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Abstracts

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mit Beteiligung der Österreichischen Gesellschaft für Herzchirurgie und thorakale Gefäßchirurgie

Salzburg, 29. Mai bis 1. Juni 2019

Tagungspräsidentin:
Univ. Prof. Dr. Andrea Podczeck-Schweighofer

Tagungssekretäre:
Univ. Prof. Dr. Bernhard Metzler
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VORTRÄGE

V-1

Molecular glucose steel phenomenon imaged by hybrid PET-MRI: 18F-FDG perfusion-metabolism mismatch 3 days after acute myocardial infarction in a translational pig model of ischemic left ventricular dysfunction

Denise Traxler[1], Johannes Winkler[1], Imre J. Pavo[2], Andras Jakab[3], Dominika Lukovic[1], Katrin Zlabinger[1], Alfred Gugerell[1], Martin Riesenhuber[1], Andreas Spannbauer[1], Mariann Gyöngyösi[1], Noemi Pavo[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria
[3]University Children's Hospital Zurich, Zurich, Switzerland

Background: Under normoxic conditions, the predominant energy metabolism of healthy cardiac cells is based on beta-oxidation of free fatty acids. Under severe myocardial hypoxia, ischemic heart cells switch their energy gain from beta-oxidation to glucose metabolism to increase ATP production per oxygen molecule. This metabolic pathway appears as perfusion-metabolism mismatch in 18F-fluorodeoxyglucose (18F-FDG) PET images, as increased 18F-FDG uptake in underperfused hypoxic myocardial areas. The aim of our study was to evaluate simultaneous perfusion, metabolism and function of the ischemic heart by hybrid 18F-FDG-PET-cMRI with late enhancement images in a translation animal model of heart failure to 1) elaborate the underlying molecular mechanisms of perfusion-metabolism mismatch, and 2) evaluate the predictive value of 18F-FDG-PET-cMRI in development of ischemia-triggered left ventricular dysfunction.

Methods: Closed-chest reperfused acute myocardial infarction (AMI) was induced in 36 domestic pigs by 90 min occlusion of the mid left anterior descending artery with a percutaneous intracoronary balloon, followed by reperfusion. Three days and 1 month after AMI, after 12 h fasting, 18F-FDG-PET-cMRI were performed by using standardized acquisition protocols ($n=30$). Cardiac functional parameter, such as ejection fraction (EF), end-diastolic volume (EDV), infarct size, and mean tracer uptake of the infarcted area were quantitatively assessed. Six animals were euthanized after the 3-day 18F-FDG-PET-cMRI images to elaborate the differences in gene expression patterns in animals with perfusion-metabolic mismatch by using next generation sequencing (NGS) and pathway network analyses.

Results: Eight (group Mismatch) of the 30 animals (group Match) with 1-month follow-up showed high 18F-FDG uptake in the infarcted area (perfusion-metabolism mismatch) at the 3-day 18F-FDG-PET-cMRI-LE images (Fig. 1). The animals in the Mismatch group had significantly lower EF at 3 days (34 ± 8.8 vs. 42 ± 3%) and at the 1-month follow-up (35.8 ± 6 vs. 43 ± 6.6%) and larger infarct size at day 3 (26.6 ± 6.6 vs. 22.1 ± 4.4%) and 1 month (28 ± 5.4 vs. 20.3 ± 4.3%) with higher EDV at 1 month. Mean tracer uptake of the infarcted area was significantly reduced in the Mismatch group at 1 month (56 ± 23.1 vs. 64.7 ± 13.2%), indicating enhanced severity and transmurality of the infarction. NGS revealed downregulation of the cholesterol metabolism pathway, and upregulation of carbohydrate derivative catabolism pathway with highly activated innate immune system and genes responsible for cytokine activation in the infarcted area 3 days post-AMI in the Mismatch group, which explains the paradox high 18F-FDG tracer uptake in the infarction zone. Accordingly, high energy demand of the severe hypoxic area led to "glucose steel phenomenon" at molecular level, subtracting the glucose (18F-FDG) from the normally perfused non-ischemic myocardial regions.

Conclusions: Molecular glucose steel phenomenon leading to 18F-FDG perfusion-metabolism mismatch in the severe ischemic area early after AMI predict development of adverse remodeling of the heart.

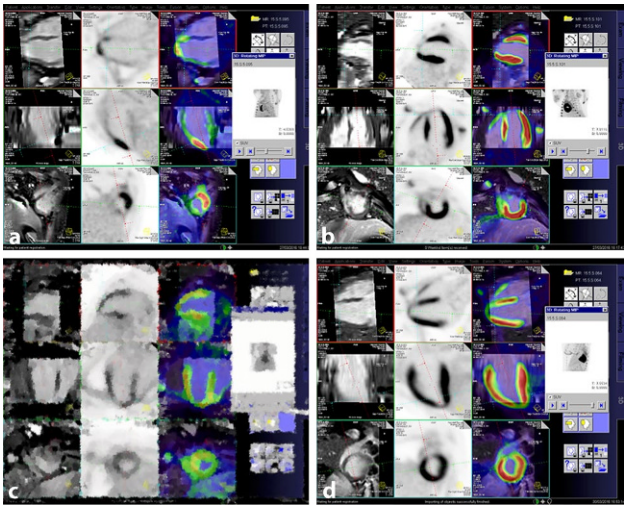


Fig. 1 | V-1

V-2

Myocardial and valvular characterization of a novel closed chest model of ischemic mitral regurgitation in pigs

Ouafa Hamza[1], Attila Kiss[1], Beáta Bódi[2], Anne Kramer[1], Sandra Trojanak[3], Eylem Acar[1], Katherina Tillmann[1], Dietmar Abraham[3], Zoltan Papp[2], Bruno K. Podesser[1]

[1]Center for Biomedical Research, Medical University of Vienna, Vienna, Austria
[2]Clinical Physiology, University of Debrecen, Debrecen, Hungary
[3]Department of Anatomy, Medical University of Vienna, Vienna, Austria

Background: Development of translational animal models of cardiovascular disease is crucial to understand the disease mechanism and pathophysiology and provide a unique platform to test novel therapies and devices. Surgical treatment of secondary mitral regurgitation remains a subject of controversy and still doesn't show a clear impact on the mortality. In addition, there is unmet need to establish less invasive approaches in patients with secondary mitral regurgitation. Therefore, the aim of the present study was to establish and characterize a clinically reliable large animal model of mitral valve regurgitation.

Methods: Young female domestic pigs were used ($n=12$, weight = 60 ± 12 kg). The induction of mitral valve regurgitation was performed by a localized posteromedial papillary muscle (PMPM) myocardial infarction. The PMPM irrigating branches

were first identified by selectively injecting contrast media into the circumflex branches and 2 ml of pure Ethanol were injected. The evaluation of the mitral valve regurgitation and cardiac function was assessed by echocardiography. After 6 weeks observation period, pigs euthanized and tissue samples from the papillary muscles and the mitral leaflets were taken for further analysis. Myocardial samples were harvested from different regions: anterior, septal, infero-posterior, infarct region and right ventricle in order to assess Ca2+-regulated force production in permeabilized isolated cardiomyocytes were obtained from control and diseased animals.

Results: Seven pigs survived the 6 weeks follow up period and showed postero-inferior wall and PMPM dyskinesia. Mitral regurgitation jet area significantly increased (jet area at baseline $0.03 \pm 0.015\ cm^2$ vs at 6 weeks $3.22 \pm 0.53\ cm^2$). A significant tenting area developed over the follow up period (Tenting area at baseline $0.35 \pm 0.21\ cm^2$ vs $2.17 \pm 0.63\ cm^2$ at 6 weeks; $p < 0.001$). These functional changes were accompanied by an increase expression levels of TGFβ, MMP9, IL1β as well as TLR2 and 4 in the posterior mitral valve leaflet while TNC expression was upregulated in the myocardial tissue but not in the valvular tissue. In addition, left ventricle enlargement was noticed (End diastolic diameter at baseline: 50.04 ± 4.34 mm vs at 6 weeks 62.12 ± 3.92 mm; $p < 0.001$) as well as left atrium enlargement (left atrium area at baseline: $7.75 \pm 0.95\ cm^2$ vs at 6 weeks $17.65 \pm 3.2\ cm^2$; $p < 0.001$) and cardiac function was declined (EF: 63 ± 3 baseline vs 47 ± 3 after 6 weeks, $p < 0.0019$). This was in line with a decreased Fmax was observed at the in isolated cardiomyocyte from postero-inferior and infarcted walls compared to control animals. Ca2+ sensitivity was also increased in those regions. Besides decreased Fmax as well as an increased Ca2+ sensitivity was observed in the right ventricle of diseased animals.

Conclusions: We established a novel, reproducible and clinically relevant model of ischemic mitral regurgitation in pigs. The functional changes of MVR were associated with a moderate remodeling on valvular level. Reduction in cardiac function was associated with a decreased maximal active force and increased Ca2+ sensitivity in cardiomyocytes were obtained from the postero-inferior, infarcted walls as well as the right ventricle. Collectively, our large animal model gives a platform to test novel pharmacological and device based therapeutic approaches for treatment and reconstructed MVR.

Funding: This study was supported by an Austro-Hungarian collaboration grant (project number: 98öu15).

V-3

Life stage determines the dual effects of IGF1 signalling on cardiac health and survival

Mahmoud Abdellatif[1], Viktoria Herbst[1], Albrecht Schmidt[1], Alina Humnig[1], Tobias Pendl[2], Angelina Gross[2], Sebastian Hofer[2], Frank Madeo[2], Andreas Zirlik[1], Daniel Scherr[1], Dirk von Lewinski[1], Peter Rainer[1], Julie McMullen[3], Tobias Eisenberg[2], Egbert Bisping[1], Simon Sedej[1]

[1]Medical University of Graz, Graz, Austria
[2]University of Graz, Graz, Austria
[3]Baker Heart and Diabetes Institute, Melbourne, Australia

Background: Cardiac outcomes of manipulating the longevity-associated insulin-like growth factor-1 (IGF1) pathway are controversial. Here we hypothesized that age (young vs. old) determines as to whether activation of IGF1 signalling improves or exacerbates cardiac function. To this end, we aimed to identify the mechanisms operating in the heart and their implications on life span upon manipulating the IGF1 pathway in mice, and investigated the alterations of IGF1 signalling cascade in human failing hearts.

Methods: Male mice with cardiomyocyte-specific overexpression of human IGF1 receptor (IGF1-R) or dominant negative phosphoinositide-3-kinase (dnPI3K) were examined by echocardiography and invasive hemodynamics at 7 and 20 months of age. Peak effort and oxygen consumption (VO2max) were determined by treadmill testing. Life span was assessed in independent longevity cohorts. Cardiac mitochondrial function was measured by high-resolution respirometry. Autophagic flux was quantified in vivo using leupeptin-based LC3 lipidation assay. IGF1 downstream targets were assessed by immunoblotting lysates of non-failing (normal and hypertrophied) and failing human heart biopsies.

Results: Young IGF1-R mice developed cardiac hypertrophy and superior contractility compared to WT mice. At old age, however, IGF1-R transgenics exhibited a significant functional decline, resulting in congestive heart failure denoted by reduced ejection fraction and preload recruitable stroke work, pathological atrial dilation as also effort intolerance and reduced VO2max. Consequently, IGF1-R mice had shortened maximal survival by 8%. Mechanistically, we identified blocked autophagic flux, which preceded a decline in mitochondrial efficiency in IGF1-R hearts and a subclinical increase in circulating pro-inflammatory cytokines at old age. Interestingly, treating aged IGF1-R mice with the autophagy inducer spermidine mitigated the transition to heart failure and preserved contractility and exercise capacity. Consistently, dampening IGF1/PI3K activity in dnPI3K mice was associated with increased maximal lifespan by 8% and a healthier cardiac phenotype in aging, despite an initial reduction in cardiac functional reserve at young age. In aged humans, we found failing hearts, and to a lower extent hypertrophic hearts, to have a higher expression of IGF1-R than non-failing hearts. In line, we detected an mTOR-dependent phosphorylation of the autophagy protein ULK-1 only in the failing hearts, implying inhibition of autophagy.

Conclusions: Activation of the IGF1/PI3K pathway, albeit essential at young age, deteriorates cardiac function at late-life stages in male mice. These results support a potential use of currently available IGF1 and PI3K antagonists to delay or even prevent cardiac disease and related mortality in the elderly essentially via reinstating autophagy.

V-4

Pregnancy-associated plasma protein A as a mortality predictor in non-heparinized chest pain patients

Tijana Andric[1], Maximillian Tscharre[2], Mona Kassem[1], Milos Tajsic[3], Kurt Huber[4]

[1]Wilhelminenspital, Vienna, Austria
[2]Landesklinikum Wiener Neustadt, Wiener Neustadt, Austria
[3]Charité – Universitätsmedizin Berlin, Berlin, Germany
[4]Wilhelminenspital and Sigmund Freud University, Vienna, Austria

Background: Pregnancy-associated plasma protein A (PAPP-A) is a metalloproteinase with insulin-like growth factor binding protein (IGFBP) cleaving activity. PAPP-A has been found in eroded and ruptured atherosclerotic but not in stable

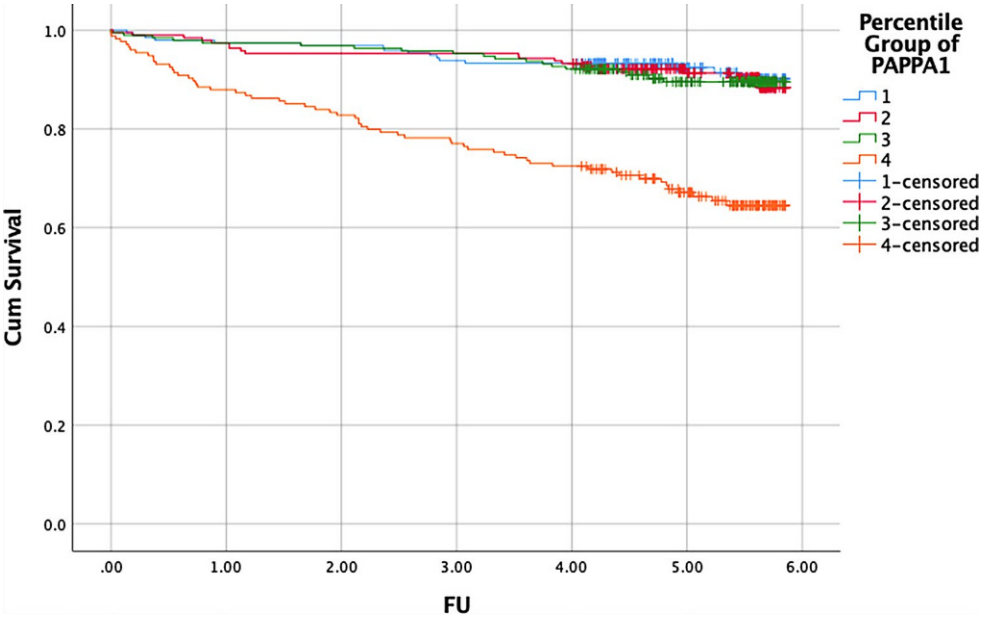


Fig. 1 | V-4 Kaplan Meier survival curves according to PAPP-A quartiles in chest pain subjects after exclusion of heparinized patients ($n = 750$)

plaques. Accordingly, it has been suggested as a useful biomarker especially in acute coronary syndromes (ACS). The fact that heparins interact with the plasma concentration of PAPP-A (increase) has not been taken into account in many previous studies. We aimed to investigate the role of PAPP-A as predictor of long-term mortality in chest pain patients admitted to our emergency department without troponin-increase and in patients presenting with type-1 or type-2 myocardial infarction (MI), according to the latest MI-definition.

Methods: PAPP-A concentrations were measured using an automated immunofluorescent assay (Kryptor, Brahms GmbH, Germany) prior to heparin administration in consecutive all-comers presenting with chest pain suggestive of ACS at our emergency department between February 2011 and December 2012. Cardiac troponin I (cTnI) was determined and clinical data were obtained in order to subgroup into non-MI, type-1 MI and type-2 MI patient cohorts. Long-term follow up survival data were retrieved from Statistik Austria database until the end of 2017. Cox regression analysis and Kaplan Maier survival curves were performed for all chest pain patients, non-MI vs. MI patients and for type-1 and type-2 MI separately.

Results: The total patient cohort consisted of 750 consecutive chest pain patients, of which 138 patients had an cTnI-related MI (type-1 MI = 98 pts., type-2 MI = 40 pts.). For the whole patient cohort, mean PAPP-A values in quartiles 1 to 4 were 6.14 mU/L, 8.33 mU/L, 10.22 mU/L and 15,27 mU/L, respectively. Kaplan Meier survival functions of the patients in the highest quartile showed significantly reduced survival with a mean survival time of 4,58 years (95% CI 4,28–4,88) and a survival rate of 66,1% (Fig. 1), as compared to lower three quartiles ($p < 0.001$) while no significant difference in survival distributions was found between the lower three quartiles. The survival analysis of the cTnI positive patients showed no significant difference between the quartiles ($p = 0.055$). After further dividing of subjects in type-1 MI and type-2 MI, cox regression analysis showed a significant mortality prediction of PAPP-A after adjustment for confounders ($p = 0.043$) in patients with type 1 MI ($n = 98$), while no mortality prediction could be shown for patients with type 2 MI ($p = 0.247$). Non-MI Patients showed a significantly reduced survival in the highest quartile of PAPP-A concentrations as compared to the first three quartiles, similarly to the total patient cohort with chest pain.

Conclusions: PAPP-A not only predicts long-term mortality in type 1 MI patients, but also in non-MI patients. These findings comply on the one hand with the hypothesis of PAPP-A being involved in instability of atherosclerotic plaques by IGFBP-cleavage-mediated disruption of fibrous cap. Other to date not fully understood pathomechanisms of PAPP-A might explain the predictive value for long-term mortality in non-MI patients based on the underlying disease states.

V-5

Appropriate and inappropriate shocks in patients with a wearable cardioverter defibrillator (WCD) – Results of the Austrian WCD Registry

Ursula Rohrer[1], Martin Manninger[1], Christian Ebner[2], Deddo Mörtl[3], Hans Keller[4], Alfred Dirninger[5], Günter Stix[6], Hannes Alber[7], Christian Steinwender[8], Ronald Binder[9], Markus Stühlinger[10], Bernadette Pratl[1], Andreas Zirlik[1], Daniel Scherr[1]

[1]Medical University of Graz, Graz, Austria
[2]Elisabethinen Hospital Linz, Linz, Austria
[3]University Hospital St. Pölten, St. Pölten, Austria
[4]Rudolfstiftung, Vienna, Austria
[5]Hospital Hochsteiermark, Bruck/Mur, Austria
[6]Medical University of Vienna, Vienna, Austria
[7]Hospital Klagenfurt, Klagenfurt, Austria
[8]Medical University of Linz, Linz, Austria
[9]Hospital Wels-Grieskirchen, Wels, Austria
[10]University Hospital Innsbruck, Innsbruck, Austria

Background: The wearable cardioverter-defibrillator (WCD) is a temporary treatment option for patients at high risk for sudden cardiac death (SCD) and/or for patients in whom implantation of a cardioverter defibrillator (ICD) is temporarily not possible. Purpose: To investigate the incidence of appropriate and inappropriate WCD shocks of all 879 patients in the Austrian WCD registry.

Methods: We performed a retrospective analysis of all shocks delivered by a WCD in the cohort of the Austrian WCD registry between 2010 and 2018. Appropriateness or inappropriateness of WCD shocks were assessed by independent review of all WCD electrograms by two cardiologists.

Of the 879 patients (age 60 ± 14, 21% female) in the Austrian WCD registry, 4% (35/879, 11% female, age 67 ± 14) received a total of 66 automatically triggered shocks. WCD indications in these patients were ischemic CMP/post PCI/CABG (n=5), NICMP (n=4), ICD associated infections (n=8), bridge to ICD implantation (n=7), delayed ICD implantation (n=6), acute myocardial infarction with LVEF< 35% (n=4), myocarditis (n=1), bridge to ablation (n=1), other indications (n=3). 66% (23/35) of the cohort with shocks had malignant arrhythmias like ventricular tachycardia (VT) or ventricular fibrillation (VF) before WCD prescription. 31/879 (3.5%) patients received 55 appropriate shocks, while the per patient shock rate was 2 [1;5]. 45 appropriate shocks in 28 patients were able to terminate a malignant arrhythmia with the first shock (86%). 6 arrhythmic events in 5 patients were effectively converted to sinus rhythm with the second shock. These shocks were induced by 25 ventricular tachycardias and 26 times ventricular fibrillation. 2 patients had ineffective shocks (1 VT event, 1 VF event). While in one patient the VT terminated spontaneously 30 seconds after the ineffective shock, the patient with VF could not be successfully defibrillated by the WCD despite appropriate detection and treatment. So the effective shock rate in Austrian WCD patients is 92%.

Results: The overall shock rate in our cohort was 0.03 shocks (3.9%) per patient-month. The mean heart rate of all 16 shocked VT events was 210 ± 33 beats per minute. The time from event onset to shock was median 60 seconds [40;1187] while the longest time to shock results from an initial haemodynamic stable patients aborting the indicated treatment for a sustained VT. 7/879 patients (0.8%) received a total of nine inappropriate shocks with a per patient shock rate of 1 [1;2]. 2 inappropriate shocks were applied due to artefacts, 3 shocks in 2 patients were delivered to non-shockable rhythms (asystole, pulseless electrical activity) and in two cases, the WCD misdetected atrial fibrillation with a bundle branch block as a ventricular tachyarrhythmia. In one patient ventricular fibrillation terminated spontaneously 3 seconds before the WCD treatment was delivered. None of the inappropriate treatments converted a benign rhythm to a malignant arrhythmia or asystole. The median time from WCD prescription to the first shock event was 8 days [1–151]. 24/35 patients (68%) received their first WCD shock within 30 days.

Conclusions: The registry shows a good overall patient compliance with 22.4 hours wearing time per day. While the WCD can detect malignant arrhythmia appropriately (85%) and treat them effectively in 92% of all cases on one hand, the registry data also shows a low inappropriate shock rate of 0,8% (7/879 patients) on the other hand. The WCD shock rate is highest within the first month of prescription but is still appearant up to several months after prescription. Summarizing the WCD is a safe and effective treatment option.

V-6

Natural history of bivalvular functional regurgitation

Gregor Heitzinger[1], Philipp Bartko[1], Henrike Arfsten[1], Noemi Pavo[1], Max-Paul Winter[1], Aurel Toma[1], Guido Strunk[2], Christian Hengstenberg[1], Martin Hülsmann[1], Georg Goliasch[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]FH Campus Vienna and Complexity Research, Vienna, Austria

Background: Bivalvular functional regurgitation (BVFR) defined as concomitant mitral and tricuspid insufficiency has not been described or systematically assessed before. The present study therefore sought to define incidence, impact and natural history of BVFR in heart failure with reduced ejection fraction (HFrEF) to provide the foundation for risk assessment and directions for potential treatment

Methods: We enrolled 1021 consecutive patients with HFrEF under guideline-directed medical therapy and performed comprehensive echocardiographic and neurohumoral profiling. All-cause mortality during a five-year follow up served as the primary endpoint.

Results: Thirty percent of patients suffered from moderate or severe BVFR. Long-term mortality increased with the presence and severity of FR with severe BVFR representing the highest risk-subset (P<0.001). Severe BVFR patients were more symptomatic and displayed an adverse remodeling and neurohumoral activation pattern (all P<0.05). Severe BVFR was associated with excess mortality (Fig. 1, Panel A) independently of clinical (adj.HR 1.52, 95%CI 1.39–1.84; P<0.001) and echocardiographic (adj.HR 1.31, 95%CI 1.11–1.54; P=0.001) confounders, guideline-directed medical therapy (adj. HR 1.55, 95%CI 1.35–1.79; P<0.001) and neurohumoral activation (adj.HR 1.31, 95%CI 1.07–1.59; P=0.009). Moderate BVFR (n=99) comprised equal baseline characteristics and similar risk as isolated severe FR (Fig. 1, Panel B) (HR 0.95, 95%CI 0.69–1.30; P=0.73).

Conclusions: This long-term outcome study shows the multi-faceted nature of FR and defines BVFR as an important clinical entity associated with impaired functional class, adverse cardiac remodeling and excess risk of mortality. Moderate BVFR conveys similar risk as isolated severe FR reflecting the deleterious impact of the global regurgitant load on the failing heart and the need of an integrated understanding for risk-assessment.

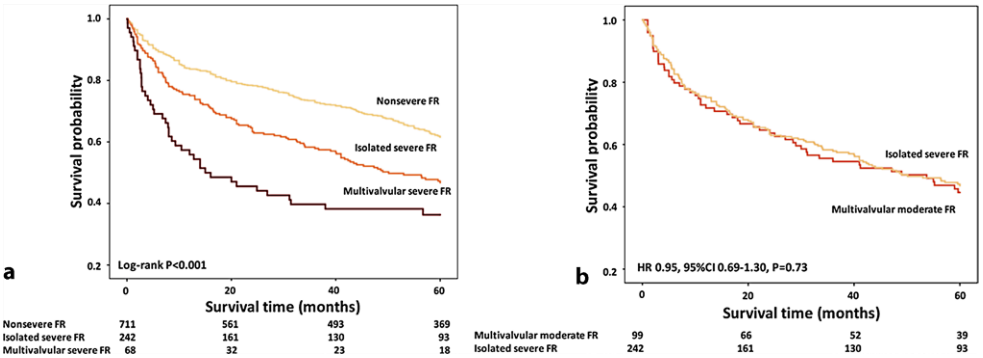


Fig. 1 | V-6

Featured Poster Session 1 – Basic Science

FP 1-1

Exosomes convey angiogenic effects in ischemic myocardium via miR-19a-3p

Leo Pölzl[1], Michael Graber[1], Jakob Hirsch[1], Felix Nägele[1], Rosalie Huber[1], Daniela Lobenwein[1], Johannes Zipperle[2], Michael Blumer[3], Rudolf Kirchmair[4], Patrick Paulus[5], Sean Davidson[6], Joost Sluiter[7], Michael Grimm[1], Johannes Holfeld[1], Can Tepeköylü[1]

[1]University Hospital for Cardiac Surgery, Department of Surgery, University of Innsbruck, Innsbruck, Austria
[2]Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, AUVA Trauma Research Center, Vienna
[3]Division of Clinical and Functional Anatomy, Medical University of Innsbruck, Innsbruck, Austria
[4]University Hospital for Internal Medicine III (Cardiology and Angiology), Department of Internal Medicine, Medical University of Innsbruck, Innsbruck, Austria
[5]Department of Anaesthesiology and Operative Intensive Care Medicine, Kepler University Hospital, Linz, Austria
[6]Cardiovascular Institute, University College London, London, Great Britain
[7]UMC Utrecht, Utrecht, Netherlands

Background: Myocardial regeneration in patients suffering from ischemic heart disease represents a major challenge in cardiovascular research. Exosomes are nano-sized vesicles crucial for intercellular communication within the heart. They have been shown to exhibit cardioprotective effects. We aimed to substantiate the pro-angiogenic impact of endogenously released exosomes, to identify their cargo and to test their therapeutic efficacy in vivo.

Methods: Extracellular vesicles (EV) were isolated from the supernatant of human coronary artery endothelial cells (HCAECs). EVs were characterized via electron microscopy, nanoparticle tracking analysis and flow cytometry. Exosome content was evaluated via miRNA sequencing array and next-generation sequencing and confirmed in functional assays. Exosomes and target miRNA were injected intramyocardially in SCID mice after left anterior descending (LAD) ligation. Heart function was analyzed via transthoracic echocardiography after 4 weeks.

Results: Characterization of released EVs via electron microscopy, nanoparticle tracking analysis and flow cytometry revealed specific exosome morphology and size with presence of exosome markers CD 9, CD81, CD63 and HSP-70. Released exosomes exhibited angiogenic properties activating Akt and ERK and enhancing endothelial tube formation and proliferation. We identified miR-19a-3p as responsible cargo, since antagomir-19a-3p antagonized exosome effects. miR-19a-3p effectively downregulated the potent angiogenesis inhibitor thrombospondin 1 resulting in VEGF receptor 2 upregulation. Exosome injection into ischemic myocardium after left anterior descending (LAD) ligation resulted in improved vascularization, increased left ventricular ejection fraction with decreased myocardial fibrosis.

Conclusions: The release of endogenous exosomes represents a physiological mechanism of angiogenesis induction. miR-19a-3p is the responsible vesicular exhibiting its angiogenic function via regulation of thrombospondin 1. Targeting miR-19a-3p containing exosomes could represent a novel therapeutic strategy for the treatment of ischemic heart disease.

FP 1-2

Mechanical stimulation of toll-like receptor 3 (TLR3) induces reprogramming of fibroblasts towards endothelial cells

Michael Graber[1], Jakob Hirsch[1], Leo Pölzl[1], Felix Nägele[1], Victor Schweiger[1], Daniela Lobenwein[1], Daniela Lener[1], Elke Kirchmair[1], Nikolaos Bonaros[1], Michael Grimm[1], Can Gollmann-Tepeköylü[1], Johannes Holfeld[1]

[1]University Hospital for Cardiac Surgery, Department of Surgery, University of Innsbruck, Innsbruck, Austria

Background: After myocardial infarction, functional myocardium is replaced by fibrotic scar tissue resulting in heart failure. Currently, therapeutic options for the regeneration of dysfunctional scar tissue are limited. Reprogramming of resident fibroblasts towards functional endothelial cells via viral vectors is a promising strategy for the regeneration of ischemic myocardium. Thereby, stimulation of the innate pattern recognition receptor Toll-Like receptor 3 (TLR3) is crucial for effective chromatin remodeling and nuclear reprogramming. Mechanical conditioning of mycoardium via shock wave therapy (SWT) has been shown to activate TLR3. We aimed to activate TLR3 in ischemic myocardium via mechanical conditioning to induce reprogramming and improve cardiac function.

Methods: Human cardiac Fibroblasts (Fb) were treated with SWT or TLR3 agonist polyI:C, transferred to Endothelial Growth Medium and analyzed for endothelial-specific markers via rt-PCR and FACS analysis after 7 and 14 days. Reprogrammed cells positive for CD31 were sorted, assessed for endothelial gene expression and subjected to functional endothelial cell assays including NO production and tube formation. Myocardial infarction was induced in FSP-1-Cre;ROSA26-lacZ reporter mice with subsequent SW treatment. Cardiac function was assessed via echocardiography and LacZ positive endothelial cells were quantified to assess reprogramming efficacy in vivo.

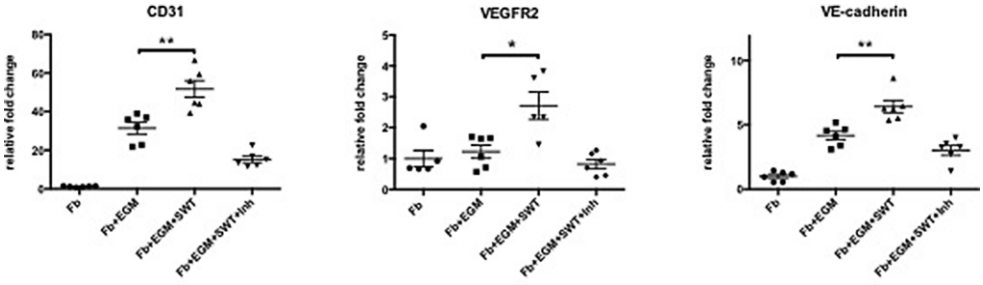


Fig. 1 | FP 1-2 Fibroblasts (Fb) showed significantly increased endothelial gene expression upon mechanical stimulation with Shock Wave Therapy (SWT). This effect could be abolished by adding a TLR3/dsRNA complex inhibitor

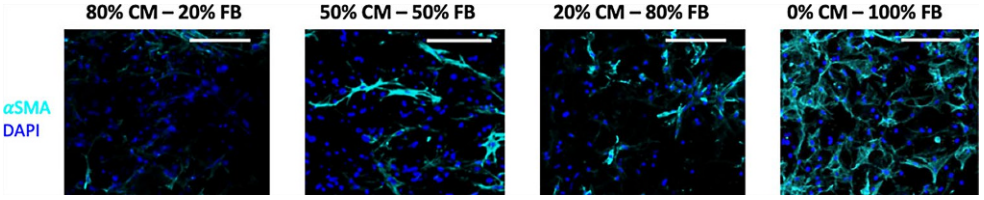


Fig. 1 | FP 1-3 Effect of Cardiomyocytes (CM) on the Fibroblast (FB) phenotype switch. αSMA (light blue) stains the proliferating myofibroblast (MyoFB), DAPI (dark blue) stains cell nucleus

Results: Human cardiac fibroblasts show abundant expression of TLR3. Mechanical stimulation activated the TRIF-dependent TLR3 signaling. TLR3 stimulation resulted in decreased expression of Histone-Deacetylase 1 (HDAC1) with increased acetylation of Histone 3 (H3). Furthermore, chromatin-modifying enzymes CIITA and PRMT8 were significantly upregulated upon TLR3 activation, clearly indicating epigenetic modifications. Upon treatment, fibroblasts showed significantly increased expression of endothelial markers CD31, VEGFR2 and VE-Cadherin. Effects were reversible using a TLR3/dsRNA complex inhibitor (Fig. 1). In line, we found an increased population of endothelial cells in FACS analysis, indicating a phenotype-switch of fibroblasts upon treatment. Reprogrammed sorted cells positive for CD31 showed indeed an endothelial gene expression profile with endothelial cell properties including NO-production and tube formation. In vivo, we found increased LacZ positive endothelial cells concomitant with improved cardiac function after treatment, indicating efficient reprogramming in ischemic myocardium.

Conclusions: TLR3 activation shows clearly an angiogenic and regenerative potential in ischemic heart disease, as it facilitates transdifferentiation of somatic cardiac fibroblasts towards an endothelial cell-type via HDAC1 dependent chromatin remodeling. Therefore, mechanical TLR3 stimulation displays an efficient treatment strategy for myocardial ischemia.

FP 1-3

A microfluidic model to study the interaction between cardiomyocytes and fibroblast in cardiac scar formation

Francesca Carminati[1], Giuseppe Isu[1], Diana Robles Diaz[1], Paola Occhetta[1], Andrea Mainardi[1], Gregory Reid[1], Stefano Ugolini[2], Marco Rasponi[2], Anna Marsano[1]

[1]University Hospital Basel, Basel, Switzerland
[2]Department of Electronic, Politecnico di Milano, IT, Milano, Italy

Background: After chronic cardiac stress or acute myocardial infarction, the injured myocardium is subjected to a remodeling process. This is characterized by the loss of functional cardiomyocytes (CM). Quiescent fibroblasts (FB) are recalled and activated in the injured area. Proliferation begins and the phenotype switches towards myofibroblasts (MyoFB). MyoFB typically express contractile proteins and synthesize extracellular matrix (ECM), stiffening the wound and leading to the formation of fibrotic tissue. Currently, there is the need of in vitro engineered cardiac models capable of recapitulating the phases of fibrotic remodeling with the aim to optimize drug discovery and screening phases of new treatments. We previously showed that mechanical stimulation alone induces FB activation and the subsequent switch in MyoFB (similarly to the supplementation of a fibrotic factor). This can, however, be prevented when FB are co-cultured with 80% CM. In this work, we developed a three-dimensional (3D) model of cardiac fibrosis within a microfluidic device (i. e. heart-scar-on-chip), with the aim of studying the interaction between different ratios of CM and FB in the early phases of cardiac remodeling.

Methods: 3D cell-laden fibrin-based hydrogels were cultured within the microfluidic heart-scar-on-chip device imposing a cyclic mechanical stretching (60 bpm, 10% strain). To simulate different heart injury cell compositions and the possible effect of the presence of CM on FB switch activation, CM and FB were co-cultured for 5 days (1×105 cells/micro.l) at different proportions: 80% CM-20% FB (80–20), 50% CM-50% FB (50–50), 20% CM–80% FB (20–80), 100% FB (0–100). The functionality of the resulting 3D micro-engineered tissues was evaluated in terms of contractility by means of external electrical pacing, while the phases of fibrotic remodeling were assessed by quantifying immunofluorescent markers of FB phenotype switch (α-SMA) and proliferation (Ki67). Separately, the 80–20 condition was supplemented with TGF-β1, the morphogen responsible for FB activation, in order to evaluate possible inhibition effects given by the interaction between CM and FB.

Results: Only 3D micro-engineered tissues generated with either 80% or 50% CM resulted to be contractile functional tissues with excitation threshold (ET) equal to 3.5 ± 1.7 V and 3.6 ± 0.7 V respectively, and maximum capture rate (MCR) equal to 3.8 ± 1.5 Hz and 2.7 ± 1.0 Hz respectively. The FB proliferation decreased together with the ratio of CM as compared to 100% FB culture. The presence of CM also reduced the FB phenotype switch into MyoFB. The percentage of MyoFB over total FB was $66.6 \pm 7\%$ when FB were cultured alone (0–100) while resulting $23.3 \pm 14.0\%$ and $17.9 \pm 11.0\%$ for 50–50 and 20–80 co-culture conditions respectively. The addition of TGF-β1 in the 80–20 synthesize showed no significant differences in the pro-fibrotic steps of cell proliferation and in the phenotype switch, with respect to the constructs without the supplementation of this pro-fibrotic factor.

Conclusions: With this study we developed a simple 3D model resembling early steps of cardiac fibrosis within a microfluidic device, allowing to assess the interaction between CM and FB populations. This model could help to further investigate the cross-talk between the two sub-populations, in order to develop an innovative drug screening tool for the possible treatment and reverse of cardiac fibrosis

FP 1-4

HDAC inhibition improves myofibrillar relaxation and metabolism in a feline model of HFpEF

Markus Wallner[1], Deborah Eaton[2], Remus Berretta[2], Natalie Bordag[3], Jichuan Wu[4], Mark Jeong[5], Ying Lin[5], Giulia Borghetti[2], Huaqing Zhao[6], Peter Rainer[1], Dirk von Lewinski[1], Sadia Mohsin[2], Elmar Zügner[7], Sandra Blass[8], Wolfgang Graier[8], Andreas Zirlik[1], Timothy McKinsey[5], Marla Wolfson[4], Steven Houser[2]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

[2]Cardiovascular Research Center, Lewis Katz School of Medicine Temple University, Philadelphia, United States of America
[3]Center for Biomarker Research in Medicine, CBmed GmbH, Graz, Austria
[4]Department of Physiology, Lewis Katz School of Medicine Temple University, Philadelphia, United States of America
[5]Division of Cardiology and Consortium for Fibrosis Research & Translation, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, United States of America
[6]Department of Clinical Sciences, Lewis Katz School of Medicine Temple University, Philadelphia, United States of America
[7]Joanneum Research Forschungsgesellschaft mbH, HEALTH – Institute for Biomedicine and Health Sciences, Graz, Austria
[8]Molecular Biology and Biochemistry, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria

Background: Heart failure (HF) with preserved ejection fraction (HFpEF) accounts for about 50% of all cases of HF and there are currently no effective therapies. Therefore, we aimed to assess the effects of histone deacetylase (HDAC) inhibition on cardiac and mitochondrial function and the plasma metabolome in a large mammalian model of slow-progressive pressure overload with features of HFpEF.

Methods: Male domestic short hair cats ($n=26$, aged 2 mo), underwent either sham (S) procedures ($n=5$) or aortic constriction with a customized pre-shaped band ($n=21$), resulting in slow progressive pressure overload during growth. 2 months post-banding, animals were treated daily with either 10 mg/kg suberoylanilide hydroxamic acid (b+SAHA) ($n=8$), a pan-HDAC inhibitor, or vehicle (b+veh) ($n=8$) for 2 months. Serial in-vivo cardiopulmonary phenotyping was performed monthly, and invasive hemodynamic and gas exchange parameters were evaluated 4 months post-banding. Ex-vivo myofibril mechanical studies and blood-based metabolomic profiling were performed. Data is presented as mean ± SEM.

Results: Echocardiography at 4-months post-banding revealed that b+SAHA animals had a significant reduction in left ventricular hypertrophy (LVH) and LA size vs. b+veh animals. Left ventricular end-diastolic pressure (LVEDP) and mean pulmonary arterial pressure (mPAP) were significantly lower in b+SAHA vs. b+veh. SAHA treatment also improved ex-vivo myofibril relaxation independent of LVH and this effect correlated with in-vivo improvements of LV relaxation. Furthermore, SAHA treatment preserved lung structure, and improved lung compliance and oxygenation, reflected by a decrease in alveolar-capillary wall thickness and intrapulmonary shunt. SAHA treatment also reduced perivascular fluid cuffs around extra-alveolar vessels, suggesting attenuated alveolar-capillary stress failure. Treatment with SAHA caused an increase in both oxygen consumption in-vivo and the percentage of type 1 skeletal muscle fibers (higher oxidative capacity). SAHA also increased mRNA levels of coactivators that regulate mitochondrial function and induced metabolic reprogramming towards mitochondrial oxidation preferentially utilizing fatty acids. SAHA treated HeLa cells showed a significant increase in oxidative phosphorylation and ATP production.

Conclusions: These results show that slow-progressive pressure overload mimics critical features of HFpEF. SAHA can improve cardiac, pulmonary, and metabolic derangements caused by chronic pressure overload. Therefore, HDAC inhibition may be an interesting therapeutic strategy to treat the ever growing HFpEF population.

FP 1-5

Dysregulated TGF-beta signaling impacts fibrotic vascular remodeling during venous thrombosis

Smriti Sharma[1], Arman Alimohammadi[1], Stella Chausheva[1], Johanna Altmann[1], Adelheid Panzenboeck[1], Max-Paul Winter[1], Bernhard Moser[1], Shahrokh Taghavi[1], Walter Klepetko[1], Irene M. Lang[1]

[1]Medical University of Vienna, Vienna, Austria

Background: Excessive transforming growth factor (TGF)-β signaling has been implicated as key derangements of vascular

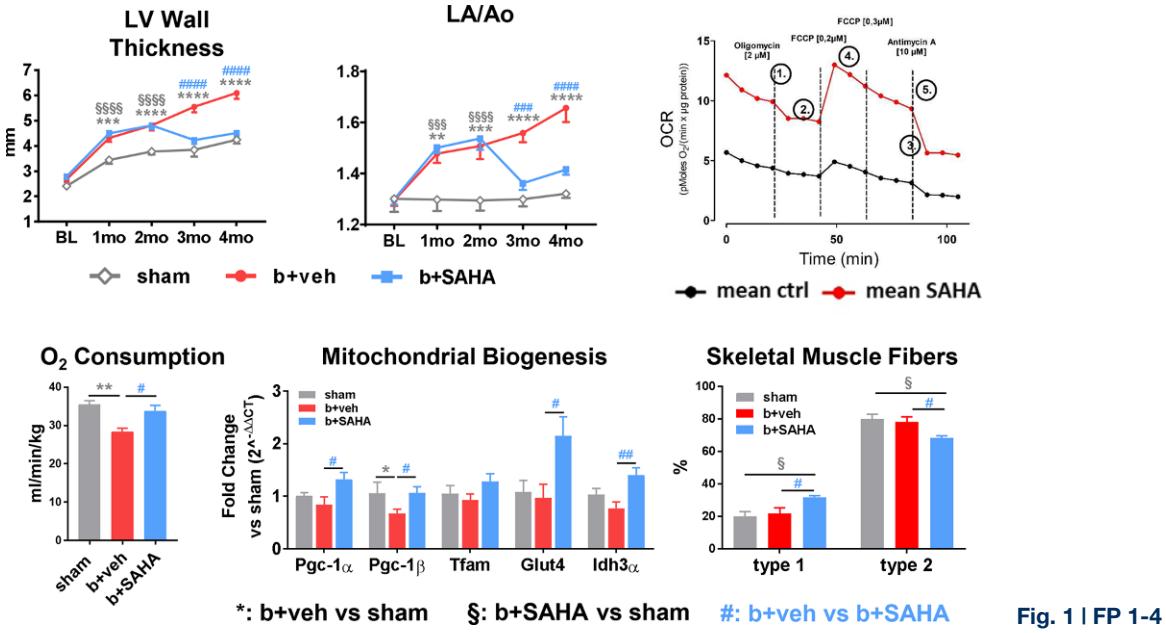


Fig. 1 | FP 1-4

disease, for example pulmonary arterial hypertension (PAH). Fibrotic vascular remodeling is a feature of PAH, but also of chronic thromboembolic pulmonary hypertension (CTEPH). Therefore, we aimed to study the role of TGF-β dysregulation in chronic thrombosis.

Methods: RNA-seq was employed to study the transcriptome of fibroblasts isolated from pairs of pulmonary artery adventitia and thrombus excised during pulmonary endarterectomy (PEA). Wild type and transgenic TBRIIΔk mice (overexpressing TGF-β in the fibroblasts) were subjected to subtotal inferior vena cava (IVC) ligation. Thrombus was harvested on days 3, 7, 14 and 21, and histological and molecular analyses were performed.

Results: RNA-seq analysis revealed significant ($P<0.05$) fold differences in 39 genes, with substantial increase of MMP-9 in thrombus fibroblasts. Most of the genes exhibiting differential expression patterns in thrombus fibroblasts were regulated by TGF-β signaling (like MMP9, SMOC1). In TGF-β overexpressing mice thrombus burden was significantly greater on days 7, 14 and 21. This was paralleled by upregulation of pro-fibrotic genes in the thrombus of TBRIIΔk mice.

Conclusions: Our results indicate that TGF-β overexpression delays thrombus resolution in a mouse model of venous thrombosis. Similar to PAH, the TGF-β pathway is significant for fibrotic pulmonary vascular remodeling as seen in CTEPH.

FP 1-6

Extracellular DNA and microvascular obstruction in STEMI patients

Andreas Mangold[1], Thomas Hofbauer[1], Anna Ondracek [1], Thomas Scherz[1], Dietrich Beitzke[1], Christoph Testori[1], Johannes Jakowitsch[1], Irene M. Lang[1]

[1]Medical University of Vienna, Vienna, Austria

Background: Microvascular obstruction (MVO) is one major determinant of infarct size and outcome of ST-elevation myocardial infarction (STEMI). Activated innate immune cells and platelets play a critical role in MVO. Their interplay and especially the release of neutrophil extracellular traps (NETs) impact cardiac function. NETs are neutrophilic chromatin with interspersed granule proteins and are highly proinflammatory, prothrombotic and cytotoxic. NETs released by activated neutrophils in culprit lesion site (CLS) thrombi are positively correlated with ST segment resolution and infarct size. dsDNA correlated with poor long-term outcome after STEMI in a Chinese cohort. Deoxyribonuclease (DNase) activity is a natural counterregulatory mechanism against extracellular DNA. CLS DNase activity is correlated inversely with NET burden and infarct size. In the present study, we analyzed neutrophils, extracellular DNA and DNase activity in a controlled prospective STEMI trial and related those to cardiac magnetic resonance (CMR) assessment of MVO.

Methods: 101 STEMI patients with symptom onset <6 hours were included in the trial. Blood samples were obtained at first medical contact (FMC), during pPCI from the femoral artery and from thrombectomy aspirates in a subset of patients ($n=56$), and consecutively until 72 hours after the event. CMR was performed at 4±2 days after the event. Neutrophil count and activation marker expression were determined by flow cytometry. Neutrophil migration was investigated by ex vivo migration assays. Citrullinated histone 3 (citH3) and dsDNA were measured using immunometric assays. DNase activity was measured using single radial enzyme diffusion assays.

Results: Neutrophil count was significantly increased at the culprit lesion site. The expression of activation markers and ex vivo migration decreased from FMC until pPCI. However, neutrophil count at the CLS and after 72 hours correlated positively with MVO. CitH3 and dsDNA were significantly increased at the CLS compared to femoral plasma, while DNase activity at the CLS was significantly reduced. dsDNA at the CLS correlated positively with MVO and negatively with ejection fraction. DNase activity at 72 hours correlated negatively with infarct size.

Conclusions: Extracellular DNA appears be an important determinant of microvascular obstruction in STEMI, and provides a mechanistic link between increased levels of extracellular DNA and poor outcome after STEMI.

FP 1-7

Imbalance between double-stranded DNA and deoxyribonuclease activity predicts mortality after out-of-hospital cardiac arrest

Anna S. Ondracek[1], Thomas M. Hofbauer[1], Raphael Wurm[2], Henrike Arfsten[1], Veronika Seidl[1], Anton Früh[1], Stefan Seidel[2], Pia Hubner[3], Andreas Mangold[1], Georg Goliasch[1], Gottfried Heinz[3], Irene M. Lang[1], Fritz Sterz[3], Christopher Adlbrecht[4], Klaus Distelmaier[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Wien, Austria
[2]Department of Neurology, Medical University of Vienna, Vienna, Austria
[3]Department of Emergency Medicine, Medical University of Vienna, Vienna, Austria
[4]Fourth Medical Department, Hietzing Hospital, and the Karl Landsteiner Institute for Cardiovascular & Intensive Care Research Vienna, Vienna, Austria

Background: Despite improved initial survival of out-of-hospital cardiac arrest (OHCA) patients, further prognostication remains challenging. In the course of systemic inflammatory responses and concomitant cell death, double-stranded (ds)DNA is released into the circulation, exerting pro-inflammatory effects. Deoxyribonuclease (DNase) is capable of degrading dsDNA. The role of DNase activity in OHCA survivors and impact on clinical outcome has not been analyzed yet. This study aimed to assess the impact of dsDNA and DNase activity on mortality in OHCA survivors.

Methods: In a prospective, single-center translational study OHCA survivors were included between October 2013 and May 2016. Blood samples available at hospital admission and 24 hours after return of spontaneous circulation were analyzed for dsDNA and DNase activity. Thirty day mortality was defined as study end point.

Results: We included a total of 95 OHCA survivors, of whom 23.4% ($n=25$) died within 30 days after hospital admission. The median age was 58 years (IQR 48–69), 20.6% of patients were female and 64.5% of patients presented with shockable rhythm. At admission, concentration of dsDNA was 519.9 [242.2, 1024.0] ng/ml but decreased significantly within 24 h to 249.1 [191.2, 423.9] ng/ml ($p<0.001$). DNase activity at admission was 1.48 [1.04, 3.18] mU/ml, with no change of activity compared to 24 h (1.11 [0.87, 1.97] mU/ml, $p=0.052$). The ratio between dsDNA levels and DNase activity as a measure of insufficient break-

down of dsDNA was independently associated with mortality at thirty days after adjustment for age, pH at admission, and shockable rhythm (HR 2.30, 95% CI 1.47–3.59).

Conclusions: Disproportionally increased dsDNA levels that are not compensated for by DNase activity predicted mortality, arguing for a protective effect of this enzyme in patients suffering from OHCA.

FP 1-8

Overexpression of sirtuin 4 accelerates the development of heart failure

Christoph Koentges[1], Katharina Pfeil[2], Christoph Bode[1], Andreas Zirlik[2], Heiko Bugger[2]

[1]University Heart Center, University Freiburg-Bad Krozingen, Freiburg, Germany
[2]Divsion of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Sirtuin 4 (SIRT4) is a mitochondrial NAD+-dependent deacylase which inhibits the oxidation of glucose and fatty acids by posttranslational modification of pyruvate dehydrogenase, malonyl-CoA decarboxylase and glutamate dehydrogenase, establishing SIRT4 as a meaningful regulator of intracellular energy metabolism. Given the importance of cardiac energy depletion during heart failure development, we aimed to define the role of SIRT4 in the development of heart failure.

Methods: Mice with deletion (SIRT4-/-) or overexpression (SIRT4 TG) of SIRT4 were subjected to transverse aortic constriction (TAC), and cardiac function and dimensions were monitored for 12 weeks by echocardiography. Oxidative stress was evaluated using levels of 4-hydroxynonenal, and mitochondria-targeted antioxidant treatment was achieved by MitoQ treatment.

Results: During physiological workload conditions, ejection fraction (EF) was not different between SIRT4 TG mice and wildtype (WT) littermates. In contrast, SIRT4 TG mice developed a more pronounced decrease in EF (35% vs. 51%; $p<0.05$) and a more pronounced increase in LV endsystolic diameter (4.5 mm vs. 3.6 mm; $p<0.05$) twelve weeks following TAC compared to WT mice undergoing TAC, indicating accelerated development of heart failure in SIRT4 TG mice. In addition, myocardial levels of the lipid peroxidation product 4-hydroxynonenal were increased in WT mice following TAC and were synergistically increased in SIRT4 TG mice following TAC (+66% vs. WT TAC; $p<0.05$). Administration of the mitochondria-targeted antioxidant MitoQ normalized myocardial 4-hydroxynonenal levels, markedly attenuated the decline in EF and almost normalized endsystolic LV diameter in SIRT4 TG mice. In contrast, cardiac function and morphology were unaffected in SIRT4-/- mice during normal or increased workload conditions.

Conclusions: Thus, SIRT4 is not required to maintain cardiac function even in response to increased energy demands. However, increased expression of SIRT4 accelerates the development of heart failure following TAC, possibly due to increased mitochondrial oxidative stress.

Featured Poster Session 2 – Clinical Science

FP 2-1

Preliminary results from the FIFA-trial – Fitness-tracker assisted frailty-assessment before transcatheter aortic valve implantation

Markus Mach[1], Victoria Watzal[2], Stephanie Wallner[2], Waseem Hasan[3], Gabriel Weiss[2], Christopher Adlbrecht[4], Andreas Strouhal[4], Georg Delle-Karth[4], Martin Grabenwöger[5], Bernhard Winkler[2]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna; Division of Cardiac Surgery, Medical University Graz, Graz, Austria
[2]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[3]Imperial College, London, UK, London, United Kingdom
[4]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[5]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research; Sigmund Freud University, Medical Faculty, Vienna, Austria

Background: Frailty is a geriatric syndrome frequently observed in elderly high-risk patients undergoing transcatheter aortic valve implantation (TAVI) which decreases the potential for functional recovery after TAVI and diminishes postoperative life expectancy. The study sought to develop a preprocedural frailty assessment based on parameters measured by a wearable health monitoring device. The predictive performance of this multimodality frailty assessment (MFA) with respect to hospital mortality after TAVI was compared to conventional frailty scoring methods.

Methods: A prospective cohort of elderly adults undergoing TAVI procedure via a transapical approach between April 2017 and December 2018 in a single center was included in the present study. Patients wore the device (Garmin Vivosmart 3) for one week prior to the procedure. Threshold levels in three categories (steps, heart rate range, stress) were calculated with ROC analysis. The patients were assigned one point per category when exceeding the cut-off value and then classified in four stages (no, borderline, frail, very frail). The MFA was then compared to gait speed category derived from 6-minute-walking-test (GSC) and the Edmonton Frailty Scale classification (EFS-C). The primary study endpoint was hospital mortality.

Results: In total, 50 patients with a mean age of 77.75 years (± 5.1) were included. All-cause hospital mortality was 8.3% ($n=3$). Depending on the frailty scores used, the prevalence of frailty ranged from 55.5% (MFA) and 60.6% (EFS-C) to 62.5% (GSC). Overall preprocedural stress level ($p=0.036$), minutes of high stress per day ($p=0.042$), minutes of rest per day ($p=0.034$) and daily heart rate maximum ($p=0.036$) as single parameters were the strongest predictors of hospital mortality. When comparing the different frailty scores, the MFA demonstrated the highest predictability of hospital mortality (MFA: AUC: 0.845 (0.657–1.000), $p=0.052$; GSC: AUC: 0.730 (0.474–0.986), $p=0.196$; EFS-C: AUC: 0.638 (0.265–1.000), $p=0.438$).

Conclusions: The preliminary findings of this study demonstrate the strong predictive performance of MFA compared to conventional frailty methods. The promising initial results warrant further evaluation of MFA as a predictor of short and long-term mortality after transcatheter structural interventions or conventional surgery.

FP 2-2

Natural history of functional tricuspid regurgitation: Implications of quantitative Doppler assessment

Philipp Bartko[1], Henrike Arfsten[1], Maria Frey[1], Gregor Heitzinger[1], Noemi Pavo[1], Anna Cho[1], Neuhold Stephanie[2], Timothy Tan[3], Guido Strunk[4], Christian Hengstenberg[1], Martin Hülsmann[1], Georg Goliasch[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Kaiser-Franz-Joseph-Spital, Vienna, Austria
[3]University of Sydney, Sydney, Australia
[4]FH Campus Vienna and Complexity Research, Vienna, Austria

Background: The present study aimed to establish the prognostic value of quantitative measures of functional tricuspid regurgitation (TR) severity i. e. effective regurgitant orifice area (EROA) and regurgitant volume.

Methods: 382 patients with HFrEF on guideline-directed medical therapy were enrolled and TR EROA as well as regurgitant volume by Doppler/2D-echocardiography were assessed. All-cause mortality was defined as the primary study endpoint.

Results: Quantitative metrics of TR severity were consistently associated with mortality with a HR of 1.27 (95%CI 1.13–1.42, $P<0.001$) for the EROA and of 1.29 (95%CI 1.14–1.45, $P<0.001$) for the regurgitant volume (Fig. 1, Panels A and B). Results remained unchanged after bootstrap- or clinical confounder-based adjustment. A spline curve pattern illustrates the association with mortality with thresholds for the EROA $\geq 0.2\ cm^2$, and the regurgitant volume ≥ 20 ml with sustained excess mortality thereafter (Fig. 1 Panels C-D).

Conclusions: This large-scale outcome study demonstrates the prognostic value of quantitative Doppler-echocardiographic measures of TR severity in HFrEF. Thresholds for EROA and TR regurgitant volume associated with mortality in the present study, fall within current ranges defining non-severe TR. This may potentially impact therapeutic decision making particularly timing of intervention.

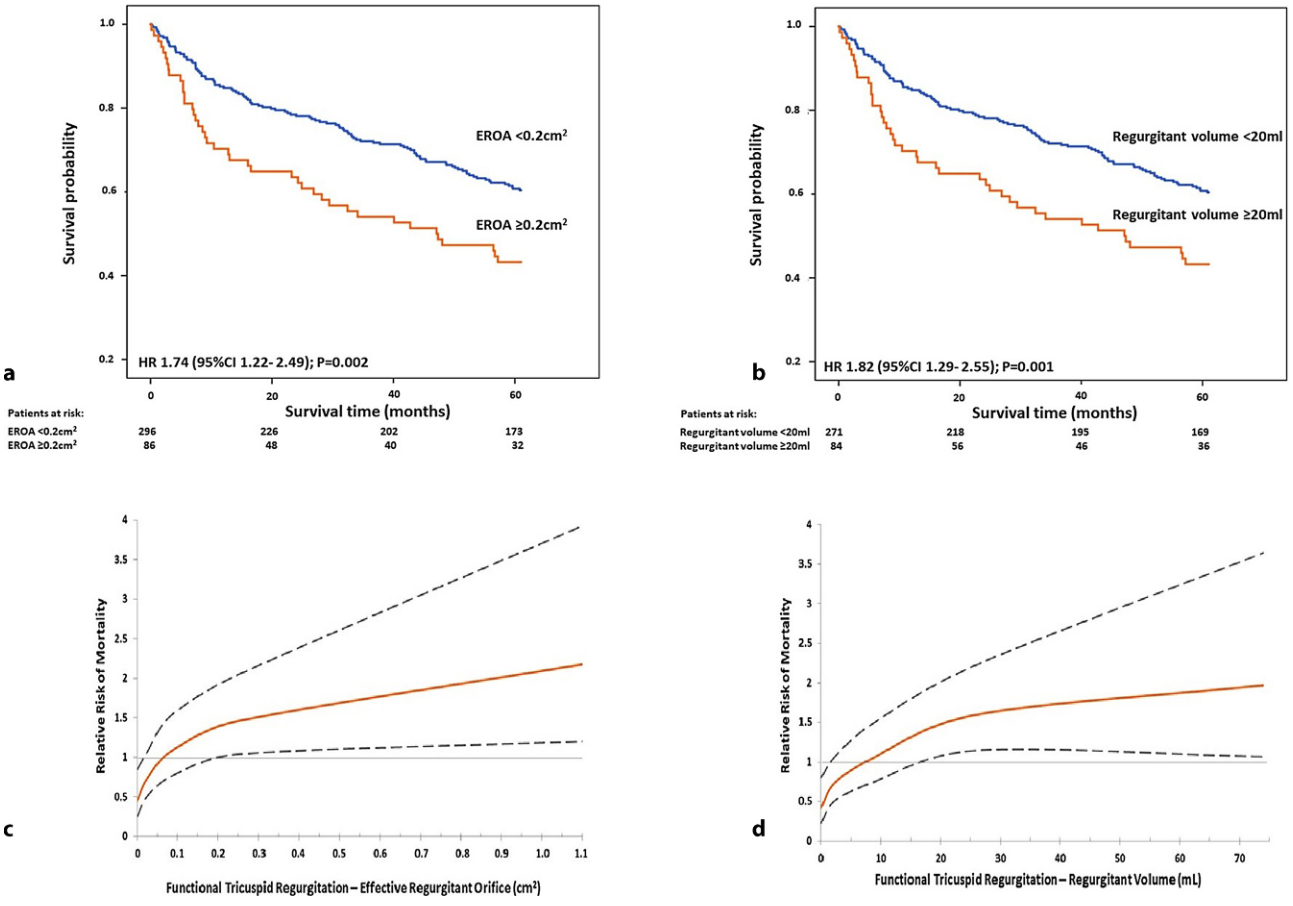


Fig. 1 | FP 2-2

FP 2-3

Aspirin for primary prevention of cardiovascular disease – a meta-analysis

Georg Gelbenegger[1], Marek Postula[2], Ladislav Pecen[3], Sigrun Halvorsen[4], Maciej Lesiak[5], Christian Schoergenhofer[1], Bernd Jilma[1], Christian Hengstenberg[6], Jolanta Siller-Matula[6]

[1]Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria
[2]Department of Experimental and Clinical Pharmacology, Centre for Preclinical Research and Technology (CEPT), Medical University of Warsaw, Warsaw, Poland
[3]Institute of Computer Science of Academy of Sciences of the Czech Republic, Prague, Czech Republic
[4]Department of Cardiology, Oslo University Hospital, Oslo, Norway, Oslo, Norway
[5]1st Department of Cardiology, Poznan University of Medical Sciences, Poznan, Poland
[6]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Platelet inhibition by aspirin reduces ischemic events but increases the risk of bleeding events. In patients with known cardiovascular disease (CVD), the benefits of aspirin to reduce further cardiovascular (CV) events significantly outweigh the risks of major bleeding and thus aspirin has since become a mainstay in secondary prevention of CVD. Yet, the role of aspirin in primary prevention of cardiovascular disease remains unclear. While updated guidelines from the American Heart Association and the U. S. Preventive Services Task Force do recommend aspirin for certain patient populations, guidelines by the European Society of Cardiology do not recommend aspirin for primary prevention of CVD. Recently, three major trials evaluating the use of aspirin in primary prevention of CVD were published. We therefore performed a meta-analysis, that additionally comprises the three large, recently published trials, ARRIVE, ASCEND and ASPREE. We aimed to produce a clinically relevant benefit-risk assessment of aspirin for primary prevention of cardiovascular disease.

Methods: PubMed was searched using predefined search-terms starting 1 January 2006 until 4 November 2018. A previous meta-analysis included studies performed prior to 2006. These were also included in this meta-analysis. Randomized-controlled trials comparing the effects of aspirin for primary prevention of cardiovascular disease versus placebo/control and including at least 1.000 patients were eligible for this meta-analysis. Two investigators independently extracted data and assessed study quality. The primary pre-specified efficacy endpoint was the composite of major adverse cardiovascular events (MACE) defined as a composite of nonfatal stroke, nonfatal MI or CVD. In order to accurately assess the rate of MACE, we performed two analyses, one comparing the calculated rate of MACE as per our definition and one comparing the rate of the study defined primary outcome as a part of a sensitivity analysis. Stroke and MI were our secondary efficacy endpoints, major bleeding was our primary safety endpoint. Risk ratios were calculated from individual studies and pooled according to the inverse variance model with 95% confidence intervals (95% CI) and reported as relative risk reduction or increase, respectively (RRR/RRI) within a mean time frame of 6.4 years (which is the mean follow up period of included studies). This meta-analysis was performed according to established methods, as described previously, and is registered in the PROSPERO database (ID 118474).

Results: Thirteen randomized-controlled trials comprising 164.225 patients were included in this meta-analysis. The mean follow-up period was 6.4 years (ranged from 3.6 to 10.3 years). Aspirin reduced the relative risk (RR) of ischemic stroke by 10% (RR: 0.90; 95%CI: 0.82–0.99), myocardial infarction by 14% (RR: 0.86; 95%CI: 0.77–0.95) and the major adverse cardiovascular events by 9% (RR: 0.91; 95%CI: 0.86–0.95) but was associated with a 46% relative risk increase of major bleeding events (RR: 1.46; 95%CI: 1.30–1.64). Further, aspirin significantly increased the RR of major extracranial hemorrhage by 49% and GI bleeding by 41%. Aspirin did not reduce the risk of cardiovascular mortality (RR: 0.99; 95%CI: 0.90–1.08), all-cause mortality (RR: 0.98; 95%CI: 0.93–1.02) or cancer (RR 1.05; 95% CI, 0.87–1.26). Aspirin-treated patients who were also treated with statins had a 12% RRR of MACE when compared with placebo plus statin (RR 0.88; 95% CI, 0.80–0.96). Aspirin use did not translate into a net clinical benefit adjusted for event-associated mortality risk (mean 0.034%; 95%CI: –0.18 to 0.25%).

Conclusions: The increased risk of major bleeding and lack of reduction of mortality might outweigh the benefits of aspirin in primary prevention of CVD. Further studies assessing patients' benefit-risk ratio and 10-year risk of CVD prior to

Table 1 | FP 2-3 Overview of study demographics

Study	patients included	mean age [yr]	mean follow-up [yr]	% statin use	% PPI use	% diabetes	% male
British Doctors' Study	5.139	61	6	unknown	unknown	2	100
US Physicians' Health Study	22.071	53	5	unknown	unknown	2	100
Thrombosis Prevention Trial	5.085	57	6.8	unknown	unknown	2	100
Hypertension Optimal Treatment Trial	18.790	61	3.8	unknown	unknown	8	53
Primary Prevention Project	4.495	64	3.6	unknown	unknown	17	43
Women's Health Study	39.876	54	10.1	unknown	unknown	3	0
POPADAD trial	1.276	60	6.7	unknown	unknown	100	44
JPAD trial	2.539	65	10.3	26	8.6**	100	55
AAA trial	3.350	62	8.2	unknown	unknown	3	28
JPPP trial	14.464	71	5	unknown	unknown	34	42
ARRIVE trial	12.546	64	5	unknown	unknown	0	70
ASCEND trial	15.480	63	7.4	75	approx. 25	94.1	63
ASPREE trial	19.114	74*	4.7	34	24.7	11	44
all studies included	164.225	62	6.4 (IQR 4.85–7.8)				

*median age, **labelled as antiulcer medication

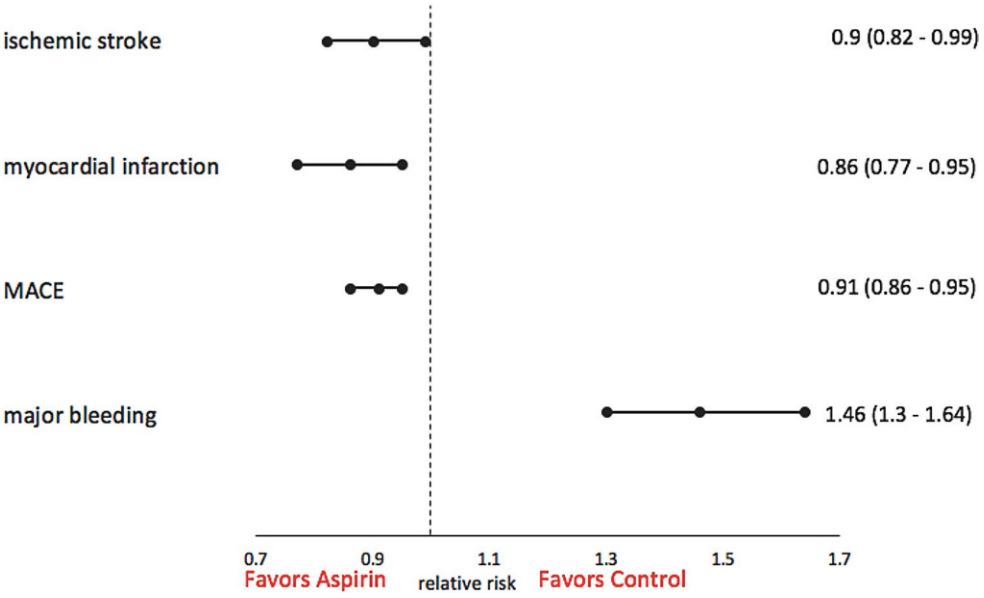


Fig. 1 | FP 2-3

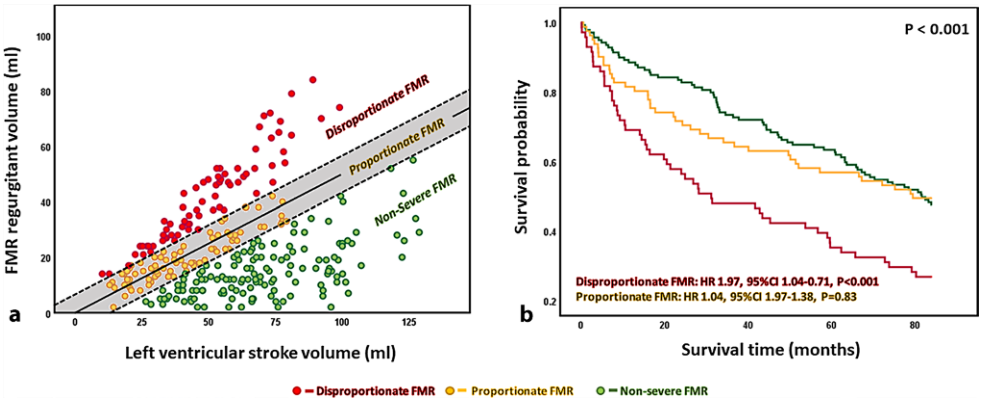


Fig. 1 | FP 2-4

treatment initiation are needed to determine the target patient cohort that potentially could benefit from aspirin treatment. Implementation of a refined bleeding-ischemic risk score could also help to identify the patients that could benefit from treatment with aspirin. The results of our analysis also call for a duly needed critical reappraisal of some current guidelines and issue a demand for repeated and more refined research projects. In conclusion, aspirin use in primary prevention is associated with a reduced risk of stroke and myocardial infarction, but at a cost of an increased risk of major bleeding.

FP 2-4

Disproportionate functional mitral regurgitation – Advancing a conceptual framework from bench to bedside

Philipp Bartko, Gregor Heitzinger, Henrike Arfsten, Noemi Pavo, Georg Spinka, Julia Mascherbauer, Martin Andreas, Christian Hengstenberg, Martin Hülsmann, Georg Goliasch

Medical University of Vienna, Vienna, Austria

Background: A recently proposed conceptual framework seeks to rearrange the effective regurgitant orifice area (EROA) and regurgitant volume (RegVol) cut-offs according to left ventricular end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF) in functional mitral regurgitation (FMR) introducing "disproportionate FMR" to describe clinically meaningful FMR. The conceptual framework, however, remains hypothetical. We sought to test the significance of FMR proportionality.

Methods: Data of 291 heart failure patients with reduced ejection fraction (HFrEF) under guideline directed therapy were embedded into this conceptual framework (Fig. 1A). The black line represents the relationship when the degree of FMR is proportionate to LVEDV with a regurgitant fraction of (RegFrac) of 50%. The dashed lines represent the degree of uncertainty determined by the imprecision inherent to the measurement of RegFrac defined as 2SD for inter- and intraobserver variability by Bland-Altmann analysis (equals ± 6.6%).

Cox-regression and Kaplan-Meier analysis were applied to assess the association between FMR proportionality and mortality.

Results: Median age was 68 years (IQR61-75), 77% were male. Median LVEF was 25% (IQR18-33) and LVEDV was 214 ml (IQR165-267). Disproportionate FMR was present in 71 patients (24%) (red dots Fig. 1A) with a median EROA of 0.26 cm^2 (IQR0.18–0.34) and a median RegVol of 42 ml (IQR28-52), proportionate FMR (yellow dots Fig. 1A) in 81 patients (28%) with a median EROA of 0.12 cm^2 (IQR0.09–0.17) and a median RegVol of 18 ml (IQR14-27). During 7-years follow-up, 166 patients died. Disproportionate FMR was associated with excess mortal-

ity compared to patients with non-severe FMR (HR 1.97, 95%CI 1.04–0.71, $P<0.001$), whereas proportionate FMR was not associated with increased long-term mortality (HR 1.04, 95%CI –1.53–0.71, $P=0.83$, Fig. 1B).

Conclusions: Every fifth patient suffers from disproportionate FMR which conveys a two-fold increased risk of mortality. Disproprtionate FMR corresponds to an EROA of roughly 0.3 cm^2 and a RegVol of 45 ml—the unifying intersection between ESC and ACC/AHA guidelines to define severe FMR. The RegFrac provides a measure proportionated to left ventricular size and function supporting its use to define clinically relevant FMR. However, RegFrac is subject to compound error due to imputation of multiple measurements limiting its use as the leading contender for FMR grading. Regardless of the term used to describe clinically significant FMR, the conceptual framework emphasizes the unmet clinical need for recalibrated cut-offs for FMR severity condensed to an algorithm that combines the strengths of several measurements of FMR severity in an integrated manner.

FP 2-5

Early left ventricular thrombus formation after ST-elevation myocardial infarction: A prospective observational CMR study

Magdalena Holzknecht[1], Sebastian J. Reinstadler[1], Martin Reindl[1], Christina Tiller[1], Agnes Mayr[2], Gert Klug[1], Bernhard Metzler[1]

[1]University Clinic of Internal Medicine III, Cardiology and Angiology, Medical University of Innsbruck, Innsbruck, Austria
[2]University Clinic of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: Left ventricular (LV) thrombus formation is a severe complication after acute ST-segment elevation myocardial infarction (STEMI). However, the incidence and determinants of LV thrombus formation are still a matter of controversy. We aimed to assess the incidence of early LV thrombus formation as detected by cardiac magnetic resonance (CMR) imaging and its determinants in a large contemporary cohort of STEMI patients treated with primary percutaneous coronary intervention (pPCI).

Methods: This observational study included 530 consecutive STEMI patients treated with pPCI. Contrast enhanced CMR was performed at a median of 3 days (interquartile range 2–4 days) after pPCI for the evaluation of LV thrombus formation, LV function and infarct severity including infarct size (IS) and microvascular obstruction (MVO).

Results: LV thrombi were detected in 3.2% of the overall cohort ($n=17$). In all patients presenting with LV thrombus, left anterior descending artery (LAD) was identified as culprit lesion. Accordingly, the incidence of LV thrombi in anterior STEMI patients ($n=247$) was 6.9%. The occurrence of thrombi was significantly associated with reduced LV ejection fraction (LVEF) ($p<0.001$), larger LV end-diastolic volume (LVEDV) ($p<0.001$) and LV end-systolic volume ($p<0.001$), larger areas of MVO ($p=0.003$) and larger IS ($p<0.001$). Furthermore, increased levels of peak high sensitivity cardiac Troponin T ($p<0.001$) and hyperlipidaemia ($p=0.038$) were significantly related to LV thrombi. After multivariable analysis, only LVEF (odds ratio (OR): 0.91, 95% confidence interval (CI) 0.87–0.96; $p=0.001$) and LVEDV (OR: 1.02, 95% CI 1.01–1.03; $p=0.004$) emerged as independent predictors of LV thrombus formation.

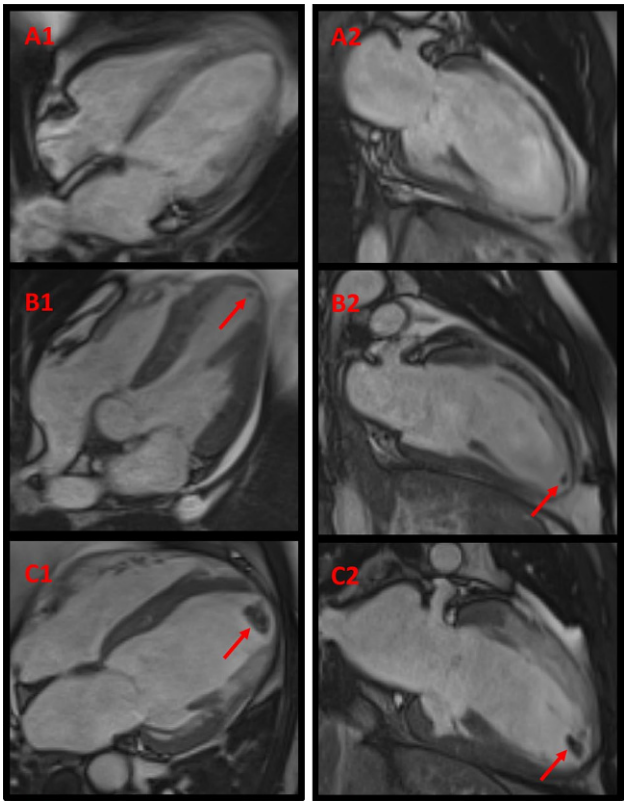


Fig. 1 | FP 2-5 Patient examples. Cine images of patients with anterior infarction (A1, 2) without thrombus, (B1, 2) with small thrombus (red arrows) and (C1, 2) large thrombus (red arrows) in the left ventricular apex

Conclusions: The risk of early LV thrombus formation remains considerable in contemporary treated STEMI patients, especially in those with LAD as culprit lesion. Among CMR parameters, only baseline LVEF and LVEDV, but not IS or MVO, independently predicted LV thrombus formation after STEMI.

FP 2-6

Flecainide but not amiodarone induces diastolic dysfunction in atrial as well as ventricular human myocardium

Christian Mayer[1], Nataša Djalinac[2], Christian Pagel[3], Burkert Pieske[4], Egbert Hubertus Bisping[2]

[1]Barmherzige Brüder Hospital Graz, Graz, Austria
[2]Medical University of Graz, Graz, Austria
[3]Georg August University Göttingen, Göttingen, Germany
[4]Charité – Universitätsmedizin Berlin, Berlin, Germany

Background: Flecainide (Flec) and Amiodarone (AM) are frequently used antiarrhythmic drugs in atrial fibrillation. In this condition diastolic function and rate dependent contractile effects are extremely important, but especially on those features the impact of both drugs has not been characterized in detail before. To assess these effects of Flec and AM on systolic and diastolic function as well as force frequency relationship (FFR), experiments using isolated atrial non-failing ($n=60$) in comparison to ventricular failing human myocardium ($n=66$) have been conducted.

Methods: Non-failing atrial trabeculae were obtained from right atrial appendages during cardiac surgery and failing ventricular trabeculae from explanted hearts during heart transplantation. Isolated trabeculae were stimulated in an organ bath under physiological conditions (1 Hz stimulation, 37 °C, 2.5 mmol/l Ca2+) and subjected to increasing concentrations of Flec and AM (0.01 to 1000 µM/l) compared to corresponding solvent controls. FFR was investigated at submaximal Flec and AM concentrations with stepwise stimulation rate increases from 1 Hz to 3 Hz. Changes in calcium transients under Flec administration were measured using the aequorin method. Additionally, phosphorylation of SERCA pump regulatory protein Phospholamban (PLB) was determined by Western blot.

Results: Flec showed a dose dependent reduction in developed systolic force (at 100 µM/l reduction to 21 ± 5% in atrial and 23 ± 7% in ventricular specimens, both $p < 0.05$) associated with reduction in intracellular calcium transients under Flec. Flec also elevated diastolic tension at higher concentrations (> 100 µM/l in atrial and significantly in ventricular specimen). But most strikingly the FFR worsened significantly at 3 µM/l Flec, with not only showing a negative inotropic effect but also an induction of diastolic dysfunction suggested by a strong rate dependent increase in diastolic tension (at 3 Hz 125 ± 10% in atrial and 136 ± 10% in ventricular specimen, both $p < 0.05$). Furthermore, PLB phosphorylation levels were significantly decreased in ventricular specimens. AM, on the other hand, only showed negative inotropic due to its solvent, but not on its own. And even in submaximal concentrations AM did not cause any deterioration of the FFR, neither for systolic nor diastolic function.

Conclusions: Flec exerts a negative inotropic effect in both healthy and failing human myocardium, impairs the diastolic function and worsens the FFR. This is linked to decreased calcium transients and decreased phosphorylation of PLB with effect on SERCA pump. On the contrary AM shows no major adverse effects on these myocardial functions in human myocardium. Proper monitoring patients' diastolic function before and during Flec therapy appears mandatory and avoidance in overt HFPEF. Furthermore, these findings underline AM's safety in patients with pre-existing heart condition, respectively in patients with pre-existing diastolic dysfunction, hence it should be preferred for this patient collective. Nevertheless, using a less cardio-depressant solvent for AM would be beneficial.

FP 2-7

High-risk plaque criteria by coronary CTA predict cardiac events but not all-cause mortality: long-term outcome

Thomas Senoner, Fabian Plank, Fabian Barbieri, Christoph Beyer, Katharina Birkl, Gerlig Widmann, Agne Adukauskaite, Guy Friedrich, Wolfgang Dichtl, Gudrun Feuchtner

Medical University of Innsbruck, Innsbruck, Austria

Background: Long-term data relating coronary computed tomography angiography (CTA) to coronary artery disease (CAD) prognosis including novel CTA imaging markers ("high-risk plaque criteria") are scarce. Objective: To define CTA imaging markers for prediction of long-term outcomes.

Methods: 1430 low-to-intermediate risk patients (57.9 ± 11.1 years; 44.4% females) who underwent CTA and coronary calcium scoring (CCS) were prospectively enrolled. CTAs were

Table 1a | FP 2-7 Study population ($n = 1430$)

Age (years)	57.9 ± 11.1
Females, *n* (%)	635 (44.4)
Body mass index (kg/m²)	26.7 ± 4.4 (15.9–52.9)
Hypertension, *n* (%)	858 (63.6)
Current smoking, *n* (%)	530 (39.3)
Positive family history, *n* (%)	504 (38.0)
Dyslipidemia, *n* (%)	824 (63.5)
Diabetes mellitus, *n* (%)	162 (13.0)
Coronary Calcium Score (AU)	140.7 ± 347

Parametric data are shown as mean ± SD (range) AU = Agatston Units

Table 1b | FP 2-7 Event rates by CTA coronary stenosis severity (CADRADS)

CADRADS	All-cause mortality *N* (%)	CV mortality *N* (%)	MACE* *N* (%)	Total *N*	
0 negative CTA	16 (3.2)	0 (0)	1 (0.2)	501	Kruskal Wallis <0.0001
1 minimal <25 %	15 (5.9)	5 (2)	7 (2.8)	254	
2 mild 25–50 %	23 (9.0)	3 (1.2)	9 (3.5)	256	
3 intermediate 50–70 %	7 (8.0)	2 (2.3)	5 (5.7)	87	
4 high grade >70 %	45 (13.6)	15 (4.5)	35 (10.5)	332	
Total, *n* (%)	**106 (7.4)**	**25 (1.7)**	**57 (4.0)**	**1430**	

**composite MACE: fatal and nonfatal events. CV = cardiovascular.*

Table 2a | FP 2-7 Multivariate Cox Proportional Hazards model for CTA and Coronary Calcium Score a) all-cause mortality

Model 1	unadjusted			adjusted*		
	HR	95 % CI	*p*	HR	95 % CI	*p*
CADRADS	1.42	1.21–1.66	<0.0001	1.30	1.10–1.53	0.002
CCS	1	1.00–1.00	0.18	1	0.99–1.00	0.903
G-score	0.98	0.93–1.03	0.355	0.99	0.94–1.04	0.652
Model 2	**unadjusted**			**adjusted***		
CADRADS	1.33	1.11–1.59	0.002	1.22	1.01–1.48	0.035
CCS >100 AU >400 AU	 1.77 0.92	 1.01–3.08 0.52–1.62	 0.045 0.770	 1.63 0.70	 0.91–2.93 0.38–1.29	 0.099 0.250
G-score cat**	0.98	0.93–1.03	0.343	0.99	0.94–1.04	0.591
Model 3	**unadjusted**			**adjusted***		
CADRADS						
1	1.80	0.89–3.65	0.101	1.86	0.88–3.92	0.102
2	2.77	1.46–5.24	0.002	2.50	1.27–4.94	0.008
3	2.77	1.14–6.73	0.025	2.38	0.95–5.98	0.064
4	4.42	2.50–7.82	<0.0001	2.97	1.59–5.57	0.001

unadjusted and adjusted for the following statistically significant values in univariate cox regression: age ≥ 75 y, nicotine, art. HT, DM. HR = Hazard Ratio; **G-score categorized into 5 increments (0–5; 6–10, 11–15, 16–20, >20) #CADRADS 1–4 categorized against CADRADS 0. CCS = coronary calcium score*

Table 2b | FP 2-7 Composite endpoint: fatal and nonfatal MACE ($n=57$)

Model 1	unadjusted			adjusted*		
	HR	95 % CI	p	HR	95 % CI	p
CADRADS	1.82	1.43–2.32	<0.0001	1.75	1.36–2.24	<0.0001
CCS	1	0.99–1.00	0.234	1	0.99–1.00	0.026
G-score	1.09	1.05–1.14	<0.0001	1.08	1.04–1.12	<0.0001
Model 2	**unadjusted**			**adjusted***		
CADRADS	1.72	1.32–2.23	<0.0001	1.58	1.20–2.08	0.001
CCS >100 >400	 1.48 0.55	 0.75–2.92 0.26–1.13	 0.257 0.104	 1.48 0.39	 0.73–3.01 0.18–0.85	 0.276 0.018
G-score cat**	1.10	1.05–1.14	<0.0001	1.08	1.04–1.12	<0.0001
Model 3	**unadjusted**			**adjusted***		
CADRADS						
1	12.86	1.58–104.57	0.017	13.37	1.64–109.18	0.015
2	15.59	1.97–123.10	0.009	14.02	1.77–111.09	0.012
3	40.51	4.72–347.61	0.001	24.61	2.72–222.96	0.004
4	57.34	7.86–418.58	<0.0001	36.48	4.94–269.67	<0.001

unadjusted and adjusted for the following statistically significant values in univariate cox regression: age ≥ 75 y, nicotine, art. HT, DM. HR = Hazard Ratio; **G-score categorized into 5 increments (0–5; 6–10, 11–15, 16–20, >20) #CADRADS 1–4 categorized against CADRADS 0. CCS = coronary Calcium Score*

Table 3a | FP 2-7 Multivariate Cox Proportional Hazards model of composite fatal and nonfatal MACE ($n=57$): High-risk plaque features

	unadjusted			adjusted*		
	HR	95 % CI	P	HR	95 % CI	P
Napkin-ring sign	3.71	1.66–8.32	0.001	4.11	1.77–9.52	0.001
LAP <60 HU	4.51	1.78–11.40	0.001	4.00	1.52–10.52	0.005
Spotty calcification	1.30	0.66–2.56	0.457	1.40	0.65–2.98	0.390
RI	0.66	0.22–2.01	0.462	0.56	0.18–1.75	0.320

unadjusted and adjusted for the following statistically significant values in univariate cox regression: age ≥ 75 y, nicotine, art. HT, Diabetes. HR = Hazard Ratio; LAP = low attenuation plaque; RI = remodeling index*

Table 3b | FP 2-7 HRP criteria (in 458 patients with non-calcified plaque)

	N	% of HRP N = 458	% of total N = 1430
LAP <30 HU	32	6.9 %	2.2 %
LAP <60 HU	92	20 %	6.4 %
SC	223	48.7 %	15.6 %
NRS	64	13.9 %	4.4 %
RI >1.1	356	77.7 %	24.9 %

HRP = high-risk plaque; LAP = low attenuation plaque; NRS = napkin-ring sign; RI = remodeling index;
SC = spotty calcification

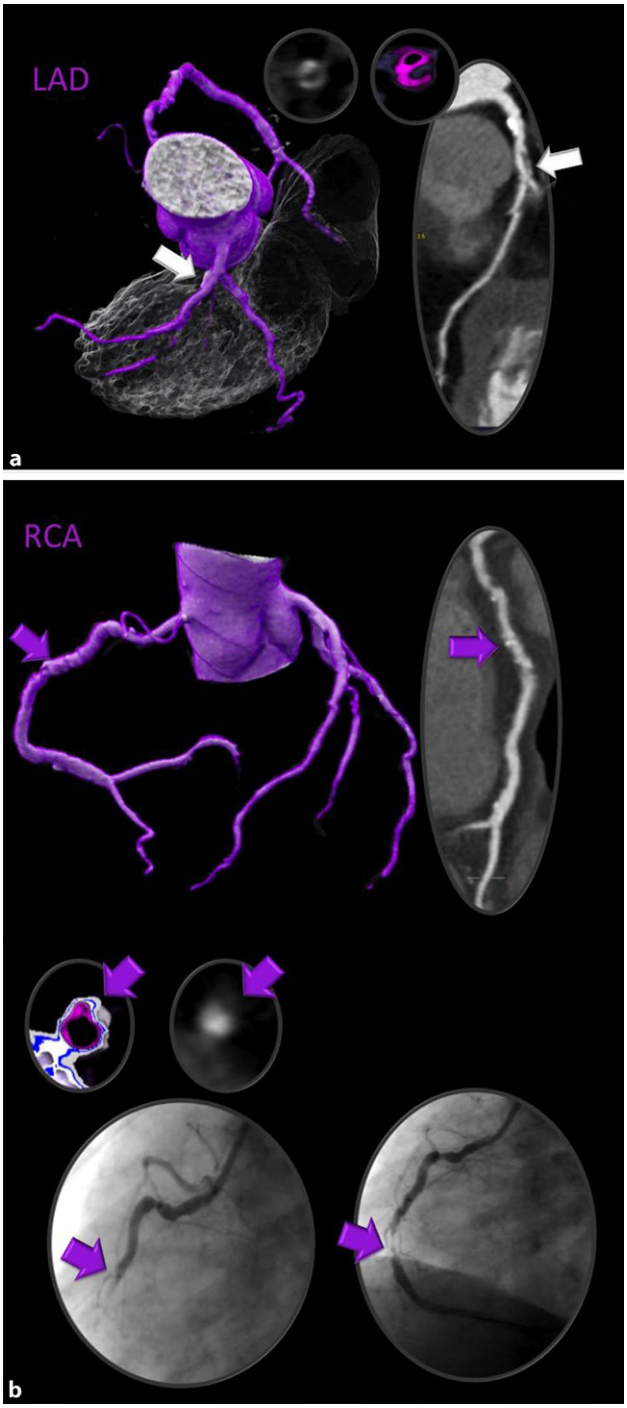


Fig. 2 | FP 2-7 A 50-year-old smoker (40 pack/yrs) with arterial hypertension, diabetes, dyslipidemia and atypical chest pain. 2a. The proximal LAD shows high-risk plaque with napkin-ring („lunar eclipse“) and intermediate (60 %) stenosis (white arrow). Inlays (mid circular) show cross-sectional images of the lesion with outer hyperdense fibrous rim (color rose = 120 HU) and hypodense lipid-rich necrotic core (black-blue <30 HU). 2b. RCA with multiple high-risk plaque and intermediate stenosis. Culprit lesion with low attenuation (HU 52 = rose color) (pink arrow) caused an acute coronary syndrome (STEMI) with CK max 5291 U/l and TropT max 13.1 ug/L 134 days after CTA due to RCA occlusion. RCA intervention was successful and a DRIVER stent was placed (Movie 1)

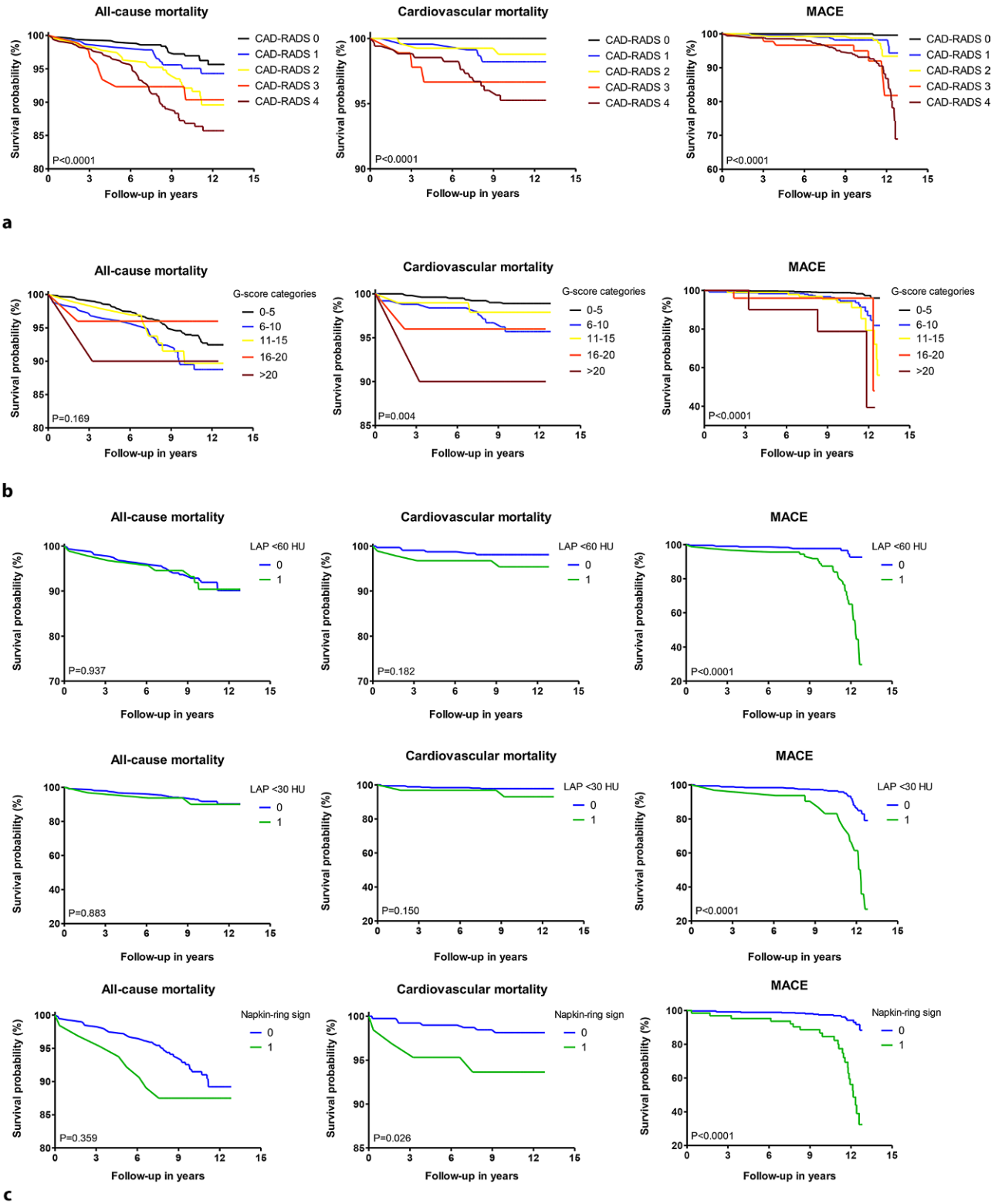


Fig. 1 | FP 2-7 Kaplan Meier Survival Curve: **a)** Stenosis severity (CADRADS) by CTA predicts all-cause mortality, cardiovascular mortality (fatal MACE) and composite MACE ($P < 0.0001$ for all three endpoints). **b)** Total plaque burden (G-score, categorized) predicts MACE and cardiovascular mortality, but not all-cause mortality **c)** The high-risk plaque criteria LAP <60 HU, <30 HU and napkin-ring („lunar-eclipse“) sign were significant predictors of MACE, but not all-cause mortality. (1 = positive)

evaluated for: (1) stenosis severity CADRADS 0–4 (minimal < 25%, mild 25–50%, moderate 50–70%, severe > 70%), (2) mixed plaque burden (G-Score), and (3) high-risk-plaque (HRP) criteria: low attenuation plaque (LAP), napkin-ring sign, spotty calcifications < 3 mm or remodeling index >1.1. Primary endpoints were all-cause and cardiovascular mortality, composite fatal and nonfatal MACE.

Results: Over a mean follow-up of 10.55 years ± 1.98 (range, 6.1–12.8), 106 patients (7.4%) died, 25 from cardiovascular events (1.75%). Composite MACE occurred in 57 (3.9%) patients. In patients with negative CTA (CADRADS 0), cardiovascular mortality and MACE rates were 0% and 0.2%, respectively. Stenosis severity (CADRADS) was the strongest predictor for all 3 endpoints on multivariate analysis (unadjusted and adjusted for risk factors, $p < 0.001$) while CCS > 100 AU predicted only all-cause mortality ($p = 0.045$) but not MACE. Total plaque burden (G-score) ($p < 0.0001$), LAP < 60 HU and the napkin-ring predicted composite MACE ($p < 0.001$) but not all-cause mortality, before and after adjusting for risk factors ($p = 0.007$ and $p = 0.001$ for LAP < 60 HU and napkin-ring, respectively), while spotty calcification and remodeling index did not. 465 had calcium score zero and in 156 (33.5%) of those, non-calcified fibroatheroma were found (total rate, 11%).

Conclusions: Long-term prognosis is excellent if CTA is negative for CAD. Stenosis severity by CTA predicts all-cause and cardiovascular mortality, while calcium score only predicts all-cause. Plaque burden and the high-risk plaque criteria LAP < 60 HU and napkin-ring are strong predictors of MACE, but not all-cause mortality.

FP 2-8

Systemic fluid status by bioelectrical impedance spectroscopy predicts outcome in patients undergoing transcatheter aortic valve replacement

Christian Nitsche[1], Matthias Koschutnik[1], Andreas Kammerlander[1], Leah Sinnhuber[1], Anna Eidenberger[1], Nabila Forutan[1], Thomas Poschner[1], Martin Andreas[2], Anahit Anvari-Pirsch[1], Christian Hengstenberg[1], Julia Mascherbauer[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria

Background: Volume overload and cardiac decompensation are cardinal signs indicating the necessity of intervention in patients with valvular heart disease. Risk stratification of patients scheduled for transcatheter aortic valve replacements (TAVR) largely relies on established risk scores, which fail to incorporate signs of fluid overload. Systemic fluid status can be easily assessed by bioelectrical impedance spectroscopy (BIS), which is a validated non-invasive tool for treatment monitoring of hemodialysis patients. The prognostic significance of fluid overload as assessed by BIS in TAVR patients is unknown.

Table 1| FP 2-8 Uni- and multivariable Cox regression analyses

	Univariable		Multivariable	
Parameter	Hazard Ratio (95% CI)	*P*-value	Hazard Ratio (95% CI)	*P*-value
Age	1.050 (0.997–1.106)	0.065		
Sex, male gender	2.013 (0.956–4.238)	0.066		
BMI	0.934 (0.863–1.011)	0.091		
Hypertension	0.890 (0.311–2.547)	0.828		
Atrial fibrillation	0.786 (0.380–1.625)	0.515		
Diabetes	1.094 (0.507–2.363)	0.819		
Hyperlipidemia	0.620 (0.312–1.232)	0.620		
CAD	0.840 (0.421–1.676)	0.621		
Previous MCI	0.177 (0.024–1.308)	0.090		
Previous PCI	1.237 (0.552–2.773)	0.606		
Previous CABG	0.457 (0.109–1.913)	0.284		
NYHA	0.813 (0.601–1.100)	0.179		
CCS	0.980 (0.703–1.368)	0.908		
Syncope	2.438 (0.923–6.439)	0.072		
Creatinine	1.428 (1.162–1.755)	**0.001**		
NT-proBNP	1.559 (1.114–2.183	**0.010**	1.813 (1.024–3.210)	**0.041**
CRP	1.042 (0.932–1.164)	0.474		
Serum albumin	0.920 (0.871–0.971)	**0.002**		
Anemia	1.608 (0.692–3.736)	0.270		
Echo EF<50%	1.606 (0.712–3.627)	0.254		
LVEDV	1.007 (0.998–1.015)	0.143		
LVESV	1.006 (0.994–1.019)	0.306		
OH>1.8 l	5.163 (1.844–14.459)	**0.002**	3.341 (1.121–9.961)	**0.030**

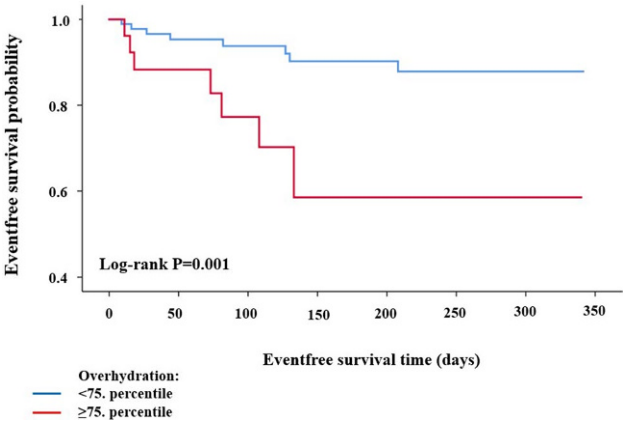


Fig. 1 | FP 2-8 Kaplan Meier Curve assessing impact of overhydration by BIS on outcome

Methods: Consecutive patients with aortic stenosis scheduled for TAVR underwent systemic fluid status assessment using BIS on the day preceding intervention, and were prospectively followed. Kaplan-Meier estimates and multivariate Cox-regression analysis were used to identify factors associated with outcome, including BIS. A composite of heart failure hospitalization and cardiovascular death was selected as primary study endpoint.

Results: In total, 135 consecutive patients (80.4 ± 7.9 years; 45.1% female) with valid BIS data were included. The study population was stratified according to the 75th percentile of overhydration (OH; +1.8 l). No associations between OH and baseline characteristics were found, including age and NYHA functional class ($p > 0.05$). However, patients in the topmost OH quartile had higher serum levels of NT-proBNP (9017 ± 9601 ng/ml vs. 3807 ± 5889; $p < 0.001$) and creatinine (1.83 ± 1.44 mg/dl vs. 1.22 ± 0.82; $p < 0.001$). A total of 35 events occurred during follow-up (27 ± 21 weeks). Patients with an OH of > 1.8 l were more likely to experience an event (log-rank, $p = 0.001$, Fig. 1). By multivariate Cox regression, including all relevant cardiovascular risk factors and routine biomarkers, OH > 1.8 l [hazard ratio 3.341 (95% confidence interval 1.121–9.961); $p = 0.030$] showed the strongest association with survival.

Conclusions: Overhydration by BIS is a strong predictor of outcome and outperformed known risk factors in TAVR patients. Routine use might help to risk stratify patients, guide fluid management, and optimize the time point for intervention.

Featured Poster Session 3 – Clinical Science

FP 3-1

Österreichisches Ablationsregister – Daten 2016 bis 2018

Lukas Fiedler[1], Daniel Scherr[2], Martin Martinek[3], Katie Bates[4], Clemens Steinwender[5], Bernhard Strohmer[6], Marcus Ammer[7], Edmund Gatterer[8], Franz Glaser[9], Florian Egger[10], Alexandra Schratter[11], Lalit Kaltenbach [4], Hanno Ulmer[4], Markus Stühlinger[12]

[1]Landeskrankenhaus Wiener Neustadt, Wiener Neustadt, Österreich
[2]Medizinische Universität Graz, Graz, Österreich
[3]Ordensklinikum Linz, Linz, Österreich
[4]Department für Medizinische Statistik, Informatik und Gesundheitsökonomie, Universität Innsbruck, Innsbruck, Österreich
[5]Klinik für Interne 1, Kepler Universitätsklinikum, Linz, Österreich
[6]Universitätsklinik für Innere Medizin II, Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Österreich
[7]Klinikum Wels-Grieskirchen, Wels, Österreich
[8]2. Medizinische Abteilung mit Kardiologie und internistischer Intensivmedizin, Krankenanstalt Rudolfstiftung, Wien, Österreich
[9]Universitätsklinikum Krems, Krems, Österreich
[10]3. Medizinische Abteilung mit Kardiologie, Wilhelminen Spital, Wien, Österreich
[11]4. Medizinische Abteilung mit Kardiologie mit Ambulanz, Krankenhaus Hietzing, Wien, Österreich
[12]Universitätsklinik für Innere Medizin III (Kardiologie und Angiologie), Medizinische Universität Innsbruck, Innsbruck, Österreich

Grundlagen: 2015 wurde von der Arbeitsgruppe Rhythmologie der ÖGK ein elektronisches Ablationsregister initiiert, um verlässliche Daten zur Anzahl, Indikation, Technik, sowie Erfolg und Komplikationen von elektrophysiologischen Prozeduren zu erheben. Die Ergebnisse der Eingaben aller Ablationen zwischen 2016 und 2018 werden in dieser Interims-Analyse beschrieben.

Methodik: Insgesamt wurden zwischen 2016 und 2018 von 14 Zentren 6399 Datensätze in das elektronische Register eingegeben. Die Zahl der eingebenden Zentren erhöhte sich von 9 im Jahr 2016 auf 14 im Jahr 2018, die Zahl der Datensätze pro Jahr von 1532 auf 2.525. ($p < 0{,}005$; Abb. 1) In einer retrospektiven Analyse wurden nunmehr alle Ablationen (ohne diagnostische Untersuchungen) in einer deskriptiven Statistik ausgewertet.

Ergebnisse: Das Alter (59; IQR 50–68 Jahre) und der Geschlechtsanteil (61 % m; 39 % w) der Patienten blieben im Beobachtungszeitraum im Wesentlichen unverändert. AVNRT-Ablationen nahmen ab (24,5 auf 22,5 %), linksatriale Ablationen bei paroxysmalem (28,5 % auf 29,9 %) und persistierendem Vorhofflimmer (8,7 % auf 12,0 %) dagegen leicht zu. Der Anteil von WPW- (6,5 %), VH-Flatter- (14,7 %), atriale Tachykardie- (4,0 %), AVN- (3,4 %) und VT-Ablationen (7,0 %) blieb relativ konstant. 79,0 % aller Prozeduren waren Erstprozeduren mit einer gesamten akuten Erfolgsrate von 96,3 %, 89,2 % wurden mit Radiofrequenz-Ablationen durchgeführt und 10,3 % mit Cryo-Ablation. Gesamt kann eine Komplikationsrate von bei

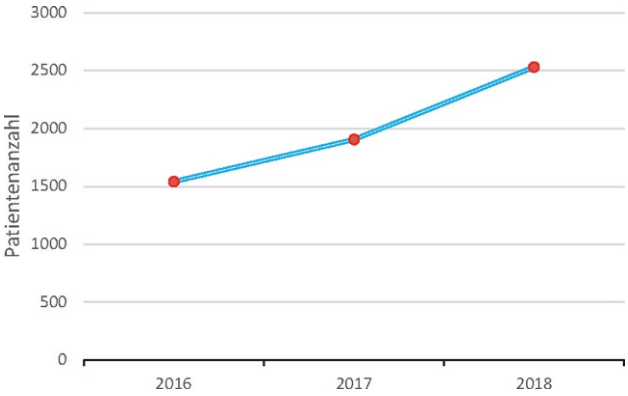


Abb. 1 | FP 3-1 Anzahl der Patienten, die in den Jahren 2016–2018 in Österreich einer Ablation unterzogen wurden

3,4 % berichtet werden, die über die Jahre tendenziell abnahmen ($p=0{,}366$). Im Median arbeiten 2 (range 1–5) Senior Elektrophysiologen und 1 (range 0–3) EP Fellow an 2,7 Tagen auf einem EP-Tisch pro Zentrum.

Schlussfolgerungen: Zwischen 2016 und 2018 wurde in diesem nationalen Register eine relative Zunahme von VH-Flimmer-Ablationen festgestellt. Die überwiegende Mehrzahl der Interventionen wird mit Radiofrequenz durchgeführt. Der Erfolg der Ablationen liegt insgesamt bei >96 % und die Komplikationsrate bei ca. 3 %.

FP 3-2

Zero-Fluoroscopy bei elektrophysiologischen Untersuchungen und Katheterablationen von rechtsseitigen Arrhythmien

Alexander Nahler[1], Hermann Blessberger[2], Denis Hrncic[2], Simon Hönig[2], Thomas Lambert[2], Christian Reiter[2], Martin Patrasso[2], Clemens Steinwender[2]

[1]Universitätsklinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum, Medizinische Fakultät Johannes Kepler Universität, Linz, Österreich
[2]Kepler Universitätsklinikum, Linz, Österreich

Grundlagen: Die Katheterablation ist bei supraventrikulären Tachykardien meist die Therapie der Wahl. Zur adäquaten endokardialen Positionierung und Darstellung der Katheter wird dabei eine fluoroskopische Bildgebung durchgeführt. Trotz zunehmend niedrigerer Strahlendosen in der Elektrophysiologie (EP) führt Röntgenstrahlung nachgewiesenermaßen bei langjähriger Anwendung mit hohen kumulativen Dosen beim im EP-Labor beschäftigten Team zu erhöhten Inzidenzen von zerebralen Tumoren oder einer Kataraktbildung. Weiters können die notwendigen Schutzmaßnahmen (Bleischürzen) zu beträchtlichen muskuloskeletalen Beschwerden führen. Durch die rasante Entwicklung der virtuellen 3D Mappingsysteme ist inzwischen eine sehr akkurate Steuerung aller Katheter auch ohne Verwendung von Fluoroskopie möglich (Zero-Fluoroscopy-Technologie, ZF) und bereits in einigen wenigen EP-Laboren weltweit in Verwendung. An unserer Institution wurde im Verlauf des letzten Jahres damit begonnen, den Großteil der rechtsatrialen und -ventrikulären Katheterablationen mittels ZF durchzuführen. Ziel dieser Analyse war es, die Sicherheit und Effektivität der ZF bei einer konsekutiven Serie von Patienten zu evaluieren.

Methodik: Seit September 2018 wurden in unserem EP Labor alle geplanten Untersuchungen mit dokumentierter Tachykardie, welche ihren Ursprung im rechten Vorhof oder Ventrikel vermuten ließ, ohne Verwendung von Röntgenstrahlung (ZF) durchgeführt. Zur Steuerung der Katheter fand das NAVX Ensite Precision System (Fa. Abbott) Verwendung. Bei Notwendigkeit einer Kontrolle der Katheterführung mittels Fluoroskopie war dies zu jeder Zeit der Prozedur mittels einer monoplanen bodenmontierten Röntgenanlage (Artis Q Zen, Fa. Siemens) möglich.

Ergebnisse: Es wurden insgesamt 43 konsekutive Untersuchungen mittels ZF durchgeführt. Das mittlere Alter der Patienten war 61 ± 14 Jahre mit einem Frauenanteil von 42 %. An wesentlichen Komorbiditäten fand sich eine arterielle Hypertonie bei 22 (51 %), eine koronare Herzkrankheit bei 14 (32 %) und eine eingeschränkte Linksventrikelfunktion bei 7(16 %) der Patienten. Folgende Arrhythmien wurden abladiert: AV-Knoten Reentrytachykardie ($n=17/40$ %) und typisches Vorhofflattern ($n=17/40$ %), ektope rechts-atriale Tachykardie ($n=2/4$ %), rechtsseitige akzessorische Leitungsbahn ($n=2/4$ %) rechtsventrikuläre Extrasystolie ($n=1/2$ %). In vier Fällen wurde lediglich eine diagnostische Untersuchung durchgeführt (10 %). Alle Ablationen waren erfolgreich, keine Prozedur musste wegen Komplikationen abgebrochen werden, auch die peri- und postinterventionelle Komplikationsrate lag bei 0 %. Die mittlere Prozedurdauer betrug 98 ± 32 Minuten (Median 90 [75;120] Minuten). In keinem Fall war von der ersten Lokalanästhesie bis zum Ziehen der Schleusen eine fluoroskopische Durchleuchtung erforderlich.

Schlussfolgerungen: Die Katheterablation von rechts-atrialen und -ventrikulären Substraten mittels ZF ist sicher und effektiv. Durch die Vermeidung von Röntgenstrahlung stellt sie für das gesamte Team eines EP-Labors die Vorgangsweise der Zukunft dar. Ihre Anwendung auch bei linksseitigen Substraten wird derzeit untersucht.

FP 3-3

NOACs vs VKA hinsichtlich asymptomatischer zerebraler Läsionen bei Pulmonalvenenisolation

Michael Derndorfer[1], Adrian Petzl[2], Kgomotso Nontsikelelo Moroka[1], Elisabeth Sigmund[1], Giorgos Kollias[1], Josef Aichinger[1], Helmut Pürerfellner[1], Martin Martinek[1]

[1]Ordensklinikum Linz, Linz, Österreich
[2]Universitätsklinik St. Pölten, St. Pölten, Österreich

Grundlagen: Die Pulmonalvenenisolation (PVI) mittels Radiofrequenzenergie geht mit einem erhöhten Risiko asymptomatischer zerebraler Läsionen (AZL) einher. Einige Studien lassen dadurch einen früheren Abbau der zerebralen Leistungsfähigkeit vermuten. Aktuelle Guidelines empfehlen zur PVI eine konsequente periprozedurale orale Antikoagulation (OAK), um Thromboembolien zu verhindern. Ziel der Studie war es, das periprozedurale Auftreten von AZL im Rahmen der PVI bei Patienten mit Vitamin-K-Antagonisten (VKA) oder NOACs (nicht-Vitamin-K-abhängige oralen Antikoagulanzien; gruppiert und Einzelvergleich) zu prüfen.

Methodik: Im Zeitraum 2013–2018 wurden 412 Patienten (73,8 % männlich) in die Studie eingeschlossen. Davon waren 184 Patienten (44,7 %) mit VKA, 228 (55,3 %) mit NOACs antikoaguliert. Die Ablation erfolgte nach allgemein gültigen Empfeh-

lungen und Ermessen des Untersuchers. Ein prä- und postprozedurales zerebrales MRT wurde bei allen Patienten angefertigt. Paroxysmales VHF lag in 67 % der Fälle vor; in 75,5 % wurde eine reine PVI ohne zusätzliche Ablationslinien durchgeführt, 26,3 % der Prozeduren waren Zweiteingriffe. Demographische und Ablations-bezogene Daten siehe Abb. 2.

Ergebnisse: AZL traten bei insgesamt 52 Patienten (12,6 %) auf, unter VKA numerisch, aber statistisch nicht signifikant seltener (17/184 Pat; 9,2 %) als unter NOACs (35/228 Pat; 15,4 %; $p=0{,}063$). Ein präinterventionelles Auslassen der letzten Tagesdosis des NOACs bewirkte keine signifikanten Unterschiede (unterbrochen 16,4 % vs kontinuierlich 13,6 %; $p=0{,}57$). Eine intraprozedurale ACT zwischen 300 und 400 Sekunden wurde angestrebt (iv Heparin-Bolus mit 100 IE Heparin/kgKG vor transseptaler Punktion + Heparin-Perfusor) und lag unter VKA höher im Normbereich als unter NOACs, wo zudem der erste gemessene Wert oft noch subtherapeutisch war. Signifikant häufiger traten AZL bei intraprozeduralen elektrischen Kardioversionen (22/111; 19,8 % vs 30/301; 10,0 %; $p=0{,}008$) sowie arterieller Hypertonie (29/172; 16,9 % vs 23/240; 9,6 %; $p=0{,}028$) oder Insult in der Anamnese (7/25; 28 % vs 45/387; 11,6 %; $p=0{,}017$) auf. Im direkten Vergleich der einzelnen NOACs zu VKA fiel einzig Dabigatran auf, worunter signifikant mehr AZL auftraten (VKA 17/184; 9,2 % vs Dabigatran 12/61; 19,7 %; $p=0{,}029$) (Abb. 1).

Schlussfolgerungen: Periprozedurale AZL bei PVI traten in 12,6 % auf und waren in der VKA-Gruppe numerisch (nicht signifikant) seltener als unter NOACs ($p=0{,}063$) bzw. signifikant seltener verglichen mit Dabigatran ($p=0{,}029$). Das Weglassen der letzten Tagesdosis des NOACs vor PVI war hierfür nicht relevant ($p=0{,}57$). Patienten mit intraprozeduraler eCV sowie Hypertonus oder Insult in der Anamnese wiesen einen signifikant höheren Anteil an AZL auf.

FP 3-4

Quantitative definition of severe functional mitral regurgitation – a matter of intercontinental debate

Georg Spinka[1], Philipp Emanuel Bartko[1], Gregor Heitzinger[2], Henrike Arfsten[1], Noemi Pavo[1], Julia Mascherbauer[1], Christian Hengstenberg[1], Martin Hülsmann[1], Georg Goliasch[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Medical University of Vienna, Vienna, Austria

Background: Recent divergence between AHA/ACC and ESC/EACTS guidelines of the quantitative definition for severe functional mitral regurgitation (sFMR) introduced uncertainty, inconsistency and continuing debate. The relation of each threshold with long-term outcome in patients under guideline directed therapy (GDT) remains however uncertain.

Methods: We enrolled 269 heart failure patients with reduced ejection fraction (HFrEF) and graded sFMR according to both guideline-recommendations [AHA/ACC: effective regurgitant orifice area (EROA) ≥ 40 mm² or regurgitant volume (RegVol) ≥ 60 ml/beat and ESC/EACTS: EROA ≥ 20 mm² or RegVol ≥ 30 ml/beat]. All-cause mortality was defined as the primary endpoint.

Results: According to AHA/ACC guidelines sFMR occurred in 17% by EROA with a median EROA of 0.5 mm² (IQR 0.4–0.6) and in 13% by RegVol with a median RegVol of 76 ml/beat (IQR 69–101). According to ESC/EACTS guidelines sFMR occurred

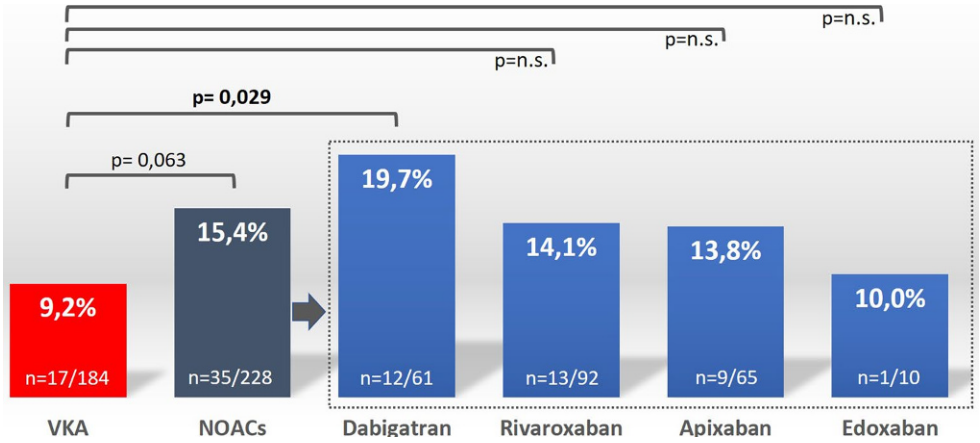


Abb. 1 | FP 3-3

	n	Alter Jahre	Gewicht kg	BMI kg/m²KOF	CHADS2VASc	LA Diameter mm, PLAX	LVEF %	Paroxysm VHF
VKA	184,0	56,8	87,8	28,3	**1,0**	**39,1**	54,2	69,6
Pradaxa	61,0	**56,2**	88,8	28,0	1,2	39,9	54,3	62,3
Xarelto	92,0	**62,2**	87,6	28,5	**1,7**	41,1	53,0	65,2
Eliquis	65,0	57,9	90,8	28,3	1,4	41,4	52,8	67,7
Lixiana	10,0	61,8	86,1	28,6	**1,7**	**41,6**	54,4	70,0
p value		<0.0001	n.s.	n.s.	0,001	0,015	n.s.	n.s.

	Total Ablation Time Minuten	LA-Time Minuten	ACT max Sekunden	ACT min Sekunden	eCV (PVI) %	Energieabgabe Ws	ReDo %	PVI only %	NOAC pausiert (%)
VKA	39,0	**141,4**	**393,9**	**322,0**	30,4	**65034,5**	25,5	73,9	
Pradaxa	34,7	132	375	268	36,1	55923	27,9	80,3	63,9
Xarelto	35,7	139	**345,1**	268	38,0	57120	30,4	75,0	23,9
Eliquis	36,2	139	354	**249,7**	50,8	58274	23,1	73,8	41,5
Lixiana	28,0	**98,0**	346	317	10,0	**46963,5**	10,0	90,0	40,4
p value	n.s.	0,0	<0.0001	<0.0001	n.s.	0,003	n.s.	n.s.	<0.0001

Abb. 2 | FP 3-3 NOACs vs. VKA hinsichtlich asymptomatischer cerebraler Läsionen bei Pulmonalvenen Ablation: Demographische und Ablations-bezogene Daten

in 53% by EROA with a median EROA of 0.4 mm² (IQR 0.2–0.4) and 40% according to RegVol with a median RegVol of 51 ml/beat (IQR 37–69). During 8-years follow-up, 165 patients died. We observed a significant association with outcome for sFMR according to AHA/ACC guidelines quantified by EROA (HR 1.66, 95%CI 1.13–2.43, $P=0.009$; Fig. 1A) as well as RegVol (HR 2.02, 95%CI 1.34–3.05, $P=0.001$; Fig. 1A). In contrast, the ESC/EACTS definition of sFMR was related with outcome exclusively if quantified by RegVol (HR 1.46, 95%CI 1.05–2.05, $P=0.026$; Fig. 1B) but not for EROA (HR 1.30, 95%CI 0.91-1.86, $P=0.15$; Fig. 1B).

Conclusions: In this contemporary HFrEF cohort under GDT there is significant association of the ACC/AHA proposed cut-off for severe FMR and long-term mortality. The ESC/EACTS definitions are associated with mortality exclusively for the RegVol. The lack of association between sFMR based on ESC/EACTS EROA cut-offs with mortality potentially results from incorporating patients where the regurgitant burden may still be compensated and has not yet become a driving force of disease progression. Contemporary definition of sFMR entails decision making for surgical/transcatheter repair. Cut-offs need to account for the competing risks of the procedure versus the potential benefit of reducing mortality. Lower thresholds may expose a significant proportion of patients to unnecessary risk of futile procedures and higher thresholds may withhold potentially life-extending therapies. The disagreement between the two guidelines does not only convey a source of uncertainty for treating physicians but also lead to inconsistent treatment allocation thereby hindering comprehensive and comparable research. Future studies need to approximate to the true nature of severe functional mitral valve disease in an attempt to facilitate a unifying definition of sFMR.

FP 3-5

Erste klinische Erfahrungen in der präinterventionellen Bildgebung und Bildintegration im Rahmen der VT Ablation

Michael Derndorfer[1], Kgomotso Nontsikelelo Moroka[1], Alexander Hofner[1], Giorgos Kollias[1], Josef Aichinger[1], Martin Martinek[1], Helmut Pürerfellner[1]

[1]Ordensklinikum Linz, Elisabethinen, Linz, Österreich

Grundlagen: Die Radiofrequenzablation ventrikulärer Tachykardien (VT) bei ischämischer oder nicht-ischämischer Kardiomyopathie stellt eine gut etablierte Therapieform zur Behandlung symptomatischer VT-Patienten dar. Eine präinterventionelle Bildgebung kann wertvolle Zusatzinformationen zur Detektion des arrhythmogenen Substrates liefern. Die gut etablierte Diagnostik mittels „Late Gadolinium Enhancement"-MRT ist jedoch häufig aufgrund implantierter Devices (Schrittmacher, Defibrillator) nur eingeschränkt möglich. Hochauflösende „Late-Iodine-Enhancement"-CT-Scans bieten hier aufgrund ihrer hohen räumlichen Auflösung mit sehr detaillierter Wiedergabe der Heterogenität und Wandstärkeunterschiede einer myokardialen Narbe, der schnellen Scan-Zeiten, höheren Verfügbarkeit und niedrigeren Kosten eine neue und gute Alternative.

Methodik: Bei 32 Patienten wurde zwischen 03/2018 und 02/2019 eine VT-Ablation mit vorangegangener Substratanalyse mittels eines hochauflösenden Herz-CTs, teilweise additivem Herz-MRT anhand des MUSIC-Protokolls (Fa. InHeart) durchgeführt. Die Bildverarbeitung erfolgte in Zusammenarbeit mit der Universität Bordeaux, die Bilder wurden ins elektroanatomische Mappingsystem integriert. Dargestellt werden können Narbenareale, die myokardiale Anatomie in Farbcodierung ihrer jeweiligen Wandstärke, die Koronarien, der Coronarsinus sowie der Nervus Phrenicus. Alle Patienten erhielten eine routinemäßige elektrophysiologische Untersuchung (EPU; Substrat- und Voltagemapping, späte abnorme ventrikuläre Aktivierung (LAVA), Spätpotentiale, Pacematch) und Ablation nach Einschätzung des Elektrophysiologen, wobei in den meisten Fällen eine Eliminierung aller pathologischen Potentiale und ein lokales Non-Capture als Endpunkt angesehen wurde. Für alle Prozeduren wurden hochauflösende Mappingkatheter verwendet (PentaRay® NAV, Fa. Biosense Webster; HD Grid, Fa. Abbott, IntellaMap ORION, Fa. Boston Scientific). Dokumentiert wurde der akute Outcome sowie ein klinisches/fallweise telefonisches Follow-Up nach 3 Monaten.

Ergebnisse: Eine ischämische Kardiomyopathie (CMP; $n=21$; 65,6 %) stellte die häufigste Diagnose bei den fast ausschließlich männlichen Patienten (90,6 %) dar. Demographische und Ablations-bezogene Daten siehe Abb. 2. Alle Patienten hatten einen Defibrillator implantiert und repetitive Schocks durch das Device erhalten. Nahezu alle Ablationen erfolgten von endokardial ($n=30$, 93,8 %), 8 Prozeduren (31,3 %) endo/epi- und 2 ARVC-Ablationen ausschließlich epikardial. Der hohe Grad an Übereinstimmung zwischen der Narbendarstellung im CT-Scan mit den Elektrophysiologischen Daten wird exemplarisch in Abb. 1 dargestellt. Anhand der farb-

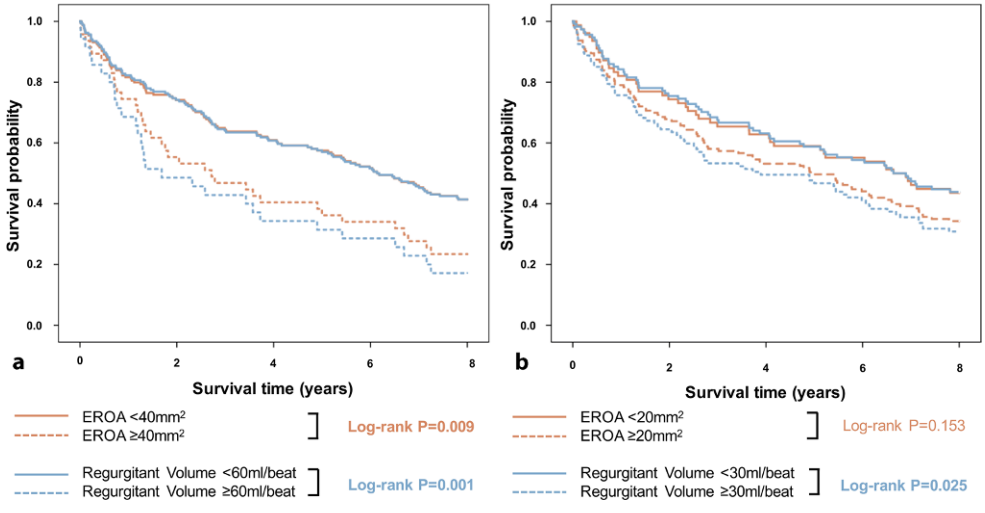


Fig. 1 | FP 3-4 Quantitative definition of sFMR

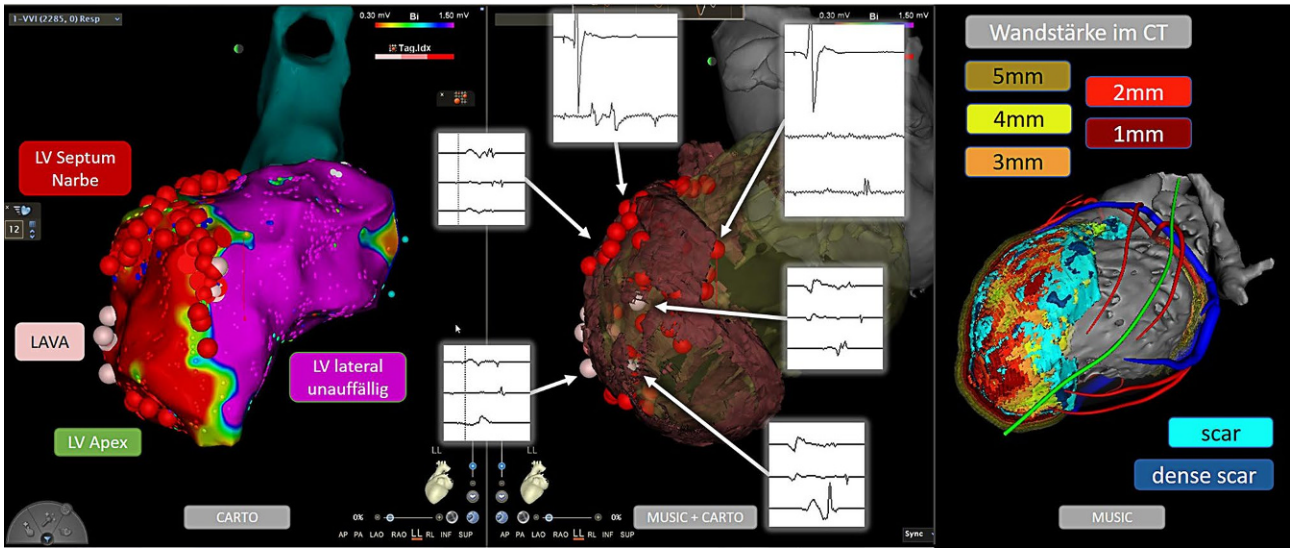


Abb. 1 | FP 3-5

	n	%	mean	min	max
männlich	29	90,6%			
Alter (Jahre)			57,3	31	77
BMI			27,4	18,7	36,1
iCMP	21	65,6%			
ICD	32	100,0%			
CRT	8	25,0%			
ATP prä	31	96,9%			
ICD-Schock prä	32	100,0%			
ReDo	10	31,3%			
Prozedurdauer (min)			219,5	105	315
Endocardial	30	93,8%			
Epicardial	10	31,3%			
FU durchgeführt	17	53,1%			
Rezidivfrei	13	76,5%			
ATP post	0	0,0%			
ICD Schocks post	3	17,6%			

Abb. 2 | FP 3-5

kodieren Bilder war eine vorab Abschätzung der möglichen Kanäle innerhalb der myokardialen Narbe möglich. Der akute Endpunkt eine LAVA-Eliminierung mit lokalem Non-Capture wurde in allen Prozeduren erreicht. Nach 3 Monaten erfolgten die ersten Follow-Up-Kontrollen, meist durch ICD-Abfrage, teils durch telefonische Kontrolle von Patienten mit Betreuung durch ein anderes Zentrum. Von 17 Patienten (53 %) war zum Zeitpunkt der Auswertung ein Follow-Up verfügbar. 76,4 % der Patienten waren frei von VTs, 1 Patient erhielt 2 ICD-Schocks im Rahmen von VTs bei schwerer Hypokaliämie, 1 Patient erlitt einen erneuten VT-Sturm und wurde erfolgreich sympathektomiert, 1 Patient mit höchstgradig eingeschränkter LVEF und repetitiven VT-Stürmen verstarb 3 Wochen post ablationem in der terminalen Herzinsuffizienz aufgrund eines erneuten therapierefraktären VT-Sturms.

Schlussfolgerungen: Die präinterventionelle Bildgebung mittels eines hochauflösenden „Late-Iodine-Enhancement"-CT-Scans stellt eine wertvolle Ergänzung zum kardialen „Late Gadolinium Enhancement"-MRT dar und liefert eine exakte vorab-Information über das zu erwartende Substrat. Die meist endokardiale und teils zusätzlich epikardiale VT-Ablation bei diesen sehr kranken und hochsymptomatischen Patienten vermag Rezidive und ICD-Schocks deutlich zu reduzieren. Durch die Weiterführung dieser Diagnostik sind zukünftig kürzere Prozedurdauern und bessere Erfolgsraten zu erwarten.

FP 3-6

Indication and outcome in patients undergoing left atrial appendage closure – Results from the Austrian LAAC Registry

David Zweiker[1], Raphael Sieghartsleitner[1], Lukas Fiedler[2], Gabor Toth[1], Olev Luha[1], Günter Stix[3], Paul Vock[4], Andreas Strouhal[5], Alexandra Schratter[5], Josef Aichinger[6], Kurt Sihorsch[7], Ronald K. Binder[8], Fabian Barbieri[9], Daniel Scherr[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Department of Internal Medicine, Hospital Wiener Neustadt, Wiener Neustadt, Austria
[3]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[4]Department of Internal Medicine III, Karl Landsteiner University Hospital St. Pölten, St. Pölten, Austria
[5]Department of Internal Medicine 4, Hospital Hietzing, Vienna, Austria
[6]Department of Internal Medicine 2, Elisabethinen Hospital Linz, Linz, Austria
[7]Department of Internal Medicine I, Johannes Kepler University Linz, Linz, Austria
[8]Department of Internal Medicine 2, Hospital Wels-Grieskirchen, Wels, Austria
[9]University Clinic of Internal Medicine III, Medical University of Innsbruck, Innsbruck, Austria

Background: Left atrial appendage closure (LAAC) is an established treatment option for stroke prevention in patients with atrial fibrillation (AF) and contra-indication to oral anticoagulation (OAC). However, the indication for LAAC and outcome in these patients outside of clinical trials is incompletely understood.

Methods: In this analysis of the national multicentre Austrian LAAC Registry, baseline characteristics, procedural details and outcome were compared between the following indication groups: patients with a history of bleeding as indication for LAAC (bleeding group) vs. a history of thromboembolism

despite OAC (thromboembolism group) vs. other patients (other group).

Results: One-hundred and eighty-six consecutive patients receiving LAAC between 2010 and 2017 at nine centres in Austria were included into the analysis. Of those, 59.7% had a history of bleeding (32.2% intracranial haemorrhage, 19.9% GI bleeding, 7.5% other), 8.1% a history of thromboembolism (7.0% stroke, 1.1% other thromboembolism) and 32.2% other indications for LAAC (7.0% predisposition for bleeding, 4.8% intolerance to OAC, 4.3% anaemia, 4.3% contraindication to OAC, 4.3% refusal of OAC, 4.3% requirement for triple therapy). $CHADS_2$ score was highest in the thromboembolism group (median 4 vs. bleeding 3 vs. other 2, $p<0.01$ for thromboembolism vs other group) and HAS-BLED score was highest in bleeding group (3 vs. thromboembolism 3 vs. other group 3, $p<0.05$ bleeding vs thromboembolism and other group). The procedural outcome was similar between groups, with major complications occurring in 7.0% of patients. During long-term follow-up (477 ± 464 days), we observed a significant relative reduction of embolic events by 57% ($p=0.035$) and a numeric reduction of bleeding events by 29% ($p=0.454$) compared to historic controls. The one-year survival free from stroke, bleeding or LAAC-associated hospitalization was similar between all groups (bleeding group 83.9%, thromboembolism group 90.0%, other group 81.4%, $p=0.891$, Fig. 1).

Conclusions: In daily clinical practice, LAAC is used in a heterogeneous patient population with AF and contraindication, inefficacy or intolerance to OAC. However, after LAAC embolic and bleeding events were reduced in all patient subgroups.

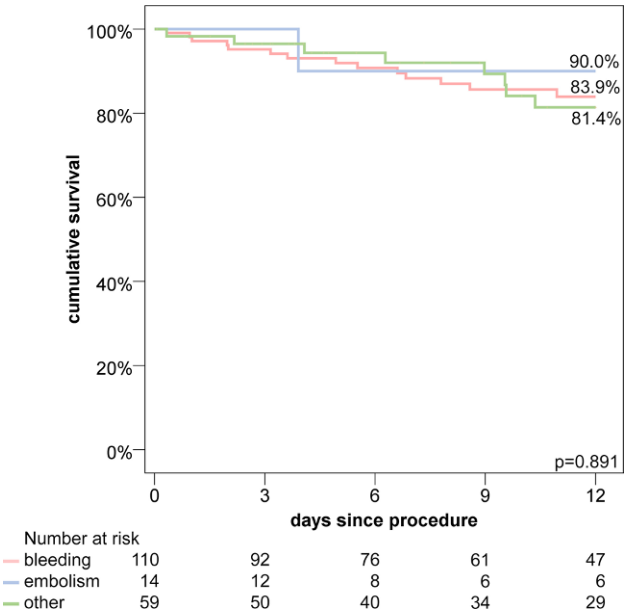


Fig. 1 | FP 3-6 One-year survival free from stroke, bleeding, or LAAC-associated hospitalization, stratified by indication groups

FP 3-7

Long-term outcome after ablation of atrial fibrillation in patients with reduced ejection fraction

Darko Trananoski, Martin Manninger, David Zweiker, Ursula Rohrer, Bernadette Pratl, Egbert Bisping, Peter Lercher, Günther Prenner, Andreas Zirlik, Daniel Scherr

Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Catheter ablation of atrial fibrillation is (AF) an established second line therapy for patients with symptomatic paroxysmal AF (PAF). Reduced ejection fraction has been proposed as a predictor for poorer outcome after ablation. On the other hand, recent studies have shown a decrease in mortality in patients with heart failure on optimal therapy that undergo AF ablation. In this study, we aimed to describe long-term outcome of patients with reduced ejection fraction.

Methods: 274 consecutive patients underwent AF ablation. 243 patients had normal left ventricular systolic function (nEF, 64 ± 5%) and 31 patients had reduced systolic function (rEF, 49 ± 10%). In rEF patients, atrial enlargement was more frequent (48 vs. 25%, $p=0.005$). Age (56 ± 12 vs. 60 ± 12), percentage of females (26 vs. 19%), BMI (27 ± 5 vs. 29 ± 4 kg/m^2, $p=0.08$), CHADS-Vasc-Score (1 [0, 2] vs. 1 [0, 2], $p=0.8$), HAS-BLED Score (1 [0, 2] vs. 1 [1, 2], $p=0.56$), arterial hypertension (54 vs. 52%, $p=0.15$), diabetes (4 vs. 7%, $p=0.26$), prior stroke (4 vs. 3%, $p=0.38$) were comparable between both groups. PVI was performed in 98.8% of nEF vs. 96.8% of rEF patients ($p=0.31$), roof lines in 3 vs. 3% ($p=0.4$), cavotricuspid isthmus ablation in 21 vs. 20% ($p=0.19$). Follow up duration was 340 (122, 555) vs. 192 (107, 452) days ($p=0.12$).

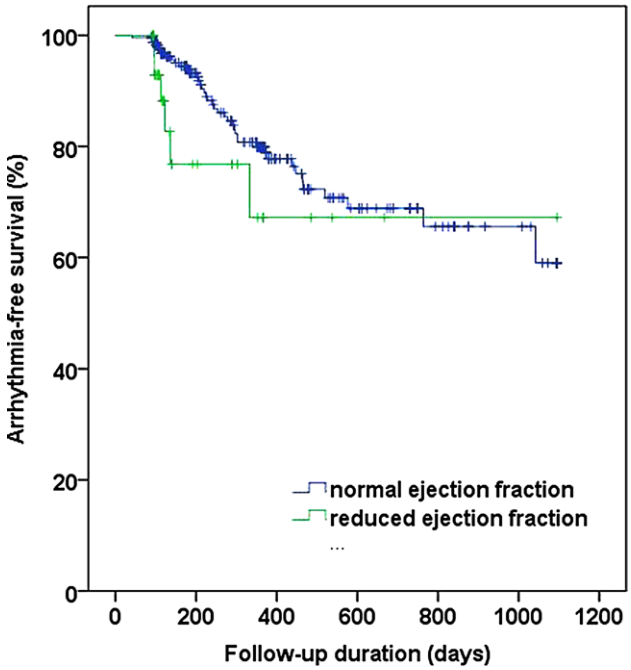


Fig. 1 | FP 3-7

Results: Complication rate was low in both groups (inguinal aneurysm in 1 nEF patient, 0.4%), 4 vs. 7% of patients required cardioversion before demission from the ward ($p=0.25$). Repeat ablations were performed in 19 vs. 23% of patients ($p=0.17$). Single procedure success rate was comparable between both groups: 59% in nEF patients vs. 67% in rEF patients (Fig. 1, log rank test: $p=0.203$). At the end of follow up, 58% of nEF patients vs. 65% of rEF patients were still on antiarrhythmic drug therapy ($p=0.12$).

Conclusions: Ablation of paroxysmal atrial fibrillation is reasonable and safe in patients with reduced ejection fraction. Outcomes and complication rates were comparable with patients with normal ejection fraction.

FP 3-8

Correlation of left atrial phasic transport function and arrhythmogenic substrate in patients with atrial fibrillation: insights from cardiac magnetic resonance feature tracking and bipolar voltage mapping

Robert Schönbauer[1], Jakub Tomala[2], Bettina Kirstein[2], Yan Huo[2], Thomas Gaspar[2], Utz Richter[2], Judith Piorkowski[2], Marie-Sophie Schönbauer[3], Lukas Fiedler[1], Franz Xaver Roithinger[1], Christian Hengstenberg[4], Julia Mascherbauer[4], Stefan Ulbrich[2], Christopher Piorkowski[2]

[1]Landesklinikum Wiener Neustadt, Wiener Neustadt, Austria
[2]Herzzentrum Dresden, Dresden, Germany
[3]Krankenhaus Hietzing, Vienna, Austria
[4]Medical University of Vienna, Vienna, Austria

Background: Bipolar voltage mapping is a widely accepted approach to identify areas of arrhythmogenic substrate in patients presenting for atrial fibrillation (AF) ablation. However, until now little is known about the correlation of left atrial (LA) bipolar voltage distribution and LA transport function.

Methods: 107 consecutive patients presenting for ablation of symptomatic AF (34 paroxysmal AF, 73 persistent AF) were prospectively enrolled. Each patient underwent cardiac magnetic resonance imaging (CMR) within 24 hours prior to the ablation procedure. 59 patients were in sinus rhythm (SR) and 48 in AF. LA phasic indexed volumes (LAVi) and ejection fractions were calculated using biplane area length formula. In addition LA phasic strains and strain rates were analyzed using dedicated software (Fig. 1A & B). LA bipolar voltage mapping was performed prior to beginning of ablation in sinus rhythm using a 3-dimensional mapping system and low voltage zones (LVZ) were defined as areas of bipolar voltage < 0.5 mV.

Results: LVZ were present in 47 patients (23 in SR). The area of LVZ was 14.6 cm^2 (5.3–34.0). For patients in AF at the time of CMR only elevated minimal and maximal LA volume indices (LAVi) ($p=0.001$ and $p=0.002$ respectively) but no LA functional parameter was predictive for the occurrence of LVZ. In contrast for patients in SR all LA phasic volumes (endsystolic, pre atrial contraction and enddiastolic LAVi) and LA function parameters (passive, active and total ejection fraction (EF), reservoir, conduit and booster pump strains and strain rates) were predictive for the occurrence of LVZ. After clustered and pooled multivariate logistic regression only impaired booster pump strain rate was still predictive for occurrence of LVZ (OR 0.974, 95% CI 0.950–0.998, $p=0.036$). In addition Pearson correlation analysis revealed a strong link between LA booster pump functional parameters and cm2 expansion of LVZ areas: LA active EF, LA booster pump strain and strain rate (r = –0.42, $p=0.044$; r = –0.47, $p=0.024$; r = –0.65, $p=0.001$ (Fig. 1C) respectively).

Conclusions: For patients in SR LA transport function is closely linked to the occurrence of LA LVZ and outperforms LA volumetric measurements for the prediction of LA LVZ. Furthermore, LA booster pump function parameters show robust correlation to the extension of LA LVZ.

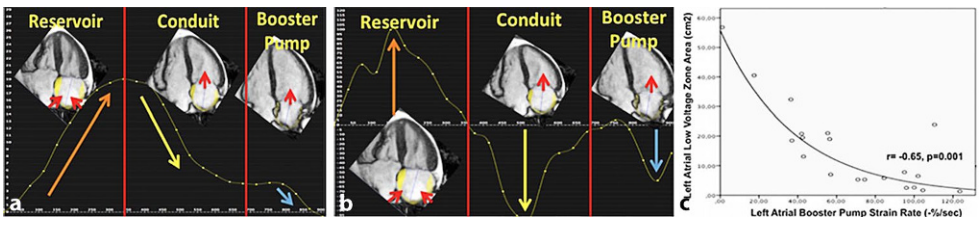


Fig. 1 | FP 3-8

POSTERSITZUNGEN 1-6

Donnerstag, 30. Mai 2019, 10.00 bis 11.00 Uhr

Postersitzung 1 – Akutes Koronarsyndrom/koronare Herzkrankheit

1-1

Blood urea nitrogen has additive value beyond estimated glomerular filtration rate for prediction of long-term mortality in patients with acute myocardial infarction

Bernhard Richter[1], Patrick Sulzgruber[1], Lorenz Koller[1], Matthias Steininger[1], Feras El-Hamid[1], David J. Rothgerber[1], Stefan Forster[1], Georg Goliasch[1], Benjamin I. Silbert[2], Elias L. Meyer[3], Christian Hengstenberg[1], Johann Wojta[1], Alexander Niessner[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Department of Intensive Care Medicine, Fiona Stanley Hospital, Murdoch, Australia
[3]Section for Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria

Background: Blood urea nitrogen (BUN) has been shown to independently predict short- and intermediate-term outcomes in patients with acute myocardial infarction (AMI). We aimed to assess the additive predictive value of BUN beyond estimated glomerular filtration rate (eGFR) in AMI patients with an 8.6-year follow-up.

Methods: This retrospective, observational single-centre study included 1332 consecutive AMI patients (median age 64 years, 58.4% male). BUN, creatinine and eGFR were determined immediately after hospital admission and before any acute intervention was performed. The study endpoint of cardiovascular mortality was determined by screening the Austrian register of death.

Results: During a median follow-up of 8.6 years (interquartile range [IQR] 4.0–11.6), 408 patients (30.6%) experienced the study endpoint of cardiovascular mortality. BUN (median 17.0 mg/dL [IQR 13.5–22.7]) was a significant predictor of cardiovascular mortality in univariate Cox regression (hazard ratio (HR) per 1 standard deviation increase 2.10, 95% confidence interval [CI] 1.94–2.28, $p<0.001$). This association remained significant after multivariable adjustment for demographics, clinical variables and eGFR (adjusted HR 1.52 [CI 1.16–2.00, $p=0.003$]). The association between BUN and outcome was more pronounced in patients with eGFR >60 mL/min/1.73 m^2 (HR 2.81 [CI 2.20–3.58, $p<0.001$]). The discriminatory abilities (Harrell's C-statistic) for BUN, eGFR and creatinine were 0.75, 0.76 and 0.67, respectively. The addition of BUN to eGFR significantly improved the C-statistic (0.78, p for comparison = 0.017), net reclassification (23.7%, $p<0.001$) and integrated discrimination (2.9%, $p<0.001$).

Conclusions: Circulating BUN on admission is an independent predictor of long-term cardiovascular mortality in AMI patients and adds predictive power beyond eGFR. BUN might be of particular value for the identification of high-risk patients in subjects with relatively normal eGFR who would be misclassified by eGFR alone. BUN reflects not only kidney function, but also acute haemodynamic and neurohumoral alterations during AMI.

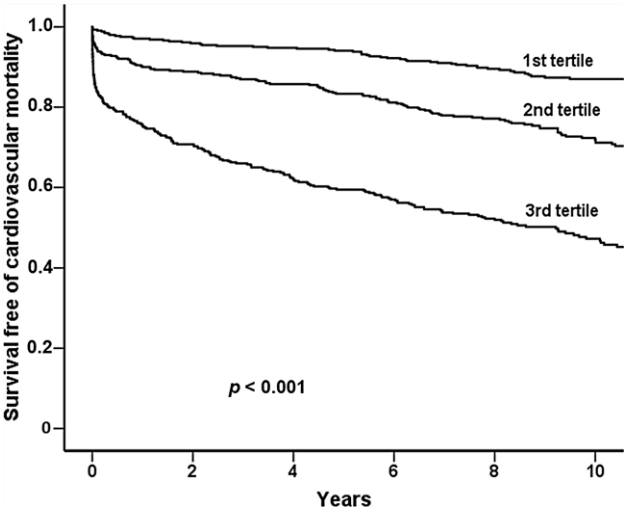


Fig. 1|1-1 Kaplan-Meier plots showing the crude cumulative survival free from cardiovascular mortality according to blood urea nitrogen (BUN) tertiles. P-value derived from log-rank test

1-2

Ticagrelor inhibits toll-like and protease-activated receptor mediated platelet activation in acute coronary syndromes

Patricia P. Wadowski[1], Constantin Weikert[1], Joseph Pultar[1], Silvia Lee[1], Beate Eichelberger[2], Renate Koppensteiner[1], Irene M. Lang[1], Simon Panzer[2], Thomas Gremmel[1], Thomas Gremmel[3]

[1]Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Department of Blood Group Serology and Transfusion Medicine, Medical University of Vienna, Vienna, Austria
[3]Department of Internal Medicine, Cardiology and Nephrology, Landesklinikum Wiener Neustadt, Wiener Neustadt, Austria

Background: Due to their distinct molecular structures, ticagrelor and prasugrel may differently affect toll-like receptor (TLR) and protease-activated receptor (PAR) mediated platelet activation. In the current study, we compared the effects of ticagrelor and prasugrel on platelet activation via TLR and PAR in acute coronary syndrome (ACS).

Methods: Platelet surface expression of P-selectin and activated glycoprotein (GP) IIb/IIIa in response to adenosine diphosphate (ADP), the TLR-1/2 agonist Pam3CSK4, the TLR-4 agonist lipopolysaccharide (LPS), the PAR-1 agonist SFLLRN and the PAR-4 agonist AYPGKF were measured by flow cytometry in 80 ticagrelor- and 80 prasugrel-treated ACS patients on day 3 after percutaneous coronary intervention. Residual platelet aggregation to arachidonic acid (AA) and ADP were assessed by multiple electrode aggregometry and light transmission aggregometry.

Results: ADP-inducible platelet activation and aggregation, and AA-inducible platelet aggregation were similar in patients on ticagrelor and prasugrel therapy, respectively (all $p \geq 0.3$). Further, LPS-inducible platelet surface expression of P-selectin and activated GPIIb/IIIa did not differ significantly between ticagrelor- and prasugrel-treated patients (both $p > 0.4$). In contrast, Pam3CSK4-inducible platelet surface expression of P-selectin and activated GPIIb/IIIa were significantly lower in ticagrelor-treated patients (both $p \leq 0.005$). Moreover, SFLLRN-inducible platelet surface expression of P-selectin and activated GPIIb/IIIa were significantly less pronounced in patients on ticagrelor therapy compared to prasugrel-treated patients (both $p < 0.03$). Finally, residual PAR-4 mediated platelet activation as assessed by platelet surface expression of activated GPIIb/IIIa following stimulation with AYPGKF was significantly lower in patients receiving ticagrelor ($p = 0.02$).

Conclusions: Ticagrelor inhibits TLR-1/2 and PAR mediated platelet activation in ACS more strongly than prasugrel.

1-3

Impella® in cardiogenic shock after acute myocardial infarction: a systematic review and meta-analysis

Kris G. Vargas[1], Alexander Geppert[1], Kurt Huber[1]

[1]3rd Medical Department, Cardiology and Intensive Care Medicine, Wilhelminenhospital, Vienna, Austria

Background: Cardiogenic shock (CS) after acute myocardial infarction (AMI) conveys a high mortality risk. Percutaneous left ventricular assist devices such as Impella may provide a bridge to patient recovery; however, individual studies are usually underpowered to adequately evaluate mortality outcomes. We aimed to provide a pooled estimate on proportions of mortality and to report on main complications (major bleeding and hemolysis) from studies evaluating the use of Impella in patients with CS after AMI.

Methods: We searched Medline OvidSP, Embase and Web of Science from 2005 until November 2018 for observational studies or clinical trials on this specific patient group. Studies were required to report on mortality at 30 days or longer. Excluded were reports with < 10 cases, entire cohort of patients on a concomitant but different assist device technology, as well as studies not stratified by CS cause. We calculated pooled proportions with 95% CIs using random-effects models and the inverse variance method.

Results: Overall, 646 patients from 10 studies (2 randomized and 8 observational) were included. Pooled proportions from 8

Study, year	Enrolment period	Region	Setting	Patients on Impella	Type of Impella	Duration of support	Comments
ISAR-SHOCK, 2008	<2008	Germany	Two-centre	12	2.5	25 [6.0-41.0] h	RCT comparing 12 patients on Impella versus 13 on IABP
Impella-EUROSHOCK, 2013	2005-2010	Germany, Netherlands, Switzerland, Sweden, Italy	Multicentre	120	2.5	43.5±49.6 h	29.2% were on IABP
USpella, 2014	2009-2012	USA	Multicentre	154	2.5	23.7[3.5-62.7] h	48.7% were on IABP
Casassus, 2015	2008-2012	France	Single-centre	22	2.5	35.5 [12.5-57.8] h	54.6% were on IABP
Schroeter, 2016	2006-2014	Germany	Single-centre	68	2.5, CP, 5.0	4.6±4.0 d	40.0% were on IABP
Meraj, 2017	2009-2015	USA and Europe	Multicentre	36	2.5	23.3±26.9 h (33 pts)	47.2% were on IABP
IMPRESS in Severe Shock, 2017	2012-2015	Netherlands, Norway	Multicentre	24	2.5, CP	49 [28-76] h	RCT comparing 24 patients on Impella versus 24 on IABP
Ouweneel, 2018	2004-2016	Netherlands	Single-centre	112	2.5, CP, 5.0	52 [22-122] h	19.6% were on IABP
Mourad, 2018	2009-2015	France	Single-centre	19	2.5, CP, 5.0	8 [4-13] d	21.1% were on ECMO
Jensen, 2018	2013-2017	Denmark	Single-centre	79	CP, 5.0, RP	62[21-135]h	15.0% were on ECMO

Fig. 1|1-3 Included studies

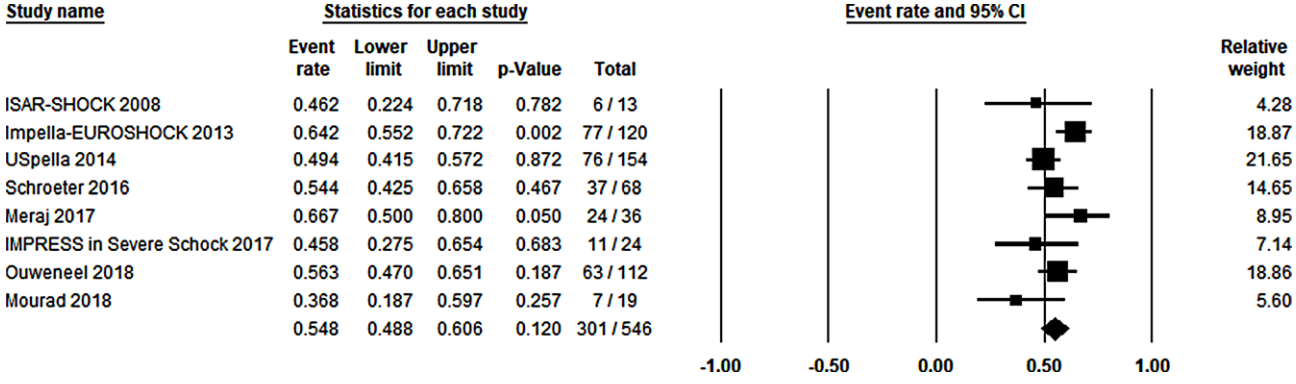


Fig. 2|1-3 Forest plot on 30-day mortality

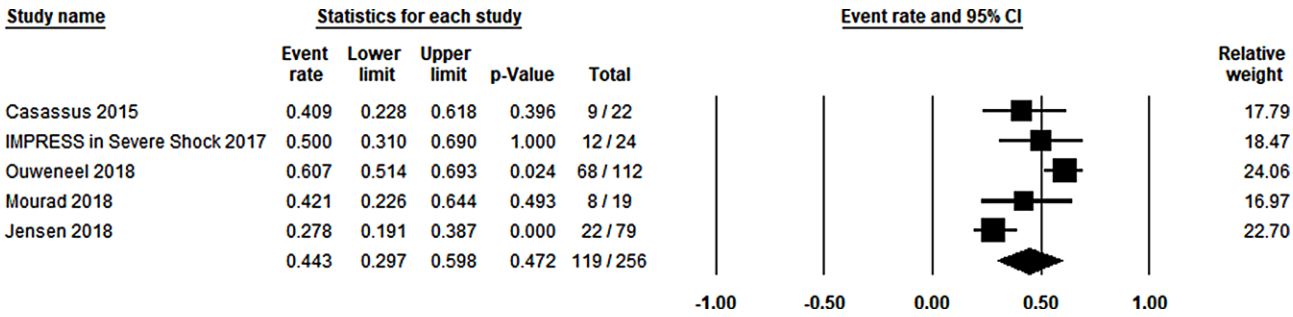


Fig. 3|1-3 Forest plot on 6-month mortality

studies showed a 30-day mortality of 54.8% (95% CI: 48.8–60.6; I2 = 39.9%; P = 0.12) and a 6-month mortality of 44.3% (from 5 studies, 95% CI: 29.7–59.8; I2 = 79.8%; P = 0.47). Major bleeding was found in 13.7% of patients (95% CI: 7.6–23.5; I2 = 78.1%; P < 0.05) and hemolysis in 7.7% (95% CI: 5.6–10.6; I2 = 0%; P < 0.05). In addition, 6 of 8 observational studies included patients who were also on intra-aortic balloon pumping (range: 19.6%–54.6%) and the remaining 2 studies included patients on extracorporeal membrane oxygenation (15.0% and 21.1% each).

Conclusions: Pooled proportion estimates of Impella in CS after AMI reveal a high (54.8%) 30-day mortality. This has also been shown in other studies in which Impella was not used. Powered randomized trials on this selected patient group are warranted for higher quality evidence.

1-4

Left ventricular thrombi and embolic events in Takotsubo syndrome despite therapeutic anticoagulation

Claudia Stöllberger[1], Josef Finsterer[1], Birke Schneider[2]

[1]Krankenanstalt Rudolfstiftung, Vienna, Austria
[2]Sana Kliniken Lübeck, Lübeck, Germany

Background: Takotsubo syndrome (TTS) may be complicated by left ventricular (LV) thrombus formation occurring in 2.2 to 12% of the patients. Embolic risk appears to be high. We present 3 patients with TTS-associated LV thrombi who developed cerebral embolism despite therapeutic anticoagulation.

Methods: Case series: Clinical characteristics and course of the patients are listed in the Table.

Table 1|1-4 Clinical characteristics and course of patients with takotsubo syndrome and left ventricular thrombi

	1	2	3
Age (years), sex	60 f	82 f	82 f
Triggering event	Conflicts within the family	Fall at home, lying on the floor for 20 hours	Pneumonia
Persisting ST-elevation	No	No	Yes
Echocardiography of the left ventricle	Apical akinesia	Mid-ventricular hypo-akinesia	Apical akinesia
Interval Oos -Echocardiography (hours)	18	68	20
Detection of LV Thrombus after Oos (hours)	41	68	94
LV thrombus	Multiple, mobile	Multiple, mobile	Single, spontaneous echo contrast
Coronary arteries	Nonsignificant plaque	Smooth, myocardial bridge LAD	Nonsignificant plaque
Anticoagulation	Enoxaparin 120 mg/day s. c.	Certoparin 3000 IE s. c., followed by unfractionated heparin i. v. in therapeutic dose	Unfractionated heparin i. v. in therapeutic dose
Initiation after Oos (hours)	20	27	18
Clinical signs of embolism	Right-sided weakness	Left-sided hemiparesis	Left sided weakness
Occured after Oos (hours)	41	120	92
Confirmed by	MRI, CT	CT	CT
Therapy	Enoxaparin continued	Unfractionated heparin continued	Unfractionated heparin continued
Discharge after	26 days	27 days	11 days
Neurologic deficit at discharge	No	Left sided hemiparesis	Left-sided weakness
Follow-up	No cardiac event after 5 months	Died after 45 days from aspiration pneumonia	Surgery for rectal carcinoma after 27 months

i.v. = intravenously; LAD = left anterior descendent coronary artery; Oos = onset of symptoms; s. c. = subcutaneously

Results: All patients were female. The age ranged from 60–82 years. Thrombocyte count was normal, whereas CRP levels were elevated. Patient #2 suffered from mid-ventricular ballooning whereas the other 2 patients showed an LV apical ballooning pattern. In patients #1 and #3, LV thrombi had not been present at the first echocardiographic examination and were detected 18 to 20 hours after initiation of anticoagulation. LV thrombi were multiple and highly mobile in 2 patients, 1 patient had a single immobile thrombus. All embolic events were ischemic strokes, occurring 41–120 hours after symptom onset and 21–93 hours after initiation of anticoagulation. At the time of embolism, all patients were under therapeutic levels of anticoagulation, either controlled by anti-factor Xa activity or by aPTT. Patients #2 and #3 additionally received acetylsalicylic acid 100 mg/d and a clopidogrel loading dose because of suspected acute coronary syndrome. Thrombolysis was not carried out in any of the patients. Two of the 3 patients were discharged with a neurologic deficit and one of them eventually died as a consequence of the stroke.

Conclusions: In TTS, LV thrombi may also occur in the mid-ventricular variant. Rapid improvement of LV function in TTS may induce detachment of the thrombus from the LV wall, transforming a mural thrombus into a protruding, floating one with high embolic potential despite optimal therapeutic anticoagulation therapy. Compared to LV thrombi in anterior myocardial infarction, this evolution makes LV thrombi in TTS extremely dangerous. In case of impending embolism from mobile thrombi in TTS, cardiac surgery with thrombectomy should be considered.

1-5

Gene expression of 1SLC8A1 is not regulated by experimental myocardial ischemia, but by NO-releasing β-blockers

Robert Gasser[1], Elisabeth Pieske-Kraigher[2], Klemens Ablasser[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2](worked in this institution) Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Cellular Ca++-homeostasis is largely maintained by the transmembrane Na+/Ca++-exchanger (NCX; 1SLC8A1 (Solute Carrier Family 8, member 16; NCX1)). 1SLC8A1 is a bidirectional transporter that normally extrudes Ca++ from the cell (forward mode), but also brings Ca++ into the cell (reverse mode) under special circumstances such as intracellular Na+ accumulation or membrane depolarisation. Changes in 1SLC8A1 function may cause abnormal Ca++ release from the sarcoplasmic reticulum (SR) and increase the propensity to abnormal cardiac electrical activity and arrhythmias of all kinds.

Methods: Here, using microarray gene expression profiling technique, validated by real time PCR, Tissue samples (60–150 mg) of right atrial auricle from patients subjected to cardiac surgery were cut into two samples and placed for 30 minutes in glucose-tyrode solution at 37 °C (Fig. 2) One sample was superfused with 100% oxygen, the other sample with 100% nitrogen in order to simulate ischemic conditions. After exposure, they were snap frozen in liquid nitrogen and stored at –70 °C until homogenization. The total RNA was isolated using the trizol method.

Results: Using real-time PCR, we have validated whether or not 1SLC8A1 gene expression is significantly down-regulated by nebivolol compared to atenolol in simulated ischemia/hypoxia (N2-perfused) preparations. We find that 1SLC8A1 gene expression is significantly down-regulated by nebivolol compared to atenolol in simulated ischemic/hypoxic (N2-perfused) preparations. In the microarray preliminary analyses we found that 1SLC8A1 gene expression is significantly down-regulated by nebivolol compared to atenolol both in O2-perfused preparations and simulated ischemia/hypoxia (N2-perfused) preparations. In the presence of atenolol, however, down-regulation of 1SLC8A1 is only minimal. It can be seen that, without the influence of beta-blockers, there is no significant regulation of 1SLC8A1-expression during myocardial ischemia. There is, however a significant difference between the expression of 1SLC8A1 during myocardial ischemia in the presence of atenolol (18.0 + 0,6) and nebivolol (13.6 + 0.3; +SEM; $P < 0.05$): 1SLC8A1-expression is decreased during ischemia in the presence of nebivolol.

Conclusions: Here, confirmed by real time PCR, the finding that 1SLC8A1 gene expression is significantly down-regulated by nebivolol compared to atenolol in simulated ischemia/hypoxia (N2-perfused) preparations may argue for a higher protective, anti-ischemic but also anti-arrhythmic potential of nebivolol compared to standard β-blockers like atenolol. Especially patients with ischemia-triggered arrhythmias—patients with ischemic cardiomyopathy, not re-vascularized ischemia, large myocardial scars may profit from this particular property of nebivolol over atenolol.

1-6

Course of immature erythropoietic and thrombopoietic cells after cessation of P2Y12-inhibitor therapy

Bernhard Jäger[1], Paul Michael Haller[1], Edith Piackova[1], Kris G. Vargas[1], Johann Wojta[2], Kurt Huber[1]

[1]Wilhelminenhospital, Vienna, Austria
[2]Medical University of Vienna, Vienna, Austria

Background: Changes in circulating cell populations may in part be responsible for an increase in ischemic events that are observed characteristically soon after discontinuation of dual antiplatelet therapy (DAPT). Aim of the study was to track the course of immature cell types of thrombopoiesis and erythropoiesis in patients with coronary artery diseases (CAD) after physician-driven cessation of chronic P2Y12-inhibition.

Methods: Sixty-two consecutive patients with CAD on DAPT maintenance dose (including aspirin 100 mg OD, plus clopidogrel 75 mg OD, or prasugrel 10 mg OD, or ticagrelor 90 mg BID) were prospectively enrolled before cessation of the P2Y12-inhibitor therapy. Immature reticulocyte fraction (IRF), reticulocyte hemoglobin content (Ret-Hb), both early markers of the of bone marrow response during mobilization of hematopoietic precursor cells, furthermore platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), and reticulated platelet count (RP) were determined at baseline (i. e. last day of P2Y12-inhibitor intake) and 10, 30, and 180 days thereafter (day–10, day–30, day–180), respectively.

Results: Cessation of P2Y12-inhibitor therapy was associated with a continuous increase of RP (baseline vs. day–180: $p<0.01$; day–10 vs. day–180: $p=0.01$; day–30 vs. day–180: $p=0.026$), IRF (baseline vs. day–180: $p=0.016$; day–10 vs. day–180: $p=0.015$; day–30 vs. day–180: $p=0.047$) and Ret-Hb (baseline vs. day–180: $p<0.01$, day–10 vs. day–180: $p<0.01$; day–30 vs. day–180: $p<0.01$), respectively. PC, MPV and PDW were not significant altered by cessation of P2Y12-inhibitor therapy.

Conclusions: In patients with CAD, discontinuation of DAPT is associated with raised thrombopoietic and erythropoietic activity in the bone marrow. This indicates elevated platelet turnover, most probably as a result of increased peripheral consumption of platelets.

1-7

Exercise-based cardiac rehabilitation is associated with a normalization of the heart rate performance curve deflection

Stefan Heber[1], Rochus Pokan[2]

[1]Center for Physiology and Pharmacology, Medical University of Vienna, Vienna, Austria
[2]Center for Sport Science and University Sports, University of Vienna, Vienna, Austria

Background: The heart rate (HR) rises with increased power output, whereby in most healthy individuals the slope of HR levels off with higher intensity. This corresponds to a downward deflection of the heart rate performance curve (HRPC). Conversely, in patients after myocardial infarction, an upward HRPC deflection is frequently observed that is especially pronounced in patients with compromised left-ventricular ejection fraction.

Methods: To investigate whether regular endurance training during cardiac rehabilitation might normalize HRPC, data of 128 male patients were analyzed. All patients performed three exercise tests: at baseline, after six weeks, and after one year. 96 patients exercised regularly according to guidelines for one year (training group, TG), 32 stopped after six weeks (control group, CG). Similarly upward deflected HRPCs were observed at baseline and after 6 weeks in both groups.

Results: After one year, TG patients had less upward deflected HRPCs compared to CG ones, corresponding to a partial normalization. Greater changes of HRPC deflection were associated with larger improvements in cardiorespiratory fitness.

Conclusions: Our results might indicate improved myocardial function due to long-term rehabilitation. Further, HRPC alterations over time should be considered when prescribing exercise intensities using a target HR, as deflection flattening might render the intensity of corresponding exercise insufficient.

1-8

Cardisiometry: a novel, artificial intelligence based screening tool for detection of stable coronary artery disease at rest

Vera Hergesell[1], Felix Vaisfeld[2], Phillipp Hölzl[1], Markus Mach[1], Ayse Gürbüz[1], Otto E. Dapunt[1], Sotirios Spiliopoulos[1]

[1]Medical University of Graz, Graz, Austria
[2]Cardisio GmbH, Frankfurt, Germany

Background: We introduce Cardisiometry (Cardisio GmbH, Frankfurt, Germany), a novel, artificial intelligence based screening tool for the detection of stable coronary artery disease at rest.

Methods: Cardisiometry is a simplified vectorcardiographic method focusing on spatial and temporal heterogeneity of cellular repolarization. Four signal electrodes and a neutral electrode placed on the thorax define two orthogonal planes. In each plane potentials between two electrodes are measured and then added together. The result is a vector that corresponds to the projection of the heart into the plane. The vectors are projected by trigonometric calculation into a Cartesian coordinate system. The orientation of the vector in this system corresponds to the direction and the length of the vector to the strength of the electrical field of the heart.

Results: 290 parameters including beat to beat variability of P-, R- and T- loops as well as superposition of T-wave and QRS complex in the transverse plane of the vector loop are fully automatically recorded and analyzed. Deviating parameters reflect impaired cellular depolarization indicating a myocardial perfusion disorder. In contrast to conventional simplified vectorcardiography, Cardisiometry additionally implements a supervised, feedforward neural network comprising an input layer of 20 input neurons, two hidden layers of twelve and eleven neurons and one output neuron. The network is trained by a backpropagation algorithm that results in an ongoing optimization of sensitivity and specificity of Cardisiometry for the detection of coronary artery disease (currently 94%/77% for male and 89%/80% for female patients respectively).

Conclusions: Cardisiometry is a novel, artificial intelligence based technology that has the potential, due to the implementation of supervised machine learning algorithms, to evolve into a first- line screening tool for the detection of stable coronary artery disease at rest.

Postersitzung 2 – Basic Science 1

2-1

Characterization of left ventricular function, proinflammatory cytokines and NRG-1 in chronic kidney disease model in rat

Eylem Acar[1], Fanni Márványkövi[2], Dalma Dajka[2], Zsuzsanna Kovács[2], Antonia Bergmeister[1], Tamás Csont[2], Bruno Podesser[1], Márta Sárközy[2], Attila Kiss[1]

[1]Center for Biomedical Research, Ludwig-Boltzmann-Cluster for Cardiovascular Research, Medical University of Vienna, Vienna, Austria
[2]Department of Biochemistry, Faculty of Medicine, University of Szeged, Szeged, Hungary

Background: The prevalence of chronic renal disease (CKD) is continuously increasing in developed countries. Uremic cardiomyopathy characterized by left ventricular hypertrophy (LVH) and diastolic dysfunction (DD) is a common cardiovascular complication of CKD. However, the underlying molecular signaling mechanisms in the development of uremic cardiomyopathy are not fully understood. Cardiac microvascular low-grade inflammation and altered expression of endothelium derived Neuregulin-1 (NRG-1) are contributed to left ventricular DD. Therefore, the present study aimed to investigate the effect of CKD on cardiac and kidney levels of NRG-1, as well as cardiac gene expression profile of fibrotic and inflammatory markers for a better understanding of the uremic cardiomyopathy pathogenesis

Methods: Male Wistar rats were used and randomized into 1) Sham operated and 2) CKD was induced by 5/6 nephrectomy. Nine weeks later serum urea and creatinine levels were measured to verify the development of CKD and transthoracic echocardiography was performed to monitor cardiac morphology and function. Furthermore total RNA was isolated and RT-qPCR was performed to evaluate the expression levels of inflammatory cytokines. In addition, NRG-1 protein levels were measured in both kidney and heart tissue by ELISA.

Results: In the 5/6 nephrectomized group, serum urea and creatinine levels were significantly higher ($p<0.05$ vs Sham operated group). There was no difference in LV ejection fraction between the groups, however CKD rats were showed impaired diastolic function (e' was significantly decreased and E/e' was significantly increased; $p<0.05$, respectively). This was accompanied by a significant decrease in NRG-1 protein levels in both cardiac and kidney tissue ($p<0.05$ vs Sham, respectively). Moreover, the expression of TNF-α, MMP-9, MCP-1 and TGF-β mRNA were increased in LV tissue samples in CKD ($p<0.05$ vs Sham, respectively).

Conclusions: CKD resulted in LV diastolic dysfunction in rats. This was accompanied by the upregulation of pro-inflammatory cytokine expression and decrease in both cardiac and kidney protein expression of NRG-1. Thus, targeting inflammation and NRG-1 represents a novel target for improving the detection, management, and prevention of CKD-induced cardiomyopathy.

2-2

Remote conditioning partially reverses myocardial ischemia and reperfusion induced vascular endothelial dysfunction in aorta

Christopher Dostal[1], Lujza Petra Szabo[1], Ouafa Hamza[1], Patrick Pilz[1], Milat Inci[1], Attila Kiss[1], Bruno Podesser[1]

[1]Center for Biomedical Research, Ludwig Boltzmann Cluster for Cardiovascular Research, Medical University of Vienna, Vienna, Austria

Background: There is growing evidence that acute myocardial infarction (MI) besides inducing irreversible myocardial damage, may also contribute to further endothelial dysfunction in the remote vascular bed. This may subsequently lead to an increased risk for additional acute atherothrombotic events. Current vascular protective strategies are limited to reverse long-term endothelial dysfunction after MI. Remote ischemic perconditioning (RIPerc) is considered as a potential clinical approach to reduce myocardial infarct size and improve endothelial function in patients with congestive heart failure. Nevertheless, there is a lack of evidence whether remote ischemic preconditioning (RIPerc) preserves endothelial function following myocardial ischemia and chronic reperfusion. Therefore, the aim of this study was to explore the effect of RIPerc on endothelial function in the abdominal aorta in rats were subjected to myocardial ischemia and reperfusion.

Methods: Male OFA-1 rats were subjected to 30 min occlusion of the left anterior descending artery (LAD) followed by 4 weeks reperfusion were allocated into the following groups: 1) sham operated (Sham, without LAD occlusion; $n=6$); (2) myocardial ischemic reperfusion (MIR) ($n=10$) and (3) MIR+RIPerc ($n=8$) group with three cycles of 5 minutes of I/R on hindlimb performed during myocardial ischemia. Assessment of vascular reactivity in isolated aortic rings was performed by a wire myograph. Accordingly, endothelium dependent relaxations were determined by administration of cumulatively increasing concentrations of Acetylcholine (1 nM–10 μM) precontracted with Phenylephrine (1 nM–10 μM). The endothelial-independent relaxation was tested by Sodium Nitroprusside (SNP, 1 nM-10 μM), precontracted with Phenylephrine (10 μM). Assessment of plasma Malondialdehyde (MDA) levels, as a marker for oxidative stress was performed by HPLC.

Results: After 4 weeks follow-up, segments of abdominal aorta from MIR group display endothelium-dependent relaxation in comparison with Sham group ($P<0.05$). In addition, rats with RIPerc showed a preserved endothelial function in aorta. Vascular response to SNP, an activator of endothelium-independent vasorelaxation pathway was not changed between groups. In addition, MIR resulted in significant upregulation of plasma MDA levels ($p<0.01$ vs Sham). Interestingly, MDA levels was not shown difference between MIR and MIR+RIPerc groups.

Conclusions: Myocardial ischemia and long term of reperfusion causes impaired peripherial vascular endothelial dysfunction. RIPerc showed a tendency to preserve endothelial function without affecting oxidative stress markers. Collectively, besides the infarct size limiting effect of RIPerc, it may also a potential therapeutic approach to enhance endothelial function and subsequently reduce risk for additional atherothrombotic events in patients with MI.

2-3

Lack of Tenascin C preserves cardiac and vascular endothelial function in diabetes

Attila Kiss[1], Zsuzsanna Arnold[1], Nagel Felix[1], A. J. Fee[2], Petra L. Szabo[1], Attila Josvai[3], Fruzsina Balogh[4], Maria Szekeres[5], György Nádasy[4], Bruno K. Podesser[1]

[1]Center for Biomedical Research, Ludwig Boltzmann Cluster for Cardiovascular Research, Medical University of Vienna, Vienna, Austria
[2]Department of Physiology, Kansas University, United States of America; Semmelweis University, Budapest, Hungary
[3]Department of Neurosurgery, Medical Centre, Hungarian Defence Forces, Budapest, Hungary
[4]Department of Physiology, Semmelweis University, Budapest, Hungary
[5]Department of Morphology and Physiology, Semmelweis University, Budapest, Hungary

Background: Tenascin-C (TNC) is a glycoprotein of the extracellular matrix, highly expressed during embryogenesis, tumorigenesis cardiac and vascular remodeling process. More recently, an enhanced expression of TN-C in patients with diabetes was associated with poor clinical prognosis. However, the contribution of TN-C for the development of cardiac and vascular dysfunction in diabetes has not been investigated. Therefore, our study was aimed to clarify the impact of lack of TN-C on diabetes associated cardiovascular dysfunctions in mice.

Methods: 18–20-weeks-old streptozotocin-induced diabetic AJ and TN-C-KO mice were used. Echocardiography was performed to assess left venticular ejection fraction (LVEF) and vascular reactivity was performed by wire myography. In addition, the whole branching system of the left descendent coronary artery, running intramurally was in situ microprepared down to about 40 micrometer of diameter and the coronary network geometry was analyzed.

Results: There was no difference in blood glucose levels between the two diabetic groups. However, TN-C-KO diabetic mice showed preserved LV ejection fraction in compared to AJ diabetic mice ($p<0.05$). In diabetic animals, a broken course of larger coronary branches was frequently encountered. TN-C-KO diabetic animals had more rich branching systems in compared to AJ diabetic mice. Aortic segments from AJ diabetic mice displayed impaired endothelium-dependent relaxation ($p<0.05$). This effect was significantly revered in TN-C-KO diabetic mice.

Conclusions: Lack of TN-C was associated with a better LV and vascular function in STZ induced diabetic mice. In addition, the richer coronary branching systems of TN-C-KO mice might contribute to a preserved ventricular tissue perfusion, subsequently delays and reduces the development of diabetic cardiomyopathy. These results suggest that targeting TN-C is a novel potential therapeutic strategy to protect vascular and cardiac function in diabetes.

2-4

The branched-chain amino acids valine and leucine predict all-cause mortality in cardiovascular disease patients independently from the presence of type 2 Diabetes mellitus

Axel Muendlein[1], Andreas Leiherer[1], Christoph H. Saely[2], Alexander Vonbank[3], Marc Schindewolf[4], Jörn F. Dopheide[4], Iris Baumgartner[4], Barbara Larcher[3], Arthur Mader[3], Simon Sternbauer[3], Lukas Sprenger[3], Peter Fraunberger[5], Heinz Drexel[4]

[1]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[2]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein
[3]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[4]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland
[5]Medical Central Laboratories Feldkirch, Feldkirch, Austria

Background: Circulating branched-chain amino acids (BCAAs) are linked with mortality in population-based studies. Whether they also predict mortality in patients with established cardiovascular disease (CVD) is unclear.

Methods: We therefore determined serum BCAAs by NMR spectroscopy in 327 patients with established CVD. Prospectively, deaths were recorded over a mean follow-up period of 8.1 ± 3.5 years.

Results: At baseline, serum valine, leucine and isoleucine were significantly associated with T2 DM (all p-values <0.001). Prospectively, death occurred in 49.5% of patients with T2 DM and in 37.2% of non-diabetic patients ($p=0.036$). Fig. 1 shows the associations of BCAAs with mortality univariately and after multivariate adjustment including presence of T2 DM in the total study cohort as well as separately for patients with T2 DM and for non-diabetic patients. Low valine as well as low leucine

		All patients	Patients with T2DM	Patients without T2DM
Valine	Univariable Cox regression analysis	HR=0.60 [0.50-0.72]; p<0.001	HR=0.41 [0.30-0.57]; p<0.001	HR=0.69 [0.54-0.87]; p=0.002
	Multivariable Cox regression analysis	HR=0.65 [0.52-0.80]; p<0.001	HR=0.49 [0.33-0.73]; p<0.001	HR=0.71 [0.55-0.92]; p=0.009
Leucine	Univariable Cox regression analysis	HR=0.74 [0.61-0.89]; p=0.001	HR=0.58 [0.42-0.80]; p=0.001	HR=0.81 [0.64-1.04]; p=0.093
	Multivariable Cox regression analysis	HR=0.77 [0.62-0.95]; p=0.015	HR=0.68 [0.46-0.99]; p=0.044	HR=0.79 [0.60-1.03]; p=0.078
Isoleucine	Univariable Cox regression analysis	HR=0.081 [0.67-0.98]; p=0.031	HR=0.83 [0.61-1.12]; p=0.223	HR=0.79 [0.62-1.01]; p=0.059
	Multivariable Cox regression analysis	HR=0.86 [0.70-1.06]; p=0.149	HR=1.04 [0.75-1.44]; p=0.826	HR=0.70 [0.53-0.93]; p=0.014

Fig. 1|2-4 Associations of BCAAS in the total study cohort: univariate and multivariate adjustment including presence of T2 DM, as well as for patients with T2 DM and for non-diabetic patients

predicted mortality independently from the presence of T2 DM in the total cohort and, in subgroup analysis, specifically in patients with T2 DM.

Conclusions: We conclude that low valine and leucine serum levels predict mortality in patients with established CVD independently from the presence of T2 DM.

2-5

Influence of dabigatran on pro-inflammatory cytokines, growth factors and chemokines in vitro

Vera Paar[1], Peter Jirak[1], Christine Prodinger[2], Bernhard Wernly[1], Uta C. Hoppe[1], Michael Lichtenauer[1]

[1]Division of Cardiology, Department of Internal Medicine II, Paracelsus Private Medical University, Salzburg, Austria
[2]Department of Dermatology, Paracelsus Private Medical University, Salzburg, Austria

Background: Blood coagulation is one of the most important host-defending mechanisms in vivo by maintaining blood pressure after injury. However, besides maintaining homeostasis, blood coagulation and the contributing factors are directly linked to pathological conditions, such as thromboembolic diseases and inflammation, leading to cardiovascular diseases among others. As anti-inflammatory drugs may reduce cardiovascular events, we hypothesized in this study that the direct thrombin inhibitor dabigatran may reduce cytokine, growth factor and chemokine expression in vitro.

Methods: Human peripheral blood mononuclear cells (PBMCs, $n=12$) were isolated and treated with different conditions by the addition of human autologous serum, heparinized plasma, EDTA plasma and thrombin. Further, the effect of the non-vitamin K antagonist oral anticoagulant on pro-inflammatory cytokines (IL-1β, IL-6 and TNF-α), growth factors (Angiogenin, TGF-β and VEGF) and chemokines (GRO-α, IL-8 and MCP-1) was measured by commercially available ELISA kits. Cells in medium (baseline), 20% autologous serum and 200 ng/ml thrombin served as negative or positive controls, respectively.

Results: Supernatant protein levels were significantly altered by the treatment with 20% serum, however no dose-dependency of cytokine levels was detected. Solely Angiogenin showed a significant increment at 20% serum (79,780.4 ± 31,888.4 pg/ml) in comparison to baseline levels (197.1 ± 682.74 pg/ml), as it is for thrombin treatment. Also chemokines increased when adding serum to cell cultures. Furthermore, the addition of dabigatran reduced cytokine and growth factor expression in both conditions in trend. Only Angiogenin expression seemed to be completely dependent on thrombin stimulation and its secretion was abrogated by the addition of dabigatran.

Conclusions: Previous studies have shown that activating stimuli on PBMC have great effects on the secretion of cytokines and chemokines by these cells and on the composition of the supernatant. These supernatants exerted cardioprotective and pro-angiogenic effects in cardiomyocytes and endothelial cells. The results of our present study outlines that the activation of the coagulation cascade leads to a triggering of the release of cytokines, chemokines and some growth factors. At least for ANG, this effect seems to be provoked by thrombin and could be reversed by dabigatran. One could hypothesize that dabigatran might elicit anti-angiogenic and anti-inflammatory effects. Future in vitro and in vivo studies are warranted in order to further elucidate these cellular mechanisms.

2-6

Analyses of UCP2 dependent modulations of cardiac electrophysiology: Nav1.5 expression and consequences of catecholaminergic stress

Vera Paar[1], Robert Larbig[2], Alexandra Kaser-Eichberger[3], Sara Reda[1], Stephanie Weichselbaumer[1], Bernhard Ohnewein[1], Peter Jirak[1], Christian Dinges[4], Uta C. Hoppe[1], Falk Schrödl[5], Lukas J. Motloch[1]

[1]Division of Cardiology, Department of Internal Medicine II, Paracelsus Private Medical University, Salzburg, Austria
[2]Division of Cardiology, Hospital Mönchengladbach, Mönchengladbach, Germany
[3]Division of Ophthalmology and Optometry, Paracelsus Private Medical University, Salzburg, Austria
[4]Department of Cardiac Surgery, Paracelsus Private Medical University, Salzburg, Austria
[5]Institute for Anatomy, Paracelsus Private Medical University, Salzburg, Austria

Background: UCP2 belongs to a superfamily of mitochondrial ion transporters. Its ability to modulate cardiac Ca2+-handling, is suspected to promote modulatory effects on cardiac electrophysiology. Indeed, compensatory mechanisms were revealed which prevent UCP2 knock out mice (UCP2-/-) from toxic Ca2+-overload at rest but are insufficient during activation of L-type Ca2+-channel (LTCC) leading to Ca2+-dependent arrhythmias. UCP2-dependent modulations promote further alterations including decreases of PR and QRS on ECG recordings as well as an increased slope factor of action potential upstrokes on the cellular level indicating modifications of Na+-channel function. However, the underlying mechanisms as well as the impact of UCP2 on catecholaminergic stress, a common etiology of cardiac arrhythmias, were not studied yet.

Methods: To investigate this issue, patch clamp recordings of the LTCC at 37°C as well as cellular and mitochondrial Ca2+-transients in cardiomyocytes and ECG recordings in mice under isoproterenol stimulation were performed in wild type (WT) and UCP2-/-. Furthermore, to evaluate the impact of UCP2 on Na+-channels, Nav1.5 expression was studied using western blot and immunofluorescence analyses.

Results: Consistent with previous results LTCC-current at 37°C was significantly decreased in UCP2-/-, indicating compensatory mechanisms. However, while UCP2 dependent alterations of ECG parameters (PR, QRS and QTc) were observed at rest, no differences were recorded after catecholaminergic stimulation. In accordance, no significant alterations in the incidence of ventricular arrhythmia were revealed. However, alterations of cytosolic and mitochondrial Ca2+-handling were preserved in cardiomyocytes indicating catecholaminergic independent effects. Nevertheless, Nav1.5 expression was not altered in UCP2-/- suggesting rather UCP2 to alter the channel's pore activity.

Conclusions: UCP2 dependent alterations of cardiac Ca2+-handling are preserved during catecholaminergic stimulation. However, in contrast to baseline function ECG parameters and the susceptibility for ventricular arrhythmias seem not to be affected. Furthermore, suspected regulatory effects of UCP2 on Na+-channel might not influence the channel's expression.

2-7

Sex differences in the pathophysiology of thoracic aortic aneurysms

Franziska Wittmann, Marie-Elisabeth Stelzmüller, Marek Ehrlich, Günther Laufer, Messner Barbara

Medical University of Vienna, Vienna, Austria

Background: Thoracic aortic aneurysms (TAAs) are the second most frequent diseases affecting the aorta and are associated with high mortality. Loss of vascular smooth muscle cells and destruction of the extracellular matrix, essential for mechanical properties of the aorta, lead to weakening and focal dilation of the aortic wall making the aorta vulnerable to dissection and/or rupture, an event associated with up to 90 percent mortality. Incidence varies but is significantly higher in men compared to women, whereas the risk for rupture is essentially higher in females. Moreover, aneurysm growth rate was shown to be significantly higher in women, contributing to a higher risk for rupture and consequently higher mortality. Possible underlying reasons contributing to these differences between men and women have already been investigated in abdominal aortic aneurysms, but data concerning sex specific differences in TAAs are rare. A sex specific view on TAA development is needed to reassess sex specific treatment to possibly equalize sex-related mortality, thus reduce mortality of TAAs in women and unravel underlying signalling pathways. Therefore the aim is to identify possible underlying gender specific pathophysiological differences also concerning tricuspid (TAV) and bicuspid (BAV) aortic valve anatomy.

Methods: Aortic tissue from patients undergoing surgery for TAA repair was collected from the Department of Cardiac Surgery of the Medical University of Vienna. Control tissue specimens were collected from heart transplant recipients/donors. The following groups were established: TAV, BAV, CTRL each female and male. Fixed tissue samples were subjected to Elastica van Gieson staining to evaluate thickness of the tunica media and intima.

Results: Elastica van Gieson staining showed a significantly thinner tunica media in BAV samples compared to the control (female BAV: $p=0.017$; male BAV: $p=0.04$). Female BAV samples showed a trend for a thinner tunica media than male BAV samples ($p=0.06$). Furthermore, female TAV samples showed to have a highly significantly thicker intimal layer compared to the control ($p=0.000$) as well as compared to male TAV samples ($p=0.008$).

Conclusions: The observed intima hyperplasia of female TAV samples might indicate an involvement of atherosclerosis in female TAA development contradictory to the current opinion that atherosclerosis and inflammation is a dominant factor in abdominal AA but not in TAA pathophysiology. Additional histological analyses are needed to perform an atherosclerosis grading for further assessment.

Postersitzung 3 – Bildgebung 1

3-1

Left atrial appendage morphology predicts cardio-embolic stroke due to atrial fibrillation

Agne Adukauskaite[1], Fabian Barbieri[1], Thomas Senoner[1], Fabian Plank[1], Michael Knoflach[1], Christian Boehme[1], Florian Hintringer[1], Silvana Mueller[1], Gudrun Feuchtner[1], Wolfgang Dichtl[1]

[1]Medical University of Innsbruck, Innsbruck, Austria

Background: In atrial fibrillation (AF) population initiation of anticoagulation therapy for primary stroke prevention might be challenging, therefore we are looking for new markers in stroke risk stratification. Since left atrial appendage (LAA) accounts for 98% of the thrombus sources in non-valvular AF, we aimed to investigate new LAA morphological parameters and their association with cardio-embolic (CE) stroke.

Methods: Based on cardiology indications a cardiac computed tomography angiography (CTA) was performed in 158 patients (56 CE and 102 controls (age median 65 (54–73), 48,7% females)), matched for sex and BMI, and analysed retrospectively. LAA morphology was classified into 5 types: Cactus, Cauliflower, Chicken-wing, Windsock and the new "Seahorse", having a distinctive "Z" shape of a 1 dominant lobe with 2 obvious bends: one being a sharp LAA tip angulation of ≤90 ^{0} and

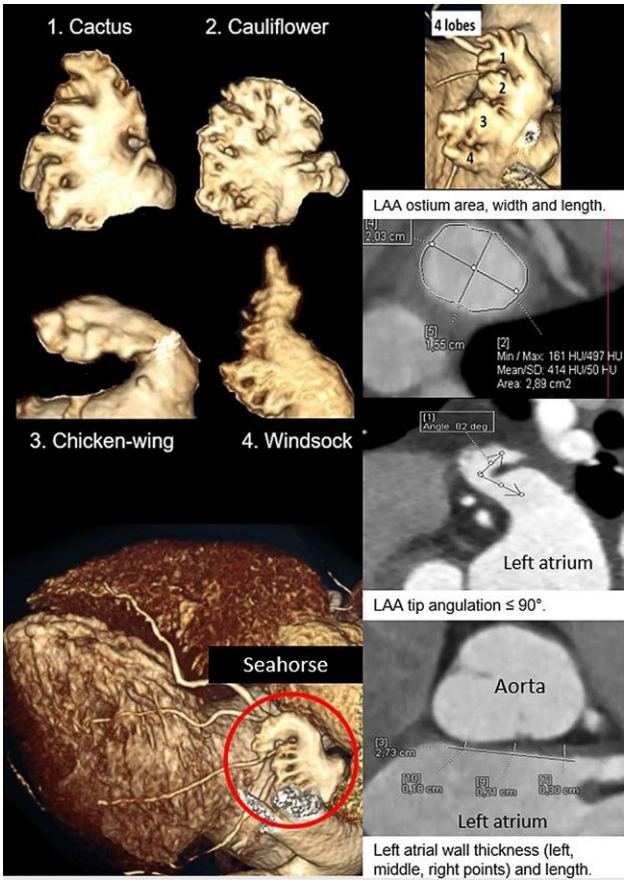


Fig. 1 | 3-1

Table 1|3-1 Left atrial appendage in cardio-embolic stroke versus non-stroke patients

Parameter	CE stroke ($n=51$) + TIA ($n=5$), $n=56$	Non-stroke, $n=102$	p value
Windsock (%)	17 (30,4)	11 (10,8)	0,002
Seahorse (%)	9 (16,1)	31 (30,4)	0,048
Lobe number	3 (2–4)	2 (2–3)	0,020
LAA ostium area (cm²)	4,73 (3,37–6,51)	2,895 (2,455–3,775)	0,000
LAWT in the middle part (mm)	2,3 (1,7–2,9)	1,5 (1,2–2,4)	0,002
Resultsgiveninmedian±IQR.CE-cardio-embolicstroke.			

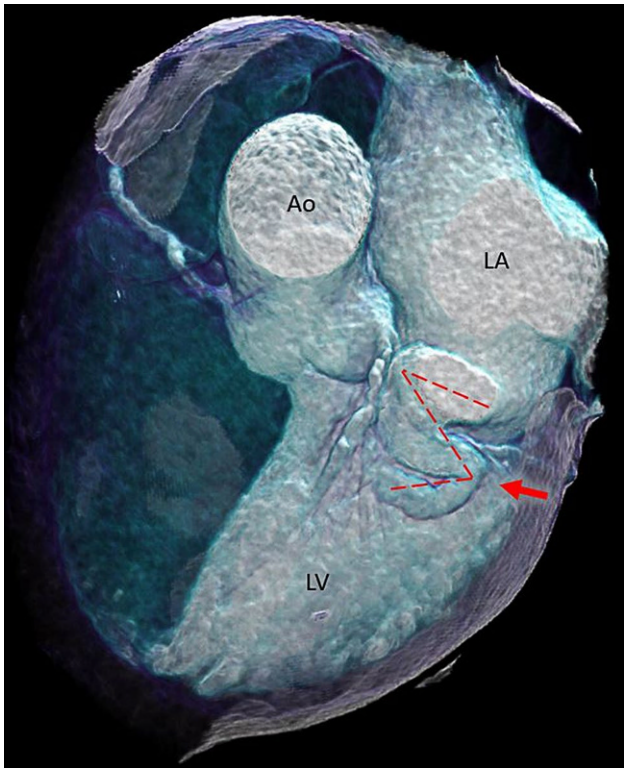


Fig. 1|3-2 A seahorse LAA type with a sharp LAA tip angulation (<90°, red arrow) in CTA 3D-reconstruction

the second one appearing in the body of the dominant lobe and having the opposite bending angle as the tip angulation. Further measurements included: LAA tip angulation (≤90 °, 91–110 °, >110 °), LAA lobe number, LAA ostium size (length, width, area) and angulation, left atrium wall thickness (LAWT).

Results: Predictors for CE stroke/TIA on multivariable analysis after adjusting for age and hypertension are: Windsock LAA (OR 5.18; CI: 1.52–17.64, $p=0.008$), greater lobe number (OR 1.44; CI:1.03–2.0, $p=0.034$), larger LAA ostium area (OR 1.95; CI: 1.42–2.68, $p<0.001$), greater LAWT in the middle part (OR 1.48; CI: 0.99–2.22, $p=0.055$), hence appear as "high-risk" parameters. A greater degree of LAA tip angulation (>110 °, $p=0.004$), LAA ostium width ($p<0.001$) and length ($p<0.001$) are also associated with CE stroke. On the contrary, a newly proposed Seahorse type shows a borderline significance of being rather protective (OR 0.48; 0.19–1.26, $p=0.048$).

Conclusions: In case a CTA is already available, these "high-risk" LAA morphological parameters could eventually provide some additional information evaluating a thromboembolic risk in decision making, whether or not an anticoagulation therapy for primary stroke prevention in AF patients is indicated.

3-2

Does a distinctive left atrial appendage morphology protect females from cryptogenic stroke?

Agne Adukauskaite, Fabian Barbieri, Thomas Senoner, Fabian Plank, Michael Knoflach, Christian Boehme, Florian Hintringer, Silvana Mueller, Gudrun Feuchtner, Wolfgang Dichtl

Medical University of Innsbruck, Innsbruck, Austria

Background: Background Stroke causes a high burden of morbidity and mortality worldwide. Approximately 30% of stroke cases remain cryptogenic (CS), of which one third is due to occult atrial fibrillation (AF) with left atrial appendage (LAA) being the most frequent thrombus source. Our study (data currently in press) already showed an association between CS and LAA morphology (a chicken-wing type, a greater lobe number, a larger and less bent LAA ostium and a thicker LA wall, whereas a sharp LAA tip angulation (≤90°) was protective). Furthermore, we aimed to investigate, if these "high-risk" LAA parameters are equally distributed between males and females, since it is known, that males have a higher incidence of both, AF and CS.

Methods: A total of 82 CS patients who underwent a cardiac computed tomography angiography (CTA) based on cardiac indications were examined retrospectively. The sex-related prevalence of the following LAA morphological parameters was compared:

1. 5 LAA shapes: windsock, chicken-wing, cauliflower, cactus and a novel 5th type – the „seahorse" with a distinctive tip angulation of ≤90° and 2 bends (Z-shape, Fig. 1).
2. Number of LAA lobes.
3. LAA ostium length and angulation.
4. Left atrial anterior wall thickness (LAWT) in the middle point and the mean of the three points (left, middle, right).
5. LAA tip angulation ≤90°.

Results: Table 1 shows no significant clinical difference between males and females in the CS group. Table 2 presents the sex-related differences in LAA morphology.

Table 1|3-2 Clinical characteristics of males vs. females in CS group

	Males ($n=61$, 74.4%)	Females ($n=21$, 25.6%)	p value
Age, y *	66.0 (57–73)	68.0 (55.5–72.5)	0.857
BMI, kg/m²	25.8 (24.1–28.7)	24.9 (20.8–27.7)	0.320
CHA2DS2-VASc score	2 (1–3)	3 (2–4)	0.390
Atrial fibrillation	0	0	–
Hypertension	51 (83.6%)	17 (81.0%)	0.780
Diabetes mellitus, type 2	12 (19.7%)	4 (19%)	0.950
Hyperlipidaemia	53 (86.9%)	15 (71.4%)	0.104
Obesity	10 (16.4%)	3 (14.3%)	0.820

Values are given in median ± IQR.
BMI – body-mass index, obesity (BMI ≥30 kg/m²), y – years.

Table 2|3-2 Left atrial morphology (LAA) parameters in cryptogenic stroke group ($n=82$, males vs. females)

LAA parameter	Males ($n=61$, 74.4%)	Females ($n=21$, 25.6%)	p value
Cactus	10 (16.4%)	3 (14.3%)	0.112
Cauliflower	20 (32.8%)	1 (4.8%)	
Chicken-wing	13 (21.3%)	8 (38.1%)	
Windsock	5 (8.2%)	3 (14.3%)	
Seahorse	13 (21.3%)	6 (28.6)	
LAA tip angulation ≤90°	**10 (16.4%)**	**8 (38.1%)**	**0.042**
Lobe number	**4 (3–4.5)**	**3 (2–4)**	**0.051**
LAA ostium length (mm)	24.05 (20.43–27.23)	21.9 (20.05–27.1)	0.644
LAA ostium angulation (°)	132.0 (109.5–140.0)	126.0 (93.5–140.05)	0.476
LAWT middle (mm)	2.4 (2.0–3.2)	2.3 (1.9–3.05)	0.573
LAWT mean (mm)	2.53 (2.27–3.13)	2.3 (2.07–2.9)	0.080

Values are given in median ± IQR.
LAA – left atrial appendage, LAWT – left atrial wall thickness.

Conclusions: The LAA tip angulation ≤90° is protective against cryptogenic stroke (data of our study currently in press) and is significantly more prevalent among females, which is also consistent with the data that females suffer from CS less often than males. Furthermore, males have a greater lobe number (borderline significance), which also proved to be independently associated with CS. These findings hypothetically offer a possible contributing pathophysiological explanation of sex-related differences in CS prevalence, although the causality needs to be proven by further prospective studies.

3-3

Transradialer Zugang bei elektiver Koronarangiographie: Duplexsonographie und Outcome im Vergleich von Kompressionssystemen

Doris Langegger[1], Nikolas Linasi[2], Andreas Valentin[2], Hubert Wallner[2], André Ewers[3]

[1]Institut für Pflegewissenschaft und -praxis, Kardinal Schwarzenberg Klinikum, Paracelsus Medizinische Privatuniversität, Schwarzach/Salzburg, Österreich
[2]Kardinal Schwarzenberg Klinikum, Schwarzach, Österreich
[3]Institut für Pflegewissenschaft und -praxis, Paracelsus Medizinische Privatuniversität, Salzburg, Österreich

Grundlagen: Der überwiegende und zunehmende Einsatz des transradialen Zugangs bei Koronarangiographien setzt präinterventionell die Abklärung einer potentiellen Kontraindikation und postinterventionell eine suffiziente und sichere radiale Kompression voraus. Die Duplexsonographie ist zur Bestimmung der Blutstromgeschwindigkeit in der Arteria radialis beziehungsweise der Diagnose einer, häufig asymptomatisch verlaufenden, radialen Okklusion geeignet. In der vorliegenden Studie wurden grundlegend zwei radiale Kompressionssysteme (TR-Band® und Seal One®) bei elektiven Eingriffen hinsichtlich klinischer und Patient Reported Outcomes (PROs) verglichen. Die Ergebnisse der prä- und postinterventionellen Duplexsonographie werden im Folgenden dargestellt.

Methodik: In der prospektiven, randomisierten und kontrollierten Querschnittstudie wurden die Daten innerhalb eines dreimonatigen Zeitraumes erhoben. Primär konnten alle konsekutiven PatientInnen mit elektiven transradialen Koronarangiographien teilnehmen ($n=168$). Nach der Selektion, mit definierten Ein- und Ausschlusskriterien, und infolge einer computergestützten Randomisierung teilte sich die Stichprobe ($n=135$) wie folgt auf: Die Interventionsgruppe inkludierte 68 PatientInnen (50,4 %) mit TR-Band®, die Kontrollgruppe 67 PatientInnen (49,6 %) mit Seal One®. Die Duplexsonographie wurde präinterventionell sowie vor Klinikentlassung durchgeführt. Hierzu erfolgte die Datenauswertung deskriptiv mit SPSS Version 24.0.

Ergebnisse: Anhand der Duplexsonographie wurden vier PatientInnen (2,4 % von $n=168$) mit einer Kontraindikation für einen transradialen Zugang detektiert. Bei drei PatientInnen wurde eine signifikante Stenose der Arteria subclavia diagnostiziert. In einem Fall lag ein asymptomatischer Verschluss der Arteria ulnaris vor. Die durchschnittlichen präinterventionellen Ausgangswerte der Stichprobe ($n=135$), zu Diameter und Blutstromgeschwindigkeit der Arteria radialis, waren in beiden Gruppen ähnlich (TR-Band®: 2,25 ± 0,35 mm, 56,25 ± 13,45 cm/s; Seal One®: 2,29 ± 0,41 mm, 55,27 ± 12,91 cm/s). Die postinterventionellen Messungen von PatientInnen mit TR-Band® (2,46 ± 0,36 mm, 54,50 ± 17,75 cm/s) und Seal One® (2,49 ± 0,32 mm, 54,40 ± 16,12 cm/s) zeigten ebenso annähernd übereinstimmende Mittelwerte. Postinterventionell wurden in der Gruppe mit TR-Band® zwei Fälle mit radialer Okklusion (2,9 %) und in der Gruppe mit Seal One® ein Verschluss (1,5 %) diagnostiziert.

Schlussfolgerungen: Die Studienergebnisse verdeutlichen die Relevanz der Duplexsonographie in der Detektion einer präinterventionellen Kontraindikation für eine transradiale Koronarangiographie als auch einer postinterventionellen Okklusion. Im Vergleich, zu vorbestehenden Studienergebnissen in der Literatur, lag die Inzidenz an radialen Verschlüssen im unteren Bereich. Da klinikintern vor Studienbeginn bevorzugt das Seal One® verwendet wurde, könnte ein Verzerrungseffekt aufgrund unterschiedlicher Routinen entstanden sein. Hieraus ergibt sich ein weiterer vergleichender Forschungsansatz mit einer Institution, in welcher vorrangig das TR-Band® verwendet wird.

3-4

Apical sparing in patients without cardiac amyloidosis

Christina Binder[1], Franz Duca[1], Christopher Mann[1], Thomas Binder[1], René Rettl[1], Stefan Aschauer[1], Luciana Camuz Ligios[1], Fabian Dusik[1], Christophe Capelle[1], Christian Hengstenberg[1], Diana Bonderman[1]

[1]Medical University of Vienna, Vienna, Austria

Background: Apical sparing describes a reduced longitudinal strain in the basal segments and preserved or supranormal longitudinal strain in the apical segments of the left ventricular (LV) myocardium. This pattern has been described as a typical finding in patients with cardiac amyloidosis (CA) and restrictive cardiomyopathy. However, apical sparing is not a quantitative parameter and is fairly subjective to the echocardiographer's

judgement. It is not known, if a certain degree of apical sparing is also present in patients with only mild LV hypertrophy and diastolic dysfunction such as it is present in heart failure with preserved ejection fraction (HFpEF).

Methods: Patients with cardiac transthyretin and light chain amyloidosis and patients with HFpEF were included in a clinical registry at our outpatient clinic. CA was diagnosed according to current guidelines. All patients underwent a comprehensive transthoracic echocardiography (TTE) exam at the time of study inclusion. The TTE protocol included standard and speckle-tracking imaging to assess the presence of apical sparing as well as the basal to apical strain gradient. Patients with known coronary artery disease were excluded.

Results: In total 115 patients were included in this study. Of these, 87 (75.7%) were diagnosed with CA and 28 (24.3%) with HFpEF. Not surprisingly, apical sparing was found in a majority (86.2%) of patients with CA, however mild forms of this phenomenon were also present in 67.9% of patients with HFpEF ($p = 0.029$, Fig. 1). Median basal longitudinal strain was significantly more impaired in patients with CA ($p < 0.001$) but there was no difference between longitudinal strain in the apical segments when comparing CA to HFpEF ($p = 0.443$). This resulted in a higher median apical to basal strain gradient in patients with CA (2.3 (IQR 1.7–3.83) versus 1.13 (IQR 1.5–1.8), $p < 0.001$).

Conclusions: Mild forms of apical sparing can be found in patients without CA. Gradual reduction in strain from base to apex could be an unspecific pathophysiologic mechanism which is remarkably pronounced in patients with CA.

3-5

Left atrial phasic function in heart failure with preserved ejection fraction: cardiac magnetic resonance feature tracking, invasive hemodynamics and outcome

Robert Schönbauer[1], Andreas Kammerlander[2], Franz Duca[2], Stefan Aschauer[2], Christina Binder[2], Caroline Zotter-Tufaro[2], Christian Nitsche[2], Lukas Fiedler[1], Franz Xaver Roithinger[1], Christian Loewe[2], Christian Hengstenberg[2], Diana Bonderman[2], Julia Mascherbauer[2]

[1]Landesklinikum Wiener Neustadt, Wiener Neustadt, Austria
[2]Medical University of Vienna, Vienna, Austria

Background: Knowledge about the correlation of phasic left atrial (LA) function with adverse events and its coupling to the left heart and to the pulmonary circulation in heart failure with preserved ejection fraction (HFpEF) is limited.

Methods: 188 HFpEF patients were prospectively enrolled and underwent baseline clinical assessment, cardiac magnetic resonance imaging (CMR) and invasive hemodynamic assessment. Coronary artery disease was ruled out by coronary angiography. 92 patients were in atrial fibrillation (AF), 96 in sinus rhythm. LA size and function were assessed by CMR including LA strain imaging by myocardial feature tracking (Fig. 1a & b).

Results: Patients in AF had more pronounced dilatation of all phasic LA volumes and reduction of all phasic LA functions when compared to sinus rhythm (each $p < 0.001$ respectively). After 31 (9–57) months 66 patients reached the combined endpoint defined as combination from hospitalization due to heart failure and cardiovascular death. In AF no atrial functional or volume parameter was correlated to outcome. In contrast in sinus rhythm several phasic LA volume and functional parameters were associated with outcome. After multivariate cox regression analysis only reduced total LA ejection fraction and conduit strain rate were still predictive for worse outcome

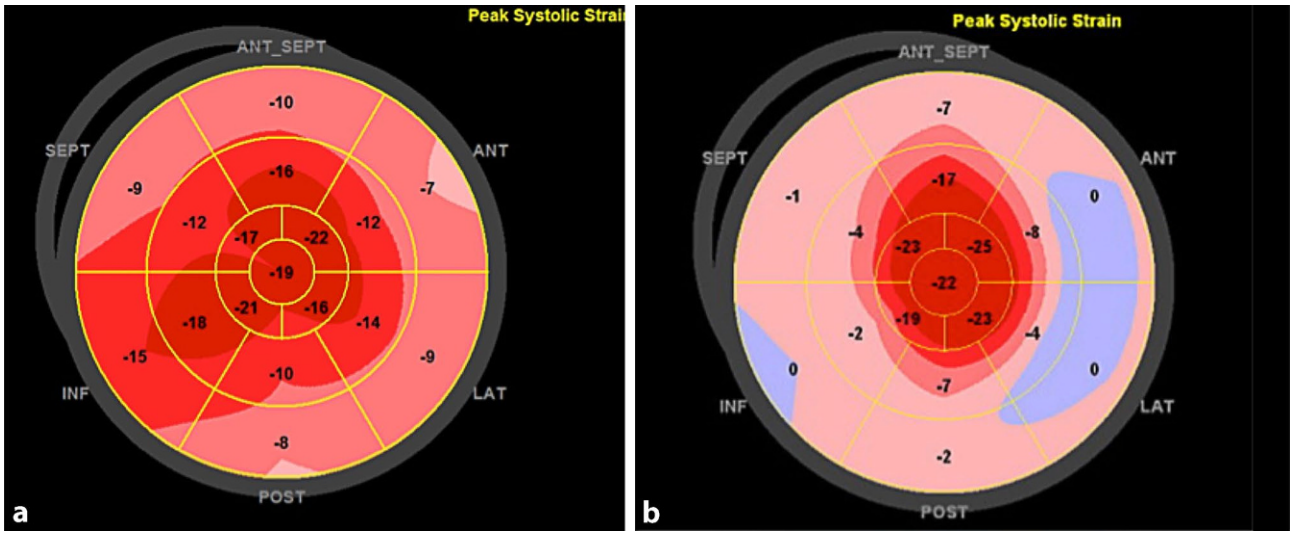


Fig. 1|3-4 Bulls-eye display of segmental left ventricular longitudinal strain in a patient with a) heart failure with preserved ejection fraction and b) cardiac amyloidosis. Panel A shows a subtle form of apical sparing in a patient with heart failure and preserved ejection fraction and mild hypertrophy with reduced strain in the basal segments compared to the apical segments. Panel B shows the typical pattern of pronounced apical sparing in a patient with light chain amyloidosis. The strain of the basal wall segments is severly reduced, while apical strain is preserved

Table 1|3-5 Univariate correlations with phasic left atrial volumetric and functional parameters

	6MWD, m		MOLLI-ECV, %		LVEDP, mmHg		sPAP, mmHg		PVR, dyn-s-cm^{-5}	
	ρ	*p*-value	ρ	*p*-value	ρ	*p*-value	ρ	p-value	ρ	*p*-value
Sinus Rhythm										
LA conduit function										
EF, %	**0.24**	**0.032**	0.21	0.107	–0.02	0.910	**–0.28**	**0.013**	**–0.40**	**0.001**
Strain, -%	**0.34**	**0.006**	0.21	0.115	–0.22	0.147	**–0.43**	**0.001**	**–0.43**	**0.001**
Strain Rate, -%/sec	**0.43**	**<0.001**	0.22	0.130	–0.25	0.095	**–0.44**	**<0.001**	**–0.41**	**0.002**
LA booster pump function										
EF, %	0.03	0.776	–0.21	0.103	0.01	0.967	0.02	0.859	–0.10	0.441
Strain, -%	0.18	0.155	–0.08	0.586	–0.08	0.582	–0.12	0.381	–0.20	0.142
Strain Rate, -%/sec	**0.28**	**0.023**	–0.12	0.395	0.03	0.866	–0.09	0.494	–0.20	0.142
LA total EF, %	0.17	0.125	–0.14	0.264	–0.11	0.396	–0.20	0.080	**–0.27**	**0.025**
LA reservoir function										
Strain, %	**0.35**	**0.004**	0.10	0.476	–0.22	0.144	**–0.35**	**0.005**	**–0.41**	**0.002**
Strain Rate, %/sec	**0.27**	**0.028**	0.19	0.187	–0.08	0.600	**–0.29**	**0.025**	**–0.32**	**0.016**
LA volumetric measurements										
VI max.,ml/m^2	<0.01	0.984	0.16	0.189	0.10	0.424	0.09	0.430	–0.07	0.587
VI pre A-wave, ml/m^2	–0.09	0.414	0.09	0.488	0.11	0.417	0.17	0.143	0.06	0.614
VI min.ml/m^2	–0.10	0.367	0.20	0.103	0.13	0.323	0.192	0.086	0.10	0.414
Atrial Fibrillation										
LA conduit function										
Strain Rate, -%/sec	0.02	0.858	–0.04	0.806	–0.19	0.237	–0.05	0.711	–0.09	0.518
LA total EF, %	0.08	0.493	0.05	0.688	0.18	0.164	–0.14	0.204	–0.06	0.582
LA reservoir function										
Strain, %	–0.05	0.737	–0.22	0.175	–0.02	0.892	0.03	0.837	–0.12	0.370
Strain Rate, %/sec	0.08	0.556	–0.18	0.273	0.01	0.949	0.05	0.710	–0.12	0.360
LA volumetric measurements										
VI max., ml/m^2	0.01	0.907	**0.26**	**0.039**	–0.07	0.600	0.01	0.908	–0.12	0.262
VI min., ml/m^2	–0.01	0.987	0.19	0.142	–0.12	0.351	0.05	0.644	–0.08	0.495

6MWD = six minute walking distance; MOLLI-ECV = modified Look-Locker inversion recovery sequence derived extracellular volume; LVEDP = left ventricular end diastolic pressure; sPAP = systolic pulmonary artery pressure; PVR = pulmonary vascular resistance; ρ = Spearman correlation; LA = left atrial; EF = ejection fraction; VI = volume index; max. = maximal; min. = minimal;

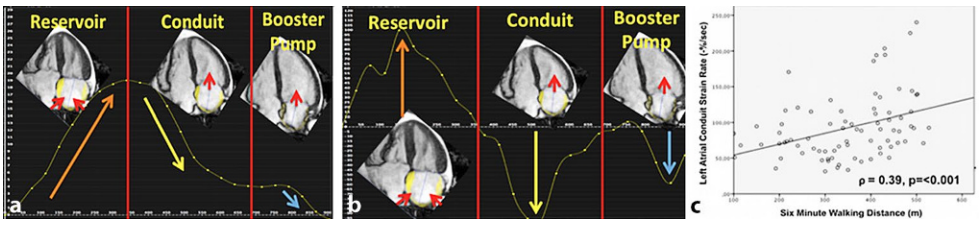


Fig. 1|3-5

($p = 0.031$ and < 0.001 respectively). After adjustment for known risk factors in HFpEF like age, six minute walking distance (6MWD), systolic pulmonary artery pressure (sPAP) and right ventricular ejection fraction as derived by CMR only impaired LA conduit strain rate remained predicitve for cardiovascular events ($p = 0.001$). In contrast to LA booster pump function LA conduit function parameters were significantly correlated to reduced 6MWD (Fig. 1c) and coupled backwards to pulmonary vasculature via correlation to sPAP and pulmonary vasculare resistance (PVR) but without coupling to CMR derived elevated LV extracellular volume and left ventricular end diastolic pressure (Table 1).

Conclusions: Total LA ejection fraction plays a key role in the prognosis of HFpEF. This effect seems to be mainly related to its LA conduit function but not to LA booster pump function. LA conduit function correlates to impaired 6MWD, sPAP and PVR.

3-6

Globaler longitudinaler Strain – ein hilfreicher Marker zur frühen Detektion der myokardialen Organmanifestation bei Morbus Fabry

Constantin Gatterer, Philipp Bartko, Matthias Schneider, Gere Sunder-Plassmann, Beatrix Buschenreithner, Thomas Binder, Christian Hengstenberg, Gerald Mundigler, Senta Graf

Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin II, Medizinische Universität Wien, Wien, Österreich

Grundlagen: Morbus Fabry ist eine der häufigsten lysosomalen Speicherkrankheiten, die durch eine x-chromosomale Mutation zu einem Mangel an Alpha-Galactosidase A führt, wodurch Sphingolipide, insbesondere Globotriaosylceramid (GB3), vermindert abgebaut und sich in weiterer Folge in allen Lysosom-enthaltenden Zellen einlagern. Die kardiale Beteiligung äußert sich in einer konzentrischen linksventrikulären Hypertrophie, welche in weiterer Folge zu myokardialer Fibrose mit Reduktion der systolischen Linksventrikelfunktion führen kann. Neben der Bestimmung der systolischen Linksventrikelfunktion durch Berechnung der Auswurffraktion hat sich als sensitiverer und im klinischen Einsatz wertvoller Marker die Bestimmung des globalen longitudinalen Strains (GLS) in der Echokardiographie etabliert, wie am Beispiel der Aortenstenose gezeigt werden konnte. Da auch bei M. Fabry die frühe Detektion von Organschäden für die Therapiestrategie maßgeblich ist, war die Untersuchung des GLS im Verlauf Ziel der vorliegenden Studie.

Methodik: 30 Patienten mit M. Fabry wurden über einen Beobachtungszeitraum von 4 Jahren mittels Echokardiographie inklusive der Bestimmung des GLS untersucht.

Ergebnisse: Bereits in der Baseline Untersuchung zeigte sich bei den 30 Patienten (20–69 Jahre, 53 % Frauen, 47 % Männer) ein leicht erniedrigter GLS von durchschnittlich –17,22 %. Im Follow-up nach durchschnittlich 39 Monaten (min. = 8 Monate, max. = 78 Monate) zeigte sich eine signifikante Reduktion des GLS auf durchschnittlich –15,51 % ($p = 0{,}009$). Es konnte kein Unterschied zwischen Patienten unter Enzymersatztherapie und therapienaiven Patienten gefunden werden. Auch zwischen Männern und Frauen unterschied sich die Reduktion des GLS nicht.

Schlussfolgerungen: Die Bestimmung des GLS ist ein sensitiver echokardiographischer Parameter zur Bestimmung der Linksventrikelfunktion, der eine frühzeitige Detektion einer myokardialen Beteiligung im Rahmen des M. Fabry ermöglicht. Dies ist für die Festlegung der Therapiestrategie hilfreich. Der Einfluss der Therapie auf den GLS ist allerdings aus den vorliegenden Daten noch nicht eindeutig erkennbar.

3-7

Native T1 time of right ventricular insertion points by CMR: relation with invasive hemodynamics and outcome in HFPEF

Christian Nitsche[1], Andreas Kammerlander[1], Franz Duca[1], Christina Binder[1], Stefan Aschauer[1], Matthias Koschutnik[1], Dietrich Beitzke[2], Christian Loewe[2], Christian Hengstenberg[1], Diana Bonderman[1], Julia Mascherbauer[1]

[1]Division of Cardiologie, Department of Internal Medicine II, Medical University of Vienna – AKH, Vienna, Austria
[2]Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria

Background: Increased afterload to the right ventricle (RV) has been shown to induce myocardial fibrosis at the RV inser-

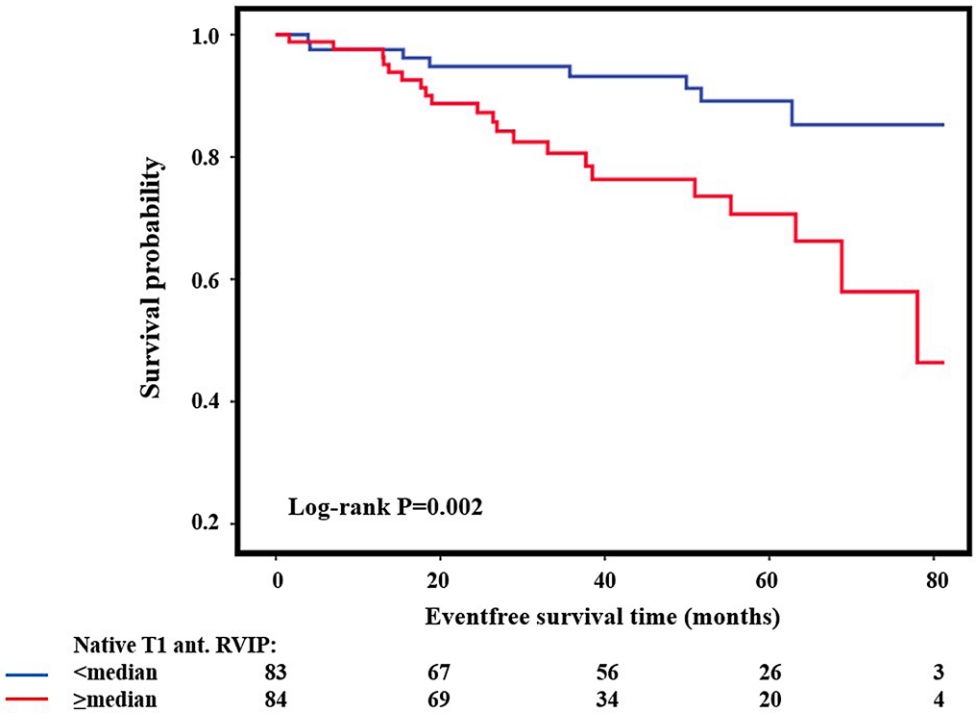


Fig. 1|3-7 Kaplan Meier plots assessing the prognostic significance of anterior right ventricular insertion point T1 times

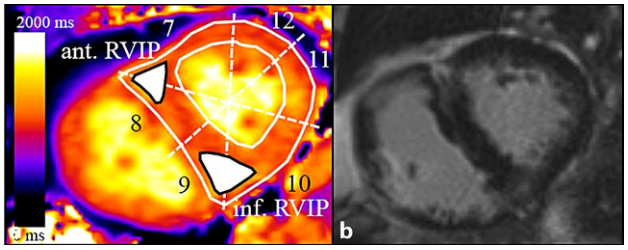


Fig. 2|3-7 Assessment of right ventricular insertion point T1 times

tion points (RVIPs). Such changes can be discrete but potentially detected by cardiac magnetic resonance (CMR) T1-mapping. Whether RVIP fibrosis is associated with prognosis in heart failure with preserved ejection fraction (HFpEF) is unknown.

Methods: We prospectively investigated 167 consecutive HFpEF patients, a population frequently suffering from post-capillary pulmonary hypertension (PH), who underwent CMR including T1-mapping. 92.8% also underwent right heart catheterization for hemodynamic assessment. Kaplan-Meier analysis, cox regression analysis and Spearman's rank order correlation were applied as statistical methods. The parameter with the strongest discriminative power of each group (clinical, hemodynamic and CMR) by receiver operating curve analysis was selected to enter the multivariate cox model.

Results: Native T1 times were 995 ± 73 ms at the anterior and 1040 ± 90 ms at the inferior RVIP. By Spearman's rank order testing, RVIP T1 times were significantly correlated with pulmonary artery pressure (mean PAP, r = 0.313 and 0.311 for anterior and inferior RVIP, respectively), pulmonary artery wedge pressure (r = 0.301 and 0.251) and right atrial pressure (r = 0.245 and 0.185; p for all < 0.05). During a mean follow-up of 43.2 ± 22.6 months, 30 (18.0%) subjects died. By multivariable Cox regression, NTproBNP [Hazard Ratio (HR) 2.105, 95% confidence interval (CI) 1.332–3.328; $p = 0.001$)], systolic PAP (HR 1.618, 95% CI 1.175–2.230; $p = 0.003$), and native T1 time of the anterior RVIP (HR 1.659, 95% CI 1.125–2.445; $p = 0.011$) were significantly associated with outcome. Also, by Kaplan-Meier analysis, native T1 time of the anterior RVIP had a significant effect on survival (log-rank, $p = 0.002$).

Conclusions: Interstitial expansion of the anterior RVIP as detected by native CMR T1-mapping reflects hemodynamic alterations, and is independently related with prognosis in HFpEF.

Postersitzung 4 – Herzinsuffizienz 1

4-1

Enzymatic RAS profiling of the human failing heart

Henrike Arfsten[1], Noemi Pavo[1], Raphael Wurm[1], Suriya Prausmüller[1], Georg Spinka[1], Georg Goliasch[1], Philipp E Bartko[1], Julia Mascherbauer[1], Marko Poglitsch[2], Andreas Zuckermann[1], Martin Hülsmann[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Attoquant Diagnostics GmbH, Vienna, Austria

Background: Prognosis of patients with heart failure with reduced ejection fraction (HFrEF) remains poor despite recent advances in pharmacologic therapy as the introduction of the angiotensin-receptor neprilysin-inhibitor (ARNI). The Renin-Angiotensin-System (RAS) is dysregulated in heart failure (HF). Research has been focusing on plasma RAS and information on tissue RAS is relatively scarce although assumedly more crucial for myocardial function. We have shown that, among all known angiotensins, only AngII and AngIII levels are detectable in the failing heart. Plasma samples in HFrEF show high AngI and AngII levels with clearly distinguishable ACE-S (AngII/AngI ratios) for different RAS-inhibitors. Interestingly, AngII and AngIII profiles in the myocardium were comparable for different RAS-inhibitors, i. e. no RAS-blocker, ACE-I, ARB or ARNI. Here

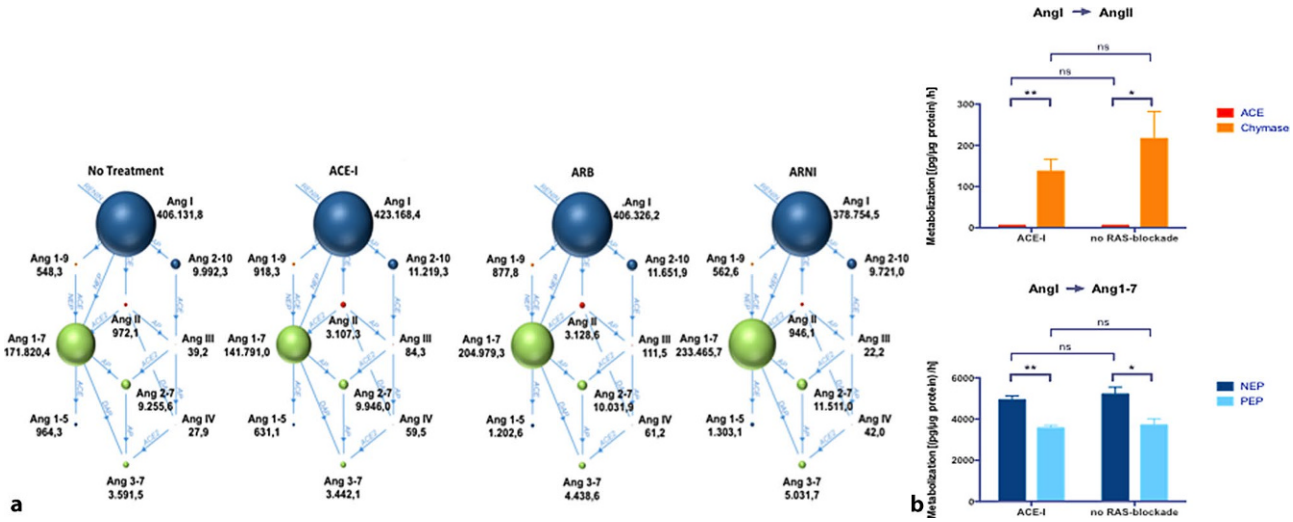


Fig. 1|4-1 Regulation and metabolic activity of myocardial tissue RAS enzymes. **a** Angiotensine peptide levels after AngI supplementation of myocardial tissue homogenates of failing hearts are shown for patients with ACE-I therapy and no RAS·blockade ($n = 3$ each) and **b** metabolic activities of ACE and chymase for the conversion of AngI >AngII and for neprilysin and PEP for the conversion of AngI >Ang1–7 are shown. Enzymatic activities were assessed in experiments using specific inhibitors, i. e. lisinopril for ACE, chymostatin for chymase, thiorphan for NEP and ZPP for PEP, respectively

we aimed to elucidate the metabolic regulation of the tissue RAS enzymes for these four different modalities of RAS-inhibition.

Methods: Enzyme regulation and metabolic activities were investigated in myocardial samples of end-stage HFrEF patients undergoing heart transplantation with a mass-spectrometry based method. Briefly, concentrations of six metabolically linked angiotensin metabolites (AngI, AngII, Ang1-7, AngIII, Ang1-5 and AngIV) were quantified after spiking a tissue homogenate with AngI or AngII and subsequently incubating the sample to visualize ongoing angiotensin metabolism. Additionally metabolic activities of distinct enzymes have been assessed in a similar fashion for the no therapy and ACE-I subgroups. Patients were stratified according to background therapy with RAS-inhibitors and variables were compared between groups by a non-parametrical test.

Results: A total of 30 patients were included ($n=6$ without RAS-blockade, $n=16$ with ACE-I, $n=6$ with ARB and $n=2$ with ARNI). Median age was 55 (IQR 45–63) years and 87% of patients were male. 40% of patients had an ischemic etiology of HF, median NT-proBNP levels were 3498 pg/ml (IQR 1761–8400). Metabolic profiles for AngI and AngII in tissue homogenate were similar for all groups, indicating comparable regulation of tissue RAS enzymes independent from therapy (Fig. 1). The formation of AngII from AngI was mainly chymase dependent with conversion rates of 99.4 (IQR 77.0–254.1) (pg/µg protein)/h for the ACE-I and 141.8 (IQR 67.9–369.2) (pg/µg protein)/h for the no RAS-blockade group, whereas ACE-related generation of AngII was below detection limit. The formation of Ang1-7 from AngI was mediated by both NEP and PEP, however the contribution of NEP was significantly higher [5022 (IQR 5002–5286) (pg/µg protein)/h vs 3555 (IQR 3351–3849) (pg/µg protein)/h, $p=0.005$ for the ACE-I group and 4729 (IQR 4438–6135) (pg/µg protein)/h vs 3601 (IQR 3052–4182) (pg/µg protein)/h, $p=0.012$ for the no RAS-blockade group]. Interestingly, there were no differences in tissue enzymatic activities between ACE-I and no therapy, as already indicated by the metabolic angiotensin profiles.

Conclusions: Enzymatic tissue profiles in end-stage HF seems to be independent of the mode of established RAS-inhibitor therapy. In contrast to plasma, AngII formation of the tissue is mainly chymase dependent, whereas ACE seems to play no significant role. Neprilysin substantially influences the generation of beneficial Ang1-7 from AngI. The impact of NEP inhibition by ARNI on tissue RAS and mechanism of action have to be further investigated.

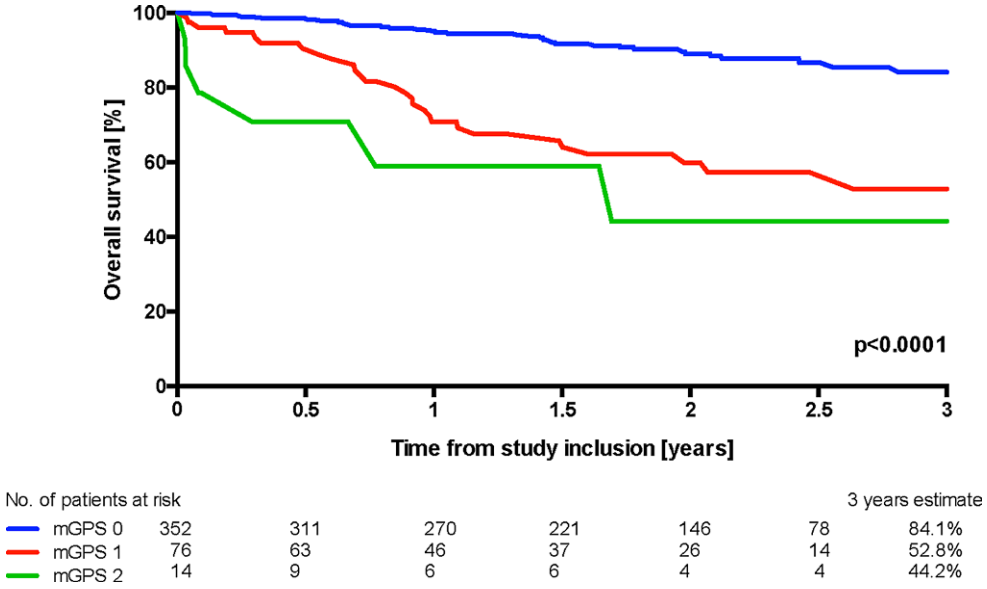


Fig. 1|4-2

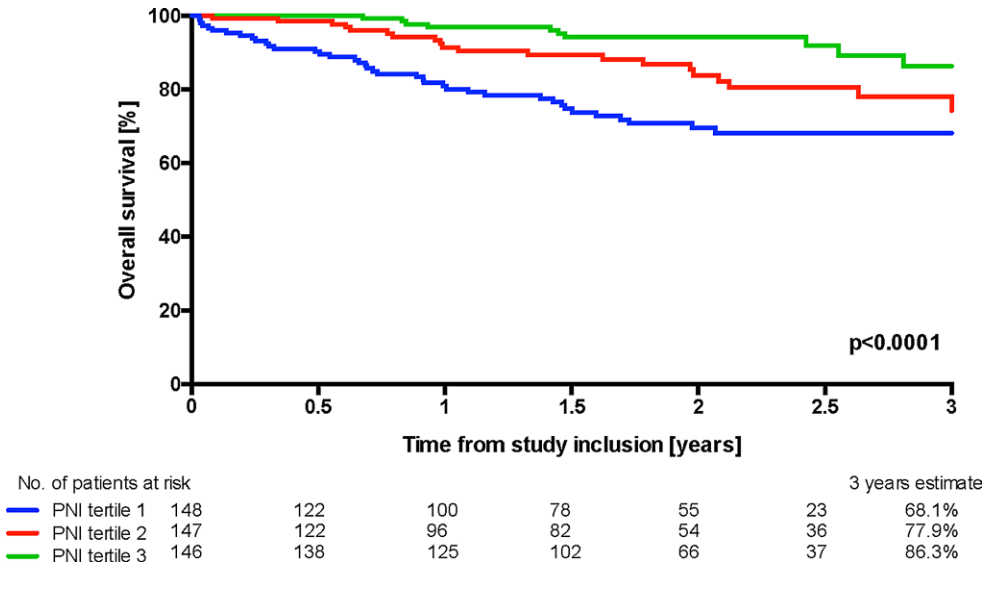


Fig. 2|4-2

4-2

Comparison of inflammation based prognostic scores in patients with stable heart failure with reduced ejection fraction

Henrike Arfsten, Anna Cho, Suriya Prausmüller, Georg Spinka, Johannes Novak, Georg Goliasch, Philipp E Bartko, Noemi Pavo, Martin Hülsmann

Medical University of Vienna, Vienna, Austria

Background: Elevated inflammatory markers and malnutrition are characteristic for heart failure with reduced ejection fraction (HFrEF) correlating with disease severity and prognosis. Nutritional decline is closely linked to inflammation. Evidence emerges that heart failure can be triggered by inflammation directly, meaning that the progression of HF is a function of individual inflammatory host response. We aimed to investigate and compare the impact of well-established inflammation based scores and inflammation-related nutritional scores on survival of stable patients with stable HFrEF.

Methods: Patients with stable HFrEF undergoing routine ambulatory care between January 2011 and November 2017 have been identified from a prospective registry at the Medical University of Vienna. Comorbidities and laboratory data at baseline were assessed. All-cause mortality was defined as the primary study endpoint. The modified Glasgow Prognostic Score (mGPS), the Neutrophil-to-Lymphocyte ratio (NLR), the Monocyte-to-Lymphocyte ratio (MLR), the Platelet-to-Lymphocyte ratio (PLR) as well as the Nutritional Risk Index (NRI) and the Prognostic Nutritional Index (PNI) were calculated. The association of the scores with heart failure severity and impact on overall survival were determined.

Results: Data was complete and analyzed for a total of 443 patients. The median age of the study population was 64 years (IQR 53–72) and 73% of the patients were male. The median body mass index (BMI) was 26.6 kg/m^2 (IQR 23.8–30.2). Median NT-proBNP levels were 2053 pg/ml (IQR 842–4345) with most patients presenting in the NYHA classes II (178, 40%) and III (173, 39%). Patients received well titrated dosages of guideline recommended heart failure therapy. The mGPS was 0 for 352 (80%), 1 for 76 (17%) and 2 for 14 (3%) patients, respectively. All scores correlated with heart failure severity reflected by NT-proBNP [$p<0.001$ for mGPS and r = –0.48, $p<0.001$ for PNI] and NYHA class [$p<0.001$ for mGPS and PNI]. All scores were associated with all-cause mortality in the univariate analysis, however after adjustment for age, gender and kidney function only the mGPS, PLR, NRI and PNI remained significantly associated with outcome. Out of these the ROC were highest for PNI and mGPS [0.674 and 0.652 respectively] and solely these scores remained significantly associated with mortality when NT-proBNP was included in the multivariate model [adj. HR 1.87 (95%CI 1.20–2.91), $p=0.006$ for mGPS and 0.62 (95%CI 0.40–0.96), $p=0.032$ for PNI]. Kaplan Meier analysis confirmed the discriminatory power of mGPS and PNI (Figs. 1 and 2).

Conclusions: Enhanced inflammation and malnutrition are more common in advanced heart failure. Among established inflammation and nutritional scores merely mGPS and PNI are associated with survival in HFrEF patients independently of NT-proBNP. This relationship emphasizes the significance of the individual proinflammatory response on prognosis. This easily available score may help clinicians to identify HFrEF patients with worse prognosis with urgent need for intensified therapy and/or alternate treatment options.

4-3

Adrenomedullin activity as an alternate mechanism of action in ARNI therapy

Henrike Arfsten[1], Georg Goliasch[1], Philipp E. Bartko[1], Anna Cho[1], Johannes Novak[1], Helmuth Haslacher[1], Guido Strunk[2], Joachim Struck[3], Martin Hülsmann[1], Noemi Pavo[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Complexity Research, Vienna, Austria
[3]Sphingotec GmbH, Hennigsdorf, Germany

Background: Background and Aim. Inhibition of neprilysin (NEP) by angiotensin-receptor neprilysin inhibitor (ARNI) therapy increases endogenous levels of natriuretic peptides (NP) in patients with heart failure with reduced ejection fraction (HFrEF). NEP however cleaves a broad spectrum of substrates which equally hold significant implications in HFrEF. This study aimed to explore the response of adrenomedullin, tachykinin and enkephalin systems to the initiation of ARNI therapy.

Methods: 55 patients with stable chronic HFrEF and recent initiation of ARNI therapy according to the heart failure guidelines were prospectively enrolled. Plasma marker were determined at baseline, at short-term (between 1 and 6 months after therapy switch) and at long-term follow-up (FUP) (between 6

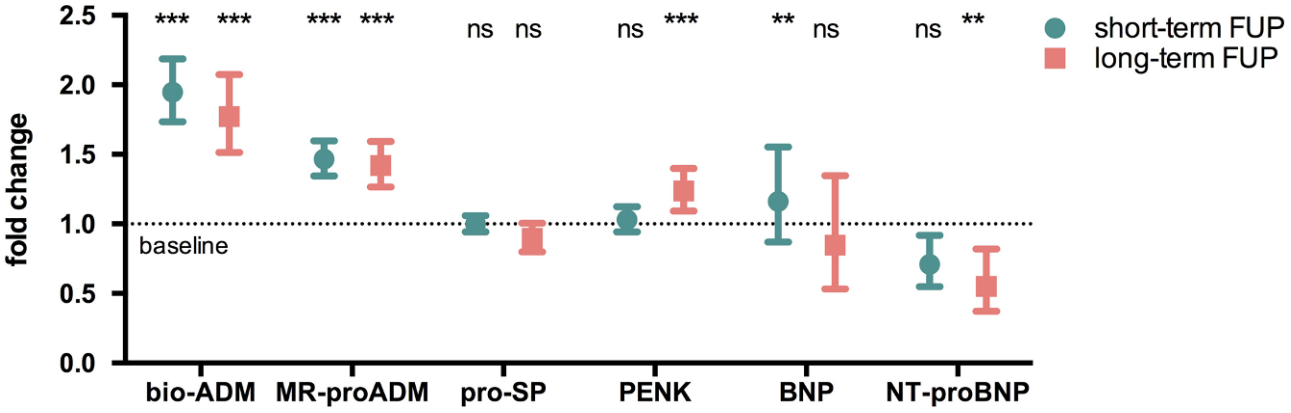


Fig. 1|4-3 Short-term ($n=47$) and long-term changes ($n=31$) in bio-ADM, MR-proADM, pro-SP and PENK after initiation of ARNI therapy

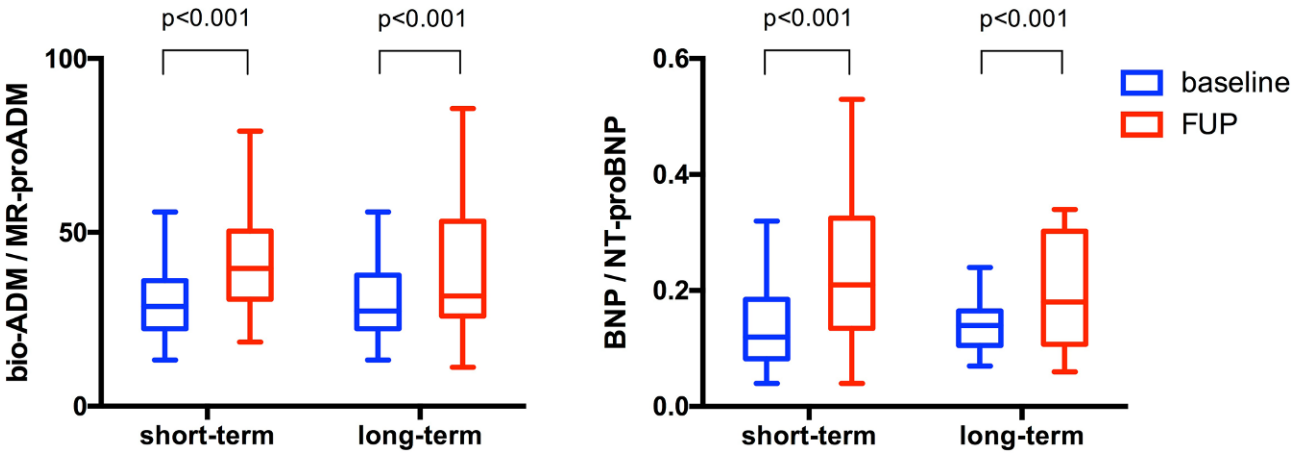


Fig. 2|4-3 Ratios of plasma concentrations of the inactive cleavage product and the biologically active peptide for BNP and ADM, respectively

and 18 months after therapy switch but closest to a follow-up time of 12 months if more than one sample was accessible). NT-proBNP was measured with the Elecsys System by Roche Diagnostics (Mannheim Germany). BNP was measured by the Siemens Advia Centaur assay. Bio-adrenomedullin (Bio-ADM) was measured using a novel chemiluminescence immunoassay (sphingotest® bio-ADM®, Sphingotec GmbH, Hennigsdorf, Germany). Mid-regional proAdrenomedullin (MR-proADM) was measured using the BRAHMS MR-proADM KRYPTOR assay (BRAHMS GmbH, Hennigsdorf, Germany). Stable pro-substance P (pro-SP) and proenkephalin A 119–159 (PENK) were determined by an immunoassay from Sphingotec GmbH, Hennigsdorf, Germany.

Results: Short-term ($n=47$) and long-term ($n=31$) FUP samples were obtained at a median of 104 (IQR: 57–132) and 350 (IQR: 246–418) days. Bio-ADM and MR-proADM levels were significantly and roboustly increased following ARNI therapy initiation [short-term: 25.4 pg/ml vs 46.0 pg/ml, $p<0.001$ for bio-ADM; 0.97 nmol/l vs. 1.28 nmol/l, $p<0.001$ for MR-proADM; long-term: 25.8 pg/ml vs. 52.0 pg/ml, $p<0.001$ for bio-ADM; 1.00 nmol/l vs. 1.27 nmol/l, $p<0.001$ for MR-proADM]. Plasma pro-SP levels remained comparable during FUP and concentrations of circulating PENK were elevated at long-term FUP [69.3 pmol/l (IQR 56.1–95.7) vs 88.3 pmol/l (IQR 61.2–121.4), $p<0.001$]. BNP levels were higher at short-term FUP [225 ng/l (IQR:107–453) vs 262 ng/l (IQR:96–664) ng/l, $p=0.006$] and NT-proBNP levels were lower at long-term FUP [1958 ng/l (IQR:1462–3508) vs 1740 ng/l (IQR:662–2690) ng/l, $p=0.007$] (Fig. 1). The proportional increase of bio-ADM exceeded BNP elevation (Fig. 1). The changes of the ratios BNP/NT-proBNP and bio-ADM/MR-proADM are displayed in Fig. 2. Patients with baseline ACE-I and ARB therapy showed similar biomarker patterns ($p>0.05$) indicating a specific effect of NEP inhibition.

Conclusions: The robust increase of MR-proADM and bio-ADM even, exceeding BNP elevation, and augmentation of bioADM/MR-proADM ratio suggest both, an enhanced production and a reduced degradation of the peptide following ARNI administration. Activation of the ADM axis represents a so far unrecognized mechanism of ARNI therapy presumably contributing to its clinical efficacy.

4-4

Sacubitril/valsartan is well tolerated in patients with heart failure and a history of cancer

Maria Klara Frey[1], Emilie Han[1], Henrike Arfsten[1], Noemi Pavo[1], Martin Hülsmann[1], Jutta Bergler-Klein[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Sacubitril/valsartan has been shown to significantly reduce cardiovascular mortality and hospitalisations due to heart failure in patients with reduced ejection fraction when compared to enalapril. Until now, sacubitril/valsartan has not been evaluated in patients with a history of cancer, as these patients were excluded from the pivotal trial, PARADIGM-HF. The aim of the current study was to assess tolerability of sacubitril/valsartan in patients with a history of cancer.

Methods: We retrospectively enrolled all patients at our heart failure out-patient unit who fulfilled the indication criteria to receive sacubitril/valsartan and had a history of cancer. Fifteen patients receiving sacubitril/valsartan had a diagnosis of histologically confirmed cancer: 26.7% breast cancer ($n=4$), 13.3% osteosarcoma ($n=2$), 13.3% colorectal cancer ($n=2$), 13.3% renal cell carcinoma ($n=2$), 6.7% non-Hodgkin lymphoma ($n=1$), 6.7% lung cancer ($n=1$), 6.7% prostate cancer ($n=1$), 6.7% bladder carcinoma and 6.7% myeloproliferative syndrome ($n=1$). Surgery due to cancer was performed in 80% of patients ($n=12$), 26.7% previously received chemotherapy ($n=6$) and 40% radiation therapy ($n=4$).

Results: Sacubitril/valsartan was withdrawn in 2 patients (13.3%) because of dizziness and pruritus respectively. After a mean follow-up of 13±8 months, NYHA functional class improved significantly (mean -0.5, $p=0.001$) and NT-proBNP was significantly decreased (mean -1552 pg/ml, $p=0.026$). There was no significant change in creatinine levels (+0.046 mg/dl, $p=0.565$).

Conclusions: In this pilot study we were able to show that sacubitril/valsartan is generally well tolerated in patients with a history of cancer. Patients with cardiotoxicity induced heart failure can be treated and uptitrated with sacubitril/valsartan to usual dosages similarly as in other causes of heart failure. Larger studies are needed to confirm these findings in cancer patients with cardiotoxicity.

4-5

Hemodynamic profiles in patients with cardiac amyloidosis

Franz Duca[1], Amir Snidat[1], Stefan Aschauer[1], René Rettl[1], Christina Binder[1], Hermine Agis[2], Renate Kain[3], Christian Hengstenberg[1], Julia Mascherbauer[1], Diana Bonderman[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Austria
[2]Division of Oncology, Department of Internal Medicine I, Medical University of Vienna, Vienna, Austria
[3]Clinical Institute of Pathology, Medical University of Vienna, Vienna, Austria

Background: Intracardiac filling and pulmonary arterial pressures play a central role in various heart failure entities, as they are strong predictors of outcome. However, their role in patients with cardiac amyloidosis (CA) is less clear. We aimed to characterize hemodynamic profiles of CA patients and assess their association with outcomes.

Methods: The present study was conducted within a prospective, national CA registry. CA was diagnosed in accordance with current recommendations. Consecutive CA patients underwent invasive hemodynamic, clinical, laboratory, and echocardiography assessment, as well cardiac magnetic resonance imaging with T1-mapping. The main outcome measure was a combined endpoint consisting of hospitalization for heart failure or death from cardiovascular causes.

Results: Between 2012 and 2018, 63 CA patients underwent invasive hemodynamic profiling. Of those, 36 had cardiac transthyretin amyloidosis (ATTR) and 25 cardiac light-chain amyloidosis (AL). In two patients amyloid subtyping was not possible. Median age of the study cohort was 74.0 years and the majority were male (61.9%). Almost half of the patients were in New York Heart Association class ≥ III (47.6%) and showed elevated N-terminal prohormone of brain natriuretic peptides (NT-proBNP) with a median of 3222 pg/mL. In comparison to AL, TTR patients were older (75.0 years versus 69.0 years, $p=0.004$), more often male (80.6% versus 40.0%, $p=0.001$), less symptomatic (NYHA class ≥ III: 38.9% versus 64.0%, $p=0.021$), and had lower NT-proBNP values (2324 pg/mL versus 5151 pg/mL, $p=0.004$). Hemodynamic profiling revealed significantly increased intracardiac as well as pulmonary arterial pressures (PAP). On an average, pulmonary artery wedge pressure was 20.0 mmHg, mean PAP (mPAP) was 30.0 mmHg, and mean right

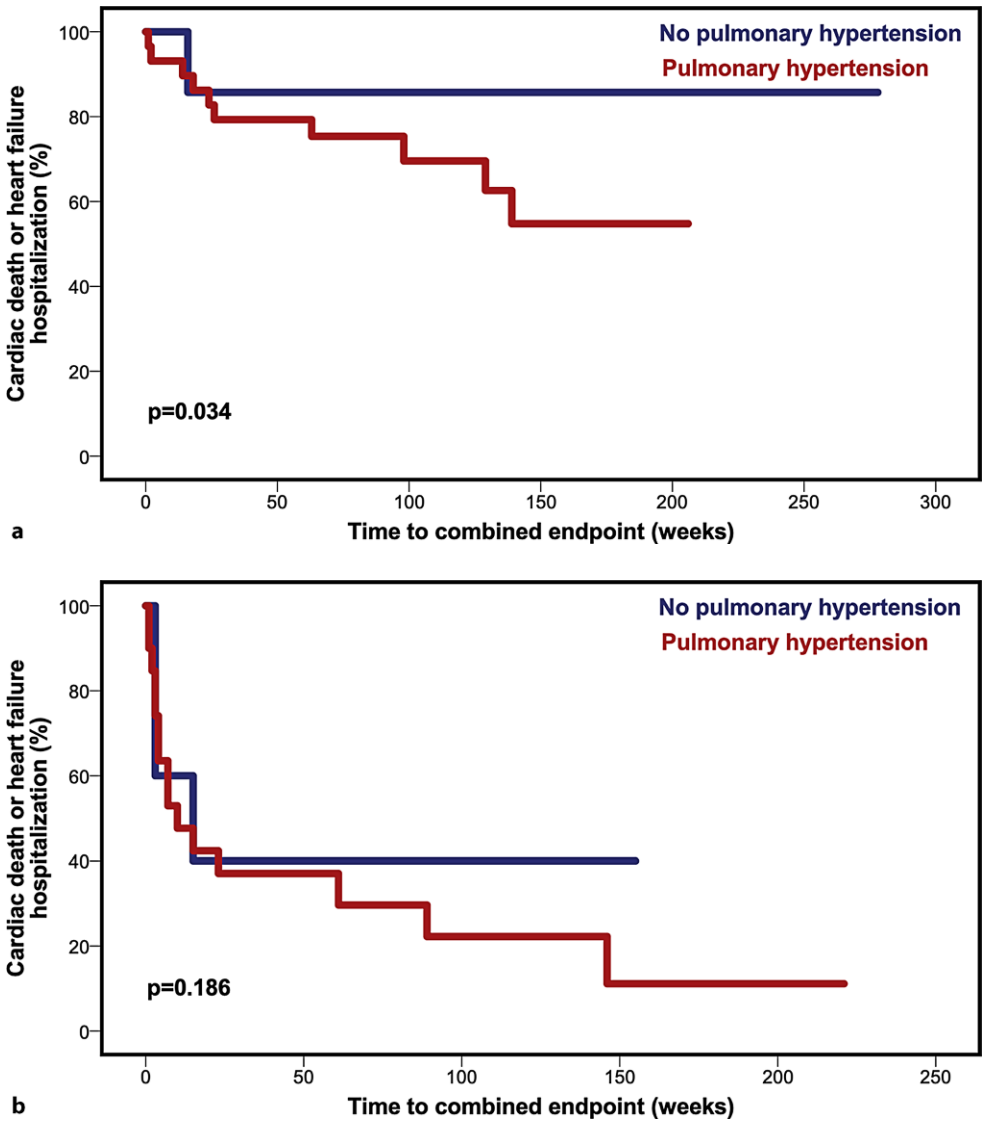


Fig. 1|4-5

atrial pressure was 11.0 mmHg. No differences between ATTR and AL patients could be detected. In ATTR patients, mPAP was significantly associated with outcome [hazard ratio (HR): 1.083, $p=0.034$, Fig. 1A], which was not the case in the AL group (HR: 1.024, $p=0.186$, Fig. 1B). Cardiac output and pulmonary vascular resistance were not associated with outcome. Neither in the ATTR ($p=0.144$; $p=0.063$) nor in AL cohort ($p=0.420$; $p=0.115$).

Conclusions: Despite differences in the severity of symptoms between cardiac AL and cardiac ATTR patients, no differences with regards to hemodynamic profiles could be detected. Furthermore, intracardiac filling and pulmonary arterial pressures seem to be of greater clinical importance in cardiac ATTR as compared to cardiac AL, as these parameters were associated with outcome in the first, but not the latter group.

4-6

Alcohol septal ablation in a patient with hypertrophic obstructive cardiomyopathy due to Anderson-Fabry disease

Verheyen Nicolas[1], Hubert Seggewiss[2], Klemens Ablasser[1], Ewald Kolesnik[1], David Zach[1], Josepha Binder[1], Andreas Zirlik[3], Gabor Toth[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Department of Cardiology, Klinikum Würzburg Mitte, Würzburg, Germany
[3]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: A 63 year-old male patient with known Anderson-Fabry disease (AFD) presented with progressive deterioration of functional capacity (NYHA III). In the medical history, he had coronary artery disease (CAD) treated with PCI, ICD-implantation due to malignant ventricular arrhythmia, chronic kidney disease stage IV and depression. Besides enzyme replacement therapy he was treated with AT-II antagonist, beta-blocker, calcium antagonist, low-dose aspirin, statin and ezetimibe.

Methods: Echocardiography showed severe global cardiac hypertrophy with pronounced interventricular septum thickening (maximal end-diastolic thickness of 31 mm). Left ventricular ejection fraction was preserved with grade II diastolic dysfunction and evidence of increased filling pressures, supporting the diagnosis of HFpEF. Maximal LVOT gradient was 52 mmHg at rest and 86 mmHg at post-extrasystolic beat. Mitral valve showed incomplete systolic anterior motion (SAM). At the time of presentation NT-proBNP levels were 1.108 pg/ml. After treatment with verapamil at maximally tolerated doses NT-proBNP was lowered to 426 pg/ml and peak LVOT gradient declined to 26 mmHg at rest. However, during bicycle echocardiography the gradient increased to 76 mmHg after maximal workload. Also, the patient did not report relevant improvement in symptoms indicating septal reduction therapy. In face of comorbidities and high perioperative risk, percutaneous transluminal septal myocardial ablation (PTSMA) was preferred.

Results: By PTSMA of the first septal branch provoked peak LVOT gradient dropped from 80 mmHg to 30 mmHg as measured invasively. Peak post-procedural levels of CK and high-sensitive Troponin T were 1.766 U/l and 6.600 pg/ml, respectively. Pre-discharge echocardiography showed a peak LVOT gradient of 16 mmHg without relevant increase during provocation and no evidence of SAM.

Conclusions: Cardiac manifestation of AFB can mimic the phenotype of hypertrophic obstructive cardiomyopathy (HOCM). Therefore, AFB patients with signs or symptoms of heart failure should undergo a comprehensive diagnostic HOCM assessment. In case LVOT obstruction is confirmed, PTSMA in experienced hands can be a safe and effective treatment option for these patients.

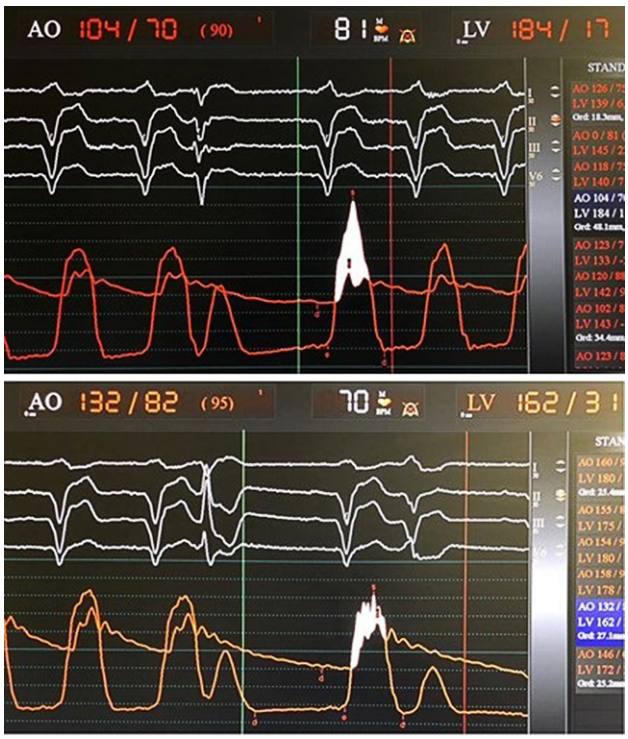


Fig. 1|4-6 Peak-to-peak gradient before and after PTSMA

4-7

Clinical utility of echocardiographic left-ventricular ejection fraction monitoring for cardiotoxicity risk assessment in patients with HER2+ early breast cancer undergoing trastuzumab-based therapy

Theresa Glantschnig[1], Florian Posch[2], Saskia Firla[1], Florian Moik[2], Klemens Ablasser[1], Josepha S. Binder[1], Gergana Stoschitzky[1], Markus Wallner[1], Dirk Von Lewinski[1], Herbert Stöger[2], Andreas Zirlik[1], Martin Pichler[2], Peter P. Rainer[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Division of Oncology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Monitoring left-ventricular ejection fraction (LVEF) is a routinely-practiced strategy to survey patients with breast cancer (BC) towards cardiotoxic treatment effects. However, whether the LVEF as a single measurement or as a trajectory over time is truly sufficient to identify patients at high risk for cardiotoxicity is currently debated. Purpose: To quantify the prognostic impact of LVEF as a single measurement or as a trajectory for predicting cardiotoxicity in women with human epi-

dermal growth factor receptor positive (HER2+) early BC undergoing trastuzumab-based therapy.

Methods: We analyzed 1,136 echocardiography reports from 185 HER2+ early BC patients treated with trastuzumab ± pertuzumab ± chemoendocrine therapy in the neoadjuvant/adjuvant setting (Fig. 1). Echocardiography was performed every 3 months during treatment, and every 6–12 months thereafter. Cardiotoxicity was defined as a 10% decline in LVEF below 50%. Joint models of longitudinal and time-to-event data were implemented to estimate the relationship between LVEF changes over time and cardiotoxicity risk.

Variable	Summary measure
Age (years, median [IQR])	55 [49-65]
Female (n, %)	185 (100%)
Body Mass Index (kg/m², median [IQR])	25.2 [22.4-29.9]
ECOG performance status (median [IQR])	0 [0-0]
HER2 positive (n, %)	185 (100%)
Estrogen receptor positive (n, %)	124 (67%)
Progesteron receptor positive (n, %)	109 (59%)
Ki-67 % (median [IQR])	35 [23-45]
Tumor grade G3 (n, %)	118 (64%)
TNM Tis-T1 (n, %)	77 (42%)
TNM T2 (n, %)	53 (29%)
TNM T3-4 (n, %)	12 (6%)
TNM TX (n, %)	43 (23%)
TNM N0 (n, %)	86 (46%)
TNM N1 (n, %)	47 (25%)
TNM N2-3 (n, %)	14 (8%)
TNM NX (n, %)	38 (21%)
TNM M0 (n, %)	185 (100%)
Neoadjuvant/Adjuvant setting (n, %)	103 (56%)
Adjuvant setting (n, %)	82 (44%)
Adjuvant radiotherapy (n, %)	148 (80%)

Fig. 1|4-7 Baseline characteristics of the study population ($n=185$). Abbreviations: IQR – Interquartile range, ECOG – Eastern Cooperative Oncology Group, HER2 – Human epidermal growth factor receptor 2, TNM – Tumor Node Metastasis classification

Results: Median baseline LVEF was 64% (25th–75th percentile: 60–69). 19 patients (10%) experienced cardiotoxicity (asymptomatic $n=12$, symptomatic $n=7$, during treatment $n=19$, treatment modification/termination $n=14$), Median time to cardiotoxicity was 6.7 months (25th–75th percentile: 3.4–10.2), and median LVEF decline in patients with cardiotoxicity was 18% (25th–75th percentile: 14–22, range: 10–35). One-year cardiotoxicity risk was 7.6% in the 35 patients with a baseline LVEF ≥60% and 24.5% in the 150 patients with a baseline LVEF <60% (HR=3.45, 95%CI:1.35–8.75, $p=0.009$, Fig. 2). During treatment, LVEF declined significantly faster in patients who developed cardiotoxicity than in patients that did not develop cardiotoxicity, respectively (1.3%/month vs. 0.1%/month, $p<0.0001$). A higher rate of LVEF decrease predicted for higher cardiotoxicity risk (HR per 0.1%/month higher LVEF decrease/month=2.50, 95%CI: 1.31–4.76, $p=0.005$), and cardiotoxicity risk increased by a factor of 1.7 per each 5% higher absolute decline in LVEF from baseline to first follow-up (HR=1.70, 95%CI: 1.30–2.38, $p<0.0001$). 36 patients (19%) developed an LVEF decline of at least 5% from baseline to first follow-up ("early LVEF decline"). One-year cardiotoxicity risk was 6.8% in those without early LVEF decline and a baseline LVEF ≥60% ($n=117$), 15.7% in those without an early LVEF decline and a baseline LVEF <60% ($n=65$), and 66.7% in those with and early LVEF decline and a baseline LVEF <60% ($n=3$, log-rank $p<0.0001$).

Conclusions: Both a single LVEF measurement and the rate of LVEF decrease strongly predict for cardiotoxicity in early BC patients undergoing HER2-targeted therapy. Routine LVEF monitoring can identify individuals at high risk of cardiotoxicity that may benefit from more sensitive screening techniques such as strain imaging.

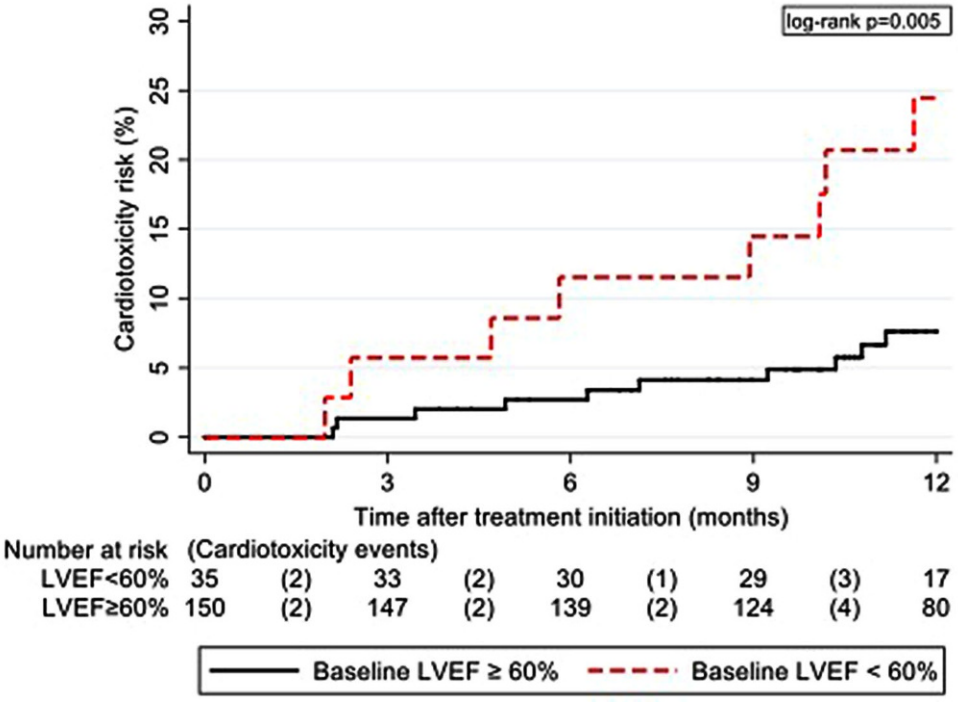


Fig. 2|4-7 1-Kaplan-Meier cumulative 1-year risk of cardiotoxicity ($n=185$). The numbers below the x-axis represent a so-called risk table, with the number of patients at risk for cardiotoxicity at the beginning of each interval, and the number of patients who developed cardiotoxicity during the pertinent interval in round brackets. Abbreviations: LVEF – Left ventricular ejection fraction

Postersitzung 5 – Interventionelle Kardiologie 1

5-1

Incidence of left atrial appendage thrombus in patients with severe aortic stenosis

Alexander Fellner, Thomas Lambert, Christian Reiter, Hermann Blessberger, Denis Hrncic, Jörg Kellermair, Alexander Nahler, Jennifer Anna Starnawski, Jürgen Kammler, Michael Grund, Clemens Steinwender

Department of Cardiology and Internal Intensive Care, Kepler University Hospital, Medical Faculty, Johannes Kepler University Linz, Linz, Austria

Background: Atrial fibrillation (AF) is the most common arrhythmia in elderly patients, especially in patients with severe aortic stenosis. In the last years, transcatheter aortic valve replacement (TAVR) has become an alternative treatment option for these patients. However, AF might lead to left atrial appendage (LAA) thrombus, which is a well known risk factor for periprocedural stroke, even in case of TAVR. We aimed to investigate the incidence of thrombotic formations in the LAA in a consecutive series of patients scheduled for TAVR and a history of AF.

Methods: Transesophageal echocardiography (TEE) was performed in all patients with severe aortic stenosis and AF prior to TAVR since June 2018. The left atrial appendage (LAA) was visualized in a mid-esophageal two chamber view using a commercially available echocardiography system (Epiq7®, Philips Health Systems, Amsterdam, The Netherlands). Absence or presence of an LAA thrombus was assessed in two orthogonal planes (xPlane function). Live 3D imaging of the LAA and echo contrast (SonoVue®, Bracco International BV, Amsterdam, The Netherlands) was used if deemed necessary. The findings were classified into three categories: 1. well circumscribed LAA thrombus, 2. spontaneous echo contrast (SEC, not well circumscribed), and 3. LAA free of thrombus or SEC. Patients with LAA thrombi or SEC were not deemed eligible for TAVR before modification of the antithrombotic medication and TEE reassessment.

Results: From June to December 2018, 38 patients (mean age: 81.55 ± 4.57 years; 42% female) were examined. According to the 2016 ESC Guidelines for the management of atrial fibrillation, AF was classified as permanent in 26 patients (68.4%), as persistent in 5 patients (5%), and as paroxysmal in 7 patients (18.4%), respectively. All patients were on sufficient oral anticoagulation for at least 4 weeks prior to the TEE (73.7% on novel oral anticoagulants and 23.7% on phenprocoumon; no intake interuptions and all INRs in therapeutic range, respectively). TEE revealed LAA thrombi or SEC only in patients with permanent AF. Thrombi were found in 4 patients and SEC in 5 patients, respectively (23.7% of all studied patients and 34.6% of patients with permanent AF, respectively). In patients with paroxysmal or persistent fibrillation no thrombi or SEC were found.

Conclusions: In patients scheduled for TAVR and a history of AF, TEE revealed a high incidence of LAA thrombotic formations despite sufficient oral anticoagulation in those with permanent AF (thrombi or SEC in 9/26 patients; 34.6%). No thrombotic formations were found in patients with paroxysmal or persistent AF. These findings underscore the importance of diligent pre-procedural cardiac imaging as well as post-procedural anticoagulation management in TAVR patients with permanent AF.

Table 1|5-1 Overview of TEE findings according to the ESC classification of Atrial Fibrillation (AF)

	Paroxysmal AF (*n*=/%) 7/18.4	Persistent AF (*n*=/%) 5/13.2	Permanent AF (*n*=/%) 26/68.4
LAA Thrombus	0	0	4
Spontaneous echo contrast (SEC)	0	0	5
LAA free of thrombus and SEC	7	5	17

5-2

Einfluss des Vorhofflimmerstatus auf das Langzeit-Outcome nach interventioneller ungeschützter Hauptstammintervention – ein retrospektives Langzeit Follow-up

Denis Hrncic, Hermann Blessberger, Jürgen Kammler, Jörg Kellermair, Thomas Lambert, Alexander Nahler, Christian Reiter, Daniel Kiblböck, Alexander Fellner, Jakob Bötscher, Jennifer Anna Starnawski, Michael Grund, Clemens Steinwender

Kepler Universitätsklinikum, Linz, Österreich

Grundlagen: Die koronare Herzkrankheit ist ein Haupt-Risikofaktor für das Auftreten von Vorhofflimmern. Es ist wenig bekannt, wie das Langzeit-Outcome von Patienten nach perkutaner Intervention einer Stenose des Hauptstamms der linken Koronararterie durch das Vorliegen einer Vorhofflimmerdiagnose zum Interventionszeitpunkt beeinflusst wird.

Methodik: Es wurden Patienten aus dem UNPROLEMA (UNPROtected LEft MAin disease) Register unserer Klinik untersucht, bei denen zwischen 11/2002 und 08/2014 eine ungeschützte Hauptstammintervention durchgeführt wurde. Dabei wurden die Patientendaten durch Informationen aus Krankengeschichten sowie aus strukturierten Telefon-Interviews und Meldeamtsanfragen bzgl. Follow-up komplettiert. Die Patienten wurden anhand des Vorhofflimmerstatus zum Zeitpunkt der Intervention in eine Vorhofflimmer- (AF) und eine Sinusrhythmus-Gruppe (SR) unterteilt. Die Gesamtmortalität und das Auftreten von major adverse cardiac and cerebrovascular events (MACCE: definiert als Myokardinfarkt, Zielgefäßrevaskularisation [interventionell oder mittels aortokoronarem Bypass], Insult/TIA oder Tod jedweder Genese) wurden mittels Kaplan-Meier Kurven analysiert. Ein Log-rank Test wurde zur Prüfung der statistischen Signifikanz durchgeführt. Zudem wurde mittels Cox Proportional Hazards Modell für potentielle Confounder (Alter, Diabetes-Status, linksventrikuläre Auswurffraktion, Raucherstatus, periphere arterielle Verschlusskrankheit, Hypercholesterinämie) adjustiert.

Ergebnisse: Insgesamt wurde bei 293 Patienten eine ungeschützte Hauptstammintervention durchgeführt. Davon war bei 237 zum Zeitpunkt der Intervention sowie aus der Anamnese kein Vorhofflimmern bekannt (SR-Gruppe, 80,9 %), während bei 56 (19,1 %) Vorhofflimmern bekannt war (AF-Gruppe: 30 paroxysmal, 5 persistierend und 21 permanent). Der CHA2DS2-VASc-Score, als Indikator einer größeren Komorbiditätslast, war in der AF-Gruppe mit 4,3 ± 1,6 signifikant höher, als in der

SR-Gruppe mit einem virtuellen mittleren Score von 3,4 ± 1,7 (p = 0,0002). Während einer medianen Follow-up-Dauer von 3,4 Jahren (IQR 1,4–6,3, Spannweite 0–12,1 Jahre) zeigte die Kaplan-Meier-Analyse bei insgesamt 90 Todesfällen jedweder Ursache (30,7 %) einen signifikanten Unterschied (p = 0,002), wobei AF-Patienten ein 2,1-fach erhöhtes Mortalitätsrisiko aufwiesen (Hazard Ratio [HR] 2,1, 95 % CI: 1,29–3,26). In der multivariaten Analyse mit Adjustierung für potentielle Confounder zeigte sich ein Verlust der statistischen Signifikanz (HR 0,46, 95 % CI: 0,09–2,37, p = 0,350). Von der MACCE-Analyse mussten 5 Patienten ausgeschlossen werden, da die Follow-up-Daten nicht vollständig erhoben werden konnten. Auch hier konnte ein signifikanter Unterschied (p = 0,046) mit einem 1,51-fach erhöhten Risiko für das Auftreten von MACCE in der AF-Gruppe beobachtet werden (HR 1,51, 95 % CI: 1,00–2,28). Nach Adjustierung für Confounder wurde wiederum ein Verlust der statistischen Signifikanz festgestellt (HR 0,75, 95 % CI: 0,33–1,74, p = 0,506).

Schlussfolgerungen: In der Analyse unserer Stichprobe beobachteten wir eine signifikante Erhöhung der Gesamtmortalität und der MACCE-Rate nach einer Hauptstamminterventionen bei Patienten mit Vorhofflimmern. Nach Adjustierung für potentielle Confounder, konnte jedoch kein Einfluss des Vorhofflimmerns im Sinne eines unabhängigen Risikofaktors auf das Langzeit-Outcome festgestellt werden. Es ist daher davon auszugehen, dass die erhöhte Gesamtmortalitäts- und MACCE-Rate durch die mit Vorhofflimmern assoziierten Komorbiditäten bedingt ist. Der Vorhofflimmer-Status kann als wichtiger Prädiktor für das Langzeit-Outcome bei Patienten nach Hauptstamminterventionen gesehen werden.

5-3

Iliofemoral tortuosity score predicting access and bleeding complications during transfemoral TAVI

Philipp Szalkiewicz[1], Thomas Poschner[1], Waseem Hasan[2], Jong Hui Lee[1], Victoria Watzal[1], Bernhard Winkler[1], Gabriel Weiss[1], Andreas Strouhal[3], Christopher Adlbrecht[3], Georg Delle-Karth[3], Martin Grabenwöger[4], Markus Mach[5]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Imperial College, London, UK, London, United Kingdom
[3]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research; Sigmund Freud University, Medical Faculty, Vienna, Austria
[5]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Graz, Austria

Background: Reliably predicting vascular complications after transcatheter aortic valve implantation remains one of the significant challenges up until today. The iliofemoral tortuosity is a known potential risk factor for vascular complications during transfemoral transcatheter aortic valve implantation, yet has been difficult to quantify. Therefore, this study evaluated the impact of novel scoring methods of iliofemoral tortuosity on the prognosis of vascular access complications and patient outcome.

Methods: Between June 2009 and December 2016, 237 TF-TAVI patients were examined retrospectively. Tortuosity of iliofemoral arteries was assessed by 3mensioValvesTM software analysis of preoperative MDCT-scans. The main access vessel has been assessed between the aorto-iliacal bifurcation and the femoral bifurcation. Single angels were measured every 15 mm in all spatial directions. Tortuosity was assessed by three quantitative methods: 1) the maximum single angle (MSA) along the entire vessel length, 2) the sum of all angles (SAA) as well as the 3) Iliofemoral tortuosity (IFT) score [((true vessel length/ideal vessel length)–1)*100]. ROC-Analysis has been performed, and cut-off values were calculated using the Youden Index. The primary study endpoint was a composite of bleeding and access complications as defined by the Valve Academic Research Consortium 2 (VARC-2) criteria. The secondary study endpoints were 30-day mortality and a composite safety endpoint.

Results: Access and bleeding complications occurred in 73 patients (13.7%). While the MSA and the SAA did not correlate with the composite primary endpoint (p = 0.990; p = 0.224) the IFT score proved to be a good predictor (p = 0.016; cut off: 21,2; sensitivity 0.77, specificity 0.43), especially of bleeding events (p = 0.005; cut off: 21.2; sensitivity 0.79, specificity 0.42). Furthermore, both the IFT and the MSA positively correlated with minor bleeding events (IFT: p = 0.009, cut-off 26.6; sensitivity 0.56; specificity 0.69; MSA: p = 0.032; cut-off 35.5°; sensitivity 0.78; specificity 0.40). For the secondary endpoints, no relation between 30-day mortality or the composite safety endpoint with neither one of the measures has been observed.

Conclusions: Vascular tortuosity is an underestimated risk factor during transcatheter aortic valve implantation. The IFT-score is a valuable tool in risk stratification prior to TF-TAVI positively predicting access and bleeding complications. As major adverse events are rarely seen nowadays in the transfemoral approach, further research is needed to validate our study's findings.

5-4

Patent hemostasis after transradial catheterization: Higher incidence after distal versus proximal radial artery access

Günter Christ[1], Thomas Hafner[1], Elisabeth Danhorn[1], Michael Kurz[1], Marcel Francesconi[1], Birgit Reiterer[2], Aneta Stopnicka[2], Brigitte Schwarzmann[2], Bianca Hofbauer[2], Claudia Ruthner-Bichler[2], Tamara Strohmer[2], Katharina Kernberger[2], Christian Zeglovits[2], Roland Graf[2], Andrea Podczeck-Schweighofer[1]

[1]5th Medical Department, Kaiser Franz Josef Hospital, Vienna, Austria
[2]Department of Radiology, Kaiser Franz Josef Hospital, Vienna, Austria

Background: Distal radial artery access (DRA) represents a novel, innovative approach for transradial catheterization with a very low rate of reported radial artery occlusion (0.3%). Patent hemostasis (i. e. documented radial patency during hemostatic compression) after standard proximal radial artery access (PRA) at wrist level is associated with lower occurrence of radial artery occlusion. We were interested to evaluate the incidence of patent hemostasis after distal versus proximal radial access.

Methods: Single-center study of consecutive transradial catheterization cases via distal or proximal radial access and evaluation of patent hemostasis. Selection of the puncture site was at the discretion of the operator. In case of PRA, a stepwise reduction protocol of the standard air-inflation volume (13 ml) without bleeding was applied. In cases of DRA, standard air-inflation volume (13 ml) was left unchanged, due to initial cases of forearm hematomas after stepwise reduction. Patent hemostasis was assessed by pulse oximetry under ipsilateral ulnar artery occlusion ("reversed Barbeau"). DRA was performed with 4F or 5F-sheaths (Glidesheath slender, Terumo; Prelude, Merit), PRA either with 4F to 6F-sheaths, and routine application of 2.5 mg Verapamil and 5000 IU heparin for diagnostic, and 100 IU/kg heparin for interventional procedures. For compression the IO-band (Comed) was used with DRA, and either IO- or the TR-band (Terumo) with PRA.

Results: Between October 2018 and January 2019, 501 consecutive cases with transradial catheterization and evaluation of patent hemostasis were included. DRA was performed in 39% ($n=197$) of cases; with a significant lower percentage of female (19% vs. 40%, $p<0.0001$) or ACS patients (16% vs. 23%, $p=0.05$), compared to PRA. Failure of DRA (20% of attempts, including learning curve) was associated with female sex (35% vs. 19%, $p=0.02$) and less body height (170 ± 10 cm vs. 173 ± 9 cm, $p=0.04$). Patent hemostasis was highly significant more present after DRA (75% vs. 34%, $p<0.0001$), even despite the significantly reduced air-inflation volume of the compression devices after PRA (10 ± 2 vs. 13 ± 0.6 ml, $p<0.0001$). Lack of patent hemostasis after DRA was associated with lower body weight (80 ± 15 vs. 86 ± 17 kg, $p=0.05$), less body height (170 ± 8 vs. 173 ± 8 cm, $p=0.02$), and with female sex (27% vs. 17%, $p=0.1$), as a trend only. Patent hemostasis after PRA was solely associated with hypertension (88% vs. 77%, $p=0.02$).

Conclusions: Discussion: DRA for transradial catheterization shows a highly significant higher incidence of patent hemostasis compared to PRA, even despite a reduction protocol for the air-inflation volume of the compression device in proximal cases. This might represent a major cause for the very low incidence of radial artery occlusions after DRA. However, due to the possible presence of a superficial palmar branch of the radial artery, which can also supply the digital branches of the thumb, a positive reversed Barbeau might not always represent patency of the compressed distal radial artery. Nevertheless, patent hemostasis with conventional PRA could only be achieved in 34% of cases. Conclusions: Although technical success seems more difficult with distal radial access and requires a longer learning curve than the proximal access, adoption of this innovative new route as default access for transradial catheterization should be widely promoted, given the possible benefits regarding radial artery occlusion.

5-5

A novel heart failure score predicts adverse outcome in patients undergoing transcatheter aortic valve implantation

Daniela Geisler[1], Christopher Adlbrecht[2], Bernhard Winkler[1], Gabriel Weiss[1], Thomas Poschner[1], Philipp Szalkiewicz[1], Victoria Watzal[1], Waseem Hasan[3], Andreas Strouhal[2], Georg Delle-Karth[2], Martin Grabenwöger[4], Markus Mach[5]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[3]Imperial College, London, UK, London, United Kingdom
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research; Sigmund Freud University, Medical Faculty, Vienna, Austria
[5]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Austria, Graz, Austria

Background: Progression of chronic heart failure (CHF) is closely linked to plasma volume expansion. Identifying the plasma volume (PV) in CHF patients can, therefore, add crucial prognostic information for risk stratification. As recently published plasma volume status (PVS) can be estimated using weight and hematocrit for calculation; a PVS of >–4 was associated with increased mortality in heart failure patients. Our objective was to determine the impact of a high PVS on early clinical safety endpoints defined by the Valve Academic Research Consortium 2 (VARC-2) after transcatheter aortic valve implantation (TAVI). Furthermore, we wanted to assess the prognostic utility of PVS for outcome prediction.

Methods: We retrospectively calculated the PVS in 516 patients between 2009 and 2016. They were then categorized into two groups depending on their preoperative plasma volume status (PVS ≤ –4; $n=193$ vs. PVS > –4; $n=323$). Relative PVS was derived by subtracting calculated ideal (iPV = c x weight) from actual plasma volume (aPV = (1-hematocrit) x (a + (b x weight in kg))).

Results: The need for renal replacement therapy (1 (0.5%) vs. 17 (5.3%); $p=0.002$) and re-operation for non-cardiac reasons (9 (4.7%) vs. 32 (9.9%); $p=0.021$) were significantly higher in patients with a PVS > –4%. Furthermore, bleeding (13 (6.7%) vs. 35 (10.8%); $p=0.075$), acute kidney injury (25 (13.0%) vs. 59 (18.3%); $p=0.065$), re-operation for bleeding (9 (4.7%) vs. 27 (8.4%); $p=0.075$) and periprocedual death (7 (3.6%) vs. 24 (7.4%); $p=0.055$) suggest a trend towards a worse outcome in patients with higher fluid retention. The composite 30-day early safety endpoint (176 (91.2%) vs. 272 (84.2%); $p=0.054$) confirms that an increased preoperative PVS is associated with a worse overall outcome after TAVI.

Conclusions: PVS as an index for congestion is an easily calculable measure that adds important prognostic information for risk stratification in patients undergoing TAVI.

5-6

Contrast medium volume does not predict acute kidney injury after transcatheter aortic valve implantation

Philipp Szalkiewicz[1], Waseem Hasan[2], Victoria Watzal[1], Carina Cuhaj[1], Thomas Poschner[1], Bernhard Winkler[1], Gabriel Weiss[1], Andreas Strouhal[3], Christopher Adlbrecht[3], Georg Delle-Karth[3], Martin Grabenwöger[4], Markus Mach[5]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Imperial College, London, UK, London, United Kingdom
[3]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research; Sigmund Freud University, Medical Faculty, Vienna, Austria
[5]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Graz, Austria

Background: The study aimed to investigate contrast-induced nephropathy after TAVI and define specific threshold values. Recent studies suggested that the contrast medium (CM) volume is associated with acute kidney injury (AKI) after TAVI. Nevertheless, in a high-risk elderly TAVI population, the prognostic value and ideal threshold of CM dosage on AKI persist in being unclear.

Methods: Data of 532 successive TAVI patients (age 81.1 ± 6.8 years, Euro- SCORE II 4.8% ± 6.0%) were analyzed. AKI was defined by Valve Academic Research Consortium 2 criteria. Based on a recently published formula, the renal function (pre-procedural serum creatinine: SCr) corrected ratio of CM and body weight (CM*SCr/BW) was calculated to determine the risk of postprocedural contrast-induced AKI.

Results: AKI occurred in 94 patients (18.3%). A significant difference in 1-year all-cause mortality between the AKI and non-AKI groups (22 (23.4%) vs. 55 (13.1%), $p = 0.001$) was shown. In contrast to recent findings, our study showed no association between CM dosage or the CM*SCr/BW ratio and the occurrence of AKI ($p = 0.968$ and $p = 0.442$ respectively). However, a significant correlation between AKI and 30-day as well as 1-year all-cause mortality was observed ($p = 0.001$; $p = 0.007$).

Conclusions: In our all-comers, all-access cohort we found no relationship between CM dosage, nor the established risk ratio models and the occurrence of postprocedural AKI. Further research needs to be directed towards different pathophysiological causes and preventive measures as AKI negatively impacts short- and long-term survival.

Postersitzung 6 – Risikofaktoren/ Stoffwechsel/Lipide 1

6-1

Intermediate density lipoprotein is associated with monocyte subset distribution in patients with stable atherosclerosis

Konstantin Krychtiuk[1], Stefan P. Kastl[1], Thomas Pongratz[2], Georg Goliasch[1], L Gaspar[3], Christian Hengstenberg[1], Kurt Huber[4], Elisabeth Dostal[2], Stefan Pfaffenberger[1], Stanislav Oravec[3], Johann Wojta[1], Walter Speidl[1]

[1]Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Krankenanstalten Dr. Dostal, Vienna, Austria
[3]Comenius University, Bratislava, Slovakia
[4]3rd Medical Department, Wilhelminenhospital, Vienna, Austria

Background: Intermediate density lipoprotein (IDL) consists mainly of chylomicron remnants and very low densitiy lipoprotein (VLDL) remnants that are thought to be proinflammatory lipoprotein particles. Atherosclerosis is considered to be an inflammatory disease of the vessel wall in which monocytes and monocyte-derived macrophages are crucially involved. Circulating monocytes can be divided according to their surface expression pattern of CD14 and CD16 into at least three subsets with distinct inflammatory and atherogenic potential. The aim of this study was to investigate whether IDL is associated with proinflammatory monocyte subsets.

Methods: We included 90 patients with stable coronary artery disease (CAD). Monocyte subsets were identified as classical monocytes (CD14++CD16-; CM), intermediate monocytes (CD14++CD16+; IM) and non-classical monocytes (CD14+CD16++; NCM) by flow cytometry. Lipoprotein subfractions were measured by an electrophoresis method on polyacrylamide gel.

Results: IDL correlated significant with the proinflammatory IM ($r = 0.24$; $p < 0.05$) whereas VLDL and low densitiy lipoprotein (LDL) were not associated with monocyte subtypes. IDL was not associated with CM ($r = -0.18$; $p = 0.09$) and NCM ($r = 0.16$; $p = 0.13$) but correlated significant with the acute phase protein C-reactive protein ($r = 0.40$; $p < 0.01$). The association of IDL with IM was independent of cardiovascular risk factors and statin treatment. Patients with IDL>median (38 mg/dL) showed a significant higher proportion of IM as compared to patients with IDL< 38 mg/dL (5.6 IQR 4.3–8.3% vs. 4.1 IQR 2.6–6.2%).

Conclusions: In conclusion, we provide a potential link between elevated levels of IDL and a proinflammatory distribution of monocyte subtypes in patients with stable atherosclerotic disease. This possible proatherogenic role of IDL warrants further studies.

6-2

Mangelernährung – Einfluss und Outcome in der kardiovaskulären Rehabilitation: Pilotstudie

Andreas Guttmann[1], Sabina Maria Hörist-Kollmann[2], Christiane Prenner[2], Alexandra Deutsch[2], Matthias Kristoferitsch[2], Angela Krautsack[2], Elisabeth Wappl[2], Werner Kullich[3], Bettina Thauerer[3], Hermann Toplak[4], Jeanette Strametz-Juranek[2]

[1]Medizinische Universität Graz, Oberwart, Österreich
[2]SKA-RZ Bad Tatzmannsdorf, Bad Tatzmannsdorf, Österreich
[3]Ludwig Boltzmann Institut für Arthritis und Rehabilitation, Department für Rehabilitation, Saalfelden, Österreich
[4]Universitätsklinik für Innere Medizin, Medizinische Universität Graz – LKH Graz, Graz, Österreich

Grundlagen: Herz-Kreislauferkrankungen stellen die häufigste Todesursache weltweit dar. Kardiologische invasive Techniken und chirurgische Verfahren (z. B. TAVI,...) steigern zunehmend den Anteil älterer und alter Personen im Bereich der stationären Rehabilitation. Mangelernährung, gekennzeichnet durch Gewichtsverlust, progredienten Muskelabbau und niedrigem Eiweißgehalt, ist assoziiert mit einer erhöhten Sturzneigung und gilt zusammen mit dem Alter als unabhängiger Risikofaktor für HKE. In der vorliegenden Pilotstudie wurde die Wirksamkeit kardiovaskulärer Rehabilitationsmaßnahmen bei älteren und alten Menschen, der Einfluss eines gezielten Screenings und die Behandlung von Mangelernährung auf Outcomeparameter, wie Gehstrecke, Muskelkraft, etc. untersucht.

Methoden: Alle PatientInnen erhielten ein AKE-Screening sowie BIA, Labor, SPPB und 6MGT am Anfang und Ende. Zusätzlich kam der Genderenergiebedarfsrechner zum Einsatz. Im Rahmen der stationären Rehabilitation auf der Bettenstation nahmen $n = 31$ Personen (19 weiblich, 12 männlich) mit einem Durchschnittsalter von 77 Jahren an der Studie teil. 13 PatientInnen wiesen ein Risiko für Mangelernährung = Studiengruppe A und 18 PatientInnen eine manifeste Mangelernährung = Studiengruppe B auf. Alle PatientInnen mit manifester Mangelernährung erhielten eine zusätzliche Nahrungsmittelsupplementation mit erhöhtem Proteinanteil. PatientInnen mit Risiko für

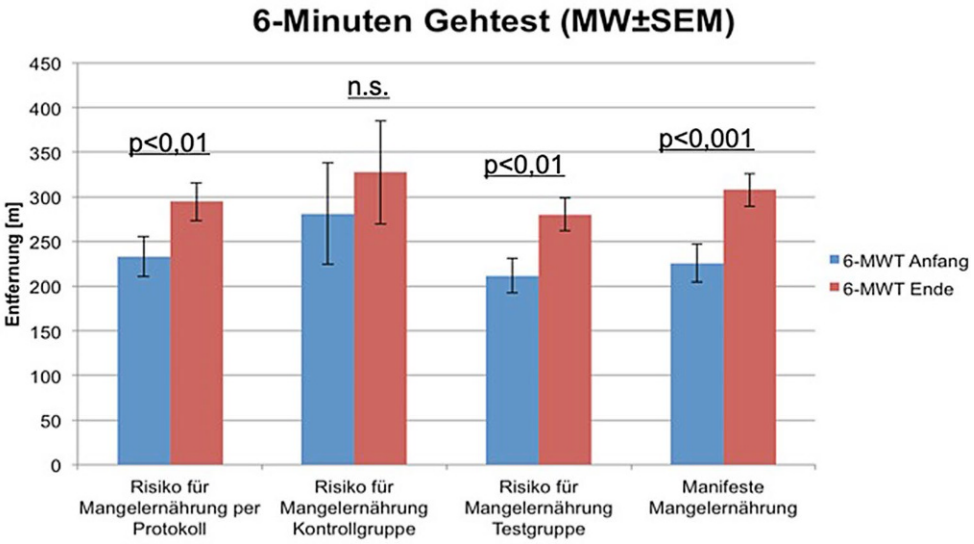


Abb. 1|6-2

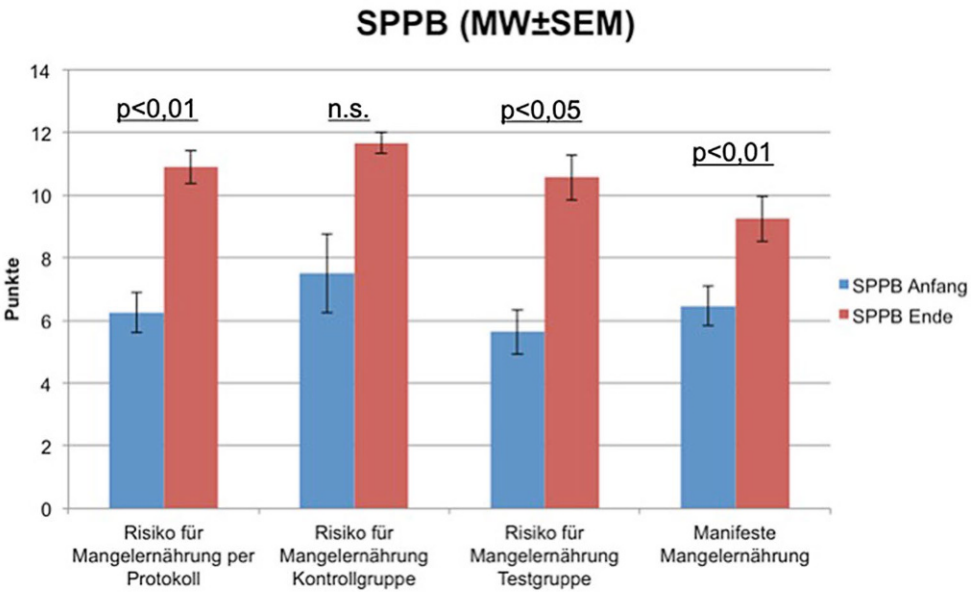


Abb. 2|6-2

Mangelernährung wurden in zwei Gruppen randomisiert. Im Gegensatz zur Kontrollgruppe erhielten PatientInnen der Testgruppe eine zusätzliche Nahrungsmittelsupplementation mit erhöhtem Proteinanteil. Die Statistik erfolgte mittels GraphPad Prism 7 mit einer „intention- to- treat" und „per protocol" Analyse.

Ergebnisse: Generell konnten wir zeigen, dass sowohl PatientInnen mit manifester als auch mit Risiko für Mangelernährung eine deutliche Zunahme der Leistungsfähigkeit beim 6MGT (A: 233,1 m ± 81 m auf 294,6 m ± 76,7 m, $p = 0{,}002$) und der SPPB (A: 6,25 ± 2,26 auf 10,9 ± 1,66, $p = 0{,}002$) aufwiesen. Bei PatientInnen mit Risiko für Mangelernährung zeigte sich, dass die Testgruppe eine deutlichere Steigerung beim 6MGT (211,7 m ± 56,9 m auf 280 m ± 54,7 m, $p = 0{,}001$) und SPPB (5,62 ± 1,99 auf 10,57 ± 1,9, $p = 0{,}015$) aufwies als die Kontrollgruppe.

Schlussfolgerungen: Mangelernährung ist ein prioritäres Thema in der Rehabilitation. 1. Ältere und alte Menschen profitieren durch eine stationäre Rehabilitation. 2. Mangelernährung beeinflusst Maßnahmen und Ziele der kardiovaskulären Rehabilitation signifikant. 3. Die gezielte interdisziplinäre Behandlung einer Mangelernährung führt zu einer signifikanten Verbesserung von Muskelkraft, Ganggeschwindigkeit und Gleichgewichts und ist eine wichtige Maßnahme zur Sturzprophylaxe und dem kardiovaskulären Outcome.

6-3

Influence of traditional cardiovascular risk factors, gender and chronic kidney disease on carotid and femoral atherosclerotic plaque volume as measured by three-dimensional ultrasound

Maria Noflatscher[1], Michael Schreinlechner[1], Philip Sommer[1], Julia Kerschbaum[2], Markus Theurl[1], Kirchmair Rudolf[1], Peter Marschang[3]

[1]University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Internal Medicine IV (Nephrology and Hepatology) Medical University of Innsbruck, Innsbruck, Austria
[3]Department of Internal Medicine, Zentralkrankenhaus Bozen, Bozen, Italy

Background: Atherosclerosis is a systemic multifocal disease with a preference for the branching points of the arteries. 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. So far, the influence of cardiovascular risk factor (CVRF) on quantitatively measured carotid and femoral plaque volume in subjects with CVRF and/or established atherosclerotic disease has not been systematically assessed. Also the influence of gender and chronic kidney disease (CKD) on carotid and femoral plaque volume has not been examined before. Therefore, we aimed to investigate the association of carotid and femoral plaque volume with traditional CVRF, gender and chronic kidney disease (CKD) using an innovative 3D ultrasound approach.

Methods: In this prospective, single centre study, we included 404 patients (median age 64; 57% men) with at least one CVRF or established cardiovascular disease. Plaque volume was measured using an automated software. Statistical analyses were performed using SPSS Statistic (version 24.0).

Results: Depending on the number of traditional CVRF and the presence of cardiovascular diseases we observed a significant increase in total, femoral and carotid plaque volume ($p < 0.001$). The strongest associations with total and femoral plaque volume were noted for smoking, hypertension, age, as well as for the presence of peripheral arterial occlusive disease ($p < 0.05$). Carotid plaque volume was best predicted by hyperlipidaemia, hypertension, age, as well as the presence of cerebrovascular disease and coronary artery disease ($p < 0.05$). The atherosclerotic plaque volume was significantly higher in men compared to women in all vascular territories ($p < 0.001$) and in patients with CKD for total plaque volume ($p < 0.001$).

Conclusions: We conclude that plaque volume increases with increasing numbers of CVRF and in the presence of cardiovascular disease and CKD. In addition men have a significant higher prevalence for total, femoral and carotid plaque burden compared to women. Smoking appears to be primarily associated with total and femoral plaque volume, whereas hyperlipidaemia appears to be associated with carotid plaque volume. Measurement of 3D plaque volume appears to be a practicable and reproducible technique with the potential to become an additional screening tool in risk stratification.

6-4

Die aortale Pulswellengeschwindigkeit als unabhängiger Prädiktor kardiovaskulärer Ereignisse – ein Vergleich invasiver mit nicht-invasiver Messung

Kathrin Danninger[1], Bernhard Hametner[2], Siegfried Wassertheurer[2], Christopher Clemens Mayer[2], Ronald Binder[1], Thomas Weber[1]

[1]Klinikum Wels-Grieskirchen, Wels, Österreich
[2]Austrian Institute of Technology, Wien, Österreich

Grundlagen: Die aortale Pulswellengeschwindigkeit (aortale PWV) steht in engem Zusammenhang mit der arteriellen Gefäßsteifigkeit und stellt einen wichtigen Risikomarker im

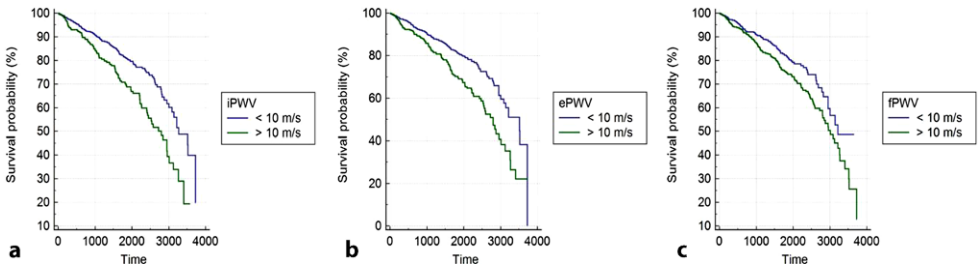


Abb. 1|6-4 Vorhersage der Überlebenswahrscheinlichkeit mittels iPWV versus ePWV

Rahmen des Konzepts der Gefäßalterung dar. Es gibt verschiedene Methoden zur Bestimmung der aortalen PWV, jedoch wird bisher keine davon in der täglichen klinischen Praxis verwendet, sei es aufgrund von Unpraktikabilität oder unklarem prognostischen Wert.

Methodik: Das Ziel dieser Studie ist die Evaluierung des prognostischen Werts zweier unterschiedlicher Methoden zur Bestimmung der aortalen PWV. Bei 1040 Patienten, bei denen eine diagnostische Koronarangiographie bei Verdacht auf koronare Herzerkrankung durchgeführt wurde, wurde bei Rückzug des Katheters die invasive Pulswellengeschwindigkeit (iPWV) gemessen. Ergänzend dazu erfolgte die Abschätzung der Pulswellengeschwindigkeit auf nicht invasive Weise (ePWV) mittels radialer Tonometrie. Als primärer Endpunkt wurde eine Kombination aus Tod, Myokardinfarkt, Schlaganfall oder ungeplanter koronarer Revaskularisation festgelegt. Zur Überlebensanalyse wurden Cox proportional hazard Modelle und Kaplan Meier Kurven verwendet. Für letztere wurden die Patienten in Gruppen anhand eines Cutoff Punktes von 10 m/s eingeteilt.

Ergebnisse: Bei einer mittleren Follow up Zeit von 1565 Tagen erreichten 24 % der Patienten den primären Endpunkt. In der Analyse zeigte sich eine signifikante Separation der Kaplan Meier Kurven (Abb.). Nach Korrektur für multiple Variablen (Alter, Geschlecht, diastolischer Blutdruck, Schweregrad der KHK, systolischer Funktion, Diabetes, Rauchstatus und Kreatininwert) lagen die Cox proportional hazard ratios per m/s bei 1,13 für iPWV und bei 1,17 für ePWV ($p<0{,}0001$ für beide Methoden).

Schlussfolgerungen: Arterielle Gefäßsteifigkeit, erhoben mittels invasiver oder nichtinvasiver Methode, konnte kardiovaskuläre Ereignisse und Tod bei Patienten mit Verdacht auf koronare Herzerkrankung vorhersagen. Dies weist darauf hin, dass beide Methoden zur Bestimmung der Gefäßsteifigkeit – unter Berücksichtigung ihrer individuellen Charakteristika – geeignet sind.

6-5

Type 2 diabetes is a strong predictor for LDL cholesterol target achievement in patients with peripheral artery disease

Alexander Vonbank[1], Christine Heinzle[2], Daniela Zanolin-Purin[2], Jörn F. Dopheide[3], Iris Baumgartner[3], Barbara Larcher[1], Arthur Mader[1], Simon Sternbauer[1], Lukas Sprenger[1], Andreas Leiherer[2], Axel Muendlein[2], Heinz Drexel[3], Christoph H. Saely[4]

[1]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[2]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[3]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland
[4]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein

Background: Patients with peripheral artery disease (PAD) are at a very high risk of cardiovascular events and strongly benefit from lowering LDL cholesterol (LDL-C). Current guidelines recommend an LDL-C target of at least <70 mg/dl for these patients. PAD patients who also have diabetes are at an extremely high risk of cardiovascular events, and an LDL-C target of < 55 mg/dl has been proposed for these patients. Whether the presence of type 2 diabetes (T2 DM) affects LDL-C target achievement in PAD patients is unknown and is addressed in the present study.

Methods: We investigated an unselected consecutive series of 481 patients with sonographically proven PAD, of whom 214 (44.5%) had T2 DM.

Results: An LDL-C target of < 70 mg/dl was met by 26.4% of PAD patients with T2 DM and by 9.0% of non-diabetic PAD patients ($p<0.001$); an LDL-C target < 55 mg/dl was met by 11.8% of T2 DM patients and by 2.7% of non-diabetic patients ($p<0.001$). Logistic regression analysis showed that the presence of T2 DM was an independent and strong predictor of LDL-C target achievement after multivariate adjustment including age, gender and statin use both for the < 70 mg/dl target (OR 3.31 [1.93–5.68]; $p<0.001$) and for the < 55 mg/dl target (OR 4.40 [1.83–10.51]; $p<0.001$).

Conclusions: We conclude that T2 DM is a strong and independent predictor of LDL-C target achievement among PAD patients; however, also among PAD patients with T2 DM the majority does not even meet the liberal LDL-C target of < 70 mg/dl.

6-6

Lipid parameters in peripheral artery disease versus coronary artery disease patients with type 2 diabetes

Christoph H. Saely[1], Alexander Vonbank[2], Christine Heinzle[3], Daniela Zanolin-Purin[3], Jörn F. Dopheide[4], Iris Baumgartner[4], Barbara Larcher[2], Arthur Mader[2], Simon Sternbauer[2], Lukas Sprenger[2], Andreas Leiherer[3], Axel Muendlein[3], Heinz Drexel[4]

[1]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein
[2]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[3]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[4]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland

Background: Whether lipid parameters differ between type 2 diabetes (T2 DM) patients with peripheral artery disease (PAD) and those with coronary artery disease (CAD) is unclear and is addressed in the present study.

Methods: We measured lipid parameters in 465 patients with sonographically proven PAD, of whom 204 had T2 DM and in 1312 patients with angiographically proven CAD, of whom 384 had T2 DM.

Results: Fig. 1 compares means ± SDs of lipid parameters between PAD and CAD patients, stratifying the analyses by the presence of diabetes. Overall, the differences between PAD and CAD patients were similar in patients with T2 DM and non-diabetic subjects. Specifically, T2 DM patients with PAD had lower total cholesterol, LDL cholesterol, non-HDL cholesterol, and apolipoprotein B but higher lipoprotein(a) than those with CAD. These differences remained significant after multivariate adjustment including lipid lowering medication ($p<0.001$ for total cholesterol, LDL cholesterol, non-HDL cholesterol, and apolipoprotein B and lipoprotein(a), respectively).

Conclusions: We conclude that total cholesterol, LDL cholesterol, non-HDL cholesterol, as well as apolipoprotein B lev-

	CAD / DM -	PAD / DM -	p-value	CAD / DM +	PAD / DM +	p-value
Total cholesterol [mg/dl]	209±46	186±42	p<0.001	197±49	173±49	p<0.001
LDL cholesterol [mg/dl]	133±39	110±35	p<0.001	121±39	98±43	p<0.001
HDL cholesterol [mg/dl]	54±16	56±18	p=0.308	48±14	48±16	p=0.895
non-HDL cholesterol [mg/dl]	155±46	130±40	p<0.001	149±49	125±47	p<0.001
Triglycerides [mg/dl]	144±94	141±86	p=0.907	174±110	180±133	p=0.608
Apolipoprotein A1 [mg/dl]	151±28	162±35	p<0.001	144±26	151±36	p=0.069
Apolipoprotein B [mg/dl]	97±28	80±23	p<0.001	98±31	77±26	p<0.001
Lipoprotein (a) [mg/dl]	32±56	44±56	p<0.001	24±43	44±54	p<0.001
LDL/ApoB ratio	1.39±0.28	1.40±0.23	p=0.037	1.26±0.28	1.29±0.33	p=0.329

Fig. 1|6-6

els are lower and lipoprotein(a) is higher in PAD than in CAD patients with T2 DM.

6-7

Type 2 diabetes and different manifestations of pre-existing cardiovascular disease as predictors of specific cardiovascular events

Christoph H. Saely[1], Alexander Vonbank[2], Christine Heinzle[3], Daniela Zanolin-Purin[3], Barbara Larcher[2], Arthur Mader[2], Simon Sternbauer[2], Lukas Sprenger[2], Marc Schindewolf[4], Iris Baumgartner[4], Andreas Leiherer[3], Axel Muendlein[3], Heinz Drexel[4]

[1]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein
[2]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[3]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[4]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland

Background: Coronary artery disease (CAD) and peripheral artery disease (PAD) confer an increased risk of cardiovascular events that is particularly high when type 2 diabetes (T2 DM) is present in addition to cardiovascular disease (CVD). Here, we aimed at investigating the impact of T2 DM and of the manifestation of pre-existing cardiovascular disease (PAD vs. CAD) as predictors of specific cardiovascular events.

Methods: We prospectively recorded cardiovascular events over 10 years in 1777 patients with established CVD, including 1312 patients with CAD, of whom 29.3% had T2 DM and 465 patients with PAD, of whom 43.9% had T2 DM.

Results: T2 DM after multivariate adjustment significantly predicted cardiovascular mortality ($n=102$; HR 1.77 [1.33–2.36]; $p<0.001$), myocardial infarction ($n=74$; HR 1.50 [1.10–2.04]; $p=0.010$), ischemic stroke ($n=54$; HR 1.69 [1.16–2.46]; $p=0.007$), and revascularization of non-coronary arteries ($n=134$; HR 1.66 [1.29–2.13]; $p<0.001$) independently from the manifestation of CVD. The presence of PAD versus that of CAD after adjustment for conventional cardiovascular risk factors including T2 DM predicted myocardial infarction (HR 2.33 [1.61–3.37]; $p<0.001$) and revascularization of non-coronary arteries (HR 7.48 [5.51–10.16]; $p<0.001$). Neither T2 DM nor the presence of PAD vs. that of CAD was significantly associated with percutaneous coronary interventions ($n=246$) or coronary artery bypass graftings ($n=94$) in our cohort.

Conclusions: We conclude that both T2 DM and the manifestation of pre-existing CVD predict cardiovascular events in patients with established CVD.

6-8

Type 2 diabetes as a predictor of cardiovascular events in peripheral artery disease versus coronary artery disease

Christoph H. Saely[1], Alexander Vonbank[2], Christine Heinzle[3], Daniela Zanolin-Purin[3], Barbara Larcher[2], Arthur Mader[2], Simon Sternbauer[2], Lukas Sprenger[2], Marc Schindewolf[4], Iris Baumgartner[4], Andreas Leiherer[3], Axel Muendlein[3], Heinz Drexel[4]

[1]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein
[2]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[3]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[4]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland

Background: Patients with established cardiovascular disease (CVD) are at a very high risk of cardiovascular events, and cardiovascular risk is considered extremely high in those with the combination of CVD and diabetes. However, the impact of type 2 diabetes (T2 DM) on cardiovascular event risk may differ between different manifestations of CVD.

Methods: To address this issue, we prospectively recorded cardiovascular events over 10 years in 1472 patients with angiographically proven stable coronary artery disease (CAD), of whom 454 had T2 DM as well as in 465 patients with sonograph-

ically proven peripheral artery disease (PAD), of whom 204 had T2 DM.

Results: Both among CAD and among PAD patients, those with T2 DM were at a significantly higher risk of cardiovascular events than those who did not have diabetes (56.0% vs. 44.5%; $p<0.001$ and 68.5% vs. 50.6%; $p<0.001$, respectively). Cardiovascular risk was significantly higher in PAD than in CAD patients, both among those with T2 DM (68.0% vs. 56.0%; $p=0.003$) and among those who did not have diabetes (50.6% vs. 44.5%; $p=0.047$). In multivariate analyses, T2 DM (HR 1.48 [1.13–1.70]; $p<0.001$) and presence of PAD versus that of CAD (HR 1.93 [1.64–2.28]; $p<0.001$) were mutually independent predictors of cardiovascular events. An interaction term T2 DM by PAD vs. CAD was non-significant ($p=0.146$), indicating that the relative risk increase conferred by T2 DM did not differ significantly between PAD and CAD patients.

Conclusions: We conclude that T2 DM increases cardiovascular event risk among patients with PAD as well as among those with CAD and that PAD confers a higher risk of cardiovascular events than stable CAD irrespective of the presence of T2 DM.

POSTERSITZUNGEN 7-12

Donnerstag, 30. Mai 2019, 15.30 bis 16.30 Uhr

Postersitzung 7 – Basic Science 2

7-1

The cardiovascular biomarkers suPAR, GDF-15, H-FABP and sST2 in ischemic heart disease

Daniel Dalos[1], Matthias Schneider[1], Georg Spinka[1], Michael Lichtenauer[2], Bernhard Wernly[2], Vera Paar[2], Uta Hoppe[2], Jeanette Strametz-Juranek[1], Michael Sponder[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Paracelsus Private Medical University, Salzburg, Austria

Background: Various biomarkers have been associated with the extent of coronary calcification resulting in significant coronary artery disease (CAD) and ischemic heart failure. The aim of this study was to investigate the course of serum plasma levels of suPAR, GDF-15, H-FABP and sST2 in CAD patients with and without reduced ejection fraction (EF).

Methods: CAD patients were divided into three groups according to their EF as measured by biplane Simpson method (84–53%, 52%–31%, £ 30%). Results were compared to a control group of healthy adults.

Results: In total, 361 subjects were analyzed. 155 CAD patients had an EF of 84–53%, 71 patients of 52–31% and 23 patients of £ 30% compared to 112 controls (age 51.3 ± 9.0 years, 44.6% female). Mean age according to EF was 62.1 ± 10.9, 65.2 ± 10.1, 66.6 ± 8.2 years, with a female proportion of 29.0, 29.6 and 13.0%, respectively. Serum levels of suPAR, GDF-15, H-FABP and sST2 were significantly higher in CAD patients compared to the control group and showed an exponential increase with decreasing EF (Table 1). In a multiple logistic regression model, serum levels of GDF-15 ($p=0.009$) and NT-brain natriuretic peptide ($p=0.003$) were independently associated with EF, adjusted for age, sex and body mass index.

Conclusions: Cardiovascular biomarkers such as suPAR, GDF-15, H-FABP and sST2 are increased in CAD patients, especially in highly impaired EF. Besides NT-proBNP as a well-known marker for risk prediction in this population, GDF-15 may provide an additional tool for diagnosis and clinical follow-up.

7-2

Pro-inflammatory macrophage polarization enhances neutrophil extracellular trap degradation

Patrick Haider, Julia Mayer, Christoph Kaun, Michael B. Fischer, Christian Hengstenberg, Walter Speidl, Johann Wojta, Philipp Hohensinner

Medical University of Vienna, Vienna, Austria

Background: Macrophages are versatile phagocytic cells, which can be polarized into different functional subsets through stimulation with pro- or anti-inflammatory cytokines. Intravascular thrombi contain neutrophil extracellular traps and these DNA-rich clots cannot be lysed completely through fibrinolytic drugs. It has been shown that macrophages are capable of infiltrating thrombi and degrade fibrin, but their ability of degrading neutrophil extracellular traps has not been studied intensively yet. Aim: To evaluate the capacity of individual macrophage subsets for clearing extracellular neutrophil traps and to identify the related enzymes and pathways.

Methods: Fresh human monocytes were differentiated into macrophages and polarized into pro-inflammatory M1 (via lipopolysaccharide and interferon-γ) and regulatory M2 (via interleukin-4 and interleukin-13) subsets. Neutrophil extracellular trap degradation was assessed in an in vitro assay by seeding differently polarized macrophages onto neutrophil extracellular traps. Secreted DNases were analyzed by a conditioned culture medium experiment, using the supernatant of individual macrophage subsets. Furthermore, DNase 1, DNase 2, DNase 1L3 and TREX1 were analyzed by fluorescence-immu-

Table 1 | 7-1

	Control ($n=112$)	EF 84–53% ($n=155$)	EF 52–31% ($n=71$)	EF ≤ 30% ($n=23$)
sST2 (pg/ml)	6476 ± 2916	7417 ± 5404	8771 ± 6082	9632 ± 6346
hFABP (ng/ml)	2.54 ± 4.16	3.84 ± 7.80	4.75 ± 5.75	5.92 ± 4.48
GDF-15 (pg/ml)	699 ± 554	1500 ± 1337	1975 ± 1405	3173 ± 3008
suPAR (pg/ml)	1852 ± 759	2178 ± 1108	2851 ± 1260	3181 ± 1387
proBNP (ng/l)	58 ± 103	1239 ± 3298	2843 ± 4306	7041 ± 8791
Mean EF (%)		63	45	23

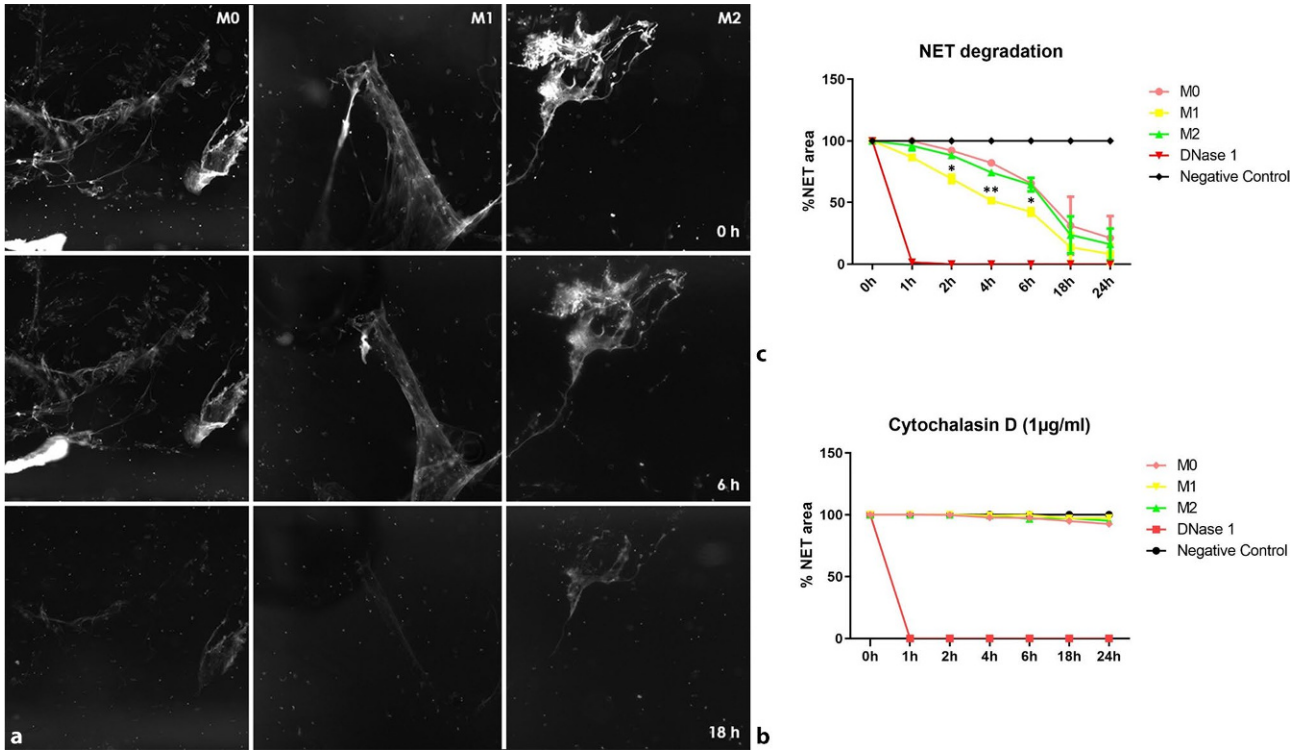


Fig. 1|7-2

nohistochemistry, quantitative ELISA and qPCR. Statistical analysis was performed in GraphPad Prism 8.

Results: Pro-inflammatory polarization of human monocyte-derived macrophages led to significantly accelerated and enhanced degradation of neutrophil extracellular traps (Fig. 1a & 1b). Inhibition of phagocytosis via 1 µg/ml Cytochalasin D resulted in nearly complete abolishment of the neutrophil extracellular trap degradation in all three macrophage subsets (Fig. 1c). Concordantly, the expression of the intracellular exonuclease TREX1 as well as the intracellular amount of DNase 1 were significantly increased after pro-inflammatory stimulation. These increased levels of intracellular nucleases were not followed by an increased secretion of DNases into the supernatant. Extracellular DNase 1 and DNase 1L3 amounts were quantified by sandwich ELISA, but there was no significant difference between the individual subsets.

Conclusions: Pro-inflammatory polarization enhances the ability of macrophages to degrade neutrophil extracellular traps and this degradation mainly occurs through phagocytosis and intracellular nucleases, because antagonizing phagocytosis through Cytochalasin D abolished nearly all degrading activity in this in vitro setting.

7-3

Echinococcus multilocularis induces proliferation of human umbilical vein endothelial cells in vitro

Christoph Kaun[1], Kariem Mahdy Ali[2], Johann Wojta[1], Philipp Hohensinner[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Medical University of Graz, Graz, Austria

Background: Echinococcus multilocularis (E. multilocularis) is a helminthic parasite. In alveolar echinococcosis tumor-like cysts grow beyond the organic borders and invade attached organs. Successful metazoan parasitism, among many other factors, requires a supply of nutrients and the removal of waste products. Similar to a tumour, successful parasitic growth might therefore be linked to neovascularization of the surrounding tissue.

Methods: E. multilocularis cysts were harvested from previously infected mice and homogenized. Human umbilical vein endothelial cells (HUVEC) were treated with the centrifuged extract at different concentrations for 72 hours. Cell proliferation, migration and cell organization was quantified. Angiogenic proteins were screened using a commercially available protein screening tool.

Results: Histochemical stainings of human cysts demonstrated a network of endothelial cells around the cyst. In vitro analysis of the effect of E. multilocularis cysts extracts revealed a strong induction of proliferation. In addition, cyst extract promoted the organization of endothelial cells on an extracellular matrix layer. However, migration was not affected by the extract. To determine if the cyst extract is capable of inducing a proangiogenic response in endothelial cells we used a screening approach. We found an induction of IL-8 protein levels after cyst extract stimulation.

Conclusions: Our results indicate that echinococcal cyst extract induces proliferation and tube formation of human endothelial cells in vitro. This proliferation induction could be due to the induction of IL-8.

7-4

Functional reduction of the pacemaker current If in left and right atrial appendages in atrial fibrillation

Susanne Scherübel[1], Eva Bernhart[2], Chintan Koyani[3], Petra Lang[1], Heinrich Mächler[4], Klaus Zorn-Pauly[1], Brigitte Pelzmann[1]

[1]Biophysics, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria
[2]Molecular Biology and Biochemistry, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria
[3]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[4]Department of Cardiothoracic Surgery, Medical University of Graz, Graz, Austria

Background: Atrial fibrillation (AF) is a highly prevalent arrhythmia and characterized by structural and electrical remodeling. There is a variety of pathophysiological factors contributing to the initiation and progression of AF, among them calcium-handling abnormalities and alterations of ionic currents. In the present study the contribution of the pacemaker current If and the inward rectifier current IK1 to the electrical remodeling process is investigated. These two currents are compared regarding their expression and functionality in tissue samples from patients in the sinus rhythm (SR) or suffering from chronic AF.

Methods: Right atrial appendages (RAA) and left atrial appendages (LAA) of patients undergoing cardiac surgery were collected and used for the PCR experiments. For the electrophysiological investigations single cells were isolated from the LAA and RAA. Patch-clamp experiments were performed in the whole cell patch clamp technique.

Results: In AF, the HCN mRNAs encoding If channels are reduced as well as their regulating microRNAs mir-1 and mir-133a. The pacemaker current shows a diminished current density and the voltage dependence of activation is shifted to more negative membrane potentials. IK1 gains function in AF since both, expression levels and current densities are increased.

Conclusions: The impairment of the pacemaker current might reflect a compensatory mechanism which renders the tissue less susceptible to ectopic activity since the amount of positive inward charge through the If channel is diminished at the resting phase of the action potential.

7-5

Sirtuin 5 deficiency exaggerates myocardial ischemia reperfusion injury

Constantin Witt[1], Christoph Koentges[2], Katharina Pfeil[3], Christoph Bode[2], Andreas Zirlik[3], Heiko Bugger[3]

[1]West German Heart and Vascular Center Essen, University Hospital, Essen, Germany
[2]Heart Center Freiburg University, Freiburg-Bad Krozingen, Freiburg, Germany
[3]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Sirtuin 5 (SIRT5) is a mitochondrial NAD+-dependent protein deacylase which regulates the enzymatic activity of numerous mitochondrial proteins due to increased succinylation and malonylation, including enzymes of energy substrate oxidation and mitochondrial antioxidant enzymes. Since energy depletion and mitochondrial oxidative stress contribute to myocardial ischemia reperfusion (IR) injury, it was our objective to evaluate the potential role of SIRT5 in IR injury.

Methods: Mice with cardiomyocyte-selective deletion (SIRT5-/-) or overexpression (SIRT5 TG) of SIRT5 were subjected to IR in Langendorff heart perfusions.

Results: LV developed pressure or dp/dt max were similar between 8 week-old SIRT5-/- mice and wildtype (WT) littermates. However, recovery of LV developed pressure and dp/dt max following ischemia was lower by 34% and 20% in SIRT5-/- mice compared to WT littermates, respectively (all $p<0.05$). In contrast, postischemic recovery of cardiac function was not impaired and even improved in SIRT5 TG mice compared to WT mice undergoing IR. Mitochondrial reactive oxygen species generation was increased in SIRT5-/- hearts compared to WT hearts following IR, and mitochondria-targeted antioxidant treatment using MnTBAP during heart perfusion completely normalized recovery of contractile function in SIRT5-/- mice following IR.

Conclusions: Thus, lack of SIRT5 aggravates myocardial IR injury, likely by increasing mitochondrial oxidative stress. Increasing SIRT5 activity may thus represent a promising therapeutic strategy to attenuate myocardial IR injury.

7-6

Tissue factor induction in macrophages is dependent on alternative polarization

Julia Mayer[1], Christoph Kaun[1], Walter Speidl[1], Kurt Huber[2], Johann Wojta[1], Philipp Hohensinner[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]3rd Medical Department, Cardiology and Intensive Care Medicine, Wilhelminenhospital, Vienna, Austria

Background: Tissue factor (TF) is a key mediator of coagulation. It is mostly secreted bound to extracellular vesicles and activates factor Xa in complex with factor VIIa. Macrophages have been implicated in coagulation, however the polarization required for TF induction remain unknown.

Methods: Human macrophages were derived from circulating monocytes using M-CSF and polarized towards classical activation using LPS and IFN-gamma (M1) and towards alternative polarization using IL-4 and IL-13 (M2).

Results: Extracellular vesicle production is induced in macrophages by alternative polarization but not by classical activation. M2 show increased shedding of total extracellular vesicles and phosphatidylserine positive extracellular vesicles. The extracellular vesicles contain more TF protein and show increased TF activity after alternative polarization. The induction of TF in M2 macrophages is dependent on STAT6 signaling and PARP14 ribosylation. Whereas monocytes upregulate TF after stimulation with LPS and IFN, macrophages did not react to this stimulation. However, this is not due to M-CSF dependent macrophage differentiation, as GM-CSF derived macrophages show a similar inability to upregulate TF after classical activation and significant upregulation after alternative polarization. We found increased methylation of the NF-kB response element of the TF promoter in macrophages compared to monocytes.

Using a demethylation agent we were able to restore the induction of TF by LPS and IFN indicating an epigenetic regulation of TF after macrophage polarization.

Conclusions: Overall, our data demonstrate a dependency on alternative polarization for increased TF expression in macrophages. This is due to an epigenetic altering within the promoter region of TF. We therefore conclude that alternatively activated macrophages display an increased coagulatory phenotype.

7-7

Effects of ranolazine on inflammation, coagulation and atherosclerotic plaque progression

Max Lenz[1], Zorica Krivaja[1], Philipp Hohensinner[1], Konstantin Krychtiuk[1], Christoph Kaun[1], Sabine Rauscher[2], Stefan Stojkovic[1], Kurt Huber[3], Johann Wojta[1], Walter Speidl[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Skin & Endothelium Research Division, Medical University of Vienna, Vienna, Austria
[3]3rd Medical Department, Cardiology and Intensive Care Medicine, Wilhelminenhospital, Vienna, Austria

Background: Cardiovascular diseases remain the leading cause of death in Europe and the western world. Taking the magnitude of the population at risk in to account it is not surprising to see that chronic angina pectoris affects a huge number of patients every year. During the last decades, several drugs were introduced in order to provide symptom-relief for those patients. Ranolazine, a piperazine derivative and inhibitor of late sodium channels is one of them. Despite the substantial reduction of symptoms and rather good tolerance of the drug overall, there is no available data on ranolazines effect on the underlying atherosclerotic pathomechanism of angina pectoris. So the objective of this project was to illuminate ranolazines effects on inflammation and atherosclerotic plaque formation in vitro as well as in vivo.

Methods: Human umbilical vein endothelial cells (HUVEC) were stimulated with interleukin-1β (IL-1β: 200 U/ml) and treated with ranolazine (500 μM) for 2–24 hours. Expression of adhesion molecules (ICAM-1, VCAM-1, E-selectin) and tissue factor (TF) was measured using flow cytometry as well as real time-PCR. Interleukin 6 (IL-6), interleukin 8 (IL-8) and phospho-I-kappa-B-alpha was quantified by specific enzyme-linked immunosorbent assays. Furthermore, 26 male Ldlr –/– mice (C57BL/6 background) were divided in two groups of equal size and fed high-fat diet starting at the age of 12 weeks. Beginning at the age of 18 weeks, one group receiving ranolazine (300 mg/kg/day) administered through the drinking water, whereas the other group received regular tap water and served as control. All animals were sacrificed at the age of 26 weeks. Subsequently the atherosclerotic plaque was analysed via En Face and cross-sections of the aortic root. IHC-stainings were performed in order to quantify plaque size as well as composition.

Results: Treatment with ranolazine strongly attenuated IL-1β-induced expression of adhesion molecules, TF, IL-6 and IL-8 in vitro. Furthermore, phospho-I-kappa-B-alpha was significantly reduced. Mice receiving ranolazine displayed a significantly smaller plaque-covered area (EnFace: 5.94% ± 2.88 vs. 9.13% ± 3.35, $p < 0.05$) as well as a reduced extent of the plaques' necrotic core (cross-sections: 14.62% ± 6.78 vs. 22.31% ± 10.0, $P < 0.05$).

Conclusions: Our in vitro findings indicate that ranolazine exhibits anti-inflammatory effects on endothelial cells by inhibition of NF-kappa-B. Moreover, our in vivo results suggest that treatment with ranolazine reduces plaque-formation and could lead to increased stability due to a reduced size of the necrotic core.

Postersitzung 8 – Vitien

8-1

Quantification of fluid status using bioelectrical impedance spectroscopy: a predictor of outcome in patients with valvular heart disease

Carolina Donà, Andreas Kammerlander, Barbara Karner, Amelie Keil, Mark Seitlhuber, Franz Duca, Christian Nitsche, Matthias Koschutnik, Christina Binder, Stefan Aschauer, Diana Bonderman, Christian Hengstenberg, Julia Mascherbauer

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Volume overload, which may finally lead to cardiac decompensation, is a major threat in valvular heart disease (VHD) patients. In clinical practice, fluid overload is estimated by evaluation of leg edema, pulmonary congestion, weight gain or distension of jugular veins; however, these parameters lack both specificity and sensitivity. Bioelectrical impedance spectroscopy (BIS) is an easy, non-invasive and reliable way to determine the extent of fluid overload. BIS it broadly used in patients on chronic haemodialysis to guide therapy. Whether fluid status as measured by BIS is associated with outcome in VHD patients without obvious volume overload is unknown.

Methods: Stable patients with moderate or severe VHD as diagnosed by transthoracic echocardiography (TTE) underwent fluid status assessment by BIS at baseline and were prospectively followed. The primary endpoint was a composition of heart failure hospitalisation and cardiovascular death. Kaplan-Meier estimates and multivariable Cox-regression analysis were

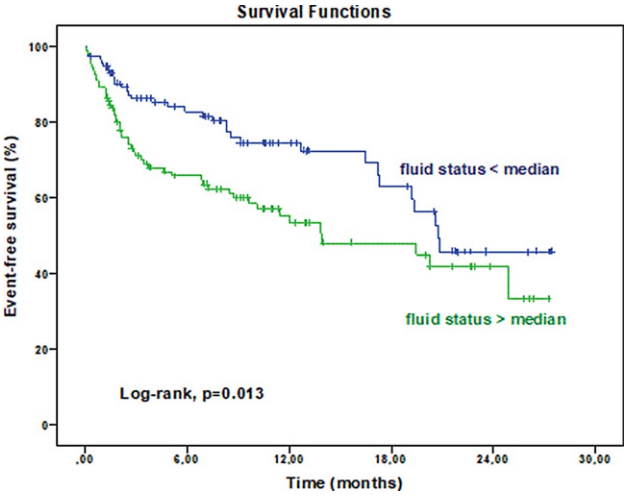


Fig. 1|8-1

used to identify factors associated with outcome. This study was registered at clinicaltrials.gov (NCT03372512).

Results: 232 patients (46.6% female, 72 ± 13 years) were included in the study. 23.7% suffered from aortic stenosis (2.5% moderate, 21.2% severe), 49.6% from mitral regurgitation (21.5% moderate, 28.1% severe). In 61.6% of the patients additional tricuspid regurgitation was present (23.2% moderate, 38.4% severe). Median overhydration (OH) was +0.6 L, and patients were stratified according to this cut-off into two groups. Fluid status by BIS was not associated with diabetes ($p = 0.776$), coronary artery disease ($p = 0.504$), renal function ($p = 0.824$), left ventricular ejection fraction ($p = 0.785$), NYHA functional class ($p = 0.809$), or leg edema ($p = 0.492$). During a follow-up of 8.8 ± 7.5 months a total of 85 events (36.6%) occurred. 71 patients (30.6%) underwent invasive treatment for VHD (either surgical or transcatheter) and were censored at the time of intervention and not treated as an event. Patients with fluid overload (OH ≥ 0.6 L) were more likely to experience an event (log-rank, $p = 0–013$; Fig. 1). By univariable Cox-regression fluid overload was significantly associated with outcome (per 1L: HR 1.152 [1.073–1.236]; $p < 0.001$). In a multivariable Cox-regression model correcting for age (HR 0.976 [0.938–1.015], $p = 0.224$), NT-proBNP (logarithmized; HR 1.485 [1.018–2.166], $p = 0.040$), LVEF (HR 0.994 [0.970–1.018], $p = 0.595$), and glomerular filtration rate (HR 0.962 [0.934–0.990], $p = 0.008$), OH remained significantly associated with the primary endpoint (HR 1.231 [1.058–1.433], $p = 0.007$).

Conclusions: Fluid status as determined with BIS is significantly associated with cardiovascular events in patients with significant VHD. This non-invasive technique may be useful as a prognostic tool and may help to guide diuretic as well as invasive treatment.

8-2

High sensitivity troponin T and N-terminal pro brain natriuretic peptide plasma levels predict long-term postoperative survival in 3595 patients with severe aortic stenosis admitted for valve implantation: the Tyrolean Aortic Stenosis Study-2 (TASS-2)

Fabian Barbieri[1], Thomas Senoner[1], Agne Adukauskaite[1], Stephan Dobner[2], Johannes Holfeld[3], Severin Semsroth[3], Thomas Lambert[4], David Zweiker[5], Thomas Theurl[6], Rainer Peter[5], Albrecht Schmidt[5], Gudrun Feuchtner[7], Clemens Steinwender[4], Uta C. Hoppe[6], Florian Hintringer[1], Silvana Müller[1], Michael Grimm[3], Bernhard Pfeifer[8], Wolfgang Dichtl[1]

[1]University Clinic of Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Cardiology, Inselspital, Bern University Hospital, Bern, Switzerland
[3]University Clinic of Heart Surgery, Medical University of Innsbruck, Innsbruck, Austria
[4]Department of Cardiology, Kepler University Hospital, Linz, Austria
[5]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[6]University Clinic of Internal Medicine II, Paracelsus Private Medical University, Salzburg, Austria
[7]University Clinic of Radiology, Medical University of Innsbruck, Innsbruck, Austria
[8]Institute of Electrical and Biomedical Engineering, University for Health Sciences, Medical Informatics and Technology (UMIT), Hall in Tirol, Austria

Background: Optimal timing of valve implantation in patients with severe aortic stenosis (AS) is under debate, considering the subjective nature of symptom onset. We aimed to investigate the pre-procedural value of routinely available cardiac biomarkers in predicting postoperative long-term outcome in a large cohort undergoing either surgical or transcatheter aortic valve implantation.

Methods: The Tyrolean Aortic Stenosis Study-2 (TASS-2) group, a consortium of four university hospital centers in Austria, analysed pre-procedural high-sensitivity troponin T (hsTnT) and N-terminal pro brain natriuretic peptide (NT-proBNP) plasma levels in 3595 patients admitted for valve implantation because of severe aortic stenosis since 2007.

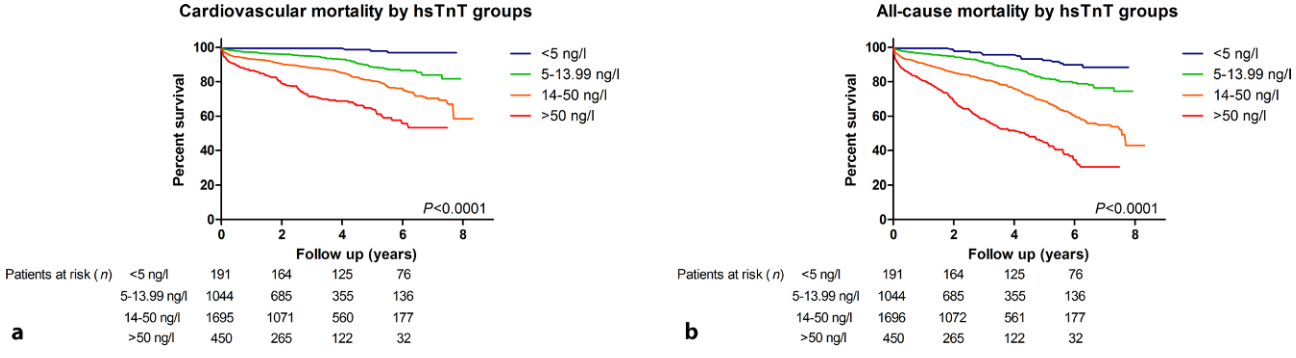


Fig. 1|8-2

Table 1|8-2 Multivariate cox regression analysis for all cause mortality (model #1)

	HR (95% CI)	P value for heterogenity
hsTnT (<5 ng/l as reference)		
hsTnT (5-13.99 ng/l)	1.595 (0.928-2.739)	0.091
hsTnT (14-50 ng/l)	1.821 (1.065-3.112)	0.028
hsTnT (>50 ng/l)	2.803 (1.605-4.894)	<0.001
NT-proBNP (normal range as reference)		
NT-proBNP (1-3 times >normal range)	1.384 (1.057-1.812)	0.018
NT-proBNP (>3 times >normal range)	1.679 (1.294-2.180)	<0.001
STS (<4% as reference)		
STS (4-8%)	1.166 (0.964-1.409)	0.113
STS (>8%)	1.227 (0.896-1.680)	0.201
LVEF (>50% as reference)		
LVEF (30-50%)	1.038 (0.872-1.236)	0.674
LVEF (<30%)	1.216 (0.887-1.667)	0.224
Age	1.028 (1.015-1.040)	<0.001
CAD	1.138 (0.979-1.324)	0.093
Sex (male gender as reference)	0.862 (0.736-1.010)	0.065
Arterial hypertension	1.086 (0.887-1.330)	0.424
Atrial fibrillation	1.567 (1.347-1.823)	<0.001
eGFR	0.993 (0.990-0.997)	<0.001
COPD	1.291 (1.069-1.559)	0.008
Diabetes mellitus	1.060 (0.893-1.258)	0.508
TAVI (SAVR as reference)	1.732 (1.435-2.092)	<0.001

Abbreviations: CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; hsTnT, high sensitivity troponin T; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro brain natriuretic peptide; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.

Table 2|8-2 Multivariate cox regression analysis for all cause mortality (model #2)

	HR (95% CI)	P value for heterogenity
hsTnT (<5 ng/l as reference)		
hsTnT (5-13.99 ng/l)	2.20 (1.29-3.77)	0.004
hsTnT (14-50 ng/l)	4.05 (2.41-6.82)	<0.001
hsTnT (>50 ng/l)	8.63 (5.07-14.70)	<0.001
NT-proBNP (normal range as reference)		
NT-proBNP (1-3 times >normal range)	1.47 (1.13-1.91)	0.004
NT-proBNP (>3 times >normal range)	1.96 (1.54-2.51)	<0.001

Abbreviations: CI, confidence interval; HR, hazard ratio; hsTnT, high sensitivity troponin T; NT-proBNP, N-terminal pro brain natriuretic peptide;

Results: Transcatheter aortic valve implantation was performed in 1517 (42.2%) of patients. During a median follow-up of 2.93 (1.91–4.92) years, 919 patients (25.6%) died, among them 556 (15.5%) due to cardiovascular causes. In multivariate cox regression analysis—adjusting for STS risk score, degree of left ventricular systolic dysfunction, atrial fibrillation, sex, age, renal function, COPD, arterial hypertension, diabetes mellitus, concomitant significant coronary artery disease and type of procedure—pre-procedural hsTnT as well as NT-proBNP plasma levels were strong independent predictors for postoperative survival: hazard ratio [HR] 1.82, 95% confidence interval [CI] 1.07–3.11, P = 0.028 for mildly to moderately elevated hsTnT (14–50 ng/l); HR 2.80, CI 1.61–4.89, P < 0.001 for severely elevated hsTnT (> 50 ng/l); HR 1.38, CI 1.06–1.81, P = 0.018 for mildly to moderately elevated NT-proBNP (defined by an increase of up to threefold of age- and sex-corrected normal range); HR 1.68, CI 1.29–2.18, P < 0.001 for severely elevated NT-proBNP (defined by an increase of more than threefold of age- and sex-corrected normal range). For direct comparison of these two biomarkers a second cox regression model was conducted including only hsTnT and NT-proBNP: HR 2.20, 95% CI 1.29–3.77; P = 0.004 for minimally elevated hsTnT (5–13.99 ng/l). HR 4.05, CI 2.41–6.82; P < 0.001 for mildly to moderately elevated hsTnT (14–50 ng/l). HR 8.63, CI 5.07–14.70; P < 0.001 for severely elevated hsTnT (> 50 ng/l).

Conclusions: hsTnT and NT-proBNP strongly predict long-term postoperative survival in patients with severe AS admitted for valve implantation.

8-3

High-molecular-weight von Willebrand Factor multimer ratio reflects aortic valve calcium burden in patients with low-flow, low-gradient aortic stenosis

Jörg Kellermair[1], Jürgen Kammler[1], Aymann Alsheikh[1], Helmut Ott[2], Hermann Blessberger[1], Christian Reiter[1], Daniel Kiblböck[1], Clemens Steinwender[1]

[1]Department of Cardiology and Internal Intensive Care, Kepler University Hospital, Medical Faculty, Johannes Kepler University Linz, Linz, Austria
[2]Department of Hemostasis/Transfusion Medicine, Ludwig Maximilians University, Munich, Germany; Augsburg, Germany

Background: Low-flow, low-gradient (LF/LG) aortic stenosis (AS) is subclassified into a true-severe and pseudo-severe form using dobutamine-stress echocardiography and/or multidetector computed tomography (MDCT). However, these imaging modalities have significant limitations, therefore, there is a demand for laboratory biomarkers to expand the diagnostic portfolio. Recently, our study group introduced high-molecular-weight (HMW) von Willebrand Factor (VWF) multimer ratio as a novel biomarker for LF/LG AS subclassification. Due to sheer-stress induced cleavage of HMW VWF multimers, this biomarker mirrors hemodynamics at the site of LF/LG AS. The aim of the present study was to highlight its association with the amount of aortic valve calcification.

Methods: 36 consecutive patients with the diagnosis of LF/LG AS (defined by a peak aortic jet velocity < 4 m/s, a mean transvalvular pressure gradient (MPG) < 40 mmHg, an AVA < 1.0 cm^2, a stroke volume index < 35 ml/m^2 and left ventricular ejection fraction (EF) < 50%) were prospectively recruited and underwent quantification of aortic valve calcification by MDCT using imaging software with calcium-scoring module (Somatom Force, syngo.via, Siemens Healthcare, Erlangen, Germany). The multimer pattern was analyzed using a densi-

tometric quantification of Western Blot bands. HMW VWF multimer ratio was calculated by dividing the total number of HMW multimers (defined as bands >15) in a patient sample by the total number in a reference standard.

Results: Study patients had a mean age of 80 ± 10 years and 28/36 (78%) were male gender. Baseline echocardiographic characteristics included a mean EF of 34 ± 10%, mean MPG 27 ± 7 mmHg and a mean AVA 0.81 ± 0.15 cm². Mean aortic valve calcium score was 2530 ± 1218 AU (male: 2835 ± 1183 AU, female: 1462 ± 589 AU). Mean HMW VWF multimer ratio was 0.91 ± 0.26 and values showed a strong negative correlation with aortic valve calcium score (r = –0.5016; $p = 0.0018$). Patients diagnosed with true-severe LF/LG AS ($n = 29$) had a significantly lower HMW VWF multimer ratio and a higher aortic valve calcium score compared to patients with pseudo-severe LF/LG AS ($n = 7$) (HMW VWF multimer ratio 0.86 ± 0.27 vs. 1.09 ± 0.11., $p = 0.0325$; calcium score male patients: 3096 ± 1135 AU vs. 1638 ± 416 AU, $p = 0.0017$; calcium score female patients: 1650 ± 561 AU vs. 895 ± 24 AU, $p = 0.0714$)

Conclusions: HMW VWF multimer ratio negatively correlates with aortic valve calcium score in patients with LF/LG AS. This finding underscores the value of HMW VWF multimer ratio as a diagnostic biomarker.

8-4

Dobutamine stress echocardiography enhances the loss of high-molecular-weight von Willebrand Factor multimers in patients with low-flow, low-gradient aortic stenosis

Jörg Kellermair[1], Sahrai Saeed[2], Helmut Ott[3], Jürgen Kammler[1], Hermann Blessberger[1], Christian Reiter[1], Clemens Steinwender[1]

[1]Department of Cardiology and Internal Intensive Care, Kepler University Hospital, Medical Faculty, Johannes Kepler University Linz, Linz, Austria
[2]Department of Heart Disease, Haukeland University Hospital Bergen, Bergen, Norway
[3]Department of Hemostasis/Transfusion Medicine, Ludwig Maximilians University, Munich, Germany; Augsburg, Germany

Background: Sheer-stress induced cleavage of high-molecular-weight (HMW) von Willebrand Factor (VWF) multimers occurs frequently at the site of low-flow, low-gradient (LF/LG) aortic stenosis (AS). The multimeric structure responds to haemodynamic changes within seconds to minutes, and therefore, may be regarded as a rapid sheer-flow sensor. The aim of the present study was to compare HMW VWF multimeric pattern in patients with LF/LG AS shortly before and shortly after dobutamine stress echocardiography (DSE) to identify a DSE induced HMW VWF multimer degradation.

Methods: Thirty 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 < 1.0 cm², a stroke volume index < 35 ml/m² and left ventricular ejection fraction < 50%) were prospectively recruited and underwent

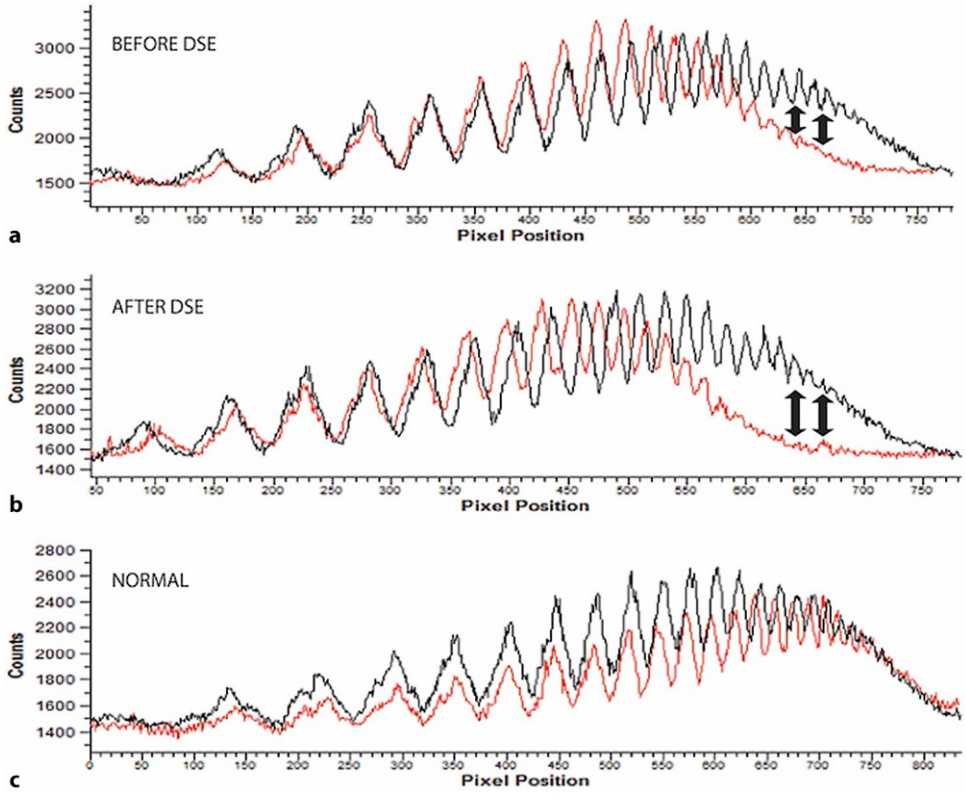


Fig. 1|8-4 Illustration of densitometrical Western Blot band quantification. Top row (a) shows a patient (red color) with HMW VWF multimer deficiency (arrows) immediately before DSE in comparison to a reference standard (black color). The middle row (b) depicts an enhanced loss of HMW VWF multimers in the same patient immediately after DSE. The bottom row (c) illustrates a normal HMW VWF multimer pattern in a healthy individual

Table 1|8-4

Baseline patient characteristics	(n = 30)
Age (mean years ± SD)	78 ± 11
Male Gender (%)	24/30 (80%)
Diabetes (%)	8/30 (26.7%)
Coronary artery disease (%)	19/30 (63.3%)
Baseline echocardiographic data	
Indexed stroke volume (mean ml/m² ± SD)	30 ± 5
Mean aortic gradient (mean mmHg ± SD)	23 ± 5
Mean peak transvalvular flow velocity (mean m/s ± SD)	3.1 ± 0.3
Echocardiographic data during final DSE stage	
Indexed stroke volume (mean ml/m² ± SD)	39 ± 9
Mean aortic gradient (mean mmHg ± SD)	36 ± 9
Mean peak transvalvular flow velocity (mean m/s ± SD)	4.0 ± 0.4
Baseline laboratory characteristics	
Hemoglobin (mean g/dL ± SD)	13.1 ± 2.2
VWF:Ag (mean % ± SD)	234 ± 104
VWF:GPIbM (mean % ± SD)	208 ± 74
HMW VWF multimer ratio (mean ± SD)	0.87 ± 0.27

low-dose DSE according to a standard protocol (2.5, 5, 10, 15, 20 µg/kg/min given at 5-minute intervals). Blood was drawn immediately before DSE and immediately after final DSE stage. The multimer pattern was analyzed using a densitometric quantification of Western Blot bands. HMW VWF multimer ratio was calculated by dividing the total number of HMW multimers (defined as bands >15) in a patient sample by the total number in a reference standard.

Results: Mean HMW VWF multimer ratio shortly after DSE was significantly lower compared to baseline levels (0.840 ± 0.31 vs. 0.870 ± 0.27; $p = 0.031$) in all patients. In detail, 6 out of 30 (20%) patients showed an enhanced loss of HMW VWF multimers after DSE. These 6 patients were characterized by significantly higher mean transvalvular pressure gradients during final DSE stage (47 ± 8 mmHg vs. 33 ± 8 mmHg; $p < 0.001$) and tended to have a higher contractile reserve (indexed stroke volume increase 44 ± 22% vs. 25% ± 17%; $p = 0.058$) compared to patients who did not feature different multimeric patterns at the two time-points. Both, baseline mean HMW VWF multimer ratio and mean HMW-VWF multimer ratio after DSE, showed a strong negative correlation with mean transvalvular pressure gradients during final DSE stage (r = –0.707; 95%CI –0.853 to –0.456; $p < 0.001$ and r = –0.712; 95%CI –0.856 to –0.464; $p < 0.001$).

Conclusions: DSE enhances the loss of HMW VWF multimers in a subgroup of patients with LF/LG AS. This finding underscores the value of HMW-VWF multimer ratio to reflect haemodynamics at the site of LF/LG AS which may have a diagnostic and prognostic implication.

8-5

Transaortic valve implantation leads to excellent outcome compared to surgical aortic valve replacement in patients aged younger than 75 years with high perioperative risk

Markus Mach[1], Ursula Slakov[1], Christian Wallmüller[2], Christoph Keil[2], Peter Stratil[2], Andreas Strouhal[2], Georg Delle-Karth[2], Gabriel Weiss[1], Martin Grabenwöger[1], Christopher Adlbrecht[2], Andreas Schober[2]

[1]Department of Cardio-Vascular Surgery, Hospital Hietzing, and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Fourth Medical Department, Hospital Hietzing, and the Karl Landsteiner Institute for Cardiovascular & Intensive Care Research, Vienna, Austria

Background: Transaortic valve implantation (TAVI) is increasingly performed in patients suffering from aortic valve stenosis at high or intermediate surgical risk at younger age levels. The aim of this study was to assess procedural short and long-term outcomes in a propensity score matched comparison of high risk patients aged 75 years or less receiving either surgical aortic valve replacement (SAVR) or TAVI.

Methods: 840 patients with a maximum age of 75 years were treated for severe aortic valve stenosis admitted to our heart center between 2005 and 2016. Propensity score matching was used to achieve two balanced cohorts. Patients were matched for sex, age, BMI, renal function, CVD, LVEF, diabetes mellitus, peripheral vascular disease and pulmonary disease. The primary study endpoint was 30-day mortality as defined by the VARC-2 criteria. Median follow-up was 5.0 years (2.2 –14.1 years).

Results: Out of 840 eligible patients 166 (26%) were included (TAVI $n = 83$ and SAVR $n = 83$). Overall 73 (44%) patients were female (TAVI 40 (48%) vs. SAVR 33 (40%); $p = 0.174$) with a mean age of 68.7 years (TAVI 68.2 y vs. SAVR 68.0 y; $p = 0.833$) and a log EuroSCORE of 11% (TAVI 13.3% vs. SAVR 8.0%; $p = 0.071$). Overall postprocedural adverse event data showed higher rates of AV conduction delay in the TAVI cohort (7 (8.4%) vs. 1 (1.2%); $p = 0.016$) and higher rates of newly acquired atrial fibrillation (4 (4.8%) vs. 15 (18.1); $p = 0.007$), prolonged ventilation (2 (2.4%) vs. 14 (16.9%); $p = 0.001$) and multi organ failure (0 (0%) vs. 5 (6.0%); $p = 0.029$) in the SAVR cohort. While procedural as well as 30-day mortality was significantly higher in the SAVR cohort (0 (0%) vs. 8 (9.6%); $p = 0.001$; 9 (10.8%) vs. 1 (1.2%); $p = 0.009$, respectively), the long-term survival of SAVR patients was superior to TAVI (log rank: $p = 0.037$).

Conclusions: Whereas the overall outcome data of our analysis match the known advantages and disadvantages of both procedures, TAVI proves to be a safe therapy option for young high-risk patients with lower perioperative and short-term mortality compared to SAVR. The superior long-term survival for SAVR might be attributed to the lower comorbidity and risk profile but needs to be vetted in a randomized trial setting.

8-6

Mid-term results with the perceval bioprosthesis for surgical treatment of severe aortic valve stenosis

Vera Hergesell, Nadine Kernspecht, Alissa Strugger, Sotirios Spiliopoulos, Helmut Suppan, Peter Oberwalder, Igor Knez, Otto E. Dapunt

Medical University of Graz, Graz, Austria

Background: We report our mid- term experience with the Perceval sutureless Bioprosthesis (LivaNoVa PLC, London, UK) for aortic valve replacement in cases of severe aortic stenosis.

Methods: From September 2017 to April 2018 the Perceval prosthesis was implanted in 100 patients (female: 51%/median age: 72; range 57–84 years/median logistical Euroscore II: 4.8; range 1.7–12.8) due to severe aortic valve pathology. 62% of the procedures were performed through a limited surgical access (right anterior minithoracotomy: 38%, hemisternotomy: 24%). Evaluation of data was performed retrospectively and was approved by institutional review board. Patients with concomitant procedures were not included in this study cohort.

Results: Median aortic cross-clamp time was 44 minutes (range 26–84 minutes) in the overall cohort and was longer in patients treated by a limited surgical access compared to patients with a conventional sternotomy (right anterior minithoracotomy: 45 min; range: 36–84 minutes; p: 0.06/hemisternotomy: 49 minutes; range: 32–78 minutes; p: 0.01). Overall 30 days mortality was 2%. At follow- up (median: 31 months; range: 11–64 months) cardiac related mortality was 0%. Thromboembolic or hemorrhagic events and cases of prosthesis endocarditis were not documented.

Conclusions: In our experience the Perceval bioprosthesis demonstrated easy implantability and an excellent safety profile at mid-term follow- up.

8-7

Klinische Ergebnisse nach Implantation der Medtronic Avalus Aortenklappenbioprothese

Vera Hergesell, Julia Kleinhapl, Markus Mach, Ayse Gürbüz, Phillipp Hölzl, Sotirios Spiliopoulos, Otto E. Dapunt

Medizinische Universität Graz, Graz, Österreich

Grundlagen: Wir berichten unsere Erfahrungen mit der Avalus Aortenklappenprothese (Medtronic, Minneapolis, MN, USA), einer neuen gestenteten pericardialen Prothese zum Ersatz der nativen Aortenklappe. Eine rezente Studie zeigte exzellente hämodynamische Eigenschaften und hervorragende klappenbezogene Ergebnisse im Beobachtungszeitraum. Für die Beobachtungsstudie liegt ein positives Ethikvotum vor.

Methodik: Es wurden alle Patienten in die Studie eingeschlossen, die aufgrund einer hochgradigen Aortenklappenstenose im Zeitraum von November 2017 bis Jänner 2019 einen Aortenklappenersatz mit der Medtronic Avalus erhielten. Die Gesamtanzahl der Patienten betrug 77 Personen, wobei 23 Patienten (29,3 %) weiblich waren. Knapp die Hälfte der Patienten ($n=36$, 46,8 %) unterzogen sich einem isolierten Aortenklappenersatz. Bei den Kombinationseingriffen erfolgte der Aortenklappenersatz im Rahmen einer koronaren Revaskularisation ($n=28$, 36,4 %). Unter den übrigen 16,98 % befanden sich Patienten mit zwei oder mehr Herzklappenvitien. Die Mehrzahl der Operationen ($n=48$, 72,7 %) wurden mittels medianer Sternotomie durchgeführt. Acht (15,2 %) Patienten wurden mittels einer rechts-anterioren Minithorakotomie und acht (12,1 %) durch eine partielle obere Sternotomie operiert.

Ergebnisse: Die mittlere Aortenklemmzeit bei isoliertem Aortenklappenersatz betrug bei der medianen Sternotomie 78,5 min (50–174 min). Die Aortenklemmzeit bei der rechts-anterioren Minithorakotomie war mit 66 min im Mittel geringer (40–105 min). Die mittlere Aortenklemmzeit bei der Hemisternotomie betrug im Median 84,5 min (58–103 min). Die zum Zeitpunkt der Datenerhebung vorliegende Nachbeobachtung von 57 Patienten zeigte einen mittleren transvalvulären Gradienten vom 8 mmHg (3–19 mmHg). Der maximale Gradient wurde mit durchschnittlich 16 mmHg (6–29 mmHg) berechnet. Eine zentrale Leckage trat bei nur 1,7 % der Patienten auf. Es wurden keine neurologische oder Blutungskomplikationen dokumentiert.

Schlussfolgerungen: Nach unserer Erfahrung ist die Medtronic Avalus Aortenklappenbioprothese eine sichere und einfach zu implantierende Prothese, die sowohl exzellente hämodynamische Eigenschaften bei einem sehr niedrigen Auftreten einer zentralen Leckage als auch ein sehr gutes Sicherheitsprofil aufweist.

Postersitzung 9 – Herzinsuffizienz 2

9-1

Influence of potassium levels on outcome in patients with heart failure and preserved ejection fraction

Öztürk Begüm, Franz Duca, Christina Binder, Stefan Aschauer, Christophe D. J. Capelle, René Rettl, Julia Mascherbauer, Diana Bonderman

Medical University of Vienna, Vienna, Austria

Background: Previous studies could demonstrate the prognostic significance of serum potassium levels in heart failure (HF) patients. However, studies investigating the association of serum potassium levels with prognosis or clinical parameters in patients with HF and preserved ejection fraction (HFpEF) have not yet been examined well. 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: Consecutive 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 October 2018, 363 HFpEF patients were included into our study. Median age of the study population was 73.0 years [Interquartile range (IQR): 67.0–77.0], 251 (69.1%) were female, median N-terminal prohormone of brain natriuretic peptide(NT-proBNP) levels were 1039 pg/mL (IQR: 412–1972) and 208 (57.3%) were in New York Heart Association class ≥ III. Median level potassium was

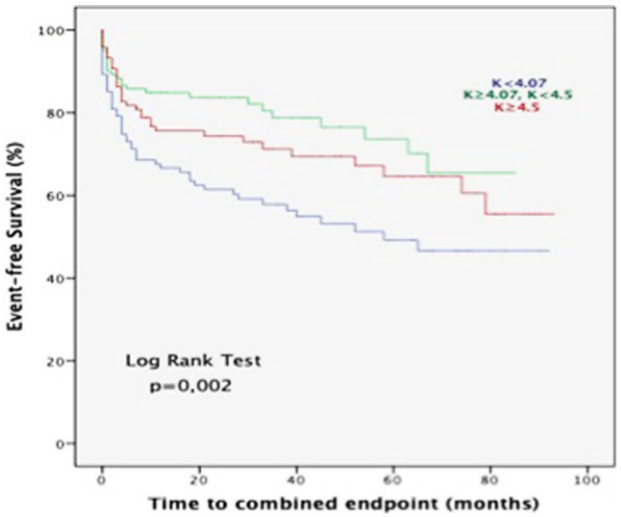


Fig. 1|9-1 Kaplan-Meier curves stratified by baseline potassium level for the combined endpoint cardiac death or heart failure hospitalization in patients with heart failure and preserved ejection fraction. 1st tertile: < 4.07 mmol/L, 2nd tertile: ≥ 4.07 mmol/L – < 4.5 mmol/L, 3rd tertile: ≥ 4.5 mmol/L

4.3 mmol/L (IQR: 4.0–4.6). 14 (3.9%) patients had hypokalemia (< 3.5 mmol/L), 37 (10.2%) had hyperkalemia (≥ 5.0 mmol/L) and 312 (86%) were normokalemic (≥ 3.5—< 5.0 mmol/L). 114 (31.4%) patients experienced the combined endpoint. Patients were grouped according to potassium tertiles tertiles (< 4.07 mmol/L, ≥ 4.07 mmol/L—< 4.5 mmol/L and, ≥ 4.5 mmol/L). Significant differences between the groups were detected with regards to estimated glomerular filtration rate [64.2 ml/min/1.73 m^2 (IQR: 49.1–75.6) versus 59.3 ml/min/1.73 m^2 (IQR: 46.9–79.1) versus 53.4 ml/min/1.73 m^2 (IQR: 39.2–66.1), ($p = 0.001$)], the combined endpoint [$n = 53$ (46.5%) versus $n = 26$ (22.8%) versus $n = 35$ (30.7%), $p = 0.001$)]. 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): 1.876, 95% confidence interval (CI): 1.300–2.706, $p = 0.006$] as well as in multivariable analyses (HR: 1.580, 95% CI: 1.056–2.363, $p = 0.026$).

Conclusions: We conclude that low serum levels of potassium (< 4.07 mmol/L) significantly predict adverse outcome in HFpEF patients; sudden cardiac death and heart failure hospitalization have been shown most often in lowest potassium tertile.

9-2

High mortality in HFrEF is independent of heart failure etiology

Elisabeth Vikoler[1], Florian Kocher[2], Alexandra Bair[1], Alex Kaser[1], Sven Dengler[1], Romina Bernardi[1], Mikael Klassnitz[1], Jakob Dörler[1], Marc-Michael Zaruba[1], Christine Mussner-Seeber[1], Gerhard Pölzl[1]

[1]University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Internal Medicine V (Haematology and Oncology), Medical University of Innsbruck, Innsbruck, Austria

Background: Heart failure can be classified into three different categories depending on the left ventricular ejection fraction: HFpEF, HFmrEF and HFrEF. Preserved ejection fraction is defined as EF ≥ 50%, mid-range ejection fraction as EF 40–49% and reduced ejection fraction as EF ≤ 39%. It was the aim of our study to investigate differences in long-term mortality in these heart failure entities with special consideration of the underlying etiology.

Methods: In this single-centre registry study we analysed 2181 patients with heart failure diagnosed between 2000 and 2018 and treated according to prevailing guidelines. CMPs were arranged after etiology in different subtypes: ischemic (25.7%), idiopathic (25.4%), hypertensive (15.3%), inflammatory (14.5%), cardiac amyloidosis (6.6%), toxic (4.4%), HCM (4.4%) and valvular (3.6%). Primary endpoint was death of any cause. 5- and 10-year mortality rates for patients with HFpEF, HFmrEF and HFrEF were estimated with the Kaplan-Meier estimator. Cox regression analysis was used to estimate the hazard for mortality in HFrEF, compared with HFmrEF and HFpEF.

Results: Median follow-up was 87 months (IQR 44–138). 5-year mortality in the whole cohort was 19.4% (AL-amyloidosis 64%, ATTR-amyloidosis 48.7%, ischemic CMP 27.3%, toxic CMP 22.3%, valvular CMP 20.1%, hypertensive CMP 18.9%, idiopathic CMP 14.7%, HCM 7.2%, and inflammatory CMP 6.9%). 5- and 10-year mortality rates of individuals with HFrEF (20.1%/37%) were significantly higher compared with HFpEF (15.5%/26.2%) and HFmrEF (14%/25%) ($p < 0.001$). No differences where seen between preserved and mid-range ejection fraction. In a multivariable model adjusting for etiology, age, and gender individuals with HFrEF were 1.4 times ([95%CI 1.08–1.87]; $p = 0.012$) more likely to die than were individuals with HFmrEF and HFpEF.

Conclusions: Data from this single-centre registry indicate that long-term mortality is high in patients with HFrEF. No differences were found between HFmrEF and HFpEF. Worse prognosis in HFrEF is independent of the underlying etiology, age, and gender. Further studies are needed to define possible differences in mode of death.

9-3

Die Rolle von Komorbiditäten bei Patienten mit chronischer Herzinsuffizienz

Sven Dengler[1], Romina Bernardi[1], Florian Kocher[2], Alexandra Bair[1], Elisabeth Vikoler[1], Mikael Klassnitz[1], Alex Kaser[1], Jakob Dörler[1], Marc-Michael Zaruba[1], Christine Mussner-Seeber[1], Gerhard Pölzl[1]

[1]Universitätsklinik für Innere Medizin III (Kardiologie und Angiologie), Medizinische Universität Innsbruck, Innsbruck, Österreich
[2]Universitätsklinik für Innere Medizin V (Hämatologie und Onkologie), Medizinische Universität Innsbruck, Innsbruck, Österreich

Grundlagen: Komorbiditäten sind häufige Komplikation bei Patienten mit chronischer Herzinsuffizienz und stellen einen Risikofaktor für den Langzeitverlauf dar. Es war das Ziel dieser Untersuchung, den Einfluss häufiger Komorbiditäten auf

den Langzeitverlauf in einem großen Kollektiv von Patienten mit chronischer Herzinsuffizienz zu untersuchen.

Methodik: In dieser Untersuchung des Innsbrucker Kardiomyopathie-Registers wurden 2292 Patienten analysiert, die zwischen 2000 und 2018 eingeschlossen und gemäß den geltenden Richtlinien für chronische Herzinsuffizienz behandelt wurden. Bei 1464 (63,9 %) Patienten konnten Informationen zu den fünf häufigsten Komorbiditäten (arterieller Hypertonus [52,3 %], Diabetes mellitus [19,7 %], eingeschränkte Nierenfunktion [eGFR < 60, 25,6 %], Unter- bzw. Übergewicht [BMI < 18,6, 2,4 % bzw. > 29,9, 16,7 %] und Vorhofflimmern [18,8 %]) erhoben werden. Keine Komorbidiät fand sich bei 25,7 %, eine bei 32,7 %, zwei bei 27,5 %, drei bei 11,1 %, vier bei 2,8 % und fünf bei 0,2 % der Patienten. Die Beobachtungszeit betrug 111 (IQR 55–144) Monate. Primärer Endpunkt war der Tod jeglicher Ursache.

Ergebnisse: In der univariaten Cox-Regressionsanalyse waren Hypertonie, Diabetes mellitus, eingeschränkte Nierenfunktion, Vorhofflimmern und Untergewicht jeweils signifikant mit dem Endpunkt assoziiert. Das Vorliegen von ≥ 2 Komorbiditäten war mit einem 1,5-fach höherem Mortalitätsrisiko (CI 1,33–1,80, P < 0,001) verbunden. In einem multivariaten Model war diese Assoziation unabhängig von Alter, Geschlecht und Ätiologie der zugrundeliegenden Kardiomyopathie.

Schlussfolgerungen: Das Vorliegen von Komorbiditäten bei Patienten mit chronischer Herzinsuffizienz ist mit einem erhöhten Mortalitätsrisiko verbunden. Die exakte Erfassung von Komorbiditäten sowohl bei der Erstuntersuchung als auch im weiteren Verlauf ist daher sinnvoll. Zukünftige Studien müssen zeigen, ob sich die eingehende Behandlung von Komorbiditäten günstig auf das Langzeitüberleben auswirkt.

9-4

Pericardial and pleural effusion in patients with cardiac amyloidosis

Christina Binder[1], Franz Duca[1], Stefan Aschauer[1], René Rettl[1], Luciana Camuz Ligios[1], Fabian Dusik[1], Christophe Capelle[1], Hermine Agis[2], Renate Kain[1], Christian Hengstenberg[1], Diana Bonderman[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Division of Oncology, Department of Internal Medicine I Medical University of Vienna, Vienna, Austria

Background: Pericardial and pleural effusion are common findings in patients with cardiac amyloidosis (CA). While this might be suggestive of a sign of right heart failure, it is not known, whether effusions correlate with right ventricular (RV) function in patients with CA. Furthermore, data on the prognostic significance of pleural and pericardial effusion in CA is scarce.

Methods: Patients with cardiac transthyretin (ATTR) and light chain (AL) amyloidosis were included in a clinical registry at our dedicated CA outpatient clinic. CA was diagnosed according to current guidelines. All patients underwent a comprehensive transthoracic echocardiography (TTE) exam at the time of study inclusion. The TTE protocol included standard and advanced parameters describing left ventricular and RV function, including speckle-tracking imaging to assess global longitudinal left ventricular and RV free wall (RV-FW) strain. The presence of pericardial and pleural effusion was determined in every patient and was verified by cardiac magnetic resonance imaging when present. The size of pericardial effusion was measured at the point of its maximum extension. The clinical endpoint was defined as all-cause death.

Results: Between March 2012 and February 2019, 177 patients were included in our CA registry, however, TTE image

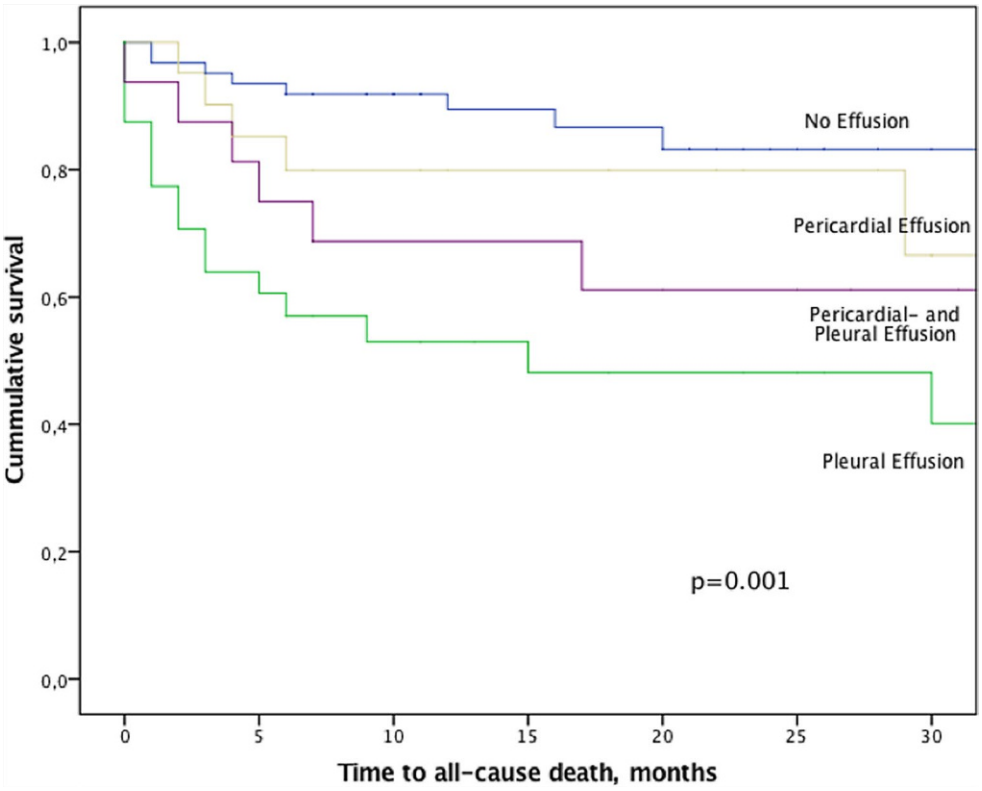


Fig. 1|9-4 Kaplan Meier plot showing time to all-cause death in patients with cardiac amyloidosis according to the presence of pericardial and/or pleural effusion at baseline

quality was only sufficient for analysis in 143 patients. Of these, 83 patients (59.4%) were diagnosed with ATTR and 60 patients (42.0%) with AL. In total, 23 patients (16.1%) presented with isolated pericardial effusion and 36 (25.2%) with isolated pleural effusion. In 17 patients (11.9%) both pericardial and pleural effusion were found and in 66 patients (46.2%) no effusion was present at baseline. Overall, there was no significant difference in the type of effusion between patients with AL and ATTR. In general, pericardial effusions were small (median diameter 7.1 mm (IQR 5.2–9.7) and none were hemodynamically compromising. Interestingly, the presence of pleural effusion correlated well with poor RV function, measured by RV-FW strain ($p=0.034$). However, no such correlation could be found for pericardial effusion and RV-FW strain ($p=0.319$). Kaplan Meier analysis showed that patients presenting with pleural effusion had a worse prognosis compared to patients with pericardial effusion alone or no effusion at baseline ($p=0.001$, Fig. 1).

Conclusions: More than 50% of patients with CA presented with pleural and/or pericardial effusions. While pleural effusion was clearly associated with poor RV function, we were not able to detect this association with pericardial effusion. In addition, patients with pleural effusions had an exceptionally poor prognosis compared to patients with pericardial effusions or no effusion at baseline.

9-5

Sex differences in invasive diagnostic testing in patients with heart failure

Romina Bernardi[1], Florian Kocher[2], Alexandra Bair[1], Elisabeth Vikoler[1], Sven Dengler[1], Alex Kaser[1], Mikael Klassnitz[1], Jakob Dörler[1], Marc-Michael Zaruba[1], Christine Mussner-Seeber[1], Gerhard Pölzl[1]

[1]University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Internal Medicine V (Haematology and Oncology), Medical University of Innsbruck, Innsbruck, Austria

Background: Cardiac catheterization is a widely applied technique to gain insight into hemodynamics and causalities in patients with heart failure. Based on evident sex-related differences in the invasive management of patients with coronary artery disease we investigated the gender-specific use of invasive testing including coronary angiography (CAG) and right heart catheterization (RHC) in patients with heart failure of various etiologies.

Methods: We analyzed the frequency of CAG and RHC in 2286 patients included from 2000 to 2018 in the Innsbruck cardiomyopathy (CMP) registry. CMPs were classified into eight groups: ischemic (25.7%), idiopathic (25.4%), hypertensive (15.3%), inflammatory (14.5%), cardiac amyloidosis (6.6%), toxic (4.4%), hypertrophic (4.4%), and valvular (3.6%). Patients were followed for a median of 87 months. Primary endpoint was death of any cause. Chi-square test was used to calculated sex differences in frequencies of invasive testing. A multivariate cox regression analysis was performed to compare survival differences between groups.

Results: Overall, frequency of coronary angiography (CAG) in 1837 (80.3%) and right heart catheterization (RHC) in 1234 (54%) patients was high in our cohort. The percentage of CAG was significantly higher in men (82.6%) compared with women (74.3%) ($P<0.001$). Likewise, RHC was applied more often in men (55.2% vs. 50.7%, $P<0.05$). Gender-specific disparities in invasive testing (CAG a/o RHC) with regard to various etiologies were evident only in idiopathic cmp (81.1% vs. 65.7%, $P<0.001$), [ischemic cmp (89.9% vs. 85.8%, $P<0.23$), hypertensive cmp (72.6% vs. 66.0%, $P<0.23$), inflammatory cmp (91.8% vs. 89.0%, $P<0.0.42$), cardiac amyloidosis (84.9% vs. 75.2%, $P<0.54$), toxic cmp (77.6% vs. 65.5%, $P<0.33$), hypertrophic cmp (55.2% vs. 61.5%, $P<0.67$), and valvular cmp (100% vs. 100.%, $P<1.0$)]. Long-term mortality was significantly worse in male patients (HR 1.29 [CI 1.09–1.53], $P=0.003$). Interestingly, invasive cardiac testing did not affect long-term outcome (HR 1.01 [CI 0.85–1.21], $P=0.89$). This was true for both sexes.

Conclusions: In this single-center cardiomyopathy registry cardiac catheterization was less frequently used in female patients with heart failure. This difference, however, did not translate into worse outcome.

9-6

Endomyocardial biopsy in patients with new-onset heart failure: an observational study

Lukas Baldinger, Veronika Eder, Thomas Sturmberger

Cardiology, Ordensklinikum Elisabethinen Linz, Linz, Austria

Background: Myocarditis is a common underlying cause in patients presenting with de-novo heart failure (HF). Albeit non-invasive imaging techniques such as cardiac magnetic resonance imaging are useful, endomyocardial biopsy (EMB) remains the diagnostic gold standard to identify myocarditis in patients with new onset heart failure. It is the definitive procedure to assess the aetiology and type of inflammation (e. g. giant cell, lymphocytic, viral), which imply various types of treatment.

Methods: In our retrospective analysis we scrutinized patients, in which EMB was performed in our institution the previous two years. Our data provide information about aetiology of heart failure, procedure safety and medical treatment. Furthermore, we assessed left ventricular ejection fraction, NYHA class and NT-pro BNP levels at the time of the index procedure and after 9 months. From January 2016 to October 2018 EMB was performed in 95 patients. 68 patients (72%) had new onset HF, whereas 27 (28%) were suspected to have specific myocardial disorder (e. g. amyloidosis). Just one adverse event (cardiac tamponade) occurred, requiring cardiac surgery.

Results: In the group with new onset HF 34 patients (50%) had dilated cardiomyopathy (DCM) and 34 (50%) had active myocarditis. Among the latter we found 15 (44%) to be from infectious/viral cause, 17 (50%) to be virus-negative inflammatory cardiomyopathy (VNICM) and 2 (6%) to be giant-cell myocarditis. All patients received neuro-humoral therapy according to HF guidelines. 6 patients with active virus myocarditis (HHV6 or Parvovirus-B19) were treated with either Peginterferon-alpha-2a or valganciclovir. 8 patients with VNICM received immunosuppression therapy with azathioprine and prednisone. 18 patients with active myocarditis were not treated with targeted therapy, either due to clinical stability or refusal. We observed clinical characteristics of 20 patients with DCM (group 1) and 14 patients with active myocarditis on specific treatment (group 2). Mean age of patients were 58 ± 11 ys. in group 1 and 48 ± 14 ys. in group 2. At baseline mean LVEF, median NT-pro BNP and mean NYHA class were 23.6 ± 7.5%, 1428 pg/ml and

3.1 ± 0.3 in group 1 and 22.9 ± 7.1%, 2363,5 pg/ml and 3.0 ± 0.8 in group 2 respectively. At follow-up at 9 months both groups improved significantly with mean LVEF of 37.4 ± 11.0% (group 1) and 40.8 ± 12.0% (group 2), a median NT-pro BNP of 446.5 pg/ml (group 1) and 255.5 pg/ml (group 2) and NYHA class of 1.7 ± 0.5 (group 1) and 1.4 ± 0.5 (group 2).

Conclusions: In our patients with new-onset heart failure we observed a high incidence of active myocarditis, confirmed by endomyocardial biopsy, leading to extended target therapy. The vast majority of patients improved in terms of symptoms and left ventricular function irrespective of the aetiology of heart failure. Finally, endomyocardial biopsy is a low risk procedure and should not be withheld in patients with suspected myocarditis due to safety concerns.

9-7

Heart failure from cardiac TTR-amyloidosis is a highly malignant disease

Alex Kaser[1], Florian Kocher[2], Alexandra Bair[1], Elisabeth Vikoler[1], Sven Dengler[1], Romina Bernardi[1], Mikael Klassnitz[1], Jakob Dörler[1], Marc-Michael Zaruba[1], Christine Mussner-Seeber[1], Gerhard Pölzl[1]

[1]University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Internal Medicine V (Haematology and Oncology), Medical University of Innsbruck, Innsbruck, Austria

Background: Cardiac amyloidosis is an underappreciated cause of morbidity and mortality. Light chain (AL) and transthyretin (ATTR) amyloidosis have different disease trajectories. Recent evidence suggests that ATTR is probably much more common than widely appreciated. ATTR was evident in patients with heart failure with preserved ejection fraction (HFpEF) and in elderly patients with aortic stenosis. Purpose: No data are available on subtype-specific comparisons of prognosis with other heart failure etiologies.

Methods: In this single-centre registry 2181 patients treated for heart failure according to prevailing guidelines between 2000 and 2018 were analysed. Underlying CMPs were classified into eight groups: cardiac amyloidosis (6.6%) [ATTR 3.0%; AL 3.6%], ischemic (25.7%), idiopathic (25.4%), hypertensive (15.3%), inflammatory (14.5%), toxic (4.4%), HCM (4.4%), and valvular (3.6%). 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: Patients were followed for a median of 87 months (IQR 44–138). Five year overall survival in the whole cohort was 80.6% (ATTR-amyloidosis 51.3%, AL-amyloidosis 36%, ischemic 72.4%, toxic 77.7%, valvular 79.9%, hypertensive 81.1%, idiopathic 85.3%, HCM 92.8, inflammatory 93.1%). In multivariate analysis adjusted for age, gender, LV-EF, and NYHA class, individuals with ATTR-amyloidosis were 2.6 time (95% CI 1.4–4.7; P = 0.002) and AL-amyloidosis 7.1 time (95% CI 4.4–11.6; $P < 0.001$) more likely to die of any reason than were individuals with inflammatory CMP. Differences in mortality between ATTR-amyloidosis and ischemic CMP were not significantly different (HR 1.5, 95%CI 0.9–2.5; $P = 0.096$). In the multivariate model, mortality was significantly higher in AL (HR 2.9, 95%CI 1.5–5.6; $P = 0.001$) compared with ATTR-amyloidosis.

Conclusions: Data from this single-centre registry study that compared cardiac amyloidosis with various reasons of cardiomyopathies indicate worst prognosis in patients with cardiac amyloidosis. Although outcome in ATTR is better than in AL, ATTR-amyloidosis is still associated with poor long-term survival. From this perspective, thorough etiologic evaluation and targeted therapy should be mandatory in patients with heart failure and suspected ATTR-amyloidosis.

Postersitzung 10 – Diverse 1

10-1

Unaffacted mRNA expression of myocardial SLC2A4 and its regulator gene SLC2A4RG during experimental hypoxia: a limiting factor for protection and recovery?

Robert Gasser[1], Klemens Ablasser[1], Elisabeth Pieske-Kraigher[2]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Worked at this institution, Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Myocardial ischemia increases glucose uptake through translocation of GLUT1 and GLUT4 from an intracellular compartment to sarcolemma. This appears to be a beneficial effect during ischemia and possibly recovery. Insulin and ischemia have additive effects to increase in vivo glucose utilisation and augment glucose transporter translocation. Delivery of glucose to the glycolytic pathway appears to be a major controlling site of glycolysis in low-flow ischemia. While many experimental studies suggest that an increase in glucose uptake and metabolism by the ischemic myocardium helps to protect myocardial cells from irreversible injury, little or nothing is known in this context about human cardiac trans-membrane glucose transport, SLC2A4-expression and its regulation.

Methods: In human cardiac tissue (right auricle), using microarray technique, we first look at general changes in expression profiles during simulated myocardial ischemia, the behaviour of SLC2A4 (GLUT4, solute carrier family 2, facilitated glucose transporter, member 4) as well as its regulator gene SLC2A4RG. Then, using Real Time PCR (Light Cycler), we quantify GLUT4 mRNA expression changes in experiments under ischemic and control conditions.

Results: Using the microarray technique, we find that both the expression of GLUT4 gene (SLC2A4) and its regulator gene remain practically unchanged. In Real Time PCR (Light Cycler), the mean ratio for GLUT4 gene expression compared to the house keeping gene G6PDH was under well oxygenated conditions –0.0052 + 0.0203 and under N2-simulated ischemia 0.0179 + 0.0196 ($n = 8$; +SEM). No statistically significant difference could be found between the two groups. Results show a trend to a slight increase in expression, however no statistical significance could be seen.

Conclusions: No significant changes are seen in the expression of the GLUT4 gene as well as in its regulatory gene after 30 minutes of N2-mediated experimental ischemia. Similarly, biological processes involved in glucose metabolism are not

significantly de-regulated as are others. This, as well as a slight trend towards up-regulation can be interpreted as an attempt of the myocyte to maintain energy metabolism also under hypoxic conditions. The facilitation by drugs like trimethazidine of shifting metabolic phenotype from adult (preferance of β-oxidation) towards fetal (preference of glucose) could thus, in this context, be seen as an important anti-ischemic property.

10-2

Therapieupdate orale Antibiose bei Endokarditis: eine Metaanalyse

Richard Rezar[1], Michael Lichtenauer[1], Eliano P. Navarese[2], Christian Jung[3], Brunilda Alushi[4], Uta C. Hoppe[1], Alexander Lauten[4], Bernhard Wernly[1]

[1]Universitätsklinik für Innere Medizin II, Kardiologie und internistische Intensivmedizin, Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Österreich
[2]INOVA Heart and Vascular Institute, Fairfax, Virginia, Vereinigte Staaten von Amerika
[3]Klinik für Kardiologie, Pneumologie und Angiologie, Universitätsklinikum Düsseldorf, Düsseldorf, Deutschland
[4]Medizinische Klinik für Kardiologie, Charité – Universitätsmedizin Berlin, Berlin, Deutschland

Grundlagen: Gemäß gültiger Guidelines erfolgt bei nicht kritisch kranken Patienten mit infektiöser Endokarditis in der Regel eine 6-wöchige antibiotische Therapie. Höhere Ausgaben für Krankenversicherungsträger durch prolongierte stationäre Aufenthalte mangels ambulanter Alternativen und auch durch höhere Kosten der i. v.-Therapie im Vergleich sind nur ein Kritikpunkt. Lange stationäre Liegedauern beeinträchtigen die Lebensqualität von PatientInnen und verlängern die Dauer der Rekonvaleszenz und Wiederintegration in den Alltag. Auch birgt die Verwendung eines intravenösen Regimes die Gefahr einer neuerlichen Infektion der Blutstrombahn durch häufige Venenpunktionen und liegende Kanülen. Die Bioverfügbarkeit oral verabreichter Substanzen im Vergleich zu parenteral applizierten Präparaten wird von Klinikern oftmals deutlich unterschätzt. Analog vieler anderer Infektionserkrankungen wird in Zeiten von Antibiotic Stewardship Programmen der Ruf nach einer zumindest partiellen oralen Therapiestrategie nach einer initialen parenteralen Stabilisierungsphase lauter.

Methodik: Unter Verwendung der Datenbank PubMed wurde eine Metaanalyse zum Thema „partielle orale antibiotische Therapie bei Endokarditis“ erstellt. Insgesamt 1848 Studien wurden anhand von Titel und Abstract gescreent. Für die endgültige Analyse in Frage kommende Publikationen wurden im Volltext geprüft. Von allen begutachteten Arbeiten wurden vier Studien mit gesamt 788 Patienten in die endgültige Analyse miteinbezogen. Als primärer Endpunkt wurde die Gesamtmortalität herangezogen. Das Auftreten eines Endokarditis-Rezidivs wurde als sekundärer Endpunkt gewählt. Zur Messung der Heterogenität wurde die I^2-Methode verwendet. Die gepoolte Ereignisrate wurde für die einzelnen Subgruppen in einer Metaanalyse mittels „Fixed-effects“-Modell berechnet. Das Chancenverhältnis (OR) wurde mittels Cochran–Mantel–Haenszel Test kalkuliert.

Ergebnisse: Im gesamt analysierten Patientengut konnten 72 PatientInnen mit Endokarditis im rechten und 765 PatientInnen mit Endokarditis im linken System identifiziert werden. Die einzelnen antibiotischen Behandlungsregime wurden nach Resistenztestung abgestimmt. Alle eingeschlossenen Patienten wurden klinisch evaluiert und als nicht kritisch krank eingeschätzt. Es verstarben deutlich mehr Patienten in der parenteralen Therapiegruppe. Während der primäre Endpunkt in der oralen Therapiegruppe in 11 von 379 Fällen eintrat, konnten in der i. v.-Gruppe 33 Todesfälle bei 409 PatientInnen beobachtet werden (OR 0,34; 95 %CI 0,17–0,68; $p = 0{,}003$; I^2 30 %). Der sekundäre Endpunkt variierte nicht zwischen den beiden Gruppen (OR 0,55; 95 %CI 0,26–1,20; $p = 0{,}13$; I^2 0 %).

Schlussfolgerungen: Wir konnten in unserer Metaanalyse keine Unterlegenheit eines partiell oralen Therapieregimes bezüglich Endokarditis-Rezidivrate bei klinisch stabilen Patienten zeigen. Es zeigte sich sogar eine geringere Mortalitätsrate in der oralen Therapiegruppe. Bei nicht kritisch kranken Patienten mit Endokarditis sollte ein partiell orales Therapieregime zumindest in Erwägung gezogen werden. Von einer intravenösen Initialtherapie kann aus derzeitiger Datenlage nicht abgeraten werden. Mittels eines partiell oralen Therapieregimes könnte in Zukunft bei unkomplizierten klinischen Verläufen die Dauer der stationären Aufenthalte reduziert und eine schnellere Genesung und Wiederintegration in den Alltag erreicht werden.

10-3

Effects of tafamidis in patients with transthyretin amyloid cardiomyopathy

René Rettl, Franz Duca, Christina Binder, Christophe Capelle, Stefan Aschauer, Julia Mascherbauer, Christian Hengstenberg, Diana Bonderman

Medical University of Vienna, Vienna, Austria

Background: Transthyretin amyloid cardiomyopathy (ATTR-CA) is caused by deposition of amyloid fibrils in the myocardium. The deposition occurs when transthyretin (TTR) becomes unstable and misfolds. Tafamidis is a kinetic stabilizer of transthyretin that prevents tetramer dissociation and amyloidogenesis by wild-type and mutant TTR.

Methods: Twenty-one patients with diagnosis of transthyretin amyloid cardiomyopathy (hATTR or wtATTR) from our national amyloidosis registry were treated with 20 mg of tafamidis for a period of six months. In our explorative analysis we aimed to evaluate the effects of tafamdis by changes from baseline of the serum N-terminal prohormone of brain natriuretic peptide (NT-proBNP) concentration, 6-minute walking distance, as well as cardiac structure and function, compared to untreated amyloidosis patients.

Results: The analysis showed a significant reduction in the serum NT-proBNP concentration in tafamidis treated patients compared to an increase in untreated patients (median difference, –1024.0 pg/mL, $p = 0.018$). Tafamidis also significantly improved the walking distance during the 6-minute walk test at month six, while reduction in untreated patients was observed (mean difference, +52.29 m, $p = 0.036$). Echocardiographic findings revealed an improvement of the global longitudinal strain (GLS) (mean, +0.46%), a decrease in left atrial size (mean, –1.00 mm) and a decrease in left ventricular size (mean, –2.26 mm) in tafamidis treated patients. T1 mapping in cardiac MRI showed a decrease in extracellular volume (ECV) (mean, –1.95%) in patients receiving tafamidis, while an increase in ECV in untreated patients was observed (mean, +2.95%). Due to insufficient power, the imaging parameters did not differ significantly between tafamidis treated and untreated patients.

		Tafamidis	No treatment	Treatment Difference	P-Value
Cardiac Biomarkers		**n=21**	**n=20**		
NT-proBNP, ng/L	Baseline, median	2740.0	2765.0		
	CFB to 6 months, median	-207.0	+817.0	-1024.0	0.018
Functional Status		**n=15**	**n=14**		
6MWT, m	Baseline, mean	408.33	403.50		
	CFB to 6 months, mean	+20.00	-32,29	+52.29	0.036
Echocardiogram		**n=19**	**n=18**		
LA, mm	Baseline, mean	63.05	62.00		
	CFB to 6 months, mean	-1.00	+0.50	-1.50	0.437
LV, mm	Baseline, mean	40.89	41.50		
	CFB to 6 months, mean	-2.26	+0.16	-2.42	0.123
LV wall thickness, mm	Baseline, mean	22.53	18.11		
	CFB to 6 months, mean	-0.01	-0.33	+0.32	0.567
Longitudinal strain, %	Baseline, mean	11.21	12,50		
	CFB to 6 months, mean	+0.46	+0,42	+0.04	0.301
MRI		**n=10**	**n=8**		
ECV, %	Baseline, mean	54.81	46.30		
	CFB to 6 months, mean	-1.95	+2.95	-4.90	0.069

Fig. 1|10-3 Change from baseline

Conclusions: Treatment with tafamidis for a period of six months in patients with transthyretin amyloid cardiomyopathy results in a significant improvement in NT-proBNP levels and walking distance compared to untreated amyloidosis patients.

10-4

Digitaler Algorithmus verbessert die Triage von Patienten mit Thoraxschmerz und Atemnot

Thomas Winter

Abteilung Innere Medizin II, Krankenhaus der Barmherzigen Schwestern Ried, Ried, Österreich

Grundlagen: Patienten mit internistischen Notfällen benötigen eine rasche Behandlung und Triage durch den Notarzt. Nach wie vor wird ein großer Teil dieser Patienten primär nicht vom Notarzt versorgt. Ein digitaler Algorithmus für Patienten oder Angehörige auf der Basis einfacher Fragen könnte die Rate primär notärztlicher Versorgung bei internistischen Notfallpatienten erhöhen.

Methodik: Nicht interventionelle, retrospektive, anonymisierte Studie. 80 konsekutive Patienten mit der Diagnose STEMI Vorderwand ($n=20$), STEMI Hinterwand ($n=20$), NSTEMI ($n=20$), Pulmonalembolie ($n=10$) und exacerbierter COPD mit resp. Insuffizienz ($n=10$). Nach positivem Votum der lokalen Ethikkommission wurden 2 Gruppen gebildet: Gruppe 1: Rate an notärztlicher Versorgung bei aktueller Versorgung Gruppe 2: Rate an notärztlicher Versorgung derselben Patienten bei Anwendung des Algorithmus Primärer Endpunkt ist der Prozentsatz des Transportes mit dem Notarzt Statistische Analyse: Fisher's exact probability test.

Ergebnisse:

Transport mit NAW	*N*	Konvent. vs Algorithmus
20	STEMI VWI	45 % vs 100 %, $p<0,01$
20	STEMI HWI	35 % vs 90 %, $p<0,01$
20	NSTEMI	20 % vs 100 %, $p<0,01$
10	PE mit Rechtsherzbelastung	30 % vs 100 %, $p<0,01$
10	COPD mit resp Insuffizienz	30 % vs 90 %, $p=0,02$

Schlussfolgerungen: Die Anwendung des patientenbasierten digitalen Algorithmus führt zu einer signifikant höheren Rate primär notärztlicher Versorgung bei Patienten mit Thoraxschmerz oder Atemnot. Damit verbunden ist bei Patienten mit STEMI ein primärer Transport in ein Katheterzentrum anstatt in das nächstgelegene Krankenhaus ohne HK Labor.

10-5

Nonbacterial thrombotic endocarditis in the context of pulmonary adenocarcinoma: a case report

Christoph Clemens Kaufmann, Emil Wessely, Kurt Huber

Wilhelminenhospital, Vienna, Austria

Background: Nonbacterial thrombotic endocarditis (NBTE) is a rare condition, usually observed in association with malignancy, lupus erythematosus or antiphospholipid syndrome. Diagnosis of NBTE remains a challenge as patients often remain asymptomatic up to their first thromboembolic event. Typical presentation includes the deposition of thrombi on

normal appearing heart valves and an increased rate of thromboembolic events without typical signs of an infectious disease.

Methods: Case summary I: A 44-year-old female patient presented to the emergency department with the chief complaint of a new numbness of her right hand. Her past medical history was unremarkable except for a history of latent hyperthyroidism. Based on the results of acute magnetic resonance imaging (MRI)-scanning of the brain the diagnosis of bilatereal supratentorial stroke was made. Additionally, bilateral peripheral pulmonary embolism (PE) was revealed on computed tomography (CT)-pulmonary angiography. Hence, therapeutic anticoagulation with enoxaparin twice daily was initiated following the tentative diagnosis of a thromboembolic stroke and PE. Within the next three months the patient had several further thromboembolic events, including recurrent strokes, acute coronary syndrome as well as renal- and splenic infarction. During the diagnostic work-up of the condition pulmonary non-small cell adenocarcinoma (NSCLC) (TTF 1 positive, ALK negative, PD-L1 90% positive, EGFR positive) was found (Fig. 1). The patient was initiated on a treatment regime with Tagrisso®, an EGFR tyrosine kinase inhibitor, secondary to the promising results of the FLAURA study ("Osimertinib in Untreated EGFR-Mutated Advanced Non-Small-Cell Lung Cancer").

Results: Case summary II: Transesophageal echocardiographic examination initially revealed a large (8×4 mm) vegetation of the right coronary aortic valve cusp with concomitant significant aortic regurgitation. While the echocardiographic findings suggested fulminant aortic valve endocarditis, several consecutive blood cultures remained negative and the patient showed no signs of infectious disease. Follow-up echocardiography demonstrated a complete resolution of the previously described aortic valve vegetation and a significant decline in the severity of aortic regurgitation. Hence, suggesting embolization of the aortic valve lesion. When the patient was hospitalized for her third stroke recurrence, another echocardiography was performed, which revealed a new 5×3 mm vegetation of the non-coronary aortic valve cusp (Fig. 2). Ultimately, the diagnosis of NBTE in the context of pulmonary adenocarcinoma was made. The patient was discharged home on long-term anticoagulation with rivaroxaban 15 mg once daily in combination with clopidogrel 75 mg once daily and temporary, prophylactic antibiotic treatment with ciprofloxacin.

Conclusions: We present a rare case of NBTE in the context of pulmonary adenocarcinoma. The diagnosis of NBTE was facilitated by the transient character of the aortic valve vegetations, the occurrence of thromboembolic events at various arterial sites of systemic circulation in combination with the diagnosis of NSCLC and the missing signs of infectious disease. While there is no randomized data available for the guidance of treatment in NBTE, effective anticoagulation remains the main treatment focus besides adequate treatment of the underlying disease.

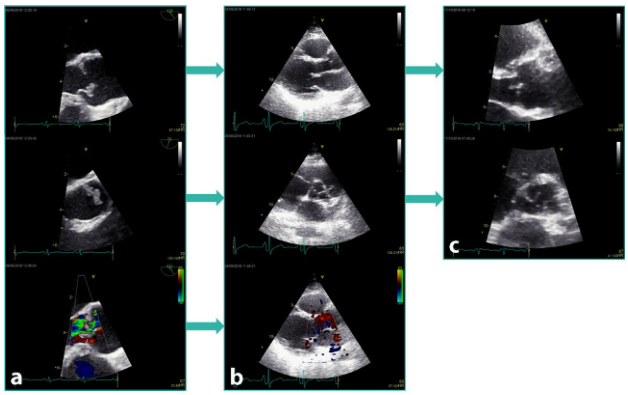


Fig. 1|10-5 Echocardiographic course. Abbreviations: TOE = transesophageal echocardiography; TTE = transthoracic echocardiography

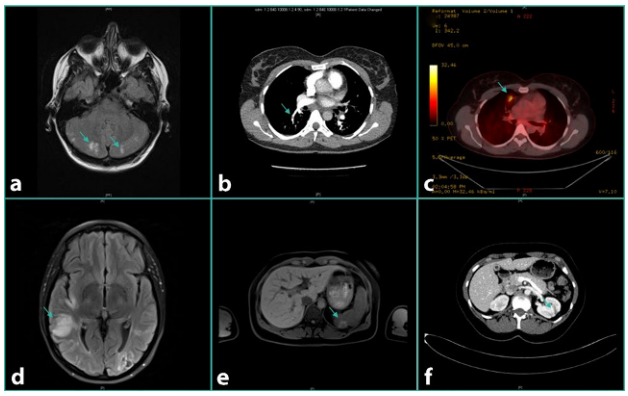


Fig. 2|10-5 Imaging of thromboembolic events/pulmonary carcinoma. Abbreviations: MRI = magnetic resonance imaging; CT = computed tomography; PET = positron emission tomography; NSCLC = non-small cell lung cancer

10-6

Produktprobleme bei Tests zur Bestimmung der B-Typ-natriuretischen Peptide BNP und NT-proBNP – Analyse der 2010–2019 vom BfArM veröffentlichten Kundeninformationen

Rüdiger Siekmeier, Jürgen Hannig

Drug Regulatory Affairs, Pharmazeutisches Institut der Universität Bonn, Bonn, Deutschland

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. Natriuretisches Peptid BNP und dessen Signalpeptid NT-proBNP sind etablierte Marker zur Diagnostik, Stratifizierung und Therapiemonitoring der Herzinsuffizienz. Neue pharmakologische Therapien der Herzinsuffizienz führen zu häufigerer Bestimmung beider Marker. Ziel der Studie war die Untersuchung der auf der Homepage des BfArM veröffentlichten FSN/FSCA auf Meldungen zu diesen Markern in Hinblick auf Produktprobleme und Risiken, Art der FSCA und Einhaltung der Kriterien der MEDDEV-Leitlinie.

Methodik: Es erfolgte eine Analyse der vom BfArM ab Anfang 2010 bis Mitte März 2019 auf der Homepage (http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html) veröffentlichten FSCA/FSN. Bei der Auswertung der BNP und NT-proBNP betreffenden

FSCA wurden Reagenzien (Tests, Kalibratoren, Kontrollmaterialien) den Analyzern (einschließlich allgemeinem Verbrauchsmaterial, z. B. Diluent, Waschlösung) gegenübergestellt.

Ergebnisse: Es fanden sich 10/11 FSCA zu Reagenzien/Analysatoren (einschl. 2 Folgemeldungen für Analyzer), z. T. mehrere Tests/Parameter und Plattformen betreffend, bei insgesamt 1943 Meldungen zu IVD 2010 bis 2019. In 5/9 Fällen waren zusätzlich weitere Parameter betroffen (Mehrfachangaben; z. B. Troponin (5/8), CK-MB (3/4) und Myoglobin (2/2)). Gründe der FSCA waren bei Reagenzien häufig Herstellungs-/Verpackungsfehler (4), Probleme der Reagenzstabilität, Kalibrations- und Messgenauigkeit (5) und Mängel der Gebrauchsanleitung (1), die zu fehlerhaften Ergebnissen (einschl. Bewertung) und Testversagen führten und bei Analyzern/Zubehör (9/2) Probleme bei der Testdurchführung (automatische Verdünnung, Transport, fehlerhafte Erfassung von Reagenzstabilität oder Füllstand, Störung durch Waschlösung (6)) und Umgebungseinflüsse (Temperatur, Luftdruck (5, einschl. Folgeinformationen), die zu fehlerhaften Ergebnissen führten. Mögliche Risiken für Patienten wurden oft beschrieben, jedoch keine bereits eingetretenen Patientenschädigungen. Abhängig vom Produktproblem erfolgten korrektive Maßnahmen, bei Reagenzien meist Rückruf/Produktvernichtung (5), bei Analyzern Maßnahmenempfehlungen, Software-Upgrade und Änderung der Gebrauchsanleitungen.

Schlussfolgerungen: Trotz der geringen Zahl an FSCA zu BNP und NT-proBNP handelt es sich um wichtige Produkte, da diese zu Diagnostik, Stratifizierung und Monitoring der Herzinsuffizienz eingesetzt werden und häufig auch andere Parameter (z. B. Troponin (T und I), CK-MB, Myoglobin) von der FSCA mitbetroffen sind, so dass auch die Differentialdiagnostik akuter Myokardschädigungen betroffen ist. Bei der Zahl der FSCA zu Analyzern ist zu berücksichtigen, dass in dieser Auswertung nur solche berücksichtigt wurden, deren FSN explizit eine Beeinträchtigung der Ergebnisse von BNP oder NT-proBNP aufführte. Aufgrund der wesentlichen Bedeutung von FSN zur Risikoverminderung bei vom Produkt ausgehenden Risiken im Falle einer FSCA sollten trotz weitgehender Einhaltung der MEDDEV-Kriterien Form und Inhalt der FSN weiter verbessert werden.

10-7

Fehlerhafte Laborwerte für kardiale Marker als Folge einer Einnahme von Biotin – Analyse der 2004–2019 vom BfArM veröffentlichten Kundeninformationen

Rüdiger Siekmeier[1], Jürgen Hannig[1]

[1]Drug Regulatory Affairs, Pharmazeutisches Institut der Universität Bonn, Bonn, Deutschland

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. Kardiale Labormarker sind wichtig bei Diagnostik (z. B. Troponin, Creatinkinase) und Therapie kardialer Erkrankungen (z. B. Digoxin). Im November 2017 publizierte die FDA eine Warnung zur Beeinflussung von Labortests (einschließlich des Berichtes eines Todesfalles in Verbindung mit einem Troponintest) durch Biotin (https://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm586505.htm), das in Form von Medikamenten/Supplementen z. T. hoch dosiert eingenommen wird. Ziel dieser Studie war die Untersuchung der auf der Homepage des BfArM veröffentlichten FSN/FSCA bei IVD zur kardiologischen Diagnostik/Therapie auf das Vorliegen einer Biotininterferenz sowie 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 ab Ende 2004 bis Mitte März 2019 auf der Homepage (http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfonode.html) veröffentlichten FSCA und FSN.

Ergebnisse: Es fanden sich 11 FSCA zur Biotininterferenz bei IVD (insgesamt 2665 FSCA zu IVD), die erste 2013, die übrigen ab 2016. Alle FSCA betrafen in geringer Konzentration vorliegende Analyte, 3 davon kardiologische Parameter (z. T. mehrere Parameter je FSCA; TnI I: 3, CK-MB Masse: 1, Digoxin: 1), z. T. mehrere Testformen/Laborplattformen betreffend. Abhängig vom Testprinzip (Sandwichassay, kompetitiver Assay) kam es zum Abfall (TnI, Digoxin) oder Anstieg (TnI, CK-MB Masse) des Ergebnisses. Hinweise zu bereits erfolgten Patientenschädigungen fanden sich nicht. In den FSN gaben die Hersteller Grenzwerte für nicht interferierende Biotinkonzentrationen an und wiesen auf entsprechende zukünftige Änderungen der Gebrauchsanweisungen hin. Die Notwendigkeit einer Retestung von Patientenproben wurde nicht berichtet.

Schlussfolgerungen: Die meisten FSCA zur Biotininterferenz bei IVD erfolgten 2017–2018, obwohl das zugrundeliegende Testprinzip seit vielen Jahren angewandt wird und das Problem einer möglichen Interferenz ebenfalls länger bekannt ist. Möglicherweise führten jedoch Änderungen der Einnahme (häufigere Einnahme von Nahrungsergänzungsmitteln in der Bevölkerung und hohe Dosierung, z. B. 1000-fache Tagesdosis bei Patienten mit Multipler Sklerose) von Biotin zum vermehrten Auftreten der Interferenz. Nur ein kleinerer Anteil der FSCA betraf Marker zum Nachweis einer akuten Myokardschädigung (TnI, CK-MB) und der kardiologischen Therapie (Digoxin). Auch wenn sich in den FSN keine Angaben über aufgetretene Patientenschädigungen fanden, sollte bei der Diagnostik eine mögliche Interferenz durch Biotineinnahme berücksichtigt werden. Darüber hinaus sollten aufgrund der Bedeutung der FSN zur Verminderung vom Produkt ausgehender Risiken im Falle einer FSCA trotz weitgehender Einhaltung der MEDDEV-Kriterien Form und Inhalt der FSN weiter verbessert werden.

10-8

Synkopenhäufigkeit und Zuweisungsart von Patienten mit suspekten T-LOC in einer Notfallaufnahme

Georg Saurer[1], Michaela Mezler-Andelberg[1], Wolfgang Weihs[1]

[1]Landeskrankenhaus Graz II, Graz, Österreich

Grundlagen: Synkope ist ein häufiges Symptom, weshalb Patienten in einer Notfallaufnahme (NFA) vorstellig werden

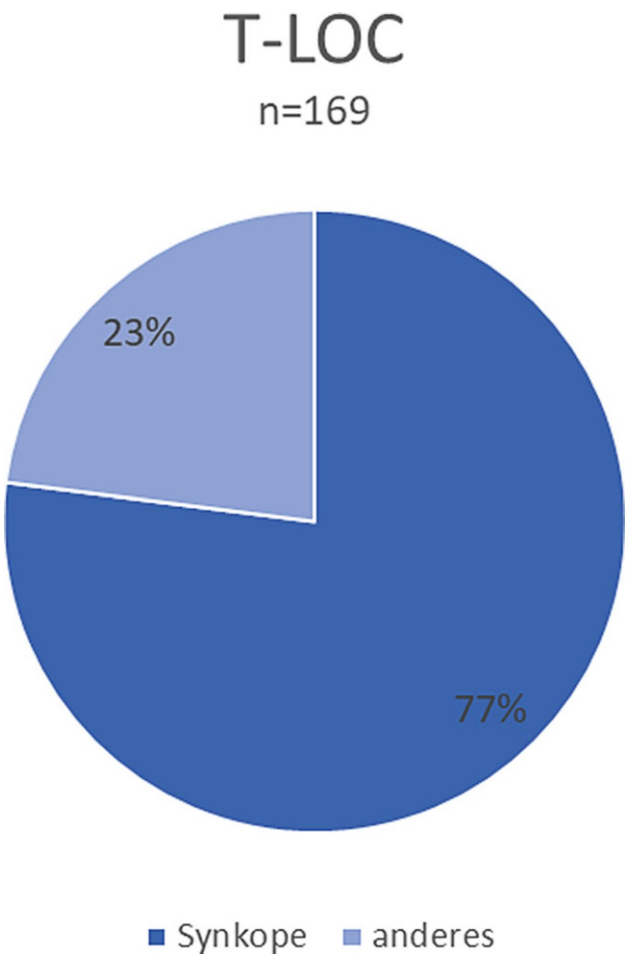


Abb. 1|10-8

(0,8–2,4 % der NFA-Präsentationen). Die Gruppe der T-LOCs (transient loss of conciouness) stellt eine große Herausforderung für NFAs dar. Es wäre sinnvoll, Patientenströme im Vorfeld zu lenken, um NFAs zu entlasten. Fragestellung: Anzahl der Patienten mit der Diagnose Synkope bei suspekten T-LOC in der NFA eines Schwerpunktkrankenhauses und Zuweisungsart dieser Patienten.

Methodik: Patienten, die von Jänner bis März 2016 die NFA wegen eines suspekten T-LOCs aufsuchten, wurden retrospektiv analysiert, ob sie entsprechend der Definition der ESC eine Synkope hatten und woher sie der NFA zugewiesen wurden.

Ergebnisse: 169 Patienten suchten die NFA mit suspektem T-LOC auf. 130 davon wurden als Synkope diagnostiziert (77 %). 70 % der Patienten kamen ohne Zuweisung von direkt in die NFA, 16 % wurden von einem anderen Krankenhaus (v. a. Unfallkrankenhaus), 6 % von Allgemeinmedizinern und 2 % von der Neurologie zugewiesen. 3 % wurden über das Notarztsystem u. 2 % aus Pflegeeinrichtungen zutransferiert. Bei 1 % war die Herkunft nicht eruierbar.

Schlussfolgerungen: In unserem Kollektiv von Patienten mit suspektem T-LOC hatten 77 % eine Synkope. 23 % hatten entweder eine andere Ursache des T-LOCs oder kein T-LOC. Patienten mit suspekten T-LOC in einer NFA stellt eine heterogene Gruppe dar, was ihre Zuweisung betrifft. Der Großteil der Patienten besteht aus Selbstzuweisern. Eine Filterung dieser Patienten zur Entlastung der NFA ist aus diesem Grund schwierig. Zu diskutieren ist die Einführung einer Allgemeinmedizinischen Akutversorgung im Vorfeld des Krankenhauses.

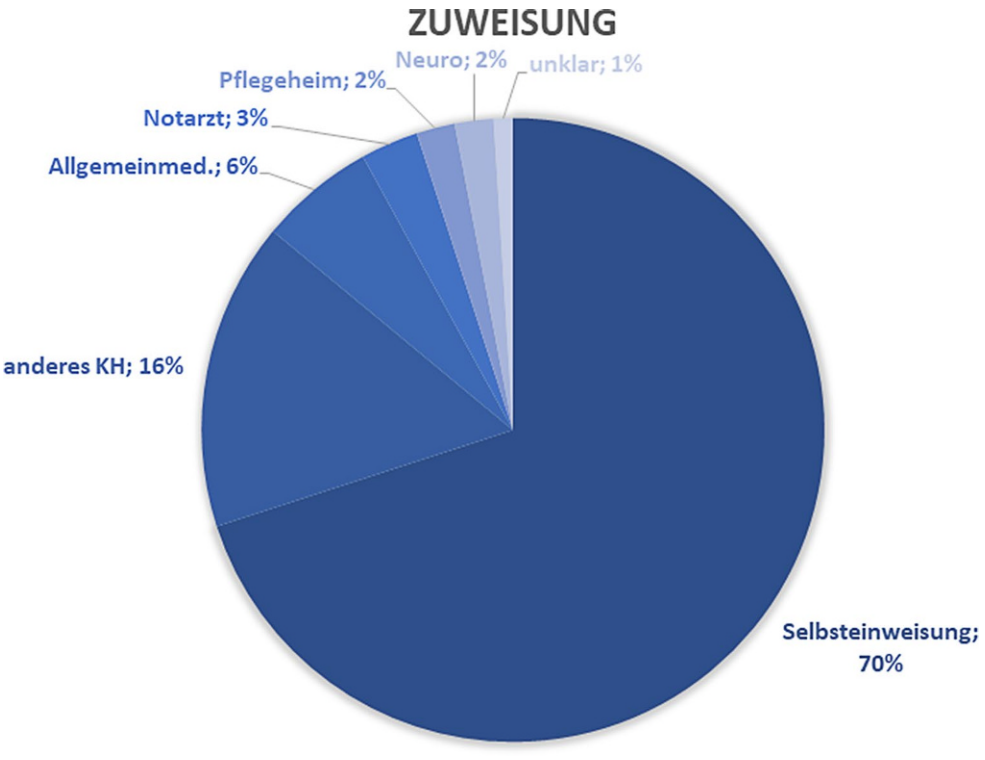


Abb. 2|10-8

10-9

Einfluss suggestiver Entspannungsverfahren auf physiologische, biochemische und neurohumorale Parameter im Herz-Kreislaufbereich

Petra Tupi[1], Corinna Haas[2], Robert Gasser[1]

[1]Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin, Medizinische Universität Graz, Graz, Österreich
[2]Abteilung für Akutgeriatrie/Remobilisation, Klinikum Klagenfurt am Wörthersee, Klagenfurt, Österreich

Grundlagen: Derzeit gibt es keine umfassende Beschreibung des aktuellen Standes der Grundlagenforschung zu diesem Thema. Der besondere Neuigkeitswert der vorliegenden Diplomarbeit liegt darin, den wissenschaftlichen Hintergrund suggestiver Entspannungsverfahren (Autogenes Training, Klinische Hypnose, progressive Relaxation nach Jacobson, Basissophronisation) im Grundlagenforschungsbereich zu erfassen und abzubilden.

Methodik: Untersucht wurde die vorhandene wissenschaftliche Literatur von peer-reviewten Fachzeitschriften in diesem Kontext zu folgenden Themen: Herz-Kreislaufphysiologie (HRV, Vasokonstriktion und -dilatation, biochemische, physiologische, elektrophysiologische Veränderungen, biologische und neuro-humorale Ansätze). Die Ergebnisse wurden statistisch-analytisch verarbeitet, die physiologischen und biochemischen Grundlagen komparativ und kritisch beurteilt, um den therapeutischen Stellenwert dieser Verfahren neu zu bewerten.

Ergebnisse: In der Literatur konnten für den kardiovaskulären Bereich folgende Anwendungsgebiete gefunden werden: Prävention (Risikofaktorenmanagement wie Stressmanagement, Raucherentwöhnung, Compliance, Körpergewichtskontrolle, Ernährungsgewohnheiten, Sport), Leistungssport, Intensivmedizin (Weaning), Anxiolyse (vor Eingriffen, ICD-Implantation, Transplantationsmanagement), Analgesie/Sedierung (Punktionen, Thoraxschmerz), begleitend bei Eingriffen, HRV, RR-Senkung. Über folgende Parameter konnten verwertbare Daten bezüglich statistisch signifikante Ergebnisse gefunden werden: Herzfrequenz, HRV (Spektralanalyse und fraktale Komplexität sind in beide Richtungen beeinflussbar), Vasokonstriktion/-dilatation, Peripherer vaskulärer Widerstand, Koronarfluss, Umbilikalarterienfluss (proof of principle), Sympathikus/Parasympathikusaktivität kann nach beiden Richtungen beeinflusst werden, Endothelfunktion beeinflussbar, Modulation nicht-dipolarer Komponenten der T-Welle, Neurohumorale Parameter: Cortisol, Wachstumshormon, Oxytocin.

Schlussfolgerungen: Der hier präsentierte Überblick über die derzeitigen Kenntnisse im Grundlagenforschungsbereich zu diesem Thema zeigt, dass neue Messtechniken zunehmend Eingang in die Valorisierung von suggestiven Entspannungsverfahren finden und letztere auch zurecht begleitend ein weites Einsatzgebiet in Kerngebieten der Kardiologie wie Risikofaktorenmanagement und Anxiolyse finden.

Postersitzung 11 – Interventionelle Kardiologie 2

11-1

Automated detection of calcified plaques in coronary optical coherence tomography images using image segmentation based on machine learning

Clemens Gangl, Christian Roth, Daniel Dalos, Georg Delle-Karth, Thomas Neunteufl, Rudolf Berger

Medical University of Vienna, Vienna, Austria

Background: Automated image recognition based on machine learning methods was proven to be feasible in several medical imaging applications recently. Apart from image classification methods to categorize input images as for example as healthy or suspicious, image segmentation allows accurate localization of pathologies and thereby facilitates a wide area of applications. Because of the unique composition of every machine learning problem the applicability of image segmentation methods for detecting coronary pathologies in optical coherence tomography (OCT) images remains unclear. Furthermore, the prediction accuracy of deep learning methods usually depends on vast amounts of training data which are often not available for particular medical challenges. Therefore special strategies need to be applied to achieve satisfying results even with smaller training sets. We aimed to investigate the applicability of machine learning methods in the special domain of plaque detection in coronary OCT images, especially considering the challenge of a small training dataset.

Methods: Originating from a dataset of 122 OCT frames containing calcified plaques, we performed image preprocessing using a custom build OCT image processing software to crop the luminal part as well as the areas outside the circular OCT signal to reduce entropy. Additionally, plaques were identified and marked by an experienced OCT analyst, drawing plaque-enclosing polygonal masks using the same software. We also performed common image augmentation strategies, primarily applying rotation and zoom operations. In a further step, we split the therefore resulting samples randomly into training, validation and test datasets (80:10.10%). To train our model, we fed the training and validation samples into an U-Net Convolutional Neural Network with domain-specific adaptions based on the publicly available PyTorch machine learning software library.

Results: After 50 training epochs, we could achieve a prediction accuracy of 74,4% with the current configuration in

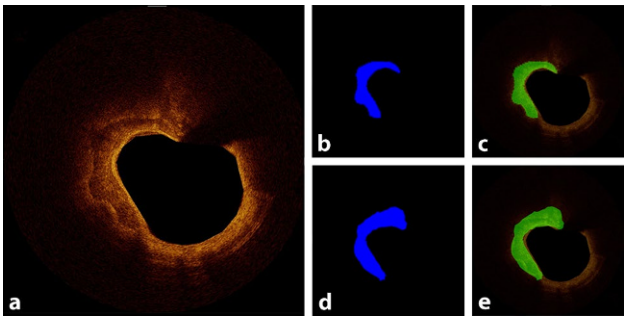


Fig. 1 | 11-1

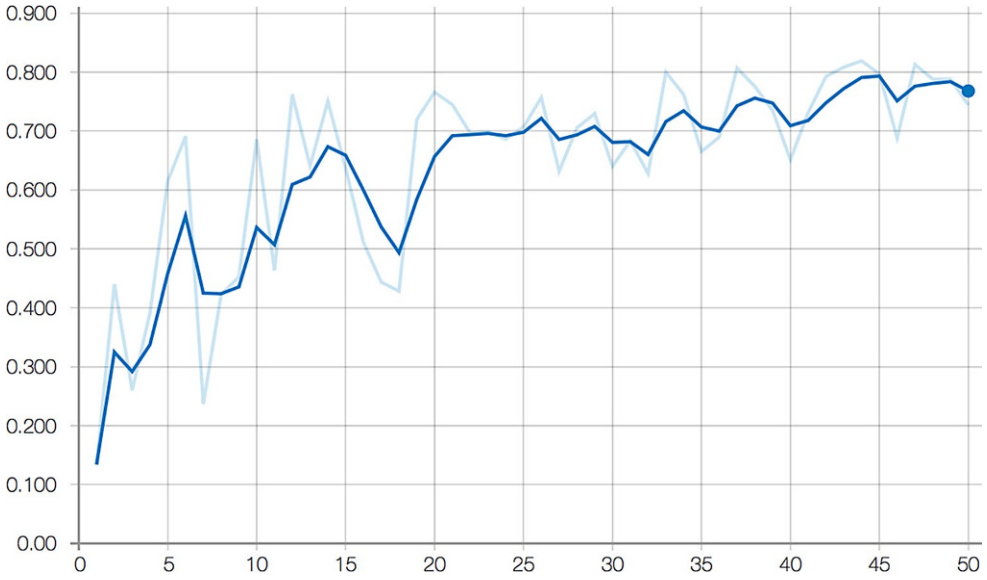


Fig. 2|11-1

terms of conformity measured by the Sørensen-Dice coefficient comparing the similarity of the predicted plaque masks with the ground truth samples (figure 1 illustrates an exemplary comparison between predicted and ground truth plaque masks). The improvement of the prediction accuracy over training time is denoted in figure 2.

Conclusions: Our results suggest that image segmentation based on machine learning strategies is a feasible way for automated plaque detection in coronary OCT imaging even based on small training datasets. Larger training datasets may be necessary to further raise prediction accuracy.

11-2

Evaluation of the Mitral Butterfly delivery and working principle in a passively perfused heart model

Claus Rath[1], Johanna Maria Ticar[2], Werner Mohl[3]

[1]Division of Anatomy, Center for Anatomy and Cell Biology, Medical University of Vienna, Vienna, Austria
[2]AVVie GmbH, Vienna, Austria
[3]Department of Cardiac Surgery (Emeritus), Medical University of Vienna, Vienna, Austria

Background: Mitral valve regurgitation is a highly widespread heart valve disease. The current guidelines recommend valve repair, if feasible. The development of minimally invasive approaches results in less surgical trauma and shortened hospitalisation. The Mitral Butterfly is a novel transcatheter mitral stent device, which can be inserted via right lateral mini thoracotomy (mini-mitral) or via a completely percutaneous approach. The device consists of a nitinol stent and a PTFE matrix. The matrix spreads from the nitinol wings along the annulus of the mitral valve towards a swing arm, covering the prolapsing segment of the insufficient valve (Fig. 1). The device is secured by leaflet penetration in the peri-annular region. An attachment to myocardial structures is not necessary as the swing arm serves as an artificial papillary muscle. This seesaw mechanism of the implant has already been proven feasible in bench testing. The aim of this study was to test the Mitral Butterfly implantation procedure in passively perfused animal hearts with valve prolapse and verify the improvement of coaptation plane and haemodynamic properties.

Methods: The feasibility of implantation and functionality of the Mitral Butterfly device was evaluated in a passively perfused heart model at the premises of LifeTec Group (Eindhoven, NL). The novel device was studied in two ovine and three porcine hearts. The chordae tendinae of the posterior leaflets were cut with endoscopic scissors. The induced prolapse of the P2/P3 segment of the respective leaflet was verified by means of endoscopic visualisation. A 30 Fr delivery system was introduced via the left atrium, the Mitral Butterfly was deployed on the posterior leaflet of the mitral valve and attached to the peri-annular region in one step. The procedural success was confirmed utilizing videoendoscopic inspection, 2D echocardiography and documenting the pressure and volume curves.

Results: The in vitro study of the Mitral Butterfly demonstrated the ease of application of the specially designed delivery system. The deployment procedure was successful in all hearts. While the deployment took twelve minutes at the first try, the time was gradually decreased with every implantation. The deployment in heart #5 was successfully performed in two minutes. Both, videoendoscopic and echocardiographic data demonstrated improvement of valve closure. It was observed, that the PTFE matrix did not cover the prolapsing segment entirely, a subject to change in the next prototype iteration. However, pressure and volume parameters omitting a regurgitant V-wave,

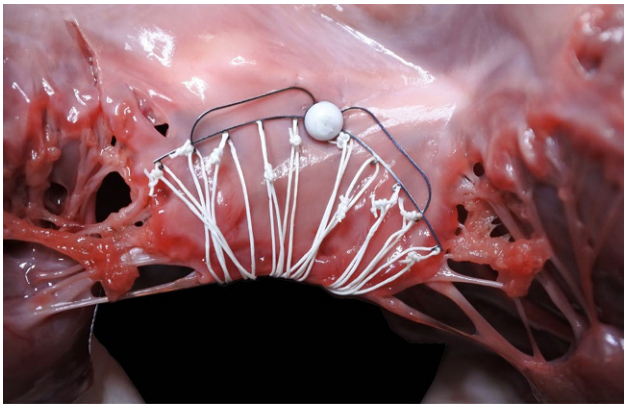


Fig. 1|11-2 Mitral Butterfly device

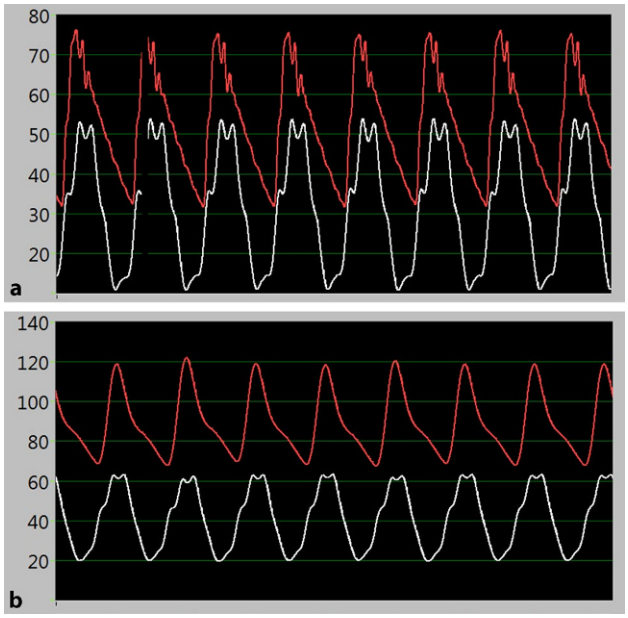


Fig. 2|11-2 Haemodynamics a) pre implantation b) post implantation. Red Aortic pressure in mmHg. White Left atrial pressure in mmHG

indicated enhanced coaptation of the anterior and posterior leaflet following implantation (Fig. 2).

Conclusions: The application of the Mitral Butterfly in a passively perfused heart model demonstrated ease of use with a specifically designed transatrial delivery system. The positioning of the implant and the fixation in the peri-annular region was successfully performed, while the PTFE matrix needs to be redesigned to guarantee full coverage of the prolapsing segment and achieve an even more satisfying coaptation of the mitral valve leaflets. Although this animal model of a human disease is sufficient to proof the concept of the Mitral Butterfly implant, a more realistic setting utilizing a thorax of a donated human cadaver will be used for further analysis.

11-3

Mitral Butterfly: A novel device for transcatheter mitral valve repair

Claus Rath[1], Johanna Maria Ticar[2], Werner Mohl[3]

[1]Division of Anatomy, Center for Anatomy and Cell Biology, Medical University of Vienna, Vienna, Austria
[2]AVVie GmbH, Vienna, Austria
[3]Department of Cardiac Surgery (Emeritus), Medical University of Vienna, Vienna, Austria

Background: Mitral valve regurgitation is the second most common heart valve disease. Surgical valve repair is the method of choice since the wide introduction of the Carpentier technique in the mid 1980s, according to current guidelines. More recently, sequential insertion of individual PTFE chordae through the apex of the heart has emerged in the clinical setting, in the beating heart as minimally invasive technique. In this transcatheter technique a multitude of artificial chordae (normally more than 3) are deployed, attached at the leaflet rim and tensioned under echocardiographic visualisation. The biomechanical properties subsequent to the repair are strongly affected by the chosen fixation point for the PTFE chordae and the experience of the surgeon.

Methods: The Mitral Butterfly implant is a one-step device. It consists of a nitinol stent and a PTFE matrix (Fig. 1). Due to the shape memory effect properties of the material, the device can be folded into a delivery system (< 30 French). This enables the implant to be deployed either via right lateral mini-thoracotomy through the roof of the left atrium or a trans-femoral transseptal approach. Therefore, the technology can be applied both by surgeons and interventionists therefore by the whole heart team. The size of the device can be chosen according to the individual size and comes in sizes small, medium and large. Depending on the sizes of the mitral annulus, the surgeon may choose the best fitting size for the patient and his/her respective prolapsing segment. A manual adjustment of the PTFE matrix length is not required, as the length solely depends on the ratio of the matrix and the swing arm.

Results: The device is attached with a clasp to the annulus of the mitral valve in one step. The PTFE matrix is intended to cover the entire prolapsing segment upon releasing the implant from the delivery system. The swing arm of the Mitral Butterfly enables a more physiological restoration of the coaptation plane by mimicking the function of a papillary muscle. Due to the seesaw movement of the entire implant, a restriction of the mitral leaflet following repair is highly unlikely. The Mitral Butterfly is primarily designed for use on the posterior leaflet, which is most commonly affected by mitral valve prolapse. It may also be used in cases of anterior valve prolapse or Barlow's disease, though. Due to its unique design and attachment mode, an excision of the prolapsing segment of the valve can be avoided. The device may also be combined with other mitral valve repair techniques and/or devices.

Conclusions: The Mitral Butterfly is a novel mitral valve repair technology. The concept has been proven feasible in in vitro studies. The device is currently in the preclinical testing stage and the first in human application is planned for 2021.

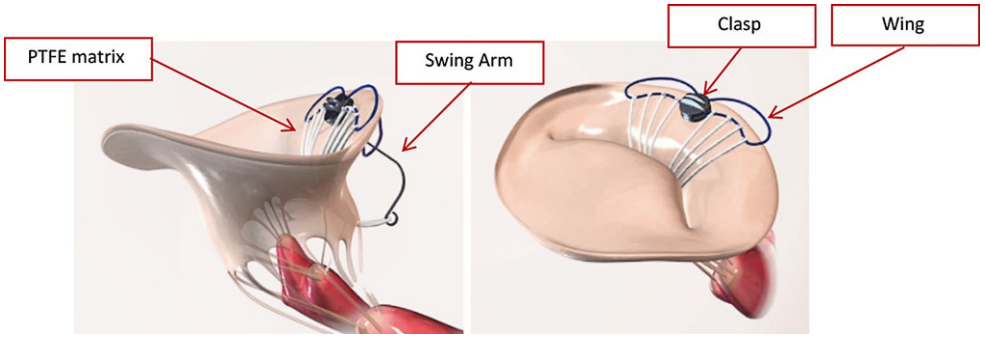


Fig. 1|11-3 Mitral Butterfly device. *Left:* Side view *Right:* Top view

11-4

Coronary sinus reducer implantation for the treatment of chronic refractory angina: the first austrian case experience

Carl Kaulfersch, Josef Brandl, Hannes Alber

Department for Internal Medicine and Cardiology, Klinikum Klagenfurt am Wörthersee, Klagenfurt, Austria

Background: Narrowing of the coronary sinus has emerged as a new therapeutic option for the treatment of patients with chronic refractory angina pectoris and myocardial ischemia not amenable to further revascularization. Recently a randomized, double-blind, multicenter clinical trial involving 104 patients, demonstrated that the implantation of coronary sinus reducing device was associated with significant improvement in symptoms and quality of life in patients with refractory angina who were not candidates for revascularization.

Methods: We report the first Austrian case experience of the implantation of the coronary sinus Reducer (Neovasc Inc., Richmond B.C., Canada) in a 56 year old male patient with chronic refractory angina (CCS 3/4) after bypass surgery despite of using five antianginal drugs. A SPECT scan showed significant ischemia in the postero-lateral wall, without an option for revascularization.

Results: After successful implantation of the device, CCS class diminished from 3/4 at baseline to 2 after 6 months of follow up. Device patency could be demonstrated by CT-scann. A second SPECT scan demonstrated significant improvement of the ischemic territory.

Conclusions: In this first Austrian case experience, Reducer implantation was safe and efficacious in reducing symptoms of angina and improving quality of life.

11-5

Safety and efficacy of cangrelor in acute and elective patients undergoing PCI regarding clinical and anatomical coronary features

Michael Grechenig[1], Fabian Plank[1], Christoph Beyer[1], Katharina Birkl[2], Guy Friedrich[1]

[1]University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: The use of cangrelor, a rapid acting intravenous P2Y12 inhibitor has been shown to be effective during PCI. We investigated the use of cangrelor in different settings with special respect to clinical and coronary anatomical features.

Methods: In a high volume tertiary care cardiology we analyzed all consecutive patients receiving cangrelor during PCI. Indications (clinical, anatomical) as well as pre-, peri- and post-procedural antithrombotic medications were compared. Intra-hospital outcome (death, bleeding and ischemic events) was also recorded.

Results: In 96 patients (78% male, 22% female) with a mean age of 62.3 years, PCI was performed. 43% were diagnosed with STEMI, 21% with NSTEMI and 17% were stable patients. Pre-procedural antithrombotic therapy was aspirin ($n=85$), heparin ($n=44$), tenecteplase ($n=4$), clopidogrel ($n=3$), NOAC or tirofiban ($n=3$). Peri-procedural therapy additionally to cangrelor was heparin ($n=82$), clopidogrel ($n=1$), aspirin ($n=11$), ticagrelor ($n=5$) and/or tirofiban ($n=2$). Out of 96 patients 21% received morphin, 26% fentanyl and 1% piritramid due to emergency therapy. In 87 patients one vessel was intervened, whereas 9 patients had PCI in 2 vessels. PCI typed anatomical lesions were 43% left anterior descending (0% type A, 36% type B, 38% type C, 15% not typed), 17% circumflex artery (6% type A, 17% type B, 33% type C, 44% not typed) 35% right coronary artery (3% type A, 33% type B, 22% type C, 15% not typed) and 5% left main stem (100% type C). In 7 patients intracoronary thrombus aspiration was performed. The mean length of hospital stay was 8.5 days. Death was observed in 12 (12.5%) patients during the hospital stay: 9 cardiogenic shock, 2 cerebral hypoxia and 1 aortic dissection. Type 4 myocardial infarction was found in 10% of the patients. Bleeding events occurred in 3 patients. The bleeding events were categorized by Bleeding Academic Research Classification (3a, 3b and 5a). Post interventional antithrombotic therapy was aspirin + clopidogrel ($n=48$), ticagrelor ($n=17$) or prasugrel ($n=15$).

Conclusions: We conclude that cangrelor may be used in acute as well as stable patients with varying coronary anatomy. Highest use was noted in complex coronary anatomy patients with mechanical ventilation or/and opioid therapy. We observed a low postprocedural ischemic and bleeding rate, despite a 99% of femoral approach.

11-6

The course of burr-speed in coronary artery rotational atherectomy – first results of an exploratory pilot-study

Johann Sipötz[1], Andreas Winter[1], Evelyn Kunschitz[1], Oliver Friedrich[2]

[1]Hanusch-Krankenhaus, Vienna, Austria
[2]Karl Landsteiner Institute for Scientific Research in Clinical Cardiology, Vienna, Austria

Background: In previous years a series of studies have indicated that burr-speed is an important parameter for treatment success in Rotational Atherectomy (RA). In in-vitro experiments it has been demonstrated that lowering burr-speed and especially burr-speed deceleration reduces heat generation and potential thermal injury, which is associated with platelet activation, smooth muscle proliferation and coronary restenosis. Two studies reported favourable clinical outcome after reducing platform speed below 160 krpm. Despite these findings studies on RA only report the pre-set platform speed and there are up to now no published data about the actual course of burr-speed in Coronary Artery RA. This study aimed to document the course of burr-speed in real world RA-procedures.

Methods: We analysed 28 RA-sequences (medium duration: 15 s; Q1: 11.75 s; Q3: 19.9 s) of 14 patients. The temporal resolution of the burr-speed recording was limited by the RA-console to 1.7 fps. We employed a standard RA-protocol (pecking technique i.e.: short runs intermittent ablation; step-up burr size beginning with small burrs of 1.25 mm or 1.5 mm up to a burr/artery ratio ≤ 0.6) with a pre-set low platform-speed of 135 krpm.

Results: The pre-set platform-speed of 135 krpm resulted in actual medium burr-speed maxima in the treated vessel of 131 krpm (Q1: 126.75 krpm; Q3: 135 krpm). Rotational ablation caused sharp burr-speed decelerations of 2.75 krpm (Q1:

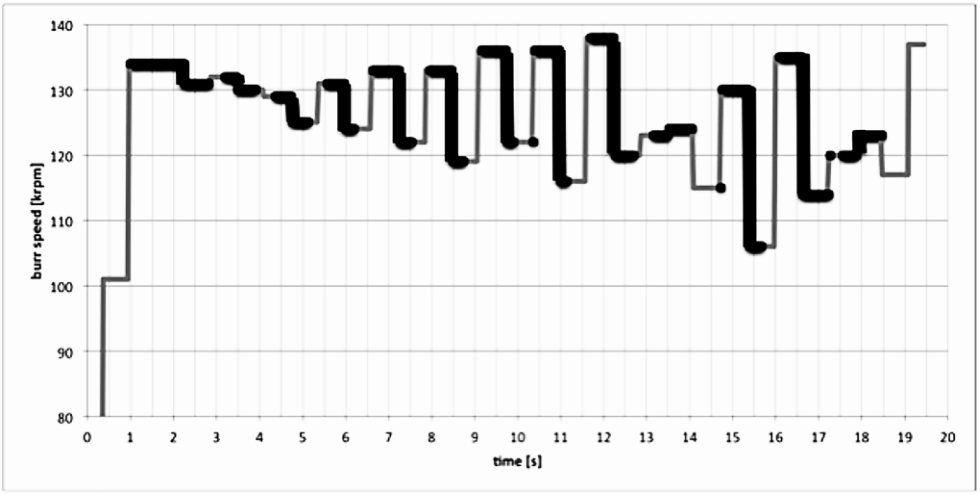


Fig. 1|11-6 Course of burr-speed in RA of a heavily calcified RCA lesion. Bold sections of the curve indicate forward movement of the burr and illustrate that sharp deceleration of burr-speed is immediately countered with retraction of the burr (temporal resolution of speed-course recording: 1.7 fps; temporal resolution of burr-movement recording: 7 fps)

2 krpm; Q3: 4.6 krpm) with maximal decelerations of 9.5 krpm (Q1: 6.75 krpm; Q3: 15.5 krpm) resulting in medium burr-speed of 125 krpm (Q1: 122.75 krpm; Q3: 128.25 krpm) over the whole procedure.

Conclusions: We found that the pre-set platform speed of 135 krpm resulted in strongly varying, substantially lower actual maximal burr-speeds in the treated vessel. Rotational ablation with the pecking technique produces short sharp decelerations in burr-speed of variable extent. Clinical studies on RA should not only report pre-set platform speeds, but also incorporate data about the actual course of burr-speed over the whole RA-procedure.

11-7

Impact of gender and on-site cardiac surgery on clinical outcomes after transfemoral transcatheter aortic valve replacement

David Zweiker[1], Florian Egger[1], Alexander Geppert[1], Miklos Rohla[1], Olev Luha[2], Gudrun Lamm[3], Matthias Hammerer[4], Edwin Maurer[5], Michael Grund[6], Thomas Sturmberger[7], Johannes Kastner[8], Eduard Zeindlhofer[9], Kurt Huber[1]

[1]3rd Medical Department, Wilhelminenhospital, Vienna, Austria
[2]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[3]Department of Internal Medicine III, Karl Landsteiner University Hospital St. Pölten, St. Pölten, Austria
[4]Clinic of Internal Medicine II, Department of Cardiology, Paracelsus Private Medical University, Salzburg, Austria
[5]2nd Medical Department with Cardiology and Intensive Care Unit, Hospital Wels-Grieskirchen, Wels, Austria
[6]Department of Cardiology, Kepler University Hospital Linz, Linz, Austria
[7]2nd Medical Department, Cardiology, Angiology and Intensive Care Unit, Hospital Elisabethinen, Linz, Austria
[8]Division of Cardiology, Department of Medicine II, Medical University of Vienna, Vienna, Austria
[9]Department of Internal Medicine, Hospital Barmherzige Schwestern, Linz, Austria

Background: A previous analysis of the prospective multicentre Austrian Transcatheter Aortic Valve Implantation (TAVI) Registry showed no significant impact of institutional on-site cardiac surgery (iOSCS) on clinical outcomes after TAVI. Current risk scores for aortic valve interventions (such as logistic EuroSCORE, EuroSCORE II, and STS/ACC score) incorporate the female gender as predictor for increased procedural risk. In this post-hoc analysis, we analysed the impact of gender on three-year mortality after TAVI in the overall cohort as well as patients treated in centres with vs. without iOSCS.

Methods: Out of 1,822 consecutive high-risk patients (median age 83 (interquartile range 79–86) years, 59.8% female) with a logistic EuroSCORE of 15.1 (9.5–23.8) %, 290 patients (15.9%) underwent TAVI without iOSCS (no-iOSCS group). Out of the remaining iOSCS group, we selected 290 iOSCS patients by 1:1 matching. We analysed (1) the prevalence of risk factors in female vs. male patients, (2) the impact of gender on survival of the whole cohort as well as (3) of no-iOSCS and matched iOSCS groups.

Results: Prevalence of female patients was similar in no-iOSCS and matched iOSCS groups (63.4% vs. 62.8%, $p=0.931$). Female patients had less coronary artery disease (50.4% vs. 73.9%, $p<0.001$), less reduced left-ventricular dysfunction (41.7% vs. 57.4%, $p=0.001$), but a higher age (84 (81–87) vs. 83 (80–87) years, $p=0.020$). The predicted risk according to

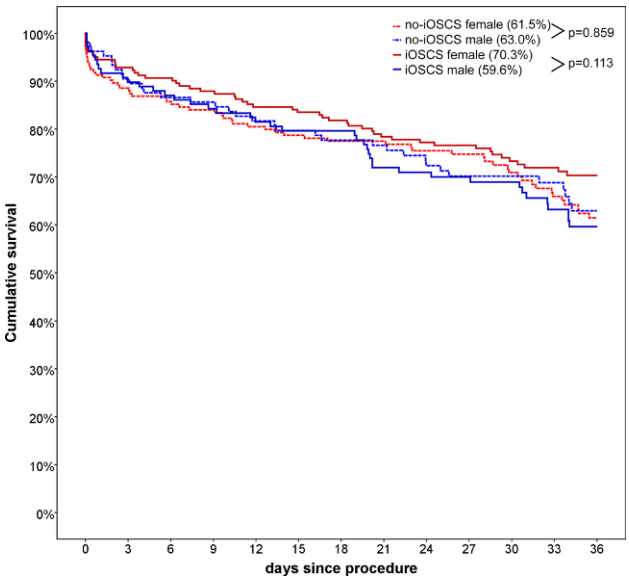


Fig. 1|11-7 Three-year survival stratified by iOSCS and gender

logistic EuroSCORE was similar between both genders (21.6 (13.9–28.8) vs. 18.05 (12.0–30.2) %, $p=0.069$). Three-year overall survival was similar in female and male patients (61.2% vs. 66.0%, $p=0.326$). We did not observe significant differences in 3-year survival between female and male patients in no-iOSCS (61.5% vs. 63.0%, $p=0.859$) and matched iOSCS groups (70.3% vs. 59.6%, $p=0.113$, Figure).

Conclusions: There were no significant differences between both genders regarding baseline predicted risk, three-year survival in the whole TAVI cohort as well as in no-iOSCS and matched no-iOSCS groups.

Postersitzung 12 – Rhythmologie 1

12-1

Leadless pacemaker implantation after transcatheter aortic valve replacement – results of a single center patient cohort

Alexander Fellner[1], Hermann Blessberger[1], Karim Saleh[1], Stefan Schwarz[1], Christian Reiter[1], Jürgen Kammler[1], Jörg Kellermair[1], Alexander Nahler[1], Daniel Kiblböck[1], Thomas Lambert[1], Michael Grund[1], Clemens Steinwender[1]

[1]Department of Cardiology and Internal Intensive Medicine, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria

Background: Leadless pacemakers (LP) have been recently introduced into clinical practice to overcome pocket- and lead-related complications of conventional pacing systems. The only commercially available LP today is the Micra® (Medtronic Inc.), an MR-conditional single-chamber LP with VVIR pacing capabilities. It is delivered to the right ventricle with a catheter through the femoral vein. Intermediate-term results of the Micra Investigational Device Exemption study and the Micra Post-Approval Registry demonstrated excellent safety and efficacy performance in more than 2,500 patients. Compared to a historical dataset of patients with conventional transvenous systems, major complications occurred 63% less often. Transcatheter aortic valve replacement (TAVR) has become a valid treatment option for selected patients (P) with severe symptomatic aortic valve stenosis. However, there still is a considerably high rate of postinterventional conduction disturbances caused by the valve prosthesis necessitating permanent pacemaker implantation. We investigated the safety and efficacy of LP implantation in P with a pacing indication after recent TAVR.

Methods: All P with recent (<10 days) transfemoral TAVR and postinterventional conduction disturbances requiring pacemaker implantation were screened for LP implantation. As pacing indications were defined: (1) The new onset of a second-degree Mobitz II or third-degree AV-block, (2) development of left-bundle-brunch block (LBBB) plus prolongation of the PR-interval (>200 ms) in P with sinus rhythm (SR) or (3) LBBB plus bradycardia or pauses in P with atrial fibrillation (AF). As suitable for LP implantation were defined: (1) P with preserved left ventricular ejection fraction (>50%) and AF. (2) P with SR, if a low pacing rate was expected (back-up pacing for new LBBB plus PR-interval prolongation). Two experienced operators performed LP implantation during the same hospital stay like TAVR. Procedural, electrical and clinical follow-up data were prospectively collected for all P. As serious adverse events were defined: (1) Cardiac effusion requiring pericardiocentesis or surgery, (2) groin hematoma requiring transfusion, (3) LP dislocation after implantation, (4) loss of LP function after implantation due to a significant rise of the pacing threshold, (5) device infection.

Results: A Micra™ LP was implanted in 32 P with a pacing indication after TAVR. The sex was balanced ($n=16/50\%$ males and females, respectively) and the mean age was 81 ± 4 years. All P had received a self-expanding TAVR (Evolut™, Medtronic or Portico™, Abbott) 7 ± 2 days before. All LP implantations were performed in a cathlab equipped for cardiac implantable electronic device implantations via the right femoral vein without serious adverse events. The mean implant procedure duration was 31 ± 6 min with a mean fluoroscopy time of 5.9 ± 2.3 min. After a mean of 1.5 ± 0.8 positions (100% septal), the LP showed a mean threshold of 0.49 ± 0.22 V, impedance of 805 ± 231 Ω and sensing of 10.9 ± 4.7 mV. No groin complications (hematoma, arterio-venous fistula, infection) occurred. All P could be discharged one to four days after LP implantation. At a mean follow-up of 1.1 ± 0.8 years, 31 P (97%) were alive. One P (3%) died 2 years and 10 months after LP implantation at home (cause of death unknown). Pacing thresholds and sensing remained stable in all P. No device-related serious adverse events occurred.

Conclusions: In suitable patients with a pacing indication after TAVR, LP may be an attractive alternative to conventional transvenous systems due to the less invasive procedure and favorable intermediate-term results.

12-2

Influence of NT-pro-BNP serum levels on the long-term outcome after cryo pulmonary vein isolation

Hermann Blessberger[1], Alexander Nahler[1], Denis Hrncic[1], Jörg Kellermair[1], Stefan Rechberger[2], Armin Windhager[2], Martin Etzelstorfer[2], Verena Kaltenberger[3], Karim Saleh[1], Stefan Schwarz[1], Christian Reiter[1], Jürgen Kammler[1], Clemens Steinwender[1]

[1]Department of Cardiology and Internal Intensive Medicine, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria
[2]Medical Faculty of the Johannes Kepler University, Linz, Austria
[3]Medical University of Graz, Graz, Austria

Background: Especially in the early course of atrial fibrillation (AF), pulmonary vein isolation (PVI) is an effective treatment modality to maintain sinus rhythm and is therefore endorsed by current guidelines. Both techniques, PVI using radiofrequency ablation or cryoablation, have recently been shown to be equivalent in terms of clinical outcomes. However, despite being more effective than conservative drug treatment, there is still a relapse rate of up to 35% in the first year after the procedure. Therefore, it is crucial to identify predictors of long-term outcome to provide a better individually-tailored treatment approach for patients. NT-pro-BNP is secreted into the bloodstream by atrial myocytes as a response to distension. NT-pro-BNP may thereby represent a surrogate parameter reflecting atrial stress or dilatation caused by increased atrial volume, pressure or a high atrial fibrillation burden. All these factors may, in turn, be associated with an inferior long-term

outcome after PVI. The aim of this study was to assess baseline NT-pro-BNP serum levels as a predictor for long-term outcome after PVI using cryoablation.

Methods: Data were retrieved from our institution's Atrial Fibrillation Cryo Ablation Registry (AFCAR). Patients were eligible if (1) they had undergone a first-ever cryoablation for atrial fibrillation at least three months ago at our department and (2) baseline NT-pro-BNP serum levels from the index stay prior to the ablation procedure were available. At first, demographic and peri-procedural data were collected retrospectively from the hospital's records. In a second step, follow-up data were collected by conducting telephone interviews (structured questionnaires) and by reviewing patients' charts. The primary outcome was defined as a combined endpoint of an ECG-documented relapse of an atrial arrhythmia or electrical cardioversion because of an atrial arrhythmia or a redo PVI procedure. Events within the first 90 days after the PVI were blanked out from the analysis. An exception to this rule was only made if a redo PVI was performed within three months after the index procedure. The impact of pre-procedural NT-pro-BNP serum levels on the primary endpoint was assessed with Kaplan-Meier survival analysis. Clinically significant effect modifiers, such as the type of atrial fibrillation, age, left ventricular ejection fraction, body mass index, kidney function or a history of coronary artery disease, were accounted for by applying a multivariate Cox proportional hazards model.

Results: We identified 404 eligible patients. Of those, 4 (1%) patients refused the telephone follow-up, and 25 patients were alive, but no contact could be established (6.2% loss to follow-up). Three hundred seventy-five subjects were finally analyzed (median follow-up time: 2.1 years, IQR: 0.8–4.1 years, age 59.1 ± 10.8 years, 108 [28.8%] female, 327 diagnosed with [87.2%] paroxysmal and 48 [12.8%] with persistent or long persistent atrial fibrillation). One or more of the conditions predefined as combined endpoint were reached by 189 individuals (50.4%). An AF relapse was associated with persistent or long persistent AF, a history of coronary heart disease and intake of antiarrhythmic drugs at the time of follow-up. Baseline NT-pro-BNP levels ranged between 5 pg/ml and 3,309 pg/ml (tertile 1 ≦ 123.8 pg/ml, tertile 2 ≦ 342.2 pg/ml, tertile 3 > 342.2 pg/ml). The Kaplan-Meier survival analysis revealed a 1.45-fold risk to meet the primary endpoint per increase of one NT-pro-BNP tertile (Hazard ratio [HR] 1.45, 95% CI: 1.21–1.74, $p = 0.0001$). This statistically significant effect was preserved in the multivariate analysis that adjusted for major confounders (HR 1.40, 95% CI: 1.12–1.75, $p = 0.003$).

Conclusions: NT-pro-BNP serum levels prior to a cryo pulmonary vein isolation may be used as a surrogate parameter of atrial stress. They proved to be a robust predictor of AF relapse in our cohort of patients.

12-3

Association of adipocytokines with left atrial remodelling and thrombus formation in atrial fibrillation – ALERT

Hermann Blessberger[1], Patrick Müller[2], Hisaki Makimoto[2], Malte Kelm[2], Anita Meissner[2], Christopher Gemein[3], Jörn Schmitt[3], Thomas Deneke[4], Franziska Fochler[4], Fabian Schiedat[5], Andreas Mügge[6], Michael Gabriel[7], Clemens Steinwender[1]

[1]Department of Cardiology and Internal Intensive Medicine, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria
[2]Department of Cardiology, Pneumology and Angiology, University Hospital Düsseldorf, Düsseldorf, Germany
[3]Department of Cardiology and Angiology, University Hospital Giessen, Giessen, Germany
[4]Heart Center Bad Neustadt, Clinic for Cardiology II, Bad Neustadt a. d. Saale, Germany
[5]Department of Medicine II, Cardiology and Angiology, Ruhr University Bochum, Germany
[6]Cardiovascular Center, St. Josef Hospital Bochum, Ruhr University Bochum, Bochum, Germany
[7]Institute of Nuclear Medicine and Endocrinology, Kepler University Hospital, Linz, Austria

Background: Atrial fibrillation is the most common sustained arrhythmia affecting 1.5–2.0% of the adult population on average. As low blood flow velocities in the left atrium during atrial fibrillation predispose to intra-cardiac thrombus formation, oral anticoagulation is an important and powerful therapeutic intervention in patients deemed to be at high thromboembolic risk. As every means of anticoagulation also bears the risk of bleeding, both the risk of thromboembolism and bleeding have to be balanced in every single patient. Risk scores like the CHA_2DS_2-VASc were shown to perform better in predicting thromboembolic risk in high-risk patients than in patients who are only at low risk. Thus, a further refinement would be desirable to better target oral anticoagulation therapy, especially in low risk patients. Novel serum markers reflecting the activation of platelets as a surrogate for intra-cardiac thrombus formation and subsequent thromboembolic events may be a possibility to accomplish this endeavor. Adipocytokines, like leptin, adiponectin, resistin or visfatin, are cell signaling proteins produced by human adipose tissue that are released into the blood stream. They were shown to influence platelet activation as well as arterial and venous thrombus formation. By doing so, adipocytokine serum levels may predict the risk of intra-cardiac thrombus formation that may, in turn, lead to debilitating ischemic strokes.

Methods: We conducted a prospective cross sectional multi-center trial to assess the association between adipocytokine serum levels and the presence of spontaneous echo contrast (SEC) or left atrial thrombi as surrogate parameters for thromboembolic events. Participating centers were located in Germany (Heart Center Bad Neustadt a. d. Saale, University Hospitals in Duesseldorf, Bochum and Giessen) and Austria (University Hospital Linz). Patients were eligible for inclusion if they were diagnosed with paroxysmal or persistent atrial fibrillation and were referred to a transesophageal echocardiography (TEE) either before undergoing electrical cardioversion or pulmonary vein isolation. TEE was performed according to the respective standards at each institution. All patients had to be

on some kind of oral anticoagulation. The primary outcome was defined as the presence of either spontaneous echo contrast (SEC) or left atrial appendage (LAA) or left atrial (LA) thrombus on TEE. Serum blood samples were drawn after an overnight fasting period and stored at -80 °C until analysis. Members of the study team administered questionnaires to record baseline characteristics. Adipocytokine serum levels were measured by using commercially available ELISA kits. A logistic regression model was fitted to evaluate the association between adipocytokine serum levels and markers of intra-cardiac thrombosis.

Results: One hundred eighty-nine patients were enrolled in the study (33% females, mean age: 67.2 ± 11.1 years, BMI 28.6 ± 4.7). The majority of patients were diagnosed with persistent atrial fibrillation (102 [54.0%]). Fourty-eight individuals (25%) exhibited the primary outcome (one or more pre-defined endpoints on the transesophageal echocardiogram—41 (21.7%) SEC, 3 (1.6%) LA thrombus, 13 (6.9%) LAA thrombus, group 1 (G1), whereas the others did not (group 2 = G2). The BMI was not statistically significantly different between both groups. Affected individuals were more likely to be in persistent atrial fibrillation ($p = 0.009$), diagnosed with chronic kidney disease ($p < 0.0001$), to have a lower left ventricular ejection fraction ($p < 0.00001$), to be on an oral anticoagulation with phenprocoumon (vs. NOAC, $p = 0.027$) or to have a history of stroke ($p = 0.018$). As opposed to adiponectin (G1: 31.3 µg/ml, G2: 26.9 µg/ml, $p = 0.126$) and visfatin (G1: 31.7 ng/ml, G2: 36.8 ng/ml, $p = 0.470$), leptin (G1: 22.6 ng/ml, G2: 12.0 ng/ml, $p = 0.025$) and resistin (G1: 6.52 ng/ml, G2: 5.31 ng/ml, $p = 0.016$) serum levels were significantly higher in patients with the primary outcome. In the logistic regression analysis, only resistin was statistically significantly associated with the primary outcome (OR 1.13, 95% confidence interval: 1.02–1.25, $p = 0.021$), whereas leptin marginally missed statistical significance (OR 1.01, 95% confidence interval: 0.99–1.02, $p = 0.061$).

Conclusions: Leptin and resistin serum levels were associated with surrogate parameters of thromboembolic events in our cohort of patients with atrial fibrillation and may constitute a link between obesity and thromboembolism. These promising new serum parameters should be further investigated in larger prospective trials with hard endpoints.

12-4

High-power short-duration ablation of complex atrial arrhythmias in patients with congenital heart disease

Thomas Wolber[1], Matthias Gass, Corinna Brunckhorst, Matthias Greutmann, Firat Duru

University Hospital Zurich, Zurich, Switzerland

Background: Radiofrequency ablation (RFA) is an important treatment option for patients with symptomatic arrhythmias. However, gaps in linear lesions may cause recurrence of arrhythmia and adjacend organs may be damaged by conductive heating. In vitro studies have demonstrated broader and shallower lesions with the use of higher power settings and shorter ablation duration. High-power short-duration (HPSD) ablation has therefore been introduced as a means to improve safety and efficacy of atrial ablation procedures. We aimed to assess safety and efficacy of HPSD in patients with complex atrial arrhythmias.

Methods: 36 patients (mean age 45 ± 15 years, 42% male) were studied. 12 patients underwent HPSD ablation and were compared to 24 matched controls. The HPSD group was treated with power settings of 50–55 W and ablation times of 5–8 seconds. In the control group, conventional settings of 25–40 W for 20–60 seconds were applied. Electroanatomic mapping and cooled catheters with force-sensing technology were used in all procedures. Procedural success was assessed by demonstration of noninducibility of a prior inducible arrhythmia and proof of bidirectional block after linear ablation. Major complications (bleeding, thromboembolism, pericardial effusion, tamponade, phrenic nerve damage, atrio-esophageal fistula) were assessed by echocardiography and chart review.

Results: HPSD ablations were performed to treat atrial arrhythmias in 12 patients with congenital heart disease (GUCH). 24 patients were included as controls. Procedural success was achieved in all patients in both groups. Ablation duration was significantly shorter (7 ± 1.2 vs. 38 +/- 19 seconds per lesion, $p < 0.01$) in HSPD ablations. HPSD ablation was associated with shorter procedure times (333 ± 122 vs. 296 ± 115 minutes). No major complications were observed in both groups.

Conclusions: This initial experience shows high procedural efficacy and low risk of complications associated with HPSD ablation in patients with complex atrial arrhythmias. Shorter ablation times may be associated with more effective lesions which might improve success rates of catheter ablations in this challenging patient group. However, further research is warranted to define optimal energy settings and ablation duration for these interventions. Safety and long-term efficacy of HPSD ablations need to be studied in larger prospective trials.

12–5

Vorhofflimmer-Ablationen in Österreich 2016 bis 2018: Ergebnisse aus dem Österreichischen Ablationsregister

Lukas Fiedler[1], Daniel Scherr[2], Martin Martinek[3], Katie Bates[4], Clemens Steinwender[5], Bernhard Strohmer[6], Marcus Ammer[7], Edmund Gatterer[8], Franz Glaser[9], Florian Egger[10], Alexandra Schratter[11], Lalit Kaltenbach[4], Hanno Ulmer[4], Markus Stühlinger[12]

[1]Landeskrankenhaus Wiener Neustadt, Wiener Neustadt, Österreich
[2]Medizinische Universität Graz, Graz, Österreich
[3]Ordensklinikum Linz, Linz, Österreich
[4]Department für Medizinische Statistik, Informatik und Gesundheitsökonomie, Universität Innsbruck, Innsbruck, Österreich
[5]Klinik für Interne 1, Kepler Universitätsklinikum Linz, Linz, Österreich
[6]Universitätsklinik für Innere Medizin II, Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Österreich
[7]Klinikum Wels-Grieskirchen, Wels, Österreich
[8]2. Medizinische Abteilung mit Kardiologie und internistischer Intensivmedizin, Krankenanstalt Rudolfstiftung, Wien, Österreich
[9]Universitätsklinikum Krems, Krems, Österreich
[10]3. Medizinische Abteilung mit Kardiologie, Wilhelminen Spital, Wien, Österreich
[11]4. Medizinische Abteilung mit Kardiologie, Krankenhaus Hietzing, Wien, Österreich
[12]Universitätsklinik für Innere Medizin III (Kardiologie und Angiologie), Medizinische Universität Innsbruck, Innsbruck, Österreich

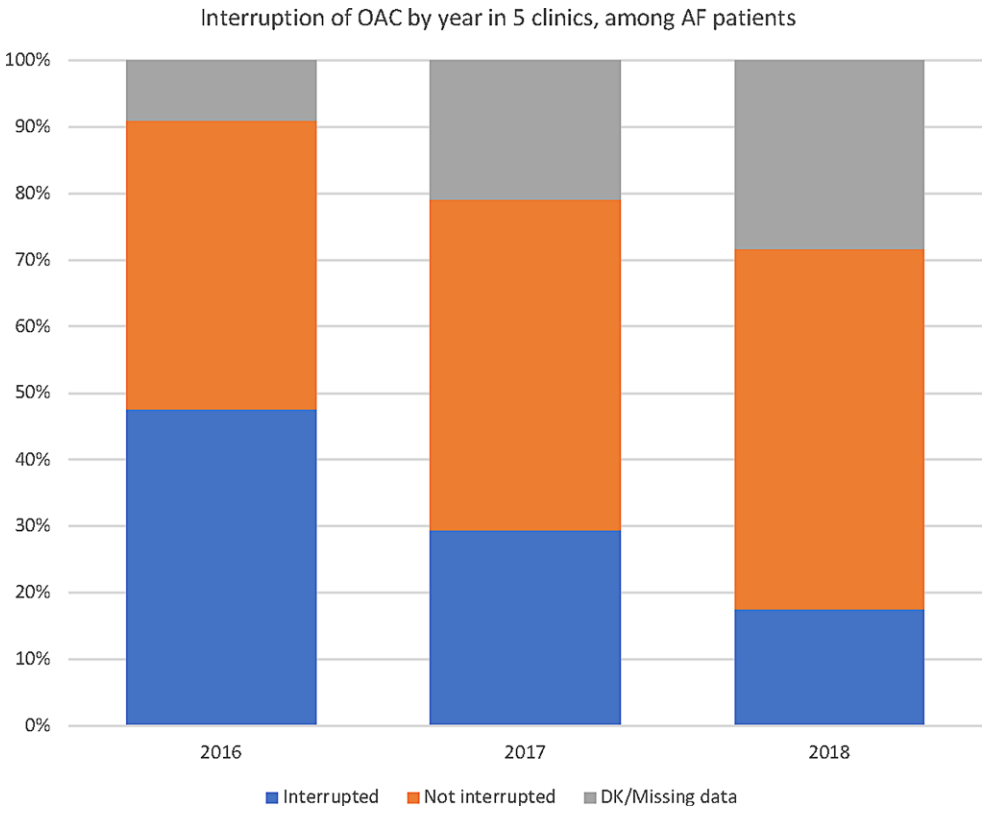


Abb. 1|12-5 Prozent der Patienten, die einer Vorhofflimmer-Ablation unterzogen wurden, bei denen die OAK periinterventionell unterbrochen wurde (*blau*); Prozent der Patienten, bei denen die OAK periinterventionell nicht unterbrochen wurde (*orange*); Missing Data (*grau*)

Grundlagen: 2015 wurde von der Arbeitsgruppe Rhythmologie der ÖKG ein elektronisches Ablationsregister initiiert, um verlässliche Daten zur Anzahl, Indikation, Technik, sowie Erfolg und Komplikationen von elektrophysiologischen Prozeduren zu erheben. In dieser Subgruppen-Analyse werden die Ergebnisse der eingegebenen linksatrialen VH-Flimmer Ablationen zwischen 2016 und 2018 beschrieben.

Methodik: Insgesamt wurden zwischen 2016 und 2018 von 13 Zentren 1860 Datensätze zu paroxysmalem und 660 Datensätze zu persistierendem Vorhofflimmern in das elektronische Register eingegeben. Die Zahl der Datensätze pro Jahr erhöhte sich von 561 auf 1508. In dieser retrospektiven Analyse wurden alle Vorhofflimmern Ablationen in einer deskriptiven Statistik ausgewertet.

Ergebnisse: Das Alter (61; IQR 54–68 Jahre) und der Geschlechts-Anteil (71 % m; 29 % w) der Patienten blieben im Beobachtungszeitraum im Wesentlichen unverändert. Der Anteil von Ablationen mit elektroanatomischem Mapping und Non-Contact Mapping Systemen nahm ab (24,7 auf 19,9 %), der der Ablationen mit dem Kryoballon (22,5 % auf 25,9 %) dagegen leicht zu. 74,8 % waren Erstprozeduren 19,8 % waren Redoprozeduren. 98 % konnten akut erfolgreich ablatiert werden. Es zeigt sich eine tendenzielle Abnahme der Komplikationen von 2017 auf 2018, 4,5 % vs 3,5 %, $p = 0{,}515$). Die Anzahl der Patienten, bei denen die die orale Antikoagualtion im Rahmen der Ablation unterbrochen wurde konnte über die letzten 2 Jahre reduziert werden (Abb. 1).

Schlussfolgerungen: Zwischen 2016 und 2018 wurde in diesem Nationalen Register eine Zunahme von eingegebenen VH-Flimmer-Ablationen festgestellt. Die überwiegende Mehrzahl der Interventionen wird mit Radiofrequenz durchgeführt. Der Erfolg der Ablationen liegt insgesamt bei 98 % und die Komplikationsrate bei 3,5 %.

12-6

Erste Erfahrungen beim Aufbau eines HIS-Bündel Pacing-Programms

Karim Saleh, Stefan Schwarz, Christian Reiter, Martin Patrasso, Roman Kneidinger, Clemens Steinwender

Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz, Linz, Österreich

Grundlagen: Die rechtsventrikuläre Stimulation verursacht je nach Stimulationsanteil und Patientencharakteristika bei bis zu 15 % der Herzschrittmacher-Patienten eine Schrittmacher-induzierte Kardiomyopathie. Als Mechanismus wird die durch die Stimulation bedingte linksventrikuläre Dyssynchronie angegeben. Um diese zu verhindern, wird seit Jahren am Konzept des HIS-Bündel Pacings (HBP) gearbeitet, bei dem die rechtsventrikuläre Stimulationselektrode nicht ins Myokard, sondern direkt in das HIS-Bündel geschraubt wird. Damit sollen eine konzentrische Aktivierung der Ventrikel bewirkt und die deletären Folgen der linksventrikulären Dyssynchronie verhindert werden. Die Technik des HBP wurde und wird durch eine eingeschränkte Steuerbarkeit der Sonden bei der Implantation sowie hohe Reizschwellen des HIS-Bündels im Vergleich zum Myokard erschwert. Mit neuen verfügbaren Tools wie der 4F Schraubelektrode SelectSecure™ Model 3830 mit den entsprechenden Schleusen C315HIS™ oder C304Deflectable™ (Fa. Medtronic) kann das HIS-Bündel bei der Implantation leichter erreicht und mit Reizschwellen unter 2,5 V stimuliert werden. Mit dieser Technologie wurde an unserer Institution ein HBP-Programm initiiert. Ziel dieser Analyse ist es, die Ergebnisse der ersten eigenen Serie von Patienten (P) mit HBP in Hinblick auf Machbarkeit und Sicherheit zu beleuchten.

Methodik: Eingeschlossen wurden nur P mit Sick-Sinus-Syndrom und niedrigem Wenckebach-Punkt bei der atrialen Stimulation, um Erfahrungen mit der neuen ventrikulären Sondenposition bei nicht Schrittmacher-abhängigen P zu sammeln. Mit der Helix der SelectSecure™ Elektrode in einer Schleuse wurde dabei mittels kleiner Bewegungen die HIS-Region gemappt, bis am Analysiergerät und einer Elektrophysiologie-Messeinheit ein eindeutiges HIS-Signal nachweisbar war. Dann wurde die Elektrode durch Einschrauben fixiert, die Schleuse in den Vorhof zurückgezogen und die Sensing- und Reizschwellenwerte ermittelt. Waren diese akzeptabel (Impedanz 400–2000 Ohm, Sensing >2 mV, Reizschwelle <2,5 V@1,0 ms), wurde eine Reizschwelle mit entsprechender Sicherheits-Marge programmiert. Anhand der Breite der stimulierten QRS-Komplexe wurde das Ergebnis als (1) selektives HBP: QRS-Komplexe ident zu denen bei AV-Eigenüberleitung bzw. als (2) para-HBP: QRS-Komplexe breiter als bei AV-Eigenüberleitung definiert. Sämtliche Prozeduren wurden von einem sehr erfahrenen Implanteur über einen linksseitigen Zugang durchgeführt. Es wurden die Prozedurdauer, Durchleuchtungszeit und periprozeduralen Komplikationen sowie die elektrischen Parameter und klinischen Ereignisse im Follow-up erfasst.

Ergebnisse: Von Mai bis inklusive Dezember 2018 wurden 8 P (5 weiblich, mittleres Alter 72 ± 8 Jahre) in die prospektive Beobachtung eingeschlossen. Bei allen P gelang es, ein HIS-Potenzial abzuleiten und die Elektrode an dieser Stelle einzuschrauben. Eine stabile Reizschwelle <2,5 V@1,0 ms wurde bei 4 P (50 %) gesehen, während bei den anderen 4 P nach erfolglosen HBP-Versuchen eine septale rechtsventrikuläre Position mit jeweils guten Parametern gewählt wurde. Die mittlere Prozedurdauer betrug 115 ± 32 min, die Durchleuchtungszeit 19 ± 10 min. Bei den 4 P mit HBP waren die mittleren elektrischen Messwerte bei der Implantation: Reizschwelle 1,65 V@1,0 ms, Impedanz 728 ± 164 Ω, Sensing 7,4 ± 2,7 mV. Der programmierte ventrikuläre output war bei allen 4 P mit HBP jeweils 3,5 V@0,4 ms und führte bei 3 P (75 %) zu selektivem HBP und bei 1 P (25 %) zu para-HBP. Es traten keine peri- oder postinterventionellen Komplikationen – insbesondere keine Sondendislokationen – auf. Bei allen P wurde ein 3-Monats-follow-up durchgeführt, der stabile elektrische Messwerte (im Trend sinkende Reizschwellen) und keine Komplikationen ergab.

Schlussfolgerungen: Der Aufbau eines HBP-Programms erfordert neben einer großen Implantations-Expertise sorgfältige Vorbereitung, Material-Know-how und Geduld während der Prozeduren. Die HIS-Region ist über einen linksseitigen Zugang mit den beschriebenen Devices und Techniken gut erreichbar. Limitierend für das Erzielen eines anhaltenden selektiven HBP scheint weniger die Stabilität der Elektroden-Fixation als das Erreichen einer ausreichend niedrigen Reizschwelle zu sein. Die Ergebnisse der ersten Implantationen und vor allem das Potential des HBP rechtfertigen fortgesetzte Bemühungen in Richtung dieser Implantationstechnik.

12-7

Diastolic function grading in the prediction of arrhythmic death during long term follow-up

Achim Leo Burger[1], Andre Diedrich[2], Herwig Schmidinger[1], Thomas Pezawas[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Vanderbilt University Medical Center, Nashville, Tennessee, United States of America

Background: Patients with HFrEF (LVEF <40%) face a different risk for ventricular arrhythmias than patients with HFmrEF (40–49%) or HFpEF (LVEF ≥50%). Exact grading of diastolic function might improve risk stratification for arrhythmic death.

Methods: We prospectively enrolled 180 heart failure patients with ischemic or dilative cardiomyopathy and 30 patients with HFpEF only. Diastolic function was graded normal (0) and dysfunction grades 1 to 3. Primary outcome parameter was arrhythmic death.

Results: Diastolic function was normal in 23 (11.0%) patients, mildly reduced in 107 (51.0%) patients, moderately reduced in 31 (14.8%) patients and severely reduced in 49 (23.3%) patients. After an average follow-up of 7.0 ± 2.6 years, arrhythmic death was observed in 28 (13.3%) patients and non-arrhythmic death in 41 (19.5%) patients. Kaplan Meier analysis revealed that patients with LVEF ≤30% and severe diastolic dysfunction had the highest risk for arrhythmic death ($p<0.001$, Fig 1a) and for non-arrhythmic death ($p=0.047$, Fig. 2a). This was also true for the group of patients with LVEF 31–40% (arrhythmic death: $p<0.001$, Fig. 1b; non-arrhythmic death: $p=0.003$, Fig. 2b). In patients with LVEF >40%, individuals with severe diastolic dysfunction had a higher risk for non-arrhythmic death ($p<0.001$), but not for arrhythmic death ($p=0.308$). In an adjusted model for relevant confounding factors, severe diastolic dysfunction was associated with an 8-fold increased risk for arrhythmic death in the overall study population (HR = 8.22, $p<0.001$).

Conclusions: Severe diastolic dysfunction is associated with an increased risk for arrhythmic death in HFrEF patients. Individuals with HFmrEF or HFpEF and severe diastolic dysfunction have an increased risk for non-arrhythmic death, but not for arrhythmic death.

POSTERSITZUNGEN 13-18

Freitag, 31. Mai 2019, 10.00 bis 11.00 Uhr

Postersitzung 13 – Kardiologisches Assistenz- und Pflegepersonal

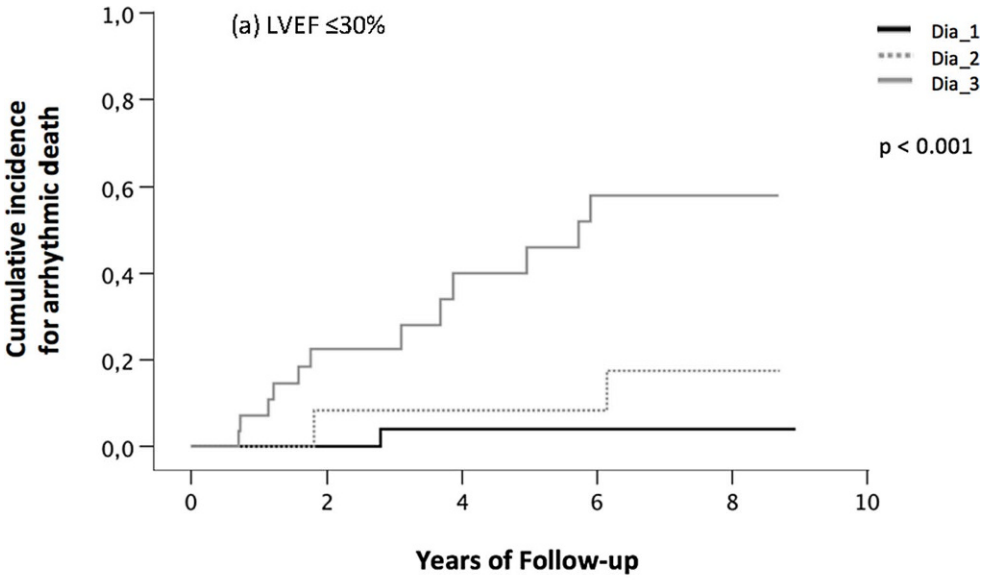
13-1

Survey on patients' perspectives about guideline-recommended disease management for chronic heart failure: results from the VISIT-HF study

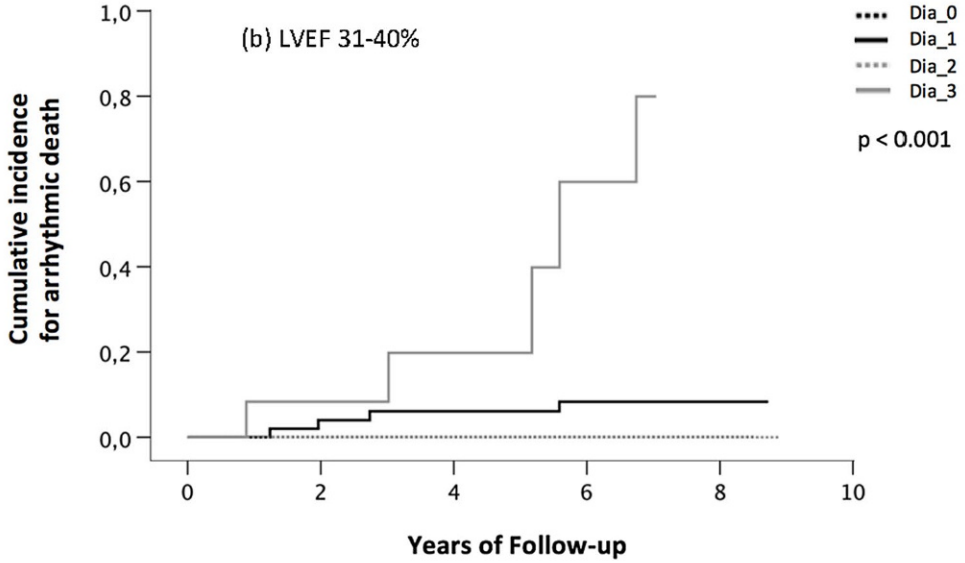
Katharina Strohmayer[1], Gernot Wagner[2], Isolde Sommer[2], Auersperg Pia[1], Renate Lechner-Bracun[1], Deddo Moertl[1]

[1]Clinical Department of Internal Medicine 3, University Hospital St. Poelten, St. Poelten, Austria
[2]Department for Evidence-based Medicine and Clinical Epidemiology, Danube University Krems, Krems, Austria

Background: Disease management programmes (DMPs) are aimed to establish guideline-recommended management in patients with chronic heart failure, thereby improving quality of life, decreasing hospitalizations and preventing premature death. Typical components of DMPs are home-based nurse care, telephone visits, tele-monitoring and patient education. Patients not accepting an integral component of a DMP are usually excluded, being left over to usual care. The magnitude of this problem is unknown, since data on patient perspectives are scarce. We therefore conducted a survey on patients' per-

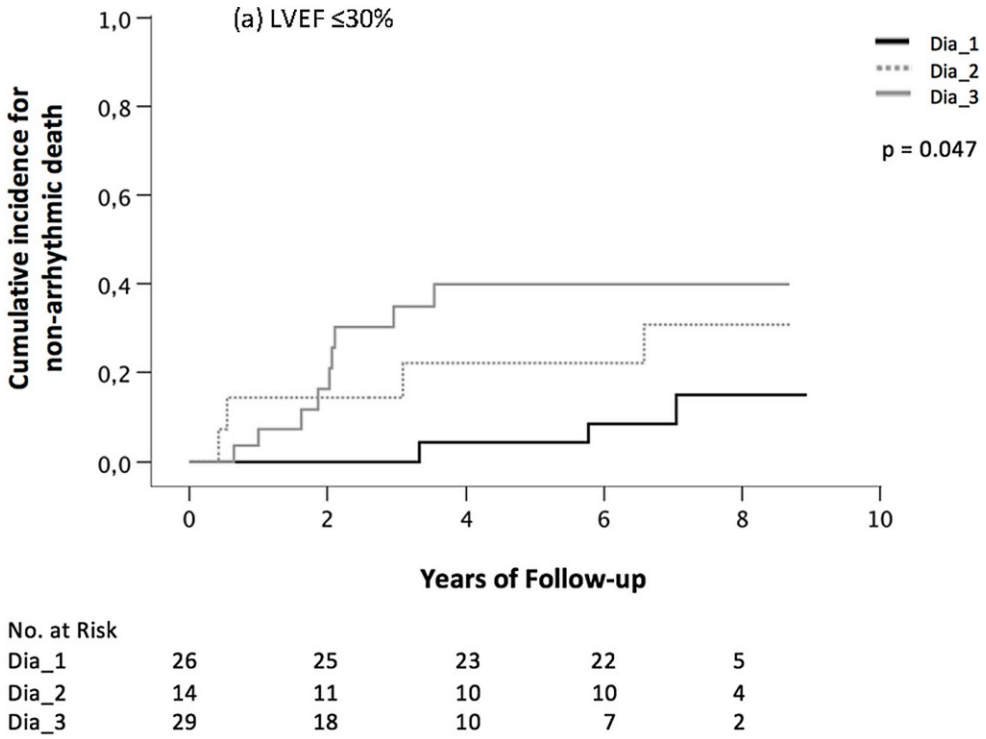


No. at Risk					
Dia_1	26	25	23	22	5
Dia_2	14	11	10	10	4
Dia_3	29	18	10	7	2

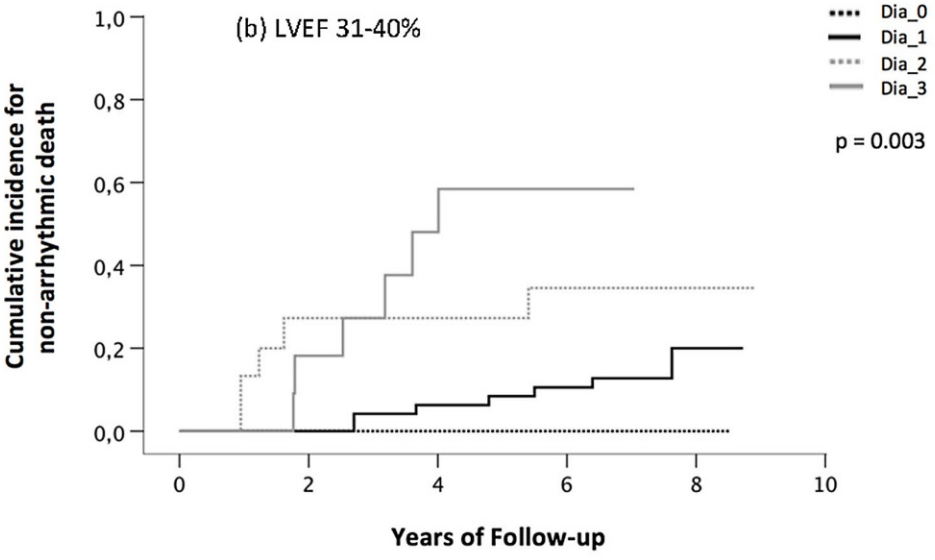


No. at Risk					
Dia_0	1	1	1	1	1
Dia_1	50	48	44	41	7
Dia_2	15	10	10	9	3
Dia_3	12	9	5	2	

Fig. 1|12-7 a,b: Kaplan-Meier estimates of the time to arrhythmic death in patients with (a) LVEF ≤30 and patients with (b) LVEF 31–40 % (DIA_0 normal diastolic function, DIA_1 mild diastolic dysfunction, DIA_2 moderate diastolic dysfunction, DIA_3 severe diastolic dysfunction)



No. at Risk					
Dia_1	26	25	23	22	5
Dia_2	14	11	10	10	4
Dia_3	29	18	10	7	2



No. at Risk					
Dia_0	1	1	1	1	1
Dia_1	50	48	44	41	7
Dia_2	15	10	10	9	3
Dia_3	12	9	5	2	

Fig. 2|12-7 a,b: Kaplan-Meier estimates of the time to non-arrhythmic death in patients with (a) LVEF ≤30 and patients with (b) LVEF 31-40 % (DIA_0 normal diastolic function, DIA_1 mild diastolic dysfunction, DIA_2 moderate diastolic dysfunction, DIA_3 severe diastolic dysfunction)

spectives about typical components of DMPs for chronic heart failure.

Methods: Patients with chronic heart failure irrespective of functional class and left ventricular ejection fraction were recruited from cardiology wards and a heart failure outpatient unit in a tertiary centre. Questionnaire-based interviews were performed covering patients' needs and preferences with respect to various components of DMPs like nurse care, tele-monitoring, and patient education.

Results: 105 patients (69 ± 12 years, 38 women, NYHA class III or IV: 65%, median NT-proBNP: 2223 pg/ml [Q1: 720 pg/ml, Q3: 5282 pg/ml]) were included and completed their interview. 46% of patients were hospitalized and 70% had heart failure with reduced ejection fraction. The majority of patients would agree on home-based nurse visits (86%) or telephone visits (83%) only if they felt very sick. However, 38% would not accept home-based nurse visits and 53% would not accept telephone visits if scheduled on a regular basis. Home-based nurse visits and telephone visits would not be accepted by 46% and 63%, respectively, if the aim of these visits was to reduce physician visits. 67% of patients would refuse tele-monitoring. Only 29% wanted to know more about their disease. No general preference on who should educate patients (general practitioner: 51%, heart failure specialist: 54%, nurse: 49% [multiple answers allowed]) was noted. None of these findings differed between hospitalized and ambulatory patients.

Conclusions: Our survey suggests that a considerable number of patients would refuse typical components of DMPs. Alternative disease management strategies with high adjustability to patients' perspectives might be needed in heart failure to improve acceptance rates and effectiveness of DMPs.

13-2

SurVey on nurses' perspectIves about paTient educAtion in chronic Heart Failure (VITA-HF)

Katharina Strohmayer, Deddo Moertl

Clinical Department of Internal Medicine 3, University Hospital St. Poelten, St. Poelten, Austria

Background: The ESC guidelines recommend patient education and self-empowerment as essential components of successful management of heart failure patients. Hospitalized heart failure patients are at very high risk for future heart failure events and are readily available for education at the wards. Therefore, they represent a reasonable target group for education by trained nurses. However, little is known about the nurses' perspectives on the need and feasibility of patient education during hospitalization in the absence of a specialized education programme. We therefore conducted a survey on staff nurses' views and perceived barriers of hospitalized heart failure patient education.

Methods: Registered nurses working at two cardiology wards and one cardiac surgery ward on a basis of 12-hour-shifts were asked to participate. They filled out paper-based questionnaires anonymously and returned them collected in a sealed envelope. The questionnaire consisted of a total of 16 questions grouped in three domains: Patient knowledge on guideline-recommended educational topics, time spent for education and topics addressed, and perceived barriers. The patient knowledge domain consisted of 12 sub-questions based on visual analogue scales (VAS) ranging from 0% (no knowledge) to 100% (sufficient knowledge, figure). For analysis, VAS score was dichotomized in adequate (≥ 80%) and inadequate (< 80%) knowledge.

Results: 25 nurses (14 from two cardiology wards, 11 from cardiac surgery wards) completed the questionnaire. 15 (60%) nurses stated that patients had no adequate knowledge in any of the investigated topics, the remaining 10 (40%) nurses found inadequate knowledge in at least half of the topics. The highest—but still inadequate—amount of knowledge was reported for smoking and devices (see figure). A median time of 15 minutes (Q1: 5 min, Q3: 30 min) was spent for heart failure education during a 12 hour dayshift. As main barriers for adequate education the nurses reported lack of time (88%) followed by insufficient nurse training to be able to educate heart failure patients (60%), and cognitive impairment of patients (60%).

Conclusions: Although staff nurses perceived considerable gaps in heart failure patient education, they only spent a small amount of time in educating heart failure patients. Lack of time and specialized nurses' training seem major but modifiable obstacles. Providing sufficient amount of time and training to staff nurses, could significantly improve patient self-empowerment and clinical outcome, and may even increase work satisfaction.

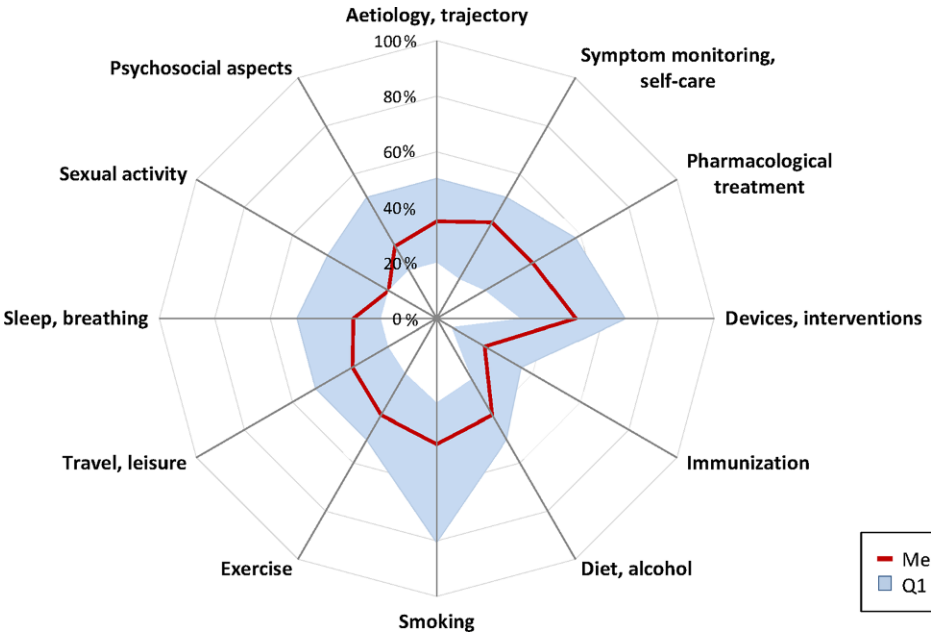


Fig. 1|13-2 Nurse-reported patient knowledge of guideline-recommended educational topics

13-3

Angst im Herzkatheter Labor – Ursachen und der Umgang mit Betroffenen

Waltraud Großschädl[1], Katrin Knödl[2]

[1]Landeskrankenhaus – Universitätsklinikum Graz, Heiligen Kreuz am Waasen, Österreich
[2] Landeskrankenhaus – Universitätsklinikum Graz, Graz, Österreich

Grundlagen: Angst wird definiert als ein bedrückendes, unsicheres Gefühl, das zu Anspannung und innerer Unruhe führt. Die Ursache ist den betroffenen Personen oft unklar oder unbekannt. Aus Studien geht hervor, dass es bei bis zu 80 % der Patientinnen und Patienten, bei denen ein medizinischer Eingriff geplant ist, zu präprozeduraler Angst kommt. Auch eine elektive, sowie akut notwendige Herzkatheter Untersuchung führt meist zu großer Verunsicherung. Pflegepersonen können jedoch durch spezielle Pflegeinterventionen Patientinnen- und Patientenängste wesentlich mindern und somit einen bedeutenden Effekt auf den Gemütszustand ausüben.

Methodik: Für diese Arbeit wurde im Zeitraum Jänner bis Februar 2019 eine Literaturrecherche auf den Datenbanken PubMed und CINAHL durchgeführt.

Ergebnisse: Pflegepersonen erzielen durch Wissen und Sensibilisierung auf das Thema Angst, dass Betroffene über ihre Befürchtungen sprechen und dadurch besser damit umgehen können. Patientinnen und Patienten machen einen ruhigeren Eindruck und bemühen sich um eine Problemlösung oder teilen mit, dass sie weniger oder keine Angst mehr haben. Auch in einem hoch technisierten Spezialbereich wie dem Herzkatheter Labor betrachten Pflegepersonen die Menschen ganzheitlich, mit all ihren krankheitsbedingten Sorgen, Nöten und Ängsten. Es ist besonders wichtig, bei Bedarf beruhigend zuzureden und eventuelle Fragen zum Eingriff kompetent und fachlich zu beantworten. Die Pflegepersonen sollten in der Lage sein zu erkennen, ob der Patientin oder dem Patienten eventuell die nötigen Informationen über den Eingriff fehlen, um Sorgen abzubauen. Falls es während der Intervention zu Schweißausbrüchen kommt, können Pflegepersonen feuchte Tücher auf die Stirn der Patientinnen und Patienten legen. Des Weiteren klagen Patientinnen und Patienten oft über die unvermeidliche Kälte, die im Labor herrscht. Wenn sich Personen fürchten und ihnen zusätzlich noch kalt ist, werden negative Emotionen häufig verstärkt. Eine warme Decke kann hier Abhilfe schaffen, um die Angst der Patienten zu mindern.

Schlussfolgerungen: Pflegepersonen sind häufig die ersten Ansprechpartner während des gesamten Krankenhausaufenthaltes. Die Auseinandersetzung mit der Angst der Patientinnen und Patienten im Herzkatheter Labor ist absolut notwendig. Das Erkennen und Auffangen dieser Emotionen können die Pflegepersonen aufgrund ihrer Kenntnisse gut bewerkstelligen.

13-4

Modernes Rhythmus Management – Die Rolle von „Advanced Practice Nurses“ bei ambulanter Implantation eines injizierbaren Loop-Recorders

Suzan Yamuti, Georg Delle-Karth

4. medizinische Abteilung für Kardiologie, Krankenhaus Hietzing, Wien, Österreich

Grundlagen: Problemstellung: Steigende Anzahl der Patientenzahlen durch demographische Entwicklung, erweiterte Indikationsstellungen und technische Möglichkeiten. Die steigende Anzahl der Indikationsstellungen und die damit benötigten Neuimplantationen stellt die Organisation der betroffenen Abteilungen vor neue Herausforderungen, die durch strukturelle Veränderungen bewältigt werden müssen. Der Pflege kann zunehmend durch die steigende Akademisierung und den damit verbundenen Zuwachs an Kompetenzen und Verantwortlichkeiten, auch im Bereich der Implantation und Nachsorge von injizierbaren Looprecordern, eine wichtige Rolle zukommen.

Methodik: Fragestellung: „Kann eine Spezialisierung der Pflege im Bereich der injizierbaren Looprecorder die Qualität und Effektivität bei Implantation und Nachsorge erhöhen?“ Deduktive Arbeit.

Ergebnisse und Schlussfolgerungen: Durch demographische Entwicklung, erweiterte Indikationsstellungen und technische Möglichkeiten werden in den letzten Jahren zur Abklärung von Synkopen, Vorhofflimmern und kryptogenen Schlaganfällen mehr Patienten mit einem ILR (injizierbaren Looprecorder) versorgt. Die steigende Anzahl der Indikationsstellungen und damit benötigten Neuimplantationen stellt die Organisation der betroffenen Abteilungen vor neue Herausforderungen, die durch strukturelle Veränderungen bewältigt werden müssen. Die Arbeit beschäftigt sich mit der Frage, ob die Pflege durch die neue Gesetzesnovelle (GuKG 08/2016) und die seit 2018 angebotenen akademischen Ausbildungen zur „Advanced Practice Nurse (ANP)“, die den Bologna-Prozess folgen, einen wichtigen Beitrag zur Qualitätssicherung bei Implantation und Nachsorge eines ILR's leisten kann? Dazu wurden Standards für Voraussetzung, Implantation, Nachsorge und Evaluation von ILR's erarbeitet, die als Anleitung für die praktische Umsetzung dienen können.

13-5

Von 100 auf 0 und wieder zurück – oder wie ich lernte mit einer LifeVest® zu leben

Mario Figo, Brigitte Strobl

Klinische Abteilung für Kardiologie, Landeskrankenhaus – Universitätsklinikum Graz, Graz, Österreich

Grundlagen: Die LifeVest® ist mittlerweile kaum noch aus dem klinischen Alltag wegzudenken. Es vergeht kaum ein Tag, an dem die Mitarbeiterinnen und Mitarbeiter der Kardiologie Ambulanz und des Herzkatheterlabors nichts mit diesem tragbaren Defibrillator zu tun haben. In Anbetracht dessen haben sich die Autoren dieses Posters dazu entschlossen, das Gerät kurz vorzustellen. In weiterer Folge wird anhand eines Fallbeispiels, sowie eines Interviews mit einem jungen LifeVest® Träger, vor allem auf die psychischen Aspekte des Lebens mit einer LifeVest®, eingegangen.

Methodik: Fallbeispiel: Juni 2017, Patient: männlich, 38a, sportlich, Nichtraucher. Zu Ostern dieses Jahres ein übergangener viraler Infekt mit Diarrhoe. Seither subjektiv nie mehr richtig fit geworden. 10 Tage vor Einweisung ins Krankenhaus ausgeprägte Belastungsdyspnoe beim Wandern, NYHA III–IV. Keine AP. Negative Familienanamnese bezüglich CMP. Erste klinische Beurteilung: EF 20–25 %. V. a. inflamm. CMP, daher Myocardbiopsie. Danach körperliche Schonung und konsequentes Tragen der LifeVest® bis die Biopsie Ergebnisse mit dem Patienten besprochen werden. Mitte Juli 2017 Ergebnis Myocardbiopsie: Keine Virus-assoziierte Myokarditis bzw.

entzündliche Kardiomyopathie nachweisbar. Dilatative Kardiomyopathie unklarer Genese. Das konsequente Tragen der LifeVest® bis auf weiteres wird empfohlen. Anfang September 2017: EF 17 %. Keine Besserung der Herzinsuffizienz trotz eingeleiteter Therapie. Patient fühlt sich subjektiv allerdings besser. LifeVest® weiter bis Implantation ICD. Anfang März 2018: Implantation ICD.

Ergebnisse: Interview mit dem Patienten:

- Wie gestaltete sich das Leben mit der LifeVest®?
- Welche Einschränkungen ergaben sich bei den Aktivitäten des täglichen Lebens?
- Wie erging es der Gattin und den beiden Kindern mit der neuen Situation?
- Wie erging es Ihnen selbst mit der neuen Situation?
- Welche Ängste und Sorgen ergaben sich durch die LifeVest®?
- Wie erging es Ihnen ohne Sport? Wann und wie begannen Sie wieder Sport zu treiben?
- Welche Bewältigungsstrategien hatten Sie in dieser Zeit?
- Fühlten Sie sich psychologisch gut betreut?
- Wie geht es Ihnen heute, knapp ein Jahr danach?

Schlussfolgerungen: Die Autoren möchten mit Hilfe dieses Fallbeispiels aufzeigen, wie sich das Leben mit einer LifeVest® für den Patienten gestaltet. Es ist sehr interessant, anhand des Interviews zu sehen, wie sich das Tragen einer LifeVest® auf die Psyche eines Patienten und seine ganze Familie auswirkt. So ist man auf der einen Seite glücklich, gut geschützt zu sein und lebt auf der anderen Seite dennoch mit der permanenten Angst, einen Stromstoß zu erhalten. Nichts desto trotz überwiegt bei einem Menschen, der auf einen ICD wartet, die Freude darüber, geschützt zu sein, über die Angst vor der Defibrillation. Aus dem Gespräch mit dem Patienten hat sich ergeben, dass er sehr dankbar war. Ihm wurde mit der LifeVest® geholfen, die Zeit bis zur ICD-Implantation mit einem ausgeprägten Sicherheitsgefühl zu überbrücken. Außerdem ermöglichte ihm die LifeVest® eine Rückkehr, wenn auch in kleinen und langsamen Schritten, in sein gewohntes Leben.

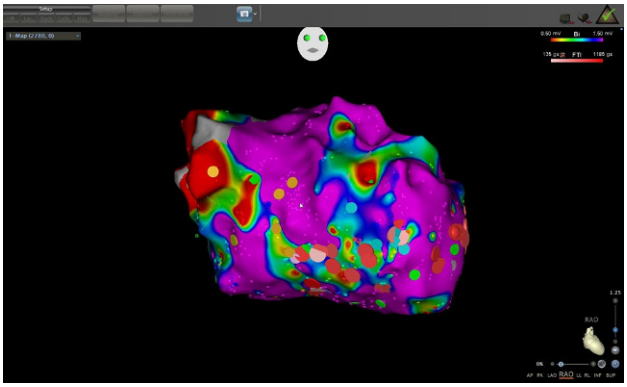


Fig. 1|13-6

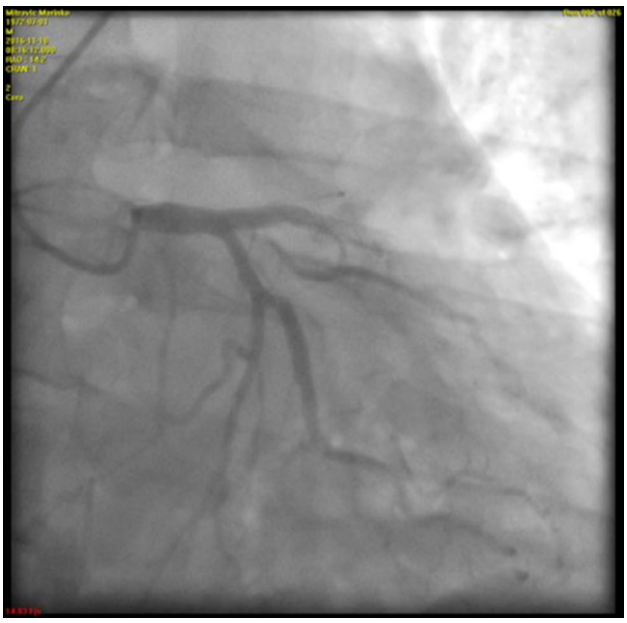


Fig. 2|13-6

13-6

Pflegevernetzung rettet Leben

Manfred Hangel[1], Martin Martinek[2], Fritz Freihoff[1], Helmut Pürerfellner[2]

[1]Sozialmedizinisches Zentrum Süd – Kaiser-Franz-Josef-Spital, Wien, Österreich
[2]Ordensklinikum Elisabethinen, Linz, Österreich

Grundlagen: Wir berichten über einen 47 Jahre alten Patienten nach einer VT-Ablation bei Z. n. elektrischem Sturm (05.01.2017).

Fallbeispiel: Am 18.11.2016 kommt der Patient mit einem Hebungsinfarkt und Kammerflimmern zur Akutangiographie ins Krankenhaus. Angiographisch zeigt sich ein Verschluss des left anterior descending, LAD, dieser wurde Primavista eröffnet. Die chronisch verschlossene, aber ausreichend kollateralisierte rechte Koronararterie (RCA) wurde vorerst belassen. Die Aufnahme auf die Intensivstation wurde veranlasst. Am 01.12.2016 wurde der Patient tracheotomiert, die Extubation erfolgte problemlos am 07.12.2016 und der Patient wurde auf die Herzüberwachung transferiert. Am 19.12.2016 wurde der Patient reangiographiert, Versuch der Wieder-Eröffnung der RCA – sowohl ante- und retrograd frustran, in der Folge kam beim Patienten eine Rhythmusproblematik hinzu.

20.12.2016 Elektrischer Sturm, neunmal defibrillationspflichtige monomorphe Kammertachykardie. Es erfolgte eine neuerliche Sedierung und die Verlegung auf die Intensivstation.

20.12.2016 Eine Terminfindung zur Katheterablation in Wien war erfolglos. In der Zwischenzeit musste der Patient immer wieder defibrilliert werden und verschlechterte sich rasant.

02.01.2017 Durch die Pflege konnte mit einem Rhythmologielabor eines anderen Bundeslandes Kontakt hergestellt werden. Dies geschah rein durch die Pflege und der Transfer wurde auch über die Pflege organisiert.

04.01.2017 Transfer in das andere Krankenhaus wurde eingeleitet.

05.01.2017 Erfolgreiche Katheterablation.

09.01.2017 Rücktransfer ad Herzüberwachung des Endsender-Krankenhauses.

10.01.2017 Transfer an die Normalstation.

17.01-2017 ICD Implantation.

19.01.2017 Patient konnte in einen sehr guten Zustand aus dem Krankenhaus entlassen werden.

Schlussfolgerungen: Das Fallbeispiel zeigt, dass das kardiologische Pflegenetzwerk in Österreich durchaus von großem Nutzen für den Patienten sein kann. Deshalb ist es wichtig, den Belastungen, die durch die Pflege und Betreuung eines

Menschen zwangsläufig entstehen können, entgegenzuwirken. Dazu braucht es eine gute Organisation und alle Berufsgruppen müssen gut informiert sein. Nur durch die Zusammenarbeit von Ärzten mit den Assistenzberufen wie DGKP, RT und DMTF kann ein ganzheitliches Therapiemodell für den Patienten entstehen. Es bilden sich umfangreiche Informationen sowie Möglichkeiten und Ideen, die zuvor nicht bekannt waren. Ein Netzwerk sollte daher auf verschiedene Pfeiler gestützt sein.

13-7

Eine Komplikation kommt selten allein – periprozedurale Komplikationen im Herzkatheterlabor und deren Behandlung

Eva Lidl, Gabriela Nagl

Kardinal Schwarzenberg Klinikum, Schwarzach im Pongau, Österreich

Grundlagen: In dieser Literaturanalyse wird versucht, anhand von zwei qualitativen Studien und sechs Reviews einen Überblick der am häufigsten auftretenden periprozeduralen Komplikationen während einer Herzkatheteruntersuchung zu geben. Zudem werden Lösungen dargestellt. Eine Herzkatheteruntersuchung ist für die meisten Patienten eine spezielle Situation, deshalb sollte das Team immer auf Komplikationen vorbereitet und dementsprechend darauf geschult sein. Anhand dieser Literaturrecherche werden die häufigsten Komplikationen, die vor, während und nach der Untersuchung auftreten können, aufgezeigt und mögliche Gegenmaßnahmen dargestellt. Es werden jährlich in Österreich ca. 56.000 Herzkatheteruntersuchungen sowie 24.000 Koronarinterventionen durchgeführt. Bei jeder dieser invasiven Untersuchungen können periprozedurale Komplikationen auftreten. Bei diesen Komplikationen kann es sich um schnell bemerkbare Komplikationen wie eine allergische Reaktion auf das Kontrastmittel oder eine ST-Streckenhebung, aber auch um nicht sofort bemerkbare Komplikationen wie eine retroperitoneale Blutung handeln. Daher hat die Prävention von Komplikationen im klinischen Alltag höchste Priorität. Es stellt sich die Frage, welche periprozeduralen Komplikationen im Rahmen einer Herzkatheteruntersuchung auftreten können und welche Behandlungsstrategien dazu angewendet werden sollen.

Methodik: Bei der systematischen Literatursuche wurden Onlinedatenbanken wie PubMed und Cinhal verwendet. Die Suche wurde auf deutsch- und englischsprachige Literatur eingegrenzt. Insgesamt wurden 14 Publikationen als relevant identifiziert. Nach einer systematischen Analyse der Texte wurden schlussendlich acht Studien eingeschlossen. Zudem wurden zwei Fachbücher miteinbezogen. Es wurde darauf geachtet, dass sich die Komplikationen und Maßnahmen einschließlich auf eine Herzkatheteruntersuchung beziehen. Für die Beantwortung der zweiten Fragestellung bezüglich der Behandlungsstrategien wurden nicht nur medikamentöse oder interventionelle Maßnahmen, sondern auch interdisziplinäre Maßnahmen wie Teambuilding oder gemeinsames Notfalltraining herangezogen.

Ergebnisse: Im folgenden Abschnitt werden die häufigsten periprozeduralen Komplikationen einer Herzkatheteruntersuchung samt Behandlungsstrategien aufgezeigt. Bei ca. 2,6 % der perkutanen Koronarinterventionen treten Komplikationen auf. Es kann sich um punktionsbedingte Komplikationen wie Fehlpunktionen oder Pseudoaneurysmen handeln. Weiters können vaskuläre Probleme wie eine Dissektion bis hin zum Verschluss oder eine Perforation auftreten. Nicht selten können Arrhythmien wie Brady- oder Tachykardien, Kammerflimmern oder eine Asystolie auftreten. Luftembolien oder ein postinterventioneller Insult zählen zu den selteneren Komplikationen. Zudem können Reaktionen auf Medikamente wie das lokale Anästhetikum oder auf das injizierte Kontrastmittel auftreten. Eine seltene, aber nicht minder gefährliche Komplikation ist der intravaskuläre Stentverlust. Diese Vielfalt an Komplikationen macht ein Komplikations- bzw. Risikomanagement unumgänglich. Die ständige Optimierung von standardisierten Prozessen und Handlungsabläufen ist von Bedeutung. Dabei werden nicht nur ein medikamentöses Management oder eine interventionelle Behandlung in diversen Dokumenten zu standardisierten Prozessen angedacht, sondern auch Weiterbildungen im Team, wie ein interdisziplinäres Notfalltraining. Dabei handelt es sich um gemeinsame Schulungen der Teams des Herzkatheterlabors oder der Intensivstation und der zuständigen Mediziner. Wichtig sind auch logistische Maßnahmen wie die gleiche Aufrüstung eines Notfallwagens.

Schlussfolgerungen: Zur Beantwortung der Forschungsfragen stehen zwar Artikel, standardisierte Prozesse, evidenzbasierte Studien und Fachliteratur zur Verfügung, jedoch ist die Anzahl solcher limitiert. Die Entwicklung der demografischen Daten der letzten Jahre weist darauf hin, dass die Anzahl der herzkranken Patienten stetig zunimmt. Daraus ergibt sich ein dringender Forschungsbedarf zu dieser Thematik. Durch die Zunahme der Untersuchungen und Anstieg des Durchschnittsalters der Patienten und deren möglicher Multimorbidität ist es unbedingt erforderlich, die richtige Indikation zur Untersuchung zu stellen. Weiters gehören mögliche Risikofaktoren für Komplikationen im Vorhinein abgeklärt bzw. limitiert. Dazu zählen Lärm, Zeitdruck, Stress oder unklare Rollenverteilung sowie schlechte bzw. fehlende Kommunikation.

Postersitzung 14 – Basic Science 3

14-1

Fibrocytes and neutrophil extracellular traps at the culprit lesion site in myocardial infarction: a role for monocyte chemoattractant protein 1

Thomas M. Hofbauer, Anna S. Ondracek, Andreas Mangold, Thomas Scherz, Veronika Seidl, Irene M. Lang

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Leukocyte-mediated inflammation is crucial in ST-segment elevation myocardial infarction (STEMI). We recently observed that neutrophil extracellular traps (NETs) are increased at the culprit lesion site CLS, promoting the activation and differentiation of fibrocytes, cells with mesenchymal and leukocytic properties. Fibrocyte migration is mediated by monocyte chemoattractant protein (MCP)-1 recognized via C-C chemokine receptor type 2 (CCR2). We investigated the interplay between fibrocyte function, NETs and MCP-1 in STEMI.

Methods: CLS and femoral blood of STEMI patients ($n=50$) was drawn during percutaneous coronary intervention. We characterized CCR2 expression of fibrocytes by flow cytometry. MCP-1 and NET marker citrullinated histone H3 (citH3) were measured by ELISA. Fibrocytes were treated in vitro with MCP-1. Human coronary arterial endothelial cells (hCAECs) were

stimulated with isolated NETs, and MCP-1 was measured by ELISA and qPCR. The influence of MCP-1 on NET formation in vitro was assessed using isolated neutrophils.

Results: Fibrocytes accumulated at the CLS in STEMI. Fibrocyte CCR2 expression was decreased compared with femoral control. MCP-1 and citH3 were increased at the CLS. CLS MCP-1 was correlated positively with fibrocyte accumulation, and negatively correlated with CCR2 expression. In vitro, MCP-1 decreased fibrocyte CCR2. NET stimulation of hCAECs induced MCP-1. MCP-1 attenuated ionomycin-induced NETosis.

Conclusions: Fibrocyte accumulation at the CLS appears to be mediated by MCP-1. NETs induce endothelial MCP-1, promoting a chemotactic gradient for fibrocyte migration. The inhibitory effect of MCP-1 on NETosis might serve as a negative feedback loop, limiting inflammation.

14-2

SGLT2 inhibitors exert no functional effects on healthy human myocardium

Natasa Djalinac[1], Ewald Kolesnik[1], Chintan Koyani[2], Heinrich Mächler[3], Egbert Bisping[1], Harald Sourij[4], Peter Rainer[1], Brigitte Pelzmann[2], Dirk von Lewinski[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Biophysics, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria
[3]Department of Cardiothoracic Surgery, Medical University of Graz, Graz, Austria
[4]Division of Endocrinology and Diabetology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Since the publication of the EMPA-REG Outcomes trial in 2015 interest has raised for studying the mechanisms behind cardiovascular protection mediated via the Sodium-glucose Cotransporter-2 (SGLT2) inhibitors. SGLT2 is not expressed in the human heart so direct transporter mediated actions are excluded. However, SGLT1 expression is present and even upregulated in conditions of ischemia and SGLT2 inhibitors are reported to inhibit SGLT1 at higher dose levels too. The study aims to elucidate whether SGLT2 and SGLT1 inhibitors exert acute functional effects on healthy human myocardium.

Methods: Human atrial trabeculae ($n=20$) were obtained from 10 right atrial appendages of patients undergoing elective heart surgery. All patients gave written consent prior surgery. Human ventricular trabeculae ($n=30$) were isolated from right ventricles of 11 donor hearts with preserved ejection fraction that were not suitable for transplantation. The trabeculae were mounted on hooks, electrically stimulated at 1 Hz, stretched to a maximum length and kept in an organ bath containing a modified Krebs-Henseleit buffer with a calcium concentration of 2.5 mM and bubbled constantly with 95% O_2 and 5% CO_2. Atrial and ventricular trabeculae were treated with the SGLT2 inhibitors empagliflozin and dapagliflozin while only ventricular trabeculae were treated additionally with the SGLT1/SGLT2 inhibitor T-1095. Drug effects were investigated by incubating the trabeculae for 30 min with sequential concentrations (0.2 µM, 2 µM and 10 µM) of respective substance. Control trabeculae were treated with the corresponding amount of the solvent. Contractility properties were measured and statistically evaluated by two-way ANOVA.

Results: The administration of increasing concentrations of empagliflozin, dapagliflozin or T-1095 had no significant effect on developed force, diastolic tension or relaxation parameters compared to vehicle treatment in ventricular tissue. In line with this finding, the administration of increasing concentrations of empagliflozin and dapagliflozin had no significant effect on developed force, diastolic tension or relaxation parameters

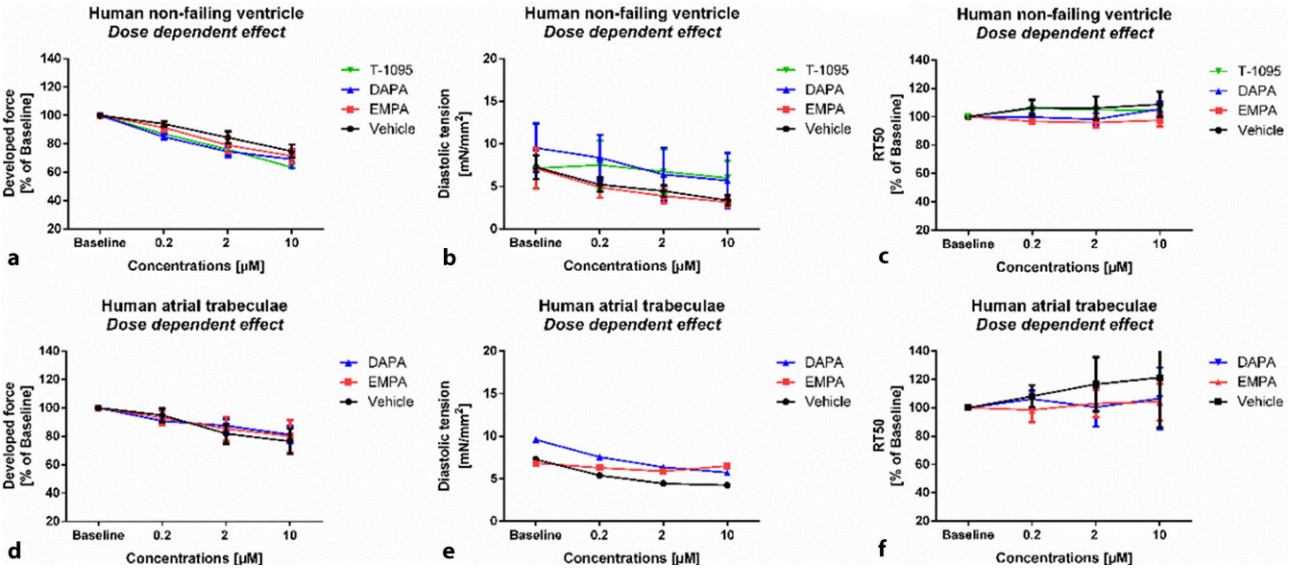


Fig. 1|14-2 Dose dependent effects of empagliflozin (EMPA), dapagliflozin (EMPA) and T-1095 on myocardial contractility. A. T-1095 shows a trend towards reduction of developed force in comparison to vehicle in non-failing human ventricular trabeculae B. Diastolic tension maintained rundown level through different concentrations C. No difference in relaxation time in human ventricular tissue. D. Developed force maintains a stable degree of rundown between groups E. No change in diastolic tension after intervention in human atrial trabeculae F. No difference in relaxation time in human atrial tissue. Results are presented as line plots ± SEM. The values are extrapolated as percentage from the maximum baseline response. Between-group difference has been determined with two-way ANOVA followed by Sidak's multiple comparisons test

compared to vehicle treatment in atrial tissue. The observed dose dependent changes from the baseline level are in correlation with the vehicle-treatment and can be attributed to physiological rundown. Like in previous observations made in failing human ventricular myocardium T-1095 shows a trend towards negative inotropy at the highest (10 μM) concentration without reaching statistical significance ($p = 0.07$).

Conclusions: Supraphysiological concentrations of SGLT2 and SGLT1/SGLT2 inhibitors exert no functional effects on non-failing human myocardium. Reported effects of SGLT2 inhibitors are likely SGLT1-independent.

14-3

Protective effects of empagliflozin against LPS-induced cardiovascular dysfunction

Ewald Kolesnik[1], Chintan Koyani[2], Cristopher Trummer[3], Natasa Djalinac[1], Margarete Lechleitner[3], Susanne Scherübel[2], Harald Sourij[4], Egbert Bisping[1], Albrecht Schmidt[1], Heinrich Mächler[5], Sasa Frank[3], Wolfgang Sattler[3], Ernst Malle[3], Brigitte Pelzmann[2], Dirk von Lewinski[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Biophysics, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria
[3]Division of Molecular Biology and Biochemistry, Gottfried Schatz Research Center, Medical University of Graz, Graz, Austria
[4]Division of Endocrinology and Diabetology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[5]Department of Cardiothoracic Surgery, Medical University of Graz, Graz, Austria

Background: Diabetes Mellitus (DM) is associated with a higher risk (2–6 fold) for developing inflammatory cardiovascular diseases. Studies performed on diabetic animal models have identified cardiac contractile dysfunction and endothelial damage due to hyperglycemia-induced inflammation. Empagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, is a glucose lowering drug that has been shown to reduce risk of heart failure in patients with type 2 DM. In the present study, we aimed to evaluate whether empagliflozin displays protective effects against lipopolysaccharide (LPS)-induced impairment of cardiac function caused by inflammation in vivo. In parallel, we assessed the impact of empagliflozin on vascular relaxation behavior ex vivo.

Methods: Mice (C57BL6, 12–16 weeks old) were treated with LPS (5 mg/kg, i. p.) alone or in combination with empagliflozin (10 mg/kg, i. p.) for 8 h. Echocardiography was performed before and after 8 h treatment. For myography experiments, thoracic aortas were isolated and cut in to 2 mm rings followed by mounting on the myograph instrument. Rings were pre-contracted with EC80 doses of nor-epinephrine followed by dose-dependent acetylcholine induced relaxation measurements.

Results: Echocardiography data show that empagliflozin treatment significantly prevented LPS-reduced ejection fraction in mice. Moreover, empagliflozin pre-treatment increased left ventricular end systolic diameter in LPS-treated mice. Myography experiments revealed that LPS-triggered impairment of acetylcholine-induced relaxation of aortic rings could be counteracted by empagliflozin administration. Next, we examined whether treatment with empagliflozin alone would affect cardiovascular function. Echocardiography and myography data reveal that empagliflozin has no obvious adverse effect on cardiac function and vasoreactivity.

Conclusions: The present data show that empagliflozin improves LPS-impaired cardiovascular function without any observed adverse effects in healthy animals. From these observations we may conclude that empagliflozin has therapeutic potential in inflammatory cardiovascular dysfunction.

14-4

LDL cholesterol promotes neutrophil extracellular trap formation

Anna S. Ondracek[1], Thomas M. Hofbauer[1], Patricia P. Wadowski[2], Andreas Mangold[1], Thomas Gremmel[2], Irene M. Lang[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Division of Angiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Pro-protein convertase subtilisin/kexin 9 (PCSK9) is a regulator of low density lipoprotein (LDL) receptor (LDLR) expression and has gained attention in the treatment of hyperlipidemia. Serum levels of LDL are correlated with numbers of activated neutrophils in the circulation of hyperlipidemic patients. Activated neutrophils can form neutrophil extracellular traps (NETs) by expelling their chromatin, and NETs have been recognized as important risk factors for acute myocardial infarction (AMI) and stroke. We analyzed the influence of serum LDL levels on neutrophil activation, their propensity to form NETs, and the correlation of NET surrogate markers with systemic inflammatory responses in AMI.

Methods: We recruited 249 consecutive patients with AMI (mean age 58 years, 20% females) and assessed laboratory parameters, inflammatory markers, and serum lipid profiles 72 h after primary percutaneous coronary intervention. Double-stranded DNA (dsDNA) and citrullinated histone H3 were determined from plasma as markers of in vivo NET formation. In a subset of patients ($n = 25$), ex vivo NET formation in response to PCSK9 and ionomycin was analyzed, neutrophils were stained for CD11b, LDLR, and lectin-like oxidized LDLR (LOX-1) using flow cytometry at baseline and after activation with phorbol myristate acetate. PCSK9 levels were measured by ELISA.

Results: Patients with serum LDL levels above the median [median (IQR) LDL 111 mg/dl (87–141), mean ± SD LDL 115 ± 41 mg/dl] had significantly higher concentrations of circulating dsDNA. Levels of dsDNA [median 121 ng/ml, IQR 101–156] were linked with levels of the specific NET marker citH3 [median (IQR) 252 ng/ml (655–1600), rs = 0.157]. Plasma concentrations of dsDNA and citH3 correlated significantly with CRP (dsDNA rs = 0.328; citH3 rs = 0.209), proBNP (dsDNA rs = 0.286; citH3 rs = 0.192), troponin T (dsDNA rs = 0.282; citH3 rs = 0.197), and IL-6 (dsDNA rs = 0.242; citH3 rs = 0.216). In the subset of patients in whom neutrophils were characterized, pre-treatment of neutrophils with PCSK9 could significantly decrease ionomycin induced NET release in a dose-dependent manner. Levels of serum LDL were associated with spontaneous NET formation (r = 0.504) ex vivo and activated CD11b on neutrophils (r = 0.495). LOX-1 expression correlated significantly with LDLR expression (rs = 0.670) and PCSK9 levels (r = 0.520). Patient neutrophil stimulation in whole blood led to a signifi-

cant decrease of the LDLR positive neutrophil population. This effect was greater when PCSK9 levels were higher.

Conclusions: Our data indicate a role for LDL in boosting neutrophil activation and formation of NETs depending on PCSK9.

14-5

Echocardiographic assessment of age associated changes in the mouse heart

Adelheid Panzenböck, Johanna Altmann, Max-Paul Winter, Smriti Sharma, Irene M. Lang

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: The elderly population is rapidly growing worldwide, and elderly patients suffer from cardiac diseases such as coronary artery disease, chronic heart failure, arrhythmias, diabetic cardiomyopathy, hypertensive heart disease and degenerative valve disease. Echocardiography has been applied to study murine models of cardiac aging, but methods and timeframes used differ vastly between studies, thereby presenting conflicting results. Aim of our study was to perform a long-time follow-up echocardiographic assessment of structural and functional changes in the aging murine heart.

Methods: Echocardiography was performed using a Vevo 2100 Imaging System with a MS 400 probe, and the corresponding software. Female ApoE-/- mice ($n=20$) on western diet were used for this study. Baseline echocardiography was performed in 12 week old mice, follow-up measurements were performed every 8 weeks thereafter, with a planned follow-up time of 64 weeks. B- and M-mode images were acquired from a parasternal long axis view to evaluate left ventricular (LV) function. Pulsed wave Doppler technique was used for aortic- and pulmonary valve function evaluation.

Results: Within the first 44 weeks of follow-up compared to baseline, we observed increasing LV systolic diameter (2.02 ± 0.38 mm vs. 2.62 ± 0.29 mm, $p \leq 0.001$), systolic volume (13.88 ± 6.34 µl vs. 25.59 ± 6.67 µl, $p \leq 0.001$) and LV mass (63.83 ± 9.16 mg vs. 104.99 ± 14.49 mg, $p \leq 0.001$). In contrast, ejection fraction (70.36 ± 9.27% vs. 56.82 ± 7.41%, $p \leq 0.001$) and fractional shortening (39.34 ± 7.23% vs. 29.40 ± 5.13%, $p \leq 0.001$) decreased, indicating the development of cardiac hypertrophy and reduced ventricular function. In addition we observed the development of aortic valve stenosis indicated by increased peak velocity (1323.97 ± 166.32 mm/s vs. 1493.01 ± 218.96 mm/s, $p=0.019$) and peak gradient (7.12 ± 1.75 mmHg vs. 9.09 ± 2.71 mmHg, $p=0.013$). The pulmonary valve showed non-significantly reduced peak velocity and peak gradient and significantly increased PAT/PET (0.29 ± 0.03 vs. 0.38 ± 0.05, $p \leq 0.001$) at 44 weeks compared to baseline.

Conclusions: In a long-time follow-up model of ApoE-/- mice on high fat diet our data demonstrate development of left ventricular cardiac hypertrophy and reduced left ventricular function as well as the development of aortic valve stenosis at 44 weeks of follow-up.

14-6

High body mass index is associated with elevated blood levels of progerin mRNA

Moritz Messner, Santhosh Ghadge, Thomas Schütz, Herbert Seiringer, Gerhard Pölzl, Marc-Michael Zaruba

University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria

Background: Obesity is a well-described risk factor with manifold effects resulting in decreased longevity and premature aging. Latest is eminently regarding the cardiovascular system (CVS). Premature aging of the CVS is the main reason of death in Hutchinson-Gilford syndrome (HGPS), a disease caused by defined mutations in the LMNA gene encoding lamin A/C. The most reported mutation in HGPS is a single C to T nucleotide substitution in exon 11 resulting in activation of a cryptic splice donor site leading to a truncated prelamin A protein known as progerin. Small amounts of progerin are also expressed in healthy individuals with physiologic ageing. In this study we aim to investigate the association of body mass index with respect to expression of progerin mRNA in blood samples of individuals presenting in an outpatient cardiology clinic.

Methods: In this cross-sectional retrospective analysis 111 patients were consecutively included of which 46 were normal (BMI < 25 kg/m²) and 65 overweight (BMI ≥ 25.0 kg/m²). Blood samples were analyzed for quantitative expression of progerin mRNA.

Results: Progerin mRNA levels were significantly higher in blood samples of individuals with BMI >25 kg/m² ($n=65$; 0.46 ± 0.16 vs. 0.83 ± 0.71, P = 0.003) compared to the normal weight group ($n=46$). Moreover, patients with BMI >25 kg/m² ($n=64$) exhibited significantly higher CRP values as the normal weight group ($n=46$; 0.28 ± 0.24 vs. 0.9 ± 1.33, P = 0.01), indicating a higher activity of systemic inflammation (P = 0.01). Linear regression analysis based on Spearman's correlation showed a positive correlation of BMI and progerin mRNA levels in patient's blood (r = 0.265, $p=0.0005$), of BMI and CRP (r = 0.300, $p=0.001$) as well as BMI and HbA1c (r = 0.336, $p=0.0003$). Furthermore, progerin mRNA levels correlate with CRP (r = 0.208, $p=0.03$).

Conclusions: We conclude that overweight and obesity are associated with increased levels of the aging related splice variant progerin and activation of systemic inflammation. Both are displaying putative mechanisms causing premature ageing of obese individuals. Targeting progerin as a new therapeutic approaches could be an achievable goal since i. e. farnesyltransferase inhibitors are already used for treatment in patients suffering from HGPS to limit disease progression.

Characteristic	Total (N=111)	BMI <25 (N=46)	BMI >25 (N=65)	P value
Age, years	56 ± 15	54 ± 17	58 ± 13	0.1
Female sex, n (%)	32 (29)	18 (39)	14 (22)	0.15
BMI, kg/m2	**26.6 ± 4.8**	**22.4 ± 1.8**	**29.6 ± 4.0**	**0.000**
NYHA class, n (%)	**2.0 ± 0.7**	**1.8 ± 0.6**	**2.1 ± 0.7**	**0.015**
I	29 (27)	15 (33)	14 (22)	
II	55 (51)	25 (54)	30 (46)	
III	24 (22)	4 (9)	20 (31)	
IV	0 (0)	0 (0)	0 (0)	
Medical history, n (%)				
Smoking, n (%)	49	17 (37)	32 (49)	0.17
Diabetes, n (%)	19 (17)	5 (11)	14 (22)	0.2
Atrial fibrill., n (%)	**42 (38)**	**10 (22)**	**32 (49)**	**0.005**
LVEF, n (%)	38.2 ± 14.9	39.9 ± 14.2	37.0 ± 15.4	0.29
Clinical features				
NT-proBNP, ng/l	2094 ± 4421	1748 ± 2118	2341 ± 5514	0.44
TroponinT, ng/l	28 ± 53	32 ± 72	24 ± 33	0.48
Creatinine, mg/dl	1.2 ± 0.46	1.19 ± 0.54	1.21 ± 0.40	0.77
GFR, ml/min	54 ± 10	54 ± 10	54 ± 10	0.55
HbA1c, %	**5.9 ± 1.0**	**5.7 ± 1.1**	**6.1 ± 1.1**	**0.017**
Triglycerides, mg/dl	**135 ± 68**	**119 ± 59**	**145 ± 73**	**0.041**
Cholesterol, mg/dl	172 ± 44	181 ± 43	166± 45	0.08
LDL, mg/dl	107 ± 37	110 ± 38	105 ± 39	0.47
HDL, mg/dl	**52 ± 19**	**59.0 ± 22.7**	**46.5 ± 14.0**	**0.003**
Hs-CRP, mg/dl	**0.64 ± 1.07**	**0.28 ± 0.24**	**0.9 ± 1.33**	**0.01**
GGT, U/I	86 ± 146	87 ± 184	86 ± 114	0.96
Leucocyte count, G/l	7.7 ± 2.2	7.5 ± 1.9	7.9 ± 2.3	0.37

Fig. 1 | 14-6 Characteristics of the patients. Means ± standard deviation. P values refer to differences in continuous variables (stud. T-test) or categorical variables (fisher's exact test). Percentages may not total 100 because of rounding

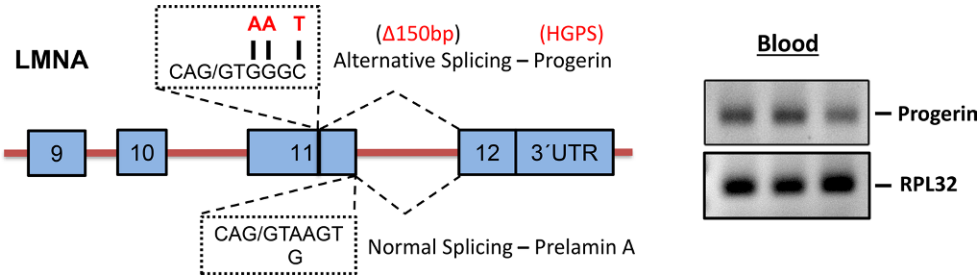


Fig. 2|14-6

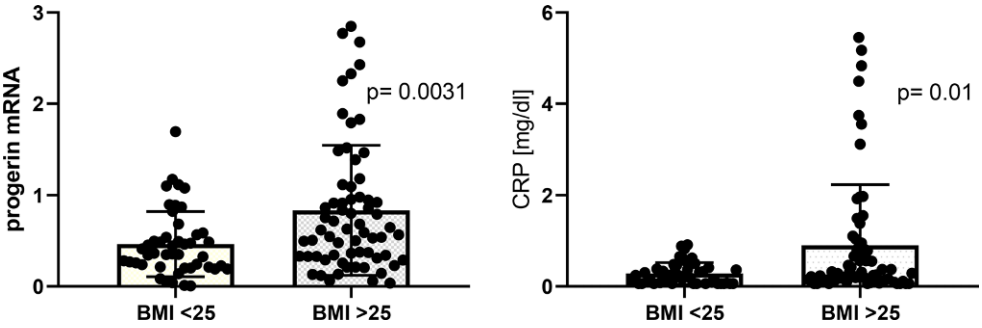


Fig. 3|14-6

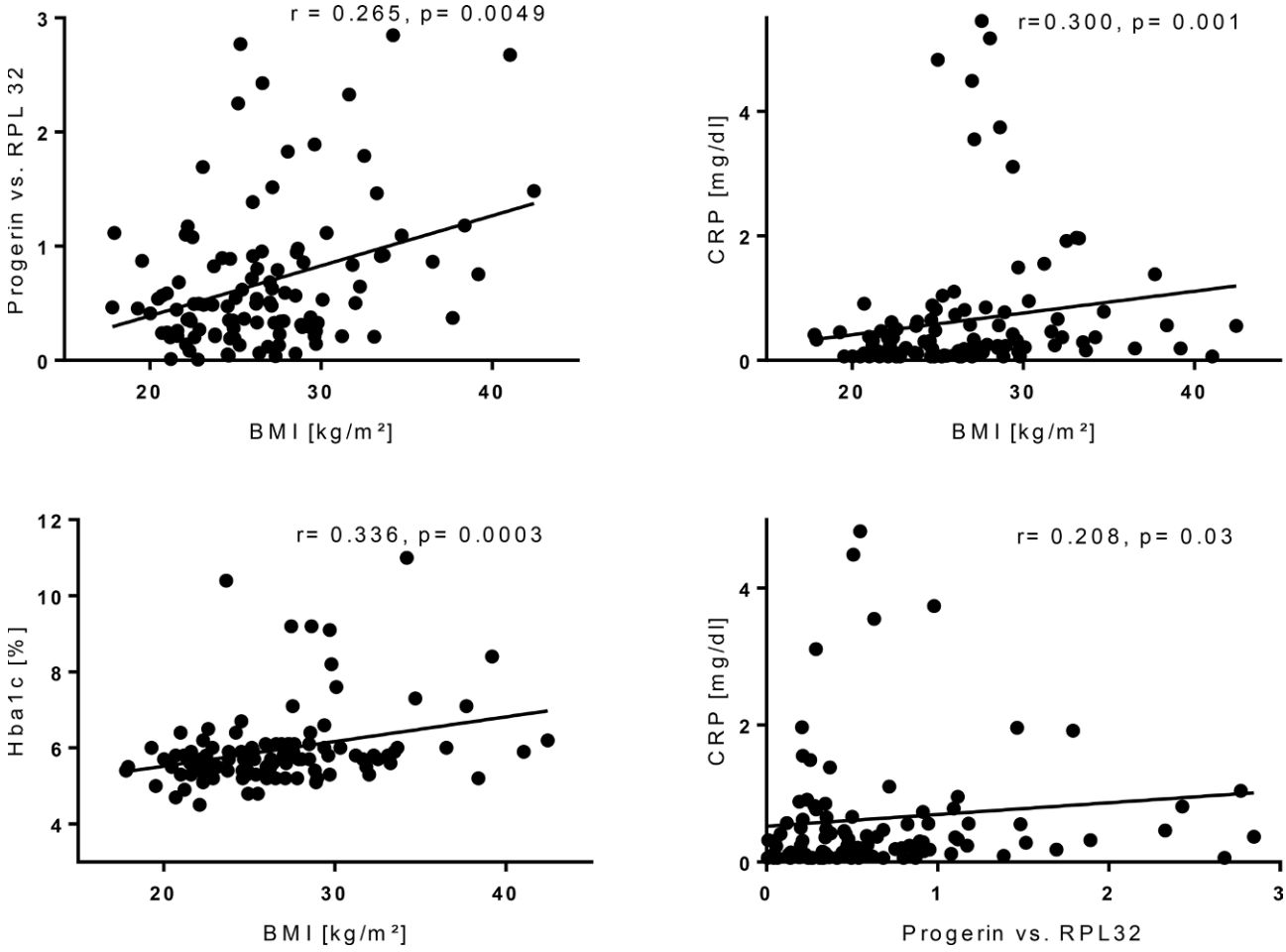


Fig. 4|14-6

14-7

Hypoxic cardiomyocytes show increased miR-210 expression indicating possible use as hypoxic marker in vitro

Nina Kastner, Johannes Winkler, Denise Traxler-Weidenauer, Julia Mester-Tonczar, Daniel Kockovsky, Mariann Pavone-Gyöngyösi, Katrin Zlabinger

Medical University of Vienna, Vienna, Austria

Background: Myocardial infarction and cardiovascular diseases persist to be the leading cause of death in the western world. The regeneration of cardiomyocytes after ischemic conditions remains difficult despite major leaps in therapy. To provide better treatment options, a better understanding of the mechanisms behind necrosis due to hypoxic conditions is crucial. The HIF-1alpha pathway is known to be the main pathway induced by hypoxia, leading to Glut-1 expression amongst many other. Lately, miR-210 expression was also described to be over-expressed in hypoxic cancer cells and hypoxic cardiac stem cells. This increased expression seems to correlate with the chance of survival.

Methods: In this work, the effect of hypoxia on human cardiomyocytes was analysed in vitro and the possibility of miR-210 as a hypoxic marker in cardiomyocytes was evaluated. The hypoxia was induced by a modular incubator chamber using a nitrogen and oxygen gas mixture in two different mixing ratios: <1% oxygen and 2% oxygen. The cells were exposed for various time periods, ranging from 1 hour to 24 hours. The hypoxic effect was evaluated by performing a qRT-PCR of the HIF-1alpha, Glut-1 and miR-210 gene expression and a HIF-1alpha ELISA. Additionally, images were taken to capture morphological changes as well.

Results: The HIF-1alpha and miR-210 expression was upregulated in all tested time points and concentrations. Yet, the Glut-1 expression in cardiomyocytes when exposed to an oxygen level of 2%, only started to significantly increase after 4 hours. The hypoxia exposure over 24 hours showed high hypoxic stress in the cardiomyocytes and cell survival was very poor, thus indicating fewer chance of cell regeneration. The exposure to an oxygen level of <1% for 2 hours showed a peak of HIF-1alpha, Glut-1 and miR-210 expression when compared to the normoxic control and other tested parameters. Furthermore, the HIF-1alpha ELISA showed matching expression results on a protein level intracellularly. When comparing the miR-210 expression change to the known hypoxic markers, it appears to take a similar course. Cell morphology showed no obvious changes and cell survival was still moderately, indicating a higher chance of regeneration possibility.

Conclusions: Since miR-210 shows a similar expression change behaviour and was significantly elevated in all tested time points and concentrations, it indicates a possible use as hypoxic marker in human cardiomyocytes in vitro. Further, the expression of the hypoxic markers showed significant increase

after short time periods, whereas cell survival was still good. This might indicate that cell regeneration is promising when exposed to severe hypoxia for only short time periods, making regeneration therapies potentially most effective when applied as soon as possible after acute ischemia due to e. g. myocardial infarction. The immediate therapy with bone-marrow-derived mesenchymal stem cells will be tested and evaluated in the further course of this project.

14-8

Hypoxia induction with cobalt chloride in human cardiomyocytes

Daniel Kockovsky, Nina Kastner, Johannes Winkler, Marian Gyöngyösi, Katrin Zlabinger

Medical University of Vienna, Vienna, Austria

Background: Hypoxia—the deprivation of oxygen supply in the cell—is intensively studied in cardiac muscle cells, as the ischaemic heart disease still remains the leading cause of death worldwide. Several methods have been developed to evaluate hypoxia and novel therapies under cell culture conditions.

Methods: In this study, induction of hypoxia in human cardiomyocytes (hCMC) was implemented with cobalt (II) chloride ($CoCl_2$), which mimics hypoxia in the cells by overexpression of the hypoxia inducible factor 1 alpha (HIF-1α). The optimal concentration (100 µM, 200 µM, 300 µM and 400 µM) and incubation time (4 h, 6 h, 8 h and 12 h) of $CoCl_2$ at which hypoxia-specific genes are overexpressed in the cells, but the cells aren't apoptotic or necrotic, was determined. The cell viability was measured with Acridine Orange/Propidium Iodide staining and with trypan blue staining. On mRNA level, the expression of genes that code for HIF-1α, vascular endothelial growth factor (VEGF) and micro RNA 208 (miR208) was quantified by qPCR. On protein level, HIF-1α protein was examined with a commercially available HIF-1α—ELISA kit.

Results: The results of the cell viability assay didn't show any dependence of cell viability on $CoCl_2$ concentration and incubation time. On mRNA level, incubation of $CoCl_2$ for 4 hours enhanced the expression of HIF-1α mRNA at all tested concentrations, whereas the mRNA of HIF-1α was only slightly increased or even decreased at $CoCl_2$ incubation times of 6, 8 and 12 hours. On protein level, the concentration peak of HIF-1α protein changed at different $CoCl_2$ concentrations. At 100 µM $CoCl_2$, the HIF-1α protein concentration peaked after incubation for 12 hours, at 200 µM after 8 hours, at 300 µM after 6 hours and at 400 µM after 4 hours.

Conclusions: These results indicate that $CoCl_2$ alters the HIF-1α expression and can be used as an in vitro hypoxia imitation in human cardiomyocytes. The results suggest the incubation of 300 µM $CoCl_2$ for 6 hours as the best method to provide distinct changes in HIF-1α expression gene and protein level. This method will be further applied to co-culture hypoxic cardiac cells with adipose derived stem cells and to analyse their regenerative effect.

Postersitzung 15 – Bildgebung 2

15-1

Prognostic implications of global longitudinal strain by feature-tracking cardiac magnetic resonance in ST-elevation myocardial infarction

Martin Reindl[1], Sebastian Reinstadler[1], Christina Tiller[1], Magdalena Holzknecht[1], Ivan Lechner[1], Mathias Pamminger[2], Agnes Mayr[2], Gert Klug[1], Bernhard Metzler[1]

[1]University Clinic of Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Clinic of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: The high accuracy of feature-tracking (FT) cardiac magnetic resonance (CMR) imaging qualifies this novel modality as potential gold standard for myocardial strain analyses in ST-elevation myocardial infarction (STEMI) patients; however, the incremental prognostic validity of FT-CMR over left ventricular ejection fraction (LVEF) and myocardial damage remains unclear. We therefore aimed to determine the value of myocardial strain measured by FT-CMR for the prediction of clinical outcome following STEMI.

Methods: This prospective observational study enrolled 451 revascularized STEMI patients. Comprehensive CMR investigations were performed 3 (interquartile range [IQR]: 2–4) days after infarction to determine LVEF, global longitudinal (GLS), radial (GRS) and circumferential strain (GCS) as well as myocardial damage. Primary endpoint was a composite of death, re-infarction and congestive heart failure (=MACE).

Results: During a median follow-up of 24 (IQR: 11–48) months, 46 patients (10%) experienced a MACE event. All three strain indices were impaired in patients with MACE (all $p<0.001$). However, GLS emerged as strongest MACE prognosticator among strain parameters (AUC: 0.73; 95%CI: 0.69–0.77) and was significantly better ($p=0.005$) than LVEF (AUC: 0.64; 95%CI: 0.59–0.68). The association between GLS and MACE remained significant ($p<0.001$) after adjustment for GRS, GCS and LVEF as well as for infarct size (IS) and microvascular obstruction (MVO). The addition of GLS to a risk model comprising LVEF, IS and MVO led to a net reclassification improvement (categorical NRI: 0.35 [95%CI: 0.14–0.55], $p<0.001$; continuous NRI: 0.63 [95%CI: 0.34–0.92], $p<0.001$).

Conclusions: GLS by FT-CMR strongly and independently predicted the occurrence of MACE in contemporary revascularized STEMI patients. Importantly, the prognostic value of GLS was superior and incremental to LVEF and CMR markers of infarct severity.

15-2

Global longitudinal strain by feature-tracking for optimized prediction of adverse remodeling after ST-elevation myocardial Infarction

Martin Reindl[1], Sebastian Reinstadler[1], Christina Tiller[1], Magdalena Holzknecht[1], Ivan Lechner[1], Mathias Pamminger[2], Benjamin Henninger[2], Agnes Mayr[2], Gert Klug[1], Bernhard Metzler[1]

[1]University Clinic of Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Clinic of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: The role of left ventricular (LV) myocardial strain by cardiac magnetic resonance feature tracking (CMR-FT) for prediction of adverse remodeling following ST-elevation myocardial infarction (STEMI) in comparison to LV ejection fraction (LVEF) and infarct severity is unclear. This study aimed to evaluate the independent and incremental value of LV strain assessed by CMR-FT for the prediction of adverse LV remodeling post-STEMI.

Methods: STEMI patients treated with primary percutaneous coronary intervention within 24 hours after symptom onset were enrolled. CMR core laboratory analysis was performed to assess LVEF, infarct pathology and LV myocardial strain. The primary endpoint was adverse remodeling defined as ≥20% increase in LV end-diastolic volume from baseline to 4 months.

Results: From the 232 patients included, 38 (16.4%) reached the primary endpoint. Global longitudinal strain (GLS), global radial strain, and global circumferential strain were all predictive of adverse remodeling ($p<0.01$ for all), but among strain values only GLS was an independent predictor of adverse remodeling (hazard ratio:1.36 [1.03–1.78]; $p=0.028$) after adjustment for strain parameters, LVEF and CMR markers of infarct severity. A GLS >–14% was associated with a 4-fold increase in risk for LV remodeling (hazard ratio:4.16 [1.56–11.13]; $p=0.005$). Addition of GLS to a baseline model comprising LVEF, infarct size and microvascular obstruction resulted in net reclassification improvement of 0.26 ([0.13–0.38]; $p<0.001$) and integrated discrimination improvement of 0.02 ([0.01–0.03]; $p=0.006$).

Conclusions: In survivors of acute STEMI, determination of GLS using CMR-FT provides important prognostic information for the development of adverse remodeling that is incremental to LVEF and CMR markers of infarct severity.

15-3

Contrast-free magnetic resonance imaging protocol for TAVI guidance: 3D ‚whole heart' and quiescent-interval single-shot angiography in comparison with contrast-enhanced CT

David Plappert, Mathias Pamminger, Gert Klug, Christof Kranewitter, Martin Reindl, Sebastian J Reinstadler, Benjamin Henninger, Christina Tiller, Magdalena Holzknecht, Christian Kremser, Werner Jaschke, Bernhard Metzler, Agnes Mayr

Medical University of Innsbruck, Innsbruck, Austria

Background: The purpose of this study is to prospectively compare a comprehensive non-enhanced cardiovascular magnetic resonance imaging (MRI) protocol with contrast-enhanced computed tomography angiography (CTA) for prosthesis sizing and access guidance in transcatheter aortic valve intervention (TAVI) evaluation.

Methods: 35 patients (82 ± 5.3 years, 18 females [51%]) with severe aortic stenosis referred for TAVI evaluation underwent non-contrast three-dimensional (3D) 'whole heart' MRI for aortic root measurements as well as non-enhanced quiescent-interval single-shot (QISS) MR angiography for evaluation of aortoiliofemoral access routes on a 1.5 T system. CTA was performed in 26 (74%) patients.

Results: Aortic annulus geometry assessed by 3D 'whole heart' MRI showed strong to very strong correlations ($r=0.68$ to 0.89, all $p\leq0.0001$) compared to CTA. QISS and CTA based measurements of aortoiliofemoral vessel diameters correlated moderately to very strong ($r=0.57$ to 0.85, all $p\leq0.002$) with good to excellent inter-observer reliability (ICC = 0.86 to 0.99, all $p<0.0001$) regarding MRI measurements. Mean diameters of the infrarenal aorta, common iliac arteries, right external iliac artery and common femoral arteries differed significantly (bias 0.37 to 0.98 mm, $p=0.041$ to <0.0001) between the two modalities. However, inter-method agreement for the decision of transfemoral accessibility was strong ($\kappa=0.87$, $p<0.0001$). Median image quality rating for QISS according to a 4-point Likert scale was 1 (IQR 1–2) for both observers (ICC = 0.93, $p<0.0001$).

Conclusions: MRI 3D 'whole heart' and QISS angiography provide contrast-free evaluation of aortic annulus and access routes in TAVI patients with moderate to strong correlations compared to CTA. Moreover, decision for transfemoral accessibility is comparable, highlighting this MRI protocol as a reliable alternative for TAVI guidance without the need of contrast agents.

15-4

Complete versus simplified Selvester QRS score for infarct severity assessment in ST-elevation myocardial infarction

Christina Tiller[1], Martin Reindl[1], Sebastian Reinstadler[1], Magdalena Holzknecht[1], Michael Schreinlechner[1], Alexander Peherstorfer[1], Nicolas Hein[1], Agnes Mayr[2], Gert Klug[1], Bernhard Metzler[1]

[1]University Clinic of Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Clinic of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: Complete and simplified Selvester QRS score have been proposed as valuable clinical tool for estimating myocardial damage in patients with ST-elevation myocardial infarction (STEMI). We sought to comprehensively compare both scoring systems for the prediction of myocardial and microvascular injury assessed by cardiac magnetic resonance (CMR) imaging in patients with acute STEMI.

Methods: In this prospective observational study, 201 revascularized STEMI patients were included. Electrocardiography was conducted at a median of 2 (interquartile range 1–4) days after the index event to evaluate the complete and simplified QRS scores. CMR was performed within 1 week and 4

months thereafter to determine acute and chronic infarct size (IS) as well as microvascular obstruction (MVO).

Results: Complete and simplified QRS score showed comparable predictive value for acute (area under the curve (AUC) = 0.64 vs. 0.67) and chronic IS (AUC = 0.63 vs. 0.68) as well as for MVO (AUC = 0.64 vs. 0.66). Peak hs-cTnT showed an AUC of 0.88 for acute IS and 0.91 for chronic IS, respectively. For the prediction of MVO, peak hs-cTnT represented an AUC of 0.81.

Conclusions: In reperfused STEMI, complete and simplified QRS score displayed comparable value for the prediction of acute and chronic myocardial as well as microvascular damage. However, both QRS scoring systems provided inferior predictive validity, compared to peak hs-cTnT, the clinical reference method for IS estimation.

15-5

Aortic pulse wave velocity adversely affects infarct healing following ST-elevation myocardial infarction

Sebastian J. Reinstadler, Martin Reindl, Christina Tiller, Magdalena Holzknecht, Agnes Mayr, Gert Klug, Bernhard Metzler

Medical University of Innsbruck, Innsbruck, Austria

Background: In patients with ST-elevation myocardial infarction (STEMI), increased aortic pulse wave velocity (PWV) is associated with worse clinical outcome; however, the underlying pathomechanisms are not completely clarified so far. Aim of the present study was to investigate the relationship between aortic PWV and infarct healing, using comprehensive cardiac magnetic resonance (CMR) imaging, in STEMI patients undergoing primary percutaneous coronary intervention (PPCI).

Methods: This was an observational study that included 103 consecutive STEMI patients. Aortic PWV was measured by phase-contrast CMR within the first week after STEMI. Infarct healing, defined as relative infarct size (IS) reduction from baseline to 4 months follow-up scan, was determined using late gadolinium enhanced CMR.

Results: IS significantly decreased from 17% of left ventricular mass (Interquartile range [IQR]:9–28) at baseline to 12% (IQR: 6–17) at 4 months follow-up ($p < 0.001$). Relative IS reduction was 36% (IQR:15–52). Patients with IS reduction > 36% were younger ($p = 0.01$), had lower baseline N-terminal pro B-type natriuretic peptide (NT-proBNP) concentrations ($p = 0.047$) and lower aortic PWV values ($p = 0.003$). In a continuous (odds ratio [OR]: 0.65 [95% confidence interval: 0.48–0.88], $p = 0.01$) as well as categorical (PWV < 7 m/s; OR: 4.32 [95% confidence interval: 1.61–11.63], $p = 0.004$) multivariable logistic regression model, the relation between aortic PWV and relative IS reduction remained.

Conclusions: In STEMI patients treated by PPCI, aortic PWV independently predicted IS reduction as assessed by CMR, revealing a novel pathophysiological link between aortic stiffness and adverse infarct healing following STEMI.

15-6

Admission Q waves predict intramyocardial haemorrhage in ST-elevation myocardial infarction

Christina Tiller[1], Martin Reindl[1], Magdalena Holzknecht[1], Lukas Innerhofer[1], Maximilian Klapfer[1], Agnes Mayr[2], Gert Klug[1], Sebastian Reinstadler[1], Bernhard Metzler[1]

[1]University Clinic of Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[2]University Clinic of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: Intramyocardial haemorrhage (IMH), depicted by T2* imaging, has emerged as novel prognostic marker in patients suffering from ST-elevation myocardial infarction (STEMI). However, to date it is unclear which clinical parameters are suitable for the detection of IMH. We therefore sought to investigate the relation between admission Q waves and IMH, assessed by cardiac magnetic resonance (CMR) imaging, in patients with revascularized STEMI.

Methods: The present observational study included 195 revascularized STEMI patients. Electrocardiography was conducted on admission to evaluate duration and depth of Q waves. CMR was performed at a median of 3 (interquartile range: 2–5) days to determine IMH.

Results: Duration and depth of admission Q waves were significantly associated with presence of IMH ($p < 0.001$). In multivariable logistic regression analysis, duration of admission Q waves ($p = 0.019$) emerged as independent predictors of IMH, although after adjustment with other clinical parameters. Both duration and depth of admission Q waves significantly predicted IMH (area under the curve (AUC) = 0.67, 95% confidence interval (CI) 0.58–0.75, $p < 0.001$; AUC = 0.66, 95% CI 0.55–0.73, $p = 0.002$, respectively).

Conclusions: In reperfused STEMI, admission Q waves emerged as independent predictors of CMR-determined IMH. Therefore, our findings emphasize the usefulness of admission Q waves as a cost-effective and non-invasive clinical tool for assessing IMH in daily routine.

15-7

Prognostische Relevanz von Delayed Enhancement in der Magnetresonanztomographie bei linksventrikulärer Noncompaction

Hanna Schnetz, Margarethe Coulibaly-Wimmer, Claudia Stöllberger, Josef Finsterer

Krankenanstalt Rudolfstiftung, Wien, Österreich

Grundlagen: Linksventrikuläre Hypertrabekulierung/Noncompaction (LVHT) ist eine kardiale Abnormität, die sich morphologisch durch ein zweilagiges Myokard und verstärkte Trabekulierung auszeichnet. LVHT kann in allen Altersgruppen auftreten und klinisch sowohl asymptomatisch bleiben, als auch mit einer erhöhten Morbidität und Mortalität assoziiert sein. Die Pathogenese von LVHT ist noch nicht geklärt. LVHT kann mit myokardialer Fibrose verbunden sein, welche mittels Delayed Enhancement (DE) Sequenzen in der kardialen Mag-

netresonsztomographie (MRT) dargestellt werden kann. Ziel dieser Arbeit war die Anwesenheit von DE und dessen Korrelation mit dem klinischen Schweregrad von LVHT zu analysieren und somit die Rolle von DE als Untersuchungsmodalität bei LVHT weiter zu untersuchen.

Methodik: Es wurden MRT-Befunde von Patienten mit echokardiographisch gesicherter LVHT retrospektiv ausgewertet und Baseline-, klinische, elektrokardiografische, echokardiografische, neurologische und Follow-up-Parameter von Patienten mit und ohne DE anhand von deskriptiver Statistik miteinander verglichen.

Ergebnisse: Es wurden die MRT-Befunde von 48 Patienten eingeschlossen, in denen explizit zur Frage des DE Stellung genommen worden ist. Das mittlere Alter war 47 Jahre, 32 % waren weiblich. Zwölf Patienten (25 %) zeigten DE. Patienten mit DE hatten signifikant häufiger pathologische Q-Zacken im EKG ($p=0{,}043$) und Stenosen in der Koronarangiografie ($p=0{,}028$), bei den restlichen getesteten Parametern gab es keine signifikanten Unterschiede zwischen den beiden Gruppen. Es gab keine Übereinstimmung zwischen der Lokalisation von LVHT in der Echokardiografie und DE in der MRT. Während eines mittleren Follow-up Zeitraums von 60,5 Monaten gab es keinen signifikanten Unterschied zwischen den beiden Gruppen bezüglich Mortalität, Auftreten von thromboembolischen Ereignissen, Durchführung einer Herztransplantation oder Versorgung mit einem kardialen elektronischen Device.

Schlussfolgerungen: In unserer Kohorte scheint DE bei LVHT-Patienten weder klinische noch prognostische Bedeutung zu haben. Weitere Studien mit prospektivem Design und größerer Patientenzahl sind notwendig.

15-8

Reversible myocardial edema as a differential diagnosis of cardiac amyloidosis

Claudia Stöllberger[1], Christine Schmid[1], Birke Schneider[2]

[1]Krankenanstalt Rudolfstiftung, Vienna, Austria
[2]Sana Kliniken Lübeck, Lübeck, Germany

Background: A reversible myocardial edema may occur after reperfusion of an occluded coronary artery, which may manifest echocardiographically as wall thickening and lead to misinterpretations, as shown in the following case.

Methods: Case report: A 68-year old male with a 10-year history of hypertension underwent acute coronary angiography because of an ST-elevation anterior myocardial infarction. A proximal occlusion of the left anterior descending coronary artery was re-canalized and 2 drug-eluting stents were implanted. Peak of creatine-kinase (5,385 U/l) and troponin T (8,835 ng/l) occurred 11 hours after the onset of symptoms and 8 hours after recanalization. Postinterventionally, the patient was haemodynamically stable but developed a pneumonia, which was treated by amoxicillin/clavulanic acid and azithromycin.

Results: Echocardiography one day after the coronary intervention showed wall motion abnormalities in the anterior wall and the interventricular septum. Since the left ventricular wall was thickened (14 mm) and of increased echogenicity, transthyretin (TTR) cardiac amyloidosis was suspected and the patient was investigated by 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) whole body bone scan. Because of a slight tracer uptake in the myocardium (Perugini score 2) and absence of a monoclonal gammopathy, cardiac TTR amyloidosis was diagnosed. The patient refused the suggested therapy with tafamidis and searched for a second opinion. Three months after the acute event, repeat coronary angiography showed a good mid-term result of the intervention. Left ventriculography revealed hypokinesia of the anterior wall with an ejection fraction of 40%. Echocardiography showed wall motion abnormalities in the anterior wall and apex and a slight left ventricular wall thickening of 11–12 mm. The 99 m-Tc DPD scan was repeated and showed no myocardial tracer uptake any more. Neither genetic testing nor cardiac magnetic resonance imaging were indicative for amyloidosis.

Conclusions: Cardiac TTR amyloidosis frequently remains undiagnosed. Only recently pharmacologic therapies have been developed. These new treatment options, however, should not lead to overdiagnosis of TTR amyloidosis and ignorance of the differential diagnoses. The 2017 consensus document of the European Association of Cardiovascular Imaging (EACVI) and the Working Group on myocardial and pericardial diseases of the European Society of Cardiology (ESC) on multimodality imaging in restrictive cardiomyopathy states that the diagnosis of cardiac TTR amyloidosis can reliably be made by 99 m-Tc DPD scintigraphy without the need for histology. A reversible edema as differential diagnosis of cardiac TTR amyloidosis is not mentioned in this document. Myocardial edema due to reperfusion of an occluded coronary artery, however, may present as cardiac TTR amyloidosis by echocardiography as well as bone scintigraphy.

Postersitzung 16 – Herzinsuffizienz 3

16-1

Serum levels of gamma-glutamyltransferase predict outcome in heart failure with preserved ejection fraction

Daniel Dalos, Theresa Dachs, Christina Binder, Franz Duca, Stefan Aschauer, Andreas Kammerlander, Christian Hengstenberg, Julia Mascherbauer, Thomas Reiberger, Diana Bonderman

Medical University Vienna, Vienna, Austria

Background: Previous studies suggested an association between heart failure (HF) and hepatic disorders. Liver function parameters have been shown to predict outcome in HF with reduced ejection fraction, but their impact in HF with preserved ejection fraction (HFpEF) has not yet been investigated.

Methods: Between January 2011 and February 2017, 274 patients with confirmed HFpEF were enrolled (age 71.3 ± 8.4 years, 69.3% female) in a prospective registry.

Results: During a median follow-up of 21.5 ± 18.6 months, 97 patients (35.4%) reached the combined endpoint defined as hospitalization due to HF and/or death from any cause. By multivariate cox regression, serum gamma-glutamyltransferase (GT) was independently associated with outcome (Hazard Ratio (HR) 1.002, $p=0.010$) along with N-terminal pro brain natriuretic peptide (HR 1.491, $p<0.001$) and hemoglobin (HR 0.851, $p=0.008$). Kaplan-Meier analysis showed that patients with serum gamma-GT levels above a median of 36 U/L had significantly more events as compared to the remainder of the group (log-rank $p=0.012$). By multivariable logistic regression, early mitral inflow velocity/mitral peak velocity of late filling (Odds Ratio (OR) 2.173, $p=0.024$), right atrial (RA) pressure (OR 1.139, $p<0.001$) and RA diameter (OR 1.070, $p=0.001$) were independently associated with serum gamma-GT.

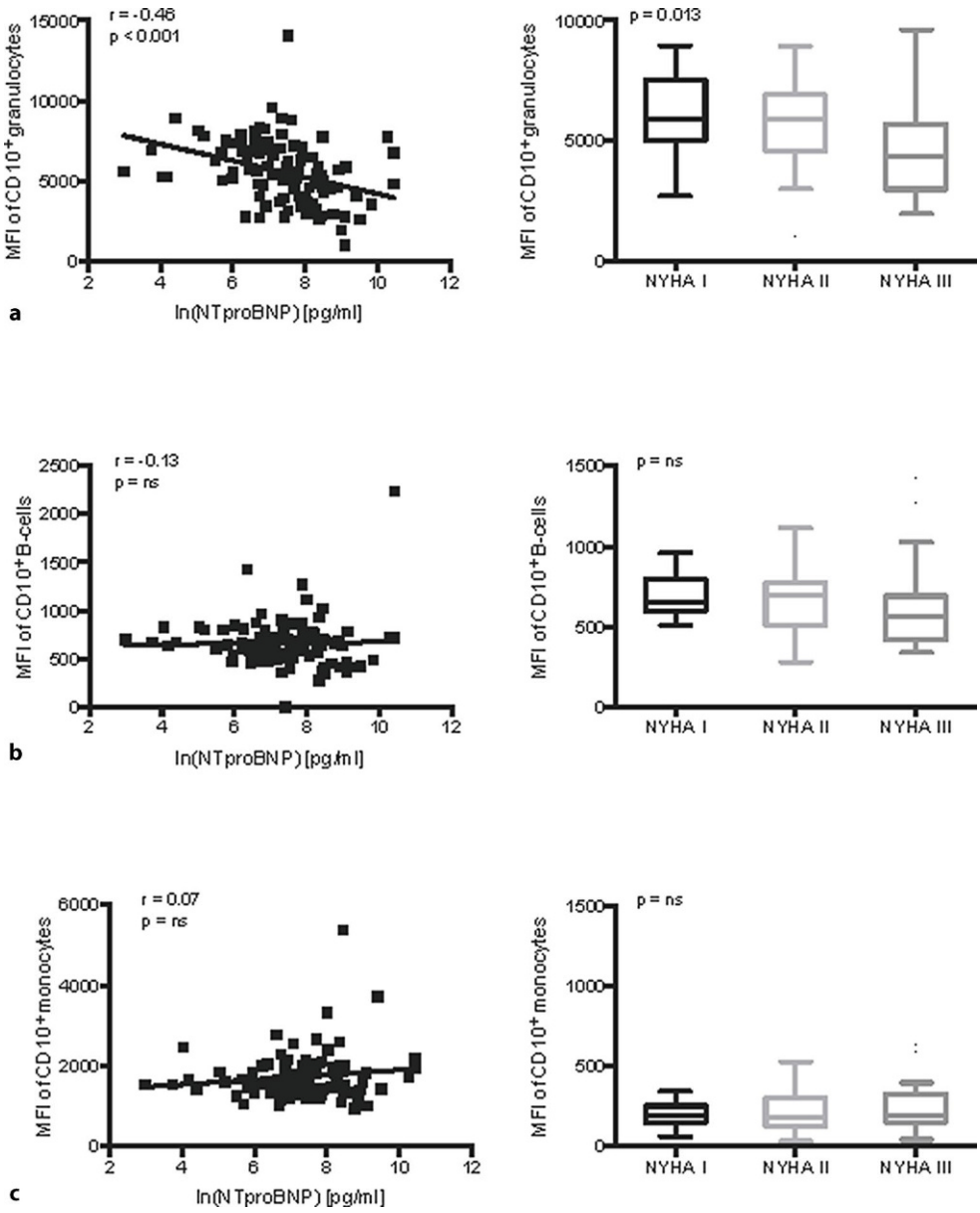


Fig. 1|16-2 Association of NEP (CD10) expression of leukocyte subsets with heart failure severity. Scatter plots with linear regression analysis and the Spearman-Rho correlation coefficient for mean fluorescence intensities (MFI) of CD10+ A. granulocytes, B. B-cells and C. monocytes with NT-proBNP as well as group comparisons using the Kruskal-Wallis-test between NYHA class are shown

Conclusions: Serum levels of gamma-GT are associated with both left and right-sided cardiac alterations and may serve as a simple tool for risk prediction in HFpEF, especially when further diagnostic modalities are not available.

16-2

Increased granulocyte membrane neprilysin (CD10) expression is associated with better prognosis in patients with heart failure with reduced ejection fraction

Noemi Pavo, Alfred Gugerell, Georg Goliasch, Philipp Bartko, Henrike Arfsten, Johannes Novak, Mariann Gyöngyösi, Martin Hülsmann

Medical University Vienna, Vienna, Austria

Background: The exact mechanism of action of neprilysin inhibition (NEPi) are still a subject of debate. The soluble form of the enzyme (sNEP), which can be detected in plasma, is similarly discussed controversially as a potential biomarker in heart failure with reduced ejection fraction (HFrEF). NEP is not only present on solid tissues but is identical to CD10, expressed on the surface of leukocytes under physiological conditions. The possible impact of NEP expression on peripheral leukocytes on prognosis and its association with sNEP levels 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. NEP (CD10) expression on peripheral blood cells were measured by flow cytometry in using a combination of six antibodies with fluorescence minus one samples as control [CD3(#555339), CD19(#555413), CD56(#335826), CD16(#561306), CD14(#562692), +/– CD10(#332777); BD Biosciences, USA]. Additionally sNEP levels were determined using a specific enzyme immunosorbent assay [SEB785Hu, USCN, China]. The association between NEP expression and heart

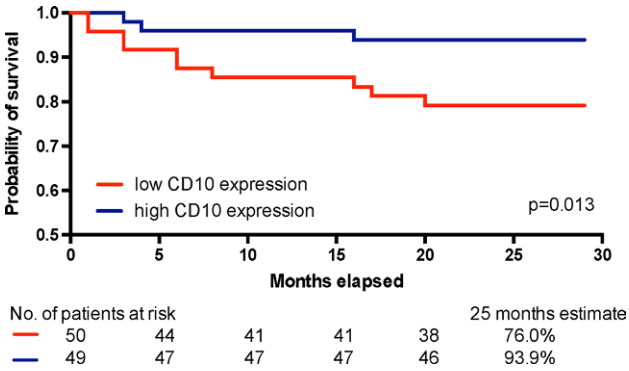


Fig. 2|16-2 Association of granulocyte NEP (CD10) expression with prognosis. Kaplan-Meier analysis for HFrEF patients with low and high granulocyte NEP (CD10) expression with the median MFI as the cut-off value. Comparison was calculated by the log-rank test

failure severity, sNEP levels and all-cause mortality were determined.

Results: Median age was 65 years (IQR:55–73), 75% of patients were male, and beta-blocker, ACE-I/ARB and MRA therapy was established for 96%, 95% and 77% of patients, respectively. Median NT-proBNP levels were 1700 pg/ml (IQR:794-4009). NEP was abundantly expressed on granulocytes with 94.8% (IQR:90.5–97.4) of CD10+cells and measurable 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+cells was 5461 (IQR:4028–6904) for granulocytes, 640 (IQR:535–740) for B-cells and 1589 (IQR:1395–1975) for monocytes. Granulocyte NEP expression, but not NEP expression on B-cells or monocytes, correlated inversely with heart failure severity reflected by NT-proBNP levels ($r=-0.46$, $p<0.001$) and NYHA class ($p=0.013$) (Fig. 1). sNEP concentrations correlated weakly with NEP expression on granulocytes ($r=0.22$, $p=0.030$) and the MFI of CD10+granulocytes ($r=0.31$, $p=0.003$). 15 (15%) out of 99 patients died during a median follow-up of 24 (IQR:23–28) months. Increased NEP expression on granulocytes was indicative for better overall survival in the univariate model [crude HR per 1-IQR increase of MFI 0.40 (95%CI: 0.17–0.90), $p=0.027$] and after adjustment for age and kidney function [adj. HR per 1-IQR increase of MFI 0.41 (95%CI: 0.18–0.94), $p=0.035$]. Kaplan-Meier analysis illustrates the impact of granulocyte NEP expression on outcome (Fig. 2).

Conclusions: In conclusion, albeit beneficial effects of NEP inhibition by ARNI therapy, NEP expression on granulocytes is inversely correlated with heart failure severity and mortality. The results support the inverse relationship between BNP and plasma NEP activity reported for a mixed population of heart failure patients. The positive correlation of granulocyte NEP expression and sNEP indicates a possible contribution of shed membrane NEP molecules to plasma NEP levels as a surrogate marker. The utility of granulocyte NEP expression or sNEP as biomarkers in HFrEF have to be further evaluated.

16-3

The myocardial tissue Renin-Angiotensin-System (RAS) of the failing heart

Noemi Pavo[1], Henrike Arfsten[1], Raphael Wurm[1], Suriya Prausmüller[1], Georg Spinka[1], Georg Goliasch[1], Philipp Bartko[1], Julia Mascherbauer[1], Marko Poglitsch[2], Andreas Zuckermann[1], Martin Hülsmann[1]

[1]Medical University Vienna, Vienna, Austria
[2]Attoquant Diagnostics, Vienna, Austria

Background: Prognosis of patients with heart failure with reduced ejection fraction (HFrEF) remains poor despite recent advances in pharmacologic therapy such as the introduction of the angiotensin-receptor neprilysin-inhibitor (ARNI). The Renin-Angiotensin-System (RAS) is dysregulated in heart failure (HF) with elevated AngII levels as a central driver of disease progression. The myocardium is capable of synthesizing all RAS components resulting in tissue specific angiotensin levels. Neprilysin (NEP) is implicated in the RAS cascade catalyzing the generation of Ang1-7 which counteracts the deleterious effects of AngII. Myocardial tissue angiotensins of the failing heart and the role of long-lasting RAS-inhibitor therapy and particularly NEP inhibition on tissue RAS have not been investigated yet.

Methods: Concentrations of the angiotensin metabolites AngI, AngII, Ang1-7, AngIII, Ang1-5 and AngIV (RAS-fingerprints) were investigated in myocardial samples of end-stage HFrEF patients undergoing heart transplantation with a mass-spectrometry based method. Patients were stratified according to background therapy with RAS-inhibitors and variables were compared between groups by a non-parametrical test.

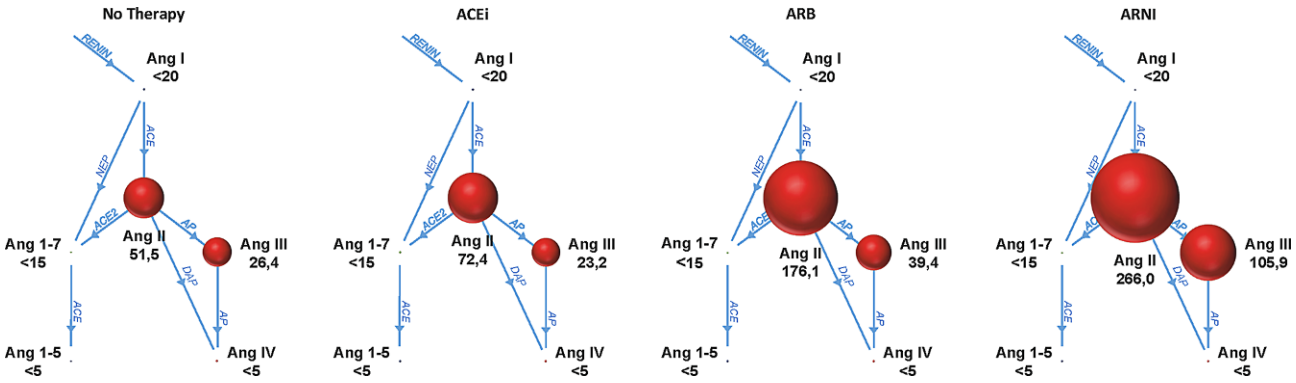


Fig. 1|16-3 Renin-angiotensin-system metabolite concentrations (RAS-fingerprints) of the failing heart according to RAS-inhibition therapy, i. e. no RAS-blockade, ACEi, ARB or ARNI. Numbers in brackets indicate the specific angiotensin peptides. Side of spheres and numbers beside represent absolute concentrations of angiotensins ((pg/g tissue), median value) analyzed by mass spectrometry

Results: A total of 30 patients were included ($n=6$ without RAS-blockade, $n=16$ with ACE-I, $n=6$ with ARB and $n=2$ with ARNI). Median age was 55 (IQR 45–63) years and 87% of patients were male. 40% of patients had an ischemic etiology of HF, median NT-proBNP levels were 3498 pg/ml (IQR 1761–8400). Tissue RAS patterns were visually similar between all groups (Fig. 1). Myocardial AngI, Ang1-7, Ang1-5 and AngIV levels were below the detection limit for all samples. Median tissue AngII and AngIII concentrations across all samples were 83.1(pg/g tissue) (IQR 29.3–196.6) and 26.4 (pg/g tissue) (IQR 5.0–64.5). Despite different background RAS-inhibitor therapy, AngII and AngIII levels were not significantly different between all groups [median (IQR) in (pg/g tissue)—AngII: 51.5 (41.5–123.8) vs. 72.4 (28.5–177.6) vs. 176.1 (22.4–286.8) vs. 266.0 (108.2–423.8); $p=$ns and 26.4 (5.0–89.2) vs. 23.2 (5.0–59.3) vs. 39.4 (5.0–94.3) vs. 105.9 (46.5–165.3); $p=$ns for no therapy, ACE-I, ARB and ARNI respectively].

Conclusions: Although only AngI and AngII are detectable at substantial concentrations in plasma of HFrEF patients, the predominant angiotensins of the failing heart are AngII and AngIII. AngII levels are high in the failing heart supporting the hypothesis that excess AngII is involved in heart failure disease progression. AngIII similarly exerts strong vasoconstrictive properties also increasing cardiac sympathetic activity presumably potentiating further HF deterioration. The modality of the long established RAS-inhibitor therapy in end-stage HF, particularly the inhibition of NEP, seems to have no (more) influence on myocardial tissue RAS regulation.

16-4

Ist Impella® einer herkömmlichen Strategie im kardionenen Schock überlegen? Metanalyse der vorhandenen Daten

Bernhard Wernly[1], Clemens Seelmaier[1], Ingrid Pretsch[1], Michael Lichtenauer[1], Christian Jung[2], Uta C. Hoppe[1], Ulf Landmesser[3], Holger Thiele[4], Alexander Lauten[3]

[1]Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Österreich
[2]Universitätsklinikum Düsseldorf, Düsseldorf, Deutschland
[3]Charité – Universitätsmedizin Berlin, Berlin, Deutschland
[4]Universitätsklinikum Leipzig, Leipzig, Deutschland

Grundlagen: Patienten im kardiogenen Schock haben eine hohe Mortalität und Morbidität. Impella®, ein perkutanes linksventrikuläres „assist device“ (LVAD), senkt die linksventrikulären Drücke, erhöht das Herzzeitvolumen und verbessert die koronare Perfusion. Ziel dieser Metanalyse war es, eine Impella®-Strategie mit einer alternativen, herkömmlichen Strategie (medikamentöse Behandlung oder „intraaortic pump“ (IABP) in Patienten mit CS aufgrund von Myokardinfarkt oder nach Reanimation zu vergleichen.

Methodik: Die Daten wurden auf Studienebene analysiert. Die Heterogenität wurde mittels I2 Statistik evaluiert. Mittels „random-effects model“ (DerSimonian and Laird) wurden Risikoraten kalkuliert. Insgesamt vier Studien mit kumulativ 588 Patienten wurden in die Metaanalyse inkludiret. Der primäre Endpunkt war die Kurzzeitmortalität (intrahospital oder Mortalität nach 30 Tagen).

Ergebnisse: Impella® war nicht mit einer Verbesserung der Mortalität (RR 0,84; 95 %CI 0,57–1,24; $p=0{,}38$; I^2 55 %) assoziiert. Das Schlaganfallrisiko war ohne Unterschied zwischen den beiden Gruppen (RR 1,00; 95 %CI 0,36–2,81; $p=1{,}00$; I^2 0 %). Das Risiko für relevante Blutungen (RR 3,11 95 %CI 1,50–6,44; $p=0{,}002$; I^2 0 %) und periphere ischämische Komplikationen (RR 2,58; 95 %CI 1,24–5,34; $p=0{,}01$; I^2 0 %) war jedoch in der Impella®-Gruppe eleviert.

Schlussfolgerungen: Der Einsatz von Impella® war in dieser Metaanalyse nicht mit einer Risikoredukton hinsichtlich der Kurzzeitmortalität verbunden. Weiters kam es in der Imeplla®-Gruppe vermehrt zu Komplikationen im Vergleich zur Kontrollgruppe, welche aus medikamentös und/oder mit IABP behandelten Patienten bestand. Es ist daher notwendig, besser Patienten zu selektionieren, welche von den hämodynamischen Vorteilen der Impella® profitieren.

16-5

Neurohumoral regulation of the low-, medium- and high-renin HFrEF phenotypes

Suriya Prausmueller, Henrike Arfsten, Georg Spinka, Johannes Franz Novak, Anna Cho, Georg Goliasch, Philipp Emanuel Bartko, Pavo Noemi, Martin Huelsmann

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Austria

Background: Previous investigations of plasma Renin-Angiotensin-System (RAS) fingerprints of patients with heart failure with reduced ejection fraction (HFrEF) revealed the existence of low, medium and high renin phenotypes independently of disease severity. Plasma renin serves as an excellent surrogate for angiotensin levels. The different renin phenotypes could not only hypothetically respond differently to RAS blockade but associated alterations of other vasoactive peptide systems could elucidate disease mechanisms and novel targets for heart failure therapy. The study aimed to investigate the relation between RAS regulation and pathophysiologically relevant vasoactive peptide systems based on different renin phenotypes.

Methods: We prospectively enrolled 369 patients with stable HFrEF. Laboratory markers including NT-proBNP and active renin concentration (ARC) were assessed. Plasma NEP levels (sNEP), bioactive adrenomedullin (bio-ADM) and big-endothelin1 (bigET-1) were measured by ELISA (R&D systems, UK; Sphingotec GmbH, Germany and Eagle Biosciences, Austria). NEP activity was determined by a fluorimetric peptide cleavage assay. The correlation between biomarkers and association with all-cause mortality was assessed. sNEP, bio-ADM and bigET-1 levels as well as NEP activity between the different renin phenotypes (i. e. <15. percentile, 15.–85. percentile and >85. percentile of ARC) was compared.

Results: Median age was 65 (IQR 53–73) years, 75% of patients were male. Median NT-proBNP levels were 1936 (IQR 855–4126) pg/mL. Median ARC was 155 (29–569) µIE/mL, the low, medium and high renin HFrEF phenotypes showed median ARC levels of 4.2 µIE/mL (IQR 2.0–7.8), 155.1 µIE/mL (IQR 43.3–353.5) and 2360 µIE/mL (IQR 1483–3250) µIE/mL. Median bigET-1 was 0.62 pmol/L (IQR 0.42–1.10), bio-ADM 26.0 pg/mL (IQR 16.1–46.7), sNEP 413 pg/mL (IQR 0–4111) and NEP activity 2.36 nmol/mL/min (IQR 1.16–4.59). There was no correlation between sNEP and NEP activity [$r=0.09$, $p=0.088$]. ARC did not show a meaningful correlation with any of the four biomarkers [$p=$ns for sNEP, NEP activity and bigET-1; $r=0.13$, $p=0.018$ for bio-ADM]. In the univariate analysis ARC, bigET-1, bio-ADM but not sNEP and NEP activity, were associated with outcome. This association remained significant after adjustment for age, gender and kidney function for all three markers and for ARC

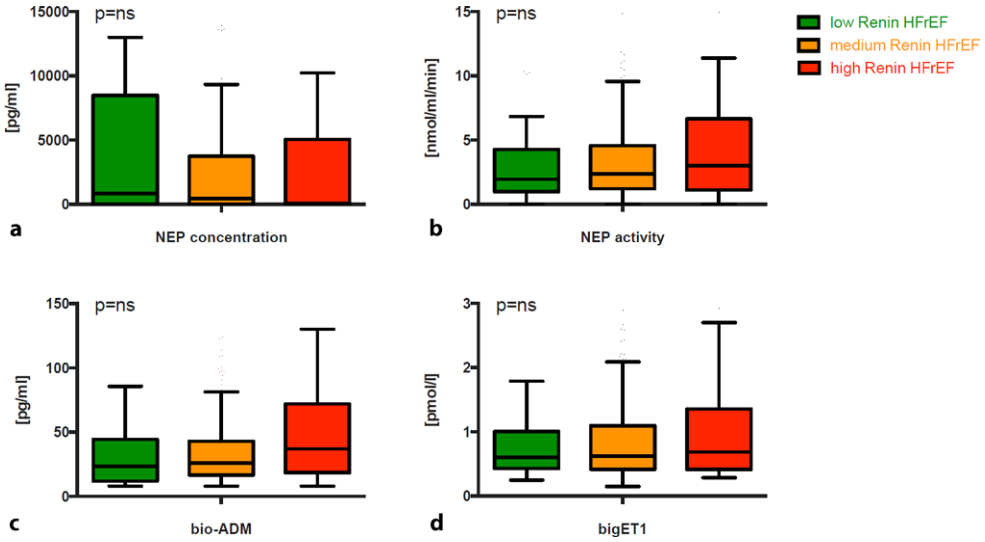


Fig. 1|16-5

after adding NT-proBNP [adj. HR per 1-IQR increase of ARC 1.27 (95%CI 1.04–1.22), $p=0.003$]. There were no differences in bigET-1, bio-ADM and sNEP or NEP activity stratified by the different renin phenotypes (Fig. 1).

Conclusions: ARC is a risk factor for mortality in HFrEF patients, independently of NT-proBNP. Plasma NEP levels and activity neither correlated with each other nor were associated with outcome. Bio-ADM and bigET-1 were strong risk factors for all-cause mortality. Interestingly, neither NEP nor bio-ADM or bigET-1 were related to RAS-activation, suggesting that there is no direct relationship with RAS regulation.

16-6

Comparison of global longitudinal strain and ejection fraction in correlation to NT-proBNP in ischemic and non-ischemic heart failure

Klemens Ablasser[1], Dirk von Lewinski[1], Ewald Kolesnik[1], Michaela Gangl[1], Lydia Kattnig[1], Vera Habenicht[1], Martin Manninger-Wünscher[1], Daniel Scherr[1], Johannes Schmidt[2], Friedrich Fruhwald[1], Andreas Zirlik[1], Nicolas Verheyen[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Department of Radiology, Medical University of Graz, Graz, Austria

Background: In chronic heart failure (CHF) NT-proBNP and left ventricular ejection fraction (LVEF) by echocardiography are standard diagnostic as well as follow-up markers and are known to correlate with prognosis. Speckle-tracking echocardiography is a more recent technique to quantify myocardial deformation as a measurement of left ventricular function with potential benefits over LVEF. The purpose of this investigation was to analyse the cross-sectional relationship between 2D speckle tracking-derived global longitudinal strain (GLS) and NT-proBNP plasma levels in a prospective cohort of ischemic and non-ischemic CHF patients.

Methods: We enrolled 205 patients with chronic heart failure. Major inclusion criteria were age over 18 years, stable disease with absence of unplanned hospitalization or change in medication or device therapy in the previous month or major surgery in the previous 3 months. CHF treatment had to be according to the recommendations of the ESC CHF guidelines 2016 and LVEF had to be below 50%. Patient history, physical examination and an extensive echocardiography exam were performed. Lab results included NT-proBNP. Manual longitudinal strain was calculated using EchoPAC (General Electric Medical Systems, Horten, Norway) by a single and blinded examiner. LVEF was measured using Simpson's biplane method.

Results: 205 patients included in the study. The baseline characteristics included mean age 65.0 years and 75% male. Mean GLS was -9.6% (SD +/- 4.5%) and median NT-proBNP 1269.5 (IQR 379.5–2759.5) ng/ml. The CHF aetiology was 70.0% ischemic vs 30.0% non-ischemic. There was a significant negative correlation between GLS and NT-proBNP (Pearson r = 0.239, $p=0.029$), this was not significant for LVEF and NT-proBNP (Pearson r = 0.149, $p=0.228$). In a multivariate regression analysis adjusted for age, sex, NYHA classification and HF aetiology, GLS remained significantly correlated with NT-proBNP (adjusted beta-coefficient = 0.289, $p=0.011$). Furthermore, in contrast to LVEF, GLS showed a significant correlation to NT-proBNP in patients with ischemic (Pearson r = 0.266, $p=0.049$) as well as non-ischemic aetiology of heart failure (Pearson r = 0.434, $p=0.034$).

Conclusions: Global longitudinal strain, not LVEF, was significantly correlated with NT-proBNP in patients with CHF, independently of age, sex, symptoms or heart failure aetiology. This shows that speckle-tracking might be superior to LVEF for the assessment of left ventricular function in CHF.

16-7

Takotsubo cardiomyopathy with left ventricular thrombus: a case report

Emilie Han, Begüm Öztürk, Jutta Bergler-Klein, Roza Badr Eslam

Medical University of Vienna, Vienna, Austria

Background: Left ventricular thrombus is a potentially life-threatening condition, with a high risk of embolic complications. These intracardiac thrombi are more likely to form in patients who have had an anterior myocardial infarction with apical dysfunction. A 25-year old male patient of Somali eth-

nicity first arrived at our hospital with worsening symptoms of chest pain and dyspnoea (NYHA III). Coronary arteries were described as normal assessed by coronary angiography in the referral hospital. Past medical history reported a left ventricular cardiac mass (33 × 15 mm, Fig. 1) on the apical wall of unknown aetiology and moderately impaired left ventricular ejection fraction (LVEF = 48%). The patient complained of headaches, vertigo and shortness of breath, but did not report any occurrence of syncope. The remaining physical examination and lab report were unremarkable, apart from an elevated NT-proBNP (218 pg/mL). Electrocardiography disclosed sinus rhythm and a complete right bundle branch block. The patient did not report suffering from a myocardial infarction, but notable taken history was that six months prior to diagnosis the patient was a refugee who fled from the insecurity of his home country under stressful circumstances. These findings support the differential diagnosis of an intracardiac thrombus, which formed post acute Takotsubo syndrome.

Methods: To evaluate the size of intracardiac thrombus as well as left ventricular function we assessed two dimensional transthoracic echocardiography and/or contrast echocardiography in each follow-up visit. NT-proBNP levels were continuously monitored.

Results: After initial diagnosis of the intracardiac thrombus, the patient continued rivaroxaban and was additionally started on heart failure medication to counteract his symptoms. At the follow-up visit his general condition was worse and he described noticeable performance loss. A follow-up TTE showed a protruding mural thrombus which had increased in size (49 × 25 mm). Thus, tumour markers and a PET-MRI were considered to exclude malignancy of the growth. Consequently, it was decided to change the patient's anticoagulation from rivaroxaban to VKA and close follow-up visits were scheduled. International normalised ratio (INR) was controlled regularly in the outpatient clinic and patient compliancy improved after repeated initial difficulties (Fig. 2). The patient suffered from no bleeding or thromboembolic event. In the one-year follow-up after anticoagulation switch to vitamin-K antagonists the thrombus had decreased in size and measured 26 × 10 mm in two dimensional TTE. VKA treatment was effective in reducing the clot size. Although the patient seemed asymptomatic in everyday life, decreased exercise capacity due to cardiac involvement was detected by spiroergometry examination done for comprehensive risk assessment. Results revealed a reduction of the predicted peak oxygen uptake value (ppV'O2 = 47%), which is an accurate parameter for myocardial impairment.

Conclusions: The established therapy option of a left ventricular thrombus is anticoagulation with VKA. In patients with cardiomyopathy and a diagnosis of left ventricular thrombus close follow-up management is crucial, due to the risk of bleeding, embolism and progression of the left ventricular function impairment. Spiroergometry should be considered as an appropriate tool for risk stratification in young cardiomyopathy patients.

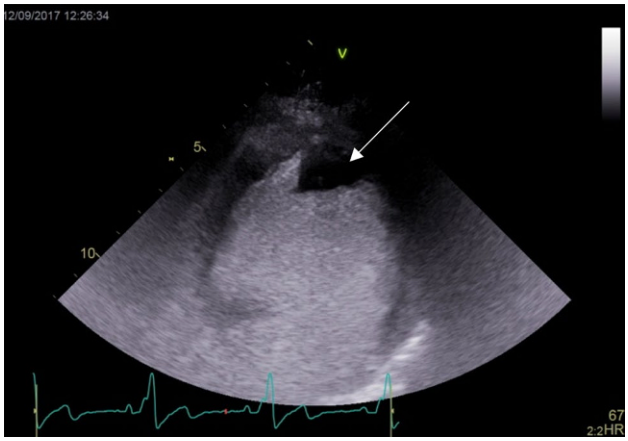


Fig. 1|16-7 Contrast echocardiography image of the intracardiac thrombus (marked by arrow) located at the left apical wall, measured 33 × 15 mm

Postersitzung 17 – Diverse 2

17-1

Cardiac complications during pregnancy are rare in childhood cancer survivors

Maria Klara Frey[1], Emilie Han[1], Varius Dannenberg[1], Stephanie Ludwig[2], Eva Frey[2], Leo Kager[2], Jutta Bergler-Klein[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2] St. Anna Children's Hospital Vienna, Vienna, Austria

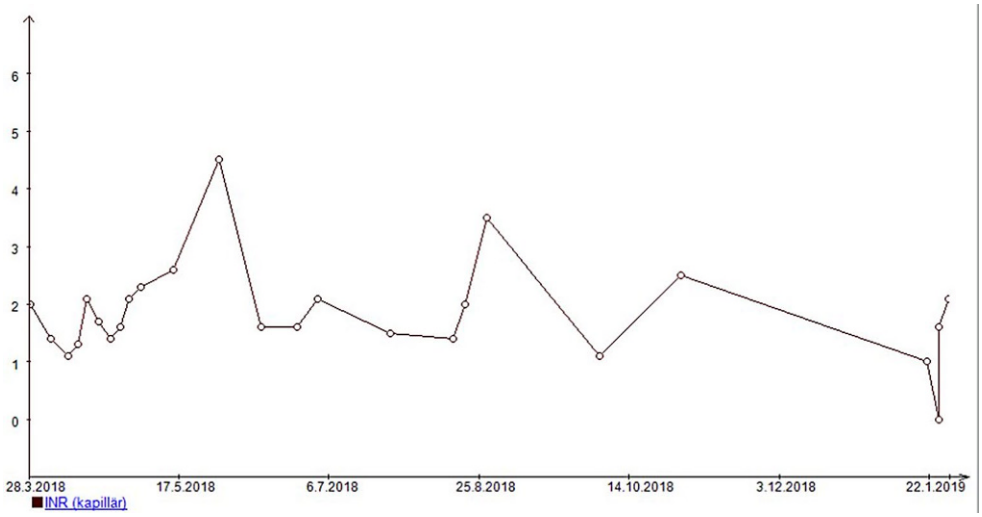


Fig. 2|16-7 INR curve of the initially non-compliant patient over time, from switch of anticoagulation to the last follow-up to date (data point 0 is recorded in error due to not enough sample material available for the laboratory)

Background: Cardiac outcomes of childhood cancer survivors are of great interest in the field of cardio-oncology. Limited data is available on the impact of pregnancy on cardiac function in these patients. The aim of the current study was to identify pregnancy-related cardiac events in childhood cancer survivors.

Methods: Consecutive female childhood cancer survivors of St. Anna Children's Hospital in Vienna aged between 25 and 50 years were called to participate in the study. Medical files were screened for documented cardiac events and patients were asked about eventual childbirths and problems associated with pregnancy.

Results: A total of 27 female childhood cancer survivors between 25 and 49 years (mean age 36 years) were successfully screened. The patients were most commonly treated for the following cancers during their youth: 22% had Hodgkin's lymphoma ($n=6$), 22% osteosarcoma ($n=6$), 15% Ewing sarcoma ($n=4$). Out of these women, 14 (51.8%) reported to have given birth to at least one child (median 2, range 1 to 7). (Six women (22%) wished to have children, but stated difficulties with natural conception. Pregnancy proceeded without complications in 11 of 14 patients (78.6%), whereas 2 patients (14.3%) developed pregnancy complications (preeclampsia and gestational diabetes). Supraventricular tachycardia following pregnancy occurred in 2 women (14.3.%). Peripartum cardiomyopathy developed in 2 patients (7.7%), in one patient with previously borderline left ventricular function.

Conclusions: In this pilot study we could show that pregnancy is well tolerated in most women with survived childhood cancer. However, cardiac events often occur following pregnancy. More data are needed to counsel this increasing number of women before pregnancy and to better identify patients a risk for cardiac events associated with pregnancy.

17-2

The prevalence of potentially inappropriate cardiovascular medication and hospitalization in elderly patients with chronic renal insufficiency: a retrospective data analysis in Austria (2008–2011)

Safoura Sheikh Rezaei[1], Andrea Haberson[2], Alexander Schöberl[2], Christoph Rinner[2], Hana Šinkovec[2], Gottfried Endel[3], Walter Gall[2], Michael Wolzt[1]

[1]Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria
[2]Center for Medical Statistics, Information and Intelligent Systems, Medical University of Vienna, Vienna, Austria
[3]Main Association of Austrian Social Security Organizations, Vienna, Austria

Background: Polypharmacy and potentially inappropriate medication (PIM) use may result in adverse drug reactions (ADR). However, the impact on the health care system in Austria is unknown. The aim of our study was therefore to evaluate cardiovascular PIM use and ADR in a population at high risk.

Methods: Prescription and demographic data as well as information on hospital discharge diagnoses for patients aged ≥70 years and chronic renal insufficiency were analyzed from 13 Austrian health insurance funds for the years 2008 to 2011.

Results: Data were available from 5,702 male and 5,845 female patients with a mean age of 78 years in 2008. In total, 40,999 hospitalizations were recorded (median: 2 hospitalizations per patient) and 2.401.434 prescriptions were filled the first 30 days after the PIM-prescription. From 11,547 patients, 95% and 79% patients received at least one EU-PIM, AT-PIM and 25% cardiovascular PIM, respectively (Table 1). In total, 34 ADR were identified during the first 30 days.

Table 1 | 17-2 Cardiovascular PIM prescription

ATC-codes	drug	Number of prescriptions (*n*)	(%)
C02CA04	Doxazosin	18.704	0,78%
C04AD03	Pentoxifyllin	12.658	0,53%
C02AC06	Rilmenidin	12.241	0,51%
C03DA01	Spironolacton	10.285	0,43%
C02CA06	Urapidil	9.491	0,40%
C01BD01	Amiodaron	8.004	0,33%
C02AC05	Moxonidin	5.654	0,24%
C08DB01	Diltiazem	5.618	0,23%
C04AX20	Buflomedil	5.013	0,21%
C08DA01	Verapamil	4.420	0,18%
C01AA04	Digitoxin	3.496	0,15%
C04AE01	Ergoloidmesylat	3.351	0,14%
C08CA05	Nifedipin	3.258	0,14%
C04AX21	Naftidrofuryl	2.904	0,12%
C01AA08	Metildigoxin	2.534	0,11%
C04AE02	Nicergolin	2.303	0,10%

Conclusions: Elderly patients with chronic renal insufficiency have a high prevalence of PIM use. However, ADR associated with PIM use are not frequent.

17-3

Diagnostic yield and time to diagnosis by Implementing a syncope pathway

Georg Saurer, Michaela Mezler-Andelberg, Wolfgang Weihs

Landeskrankenhaus Graz II, Graz, Austria

Background: Syncope is a common presenting symptom in emergency departments (0.8–2.4%) and is associated with high health care costs. In up to 40% of cases etiology remains unknown after initial evaluation. Purpose: To assess the increase in diagnostic yield and the time to diagnosis by implementing a structured pathway in syncope evaluation according ESC-Guidelines in a secondary hospital.

Methods: In the study we compared 2 groups of patients with T-LOC. We evaluated the diagnostic yield and the time to diagnosis. The first group compromised all patients with T-LOC referred to the emergency department (ED) of the hospital from January to March 2016. The work up was done according to common clinical practice. After implementation of a structured pathway in syncope evaluation according to ESC-Guidelines, we reevaluated the diagnostic yield and the time to diagnosis in all patients referred to ED with T-LOC from July to September 2017. The implementation consisted of an initial evaluation (careful history with a checklist, physical examination, ECG,

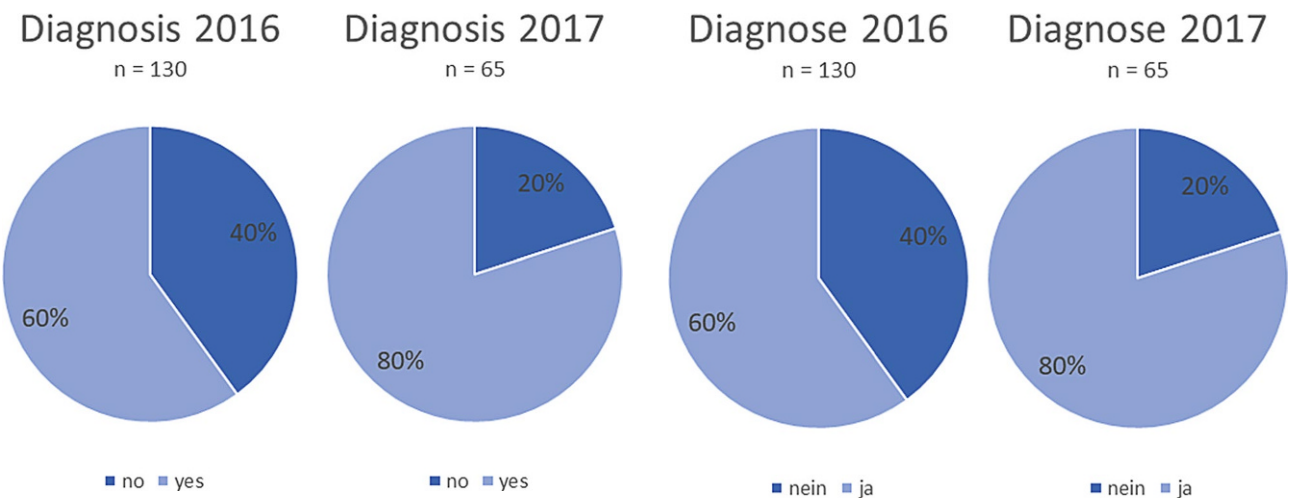


Fig. 1|17-3

Abb. 1|17-4 Diagnoserate

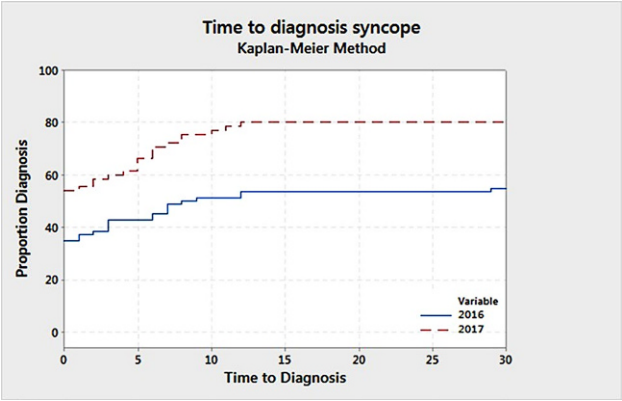


Fig. 2|17-3

orthostatic challenge done by nurses), risk assessment and instructing the medical staff.

Results: There were 169 vs. 85 pts with suspected T-LOC presenting in the ED. 130 (77%) vs. 65 (76.5%) were classified as having a syncope. The diagnostic yield in the syncope patients was 60 vs. 80% ($p = 0.013$). The rate of correct diagnosis within 14 days increased from 55 to 80%.

Conclusions: By implementing a structured pathway and educating the staff, we succeeded in increasing the diagnostic yield from 60 to 80%. This could be achieved in a reduced referral to diagnosis time.

17-4

Diagnoserate und Klassifikation von Synkopen nach Implementierung eines Synkopenpfades

Georg Saurer, Michaela Mezler-Andelberg, Wolfgang Weihs

Landeskrankenhaus Graz II, Graz, Österreich

Grundlagen: Die Synkope ist definiert durch einen Bewusstseinsverlust bedingt durch eine globale cerebrale Hypoperfusion. Diese ist charakterisiert durch plötzlichen Beginn, kurze Dauer und spontane vollständige Erholung. Die Ursache bleibt in bis zu 40 % ungeklärt. Ziel: Erhöhung der Diagnoserate und Verbesserung der Klassifizierung von Synkopen in einem Schwerpunktkrankenhaus nach Implementierung eines Synkopenpfades entsprechend der ESC-Leitlinien.

Methodik: Wir verglichen 2 Gruppen von Patienten mit Synkope, die die Notfallaufnahme (NFA) unseres Krankenhauses aufsuchten und abgeklärt wurden. Die erste Gruppe wurde zwischen Jänner und März 2016 retrospektiv analysiert. Diese Patienten wurden entsprechend allgemeiner klinischer Praxis abgeklärt. Nach Implementierung eines Synkopenpfades mit einer Basisdiagnostik (ausführliche Anamnese mit Checkliste, EKG, physikalische Untersuchung, Orthostasetest) und Schulung der Ärzteschaft und Pflege wurde ein zweites Patientenkollektiv mit Synkope von Juli bis September 2017 evaluiert.

Ergebnisse: Es fanden sich 130 bzw. 65 Patienten mit Synkope in der NFA. Die Diagnoserate konnte von 60 auf 80 % gesteigert werden ($p = 0{,}013$). Den größten Anteil der Synkopen bildete in beiden Gruppen die orthostatische Synkope (47 vs. 51 %). Der Anteil der Reflexsynkopen stieg von 1 auf 22 %. Kardiale Synkopen wurden zu 10 vs. 5 % diagnostiziert.

Schlussfolgerungen: Durch Implementierung eines Synkopenpfades und Schulung des Personals konnte die Diagnoserate signifikant gesteigert werden. Durch die eingeführten Maßnahmen wurde vor allem das Bewusstsein für Reflexsynkopen gehoben.

17-5

A novel in vitro hybrid mock circulatory loop for evaluation of ventricular assist devices

Emmanouil Agrafiotis[1], Markus A. Geith[1], Gerhard Sommer[1], Gerhard A. Holzapfel[1], Vera Hergesell[2], Otto E. Dapunt[2], Sotirios Spiliopoulos[2]

[1]University of Technology Graz, Graz, Austria
[2]Medical University of Graz, Graz, Austria

Background: We introduce a novel mock circulatory loop (MCL) capable of simulating the ventricular physiology to evaluate the performance of ventricular assist devices (VADs).

Methods: The MCL consists of two piston-cylinders driven by two servo motors and a software interface to control the motors precisely. The first piston-cylinder is attached to a ven-

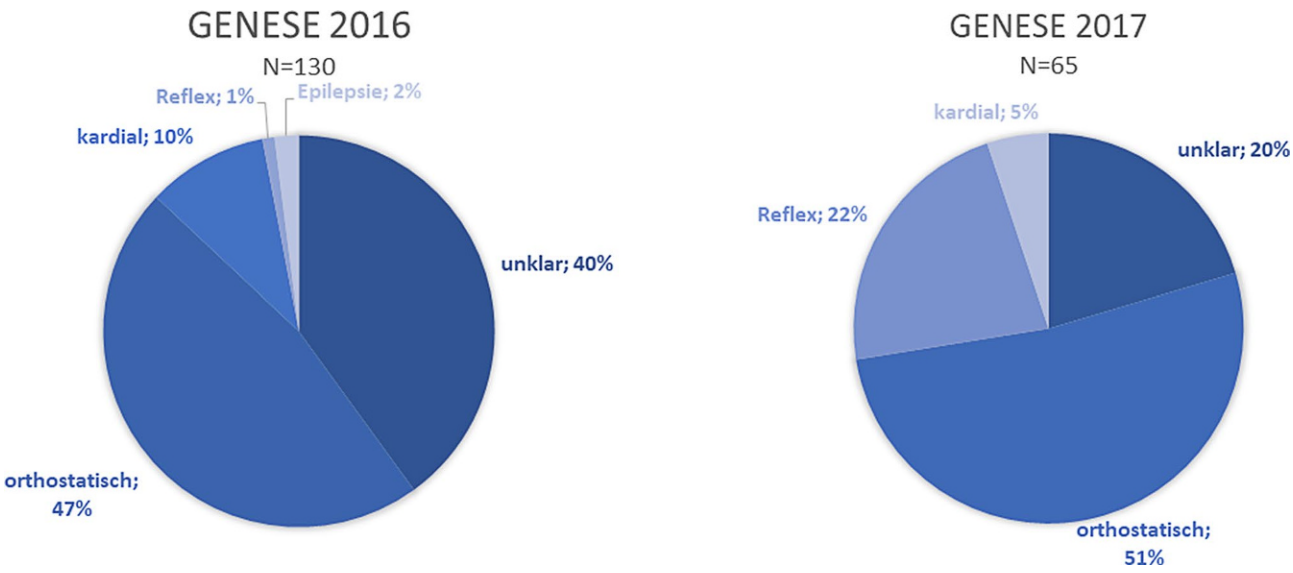


Abb. 2|17-4 Klassifikation

tricular-like shaped part with two mechanical bileaflet heart valves implanted acting as mitral valve (MV) and aortic valve (AV) respectively. The second piston-cylinder, namely compliance chamber, has a pressure sensor attached in-line and is regulating the compliance of the loop by alternating the volume when it senses a pressure difference. The VAD is placed to the in vitro MCL similar to the in vivo implantation. The two cylinders are being bridged via an artificial aortic arch, in which the outflow graft of the VAD is connected. During operation, when the ventricular piston retracts the MV opens and the ventricle is filling. Afterward, the piston ejects the stroke volume to the artificial ascending aorta and the AV opens, while the MV remains closed.

Results: Under operation, the ventricular motor has a maximum speed of 5000 mm/s and position repeatability of 2 ms which enables reproduction of healthy, heart failure, and exercise scenarios. The volumetric capacity of the in vitro ventricle is up to 150 ml, which is sufficient for parallel synchronous operation with VADs. The bileaflet valves facilitate unidirectional flow. Pre- and after-ejection, the compliance chamber regulates the volumetric expansion of the increase in preload and incorporates the Frank-Starling law. The in vitro circulation is fully-controlled via the control unit and the software in real time

Conclusions: The ventricular-like shape of the MCL can reproduce realistic physiological values such as blood pressure and volumetric flow. Its sophisticated design mimics the in vivo implantation of VAD and facilitates real-time testing. Uniquely, this innovative in vitro set-up can evaluate the performance of the VADs prior to animal and clinical trials.

17-6

Genetic profiles of patients with hereditary transthyretin amyloidosis in Austria

Michaela Auer-Grumbach[1], Franz Duca[1], René Rettl[1], Christina Binder[1], Daniel Dalos[1], Stefan Aschauer[1], Martin Gattermeier[2], Wolfgang Löscher[3], Christian Lampl[4], Helmut Rauschka[5], Gerhard Pölzl[3], Fritz Zimprich[1], Gabor Kovacs[1], Hermine Agis[1], Diana Bonderman[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Landesklinikum Waidhofen/Ybbs, Waidhofen/Ybbs, Austria
[3]Medical University of Innsbruck, Innsbruck, Austria
[4]Ordensklinikum Linz, Linz, Austria
[5]SMZ-Ost Donauspital, Vienna, Austria

Background: Hereditary transthyretin amyloidosis (hATTR) is an ultra-rare disease that is caused by mutations in the transthyretin (TTR) gene, which leads to amyloid deposition mainly in the heart and the peripheral nerves. The disease is endemic in Portugal and Sweden with the recurrent mutation in the Val-30Met, which has led to the subdivision into Val30Met and non-Val30Met patients. The prevalence and genetic characteristics of hATTR in Austria have not been studied so far.

Methods: Between 2014 and 2019, consecutive patients with clinically and genetically confirmed hATTR have been registered in referral centers throughout Austria. Cardiological and neurological evaluation was carried in all patients and available relatives who were clinically and genetically affected.

Results: A total of 5 different variants in the TTR gene have been identified: His88Arg was found in 4 unrelated index patients, the Ile107Phe, Val20Ile and Val30Met were identified in 2 families each, and the Val93Leu variant was found in 1 proband. In contrast to genetic profiles from Portugal and Sweden, where more than half of the affected individuals display the Val30Met mutation, only 2 index patients in the Austrian cohort were identified. Fig. 1 demonstrates genetic profiles of Austrian hATTR according to geography. All patients with the His88Arg mutation were located in Vienna, all others were distributed across other Austrian provinces.

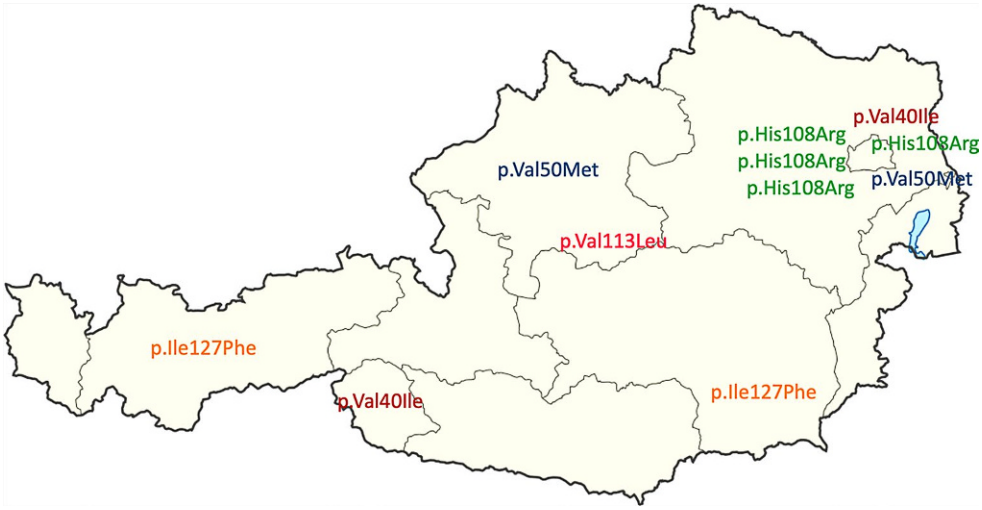


Fig. 1|17-6 Austrian transthyretin mutation gene map

Conclusions: For the first time, we provide an Austrian gene map for mutations in the TTR gene of clinically affected families. An unexpected finding was the high individuality of mutations, which may hamper predictions with regards to therapeutic responses or prognosis. Recruitment of further patients with hATTR is ongoing and will enable to expand the genotypic spectrum of this treatable orphan disease in Austria.

17-7

The prognostic impact of therapeutic anticoagulation after biological aortic valve replacement

Andreas Hammer[1], Patrick Sulzgruber[1], Sebastian Schnaubelt[2], Lorenz Koller[3], Niema Kazem[1], Günther Laufer[4], Barbara Steinlechner[5], Aurel Toma[1], Tatjana Fleck[4], Johann Wojta[1], Alexander Niessner[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Department of Emergency Medicine, Medical University of Vienna, Austria
[3]Medical University of Vienna, Vienna, Austria
[4]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[5]Division of Cardiothoracic and Vascular Anesthesia, Medical University of Vienna, Vienna, Austri Austria

Background: Recent guidelines state that in patients with surgical biological aortic valve replacement (AVR), the use of anti-platelet therapy is as a valid alternative to postoperative anticoagulation (AC) in the absence of a further indication for AC. However, the prognostic impact of different anti-thrombotic strategies after biological AVR has not clearly been investigated so far and outcome data remain scare and inconclusive. Moreover, the AC strategy of patients presenting with post-operative atrial fibrillation (POAF), a common post-operative phenomenon, has not clearly been investigated so far. Therefore, we aimed to picture the therapeutic AC approach after biological AVR and whether the presence of POAF effects decision making with regard to anti-thrombotic management. Additionally, we aimed to investigate the prognostic impact of a post-operative AC therapy on the patient outcome.

Methods: Within this prospective observational study 515 patients undergoing elective cardiac valve and or coronary artery bypass graft (CABG) surgery at the Department of Cardiac Surgery of the Medical University of Vienna (Austria) were enrolled. All patients were continuously screened for the development of POAF and followed until the primary endpoint (mortality) was reached. Logistic regression analysis was performed to elucidate the effect of AC on outcome.

Results: A total of 200 individuals underwent biological AVR (including 81 [40.3%] combined AVR+CABG surgeries, median age: 77 years [IQR: 71–80 years]; 133 [66.3%] male gender). We found that 97 (48.3%) patients received therapeutic AC at the time of discharge, including 42 (43.4%) on vitamin K antagonists (VKA), 53 (54.6%) on low-dose low-molecular weight heparin (LMWH) and 2 (2.0%) non-vitamin K antagonist oral anticoagulants (NOACs). One-hundred and three (51.2%) patients received another anti-thrombotic approach including 23 (22.3%) on dual anti-platelet therapy (DAPT) and 72 (69.9%) with prophylactic LMWH. Interestingly, the fraction of patients that received AC were comparable between POAF (CHA_2DS_2-VASc-Score 4, IQR: 3–5) and non-POAF individuals (51.9% vs. 44.6%; $p=0.304$). After a median follow-up time of 1069 days (IQR: 673–1475 days) 21 patients (10.4%) died, referring to 9 (8.3%) non-POAF and 12 (13.0%) POAF individuals. We found that a therapeutic AC after surgery showed a strong and inverse association with 3-year mortality with a crude odds ratio (OR) of 0.31 (95%CI 0.12–0.79; $p=0.015$). The prognostic potential remained stable after adjustment for potential confounders ($p=0.029$).

Conclusions: We found, that therapeutic AC showed a strong and independent inverse association with 3-year mortality, mirroring a potential benefit on outcome compared to anti-platelet therapy or low-dose LMWH. However, the fraction of patients receiving therapeutic AC was considerably low—especially NOACs were not commonly used. Despite its association with fatal cardiac adverse events, the presence of POAF was not a relevant value for decision making for the initiation of AC. Future prognostic data on both thromboembolic and bleeding events are needed to elucidate a net-benefit of therapeutic AC in patients with surgical biological AVR who have an indication for AC or present with POAF.

17-8

Epicardial ablation of Brugada syndrome

Georgios Kollias, Martin Martinek, Michael Derndorfer, Stefan Sieghartsleitner, Kgomotso Moroka, Josef Aichinger, Helmut Pürerfellner

Ordensklinikum Linz Elisabethinen, Linz, Austria

Background: Brugada syndrome (BrS) is a cardiac rhythm disorder characterised by a typical ECG and a high incidence of ventricular fibrillation (VF) and sudden cardiac death. There is growing evidence supporting that BrS depends on functional epicardial substrates, which may be eliminated by radiofrequency ablation. We report the first (to our knowledge) 3 cases of epicardial substrate ablation of BrS in Austria.

Methods: Three patients (P1, P2 and P3, aged 33, 26 and 44 years old respectively) with BrS and recurrent ICD~Shocks due to VF were referred to our hospital between July 2018 and January 2019 for ablation. All patients had more than 3 episodes of appropriate ICD discharge within the last year. P1 and P3 had a transvenous ICD-system, P2 had an sICD. P2 and P3 had spontaneous type I Brugada ECG, whereas P1 had a type I ECG after provocation with ajmalin. All patients underwent epicardial substrate ablation of the RVOT with the use of 3D mapping systems and high density multipolar mapping (NavX Ensite and HD-Grid catheter for P1, Carto 3 and PentaRay catheter for P2 and P3). Abnormal electrograms (AE) were defined according to previous studies as those with amplitude < 1.5 mV or associated wide duration (> 80 ms), multiple (> 3), or delayed components extending beyond the end of the QRS complex. During the procedure ajmalin (1 mg/kg) was administrated to augment the AE area. Area of AEs and subsequent ablation ranged from 13.3 to 22.8 cm^2 (Fig. 1). Radiofrequency was delivered at these areas up to 45 Watts, lasting 30 to 60 s, depending on elimination of the targeted AEs, and all AEs were completely abolished.

Results: The ablation procedure was successful and free of complications in all 3 patients. All patients developed ST-elevation in the right precordial leads during ablation, also described in previous studies. However, in all 3 patients coronary angiography was performed and a coronary lesion was excluded. A persistent diffuse ST-elevation was observed in P1, attributed to ablation induced pericarditis. Ajmalin test the next day after ablation failed to produce type I Brugada ECG in P1 and P3. All three patients are free of VF or other relevant ventricular arrhythmias since the ablation procedure (follow up of 8, 3 and 2 months respectively).

Conclusions: Substrate epicardial mapping and ablation guided by provocative testing could be considered in patients with BrS and recurrent ICD-shocks in experienced centres trained in epicardial ablation. However large studies with long follow-up are required to assess the efficacy of epicardial substrate ablation as a potential definitive treatment of the phenotypic manifestations of BrS.

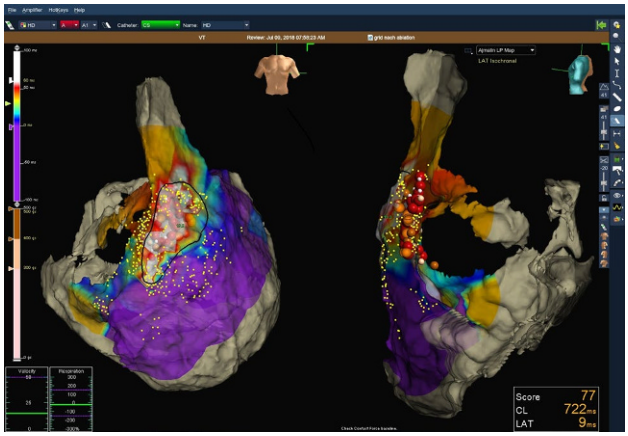


Fig. 1|17-8 Area of abnormal electrograms and ablation points in RVOT

17-9

Bilateral sympathicotomy for treatment of refractory ventricular tachycardia

Georgios Kollias, Reinhold Függer, Martin Martinek, Michael Derndorfer, Kgomotso Moroka, Stefan Sieghartsleitner, Josef Aichinger, Helmut Pürerfellner

Ordensklinikum Linz Elisabethinen, Linz, Austria

Background: Ventricular tachycardia (VT) commonly occurs in patients with ischemic (ICM) or nonischemic cardiomyopathy (NICM) and requires antiarrhythmic drugs, ablation, or advanced circulatory support. Though radiofrequency ablation (RFA) is usually effective in treating such patients, VT may be refractory to RFA and thus potentially life-threatening, causing also frequent ICD discharges. Cardiac sympathetic denervation reduces the occurrence of potentially fatal VT by inhibiting the sympathetic outflow to the cardiac tissue. We report the 2 first cases of bilateral sympathicotomy for refractory VT in our center.

Methods: Two patients (P1 and P2, aged 63 and 59 years old respectively) with ICM and recurrent ICD~Shocks due to VT were referred to our hospital between October 2018 and January 2019 for ablation. VT Ablation was performed in both patients. P1 underwent an epicardial and endocardial RFA api-

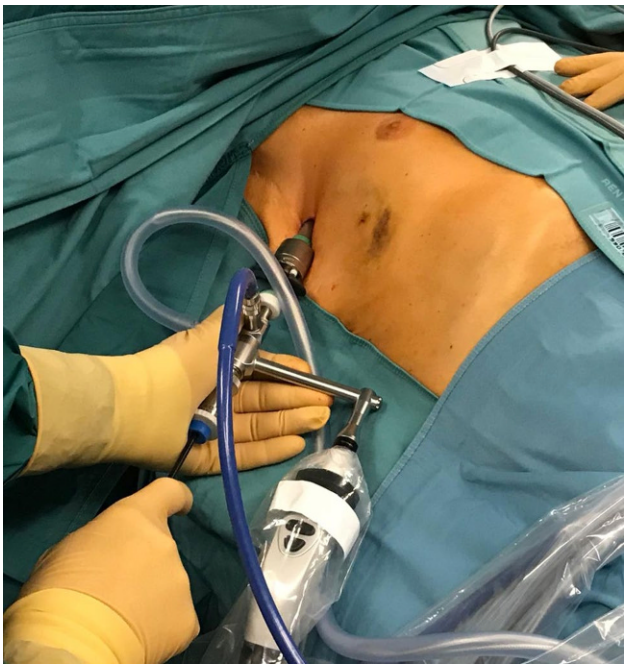


Fig. 1|17-9

cal and anterolateral, as it was a redo procedure with a history of VT storm. P2 underwent an endocardial RFA inferobasal and septal. Despite extensive Ablation with abolition of all local abnormal activation (LAVAs) and non-inducibility at the end of the procedure, early VT recurrence occurred in both patients. Furthermore P2 suffered from severe vasospastic angina, triggering VT episodes. Consequently both patients underwent a transthoracal endoscopic bilateral sympathicotomy (not sympathectomy) with interruption of sympathetic chain at the T2 to T3 level.

Results: Transthoracal endoscopic bilateral sympathicotomy was performed in a one-stage procedure by the same surgeon under general anaesthesia and selective ventilation. The sympathicotomy procedure was successful and free of acute complications in both patients. Procedural complications such as neuropathic pain, paravertebral venous plexus injury or pneumothorax were not observed. Both patients are free of VT or other relevant ventricular arrhythmias since the sympathicotomy procedure (relative short follow up of 3 and 2 months respectively). P2 is also free of recurrence of vasospastic angina after the procedure.

Conclusions: Bilateral cardiac sympathetic denervation may be an effective option and a bail-out strategy for patients with ICM and refractory VT when conventional and ablative treatment fails.

Postersitzung 18 – Rhythmologie 2

18-1

Fallbericht: Erfolgreiche Ablation von Vorhofflimmern durch stufenweises Mapping und Isolation der Vena cava superior

Adrian Petzl[1], Georgios Kollias[2], Michael Derndorfer[2], Kgomotso Moroka[2], Martin Martinek[2], Josef Aichinger[2], Helmut Pürerfellner[2]

[1]Klinische Abteilung für Innere Medizin 3 (Kardiologie), Universitätsklinikum St. Pölten, St. Pölten, Österreich

[2]Abteilung Interne 2 (Kardiologie, Angiologie & Interne Intensivmedizin), Ordensklinikum Linz Elisabethinen, Linz, Österreich

Grundlagen: Die hauptverantwortlichen Trigger für Vorhofflimmern (VHF) befinden sich in den Pulmonalvenen (PVs), weshalb die primäre Strategie der VHF-Ablation in der Pulmonalvenenisolation (PVI) liegt. Jedoch existieren bei einer signifikanten Minderheit der Patienten extrapulmonalvenöse Foci, die VHF induzieren können. Kasuistik: Ein 54jähriger Patient wurde zur Ablation bei einem Rezidiv von paroxysmalem VHF und Zustand nach PVI vorstellig. Trotz Reablation im Bereich der Rekonnektionen und anschließend nachgewiesener Dichtigkeit der Isolationslinien kam es zur inzessanten, spontanen Reinduktion von VHF. Durch stufenweises Mapping der Re-Induktion nach Elektrokardioversion (ECV) konnte die Vena cava superior (SVC) als Trigger identifiziert werden.

Methodik: Elektrophysiologische Untersuchung, 3-D Map des linken Atriums und der SVC, RF-Ablation, ECV.

Ergebnisse: Die SVC konnte erfolgreich isoliert werden, wodurch sich ein stabiler Sinusrhythmus erzielen ließ, und es zu keiner weiteren spontanen VHF-Induktion kam.

Schlussfolgerungen: Bei rezidivierender spontaner Induktion von VHF trotz nachgewiesener Isolation der PVs, sollte systematisch nach dem Triggerareal gesucht und dieses abliert werden. Die SVC kann als Trigger von VHF fungieren und eignet sich für eine Isolation mittels RF-Ablation.

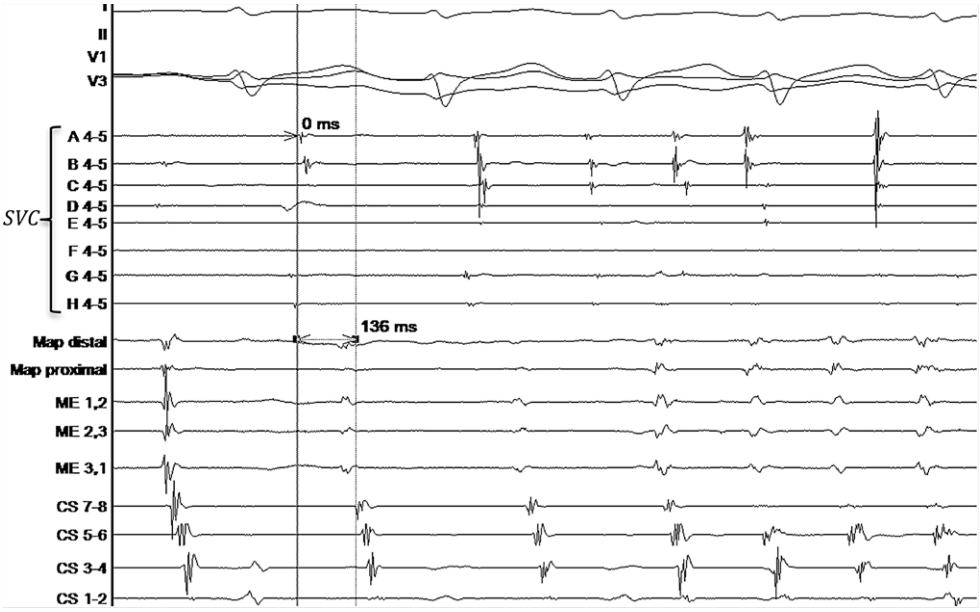


Abb. 1|18-1 Initiierung von Vorhofflimmern aus der SVC. Die auslösende atriale Extrasystole in der SVC geht der Aktivierung des CS um 136 ms voraus; im Anschluss sind weitere, aus der SVC stammende, kurz gekoppelte Extrasystolen ersichtlich, welche schließlich in Vorhofflimmern übergehen

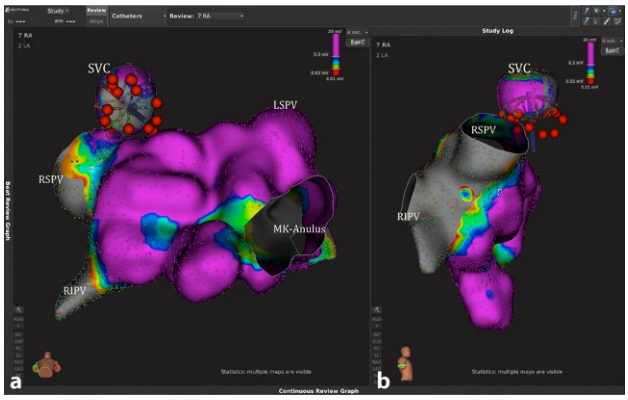


Abb. 2|18-1 3-D Map des linken Atriums und der SVC, sowie die entsprechenden Ablationspunkte (*rot*) am proximalen Ende der SVC (mitdargestellt ist der Mapping-Katheter in der SVC). A: Ansicht in caudaler Ausrichtung. B: Ansicht in rechts-lateraler Ausrichtung. (SVC: Vena cava superior, RSPV: rechte superiore Pulmonalvene, RIPV: rechte inferiore Pulmonalvene, LSPV: linke superiore Pulmonalvene, MK-Anulus: Mitralklappenanulus)

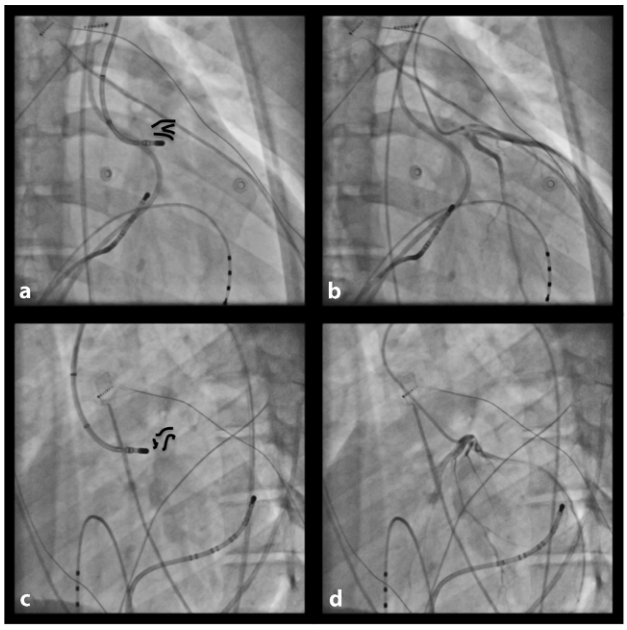


Abb. 1|18-2 Gegenüberstellung der Katheterposition bei Ablation und der angiographischen Darstellung des Hauptstammes des linken Koronargefäßes. A: Position des Ablations-Katheters am Ursprungs der VES im Bereich des LCC, in RAO-Projektion (eingezeichnet ist der Hauptstamm des linken Koronargefäßes). B: Angiographie des linken Koronargefäßes in RAO-Projektion. C: LAO-Projektion der Position des Ablations-Katheters (eingezeichnet ist der Hauptstamm des linken Koronargefäßes). D: LAO-Projektion der Angiographie des linken Koronargefäßes

18-2

Fallbericht: Ablation einer inzessanten Ausflusstrakt-Extrasystolie im Bereich der linkskoronaren Klappentasche, in unmittelbarer Nähe zum Ostium des linkskoronaren Hauptstammes

Adrian Petzl[1], Georgios Kollias[2], Michael Derndorfer[2], Kgomotso Moroka[2], Martin Martinek[2], Josef Aichinger[2], Helmut Pürerfellner[2]

[1]Klinische Abteilung für Innere Medizin 3 (Kardiologie), Universitätsklinikum St. Pölten, St. Pölten, Österreich
[2]Abteilung Interne 2 (Kardiologie, Angiologie & Interne Intensivmedizin), Ordensklinikum Linz Elisabethinen, Linz, Österreich

Grundlagen: Ausflusstrakttachykardien sind einer Ablationsbehandlung gut zugänglich, verbunden mit einer geringen Komplikationsrate. Wenn allerdings im linksventrikulären Ausflusstrakt (LVOT), supravalvulär im Bereich des Aortensinus, abliert wird, muss man sich der Nahebeziehung zu den Ostien der Koronarien bewusst sein. Eine Verletzung jener Gefäße kann bedrohliche Folgen nach sich ziehen. Kasuistik: Ein 18jähriger männlicher Patient wurde aufgrund inzessanter ventrikulärer Extrasystolie (VES) vorstellig. Der Ursprung der Extrasystolen konnte in den Bereich der linkskoronaren Klappentasche (LCC) lokalisiert werden. Der Fokus lag nur etwa 1 cm unter dem Ostium des linken Hauptstammes und stellte somit ein potentielles Risiko für die Ablation dar.

Methodik: Elektrophysiologische Untersuchung, 3-D Map des RVOT und LVOT, Katheterangiographie der linken Koronararterie, RF Ablation in der LCC.

Ergebnisse: Die VES terminierte mit Beginn der Ablation. Es wurden keine Anzeichen einer koronariellen Gefäßverletzung beobachtet. Im dreimonatigen Follow-up kam es weder zu einem Rezidiv der VES, noch zum Auftreten von Symptomen einer koronariellen Stenose.

Schlussfolgerungen: Wenn im LVOT im Bereich der Klappentaschen abliert wird, muss darauf geachtet werden, die Koronargefäße nicht zu verletzen. Daher ist eine koronare Bildgebung vor Beginn der Energieabgabe essentiell.

18-3

Case Report: Successful ablation of a scar associated left atrial macro-reentry-tachycardia by radiofrequency ablation at the septal mitral valve annulus in a patient with previous left atrial ablation for atrial fibrillation and a peri-mitral flutter

Kgomotso Moroka[1], Adrian Petzl[2], Helmut Pürerfellner[3], Josef Aichinger[3]

[1]Ordensklinikum Linz, Elisabethinen Krankenhaus, Linz, Austria
[2]Department of Internal Medicine 3 (Cardiology), University Hospital St. Poelten, Karl Landsteiner University of Health Sciences, St. Poelten, Austria
[3]Ordensklinikum Linz Elisabethinen, Linz, Austria

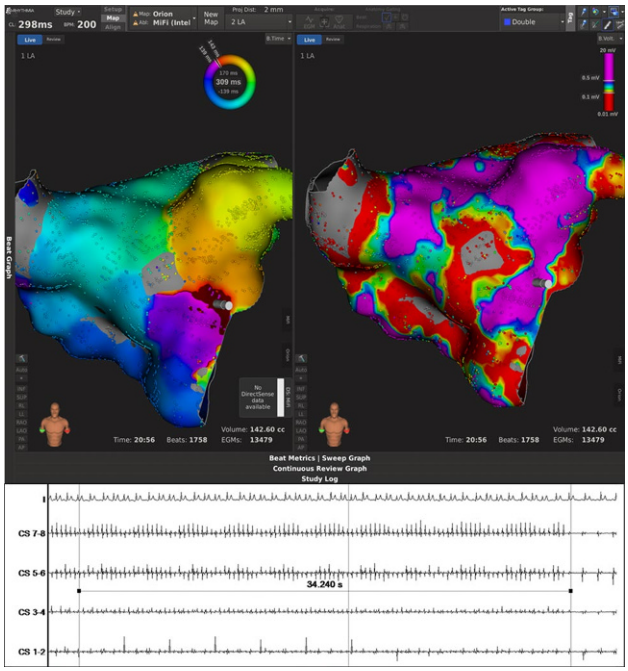


Fig. 1|18-3 Activation (left) and Voltage (right) maps generated by the Rhythmia system reveal the macro reentry circuit and the critical isthmus located at the mitral valve area borded by scar. Single point ablation at the critical isthmus resulted in termination of the tachycardia after 34 seconds as demonstrated by the electrogram tracings

Background: The majority of post atrial fibrillation tachyarrhythmias are left atrial macro-reentry-tachycardias (LAMT) in nature (1). The most common forms are mitral isthmus and left atrial roof dependent tachycardias. We present a case of a macro-reentry left atrial tachycardia localised to an anteroseptal scar from a previous ablation. Patient history: A 67 year old male patient presented with ongoing atrial tachycardia for several months with evidence of a LAMT on a 12 lead electrocardiogram. This patient had undergone 2 previous left atrial ablation procedures. Diagnosis: Left atrial peri-mitral flutter involving a scar on the anterior wall occurring late after atrial fibrillation ablation.

Methods: Left atrial tachycardia had a cycle length of 318 ms with a distal to proximal coronary sinus activation in keeping with a left sided peri-mitral tachycardia. During ongoing tachycardia a high density map of the left atrium using a dedicated basket catheter (Orion™, Boston Inc.) was created. Analysis by the 3-D mapping system (Rhythmia™, Boston Inc.) revealed evidence of a LAMT with a critical isthmus located at the mitral valve in the septal area bordered by a scar on the anterior wall showing fractionated low amplitude signals. The critical isthmus area was also identified as site of wavefront narrowing and slowing of conduction. Using dedicated pacing techniques all criteria could be demonstrated which confirmed the site as critical for this LAMT (entrainment without *p*-wave fusion as well as identical intracardiac activation sequence in neighboring coronary sinus leads, post pacing inverval exactly equaling tachycardia cycle elength, stimulation to P-wave interval equaling electrogram to P wave interval). There was evidence that the pacing site was within the entrance of the protected isthmus. Using radiofrequency current at this point resulted in termination of the tachycardia after 34 seconds.

Results: Termination of a LAMT with ablation. During 3 months follow-up there has been no recurrence of the arrhythmia.

Conclusions: A case of a LAMT localised to site of previous ablation scar proved the usefulness of left atrial geometry creation with a high density high resolution catheter including detailed activation mapping. Classical pacing techniques reconfirmed the critical isthmus. This served to aid rapid targeted ablation. Further studies are needed to clarify the current role of entrainment pacing in the era of high density mapping.

18-4

Weltweit erstes Twiddler Syndrom bei S-ICD Patient

Stefanie Hennig

Kaiser Franz Josef Spital, Wien, Österreich

Grundlagen: Unsere 57jährige Patientin erhielt aufgrund einer hochgradig reduzierten Linksventrikelfunktion bei ischämischer Kardiomyopathie einen S-ICD (subkutan implantierbarer Defibrillator) der Fa. Boston Scientific. 3 Wochen nach der Implantation kam es plötzlich zu einer starken Schmerzsymptomatik im Bereich des Generators und in der linken Scapula, 5 Stunden später kam es zu einer Schockabgabe bei einer kardiorespiratorisch völlig stabilen Patientin. Im kurz daraufhin durchgeführten Thoraxröntgen zeigte sich eine deutlich retrahierte Sonde, deren Spitze neben dem um die eigene Achse rotierten Generator lag. In der Abfrage des S-ICDs konnte der Verdacht einer inadäquaten Schockabgabe bestätigt werden, somit war die Indikation für eine Revisions-OP gegeben.

Methodik: Die Patientin wurde planmäßig am 25.02.2019 zu einer geplanten RCA CTO aufgenommen; bereits im Rahmen des letzten Aufenthaltes wurde die LAD im Rahmen eines STEMIs mit kardiogenem Schock erfolgreich interveniert; auch in der Vergangenheit hatte die Patientin zwei NSTEMIs 2011 und 2016, wo bereits die LAD und die RCA interveniert wurden. Als Folgeerkrankung hatte sie eine ischämische Kardiomyopathie mit einer EF von 20 %, aufgrund des Alters und fehlender ventrikulärer Tachykardien wurde die Indikation zu einer S-ICD Implantation gestellt und diese am 1.2.19 komplikationslos durchgeführt. Die Kontrollabfrage des ICD sowie das Thoraxröntgen waren unauffällig. Bei der Aufnahme schilderte die Patientin Schmerzen im Bereich der linken Scapula und des Generators und berichtete über eine Schockabgabe vor 2 Tagen. Bei Verdacht auf S-ICD Fehllage wurde ein C/P durchgeführt, das ein Twiddler Syndrom bestätigen konnte, in der Kontrollabfrage zeigte sich eine inadäquate Schockabgabe bei normofrequentem Sinusrhythmus, sodass eine Revisions-OP erfolgte. Postoperativ zeigten sich bis heute gute Sensingwerte sowie eine gute Lage der Sonde und des Generators; danach erfolgte noch die RCA CTO.

Ergebnisse: Das Twiddler- Syndrom beschreibt eine sehr seltene Komplikation nach Herzschrittmacher-/Defibrillatorimplantationen und ist durch die spontane, mehrfache Rotation des Generators in der subpektoralen Tasche gekennzeichnet. In unserem Fall handelt es sich um das erste Twiddler-Syndrom bei einem S-ICD Patienten. Es kam zu mehrfacher Rotation des Generators um die eigene Achse und in Folge zur totalen Dislokation (Retraktion) der Defibrillatorsonde (siehe Röntgenbild). Alle Fixationsnähte (Sonde und Generator) inkl. ein Teil des umliegenden Gewebes waren ausgerissen. Bei Patienten mit einem Twiddler Syndrom kann es zu starken Schmerzen und inadäquaten Schockabgaben kommen (beides traf bei unserer Patientin zu), zusätzlich ist die Primär und Sekundärprophylaxe von lebensgefährlichen ventrikulären Arrhythmien nicht mehr vorhanden, somit besteht immer

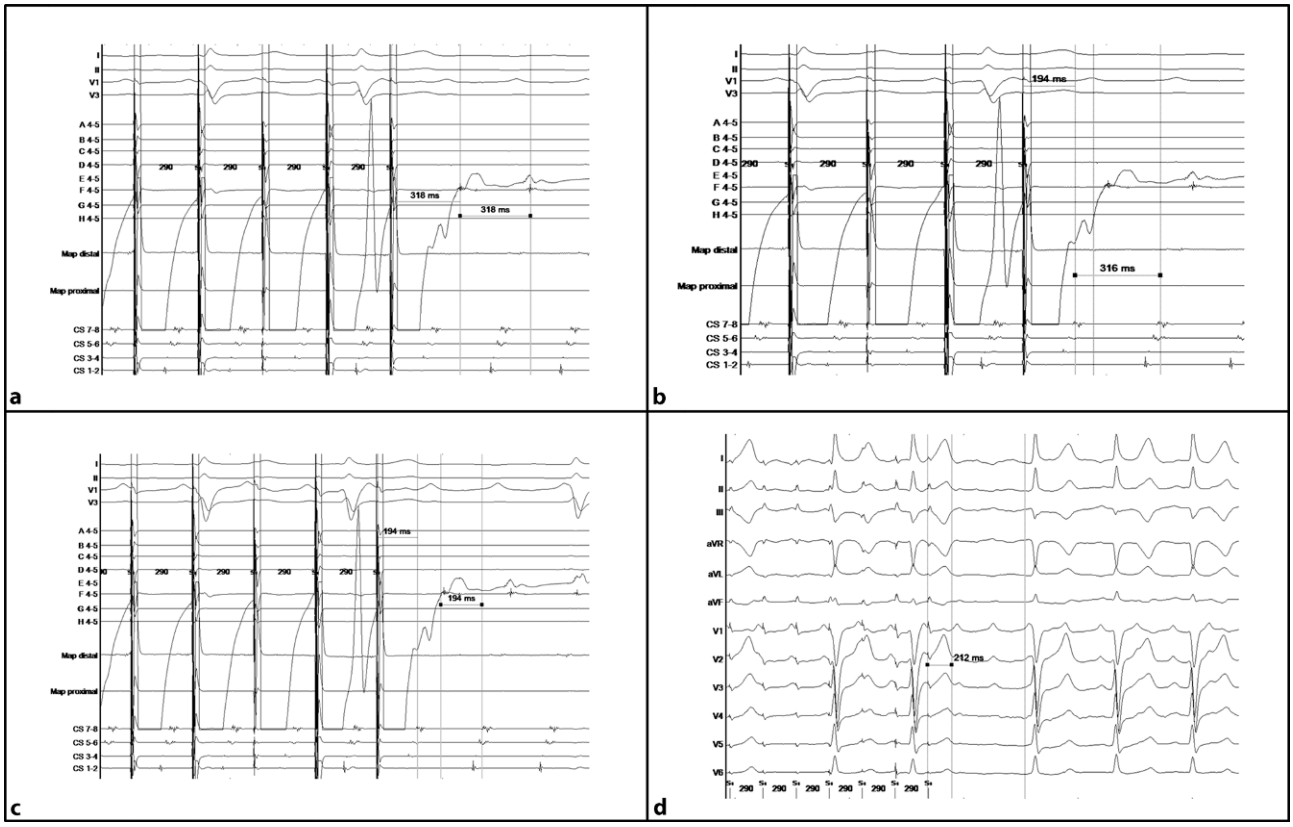
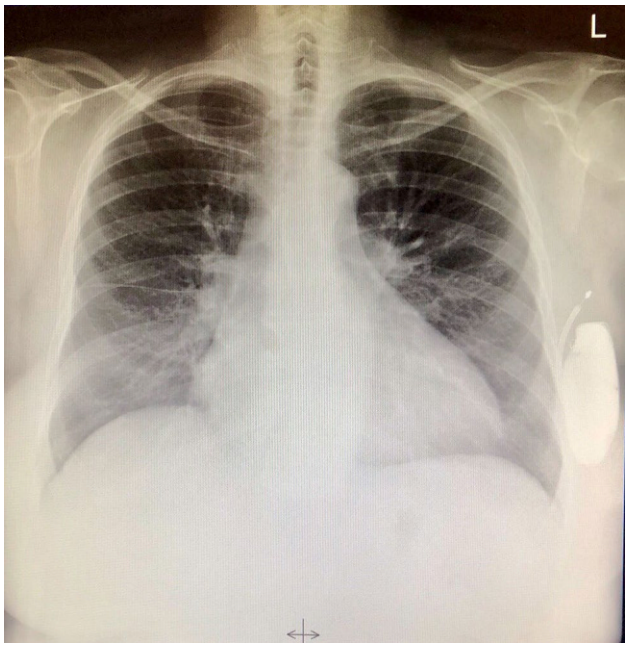


Fig. 2|18-3 Criteria which confirmed the site of the critical isthmus for the LAMT by dedicated pacing techniques A. post pacing inverval exactly equaling tachycardia cycle length at 318 ms B. the ration of the stimulation time to the tachycardia cycle length divide by 100 equaling 61 % i keeping with pacing in the entrance of the re-entrant circuit C: stimulation to P-wave interval equaling electrogram to P wave interval at 194 ms D. concealed entrainment without p-wave fusion with identical intracardiac activation sequence in neighboring coronary sinus leads



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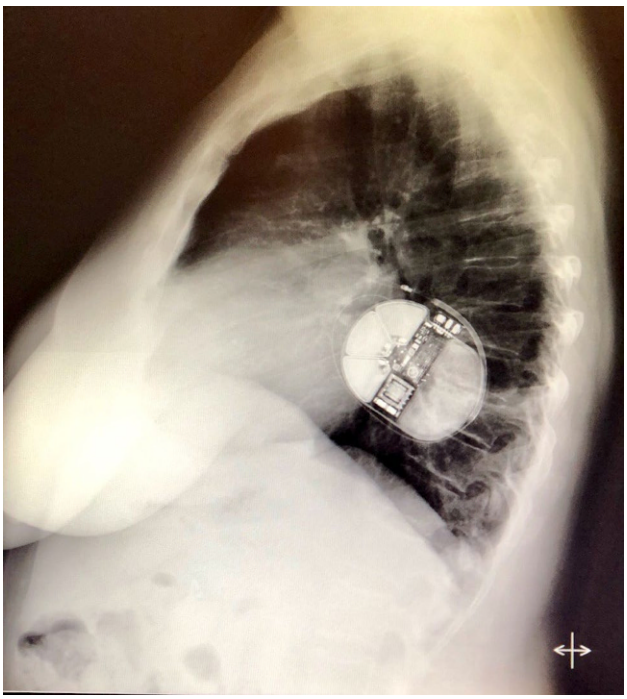


Abb. 2|18-4

die Indikation zur Revisions-OP. Das worst case Scenario wäre eine ventrikuläre Tachykardie oder Kammerflimmern und die Unfähigkeit einen suffizienten Schock abzugeben und somit ein Sudden Cardiac Death.

Schlussfolgerungen: Die Ursachen des Twiddler Syndroms sind, wie bei unserer Patientin, oft nicht klar. Einige prädisponierende Faktoren, die bislang allerdings nur für den pektoral implantierten ICD galten, könnten in Zukunft auch für den S-ICD zutreffen: eine zu große subkutane (bzw. submuskuläre) Tasche, Adipositas, rezidivierendes Hochheben des linken Armes post Implantation, manuelle Manipulation des Generators oder zu locker geknüpfte Haltenähte. Bei unserer Patientin traf außer der Adipositas (BMI von 32) nichts zu. Die Muskulatur zwischen M. serratus anterior und M. latissimus dorsi wurden präoperativ evaluiert und für ausreichend gut befunden, somit sollte auch dies ein Ausschluss für die Ursache des Twiddler-Syndroms sein. Eine sichere und am besten 4fache Fixierung der Elektrode (über eine 3-Schnitt-Technik) und des Generators mittels nicht resorbierbarer Fäden (z. B. Ethibond der Stärke 2.0 oder 3.0) und ggf. anschließendem manuellem Zug zur Überprüfung der Nahtstabilität ist von höchster Priorität – insbesondere bei Patienten, die ein lockeres subkutanes Fettgewebe und/oder wenig Muskelmasse besitzen.

18-5

Voltage mapping of the compact AV-nodal area facilitates selective permanent His bundle pacing

Johannes Kraus, Franz Danmayr, Uta C. Hoppe, Bernhard Strohmer

Clinic of Internal Medicine II, Department of Cardiology, Paracelsus Medical Private University Salzburg, Salzburg, Austria

Background: Several studies and registries have shown clinical improvement with permanent His bundle pacing (PHBP) compared to permanent right ventricular pacing. In cases of heart failure, PHBP can alleviate ventricular dyssynchrony and potentially substitute conventional CRT pacemaker systems in the absence of distal left bundle branch block. In clinical routine, the most commonly used approach to achieve PHBP is fluoroscopic imaging in combination with recorded electrograms. We present a novel technique to localize the optimal His bundle region with help of 3D voltage mapping of the compact AV node.

Methods: Before pacemaker implantation, the right groin was prepared to introduce a deflectable D-type quadripolar diagnostic catheter (Biosense Webster™) to the His bundle region. Detailed mapping of the His bundle region was carried out with a 3D mapping system (EnSite™ Velocity™). The threshold of voltage mapping was adjusted to obtain a focal spot according to the highest amplitude of the His deflection as a surrogate of the true His bundle. The pacing lead (Medtronic Select Secure™ 3830) was inserted via left subclavian access using a His sheath (Medtronic™ C315), otherwise, a deflectable His sheath was introduced. Wall contact and correct anatomic position were confirmed with fluoroscopy in LAO and RAO projections. The pacing lead was connected via alligator clips to the mapping system to allow visualization of the lead tip in real-time, to record signals and to ensure a proper position on the largest His deflection. After screwing in the pacing lead, the bipolar signals were displayed to confirm an injury potential with inversion of the His spike. Thereafter threshold testing was performed with special attention to the electrical axis and width of the paced QRS complexes.

Results: Case #1: A 73-year-old woman presented with permanent atrial fibrillation (brady-tachy syndrome), pulmonary hypertension and mildly impaired left ventricular function. Her intrinsic QRS complex measured 82 ms. PHBP was chosen to avoid ventricular dyssynchrony and deterioration of the pre-existing tricuspid valve insufficiency. In case #1 selective His bundle stimulation was achieved at an acute pacing threshold of 1.0 V @ 1.0 ms. The paced QRS duration measured 110 ms with a similar electrical vector on the surface ECG. Case #2: An 18-year-old man with congenital total AV block and narrow junctional escape rhythm (QRS-width 94 ms) reported dyspnea and fatigue on minimal exertion. Due to the expected high percentage of pacing, the patient underwent permanent atrial-his-ventricular sequential pacing. In case #2 mapping of the AV nodal area revealed a proximal AV nodal block. Selective His bundle stimulation resulted in a QRS duration of 98 ms, the acute pacing threshold was 0.75 V @ 1.0 ms. PHBP resulted in nearly identical electrical activation compared to the intrinsic QRS axis.

Conclusions: Permanent His bundle pacing (PHBP) is a promising tool for patients who need frequent ventricular pacing. Careful mapping of the HB region using a 3D mapping system can help in identification of the level of disease or delay and facilitate successful implantation at a spot distal to the site of disease. Meticulous voltage mapping of the His bundle region may obtain the highest His deflection as target region for lead placement ensuring selective His bundle stimulation at low pacing thresholds. Beyond the conventional technique, non-fluoroscopic visualization is helpful to achieve successful PHBP in challenging cases or complex anatomy.

18-6

Rotor mapping in a patient with persistent atrial fibrillation

Martin Manninger, Ursula Rohrer, Egbert Bisping, Peter Lercher, Bernadette Pratl, Günther Prenner, Andreas Zirlik, Daniel Scherr

Medical University of Graz, Graz, Austria

Background: Atrial fibrillation (AF) is the most common arrhythmia with an increasing burden in the overall population. Invasive catheter ablation with pulmonary vein isolation is an established second line therapy in symptomatic patients with

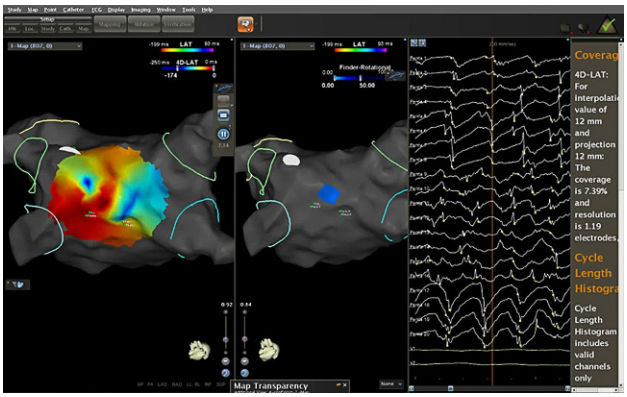


Fig. 1 | 18-6

paroxysmal AF with multiple procedure success rates around 85%. Success rates in patients with persistent AF are significantly lower (50–70%). Many ablation and mapping techniques have been proposed for patients with persistent AF, all of which showed no benefit compared to pulmonary vein isolation. We aimed to investigate the incidence of focal and rotational repetitive activational patterns (RAP) in a patient with persistent atrial fibrillation with the novel multielectrode mapping system CartoFinder.

Methods: This is the first Austrian case of invasive rotor mapping for symptomatic persistent AF in a patient undergoing a routine AF ablation. A Pentaray catheter was used to acquire unipolar signals, which were processed by the mapping system to generate wavefront propagation maps. A computational analysis was used to identify and characterize either focal or rotational RAP prior to pulmonary vein (PV) isolation. We performed a retrospective offline analysis of all detected focal or rotational RAPs during a routine electrophysiological procedure.

Results: We report a clinical case about a 74 years old male patient suffering from symptomatic episodes of atrial fibrillation for two years before presenting in our out-patient-clinic. He had multiple emergency room visits due to tachycardic atrial fibrillation and attempts of electrical cardioversions in his past medical history. At time of presentation he was in persistent atrial fibrillation for two months. According to the patients' desire and due to contraindications for an antiarrhythmic medication a primary strategy of catheter ablation for invasive rhythm control was scheduled. The procedure was performed one month later. A routine fast atrial map was done to exlcude low voltage areas (threshold 0.05 mV). In order to identify potential RAPs, 405 points were obtained with a Pentaray catheter to cover the whole left atrium (LA). The unipolar signals at each point were recorded for 30 seconds at every spot. These unipolar signals were analyzed and annotated by a rotor mapping software. 10 focal RAP and one rotational RAP could be detected in the left atrium. The focal activation patterns were detected at the roof near the LSPV (1), at the posterior roof (2), at the os of the RIPV (3), at the inferior part of the LA (1), at the ridge (1) and at the mid-anterior right part of the LA (2). The only rotational RAP was detected at the lateral posterior wall of the LA. We could not identify a correlation to low voltage areas as there were none of these identified.

Conclusions: After the rotor mapping a pulmonary vein isolation was performed. No ablation in the RAP regions was performed, since the study was performed to evaluate the feasibility of the procedure and there is no evidence of ablation in RAP regions yet. Conclusion: Rotor mapping is a new approach to understand the complexity of AF in advanced stages of AF. This method is easy feasible and might be a future option to determinate ablation targets that might be performed additional to pulmonary vein isolation in patients with persistent atrial fibrillation. Further investigation and evaluation will be needed until this method will find its way into clinical routine.

18-7

Mid-term outcome after ablation of paroxysmal atrial fibrillation using the CLOSE protocol

Martin Manninger, Zweiker David, Darko Trananoski, Ursula Rohrer, Bernadette Pratl, Egbert Bisping, Peter Lercher, Günther Prenner, Andreas Zirlik, Daniel Scherr

Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background: Catheter ablation of atrial fibrillation is (AF) an established second line therapy for patients with symptomatic paroxysmal AF (PAF). The novel ablation tool Ablation Index (AI) combines information of contact force sensing, stability and energy output monitoring to predict lesion formation. Standardisation of inter-lesion distance (ILD) and differential AI threshold for the anterior and posterior wall within the CLOSE protocol have shown to increase procedural outcome in single centre studies. We aimed to describe mid-term outcome of CLOSE protocol guided ablation.

Methods: Forty-five consecutive PAF patients underwent pulmonary vein using a contact force sensing catheter targeting an ILD ≤6 mm and AI ≥400 at the posterior and ≥550 at the anterior wall. Mean age was 58 ± 10 years, 18% were female, mean BMI was 27 ± 4 kg/m², median CHA_2DS_2-VASc Score 1 (0, 2), median HAS-BLED Score 1 (0, 1), history of AF was 54 (18, 67) months, mean left ventricular ejection fraction was 61 ± 7%. Follow up duration was 158 (101, 184) days.

Results: Primary success rate to meet CLOSE protocol criteria as well as pulmonary vein isolation was achieved in all patients. Two patients (4%) had recurrences before being dismissed from the ward (both were successfully cardioverted). Arrhythmia-free survival was 93.3% (Fig. 1). There were no procedure-related complications or complications during follow-up.

Conclusions: Strict application of criteria for contiguity and ablation index using the CLOSE protocol is safe and results in a high mid-term success rate after PVI. A randomized controlled multicentre trial is needed to compare outcome to conventional PVI approaches.

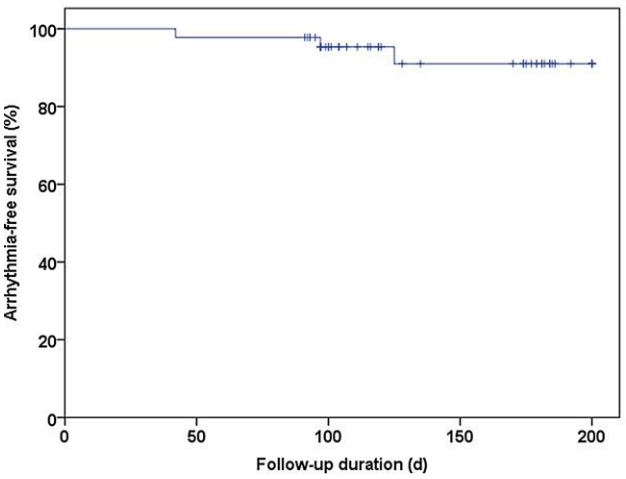


Fig. 1 | 18-7

POSTERSITZUNGEN 19-24

Freitag, 31. Mai 2019, 15.30 bis 16.30 Uhr

Postersitzung 19 – Basic Science 4

19-1

Depletion of the acquired immune system does not halt neonatal cardiac regeneration

Theresa Dolejsi[1], Thomas Schuetz[1], Alexander Bild[1], Josef M. Penninger[2], Bernhard J. Haubner [1]

[1]Medical University of Innsbruck, Innsbruck, Austria
[2]Institute of Molecular Biotechnology, Vienna, Austria

Background: Myocardial infarction (MI) represents a major health burden due to subsequent reduction of cardiac function leading to ischemic cardiomyopathy. In contrast to other adult tissues i. e. liver, myocardium cannot be sufficiently regenerated following hypoxic injury. Recently our group demonstrated efficient cardiac regeneration in a neonatal mouse MI model of left anterior descending artery (LAD) ligation. Previous work demonstrated the pivotal role of the innate immune system during murine neonatal cardiac regeneration by clodronate facilitated macrophage depletion.

Methods: Since the innate immune system is required for neonatal cardiac regeneration, we hypothesized that the acquired immune system is mechanistically relevant for cardiac regeneration.

Results: Ligation of the left anterior descending artery (LAD) or SHAM surgery was performed on Rag2 knock-out mice on their first day of life (P1). Rag2 is essential for generation of B and T lymphocytes, therefor Rag2 knock-out mice lack the acquired immune system. Successful induction of myocardial infarction was confirmed by echocardiography one day post injury (dpi). 21 dpi final echocardiography was performed and hearts were harvested for further histological assessment. The amount of fibrosis as a marker of cardiac injury was quantified by Massons-Trichrome stained tissue sections. No marked difference was observed between the groups.

Conclusions: Whereas the innate immune system is crucial for cardiac regeneration in mice during the first week of life, we proved the nonrelevant role of the lymphocyte dependant adaptive immune response.

19-2

Detection of circular RNA CDR1as in pig hearts using qPCR and Sanger sequencing

Julia Mester-Tonczar, Johannes Winkler, Dominika Lukovic, Mariann Gyöngyösi

Medical University of Vienna, Vienna, Austria

Background: Non-coding RNAs (ncRNAs) are attractive novel potential biomarkers and drug targets in cardiovascular diseases. To examine their role and function, adequate animal models with close correlation of genetic characteristics and function of ncRNAs to humans are necessary. Circular RNAs (circRNAs) represent a novel ncRNA family, forming a covalently closed loop lacking 5'-cap structure and 3'-poly(A)-tails (Figure). CircRNAs have been found in blood and cardiac tissues of failing heart of mice, suggesting their potential functional role as biomarker. Since circRNAs are more stable than linear mRNAs because of their inaccessibility to exonucleases, they may represent a new valuable diagnostic tool to predict disease entities and outcomes. One of the most studied circRNAs is cerebellar degenerated-related protein 1 antisense (CDR1as/ciRS-7), abundantly expressed in the brain, but has also been reported to have increased expression in infarcted murine heart, as compared to healthy heart. CircRNAs were found in humans, mice, drosophila and nematodes, yet little is known about circRNAs in pigs. Therefore the aim of our study was to develop a method to identify and characterise CDR1as in a pig heart.

Methods: Prior to AMI (acute myocardial infarction), the animal was sedated with 12 mg/kg ketamine hydrochloride, 1 mg/kg xylazine and 0.04 mg/kg atropine by intramuscular injection. AMI was induced in a closed-chest reperfusion pig model by balloon occlusion of the mid-LAD (left anterior descending coronary artery) for 60 minutes, 5 atm, followed by balloon deflation. A tissue sample of a pig heart, collected from the AMI region, 60 days post AMI was dipped in RNAlater and stored at –80 °C. RNA was isolated from tissue using a column-based chloroform extraction. To enrich circCDR1as and diminish linear counterparts, total RNA was digested with RNase R.

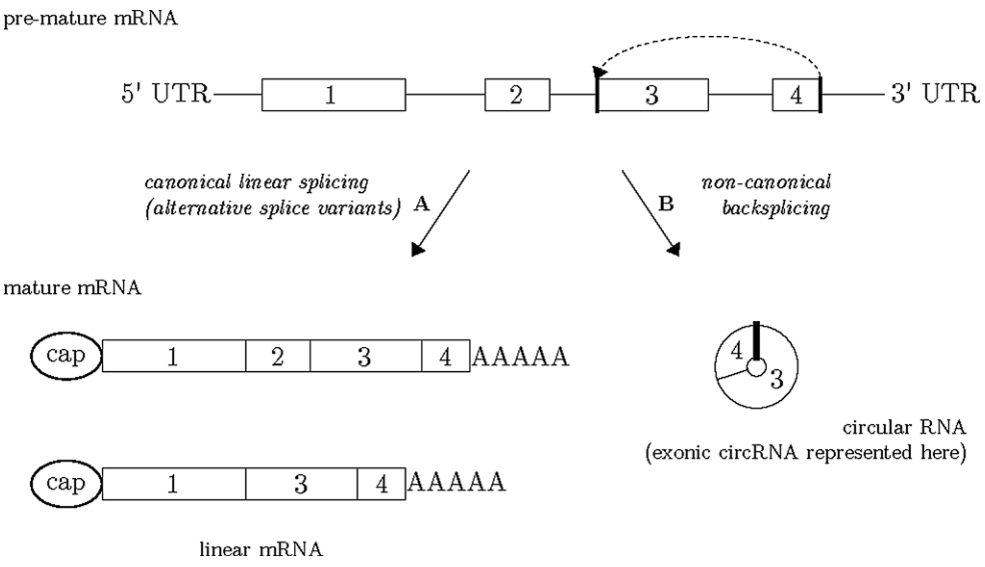


Fig. 1|19-2 Difference in the formation of mature mRNA and circular RNA

Afterwards RNA was reverse transcribed into cDNA and stored at –20 °C. Genetic information of respective human, murine and porcine sequence were compared using NCBI and UCSC databases. Divergent primers were used by qPCR, allowing only the amplification of the circRNAs, and not the linear mRNA counterpart by spanning the backsplice junction. Furthermore, we analysed CDR1as expression in AMI tissue and control animals (no AMI) to evaluate CDR1as as potential biomarker after AMI.

Results: Using genomic database information, a putative sequence of CDR1as from pigs (Sus scrofa domesticus) was obtained by identifying homology with human and murine sequences. As in other species, the respective genomic sequence is flanked by short interspersed nuclear elements (SINEs), repeat sequences, which are instrumental for the splicing which forms the circRNA. Treatment of RNA with RNase R resulted in decreased amount of linear mRNA compared to circRNA. This shows increased stability of circRNA to exonucleases compared to linear RNA. Quantitative PCR using divergent primers indicated the presence of potential CDR1as. The PCR product was analysed in an agarose gel for purity and the molecular weight. Afterwards Sanger sequencing was performed. In the end, the sequencing results of several overlapping amplicons were combined in order to obtain the majority of the sequence. Expression of CDR1as increased 11-fold in tissue of the AMI group compared to the control group.

Conclusions: Here we confirmed the presence and elucidated the sequence of porcine CDR1as, which is homologous to the human sequence. This homology can be of particular importance as the pig hearts anatomy and physiology resemble human hearts more closely than rodents, and may represent a valuable tool in translational research to study circRNAs in vivo in a cardiovascular context. Finally, CDR1as shows potential as a novel diagnostic biomarker after AMI.

19-3

Macrophage derived Igf1 is not required for neonatal cardiac regeneration

Thomas Schuetz[1], Theresa Dolejsi[1], Alexander Bild[1], Nadia Rosenthal[2], Josef M. Penninger[3], Bernhard J. Haubner[1]

[1]Medical University of Innsbruck, Innsbruck, Austria
[2]The Jackson Laboratory, Bar Habor, United States of America
[3]Institute of Molecular Biotechnology, Vienna, Austria

Background: Cardiac remodeling and subsequent heart failure remain critical issues after myocardial infarction despite improved treatment and reperfusion strategies. Recently, we demonstrated complete cardiac regeneration in a neonatal mouse model of myocardial infarction. This regenerative potential of the heart is lost within the first week of life. Other groups have shown that macrophages play a key role in neonatal cardiac regeneration. In skeletal muscle regeneration macrophages are known to promote the regenerative process by secreting Insulin-like growth factor 1 (Igf1). It is not yet known if the same mechanism applies to cardiac regeneration.

Methods: Ligation of the left anterior descending artery (LAD) or SHAM surgery was performed on Igf1f/f/LysMCretg/+ and Igf1f/f/LysMCreWT mice on their first postnatal day of life (P1). Successful induction of myocardial infarction was confirmed by echocardiography one day post injury (dpi). 21 dpi a final echocardiography analysis was performed, hearts were harvested and underwent histological analysis. Fibrosis was quantified in histological sections stained with Massons-Trichrome protocol.

Results: No difference in cardiac function or fibrosis content was observed between the groups.

Conclusions: Macrophage specific knock-out of Igf1 does not perturb the process of neonatal cardiac regeneration.

19-4

Differential regulation of miR-212 in ischemic pre- and postconditioning

Andreas Spannbauer, Katrin Zlabinger, Mariann Gyöngyösi, Nina Kastner, Daniel Kockovsky, Johannes Winkler, Denise Traxler-Weidenauer, Julia Mester-Tonczar, Martin Riesenhuber, Claudia Müller

Medical University of Vienna, Austria

Background: Most research regarding Ischemic Preconditioning (IPC) and Ischemic Postconditioning (PostC) has focused on their effect on ischemia-reperfusion (I/R) injury, especially regarding myocardial function and ejection fraction (EF). Very little attention has been paid to their potential effects on electrophysiological parameters and acute myocardial infarction (AMI)-associated arrhythmias like ventricular tachycardia or ventricular fibrillation. In the last decade, MicroRNAs (miRs) have emerged as important and versatile effectors of cellular communication across many different tissues, including the heart. In this project, we have investigated the differential regulation of cardiac-conduction-related-miRs in ischemic pre- and postconditioning.

Methods: 9 domestic pigs were split into 3 groups: IPC-AMI ($n=3$), AMI-PostC ($n=3$) and AMI ($n=3$). The IPC protocol was as follows: 3 cycles of 5 min I/R using a balloon catheter in the mid LAD prior to infarction. Myocardial infarction was induced via inflation of a balloon in the mid LAD for 90 minutes. PostC was accomplished by inflating and deflating the balloon for 6×30 second cycles of I/R immediately after infarction (Fig. 1). EDTA plasma samples were collected prior to first occlusion and after reperfusion. miRs were isolated using QIAGEN miRNeasy Serum/Plasma kits, reverse transcribed using QIAGEN miScript RT kit and qPCR was performed using miScript SYBR® Green PCR Kit. Fold changes were normalized using ce-miR-39 Spike-in-Control of the QIAGEN Serum/Plasma kit. Relative fold changes before occlusion and after begin of reperfusion were evaluated.

Results: Fig. 2 shows the relative fold changes of miR-212 at baseline and immediately after reperfusion in the IPC-AMI, AMI and AMI-PostC groups. There is no significant difference in expression between the IPC-AMI, AMI and AMI-PostC groups at baseline. After reperfusion, however, there is a clear downregulation of miR-212 in the IPC-AMI and AMI group compared to an upregulation in the AMI-PostC group.

Conclusions: miR-212 has anti-apoptotic and anti-arrhythmic properties and is known to be downregulated after myocardial infarction. Our results show that PostC causes a slight but significant upregulation of this beneficial miR following an AMI.

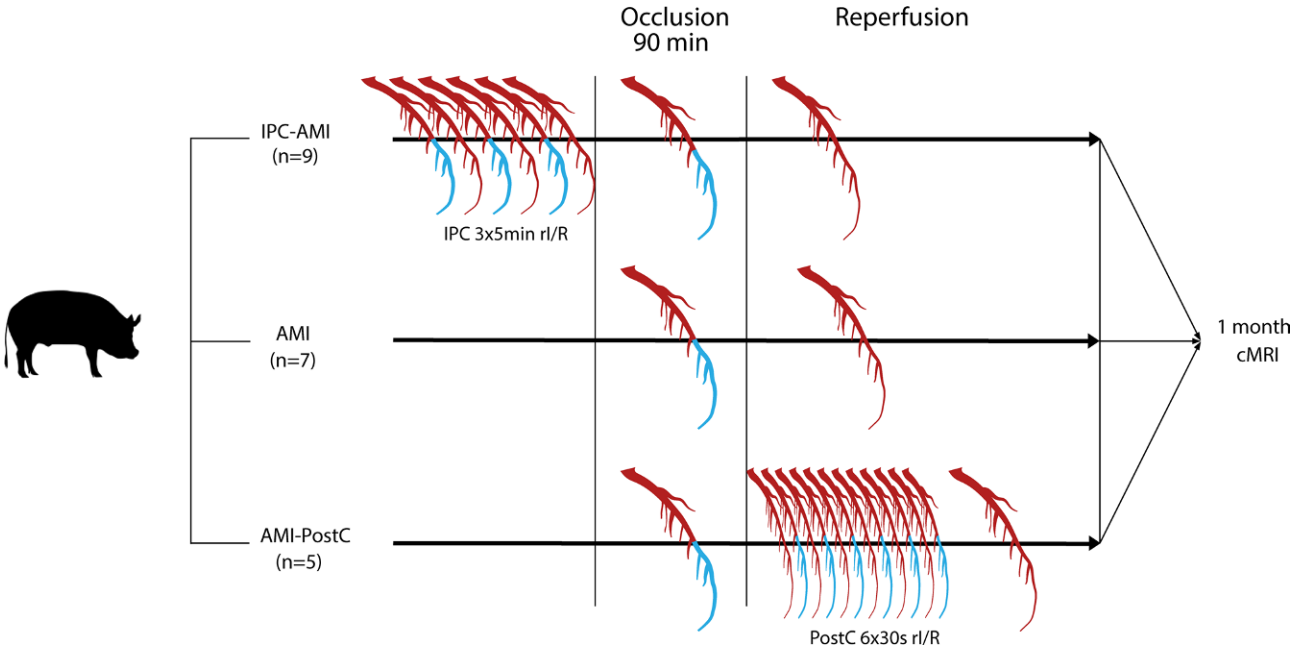


Fig. 1|19-4

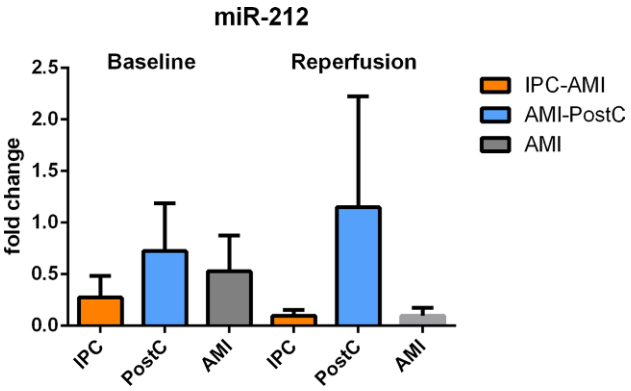


Fig. 2|19-4

19-5

Effect of ischemic pre-conditioning on expression of cardio- and thrombomiRs in a porcine model of acute myocardial infarction

Denise Traxler, Alfred Gugerell, Martin Riesenhuber, Jakob Prömer, Katrin Zlabinger, Andreas Spannbauer, Johannes Winkler, Mariann Gyöngyösi

Devision of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Several microRNAs play role in cardioprotection. The aim of this work was to assess the effect of ischemic pre-conditioning on circulating cardio- and thrombo-microRNAs (miR) in a pig model of acute myocardial infarction (AMI).

Methods: Closed chest reperfused AMI was induced in farm pigs by 90 minutes percutaneous balloon occlusion of the LCX, followed by balloon deflation. In four pigs IPC in the LAD for 60 minutes (3 circles of 10 min occlusion + 10 min reperfusion) was performed 24 h prior to AMI to induce cardioprotection in the late window. Blood sampling was performed before and after IPC, before AMI induction, at the 25th and 90th min during balloon occlusion, and 60 min after reperfusion. We measured expression levels of six cardiomiRs and four thrombomiRs using qPCR.

Results: Hypoxia led to downregulation of miR-130a, miR-146a, miR-92a, miR-221, mir-150, miR-191 and mir-21, while reperfusion increased the level of miR-1-3p, miR-27b-3p, and miR-126-3p, not influenced by IPC. However, IPC induced decrease in circulating miR-143 and miR145-5p, and a trend to lower level of miR-223-3p, miR-92a-3p during coronary occlusion, with inhibitory effect on apoptosis, inflammation and necrosis.

Conclusions: Hypoxic myocardial stress followed by reperfusion resulted in deregulation of several cardiac- and platelet-associated miRs playing role in angiogenesis, cell proliferation and migration. IPC further decreased the level of circulating miR-s responsible for vascular injury, thereby exerting protective effect in the ischemic heart in the late window of cardioprotection.

19-6

Proteomics analysis of in vitro conditioning of cardiosphere derived cells (CDCs) with secretome from PBMECs (Aposec)

Johannes Winkler[1], Dominika Lukovic[1], Julia Mester-Tonczar[1], Alfred Gugerell[1], Katrin Zlabinger[1], Eduardo Marbán[2], Hendrik Jan Ankersmit[3], Mariann Gyöngyösi[1]

[1]Divison of Cardiology, Department of Internal Medicine, II, Medical University of Vienna, Vienna, Austria
[2]Cedars-Sinai Heart Institute, Los Angeles, United States of America
[3]Department of Surgery, Medical University of Vienna, Vienna, Austria

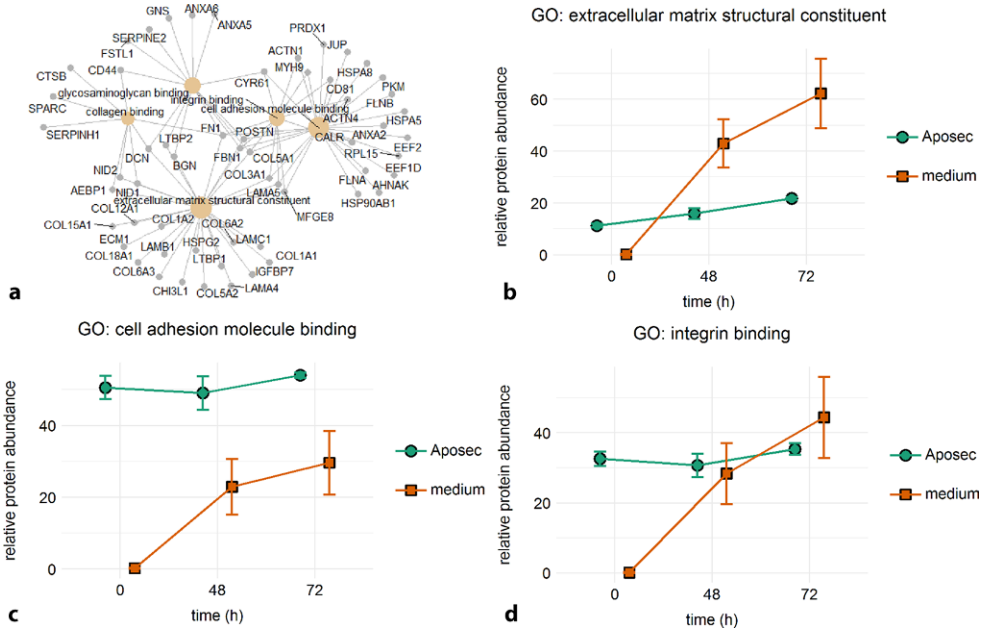


Fig. 1|19-6 Gene ontology network map of proteins with stronger secretion in standard medium (a) and summarized protein concentrations for selected gene ontology terms in absence and presence of Aposec (b–d)

Background: Recent clinical trials of stem cell therapy for myocardial infarction (MI) have generally resulted in insufficient therapeutic outcomes. Cardiosphere-derived cells (CDCs) are stem cells which are extracted from cardiac tissue, and have shown promising results in preclinical models and initial clinical evaluation. Recent data suggest that CDCs might be superior to mesenchymal stem cells for cardiac repair. In vitro conditions during cultivation of cardiac stem cells prior to cardiac delivery are essential for the cellular and molecular properties and therapeutic effects. Aposec, the secretome of irradiated peripheral blood mononuclear cells (PBMECs) has been shown to mitigate the effects of acute and chronic myocardial infarction (MI) in small and large animal models. We have previously reported the beneficial effects of Aposec-preconditioned CDCs in reducing infarct size in a porcine acute MI model. Here, we investigate the mechanism of Aposec-preconditioning using a proteome analysis of the cell culture supernatant.

Methods: Porcine CDCs were incubated in vitro in 6-well plates (2×105 cells per well) in presence or absence of porcine Aposec in serum-free cell culture medium. Aposec was applied in a concentration of the secretome derived from 106 PBMECs per mL cell culture medium. After 48 and 72 h, the proteins of the cell culture supernatant were quantified by shotgun proteomics in three biological and three technical replicates for each time point and treatment. Medium with and without Aposec supplementation served as control (time 0 h). Statistically significant alterations were calculated in a time- and treatment dependent manner with R software and the limma package. Proteins were clustered according to gene ontology (GO) with the clusterProfiler package and relative normalized concentrations of proteins of selected GO terms were summarized. Protein secretion was assessed by calculating the difference between concentrations at 72 and 0 h.

Results: Aposec itself contains many proteins, which were detected before incubation with CDCs (time 0 h), including several that are secreted by CDCs. The protein composition of porcine Aposec is equivalent to the well documented human Aposec. Significant alterations in proteins secretion were identified when CDCs were cultured in presence or absence of Aposec. Under standard, serum-free cell culture conditions the concentrations of collagens and other extracellular matrix (ECM) proteins and proteins that are instrumental for cell adhesion and cell binding were increased during the incubation time. On the other hand, Aposec-conditioning reduced protein concentration differences of these proteins between the end and start of the incubation period. Fig. 1a shows the GO annotation of proteins with significantly higher secretion (concentration difference between the start and end of the 72 h incubation period) in absence of Aposec. Fig. 1b–d depicts the relative protein concentrations, summarized to the indicated gene ontology terms, in cell culture medium at the time of analyses in presence and absence of Aposec.

Conclusions: Supplementation of the cell culture medium with Aposec decreases the secretion of ECM proteins and others by CDCs. According to the proteomics analysis, Aposec conditioning reduces the transition of CDCs towards a myofibroblast phenotype and preserves their multipotent paracrine potential.

19-7

MiR-29a and MiR-21 regulate MEF2c and GATA-4 expression in stimulated human cardiomyocyte hypertrophy

Katrin Zlabinger, Johannes Winkler, Denise Traxler-Weidenauer, Andreas Spannbauer, Julia Mester-Tonczar, Mariann Pavone-Gyöngyösi

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Cardiac hypertrophy is a major problem in clinics due to remodelling of heart tissue, increase of heart muscle size and mass and fibrotic tissue formation that further can lead to heart failure and death. There is a need for therapeutic agents to reverse remodel diseased heart tissue, which is not sufficiently possible with the current medical treatment. Before going into clinics it is necessary to test future therapeutics in vitro in cell culture models. MicroRNAs (miRNA) have shown to play a key role in the molecular regulation of pathological processes. The overall goal of this study was to establish a human cardiomyocyte hypertrophy model using Endothelin-1 (ET-1) or Angiotensin II (AngII) as stimulation agents, and to define new miRNA pathways in cardiac remodelling.

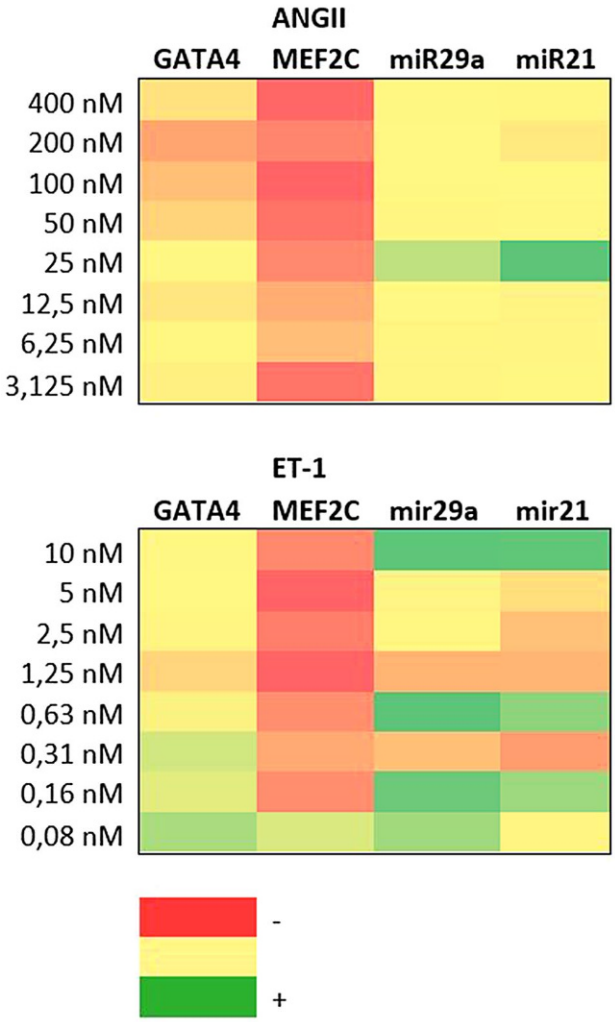


Fig. 1|19-7 Heat maps of gene expression after stimulation with Ang II and ET-1

Methods: Human cardiomyocytes were seeded to 48- and 96-well plates and stimulated for 6 h, 18 h and 24 h hours with different concentrations of ET-1 and AngII. Immunofluorescence staining for phalloidin f-actin was performed and the area of signal of each cell was used to calculate the cardiomyocyte size. Furthermore the expression of MEF2C, GATA-4, miR-21 and miR-29a on the mRNA/miRNA level was examined by qPCR. An ELISA Kit for human proBNP was used to measure the secretion of BNP into the cell culture supernatant.

Results: The measured cardiomyocyte area was unexpectedly reduced in both ET-1 (6 h: 9969 ± 2599 µm²; 18 h: 12452 ± 1857 µm²; 24 h: 10732 ± 2945 µm²) and AngII (6 h: 12844 ± 4027 µm²; 18 h: 13517 ± 585 µm²; 24 h: 12646 ± 1893 µm²) treated cells at all time points compared to untreated cells (18812 ± 2333 µm²). BNP secretion into the cell culture supernatant showed a dose dependent course with highest expression with 100 nM AngII (13.45 ng/ml) and 5 nM ET-1 (7.45 ng/ml) compared to the control (< 0.4 ng/ml). Gene expression analysis of MEF2c and GATA-4 (myocyte function and development) revealed a downregulation in all treated samples compared to untreated cells. MiR-21 and miR-29a seem to be differently expressed depending on the stimulation type. miR-21 and miR-29a were downregulated when stimulated with ET-1. AngII stimulation leads to a controversial miR-21 and miR-29a expression and seems to have an unclear expression pattern depending on treatment dose.

Conclusions: The results confirm that hypertrophy was successfully induced in human cardiomyocytes with increased protein expression of BNP and decreased expression of MEF2c and GATA-4 on gene expression level with both simulating agents. Cardiomyocyte size was reduced, but in further experiments longer stimulation could lead to an increase in cardiomyocyte size. The expression of miR-21 and mir29a indicate their potential role in the molecular regulation of pathological processes in cardiac hypertrophy.

Postersitzung 20 – Herzinsuffizienz 4

20-1

Gastrointestinal bleeding risk is linked to hemodynamics in patients with heart failure and preserved ejection fraction

Lore Schrutka, Benjamin Seirer, Franz Duca, Christina Binder, Daniel Dalos, Andreas Kammerlander, Stefan Aschauer, Lorenz Koller, Alberto Benazzo, Marianne Gwechenberger, Christian Hengstenberg, Julia Mascherbauer, Diana Bonderman

Medical University of Vienna, Vienna, Austria

Background: Two thirds of patients with heart failure and preserved ejection fraction (HFpEF) have an indication for oral anticoagulation (OAC) to prevent thromboembolic events. However, evidence regarding safety of OAC in HFpEF is limited.

Methods: We recorded bleeding events in a prospective HFpEF cohort over 8 years.

Results: Out of 328 patients (median age 71 years (IQR 67–77); 71.0% female), 64.6% ($n = 212$) were treated with OAC. Of those, 65.1% ($n = 138$) received vitamin-K-antagonists (VKA) and 34.9% ($n = 72$) non-vitamin K oral anticoagulants (NOACs). During a median follow-up time of 42 (IQR 17–63) months, a total of 54 bleeding events were recorded. Overall, patients on OAC experienced more bleeding events [$n = 49$ (23.1%) versus $n = 5$ (4.3%), $p < 0.001$]. Major drivers of events were gastrointestinal (GI) bleedings [$n = 18$ (36.7%)]. Bleeding rate was higher in VKA-treated patients compared to those on NOACs [$n = 33$ (23.9%) versus $n = 16$ (21.6%), $p < 0.001$]. HAS-BLED score [HR of 2.15 (95% CI 1.65–2.79, $p < 0.001$)] was the strongest independent predictor for overall bleeding. In the subgroup of GI bleedings mean right atrial pressure [mRAP: HR of 1.13 (95% CI 1.03–1.25, $p = 0.014$)] and HAS-BLED score [HR of 1.74 (95% CI 1.15-2.64, $p = 0.009$)] remained significant association with bleeding events after adjustment. Likewise, Kaplan Meier analysis demonstrated significantly more GI bleeding events in patients with higher mRAP (Fig. 1a; $p = 0.037$), and higher HAS-BLED scores (Fig. 1b; $p = 0.038$). mRAP provided additional prognostic value beyond the HAS-BLED score with improvement of the predictive model in C-Statistic of 0.63 versus 0.71 (95% CI 0.58–0.84, p for comparison 0.

Conclusions: High mRAP was predictive for GI bleeding events in OAC-treated HFpEF patients. Our data suggest that OAC-dosage should be cautiously chosen in this high-risk heart failure population (Fig. 2).

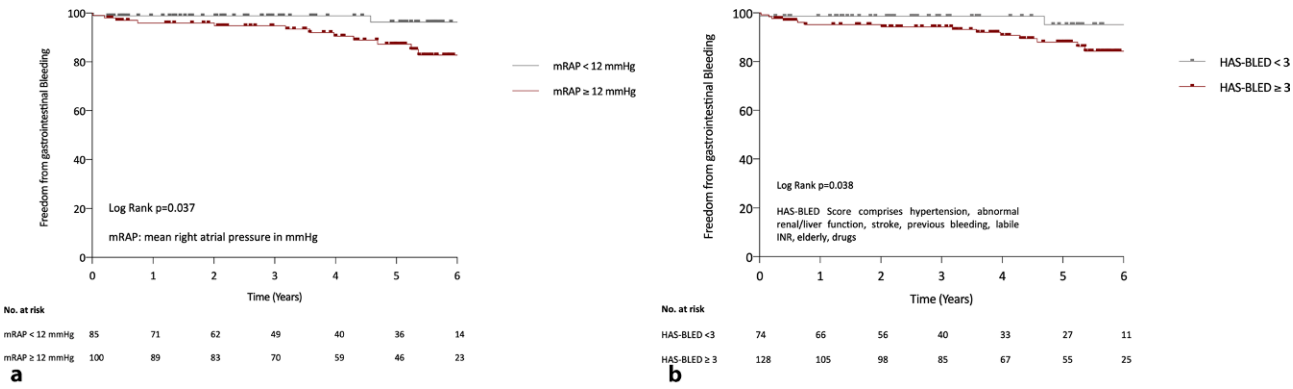


Fig. 1|20-1

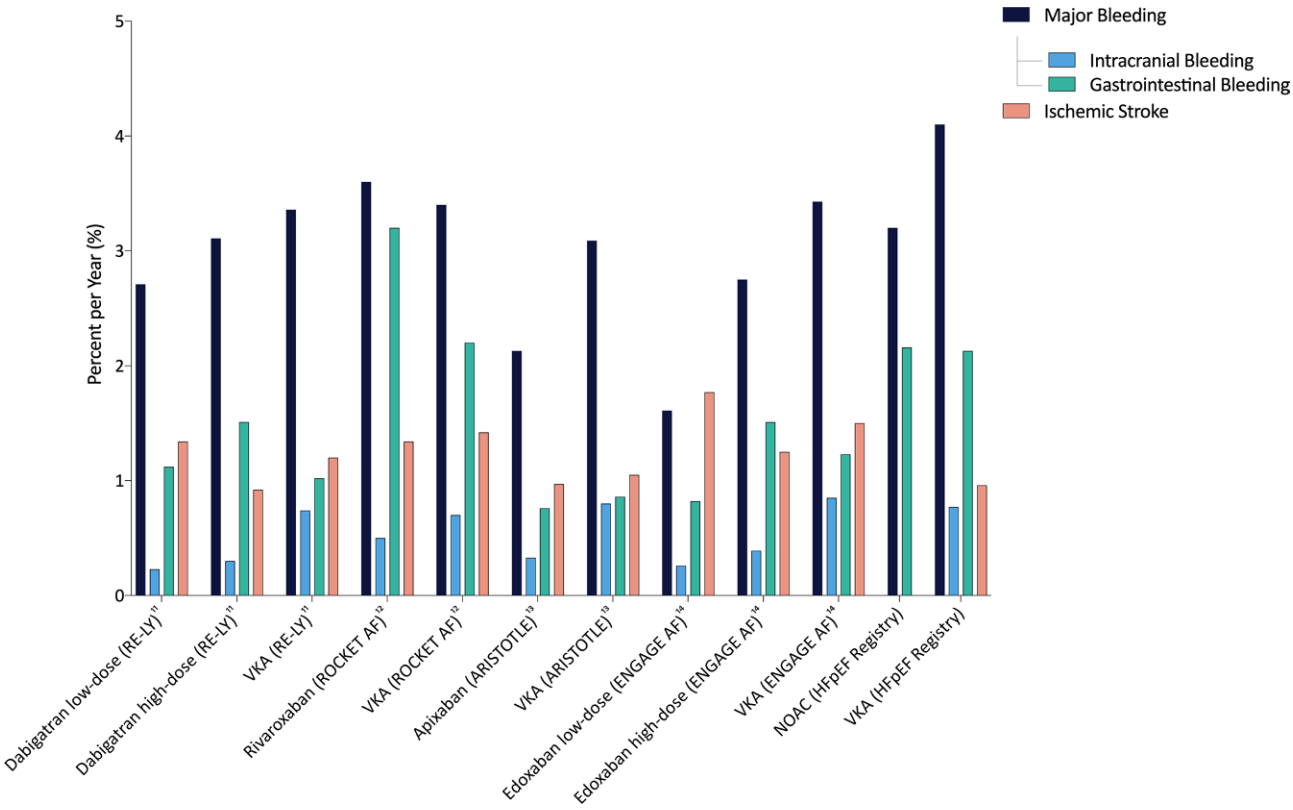


Fig. 2|20-1

20-2

Low heart rate at follow up predicts improvement of ejection fraction in a large-volume cohort of women with wearable cardioverter defibrillator

Lore Schrutka[1], Julia Erath[2], Valentina Kutiyfa[3], Birgit Assmus[4], Ashley Burch[5], Andrea M. Russo[6], Diana Bonderman[1]

[1]Medical University of Vienna, Vienna, Austria
[2]J. W. Goethe University, Frankfurt, Germany
[3]University of Rochester Medical Center, Rochester, United States of America
[4]University of Giessen, Giessen, Germany
[5]East Carolina University, Greenville, United States of America
[6]Cooper Medical School of Rowan University, Camden, United States of America

Background: Wearable cardioverter defibrillators (WCD) are effective in short-term therapy of ventricular arrhythmias and serve as diagnostic tools with continuous heart rate (HR) monitoring. Previous studies highlighted the importance of adequate HR control in heart failure patients. Women at risk for sudden cardiac death are often underrepresented in defibrillator trials and are therefore not well studied. The objective was to evaluate the impact of HR on improvement of ejection fraction (EF) in women provided with WCDs.

Methods: Data from women fitted with WCD from 2015 to 2018 were obtained from the manufacturer's database (ZOLL, Pittsburgh, PA). Quartiles of HR were compared between

Table 1 | 20-2 Logistic regression model of lowest HR quartile in registered patients with regard to EF improvement

Variable	Quartile 1	Odds ratio	95% Confidence interval	*P* value	Adjusted Odds ratio	95% Confidence interval	*P* value
Daytime HR at baseline, bpm							
Ref Quartile 4: HR>87	≤70	1.53	(1.41–1.65)	**<0.001**	1.11	(0.93–1.33)	0.263
Daytime HR at follow up, bpm							
Ref Quartile 4: HR>84	≤67	1.99	(1.84–2.15)	**<0.001**	1.32	(1.11–1.56)	**0.001**
Daytime delta HR, bpm							
Ref Quartile 4: delta HR>8.72	≤2.29	0.77	(0.71–0.83)	**<0.001**	1.02	(0.87–1.18)	0.846
Nighttime HR at baseline, bpm							
Ref Quartile 4: HR>84	≤67	1.53	(1.42–1.65)	**<0.001**	1.12	(0.93–1.34)	0.227
Nighttime HR at follow up, bpm							
Ref Quartile 4: HR>82	≤65	2.06	(1.90–2.23)	**<0.001**	1.36	(1.15–1.61)	**<0.001**
Nighttime delta HR, bpm							
Ref Quartile 4: HR>9.51	≤–1.36	0.72	(0.67–0.78)	**<0.001**	0.78	(0.67–0.91)	**0.001**

EF, ejection fraction; ICD, implantable cardioverter defibrillator; bpm, beats per minute; WCD, wearable cardioverter defibrillator
Delta indicates the difference between HR at baseline and follow up. Bold indicates $p<0.05$.
Multiple regression model was performed through adjustment for all variables in the respective category,

patients showing improvement of EF (>35%) and patients who either had indication for implantable cardioverter defibrillators (ICD) or died as a reason for WCD discontinuation.

Results: A total of 15 321 women with mean age of 66±13 years were included for analysis. Mean time of WCD use was 96±50 days. Patients with improvement of EF had significantly lower HR compared to patients who died or received an ICD. Univariable logistic regression analysis revealed that lower HR variables were predictive for improvement of EF, with nighttime HR at follow up showing strongest predictive power with an odds ratio of 2.06 (95%CI 1.90–2.23, $p<0.001$; Table 1). Multivariable adjustment revealed that daytime, nighttime and delta nighttime HR at the end of WCD use was predictive for improvement with nighttime HR remaining strongest predictor with an odds ratio of 1.36 (95%CI 1.15–1.61, $p<0.001$).

Conclusions: HR was significantly lower in patients showing improvement of EF. Absolute daytime, nighttime and delta nighttime HR at follow up showed predictive ability for recovery.

20-3

Optimal variable selection for simple prediction model of cardiac amyloidosis by routine laboratory parameters

Asan Agibetov[1], Benjamin Seirer[2], Stefan Aschauer[2], Daniel Dalos[2], Rene Rettl[2], Franz Duca[2], Hermine Agis[3], Renate Kain[4], Christina Binder[2], Julia Mascherbauer[2], Christian Hengstenberg[2], Matthias Samwald[1], Georg Dorffner[1], Diana Bonderman[2]

[1]Section for Artificial Intelligence and Decision Support, CeMSIIS (Center for Medical Statistics, Informatics and Intelligent Systems), Medical University of Vienna, Vienna, Austria
[2]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[3]Division of Oncology, Department of Internal Medicine I, Medical University of Vienna, Vienna, Austria
[4]Department of Pathology, Medical University of Vienna, Vienna, Austria

Background: Cardiac amyloidosis (CA) is a rare and complex condition with poor prognosis. Novel therapies have been shown to improve outcome, however, most of the affected individuals remain undiagnosed, mainly due to a lack in awareness among clinicians. One approach to overcome this issue is to use automated diagnostic algorithms that act based on routinely available laboratory results. We thus focus here on automated parameter (variable) selection, in order to build the best performing prediction model for cardiac amyloidosis that only requires routine lab parameters.

Methods: Our cohort consisted of 466 clinically accepted patients with various types of heart failure. Of these, 159 were diagnosed with CA via endomyocardial biopsy (positives), and

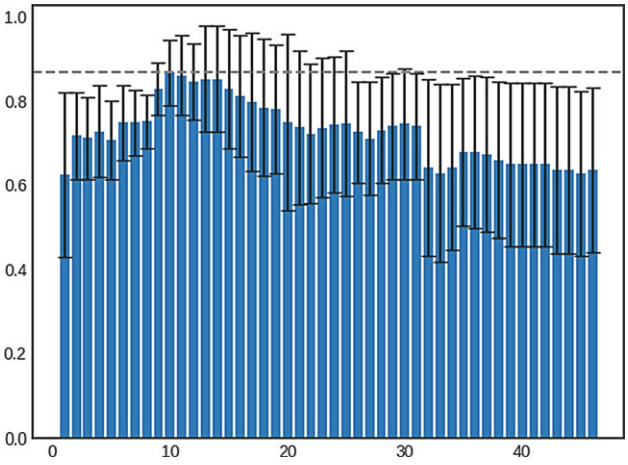


Fig. 1 | 20-3 Performance plot of linear prediction models with gradual inclusion of most important variables (from 1 to all variables, left to right). Cases (rows) with missing values are deleted. All ROC AUC scores are averaged over 10-fold cross-validation (mean +/– SD). Best prediction model (ROC AU 0.867 +/– 0.0.788) with 10 variables

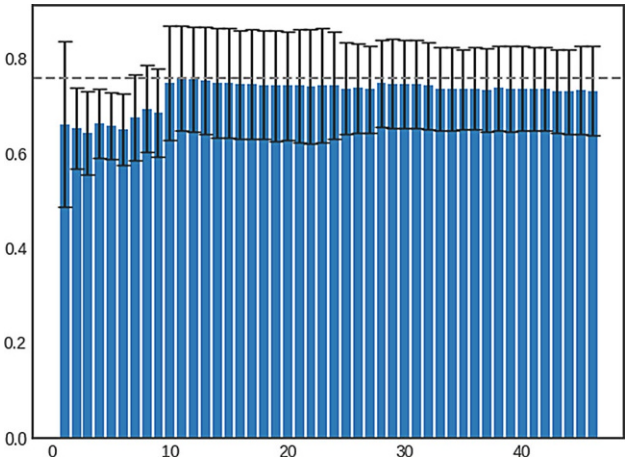


Fig. 2|20-3 Performance plot of binary logistic models with gradual inclusion of most important variables (from 1 to all variables; left to right). Cases (rows) with missing values are deleted. All ROC AUC scores are averaged over 10-fold cross-validation (mean +/– SD). Best prediction model (ROC AUC 0.867 +/– 0.0788) with 10 variables

307 had unrelated cardiac disorders (negatives). A total of 62 routine laboratory parameters were collected from these patients; some parameters had a high incidence of missing values. To boost the performance of a prediction model and prevent overfitting, we excluded parameters with high missing values ratio (cut-off at 60% missing ratio; 14 excluded), and highly collinear parameters (cut-off at 0.98 Pearson correlation; 3 excluded). After the exclusion we considered 45 laboratory parameters. Next, to enable optimal variable selection we resorted to a machine learning algorithm (gradient boosted tree ensembles). We started with one variable ($n=1$) and gradually added more variables ($n=2$, 3…), while recording each time the change in prediction performance of the ensemble model (10-fold CV) with and without the n-th variable. Averaged contribution factors (over 10 folds) were used to identify the most important variables. Finally, we iteratively built logistic regression models by gradually including ordered predictor variables and cross-validating (10 folds) the performance of each model. In all our experiments the performance of models was measured with an area under curve for receiver-operator characteristic (ROC AUC) measure.

Results: The overall best linear model was obtained with 10 most important variables (as identified through a machine learning algorithm), and a case deletion strategy for missing values, with a good average diagnostic accuracy (ROC AUC 0.867 +/– 7.8%, 10-fold CV). The inclusion of more variables led to the decrease of cross-validated performance, indicating strong overfitting (Fig. 1). Feature-wise mean imputation of missing values yielded worse performance with bigger variance for the best linear model requiring 11 most important variables (ROC AUC 0.758 +/– 11%, 10-fold CV). An inclusion of more variables, in case of statistical mean imputation, resulted in more stable and less overfitting performance of models, i. e., the tail of the distribution stayed close to 0.758 (Fig. 2). The latter can be explained by a bigger event per variable (EVP) rate in case of feature-wise mean imputation (19 events/variable for 11 variables, 9.9 with 20 variables). Case deletion, on the other hand, triggered a deflation of the EVP rate (e. g., 7.1 events/variable with 10 variables, 5.8 with 20 variables); low EVP rate causes decreased performance.

Conclusions: We obtained a good average diagnostic prediction accuracy (ROC AUC 0.867 +/– 7.8%) for cardiac amyloidosis, with 10 routine lab parameters, via a simple and interpretable linear prediction model that uses a complex machine learning algorithm for variable selection. Such automatic prediction models based on routine laboratory results may be used to help establish or suggest the diagnosis of cardiac amyloidosis in patients with heart failure symptoms, even in the absence of specialized experts.

20-4

Regulation of the Renin-Angiotensin-System (RAS) in a translational model of heart failure

Claudia Müller, Noemi Pavo, Katrin Zlabinger, Dominika Lukovic, Marko Poglitsch, Martin Hülsmann, Mariann Gyöngyösi

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: The Renin-Angiotensin-System (RAS) is dysregulated in heart failure (HF) and elevated circulating and tissue AngII levels are accused to be a central driver of disease progression. Renin is an enzyme principally exerting its activity upon secretion into plasma on angiotensinogen forming AngI thereby catalyzing the rate limiting step of the RAS cascade. We have previously reported that plasma renin shows an excellent correlation with circulating (AngI+AngII) levels in HFrEF patients independent from RAS inhibitor therapy. The myocar-

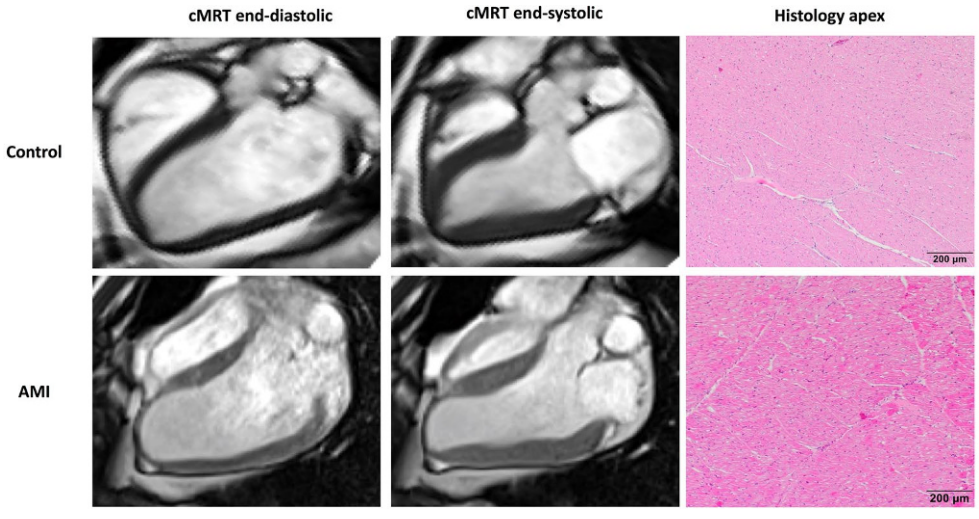


Fig. 1|20-4 Representative cMRT images and apex histology for control and HF animals

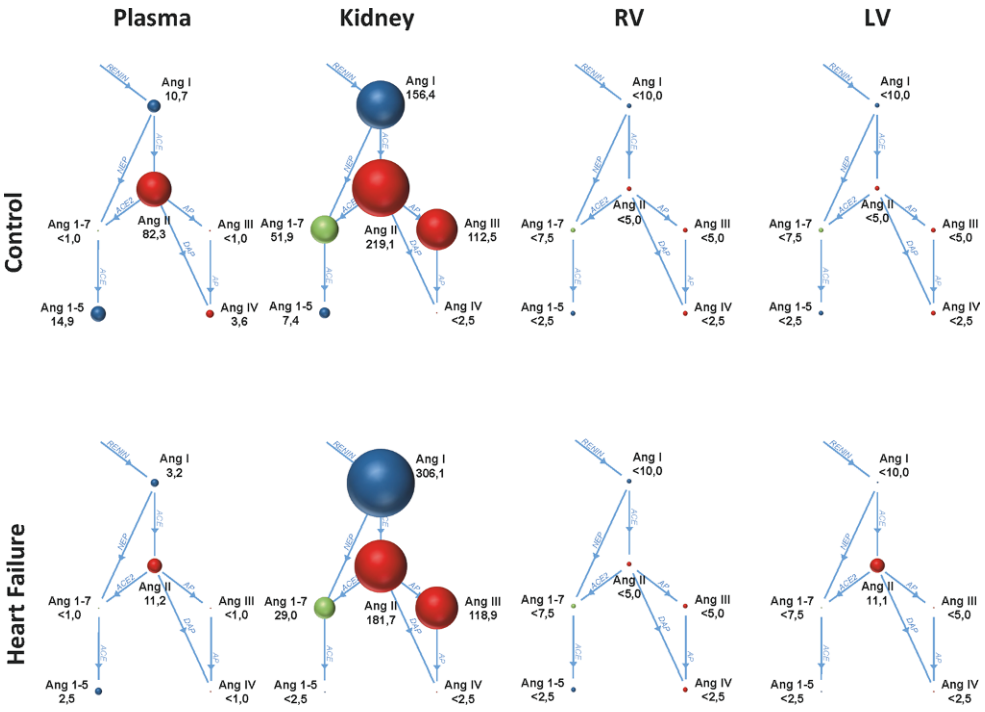


Fig. 2|20-4 Renin-angiotensin-system metabolite concentrations (RAS-fingerprints) of plasma, myocardial LV and RV and kidneys. Numbers in brackets indicate the specific angiotensin peptides. Side of spheres and numbers beside represent absolute concentrations of angiotensins (pg/ml, median value) analyzed by mass spectrometry

dium and kidneys however, are equally capable of synthesizing all RAS components resulting in tissue specific angiotensin levels. The particular relationship between plasma and tissue RAS in heart failure has not been investigated yet.

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, plasma samples were obtained and left and right ventricular tissues of the myocardium and kidneys were harvested. Plasma renin activity (PRA) was measured in plasma. Concentrations of the angiotensin metabolites AngI, AngII, Ang1-7, AngIII, Ang1-5 and AngIV (RAS-fingerprints) were investigated in plasma and tissues with a mass-spectrometry based method. Variables were compared between groups by a non-parametrical test.

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 (Fig. 1). PRA levels were higher in control compared to HF animals [0.16 (ng/ml)/h (IQR 0.13–0.39) vs 0.04 (ng/ml)/h (IQR 0.04–0.06), $p=0.016$]. RAS-fingerprints of plasma and tissues are displayed in Fig. 2. Kidneys showed a vast amount of angiotensins whereas almost all angiotensin peptides were below the detection limit for LV and RV. There were no differences in tissue angiotensin levels between HF and control animals. Plasma (AngI+AngII) levels were higher for control animals according to higher circulating renin activity [PRA: 93.0 pM (IQR 83.1–178.0) vs 12.9 pM (IQR 12.7–19.7), $p=0.008$]. PRA correlated well with circulating (AngI+AngII) levels [r = 0.88, $p<0.001$] but not with tissue angiotensin levels of the kidneys [p = ns]. There was also no relationship between total circulating and tissue angiotensin levels [p = ns].

Conclusions: Excess activation of the neurohumoral system could not be observed in heart failure animals without RAS-inhibitor treatment. Although dysregulation of myocardial tissue RAS is discussed as an important cofactor for disease progression, angiotensin peptide concentrations were minimal in myocardial LV and RV specimens. On the contrary, the kidneys displayed vast amount of angiotensin concentrations with a wide interindividual variation. Plasma renin activity, as a surrogate for RAS activation, correlated excellent with circulating angiotensin levels, as already observed for humans. Interestingly, tissue angiotensin levels seem to be unrelated to systemic RAS regulation. Effects of different renin levels and RAS inhibitor therapy should be further investigated on the tissue level in the kidneys in order to better understand the cardiorenal axis.

20-5

TLR-4 expression predicts mortality in patients with acute heart failure

Konstantin Krychtiuk[1], Max Lenz[1], Kurt Huber[2], Christian Hengstenberg[1], Johann Wojta[1], Gottfried Heinz[1], Walter Speidl[1]

[1]Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]3rd Medical Department, Wilhelminenhospital Vienna, Vienna, Austria

Background: Inflammation is regarded as an important trigger for disease progression in heart failure (HF) and activation of the inflammatory system was implicated in the pathophysiology of acute heart failure (AHF). Toll-like receptors (TLRs) play an important role in acute inflammatory processes in critically ill patients by binding to pathogen associated molecular patterns (PAMPs) and danger associated molecular patterns (DAMPs). However, it is not known whether the

expression patterns of TLRs on neutrophils and monocytes are associated with outcome in patients with severe AHF requiring intensive care unit (ICU) admission. The aim of this prospective, observational study was to analyze whether TLR-expression on monocytes or neutrophils is associated with 30-day survival in patients with severe AHF.

Methods: We included 84 patients with severe AHF admitted to our cardiac ICU. Blood was taken on admission and mean fluorescence intensity (MFI) of TLR-2, TLR-4 and TLR-9 on monocytes and neutrophils was analyzed by flow cytometry.

Results: Median age was 64 (IQR 48–74) years and 76.2% of patients were male. Median NT-proBNP was 4941 (IQR 1298–12273) pg/mL and 30-day mortality was 33.3%. TLR-4 expression on monocytes in survivors (740 IQR 694–854) was significantly lower than in non-survivors (871 IQR 723–979; $p<0.05$). TLR-2 and TLR-9 expression on monocytes and TLR expression on neutrophils was not associated with survival. TLR-4 expression on monocytes was significantly associated with survival independent of age, sex, creatinine and NT-proBNP levels.

Conclusions: Monocyte TLR-4 expression predicts mortality in patients admitted to a cardiac ICU for severe AHF. This suggests that activation of the innate immune system by TLR-binding of DAMPs may play a significant role in critically ill AHF patients.

20-6

Heart-type fatty acid binding protein correlates with troponin T in patients with cardiac amyloidosis

Safoura Sheikh Rezaei[1], Christina Binder[2], Rene Rettl[2], Franz Duca[2], Monika Fritzer-Szekeres[3], Rosa Badr Eslam[2], Julia Mascherbauer[2], Christian Hengestenberg[2], Diana Bonderman[2]

[1]Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria
[2]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[3]Department of Medical-Chemical Laboratory Analysis, Medical University of Vienna, Vienna, Austria

Background: Heart-type fatty acid-binding protein (H-FABP) is a novel biomarker, which was found to be sensitive for the early diagnosis of acute myocardial infarction. It has also been shown to be more accurate than troponin T (TNT) in risk stratifying patients with chronic heart failure. Myocardial damage by amyloid deposition and TNT elevation is one of the diagnostic hallmarks in patients suffering from cardiac amyloidosis (CA). The aim of this prospective study was to generate H-FABP profiles of patients with CA at rest and during exercise as well as to test their prognostic abilities.

Methods: 48 consecutive CA patients were enrolled in this prospective, observational study. Confirmatory diagnostic tests including laboratory assessments, bicycle ergometry, and echocardiography were performed. Troponin T and H-FABP were measured at baseline, pre- and post-bicycle ergometry.

Results: Patients' baseline characteristics are summarized in Table 1. In total, data from 46 patients with TTR-CA, one with AL-CA, and one with unspecified CA were analysed. Mean H-FABP plasma concentrations were 8.13 (SD ± 8.38) with a detection rage between 1.10–48.70 ng/ml (assay detection range between 0.747 and 120 ng/ml). H-FABP plasma concentrations correlated significantly with TNT levels ($n=48$; r2 = 0.405; $p=000$). There was a significant increase in H-FABP after ergometry ($n=11$; $p=0.008$), but not for TNT plasma concentrations ($n=11$, $p=0.092$). In a multiple regression model age and NT pro-BNP plasma concentrations were significantly associated with hospitalization due to cardiac decompensation ($n=15$; $p=0.003$), but not with H-FABP, TNT or interventricular septum thickness ($p=0.627$; $p=0.317$, $p=0.999$; respectively).

Table 1 | 20-6 Patients demographic data and laboratory assessments

Patients characteristics	*n*=
Male/female	36/12
TTR_A	46
AL_A	1
Not specified amyloidosis	1
Age years	77 (±8)
Number of Diagnosis	3(±0.54)
BMI kg/m^2	26.24(±0.43)
H-FABP ng/ml	8.13 (±8.38)
TNT ng/L	66.52 (±48.87)
IVS mm	19.84 (±4.54)
NT pro-BNP pg/ml	3727.79 (±3631.30)

Numbers in parenthesis indicate means and standard deviations. TTR-A transthyretin amyloidosis; AL-A, Light-Chain Amyloidosis; BMI, body mass index; H-FABP, heart type fatty acid-binding protein, TNT, troponin T, NT pro-BNP, N-terminal pro brain natriuretic peptide

Conclusions: H-FABP correlates with TNT in patients with CA. Further studies are warranted to establish the importance of H-FABP in this specific patient cohort.

20-7

Erfahrungen in der Betreuung von HerzinsuffizienzpatientInnen in einer Spezialambulanz

Fabienne Moser, Elisabeth Pichlbauer

Krankenanstalt Rudolfstiftung, Wien, Österreich

Grundlagen: Obwohl sich die Therapiemöglichkeiten für Herzinsuffizienz (HI) in den letzten Jahren weiterentwickelt haben und die Erkrankung in ihrer Progression mittlerweile gut hinausgezögert werden kann, ist eine Heilung in den meisten Fällen noch immer nicht möglich. Wichtig für den Krankheitsverlauf ist, neben einer eng an den Evidenz-basierten Guidelines orientierten Therapie, auch eine gute Adhärenz des Patienten sowie engmaschige Kontrollen bei ausgebildeten Spezialisten. Um dies zu gewährleisten wurden Disease Management Programme entwickelt, welche zu verbesserten Krankheitsverläufen und besserer Lebensqualität führen. Die Etablierung und Akzeptanz dieser stellt sich jedoch besonders in Wien als schwierig heraus.

Methoden: Im Rahmen dieser retrospektiven Diplomarbeit werden die Daten jener Patienten, die in den Jahren 2016 und 2017 zum ersten Mal die HI-Ambulanz einer kardiologischen Krankenhausabteilung in Wien aufgesucht haben, deskriptiv analysiert und die Fragestellung beantwortet, von welchen Parteien Patienten am häufigsten an die HI-Ambulanz überwiesen wurden, sowie ob Unterschiede im klinischen Zustand der Patienten zwischen den Zuweisergruppen bestehen.

Ergebnisse: Das Patientengut bestand aus 20 (22 %) Frauen und 70 (78 %) Männern, von denen 9 (10 %) an Herzinsuffizienz mit erhaltener Ejection Fraction (HFpEF) und 79 (90 %) an Herzinsuffizienz mit reduzierter Ejection Fraction (HFrEF) litten. Die Hälfte aller Ätiologien machte die ischämische Kardiomyopathie (CMP) (50 %) aus. Hypertonie (69 %), Hyperlipidämie (66 %) und koronare Herzerkrankung (56 %) stellten die häufigsten Komorbiditäten dar. Es wurden weitaus mehr Patienten von der kardiologischen Abteilung (82 %) an die HI-Ambulanz überwiesen als von anderen internistischen Abteilungen (10 %) und niedergelassenen Ärzten (8 %). In den wichtigsten klinisch-diagnostischen Parametern konnte jedoch kein Unterschied bezüglich der drei Zuweisergruppen festgestellt werden.

Schlussfolgerungen: Eine geringe Inanspruchnahme der Spezialambulanz durch den niedergelassenen Bereich konnte durch die Aufschlüsselung der Patienten nach Zuweisergruppen bestätigt werden. Patienten werden folglich noch immer primär von der kardiologischen Station selbst nach dortigem stationärem Aufenthalt an die HI-Ambulanz überwiesen. Die Hypothese, dass Patienten, die von der Station kommen und folglich eine Dekompensation hinter sich haben, in klinisch-diagnostischen Parametern schlechter abschneiden als andere Patienten, konnte jedoch nicht bestätigt werden.

Postersitzung 21 – Risikofaktoren/ Stoffwechsel/Lipide 2

21-1

Fatal recurrent Staphylococcus aureus infection in a patient with an aortic endostent under alirocumab

Claudia Stöllberger[1], Gerard Mertikian[2], Josef Finsterer[1], Christine Schmid[1], Dorit Stahl[1]

[1]Krankenanstalt Rudolfstiftung, Vienna, Austria
[2]Krankenhaus Hietzing, Vienna, Austria

Background: Aortic stent-graft infection (SGI) entails a high mortality. Alirocumab is a monoclonal antibody to proprotein-convertase-subtilisin/kexin-type 9 (PCSK9), approved for treatment of therapy-refractory hypercholesterolemia. There are indications that PCSK9, a ubiquitously expressed serine proteinase, plays a role in bacterial infections, and up to now, it is unclear whether it protects against or favors infections.

Methods: A 68-years old Caucasian male was admitted in July 2018 because of fatigue, fever and back pain. He had lost 14 kg within the previous month. He had a history of arterial hypertension, paroxysmal atrial fibrillation, coronary artery disease, stroke due occlusion of the left posterior cerebral artery, schizoaffective disorder, chronic sinusitis, sigma resection because of diverticulitis, diabetes mellitus, hyperlipidemia and chronic renal failure.

Results: Twelve months previously, a 4-fold-fenestrated aortic endoprosthesis was implanted because of an aortic aneurysm. Four months later, alirocumab 150 mg was initiated. Staphylococcus aureus grew in several blood cultures, and he received cefazoline and fosfomycin. Fludeoxyglucose Positron-Emission-Tomography computed-tomography indicated an infected endoprosthesis. Puncture of the periprosthetic space under antibiotics revealed different strains of Staphylococcus epidermidis. The therapy was changed to dalabavancin. The patient died suddenly 11 days later after complaining about back pain for several days. No autopsy was carried out.

Conclusions: From this observation we conclude that data about infections in patients under PCSK9-inhibitors should be collected systematically. Furthermore, it seems reasonable to debate whether patients with endovascular implanted grafts should receive antibiotic prophylaxis before invasive interventions or surgery, especially when they are treated with drugs which are known or suspected to affect the immune system.

21-2

The monitoring of performance progress due to long-term physical activity by paper-based training diaries: do training diaries reflect training progress?

Christoph Schukro[1], Michael Emich[2], Monika Fritzer-Szekeres[1], Jeanette Strametz-Juranek[3], Sponder Michael[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Federal Ministry of Defence and Sports, Vienna, Austria
[3]Rehabilitationszentrum Bad Tatzmannsdorf, Bad Tatzmannsdorf, Austria

Background: The European Society of Cardiology proposes a minimum of 75 min/week of high or 150 min/week of moderate intensity training. A modern patient care, in particular concerning patient with cardiovascular risk factors and/or cardiovascular disease, should comprise the motivation to be physically active and the observation of the patient's activity status. Training diaries are a cheap, simple and common method to monitor the training effort but there is hardly any data whether a monitoring with training diaries really reflects an improvement of the performance. The aim of this prospective study was to investigate whether the monitoring of training by paper-based training diaries reflects the training progress, measured by bicycle stress tests, in hobby athletes.

Methods: 98 participants were instructed to work out for 8 months within a calculated training pulse. They recorded their training pensum (intensity and time) by leading training diaries. Bicycle stress tests were performed at the beginning and end of the study to objectively determine the performance gain/change. Surrogate parameters, which are associated with increased physical activity were also recorded.

Results: From 98 participants, 27 did not achieve a performance gain of more than 2.9% (group 1+3), the remaining subjects (group 2+4) showed a performance gain of at least 3%. Concerning moderate intensity training, all cohorts met the specification of 150 min/week or more. Group 1 und 3 wrote down the highest amount of minutes in moderate intensity (853 resp. 672 min/month) followed by group 2 and 4 (657 resp. 600 min/month). Regarding high intensity training, the initially athletic groups showed a much higher amount of minutes/month (212 and 188 min/month) compared to the initially unathletic groups (25 and 95 min/month). None of the groups had an amount of >75 min/week. The performance gain was 0.4% in group 1, 12.2% in group 2, –3.8% in group 3 and 12.2% in group 4. There was no significant positive correlation of the performance gain with the total minutes of moderate or intensive training or the minutes per month of moderate or intensive training (p-values for group 2: 0.685/0.157/0.685/0.157; p-values for group 4: 0.257/0.052/0.275/0.052), however, the correlation of the per-

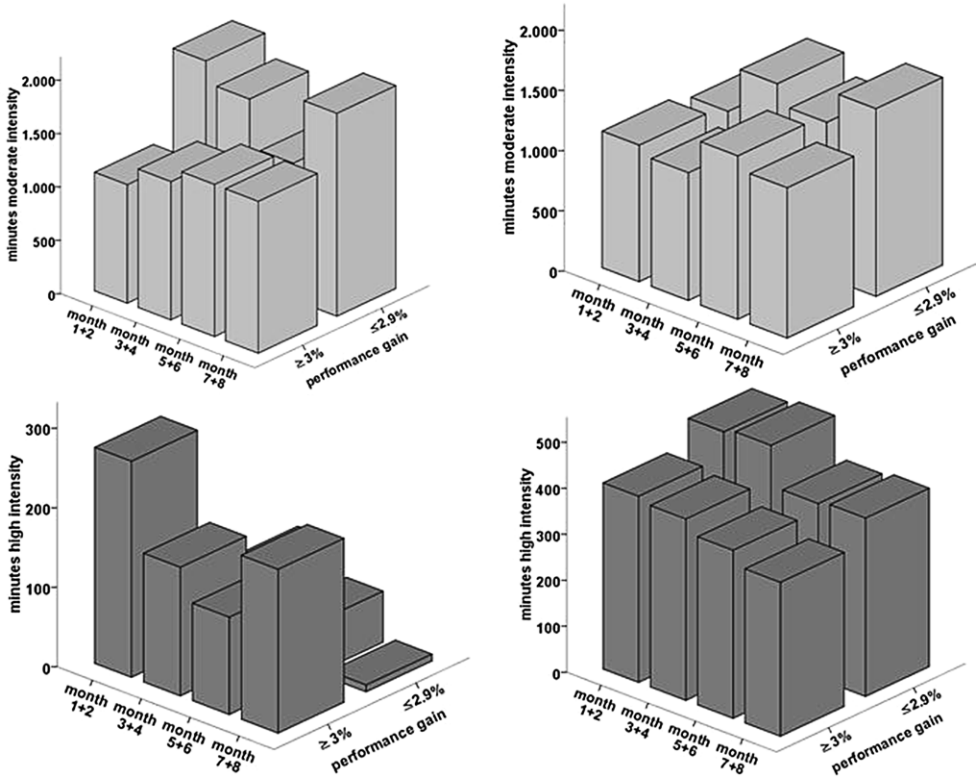


Fig. 1|21-2

formance gain and the total minutes of intensive training as well as the monthly minutes of intensive training were very close to statistical significance in group 4.

Conclusions: Our results show that there is a significant discrepancy between the reported work load and the objectively measured performance gain. The initially unathletic group 1 reported the highest amount of monthly training minutes in moderate intensity but had a performance gain of only 0.4%. In contrast, the initially unathletic group 2 with a performance gain of ca. 12% reported "only" 657 minutes of moderate training per month. A similar picture emerges regarding the initially unathletic group 3 which reported a higher work load (672 min/month of moderate and 212 min/month of high intensity training) compared to group 4 (600 min/month of moderate and 188 min/month of high intensity training). There was no correlation of work load with performance gain, however, it should be mentioned that in group 4 the correlation between reported minutes/month of high intensity training and performance gain was nearly significant. In conclusion paper-based training diaries might serve as accompanying tool in the monitoring of a training progress but due to the discrepancy between reported training loads and durations respectively, and the objectively measured training progress they are not suitable to replace regular (bicycle) stress tests for an exact determination of a performance gain.

21-3

Effect of PCSK9 inhibition on platelet reactivity in coronary artery disease patients

Lukas Galli, Anna Ondracek, Veronika Seidl, Thomas Hofbauer, Yasmin Zedan, Lore Schrutka, Konstantin Krychtiuk, Irene M. Lang, Walter Speidl, Klaus Distelmaier

Medical University of Vienna, Vienna, Austria

Background: Increased levels of circulating proprotein convertase subtilisin/kexin type 9 (PCSK9) are associated with higher platelet reactivity and the occurrence of future cardiovascular events in patients with coronary artery disease (CAD). The impact of PCSK9 inhibition on platelet reactivity in CAD patients has not been analyzed yet. We therefore assessed the effect of therapy with monoclonal antibody anti-PCSK9 on platelet function in CAD patients treated with dual antiplatelet therapy (DAPT) by Multiplate Electrode Aggregomer.

Methods: We prospectively enrolled patients receiving DAPT after coronary stent implantation who were routinely prescribed PCSK9 inhibitors due to low-density lipoprotein cholesterol (LDL-C) levels ≥ 70 mg/dl despite intensive statin and ezetimibe therapy. At baseline and 4 weeks after starting PCSK9 inhibition, adenosine diphosphate (ADP), arachidonic acid (AA) and thrombin receptor activating peptide (TRAP)-6 inducible platelet reactivity was measured by multiple electrode aggregometry.

Results: A total of nine patients (age 58 ± 6 years, male 72%) treated with PCSK9 inhibitors and DAPT (ticagrelor $n = 3$, clopidogrel $n = 6$) were enrolled. Median baseline LDL-C decreased from 88 (IQR 81–124) mg/dL to 33 (IQR 19–44) mg/dL ($P = 0.008$) after four weeks of PCSK9 inhibition. PCSK9 inhibition had no effect on platelet reactivity in response to ADP (42.5 IQR 7.5–

78.0 AU vs 40.0 IQR 7–50 AU; $p=0.33$), AA (19.0 IQR 9.0–30.5 AU vs 18.5 IQR 6.5–25.5 AU; $p=0.29$) and TRAP-6 (78.0 IQR 58.5–100.0 AU vs 91.0 IQR 67.5–124.0 AU; $p=0.67$).

Conclusions: Four weeks of PCSK9 inhibition significantly improved lipid profile but has no impact on platelet reactivity in CAD patients treated with DAPT.

21-4

Long-term clinical outcome in patients with hyperlipidemia and pacemakers: a single-center cohort study

Ena Hasimbegovic[1], Claudia Müller[2], Andreas Spannbauer[2], Friedrich Rauscha[2], Herwig Schmidinger[2], Thomas Pezawas[2], Cristoph Schukro[2], Marianne Gwechenberger[2], Cesar Khazen[3], Martin Andreas[3], Günther Laufer[3], Günter Stix[2], Anahit Anvari-Pirsch[2], Thomas Wrba[4], Denise Traxler-Weidenauer [2], Christian Hengstenberg[2], Mariann Pavone-Gyöngyösi[2], Martin Riesenhuber[2]

[1]Medical University of Vienna, Vienna, Austria
[2]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[3]Divsion of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[4]IT Systems & Communications, Medical University of Vienna, Vienna, Austria

Background: Hyperlipidemia is a major cardiovascular risk factor and affects the myocardial tissue composition and energy metabolism. Subclinical changes in myocardial properties of hyperlipidemia patients are frequent. Pacing threshold (PT) correlates with myocardial viability and is increased by myocardial ischemia. Lead impedance (LI) is influenced by patients' fluid status and lead dysfunction. We hypothesize that hyperlipidemia affects pacemaker (PM) implantation parameters, survival and functional lead parameters reflecting the influence of hyperlipidemia to the myocardium.

Methods: Clinical and PM data were retrospectively analyzed and combined with survival in a 10-year follow-up. Patients with all complete clinical (sex, age at the time of first implantation, survival data) and PM data were included. Survival data were retrieved from the Federal Institute "Statistics Austria".

Table 1 21-4 Outcome parameters

	Hyperlipidemia	No Hyperlipidemia	P Value
	N=1809	*N*=3289	
Device type			
–- Single-chamber PM	450 (26.9%)	1041 (34.7%)	<0.001
–- Dual-chamber PM	1225 (73.1%)	1963 (65.3%)	<0.001
10-year survival (*N*=3438)	52.0%	47.7%	0.026
Cause of death			
–- Total deaths	*N*=764	*N*=1666	
–- Cardiovascular death	396 (51.8%)	885 (53.1%)	0.555
–- Tumor-related death	98 (12.8%)	245 (14.7%)	0.217
–- Other death	270 (35.3%)	536 (32.2%)	0.124

Results: In total, 5098 patients were included in this study. Hyperlipidemia was diagnosed in 1809 of 5098 PM patients (35.5%): significantly fewer female than male patients had hyperlipidemia ($n=653$ (33.2%) vs. $n=1156$ (36.9%); $p=0.006$). Patients with hyperlipidemia were significantly younger at the time of PM implantation (73.56 years (IQR 63.85–80.40) vs. 71.84 (IQR 63.53–78.28) with hyperlipidemia, $p<0.001$). Patients suffering from hyperlipidemia received dual chamber PM significantly more often than patients without hyperlipidemia ($n=1225$ (73.1%) vs. 1963 (65.3%) without hyperlipidemia; $p<0.001$; Table 1). Patients with hyperlipidemia had a significantly better 10-years survival and remotely lower rates of cardiovascular and tumor-related deaths compared to patients without hyperlipidemia, although not statistically significant (Table 1), probably due to guidelines-related primary and secondary prevention. Ventricular and atrial PT was not influenced by hyperlipidemia at time point of first PM implantation (ventricular: 0.81 V vs. 0.85 V without hyperlipidemia, n. s.; atrial: 0.89 V vs. 0.92 V without hyperlipidemia, n. s.). Over the follow-up period of patients' first PM, ventricular PT increased significantly more in patients with hyperlipidemia compared to patients without hyperlipidemia (+0.17 V vs. +0.09 V, $p=0.003$). Regarding the longitudinal atrial PT, a borderline significance was found (+0.06 V vs. –0.003 V, $p=0.057$).

Conclusions: PM-patients suffering from hyperlipidemia had a better 10-year survival rate than patients without hyperlipidemia. This could be due to intensive primary/secondary prevention combined with the regular follow-up for patients with hyperlipidemia. A stronger increase of PT in patients with hyperlipidemia could be interpreted as the negative influence of cholesterol on the myocardial tissue compositions.

21-5

The Ceramide-Based Coronary Event Risk Test (CERT) predicts cardiovascular mortality in cardiovascular disease patients with type 2 diabetes mellitus as well as in those without diabetes

Andreas Leiherer[1], Axel Muendlein[1], Christoph H. Saely[2], Reijo Laaksonen[3], Mitja Laaperi[3], Alexander Vonbank[4], Barbara Larcher[4], Arthur Mader[4], Simon Sternbauer[4], Lukas Sprenger[4], Iris Baumgartner[5], Peter Fraunberger[6], Heinz Drexel[5]

[1]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[2]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein
[3]Zora Biosciences, Espoo, Finland
[4]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[5]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland
[6]Medical Central Laboratories Feldkirch, Feldkirch, Austria

Background: The recently introduced Coronary Event Risk Test (CERT) is a validated cardiovascular risk predictor that uses circulating ceramide concentrations to allocate patients into one of four risk categories.

Methods: We here aimed at investigating the power of CERT to predict cardiovascular mortality in 1087 patients with established cardiovascular disease (CVD) including 360 patients with type 2 diabetes (T2 DM). At baseline, the prevalence of T2 DM

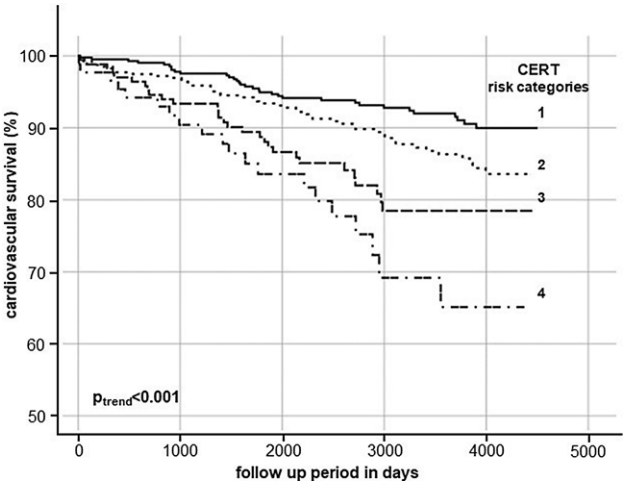


Fig. 1|21-5 Cardiovacular 45 of CVDpatients with respect to CERT risk categories. The Kaplan Meierplot indicates the survival without vascular death of the total study population according to the ceramide-based CERTrisk categories ranging from low risk (1) to high risk (4) with a log Rank *p*-value <0.001

increased through CERT categories (29.1, 31.1, 37.4, and 53.4%, respectively, ptrend <0.001). Prospectively, we recorded 130 cardiovascular deaths during a mean follow-up time of 8.1 ± 3.2 years.

Results: Overall, cardiovascular mortality increased with increasing CERT categories (Fig. 1) and was higher in T2 DM patients than in those who did not have diabetes (17.7 vs. 9.4%; $p < 0.001$). In Cox regression models, CERT categories predicted cardiovascular mortality in patients with T2 DM (unadjusted HR 1.60 [1.28–2.01]; $p < 0.001$; HR adjusted for age, gender, BMI, smoking, LDL cholesterol, HDL cholesterol, hypertension, and statin use 1.65 [1.27–2.15]; $p < 0.001$) and in those without diabetes (unadjusted HR 1.43 [1.10–1.85]; $p = 0.008$ and adjusted HR 1.41 [1.07–1.85]; $p = 0.015$).

Conclusions: We conclude that CERT predicts cardiovascular mortality in CVD patients with T2 DM as well as in those without diabetes.

21-6

Hand grip strength predicts mortality independently from type 2 diabetes and the presence of coronary artery disease

Barbara Larcher[1], Alexander Vonbank[1], Christine Heinzle[2], Daniela Zanolin-Purin[2], Arthur Mader[1], Abdurahman Said[3], Simon Sternbauer[1], Lukas Sprenger[1], Heinz Drexel[4], Christoph H. Saely[3]

[1]Department of Medicine I, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
[2]Vorarlberg Institute for Vascular Investigation & Treatment (VIVIT), Feldkirch, Austria
[3]Private University of the Principality of Liechtenstein, Triesen, Liechtenstein
[4]Division of Angiology, Swiss Cardiovascular Center, University Hospital Bern, Bern, Switzerland

Background: Hand grip strength (HGS) is widely used as a simple, inexpensive and non-invasive diagnostic parameter for frailty and sarcopenia. Low HGS in community-dwelling populations has been reported to predict a higher mortality risk. Whether this association is independent from the presence of type 2 diabetes (T2 DM) and pre-existing coronary artery disease (CAD) is not known and is addressed in the present study.

Methods: We prospectively recorded deaths over a mean follow up time of 9.2 ± 3.1 years in a cohort of 845 subjects in whom the baseline CAD state was determined angiographically.

Results: At baseline, HGS was higher in male than in female participants (41.5 ± 10.3 vs. 24.0 ± 5.06 kg; $p < 0.001$); it did not differ significantly between patients with T2 DM and non-diabetic subjects. Prospectively, low HGS predicted overall mortality both in men and women, with standardized adjusted HRs of 0.90 [0.83–0.99]; $p = 0.035$ and HR 0.65 [0,50–0,82]; $p < 0.001$ after multivariate adjustment including T2 DM and the presence of CAD at baseline.

Conclusions: We conclude that low hand grip strength predicts mortality independently from T2 DM and the presence of CAD.

21-7

Bariatric surgery reduces markers of metabolic syndrome in morbidly obese patients

Philipp Hohensinner[1], Christoph Kaun[1], Manfred Prager[2], Johann Wojta[1], Gersina Rega-Kaun[1]

[1]Medical University of Vienna, Vienna, Austria
[2]Krankenhaus Hietzing, Vienna, Austria

Background: Obesity is considered to be a global epidemic associated with numerous comorbidities including cardiovascular disease and metabolic syndrome. Current guidelines recommend gastric bypass surgery at a body mass index (BMI) >40 kg/m^2 or a BMI >35 kg/m^2 with secondary disease. This surgical intervention results in massive weight loss within the first year after surgery. The weight loss is associated with dramatic changes such as a reduced inflammatory state and reduced premature aging. In addition, previous work already demonstrated the possibility of complete remission for insulin-dependent patients after Roux-en-Y gastric bypass surgery. The aim of our study was to analyze metabolic plasma markers in order to understand the effect of Roux-en-Y gastric bypass surgery on the metabolic syndrome.

Methods: Obese patients with a body mass index (BMI) >40 undergoing Roux-en-Y gastric bypass surgery were enrolled in the study. Citrated blood was drawn before surgery and one year after. Samples were stored at -80 °C in multiple aliquots. All human material was obtained and processed according to the recommendations of the hospital's ethics committee and security board, including informed consent. Insulin and C-peptide was determined on a Cobas system, proinsulin was determined using specific ELISA. miRNA related to metabolic syndrome were isolated from plasma using an automated Maxwell system and determined via qPCR.

Results: The cohort consisted of 59 patients. Patients with diabetes only differed in HOMA-1 index from non-diabetic patients within our cohort. Other markers of metabolic syndrome were similar. When analyzing changes induced by bariatric surgery we observed similar fold changes in the reduction of markers related to the metabolic syndrome in both groups. Obesity is associated with an alteration of insulin signaling. Our data indicate that both insulin and C-peptide are dramatically reduced one year after bariatric surgery. Similarly the precursor molecule proinsulin was also reduced after gastric bypass

surgery. Insulin and C-peptide correlated strongly before surgery, this association was lost after bariatric surgery. In contrast, proinsulin did not correlate with either insulin or C-peptide before surgery but with both after bariatric surgery. Proinsulin was furthermore the only one where the fold levels of reduction after surgery correlated with weight loss. To further understand changes within the pancreatic system, we decided to measure four miRNAs associated with the pancreas. For this purpose we analyzed mir-130b-3p, mir-132-3p, mir-409-3p, and mir-451a before and after bariatric surgery. miRNAs were not different in patients with or without diabetes. All four miRNAs correlated with each other significantly at baseline. miRNAs analyzed were reduced after bariatric surgery. We did not observe a correlation of miRNAs with BMI, HOMA-1, insulin, or C-peptide.

Conclusions: We demonstrate in our cohort of previously morbid obese patients that bariatric surgery ameliorates markers of the metabolic syndrome regardless of prior diabetic status. As all patients analyzed showed marked reduction in all markers analyzed we suggest that, at least in this cohort, a healthy morbidly obese patient does not exist. Our data further indicate that surgery also lead to reduced pancreatic stress suggested by the reduction of 4 miRNAs associated with pancreatic stress. Finally, we suggest that proinsulin might be more reflective of BMI related changes as it correlated with weight loss.

21-8

A large bifurcation angle is strongly associated with increased plaque volume and plaque progression in subclinical carotid atherosclerosis

Michael Schreinlechner[1], Maria Noflatscher[1], Sommer Philip[1], Christian Kremser[1], Ruth Steiger[1], Agnes Mayr[1], Markus Theurl[1], Rudolf Kirchmair[1], Peter Marschang[2]

[1]Medical University of Innsbruck, Innsbruck, Austria
[2]Central Hospital of Bolzano, Bozen, Italy

Background: Although the exposure to systemic cardiovascular risk factors affects the entire vascular tree, atherosclerotic plaques are predominantly found at specific regions like arterial bifurcations. These observations suggest that geometric factors may be crucial in the atherosclerosis pathogenesis. The aim of our study was to analyse the influence of geometric factors on the extent and progression of carotid plaque volume (cPV). Additionally, we compared the performance of three-dimensional ultrasound (3D-US) with magnetic resonance imaging (MRI) for the detection of geometric risk factors.

Methods: This study (ANGLE study, ClinicalTrials.gov identifier: blinded) was a prospective, observational, single-center cohort study. A total of 51 study participants (mean age 65 ± 9 years; 55% men) with subclinical atherosclerosis and asymmetrical cPV (≥ 50% side to side difference) were included. Since geometric parameters we measured on both sides, every patient served as his own control. cPV was quantified with 3D-US as described (2). Arterial geometry was assessed with MRI using a semiautomatic in-house software (Fig. 1a). Carotid bifurcation angle (cBA) was measured with 3D-US and MRI. Atherosclerotic plaque progression (PPr) was evaluated after 12 months.

Results: As displayed in Fig. 1b, pairwise comparison revealed that the side with higher cPV showed a significantly larger cBA than the side with lower cPV (median 38.1° vs. 26.1°; $p < 0.001$). Conversely, in 49 individuals with symmetrical cPV, we did not observe significant differences in cBA (median 27.3°

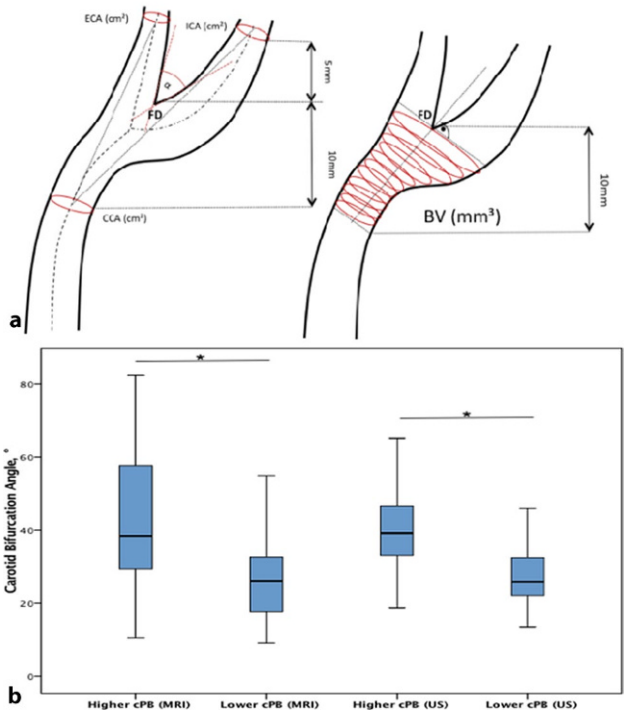


Fig. 1 | 21-8

vs. 28.1°; $p = 0.97$). We observed that similar to cPV, a larger cBA was associated with higher PPr (median 35.5° vs. 26.5°; $p = 0.004$). Particularly this observation suggests a sequential relationship of a large cBA with atherosclerotic progression. These results were confirmed in multivariate regression where only cBA (b = 0.26) and internal carotid artery (ICA) tortuosity (b = 0.23) were significant predictors of cPV and PPr. The strong correlation (r = 0.48; $p < 0.001$) between bifurcation angle and ICA tortuosity may be interpreted as two markers measuring similar geometric parameters. In addition, we evaluated the performance of 3D-US based measurements of the cBA in comparison to MRI. We found a very strong correlation (r = 0.90, $p < 0.001$) and a coefficient of variation of 20%, indicative of a very good agreement of the two methods. In 91% of all cases, cBA could be assessed with 3D-US. In receiver operating characteristics analysis, the cBA as determined by MRI and US were significant predictors for higher cPV (area under curve 0.79 vs. 0.83; $p < 0.001$) but showed no significant difference comparing the two imaging modalities ($p = 0.106$).

Conclusions: With increasing availability of 3D-US for peripheral arteries, the measurement of the cBA may become an additional tool for risk stratification. This may aid in the identification of patients with high-risk geometric features that are likely to profit from a more aggressive treatment approach.

Postersitzung 22 – Interventionelle Kardiologie 3

22-1

Prevalence of transthyretin and immunoglobulin light chain cardiac amyloidosis in patients undergoing transcatheter aortic valve replacement

Christian Nitsche[1], Andreas Kammerlander[1], Matthias Koschutnik[1], Stefan Aschauer[1], Matthias Schneider[1], Georg Goliasch[1], Thomas Poschner[1], Julian Stiftinger[1], Christina Binder[1], Franz Duca[1], Anahit Anvari-Pirsch[1], Martin Andreas[2], Hermine Agis[3], Marcus Hacker[4], Diana Bonderman[1], Christian Hengstenberg[1], Julia Mascherbauer[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[3]Division of Oncology, Department of Internal Medicine I, Medical University of Vienna, Vienna, Austria
[4]Division of Nuclear Medicine, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria

Background: A significant number of aortic stenosis (AS) patients suffer from coexisting cardiac amyloidosis (CA). Only transthyretin (TTR) CA has so far been described in AS although immunoglobulin light chain (AL) is the most common CA form. The present study evaluated the prevalence of TTR- and AL-CA in AS patients scheduled for transcatheter aortic valve replacement (TAVR), and was designed to establish abundant parameters to reliably discriminate CA-AS from AS alone.

Methods: 191 consecutive patients (82.0 ± 8.2 years; 50.2% female) were screened for CA between October 2017 and February 2019 and were prospectively enrolled. Patients underwent echocardiography with strain analysis, ECG, cardiac magnetic resonance imaging (CMR), 99mTc-DPD bone scintigraphy, and serum and urine free light chain assessment. Myocardial biopsy was performed in AL-CA. ROC curve and binary logistic regression analysis were performed to evaluate the discriminative power of respective parameters.

Results: CA was found in 11.0% ($n=21$) of patients, including TTR-CA ($n=19$), AL-CA ($n=1$), and one case of combined TTR-AL-CA. Native T1 relaxation time and left ventricular mass index by CMR, as well as relative apical longitudinal strain by echo did not differ significantly between AS and CA-AS patients (P for all >0.05). Typical pattern of late gadolinium enhancement was only present in 26.8% of CA. Voltage/mass-ratio (VMR) as well as "out-of-proportion-hypertrophy" (OPH; aortic peak gradient/LV mass index x stroke volume index on echocardiography) showed excellent discriminative power for the detection of CA (AUC 0.770 and 0.812, respectively). Furthermore, by multivariate binary logistic regression analysis, VMR (OR 0.304; 95% CI 0.130–0.710; $p=0.006$) and OPH (OR 0.121; 95% CI 0.038–0.389; $p=0.000$) were significantly associated with the presence of CA.

Conclusions: Comprehensive screening for CA in AS patients scheduled for TAVR revealed a significant number of TTR-CA, but also AL-CA cases. Since characteristic diagnostic features of CA and AS may overlap, easily accessible parameters derived from abundant diagnostic modalities, such as VMR and OPH, are needed. High suspicion of CA should entail further testing including bone scintigraphy and light chain assessment.

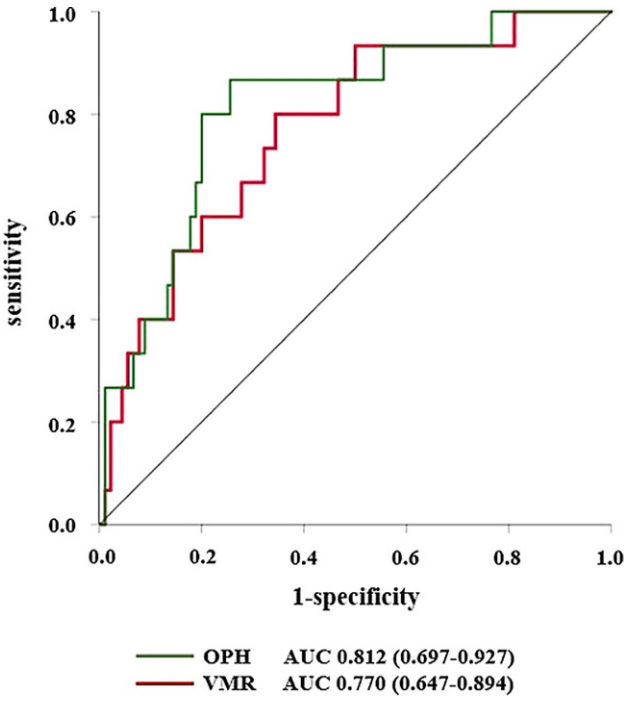


Fig. 1|22-1

22-2

The right heart in patients undergoing transcatheter aortic valve replacement: insights from cardiac magnetic resonance imaging

Matthias Koschutnik[1], Christian Nitsche[1], Andreas Kammerlander[1], Stefan Aschauer[1], Georg Goliasch[1], Jolanta Siller-Matula[1], Max-Paul Winter[1], Martin Andreas[2], Christian Loewe[3], Christian Hengstenberg[1], Julia Mascherbauer[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[3]Division of Cardiovascular and Interventional Radiology, Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria

Background: Cardiac magnetic resonance (CMR) provides the gold standard for the assessment of ventricular volumes and mass. However, data on right ventricular systolic dysfunction (RVSD) and its prognostic significance on outcome in patients undergoing transcatheter aortic valve replacement (TAVR) are lacking.

Methods: We consecutively enrolled patients with severe aortic stenosis scheduled for TAVR who underwent preprocedural CMR. Kaplan-Meier estimates and multivariate Cox-regression analysis were used to identify factors associated with outcome, including RVSD. A composite of heart failure hospi-

talization and/or cardiovascular death was selected as primary study endpoint.

Results: 145 consecutive patients (80.5 ± 7.6 years; 51.7% female) were prospectively included, 25 (17.2%) of which had RVSD defined as RV ejection fraction (RVEF) < 40%. RVSD was significantly associated with male sex, atrial fibrillation, reduced left ventricular (LV) EF (< 50%) and RV endsystolic volume on CMR (all $p < 0.05$). Serum NT-proBNP (14065 ± 12042 vs. 3203 ± 4615 ng/ml; $p < 0.001$) and creatinine levels (1.59± 0.96 vs. 1.29 ± 1.03 mg/dl; $p = 0.201$) were elevated in patients with RVSD. A total of 27 events occurred during follow-up (29 ± 13 weeks). While LVSD was not significantly associated with outcome ($p = 0.654$), RVSD showed a strong and independent association with event-free survival in the multivariate Cox-regression analysis [hazard ratio 3.836 (95% confidence interval 1.670–8.810); $p = 0.002$], which included all relevant CMR parameters, cardiovascular risk factors and routine biomarkers.

Conclusions: RVSD rather than LVSD, as determined by CMR, is an important predictor of outcome in patients undergoing TAVR. RV function might thus add useful prognostic information on top of established risk factors.

22-3

Percutaneous mitral valve repair via the MitraClip in patients with vs. without atrial fibrillation

Felix Nägele[1], Can Gollmann-Tepeköylü[1], Cenk Özpeker[1], Mert Savci[2], Silvana Müller[3], Gerhard Pölzl[3], Florian Hintringer[3], Agne Adukauskaite[3], Ludwig Müller[1], Michael Grimm[1], Nikolaos Bonaros[1]

[1]University Hospital for Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]Medical University of Innsbruck, Innsbruck, Austria
[3]University Hospital for Internal Medicine III, Medical University of Innsbruck, Innsbruck, Austria

Background: Atrial fibrillation is common in the general population, with a prevalence increasing with age. It frequently coincides with mitral regurgitation. Population-based studies indicated impaired long-term survival of patients with atrial fibrillation. Some studies on surgical mitral valve repair reported worse outcome for patients with atrial fibrillation. Data on the influence of atrial fibrillation on transcatheter mitral valve edge-to-edge repair (MitraClip) are limited.

Methods: Patients who underwent mitral valve edge-to-edge repair (MitraClip implantation) were included into the study. All patients were adjudicated as not amenable to surgery by heart team consensus prior to intervention. All patients provided written informed consent for the study.

Table 1 | 22-3 Patient characteristics

patient characteristics	no aFib (total = 23) (%)	aFib (total = 45) (%)	p-value
age	71.04 ± 3.08	81.36 ± 1.31	0.001
EURO Score 2	6.87 ± 1.2	6.14 ± 0.58	0.54
STS Score	3.35 ± 0.72	3.94 ± 0.45	0.47
previous cardiac surgery	6 (8.8)	8 (11.8)	0.42
sPAP	51.00 ± 3.42	55.06 ± 2.19	0.32
BMI	24.52 ± 0.86	24.21 ± 0.63	0.77
hypercholesterinemia	15 (65.2)	25 (55.6)	0.44
COPD	6 (26.1)	5 (11.1)	0.12
diabetes	7 (30.4)	11 (24.4)	0.6
peripheral artery disease	3 (13)	3 (6.7)	0.38
history of smoking	2 (8.7)	2 (4.4)	0.48
isch. CMP	6 (26.1)	9 (20)	0.57
other CMP	6 (26.1)	11 (24.4)	0.88
preOP cardiogenic shock/decomp.	11 (47.8)	26 (57.8)	0.44
other valve pathology	16 (69.6)	7 (15.6)	0.34
preOP NT proBNP	4692 ± 1317	4468 ± 986.6	0.92
ejection fraction	40.82 ± 3.38	43.96 ± 2.27	0.44
GFR	45.41 ± 3.34	46.32 ± 2.27	0.82
last pre-OP crea (mg/dl)	1.59 ± 0.20	1.48 ± 0.10	0.62
LVEDD	62.57 ± 2.73	71.63 ± 15.51	0.68
LVESD	48.49 ± 3.37	44.36 ± 1.83	0.25
MI Type Iib	13 (56.5)	17 (37.8)	0.15
male	14 (60.9)	7 (15.6)	0.95
history of stroke	3 (13)	6 (13.3)	0.97

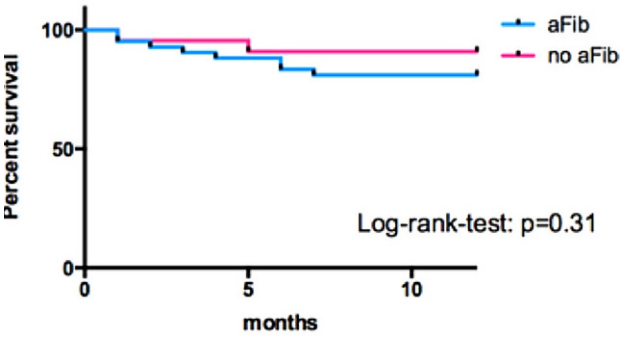


Fig. 1|22-3

Results: 68 consecutive patients (45 with, 23 without atrial fibrillation) underwent clinical and echocardiographic follow-up for 1 year. Patients with atrial fibrillation who underwent MitraClip implantation were significantly older (aFib 81.36 ± 1.31, no aFib 71.04 ± 3.08). Nonetheless, 1-year survival was equal in patients with and without atrial fibrillation (Log-rank-test $p = 0.31$).

Conclusions: Atrial fibrillation does not impact clinical outcome, mortality rate or improvement of symptoms in patients undergoing MitraClip implantation. Age should not be considered a limiting factor in patients with atrial fibrillation.

22-4

Gender-specific outcome after transcatheter mitral valve edge-to-edge repair of surgical high-risk patients

Felix Nägele[1], Can Gollmann-Tepeköylü[2], Johannes Holfeld[2], Cenk Özpeker[2], Mert Savci[3], Silvana Müller[4], Gerhard Pölzl[4], Florian Hintringer[4], Agne Adukauskaite[4], Ludwig Müller[2], Michael Grimm[2], Nikolaos Bonaros[2]

[1]University Hospital for Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
[3]Medical University of Innsbruck, Innsbruck, Austria
[4]University Hospital for Internal Medicine III, Medical University of Innsbruck, Innsbruck, Austria

Background: Gender has been an important factor of outcome in surgical mitral valve repair. Female gender has previously been reported to be an independent risk factor for mortality following valvular heart surgery. Data on the influence of gender on transcatheter mitral valve edge-to-edge repair (MitraClip) are limited. Analysis emphasizing gender-related differences in 1-year survival following MitraClip implantation are rare.

Methods: Patients who underwent mitral valve edge-to-edge repair (MitraClip implantation) were included into the study. All patients were adjudicated as not amenable to surgery

Table 1|22-4

patient characteristics	male (total = 41)	female (total = 27)	p-value
age	76.9 ± 13.95	79.33 ± 8.58	0.6
EURO Score 2	5.99 ± 0.75	7.02 ± 0.73	0.36
STS Score	3.92 ± 0.55	3.45 ± 0.43	0.56
previous cardiac surgery	12	2	0.01
sPAP	53.74 ± 2.19	52.53 ± 2.96	0.74
BMI	24.15 ± 3.365	24.6 ± 4.44	0.89
hypercholesterinemia	24	16	0.95
COPD	7	4	0.81
diabetes	13	5	0.23
peripheral artery disease	3	3	0.59
history of smoking	3	1	0.54
isch. CMP	13	2	0.02
other CMP	10	7	0.89
preOP cardiogenic shock/decomp.	27	10	0.02
other valve pathology	32	20	0.71
preOP NT proBNP	5313 ± 1229	3054 ± 487	0.2
ejection fraction	41.67 ± 2.52	45.06 ± 2.74	0.39
GFR	46.44 ± 2.18	45.3 ± 3.47	0.77
last pre-OP crea (mg/dl)	1.61 ± 0.12	1.36 ± 0.16	0.19
LVEDD	62.44 ± 1.65	78.03 ± 26.28	0.47
LVESD	48.06 ± 2.03	41.91 ± 2.68	0.072
MI Type Iib	20	10	0.49
atrial fibrillation	23	13	0.75

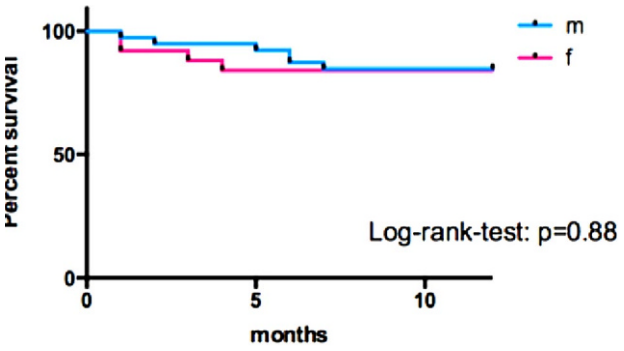


Fig. 1|22-4

by heart team consensus prior to intervention. All patients provided written informed consent for the study.

Results: 68 consecutive patients (41 male, 27 female) underwent clinical and echocardiographic follow-up for 1 year. Female patients showed a significantly better postoperative renal function (postop Creatinin female: 1.1 ± 0.9, male: 1.4 ± 0.09; *p*-value = 0.03). Postoperative proBNP was markedly higher in men, although not significant (postop proBNP female: 886 ± 581, male: 3760 ± 832; *p*-value = 0.14).

Conclusions: Although female gender is an independent risk factor for surgical mitral valve repair, this is not true for the MitraClip procedure. 1-year outcome after MitraClip implantation is equal in male and female patients.

22-5

Beating heart porcine high-fidelity simulator for the training of edge-to-edge mitral valve repair

Felix Nägele[1], Can Gollmann-Tepeköylü[1], Johannes Holfeld[1], Gerhard Pölzl[2], Bernhard Metzler[2], Florian Hintringer[2], Agne Adukauskaite[2], Ludwig Müller[1], Michael Grimm[1], Nikolaos Bonaros[1]

[1]University Hospital for Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]Medical University of Innsbruck, Innsbruck, Austria
[3]University Hospital for Internal Medicine III, Medical University of Innsbruck, Innsbruck, Austria

Background: Transcatheter treatment of structural heart disease is becoming an everyday reality for an increasing number of surgeons, and effective training modalities for basic guide-wire skills, catheter handling, and periprocedural imaging are of growing relevance. In this video tutorial we present a beating-heart porcine model used as a high-fidelity training simulator for transcatheter cardiac valve procedures.

Methods: We use the Cardiac Biosimulator Platform (LifeTec Group™, Eindhoven, NL), a porcine beating-heart model for high-fidelity training purposes. A pulsatile piston pump is connected to a porcine heart via a sealed apical cannula. It is rinsed with saline solution and a beating-heart condition simulating physiological flow is achieved. Various mitral valve pathologies can be simulated, e. g. complete transcatheter edge-to-edge mitral valve repair, including periprocedural imaging, clip deployment, and quality control. Trainees practice clip navigation within the left atrium, transmitral passage, and clip orientation as well as grasping mitral valve leaflets to treat mitral regurgitation.

Results: Periprocedural imaging is achieved via epicardial echocardiography and left ventricular cardioscopy, and these imaging modalities are also relied on to guide surgeons during the simulations, as required. Due to the chosen configuration of the experimental set-up, demonstrations of procedures involving the right heart are not possible (for example, transseptal puncture). However, the set-up described here allows us to test and train using a range of transcatheter devices, and we believe this simulator could be advantageously implemented in resident programs for the benefit of surgeons, cardiologists, and patients.

Conclusions: The beating heart model enables realistic demonstration of the hemodynamic consequences of valve repair, and we believe that this simulator represents a valuable adjunct to surgical training.

22-6

Vergleich von „drug-coated balloon“ versus „drug-eluting stents“ in „small vessel disease“: „Trial sequential analysis“ und Metaanalyse

Bernhard Wernly[1], Sarah Eder[2], Richard Rezar[1], Michael Lichtenauer[1], Christian Datz[2], Alexander Lauten[3], Uta C Hoppe[1], Bruno Scheller[4], Raban Jeger[5], Christian Jung[6]

[1]Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Österreich
[2]Krankenhaus Oberndorf, Oberndorf, Österreich
[3]Charité – Universitätsmedizin Berlin, Berlin, Deutschland
[4]Universitätsklinikum Saarland, Homburg, Deutschland
[5]Universitätsklinikum Basel, Basel, Schweiz
[6]Universitätsklinikum Düsseldorf, Düsseldorf, Deutschland

Grundlagen: In den letzten Jahren wurden sowohl klinische als auch primär angiographische Studien in Patienten mit „small vessel disease“ (Koronargefäße mit ≤ 2 mm Durchmesser; SVD) publiziert. Ziel unserer Analyse war es, die vorhandene Evidenz zu diesem Thema einer formalen Metaanalyse zu unterziehen.

Methodik: Insgesamt wurden 959 Studientitel und Abstrakts untersucht. Sechs Studien (zwei retrospektive Register und vier randomisierte kontrollierte Studien; RCTs) mit insgesamt 1847 Patienten wurden in unsere Analyse inkludiert. Der primäre Endpunkt war „major adverse cardiac event“ (MACE). Die Heterogenität wurde mittels I2 Statistik untersucht. Es wurden auf Studienlevel Eventraten in einer „random-effect“ Metaanalyse berechnet (DerSimonian and Laird Random Effects Model).

Ergebnisse: Insgesamt wurden 959 Studientitel und Abstrakts untersucht. Sechs Studien (zwei retrospective Register und vier randomisierte kontrollierte Studien; RCTs) mit insgesamt 1847 Patienten wurden in unsere Analyse inkludiert. Der primäre Endpunkt war „major adverse cardiac event“ (MACE). Die Heterogenität wurde mittels I2 Statistik untersucht. Es wurden auf Studienlevel Eventraten in einer „random-effect“ Metaanalyse berechnet (DerSimonian and Laird Random Effects Model).

Schlussfolgerungen: In Patienten welche an SCD leiden, konnten keine Unterschiede zwischen einer Strategie welche DCB einsetzt und einer herkömmlichen DES Implantation hinsichtlich MACE, Mortalität und Komplikationen gezeigt werden. Die DCB Strategie erlaubt ein früheres Absetzen von dualer Plättchenhemmung und hinterlässt kein Fremdmaterial und könnte daher in diesem Kontext einen Vorteil gegenüber der DES-Implantation bieten.

22-7

Ist der akute transkatheter Aortenklappenersatz oder die Ballonvalvuloplastie im kardiogenen Schock bei dekompensierter Aortenklappenstenose zu bevorzugen?

Bernhard Wernly[1], Peter Jirak[1], Michael Lichtenauer[1], Uta C Hoppe[1], Alexander Lauten[2], Christian Frerker[3], Christian Jung[4]

[1]Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Österreich
[2]Charité – Universitätsmedizin Berlin, Berlin, Deutschland
[3]Asklepios Klinik Hamburg, Hamburg, Deutschland
[4]Universitätsklinikum Düsseldorf, Düsseldorf, Deutschland

Grundlagen: Patienten im kardiogenen Schock (CS) aufgrund einer dekompensierten Aortenstenose (AS) weisen eine sehr hohe Mortalität auf. Als Behandlungsoptionen stehen sowohl „emergenvy transcatheter aortic valve replacement" (eTAVR) als auch „emergency balloon valvuloplasty" (eBAV) zur Verfügung. Ziel unserer Analyse war es, diese beiden Verfahren im Rahmen einer Metaanalyse zu vergleichen.

Methodik: Die Daten wurden auf Studienebene analysiert. Die Heterogenität wurde mittels I2 Statistik analysiert. In einem „random-effects model" (DerSimonian and Laird) wurden Eventraten kalkuliert. Es wurden insgesamt acht Studien 311 Patienten inkludiert. Der primäre Endpunkt war die Mortalität nach 30 Tagen.

Ergebnisse: Für Patienten, welche einer eBAV ($n=238$) unterzogen wurden, war die Mortalität nach 30 Tagen 46,2 % (95 %CI 30,3–62,5 %; I2 74 %). Die Rate an relevanten Blutungen war 10 % (95 %CI 5,4–15,7 %; I2 13 %), die Schlaganfallrate 0,7 % (95 %CI 0,0–2,7 %; I2 0 %). Postinterventionell war eine Aorteninsuffizienz (AR) ≥ II in 8,6 % (95 %CI 0,4–23,5 %; I2 86 %) der Patienten nachweisbar. Die Mortalität nach 30 Tagen in der eTAVR ($n=73$) Gruppe war 22,6 % (95 %CI 12,0–35,2 %; I2 26 %). Die Rate an relevanten Blutungen war 5,8 % (95 %CI 0,5–14,7 %; I2 0 %), die Schlaganfallrate 5,8 % (95 %CI 0,5–14,7 %; I2 0 %). Postinterventionell war eine AR ≥ II in 4 % (95 %CI 0,0–12,1 %; I2 0 %) nachweisbar.

Schlussfolgerungen: Unabhängig von der gewählten interventionelle Strategie ist die Mortalität in Patienten mit CS aufgrund einer dekompensierten AS sehr hoch. Sowohl eTAVR als auch eBAV erscheinen technisch machbar. Eine primäre eTAVR Strategie hat jedoch den Vorteil, dass es zu besseren initialen hämodynamischen Ergebnissen kommt und kein Zweiteingriff notwendig ist. Daher könnte eTAVR in selektionierten Patienten einer eBAV Strategie überlegen sein. Sollte eTAVR nicht verfügbar sein, so kann eBAV als „bridge-to" elective TAVR sinnvoll sein.

Postersitzung 23 – Pulmonale Hypertension

23-1

Iron deficiency in chronic thromboembolic pulmonary hypertension

Ioana-Alexandra Campean[1], Roela Sadushi-Kolici[1], Hannah Magdalena Beckmann[2], Inbal Shafran[1], Nika Skoro-Sajer[1], Irene Marthe Lang[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Medical University of Vienna, Vienna, Austria

Background: Iron deficiency is common in patients with pulmonary hypertension and has been associated with worse clinical outcome. This retrospective observational study investigated the prevalence of iron deficiency in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: 147 patients diagnosed with CTEPH and 190 patients with pulmonary arterial hypertension (PAH) were analyzed. Iron deficiency (ID) was defined by serum levels of ferritin below 100 µg/L or levels of ferritin between 100 and 299 µg/L, and by a transferrin saturation (TSAT) less than 20% and raised levels of soluble transferrin receptor (sTfR) (>4.5 nmol/L for women, and >5.0 nmol/L for men). A sub-analysis of patients with elevated ferritin levels (defined as ferritin >500 µg/L) was performed. Furthermore, the association of ID with laboratory markers, 6 minute-walking distance (6MWD), WHO functional class (FC), and hemodynamic parameters was evaluated.

Results: Iron deficiency was present in 109 patients (74.1%) with CTEPH. Mean age was 64.7 ± 15.5 years. The number of female patients in the study group was 78 (53.1%) and males 69 (46.9%). 6MWD was 394.6 ± 129.9 m compared with 348.3 ± 130.8 m ($P=0.016$) in a control group with PAH. In-depth analysis revealed a significantly higher TSAT in CTEPH (23.2 ± 24.9%) compared with PAH (17.6 ± 12.2%, P = 0.008). However, in CTEPH patients mean levels of hemoglobin (13.3 ± 2.6 mmol/L), transferrin (271.8 ± 54.5%), and ferritin (139 ± 280.9 µg/L) were similar to those in PAH (13.1 ± 2.6 mmol/L, $P=0.370$; 137.4 ± 311.6, $P=0.961$; 273.8 ± 65.3, $P=0.771$). ID—CTEPH patients had a lower 6MWD (378.7 ± 130.7 m) than non-ID CTEPH patients without elevated ferritin levels (444.33 ± 121.65 m, P = 0.046).

Conclusions: There is a high prevalence of iron deficiency in CTEPH. Iron deficiency in CTEPH was associated with lower exercise capacity, but did not correlate with WHO FC, hemodynamics and survival.

23-2

Deficiency in milk fat globule-epidermal growth factor 8 delays thrombus resolution

Thomas M. Hofbauer, Arman Alimohammadi, Johanna Altmann, Smriti Sharma, Anna S. Ondracek, Roela Sadushi-Kolici, Veronika Seidl, Andreas Mangold, Irene M. Lang

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by the obstruction of pulmonary vessels by organized thrombotic and fibrotic lesions. Efferocytosis refers to the engulfment of apoptotic cells (ACs) by phagocytes, a process that is facilitated by bridging proteins. Milk fat globule-epidermal growth factor 8 (MFG-E8) connects phosphatidylserine on ACs with integrin alpha-v beta-III on phagocytes. MFG-E8-deficient mice develop auto-immune disease closely resembling systemic lupus erythematosus. In humans, decreased MFG-E8 levels were observed in patients with coronary heart disease and chronic obstructive pulmonary disease. Whether defective efferocytosis is involved in failure to resolve thrombi in CTEPH remains unknown. We aimed to assess whether deficiency in MFG-E8 is responsible for of chronic non-resolving thrombosis in CTEPH.

Methods: We employed a murine model of chronic thrombosis by inferior vena cava ligation, in MFG-E8 knockout (KO) or wild-type (WT) mice to assess thrombus formation and resolution. Thrombus size at days 3, 7, 14 and 28 after ligation was assessed using either histologic trichrome stainings ($n=4$–13 per group and time point) or in vivo high-frequency ultrasound ($n=10$ per group and time point). We furthermore recruited CTEPH patients ($n=60$, 53% female, mean age 56 ± 11 years) and sex- and age-matched healthy controls for measurement of MFG-E8 plasma levels using ELISA. In CTEPH patients, hemodynamic measurements were performed. Human lung specimens harvested during surgery for CTEPH or from healthy controls, and isolated monocytes from whole blood of CTEPH patients or controls were analyzed using RT-qPCR.

Results: We observed substantially increased thrombus volume in MFG-E8 KO mice compared to WT, which persisted until day 14 after ligation. In human CTEPH patients, MFG-E8 in plasma was increased compared to healthy controls. Similarly, CTEPH monocytes displayed higher concentrations of MFG-E8 mRNA. Conversely, MFG-E8 expression of CTEPH pulmonary artery specimens was downregulated. No correlations between MFG-E8 levels and hemodynamic parameters were observed.

Conclusions: MFG-E8 plays an important role in thrombus resolution. In CTEPH, dysregulation of efferocytosis via impaired MFG-E8 expression in the pulmonary arteries, might drive persistence of thrombus in pulmonary arteries. The absence of a correlation between MFG-E8 and hemodynamic measures argues against pressure as a confounder of the observation.

23-3

Combination of balloon pulmonary angioplasty and subcutaneous treprostinil for the treatment of chronic thromboembolic pulmonary hypertension

Christian Gerges[1], Grzegorz Kopec[2], Roela Sadushi-Kolici[1], Nika Skoro-Sajer[1], Mario Gerges[1], Walter Klepetko[3], Hiromi Matsubara[4], Irene M. Lang[1]

[1]Division of Cardiology, Department of Internal Medcine II, Medical University of Vienna, Vienna, Austria
[2]Department of Cardiac and Vascular Diseases, Jagiellonian University Medical College, John Paul II Hospital, Krakow, Krakow, Poland
[3]Division of Thoracic Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[4]Division of Cardiology, National Hospital Organization Okayama Medical Center, Okayama, Japan

Background: Balloon pulmonary angioplasty (BPA) is an effective treatment modality for patients with chronic thromboembolic pulmonary hypertension (CTEPH) not undergoing surgical endarterectomy. The recent randomized controlled CTREPH trial demonstrated that subcutaneous (sc) treprostinil improves hemodynamics, symptoms and exercise capacity of patients with inoperable CTEPH and patients with persistent or recurrent PH after pulmonary endarterectomy (PEA). Whether medical treatment in combination with BPA leads to an additional hemodynamic improvement needs to be determined. We compared hemodynamic change in patients receiving sc treprostinil in combination with BPA to those treated with BPA alone.

Methods: Between April 2014 and October 2018 40 CTEPH patients (36 inoperable and 4 persistent/recurrent PH after PEA) underwent complete BPA. Of these, 13 patients underwent BPA after finishing the CTREPH trial and continued receiving sc treprostinil within the open label phase of the study. Hemodynamics were assessed at study entrance (CTREPH group only), before BPA and 6 months after the last BPA session (both groups).

Results: At baseline, CTREPH patients exhibited similar mean pulmonary artery pressure (mPAP; 43.4 ± 7.6 mmHg vs. 40.3 ± 9.4 mmHg, $p=0.307$) but lower cardiac output (CO; 3.8 ± 1.3 L/min vs. 4.7 ± 0.9 L/min, $p=0.015$) and higher pulmonary vascular resistance (PVR; 10.7 ± 4.1 WU vs. 6.9 ± 3.4 WU, $p=0.004$) compared with patients who underwent BPA only. At 6-months follow-up, relative change in PVR (–58.3% [–68.3; –42.7] vs. –33.0% [–47.1; –15.1], $p=0.007$) and CO (+32.1% [9.9; 56.6] vs. +4.6% [–13.0; 14.8], $p=0.007$) was significantly higher in the CTREPH group compared to patients treated with BPA only, while change in mPAP was similar (–36.7% [–43.3; –19.5] vs. –25.7% [–37.7; –10.7], $p=0.500$, compared with –7% in the 24-week CTREPH trial).

Conclusions: Improvement in PVR and CO is enhanced by the addition of (sc) treprostinil in CTEPH patients undergoing BPA. However, a robust change in mPAP appears to be only achieved by BPA.

23-4

Improvement of right ventricular function after balloon pulmonary angioplasty in patients with chronic thrombembolic pulmonary hypertension

Maria Klara Frey, Christian Gerges, Roela Sadushi-Kolici, Nika Skoro-Sajer, Irene M. Lang

Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

Background: Ballon pulmonary angioplasty (BPA) is an emerging treatment option for patients with chronic thromboembolic pulmonary hypertension (CTEPH), who are ineligible for pulmonary endareterectomy (PEA) or who have recurrent or persistent pulmonary hypertension after surgery. BPA improves hemodynamics and exercise tolerance in these patients. The impact of BPA on right ventricular function is less clear.

Methods: Right ventricular (RV) function was assessed using echocardiography in 15 consecutive patients with CTEPH (69 ± 12 years old, 6 female) before and after BPA ($n=5 \pm 2.5$) according to current guidelines.

Results: After BPA, all measures of RV function assessed by echocardiography improved significantly, including fractional area change (+7%, $p<0.001$), TAPSE (+3.4 mm, $p=0.0028$) and RV free wall global strain (–6%, $p=0.0017$). Changes in RV func-

tion were accompanied by a significant decrease in NT-proBNP levels (–431 pg/ml, $p=0.001$).

Conclusions: RV function as assessed by echocardiography improves significantly after BPA in patients with CTEPH.

Postersitzung 24 – Rhythmologie 3

24-1

The prognostic impact of volume substitution on cardiac strain and the development of postoperative atrial fibrillation after cardiac surgery

Patrick Sulzgruber[1], Arnold Pilz[2], Sebastian Schnaubelt[3], Lorenz Koller[2], Niema Kazem[1], Andreas Hammer[1], Günther Laufer[4], Barbara Steinlechner[5], Tatjana Fleck[4], Aurel Toma[1], Johann Wojta[1], Alexander Niessner[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]Medical University of Vienna, Vienna, Austria
[3]Department of Emergency Medicine, Medical University of Vienna, Austria
[4]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[5]Division of Cardiothoracic and Vascular Anesthesia, Medical University of Vienna, Vienna, Austria

Background: Postoperative atrial fibrillation (POAF) represents a common complication after cardiac valve or coronary artery bypass surgery. Etiologically, multifactorial causes such as the patients' age, weight, comorbidities or local remodeling proved a strong association with this common arrhythmia. While strain of atrial tissue is known to induce atrial fibrillating impulses, less attention has been paid to potentially strain-promoting values during the peri- and post-operative period. Therefore, we aimed to determine the association of peri- and post-operative volume substitution on markers of cardiac strain and subsequently its impact on the promotion and development of POAF.

Methods: In this prospective observational study 271 patients undergoing elective cardiac surgery at the Medical University of Vienna were enrolled (median age: 69 years [IQR: 60–75 years]; 195 [72%] male gender). Intra- and post-operative data was collected from anesthesiologic and intensive care unit protocols. Multivariate binary logistic regression analysis was used to identify the prognostic value of volume substitution on the development of POAF.

Results: A total of 123 (45.4%) individuals developed POAF. The average intra-operative transfusion volume was significantly elevated in the POAF subgroup (605.6 ml [POAF] vs. 227.1 ml [non-POAF]; $p<0.001$). Moreover, the fluid balance within the first 24 hours after surgery was significantly higher in patients developing POAF (+1129.6 ml [POAF] vs. +544.9 ml [non-POAF]; $p=0.044$). We found that N-terminal pro brain natriuretic peptide (NT-proBNP) values were significantly elevated in patients that received any volume substitution (2860.0 pg/mL [Transfusion] vs. 1486.5 pg/mL [no-Transfusion]; $p=0.002$). In line with those results, the postoperative fluid balance was also found to have a direct and significant correlation with post-operative NT-ProBNP values ($r=0.287$, $p=0.002$). Of note, the amount of substituted volume proved to be a strong and independent predictor for POAF with an adjusted odds-ratio (OR) per one standard deviation (1-SD) of 2.49 (95% CI: 1.25–4.96; $p=0.009$).

Conclusions: Within the present analysis we were able to demonstrate that substitution of larger transfusion volumes presents a strong and independent predictor for the development of POAF. Via the observed distinct association with NT-proBNP values, it can reasonably be assumed that post-operative atrial fibrillating impulses are triggered via volume-induced cardiac strain.

24-2

Pacing threshold is influenced by cardiotoxic effects of anticancer therapies and predicts survival: A retrospective trial

Martin Riesenhuber[1], Andreas Spannbauer[1], Friedrich Rauscha[1], Herwig Schmidinger[1], Adelinde Boszotta[1], Thomas Pezawas[1], Christoph Schukro[1], Marianne Gwechenberger[1], Günter Stix[1], Anahit Anvari[1], Thomas Wrba[2], Cesar Khazen[3], Martin Andreas[3], Günther Laufer[3], Christian Hengstenberg[1], Mariann Gyöngyösi[1]

[1]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[2]IT Systems & Communications, Medical University of Vienna, Vienna, Austria
[3]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria

Background: Chemotherapy is an effective treatment strategy for the vast majority of malign tumor diseases. However, chemotherapy is also known for its cardiotoxic side effects. In patients with pacemakers (PM), pacing thresholds can be influenced by various cardiovascular circumstances, such as myocardial ischemia or electrolyte disorders as well as antiarrhythmic

	Cancer	Non-Cancer	p Value
Total (n)	321 (6.3%)	4749 (93.7%)	
- Women	110 (34.3%)	1920 (40.4%)	0.03
- Men	211 (65.7%)	2829 (59.6%)	
First implantation age	70.6±11.7	71.3±14.9	0.29
- Dual chamber PM	219 (68.7%)	3052 (64.8%)	0.16
- Single chamber PM	100 (31.3%)	1661 (35.2%)	

Fig. 1|24-2 Baseline parameters: Total and relative amount of women/men and dual- or single-chamber PM (chi-squared test). Mean and standard deviation of patients age at first PM implantation (years, t test)

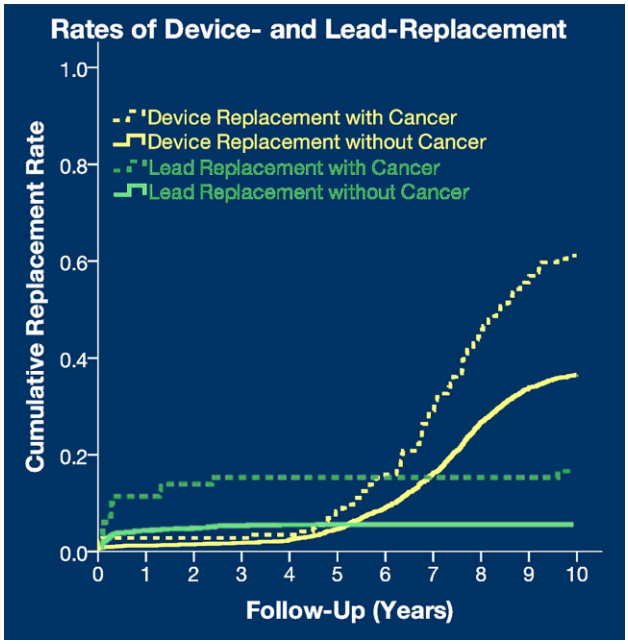


Fig. 2|24-2 Cumulative rates of device- and lead-replacements in a 10-year follow-up and PM-patients with/without cancer

drugs. Myocardial fibrosis or damage increase the pacing threshold. The aim of this study was to demonstrate the relation of pacing threshold with cardiotoxicity of cancer treatments compared to non-cancer patients and to evaluate the incidence of device and lead replacements in cancer and non-cancer patients.

Methods: This retrospective study is based on PM patients of the Medical University of Vienna between 2000 and 2015. In total, 5070 patients with PM and regular follow-up, complete mortality data, and available comorbidities were enrolled. Pacing threshold was measured at routine check-up's in our clinic. The clinical-wide electronic patient database was queried for ICD-10 Codes from the category C (malignant neoplasms) and I42 (cardiomyopathy). The dates of the first occurrence of the ICD-10 Codes were reported. Survival data was retrieved from the Federal Institute "Statistics Austria".

Results: Out of 5070 patients with PM, cancer was diagnosed in 321 patients after first PM implantation but prior to the last documented follow-up of the PM. Baseline patient data is presented in Fig. 1. Out of the 287 patients with cancer, 47 (16.4%) had cardiomyopathy. Out of the 4749 patients without cancer, 574 (12.1%) had cardiomyopathy ($p=0.03$). As indicated in Fig. 2, significant higher rates of device replacement occurred if malignant neoplasms were diagnosed within the 10-year follow-up (61.1% vs. 36.6%, HR 2.0, 95% CI 1.6–2.5, $p<0.001$). Furthermore, lead replacement was significantly more prevalent in PM-patients with cancer (17.6% vs. 5.3%, HR 3.5, 95% CI 1.9–6.5, $p<0.001$). Ventricular pacing threshold showed no difference at the time of first PM follow-up (0.6V IQR 0.5–1.0 in the non-cancer-group; 0.5V IQR 0.4–1.13 in the cancer-group, $p=0.07$). The mean follow-up period was 4.0 years. The ventricular pacing threshold increased in the cancer-group by 0.2V (IQR –0.25—+0.5). In contrast, there was no change in the non-cancer group (0V IQR 0–0.25, $p<0.001$). Mean survival times starting from patients first PM implantation were 14.3 years (95% CI 13.5–15.1) in patients without cancer and 12.2 years (95% CI 11.1–13.3) in patients with cancer. In a univariate COX regression of the cancer-group, a stronger increase of ventricular pacing threshold during the follow-up period was associated with worse 10-years survival outcome (HR 1.4, 95% CI 1.3–1.6, $p<0.001$).

Conclusions: In patients with PM and cancer, pacing threshold increases significantly stronger compared to patients without cancer. In PM-patients with cancer, an increase of the pacing threshold was a predictor for worse survival. Patients with cancer had a significantly increased rate of device- and lead-replacement compared to patients without cancer. These findings might be closely related to the cardiotoxic effects of anticancer chemotherapy.

24-3

Use of implantable cardioverter defibrillators in young patients – a single center experience

Martin Manninger[1], Felix Bäcker[1], Ursula Rohrer[1], Egbert Bisping[1], Peter Lercher[1], Rita Riedlbauer[1], Günther Prenner[1], Michael Sereinigg[2], Andreas Zirlik[1], Daniel Scherr[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Division of Transplantation Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

Background: Implanted cardioverter defibrillators (ICD) are effective in primary and secondary prevention of sudden cardiac death. ICD implantation in young patients is potentially problematic due to the increased cumulative risk of device-related complications. Recent ESC guidelines promote implantation of a subcutaneous ICD (S-ICD) for young patients without need of antibradycardic or antitachycardic pacing to prevent complications related to intravascular leads. In this study, we aimed to describe indications, arrhythmic recurrences and complications of the ICD therapy in young patients and answer the question, how many of these patients could have been supplied with an S-ICD.

Methods: We included all patients that have been implanted with an ICD at an age of 30 years or younger at the Medical University of Graz since 1999 into this retrospective analysis. Follow-up data was collected from the hospital information system and included data on ICD indication, tachyarrhythmias, ICD therapies, complications, battery longevity and pacing rates. Potential S-ICD candidates were assessed retrospectively, if they either had no indication for permanent antibradycardic pacing or frequent antitachycardic pacing. The study was approved by the local ethics committee.

Results: We included 28 patients (median (IQR) age at ICD implantation: 21.5 (17, 25) years; 80% males). Median follow-up duration was 8 (2.6, 10.9) years. Indications for ICD implantation were cardiomyopathies (40%), channelopathies (20%), congenital heart disease (20%), idiopathic ventricular fibrillation (13%) and ischemic cardiomyopathy (7%). 87% of patients received an ICD as secondary prevention, 47% after aborted sudden cardiac death. Most patients ($n=20$, 67%) were implanted with single chamber devices, nine patients (30%) were implanted with dual chamber devices and one patient received a CRT-D device. Median time to device revision was 5 (4.3, 6.3) years, median battery longevity was 7 (6.2, 7.6) years. Most common device complications were lead dislocations ($n=9$) and device-pocket related complications ($n=7$). 60% of patients received appropriate device therapies (13% for ventricular fibrillation), while more patients received appropriate device therapy if they were implanted for secondary prevention (65 vs. 25%). Inappropriate shock rate was 17%, inappropriate shocks occurred

only in patients who also received adequate shocks. Only 5 of 28 patients fulfilled criteria for S-ICD implantation.

Conclusions: In our cohort, young ICD patients had a high number of arrhythmic events and device-related complications. S-ICD implantation could have prevented some of these complications, but, retrospectively, only a few patients fulfilled S-ICD criteria.

24-4

Physical activity is reduced in patients with a wearable cardioverter defibrillator who experience ventricular arrhythmias

Martin Manninger[1], Ursula Rohrer[1], Ashley Burch[2], Benjamin D'Souza[3], J. Rod Gimbel[4], Tsuyoshi Masuda[5], Samuel Sears[6], Andreas Zirlik[1], Daniel Scherr[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]East Carolina Heart Institute, Greenville, NC, United States of America
[3]University of Pennsylvania, Philadelphia, PA, United States of America
[4]Cardiac Rhythm Specialist, Bayside, WI, United States of America
[5]ZOLL Medical, Pittsburgh, PA, United States of America
[6]East Carolina University, Greenville, NC, United States of America

Background: The utility of accelerometer-based activity data to identify patients at risk of sustained ventricular tachycardia or fibrillation (VT/VF) has not been investigated. The aim of the current study was to determine whether physical activity is associated with shocked VT/VF in patients with an ejection fraction ≤35%. Specifically, differences in daily step count were examined for patients who received a shock for sustained VT/VF and those who did not.

Methods: A database of German patients who were consecutively prescribed a WCD from April 2015 to May 2018 was used for this study. Consent was obtained from all patients. Four weeks of physical activity and shock data, beginning with the first week of WCD wear was used for the current study.

Results: Based on the ROC curve outcome, daily step count during week 1 demonstrated good accuracy in predicting group (Shocked versus Non-Shocked (area under the curve, c-index = 0.71, 95% CI = 0.65–0.77, $p < .001$). A cut-off daily step count of 3,637 during week 1 was identified. Patients who walked fewer than 3,637 steps per day during the first week of WCD prescription were 4.6 times more likely to experience a shock than those who walked more than 3,637 steps per day (OR = 4.64, 95%CI = 2.81–7.67, $p < .001$).

Conclusions: Engaging in regular physical activity is critical for optimal heart failure management. Among patients at risk for sudden cardiac arrest, encouraging a minimum step count of 4,000 steps per day could reduce the likelihood of sustained VT/VF.

24-5

Endoscopic thoracic bilateral sympathectomy as a bailout therapy in refractory electrical storm

Martin Manninger[1], Alfred Maier[2], Christoph Theuermann[3], Ursula Rohrer[1], Egbert Bisping[1], Peter Lercher[1], Günther Prenner[1], Andreas Zirlik[1], Daniel Scherr[1]

[1]Division of Cardiology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Division of Thoracic Surgery, Department of Surgery, Medical University of Graz, Graz, Austria
[3]Department of Anaesthesiology and Intensive Care Medicine, Medical University of Graz, Graz, Austria

Background: Therapeutic options in electrical storm are antiarrhythmic drug therapy, sedation, overdrive pacing and urgent catheter ablation. In case of electrical storm refractory to these treatments, several bailout therapies such as sympathectomy, blockade of the stellate ganglion, renal denervation, stereotactic radiation and heart transplantation have been proposed in case series. We report the first case of bilateral sympatectomy in a patient with electric storm in Austria.

Methods: Case presentation:

Results: A 79-year-old patient with non-ischemic cardiomyopathy was implanted with a CRT-D in 2011 for primary prevention of sudden cardiac death and due symptomatic heart failure and left bundle branch block. The patient presented with electrical storm due to incessant ventricular tachycardia (VT) in November 2017. Amiodarone was started, beta blocker therapy was up titrated, potassium and magnesium levels were increased but the patient refused catheter ablation. After three subsequent hospital admissions due to electrical storms within two months, the patient consented with endocardial ablation. Substrate mapping showed no scar areas, no critical isthmus, just fractionated potentials in the left ventricular infero-basal, lateral-basal and mid anterior regions. Substrate modification was performed. The clinical VT was still inducible in non-invasive programmed stimulation. Four days later, the patient experienced electrical storm and was planned for epicardial ablation. Epicardial mapping revealed small low voltage areas in the left basolateral, no late potentials. A VT pacemap was created and showed good match at the left laterobasal region. A linear lesion was performed, and the clinical VT was no longer inducible. Twelve days later, the patient presented with recurrent electrical storm and was intubated due to incessant VTs and five adequate shocks within 8 hours. A bailout therapy with endoscopic thoracic bilateral sympathectomy was off

Conclusions: Endoscopic thoracic sympathectomy after failed endocardial and epicardial ablation for electrical storm resulted in good short-term outcome and may be a valid bailout therapy in selected cases.

24-6

Edoxaban Treatment in routiNe clinical prActice for patients with atrial fibrillation (AF) in Europe (ETNA-AF-Europe): Baseline characteristics of the Austrian patients

Thomas Weiss[1], Marianne Gwechenberger [2], Johann Auer[3], Carl Kaulfersch[4], Alexander Kober[5], Peter Siostrzonek[6]

[1]Institute for Cardiometabolic Diseases, Karl Landsteiner Society, Vienna, Austria
[2]Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[3]Department of Cardiology and Intensive Care, St Josef Hospital, Braunau, Austria
[4]Department of Cardiology, Klinikum Klagenfurt am Wörthersee, Klagenfurt, Austria
[5]Praxis St. Aegyd am Neuwalde, St. Aegyd am Neuwalde, Austria
[6]Department of Internal Medicine II (Cardiology), Hospital Barmherzige Schwestern Linz, Linz, Austria

Background: Non-vitamin K antagonist (VKA) oral anticoagulants (NOACs) have substantially improved anticoagulation therapy for prevention of stroke and systemic embolism in patients with atrial fibrillation (AF). The available routine care data have demonstrated the safety of different NOACs in routine practice; however, such data for edoxaban are scarce. Here, we report baseline characteristics of the Austrian patients in comparison to the European population recruited for this study.

Methods: ETNA-AF-Europe is a multinational, multi-centre, post-authorisation, observational study (NCT02944019) conducted in 825 sites in 10 European countries. Patients will be followed up for four years.

Results: Overall 299 were recruited in Austria, 5 were lost to follow up. Mean patient age was 73.8 years with an average creatinine clearance of 66.5 mL/min, 53.8% of the patients were male. The calculated CHA_2DS_2-VASc and HAS-BLED mean scores were 3.2 and 2.4, respectively. Interestingly, the reported CHA_2DS_2-VASc and HAS-BLED mean scores were 3.4 and 2.0. Patient numbers for low (CHA_2DS_2-VASc = 0), intermediate (CHA_2DS_2-VASc = 1) and high (CHA_2DS_2-VASc ≥ 2) risks of stroke including dosing patterns are shown in Table 1. High-risk patients (those with prior stroke, prior major bleeding, prior intracranial bleed or CHA_2DS_2-VASc ≥ 4) comprised 40.6% of the overall population. Fifty-five percent of patients were not on anticoagulation prior to initiating edoxaban whilst 14.0% switched from a VKA and 10.9% switched from another NOAC. In Austria a total of 32.8% of patients in ETNA-AF-Europe received the reduced dose of edoxaban 30 mg which was similar to the percentage of patients eligible for dose reduction in the pivotal ENGAGE AF-TIMI 48 trial. Overall, 83.8% of patients received an edoxaban dose in line with the criteria outlined in the label.

Conclusions: Conclusion: Edoxaban was majorly prescribed to elderly, mainly anticoagulation-naïve patients with AF, with an overall good adherence to the approved label.

Table 1 | 24-6

Baseline Characteristics: CHA_2DS_2-VASc Risk Classes [calculated] (by dose)		
ETNA-AF		
Edoxaban Dose	30 mg	60 mg
Patients (N)	96	197
Low Risk (0)	1.0%	6.1%
Low-moderate Risk (1)	4.2%	11.7%
Moderate to High Risk (≥2)	94.8%	82.2%

24-7

Advanced cryoablation: the „Flushing Maneuver“

Alexander Weber[1], Hanno Oswald[2], Heiko Frank[2]

[1]Klinikum Güstrow, Güstrow, Germany
[2]Universitätsklinikum Oldenburg, Oldenburg, Germany

Background: Cryoablation of pulmonary veins is a cornerstone in ablation of atrial fibrillation. Large randomised trials proofed safe and effective treatment of patients with symptomatic paroxysmal atrial fibrillation.

Methods: According to recent recommendations a successful freeze should isolate a PV within the first 60 seconds. Otherwise another freeze should be applied. As a consequence real time PV signals are mandatory. Most procedures are performed with a stable cryoballon and good PV occlusion and a proximal achieve wire position. Real time PV isolation can be monitored and judged in this setting during the freezing periode. Sometimes one can only get a stable position of the cryoballon with patent PV occlusion after pushing the achieve wire in a further distal part of the treated PV. In this setting loss of real time PV signals on the achieve wire occurs, preventing instantly judging the effectiveness of the applied freeze. To overcome this dilemma we developed the “Flushing maneuver” which is described now (and will be illustrated @ the poster).

Results: Step 1: Stable cryoballon position with good RSPV occlusion. Distal achieve wire position without PV signals. Step 2: Flushing the PV with contrast dye after freezing the ballon delays the temperature dip in the PV, preventing early freezing inside the vein. In comparison temperature curve w/o prolonged flushing. Step 3: Withdrawal of the achieve wire after antral freezing with PV signals in a persisting stable ballon position. Step 4: Successful real time PV Isolation.

Conclusions: The flushing maneuver can be a useful technique to get realtime PV signals in unstable cryoballon positions.

Chirurgie-Abstrakts

C-1

Positive family history of cardiovascular disease and long-term outcomes after coronary artery bypass grafting in younger patients: a genetic paradox?

Hannes Abfalterer[1], Marion Dietl[1], Julian Wagner[1], Katherine Bates[2], Michael Grimm[1], Josef Fritz[2], Hanno Ulmer[2], Elfriede Ruttmann[1]

[1]University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Medical Statistics, Informatics, and Health Economics, Medical University of Innsbruck, Innsbruck, Austria

Background: Parental cardiovascular disease (CVD) is a known risk factor for premature CVD. It is unknown whether a positive family history (PFH) also affects long-term outcomes after coronary artery bypass grafting (CABG).

Methods: Data come from a prospective longitudinal study of first, non-emergent, CABG patients ($n=5389$). From this study, 2553 patients with premature CAD undergoing CABG <60 years were identified. In line with the Framingham offspring study, a premature PFH was defined when a patient's father and/or mother experienced their first CV event at <55 (father) and <65 (mother) years of age, respectively. Adjusted multivariable Cox proportional hazards regression was used to assess the effect of PFH on overall and MACCE-free survival.

Results: Premature PFH was found in 54.2% of patients ($n=1375$). Within these patients, 66.1% had a father who experienced a premature CV event ($n=909$), 27.8% a mother ($n=382$) and 6.1% both parents ($n=84$). Following CABG, PFH was associated with improved long-term survival (adjusted HR, 0.66; 95% CI, 0.50–0.91; $p=0.011$) and MACCE-free survival (adjusted HR, 0.73; 95% CI, 0.68–0.89; $p=0.01$). In contrast, multiple arterial grafting by bilateral internal thoracic arteries improved both survival (adjusted HR, 0.52; 95% CI, 0.36–0.74; $p<0.001$), and MACCE-free survival (adjusted HR, 0.41; 95% CI, 0.31–0.54; $p<0.001$).

Conclusions: In this cohort of patients undergoing CABG under 60 years of age, PFH was highly prevalent. Whilst it is evident that a PFH increases the risk of requiring CABG at younger ages, this study shows that PFH is also, paradoxically, protective regarding long-term outcomes.

C-2

16 years' experience of lead extractions: Does success depend on expertise?

Tandis Aref, Cesar Khazen, Frieda-Maria Kainz, Thomas Aschacher, Günther Laufer, Martin Andreas

Division of Heart Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria

Background: The number of pacemaker and ICD implantations increased steadily by extending the indications for cardiac rhythm management devices (CRMs) which consequently led to an increase in lead-related hazards requiring lead removal in the long run. This study focuses on the safety, effectiveness and long-term outcomes of lead extractions performed at a large-volume centre.

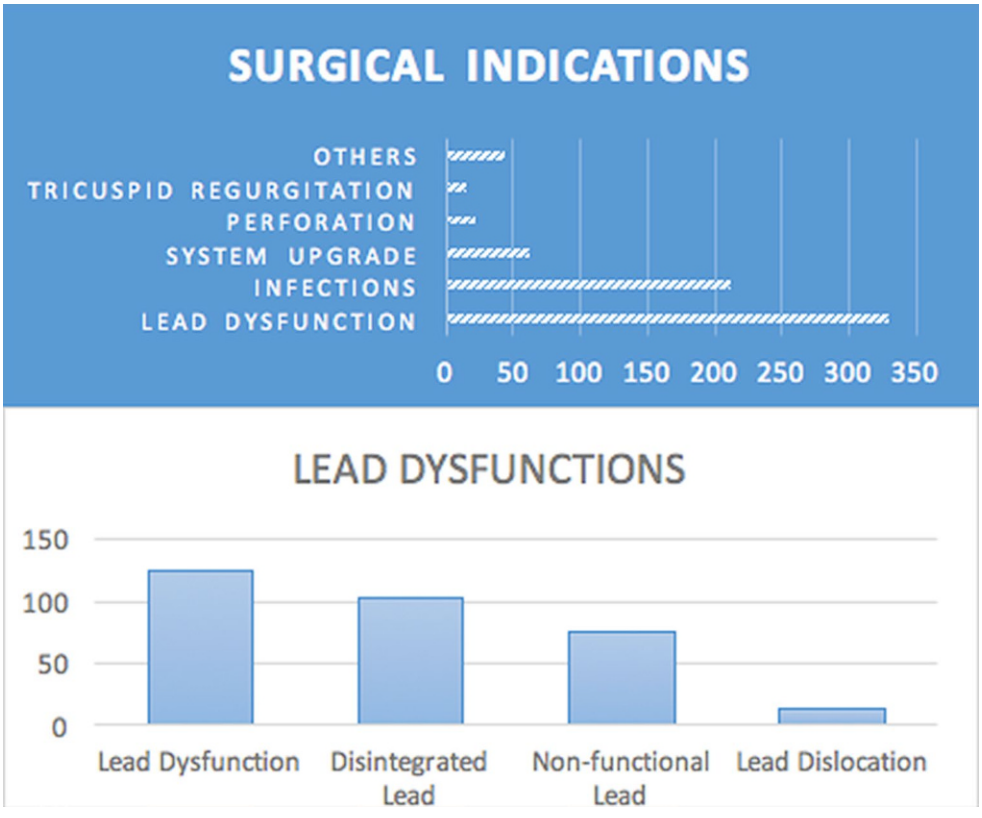


Fig. 1 | C-2

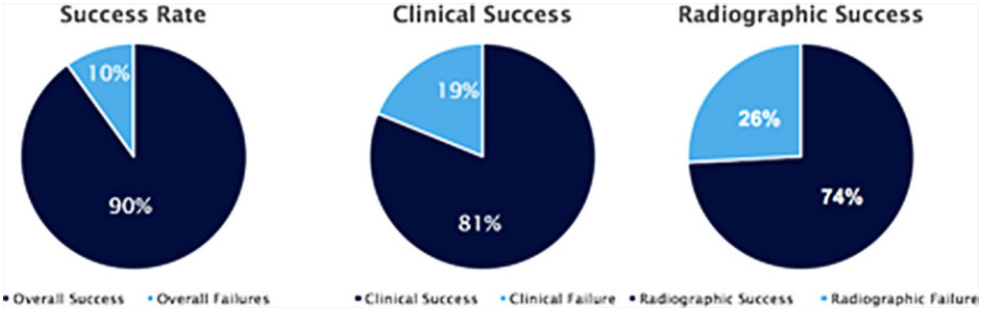
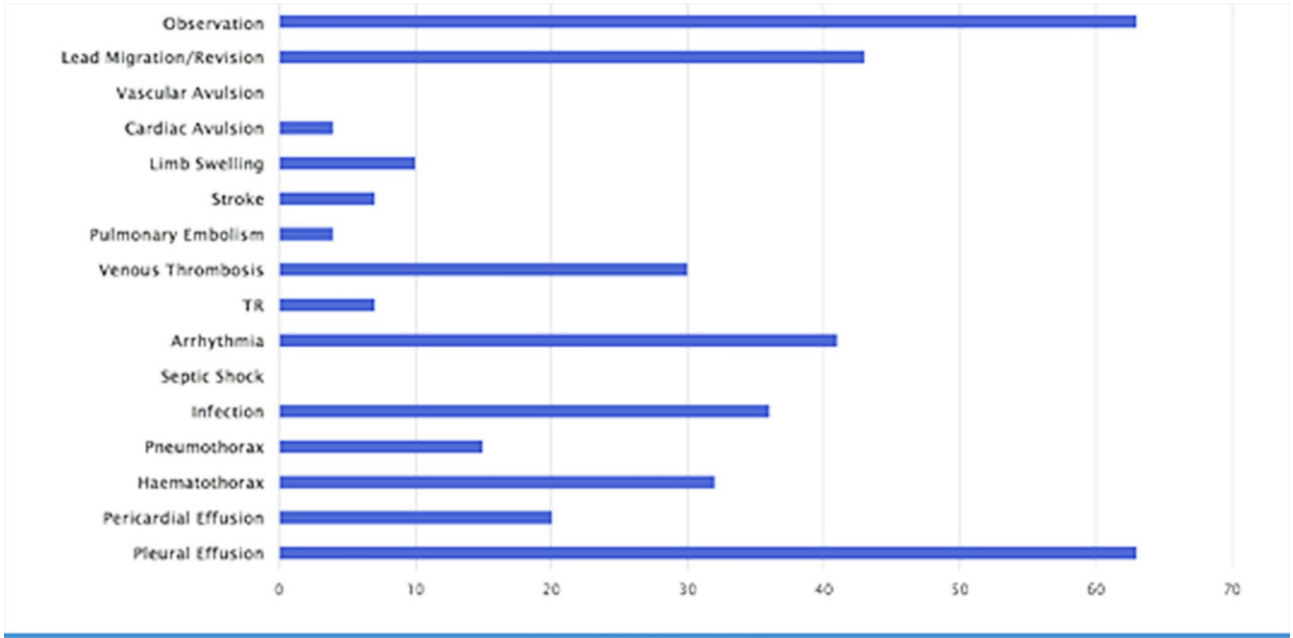


Fig. 2 | C-2



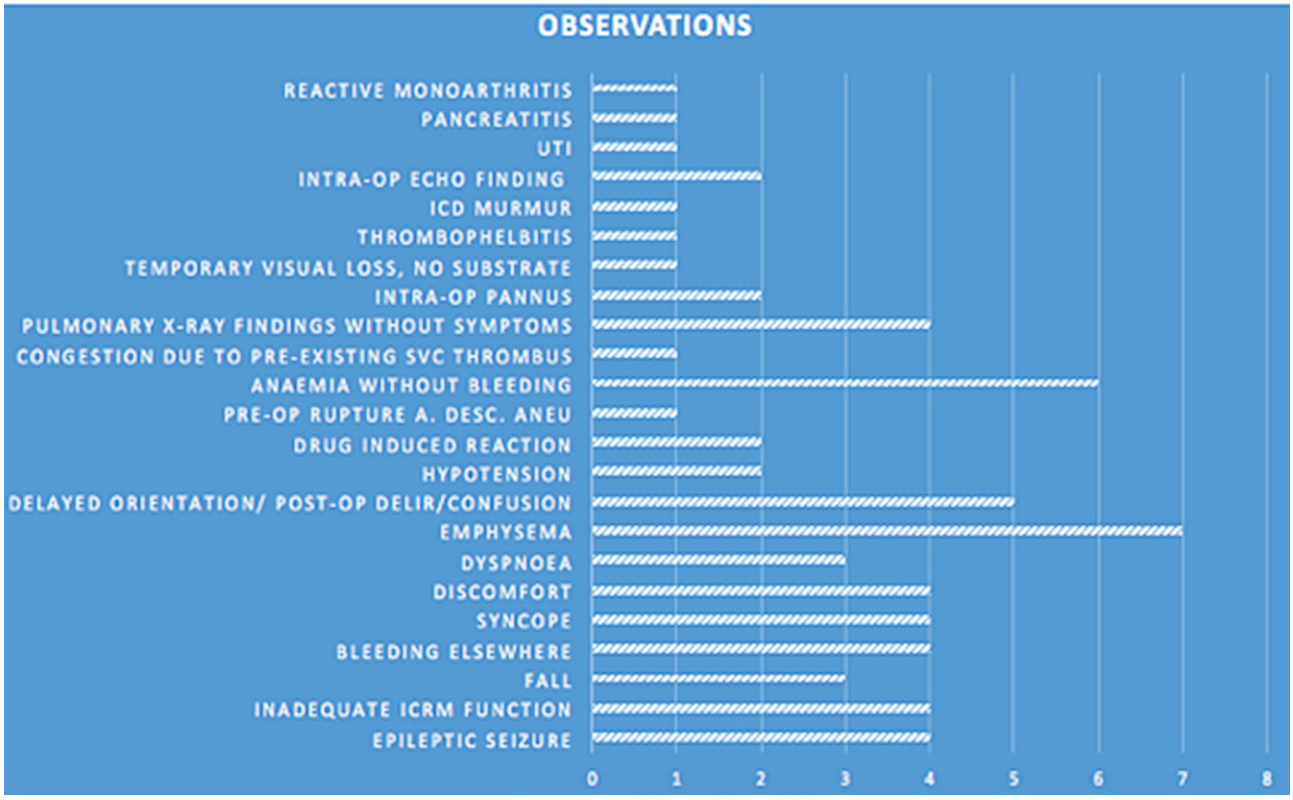


Fig. 3 | C-2

Methods: We conducted a retrospective cohort study under prospective application methods (cross-sectional telephone follow-up) including all lead extractions performed from January 2000 until December 2016 at the General Hospital of Vienna as defined by the Heart Rhythm Society. A total number of 466 patients were enrolled yielding 542 procedures within this time period. Procedures were performed by a dedicated team in the cardiac operating theatre or the cardiac hybrid room with cardiopulmonary bypass standby.

Results: 144 (31%) female and 322 (69%) male patients with a mean age of 64 ± 17 years were analysed. Eight extraction-related deaths were observed (Traction: 4; Laser: 0; Mechanical Extractor: 4): Three due to pre-existing active endocarditis, embolism and multi-organ failure, three due to bleedings, one owing to high-grade MR based on PMVL rupture and only one patient died peri-procedural because of pulseless electrical activity (intraoperative mortality: 0.2%). 30-day mortality was 3%. Leading surgical indications were lead dysfunctions (n = 329, 48%), followed by infections (n = 211, 31%) and system upgrades (n = 62, 9%). Overall success was achieved in 90% (n = 488). 406 cases (75%) were successfully completed, 82 (15.1%) were partially accomplished (e. g. remaining tips) and 54 (9.9%) failures were recorded. Leads were efficiently removed by manual traction (39%), extractors and mechanical sheaths (37%), laser (15%), femoral snares (2%) or through sternotomy and thoracotomy (7%). Life-threatening extraction-related complications were rare.

Conclusions: Our results disclose excellent success rates and low incidences of extraction-related complications due to the specific team expertise at a tertiary care centre. Failures were mainly attributable to early years of experience, extractions performed by manual traction or whenever severe fibrous lead attachments were present. A hybrid room and cardiopulmonary bypass standby are specifically increasing patient safety.

C-3

Kontrollierte Membran-Ruptur in TEVAR – Erfahrungen mit der STABILISE-Technik in 9 Patienten mit De Bakey Typ I und IIIb Dissektion

Oliver Bernecker, Felix Nagel, Elisabeth Dunkel, Florian Koutny, Christoph Holzinger

Klinische Abteilung für Herzchirurgie, Universitätsklinik St. Pölten, St. Pölten, Österreich

Grundlagen: Der Entry-Verschluss mittels TEVAR (Thoracic endovascular aortic repair) in der akuten oder subakuten Phase einer De Bakey Typ IIIb oder subakuten Phase einer operierten De Bakey Typ 1-Dissektion bietet bei vielen Patienten eine vielversprechende Therapiealternative zum „Watchful-waiting". Bisherige TEVAR-Techniken zeigen jedoch eine relativ hohe Zahl an Re-interventionen und Wachstum des falschen Lumens aufgrund weiterer Entries distal der gestenteten Aorta. Die STABILISE-Technik (Stent-assisted balloon induced intimal disruption and relamination in aortic dissection repair) stellt den Zustand einer uniluminären Aorta wieder her um diese langfristig zu stabilisieren und könnte damit die Anzahl an aortalen Re-interventionen reduzieren.

Methodik: 9 Patienten mit akuter oder subakuter Typ B Dissektion oder Restdissektion nach einer operierten Typ A Dissektion wurden mit TEVAR und STABILISE-Technik behandelt. Alle Patienten wurden mit einer Kombination aus Stentgrafts und Barestents von Zone 0, 2 oder 3 bis infrarenal gestentet. Anschließend erfolgte die kontrollierte Ruptur der Dissektionsmenbran mittels Ballon. Das Follow-up betrug 2–11 Monate.

Ergebnisse: Im Zeitraum 06/2018 bis 01/2019 wurden 9 Patienten mit der STABILISE-Methode behandelt. Das Follow-up betrug 100 %, der Nachbeobachtungszeitraum 60 bis 277 Tage. Das Patientenalter betrug 58 ± 7 Jahre. Die STABILISE-Technik konnte in 8 von 9 Fällen erfolgreich durchgeführt werden. Die Gesamtmortalität, Paraparese/-plegierate und Reinterventionsrate im beobachteten Zeitraum betrug 0 %. Die renale Malperfusion konnte von präoperativ 39 % auf postoperativ 6 % gesenkt werden. Die Thrombosierung des falschen Lumens im gestenteten Bereich betrug 100 %

Schlussfolgerungen: Intraoperativ zeigte die STABILISE-Technik eine sehr gute technische Reproduzierbarkeit. Die

Tab. 1 | C-3

Follow-up	100 %	Komplikationen	
Gesamt-Mortalität	0 %	Paraparese/-plegie	0 %
Alter	58 ± 7 Jahre	Endoleak	1/9 (11 %)
Geschlecht	22 % weibl.	Leistenrevision	0 %
Strahlungsdauer	36 ± 20 min.	Re-Intervention	0 %
KM-Verbrauch	97 ± 47 ml	Wachstum gesamte Aorta	3 ± 2 mm
Liquordrainage	0 %	Technischer Erfolg	8/9 (89 %)
Prox. Landungszone		Wachstum False Lumen	0 %
Aortenbogen (Zone 0–2]	4/9 (44 %)	(Stentbereich)	
A.Descendens	5/9 (56 %)		
Indikation TEVAR		Thrombosierung False Lumen	100 %
Wachstum nach A-Diss	4/9 (44 %)	(Stentgraftbereich)	
High Risk B-Diss	5/9 (56 %)		
Präop. Malperfusion	8/9 (89 %)	**Postop. Malperfusion**	1/9 (11 %)
Viszeral	2/18 (11 %)	Viszeral	0/18 (0 %)
Renal	7/18 (39 %)	Renal	1/18 (6 %)

Nachuntersuchungen der Patienten zeigten einen sehr stabilen Verlauf mit vollständigem Verschwinden des falschen Lumens im behandelten Teil der Aorta. mit einer sehr geringen Wachstumsdynamik im Beobachtungszeitraum. Weltweit wurden bisher 80 STABILISE-Fälle mit sehr gutem Ergebnis publiziert. Sollten sich diese Ergebnisse im laufenden internationalen multicenter STABILISE-Registry auch mittel- und langfristig bestätigen, könnte die kontrollierte Membran-Ruptur zu einem Paradigmenwechsel in der Behandlung von akuten und subakuten Typ B Dissektionen sowie Typ A Restdissektionen führen.

C-4

A case of a giant left atrial myxoma

Wolfgang Dietl[1], Igor Schor[1], Lena Haindl[2], Lukas Ameri[2], Alexander Farag[3], Michael Wimmer[3], Christoph Holzinger[1]

[1]Department of Cardiac Surgery, University Hospital St. Poelten, Karl Landsteiner University of Health Sciences, St. Poelten, Austria
[2]Department of Internal Medicine 3, University Hospital St. Poelten, Karl Landsteiner University of Health Sciences, St. Poelten, Austria
[3]Department of Anaesthesiology and Intensive Care Medicine, Karl Landsteiner University of Health Sciences, St. Poelten, Austria

Case Report: A previously healthy 39 year old female patient was referred to our emergency department by a local physician. She had experienced shortness of breath and noticed a significant worsening over the past two weeks. The initial lab test showed a slightly elevated D-Dimer, indicative of a pulmonary embolism. By using bed-side echocardiography, a huge tumor (8×6×4 cm) was detected in the left atrium, originating from the intra-atrial septum and prolabating through the mitral valve into the left ventricle. A left atrial myxoma was suspected. The tumor caused a functional stenosis of the left ventricular outflow tract. A CT scan of the thorax confirmed the tumor location and showed neither signs of pulmonary embolism nor coronary artery disease. The size of the tumor and the hemodynamically significant stenosis of the left-ventricular outflow tract were determinative to immediately excise the tumor. A surgical intervention was done via median sternotomy, cardio-pulmonary bypass was established using bi-caval cannulation. After aortic cross-clamping, both venae cavae were snared and the right atrium was opened. Subsequently, the intra-atrial septum was opened at the foramen ovale in order to locate the basis of the tumor. The septum was excised and the tumor removed. The mitral valve and the tricuspid valve showed annular enlargement in the TEE and were reconstructed using Edwards Physio Rings. The intra-atrial septum was reconstructed with an autologous, formaldehyde-fixated pericard

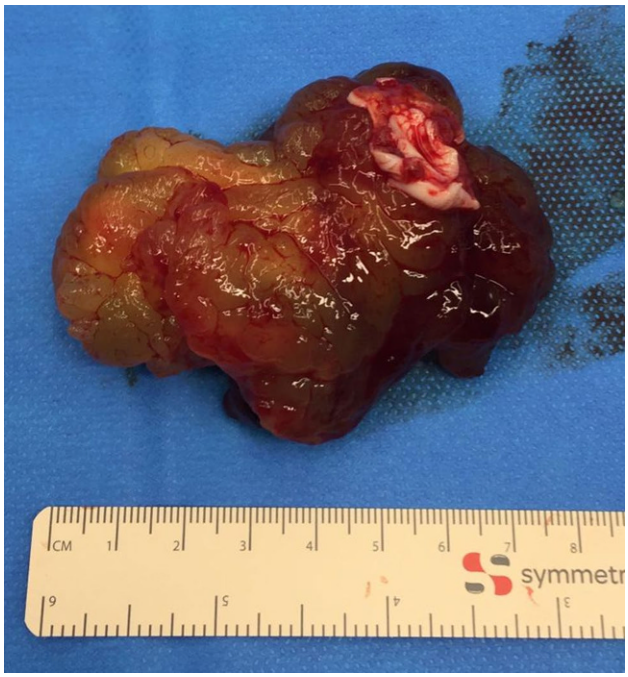


Fig. 1 | C-4 Intra-operative specimen

C-5

Cardial malperfusion in type A dissection: rare complication?

Julia Dumfarth, Simone Gasser, Lukas Stastny, Markus Kofler, Severin Semsroth, Christoph Krapf, Vitalis Zujs, Michael Grimm

University Hospital for Heart Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background: Coronary artery malperfusion secondary to type A aortic dissection has been reported in 10–15% of all patients. Aim of this study was to evaluate impact of cardial malperfusion on surgical treatment and outcome after repair.

Methods: Between January 2000 and December 2018 362 patients were deemed surgical candidates for repair of type A dissection. In a total of 77 patients (21.3%) cardial malperfusion was observed. Surgical treatment as well as hospital outcome in these patients was evaluated. Survival was compared to patients without preoperative coronary artery malperfusion.

Results: Median time from onset of chest pain to surgery was 415 minutes. Despite this rapid approach 8 (10.4%) patients died before cardiopulmonary bypass could successfully be installed. 15 patients showed severe calcification of coronary arteries in imaging scans, which could be reconfirmed during surgery by palpability. Root replacement was performed in 25 patients (32.5%), additional coronary artery bypass grafting was in 15 patients (20%). Extracorporeal membrane oxygenation had to be implanted in 7 patients (10.4%) due to severe low cardiac output syndrome, only four patients could successfully be weaned from support. Hospital mortality of patients with coronary malperfusion was 20.3%. Kaplan Meier analysis revealed significantly lower survival rates in patients with preoperative cardial malperfusion ($p = 0.026$).

Conclusions: Coronary malperfusion remains a dreaded complication in type A aortic dissection. Despite a rapid approach toward revascularization of the ischemic myocardium, cardial malperfusion has negative impact on survival in patients undergoing surgery for type A aortic dissection.

C-6

Percutaneous femoral access for complex open cardiac surgery and endovascular aortic repair – Experience with the Perclose ProGide™ vascular closing device

Elisabeth Dunkel, Felix Nagel, Christoph Holzinger, Oliver Bernecker

Department of Cardiac Surgery, University Hospital St. Poelten, Karl Landsteiner University of Health Sciences, St. Poelten, Austria

Background: Access to the femoral vessels is becoming increasingly important due to transcatheter aortic valve implantation (TAVI), endovascular aortic repair or minimally invasive mitral valve repair. While many cardiologists and radiologists have adopted a percutaneous approach using vascular closing devices (VCD), cardiac surgeons routinely use a surgical cut down to access the femoral vessels. In this retrospective report, we evaluate our experience with percutaneous femoral access via a suture mediated VCD in TEVAR, minimal invasive and open surgery.

Methods: In all patients the Perclose ProGlide™ Suture-Mediated Closure System (Abbott) was used for femoral access. For each vessel, two devices were routinely used. Maximal outer device diameter was 25.5 French for arterial access and 25 French for venous access. All femoral vessels were percutaneously accessed with the use of the Perclose ProGlide™ Device. Using ultrasound-guided single puncture of the common femoral artery or the femoral vein facilitated vessel access. All vessels were consecutively dilated to the final size of the used stentgraft or CPB-cannula. Arterial vessel-diameter was evaluated in all patients treated with TEVAR preoperatively via CT-angiography.

Results: A total of 47 femoral vessels, including 22 femoral arteries and veins for Cardiopulmonary Bypass (CPB) and 25 arteries for TEVAR, were analysed in our study. 44 ProGlides were used for femoral cannulation in patients undergoing Cardiopulmonary Bypass (CPB) and 53 ProGlides for patients treated with TEVAR. 32 (68,1%) of the procedures were elective, 11 (23,4%) urgent and 4 (8,5%) emergent. Technical success was obtained in 100%. Complications occurred in four cases (8.5%), three (12%) in TEVAR and one (4.5%) in CPB with need for surgical revision due to hematoma/bleeding in three cases (6.4%) and pseudoaneurysm in one (2.1%). No dissection, stenosis, vessel occlusion, infection or seroma was noted.

Conclusions: Percutaneous femoral access using a VCD is a well-established technique for TAVI and TEVAR procedures with a very low rate of adverse events being in many ways superior to a surgical cutdown. In our experience this technique can be safely reproduced for femoral CPB-cannulation in complex cardiac surgery. While prospective data is lacking, it is very

Table 1 | C-6 Results

Proglides	TEVAR	CPB	Total
Number of femoral vessels	25	22	47
Number of femoral arteries	25	13	38
Number of femoral veins	0	9	9
Number of Proglides	53	44	97
Mean age ± SD (years)	56 ± 13,5	59 ± 12,2	58 ± 12,8
Gender			
Female	5 (20 %)	0	5 (10,6 %)
Male	20 (80 %)	22 (100 %)	42 (89,4 %)
Mean EuroSCORE II	4,8 % ± 9,1 %	6,4 % ± 12,5 %	5,6 % ± 10,8 %
Number of reoperations	16 (64 %)	17 (77,3 %)	33 (70,2 %)
Number of second intervention femoral vessels	5 (20 %)	4 (18,2 %)	9 (19,2 %)
Vascular pathology			
Marfan syndrome	3 (12 %)	2 (9,1 %)	5 (10,6 %)
Other connective tissue disease	0	1 (6,7 %)	1 (2,1 %)
Arteriosclerosis	2 (8 %)	2 (9,1 %)	4 (8,5 %)
Duration of procedure (min)	126 ± 55	292 ± 105	203 ± 117
Outer device diameter (French)	21,6 ± 2,5	21 (arterial) 25 (venous)	
Acuity			
Elective	15 (60 %)	17 (77,3 %)	32 (68,1 %)
Urgent	8 (32 %)	3 (13,6 %)	11 (23,4 %)
Emergent	2 (8 %)	2 (9,1 %)	4 (8,5 %)
Overall complications	3 (12 %)	1 (4,5 %)	4 (8,5 %)
Pseudoaneurysm	1 (4 %)	0	1 (2,1 %)
Hematoma/bleeding	2 (8 %)	1 (4,5 %)	3 (6,4 %)
Arteries	3	0	3
Veins		1	1

likely that a percutaneous access might be the better alternative for femoral CPB-cannulation than a surgical cutdown.

C-7

Später mechanischer Aortenklappenersatz mit intakt belassener Pulmonalarterie nach arterieller Switch Operation

Petra Filzmaier[1], Igor Knez[1], Alissa Strugger[1], Ayse Gürbüz[1], Jakub Krumnikl[2], Gernot Grangl[3], Martin Köstenberger[3], Siegfried Rödl[4], Andreas Gamillscheg[3], Otto Dapunt[1]

[1]Klinische Abteilung für Herzchirurgie, Universitätsklinik für Chirurgie, Medizinische Universität Graz, Graz, Österreich
[2]Klinische Abteilung für Herz-, Thorax-, Gefäßchirurgische Anästhesiologie und Intensivmedizin, Medizinische Universität Graz, Graz, Österreich
[3]Klinische Abteilung für Pädiatrische Kardiologie, Universitätsklinik für Kinder- und Jugendheilkunde, Medizinische Universität Graz, Graz, Österreich
[4]Universitätsklinik für Kinder- und Jugendheilkunde, Medizinische Universität Graz, Graz, Österreich

Grundlagen: Die arterielle Switch Operation (ASO) ist seit der Einführung 1975 die Standard Herangehensweise bei Patienten mit Transposition der großen Arterien (TGA). Dabei werden der Truncus pulmonalis und die Aorta durchtrennt und nach dem Lecompte Manöver getauscht, sodass die Pulmonalarterienäste in ap Stellung vor der Aorta zu liegen kommen. Somit fungiert die Pulmonalklappe als Neoaortenklappe und umgekehrt. Diese atypische anatomische Konstellation beeinflusst das Langzeitergebnis und mögliche Reoperationen. Zu den bekannten Spätkomplikationen gehören RVOT Obstruktion, Koronararterienstenosen, Wurzelaneurysma der Neoaorta und/oder Neoaorteninsuffizienz (AI). Die Inzidenz für eine Reoperation beträgt 5–10 %. Wir berichten über zwei Fälle mit mechanischem Aortenklappenprothesenersatz aufgrund von Neoaortenklappeninsuffizienz als Spätkomplikation nach ASO.

Methodik: Die Eingriffe wurden bei zwei Patienten an unserer Klinik durchgeführt. Eine zu korrigierende Aortenwurzeldilatation lag in beiden Fällen nicht vor. Ebenso konnten bei beiden Patienten die Pulmonalarterien ausreichend mobilisiert und daher intakt belassen werden um die Aorta zu erreichen. Pat. A: 12-jährige Patientin mit 155 cm und 44 kg. Die primär vorhandene congenitale Fehlbildung war DORV mit d-TGA Stellung (Taussig-Bing Anomalie). Operativ wurde bis dato ein Blalock Taussig Shunt links sowie spätere Ligatur dieses, eine Ballonatrioseptektomie, Pulmonalarterienbanding, VSD-Patchverschluss sowie PFO Direktnaht und schließlich Switch Operation vor 12 Jahren im Alter von 1,5 Monaten durchgeführt. Es zeigte sich im USKG ein vergrößerter LV, die Aortenklappe dysplastisch mit einer Aortenklappeninsuffizienz (AI) III-IV Grades und PHT von 225 ms sowie Insuffizienzjet fast bis zur Herzspitze. Die Aorta asc. war auf 3,3 bis 3,5 cm dilatiert. Pat. B: 28-jähriger Patient mit 172 cm und 69 kg. Die congenitale Fehlbildung war eine l-TGA mit VSD und AOIST. Beim Patienten wurde ein Pulmonalarterienbanding mit Ductusligatur sowie End/End Anastomose der AOIST durchgeführt, bevor die Switch Operation im Alter von 6,5 Monaten stattfand. Im USKG zeigte die Aortenklappe eine moderate bis höhergradige AI mit einer PHT von 367 ms und breitem Insuffizienzjet bis zur Hälfte des LV, sowie ein Vmax. von 1,6 m/s. Der Aortenbulbusbereich mit einem Durchmesser bis max. 3,8 cm.

Ergebnisse: Bei Pat. A wurde die Operation als Vierteingriff durchgeführt mit Implantation einer 19 mm mechanischen Prothese bei nicht rekonstruierbarer Neoaortenklappe sowie Patchplastik der Aorta asc. Es kam nach Entfernen der passageren Schrittmacherelektroden zum Auftreten eines Hämatoms, welches am 9. postoperativen Tag chirurgisch saniert werden musste. Sie konnte danach am 16. postoperativen Tag entlassen werden. Bei Pat. B wurde eine 23 mm große mechanische Doppelflügelprothese als Dritteingriff bei nicht zur rekonstruierender Neoaortenklappe implantiert. Der postoperative Verlauf zeigte sich komplikationslos, sodass die Entlassung am 8. postoperativen Tag stattfand. Leider kam es bei Pat. A im weiteren Verlauf zu einer hochgradigen supravalvulären Aortenstenose im Bereich des Perikadpatches sowie einer Ektasie des Bulbus Aortae, sodass die Patientin 4,5 Jahre später mit einem supracoronaren Ascendensersatz reoperiert werden musste.

Schlussfolgerungen: Aortenklappenersatz nach arterieller Switch Operation ist eine bekannte jedoch nicht allzu häufige Spätkomplikation, wobei häufig eine zusätzliche Aortenwurzeldilatiation vorhanden ist. In der Literatur wird u. a. späte ASO, Pulmonalarterienbanding, DORV, VSD, bikuspide Neoaortenklappe, präoperative pulmonale Hypertonie, perioperative milde AI, milde LVOT Obstruktion und längeres Follow-up als Risikofaktor für eine AI beschrieben. Ebenso wurde berichtet, dass eine Taussig-Bing Anomalie eine höhere Rate an AI hat. Eine Reoperation nach ASO ist aus chirurgischer Sicht sicherlich aufgrund der anatomischen Verhältnisse herausfordernd, jedoch zeigten sich gute Daten bzgl. Outcome und Überleben in der Literatur. Lebenslange Kontrolluntersuchungen sind allerdings essentiell.

C-8

Comparative aortic arch mapping for targeted endovascular treatment

Fernando Frick[1], David Vesely[1], Niusha Taheri[1], Bernhard Winkler[1], Gabriel Weiss[1], Martin Grabenwöger[2], Markus Mach[3]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Sigmund Freud University, Medical Faculty, Vienna, Austria, Vienna, Austria
[3]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Austria, Graz, Austria

Background: The improvement of endovascular therapy options is a key issue in the future treatment of aortic arch pathologies. Therefore, extensive knowledge of the aortic arch anatomy and adjacent structures is of great importance, especially for individual therapy adaption and development of endovascular stent-grafts.

Methods: The study comprises 68 patients who underwent treatment at our institution between 2005 to 2018. Twelve patients (17.6%) had been referred for treatment of aortic arch pathologies, fifty-seven patients (82.4%) had been treated due to different other pathologies not involving the thoracic aorta. In the course of a subsequent computer tomographic examination anatomical characteristics of the aortic arch and supra-

aortic branches were evaluated. Especially the diameter of the individual vessels and the distance to each other, as well as the patient's age, sex, height, and weight, were considered.

Results: Distances and diameter of the supra-aortic branches showed no significant differences between the pathological and physiological cohort. However, the diameter of the ascending aorta differed significantly between the two cohorts (path. 43.1 mm ± 8.1 mm vs. phys. 37.8 mm ± 5.9 mm, $p=0.012$). Moreover, no difference has been found between the diameter or the length of the A. subclavia sinistra measured to the take-off of the A. vertebralis between the two cohorts (diameter path. 3.4 mm ± 1.3 mm vs. phys. 4.2 mm ± 1.5 mm, $p=0.136$; length: path. 40.5 mm ± 9.2 mm vs. phys. 43.3 mm ± 7.7 mm, $p=0.351$). While gender or age-related differences have not been observed, patients with aortopathological presentation had higher rates of concomitant atrial fibrillation (6 (54.5%) vs. 6 (13.3%), $p=0.008$) and arterial hypertension (11 (91.7%) vs. 28 (60.9%) $p=0.040$).

Conclusions: Endovascular treatment of aortic arch pathologies remains challenging. However, this study showed consistent measurements between pathologic and physiologic aortic arch anatomy, creating a benchmark for the development of an "off-the-shelf" stent-graft incorporating the aortic arch vessels. Nevertheless, the three-dimensionality, the dynamic and the structural complexity of the (pathological) aorta require further research and a larger data pool.

Tab. 1 | C-9 Operative Data and Outcome_nighttime surgery

	All patients ($n=319$)	Nighttime ($n=129$)	Daytime ($n=190$)	*p*-value
ECC time (median, min)	220	228.5	218	0.389
Selective antegrade cerebral perfusion	214 (67%)	81 (63%)	133 (70%)	0.389
Postoperative ECMO support	14 (4%)	9 (7%)	5 (3%)	0.723
Postoperative malperfusion syndrome	49 (15%)	18 (14%)	31 (16%)	0.725
Postoperative neurologic injury	54 (17%)	22 (17%)	32 (17%)	0.961
Need for postoperative hemofiltration	97 (30%)	44 (34%)	53 (28%)	0.194
Revision for bleeding	81 (25%)	32 (25%)	49 (26%)	0.938
30-day mortality	51 (16%)	21 (16%)	30 (16%)	0.923

C-9

Nighttime surgery for acute aortic dissection Type A – a single-center experience

Simone Gasser[1], Lukas Stastny[1], Markus Kofler[1], Severin Semsroth[1], Christoph Krapf[1], Nikolaos Bonaros[1], Thomas Schachner[1], Michaela Plaikner[2], Michael Grimm[1], Julia Dumfarth[1]

[1]University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria

Background: Objectives Recent literature highlighted worse outcome of patients undergoing nighttime surgery for Type A aortic dissection (AADA). The objectives of our study were to evaluate whether surgery during nighttime has a negative impact on mortality and postoperative morbidity and if patients in a stable preoperative condition benefit from an elective daytime setting.

Methods: Our hospital database for was screened for time of skin incision for repair of AADA. Mortality and morbidity were compared between nighttime (time of skin incision 19.00–5.00) and daytime (time of skin incision 05.01–18.59) surgery. Liberal surgical approach with a short time interval from symptom onset to surgery is persued at our institution for all patients with AADA, regardless patient's preoperative state. Baseline and operative data did not differ between the two groups except for a higher rate of axillary arterial cannulation site in the daytime group ($p=0.011$). Preoperative risk factors, operative data as well as outcome parameters were evaluated for 30-day mortality.

Results: From May 2000 to March 2018 345 patients underwent surgery for AADA. Time of skin incision was available in 92% ($n=319$). 46.7% ($n=149$) of all patients were already suffering from a complication of the underlying AADA and presented

	univariate			*multivariate*		
	HR	IQR	P-value	HR	IQR	P-value
Age	**1.042**	**1.017 – 1.069**	**<0.01**	**1.043**	**1.015 – 1.071**	**<0.01**
Diabetes	**4.167**	**1.751 – 9.915**	**<0.01**	**3.282**	**1.268 – 8.496**	**0.01**
Preoperative Creatinine	2.205	1.013 – 4.801	0.04	1.595	0.686 – 3.706	0.28
Preoperative malperfusion	**2.538**	**1.360 – 4.740**	**<0.01**	**2.524**	**1.210 – 5.266**	**0.01**
Preoperative CPR	5.676	2.267 – 14.21	<0.01	2.181	0.634 – 2.181	0.22
Preoperative tamponade	**3.541**	**1.841 – 6.804**	**<0.01**	**2.491**	**1.177- 5.271**	**0.02**
Preoperative intubation	**3.493**	**1.673 – 7.293**	**0.01**	**4.072**	**1.275 – 13.003**	**0.02**
Nighttime surgery	1.031	0.561 – 1.894	0.92			

Fig. 1 | C-9 Univariate and multivariate analysis for 30-day mortality

in a critical preoperative state. Overall 30-day mortality was 15.6% ($n=51$). Surgery during nighttime was performed in 41% ($n=131$) of our study cohort. Multivariate analysis excluded nighttime surgery to be an independent risk factor for 30 day mortality, but identified age (OR 1.043, 95% CI 1.015–1.071, $p=0.002$), pericardial tamponade (OR 2.491, 95% CI 1.177–5.271, $p=0.017$), malperfusion syndrome (OR 2.524, 95% CI 1.210–5.266, $p=0.014$) and intubation (OR 4.072, 95% CI 1.275–13.003, $p=0.018$) as independent preoperative risk factors. There was no significant difference in survival and morbidity between nighttime- and daytime group.

Conclusions: We could not confirm recent finding of worse outcome in patients undergoing surgery during nighttime.

C-10

Identifying patients unlikely to benefit from transcatheter aortic valve implantation

Daniela Geisler[1], Philipp Szalkiewicz[1], Thomas Poschner[1], Victoria Watzal[1], Jong Hui Lee[1], Slakov Ursula[1], Stephanie Wallner[1], Bernhard Winkler[1], Gabriel Weiss[1], Andreas Strouhal[2], Christopher Adlbrecht[2], Georg Delle-Karth[2], Martin Grabenwöger[3], Markus Mach[4]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria, Vienna, Austria
[3]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Sigmund Freud University, Medical Faculty, Vienna, Austria, Vienna, Austria
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Austria, Graz, Austria

Background: TAVI has extended the treatable spectrum of patients with severe aortic stenosis towards a multimorbid collective often denied for surgical valve replacement (SAVR) and already exceeding their average life expectancy. Therefore, a lack of clinical benefit due to early mortality or no improvement in the quality of life is frequently observed. Surgical risk scores and frailty assessment tools show considerable limitations in predicting mortality after TAVI and allocating scarce societal resources becomes increasingly challenging. This study aims to identify patients unlikely to benefit from TAVI and determine risk factors predicting futility.

Methods: 532 consecutive patients undergoing TAVI (transapical access $n=266$ [50%], female $n=335$ [63%]) between June 2009 and December 2016 were prospectively enrolled in the institutional registry and retrospectively analyzed to identify predictors associated with 1-year mortality. The median age was 82 ± 7.3 years, 335 (63%) were female.

Results: A total of 91 (17.1%) patients died within the first year after TAVI. By multivariate analysis preprocedural predictors of futility were peripheral vascular disease (PVD), cerebrovascular disease (CVD) and home oxygen dependence (odds ratio [OR]: –.099; 95% confidence interval [CI]: –.178 to –.020; $p=0.014$, OR: –.113; 95% CI: –.201 to –.025; $p=0.012$, OR: –.348; 95% CI: –.589 to –.107; $p=0.005$, respectively), whereas postprocedural factors for futility were identified as dialysis, conversion to open heart surgery and total ventilation time in hours (OR: –.278; 95% CI: –.472 to –.083; $p=0.005$, OR: –.601; 95% CI: –.841 to –.361; $p<0.001$, OR: –.002; 95% CI: –.003 to –.001; $p<0.001$, respectively).

Conclusions: In this retrospective analysis, we were able to identify predictors of 1-year mortality after TAVI. While factors such as PVD and CVD are incorporated in traditional risk scores, home oxygen dependence is an often underestimated risk factor in preprocedural risk assessment. Since the reasons for conversion to open surgery and prolonged ventilation can be diverse, our study stresses the importance of future research directed towards nephroprotection to spur progress in making TAVI safer for its old and frail patient collective.

C-11

Comparison of direct vision mini thoracotomy and 3D fully endoscopic mitral valve surgery

Daniel Höfer[1], Herbert Hangler[2], Johannes Holfeld[2], Michael Grimm[1], Ludwig Müller[2], Nikos Bonaros[2]

[1]University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background: Various "minimally invasive" methods for mitral valve (MV) procedures are established, however, no consent exists concerning superiority of one distinct procedure. We evaluate the outcome of two different minimally invasive mitral valve procedures.

Methods: Between 2001 and 2018 a total number of 900 minimal invasive valve procedures were performed at our center. In group 1 ($n=600$) a video assisted direct vision mini thoracotomy was performed, group 2 ($n=300$) was treated with 3D fully endoscopic MV surgery. Various reconstructive methods (artificial chords, resection, sliding leaflet plasty, patch augmentation, ring implantation) or valve replacement were applied in both groups.

Results: Demographic data and etiology of MV disease (79% degenerative) were not significantly different between the two groups. Operative times were almost equal (group 1 vs. group 2: mean extracorporeal circulation time 204 minutes vs. 210 minutes, mean aortic cross clamp time 112 minutes vs. 113 minutes). Conversion to sternotomy occurred more often in group 1 (7.4% vs. 3%; $p=0.04$), as well as conversion to MV replacement (4.7% vs. 1.3%; $p=0.05$). Blood transfusions were necessary in 9.6% in group 1, in 6.5% in group 2 ($p=0.07$), revisions for bleeding occurred significantly more often in group 1 (12.9% vs. 4.4%; $p=0.003$). In both groups the procedure was safe with perioperative death rates of 5% vs 0.7%; $p=0.04$. Repair results were even better in group 2 with no sign of MI at discharge in 75% vs 65% in group 1; $p=0.02$). Reoperation for recurrent MI also was a rare event in both groups (5% in group 1 vs. 0.5% in group 2; $p=0.01$).

Conclusions: Patients, types of lesions and operative techniques were comparable within the two groups. Operative times show no significant difference despite technically more demanding procedure in endoscopically treated patients. Repair rates and incidence of severe complications as well as mortality were even better in the fully endoscopic group. Both methods are feasible and safe, however, the totally endoscopic procedure is even less invasive with equal or better results and therefore superior.

C-12

Total endoscopic mitral valve surgery for endocarditis

Daniel Höfer, Lukas Stastny, Johannes Holfeld, Herbert Hangler, Michael Grimm, Nikos Bonaros, Ludwig Müller

University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background: To evaluate feasibility, safety and outcomes of total endoscopic mitral valve (MV) surgery in patients with MV endocarditis.

Methods: Between 2015 and 2018 a total number of 237 minimal invasive mitral valve procedures were performed. In 17 cases (7.2%) the indication was MV endocarditis (5 acute and 12 sub-acute procedures). Surgery was performed totally endoscopic with the use of a 3D endoscope via lateral micro incision.

Results: Mean age was 61 years, 9 (53%) were male, 8 (47%) female. Both MV leaflets were affected in 8 (43%) cases, in all patients MV repair was successfully accomplished. Repair techniques included resection, pericardial patch plasty, sliding leaflet plasty and neochordae. Ablation for atrial fibrillation ($n=1$) and tricuspid valve repair ($n=1$) were concomitant procedures. Mean bypass time was 204 minutes, mean aortic cross clamp time was 118 minutes. Conversion to sternotomy was required in 1 (5.9%) patient, in 2 (11.8%) patients revision for bleeding was necessary. Due to pulmonary edema 2 (11.8%) patients were successfully treated with ECMO. All patients were discharged home alive with excellent repair results (82% grade 0 MV insufficiency). Three patients (18%) required reoperation due to recurrent endocarditis.

Conclusions: Patients presenting with MV endocarditis require complex MV repair under complicated circumstances. Endoscopic procedure might reduce trauma and facilitate success of MV repair. Our series demonstrate feasibility and safety of total endoscopic MV surgery due to endocarditis with no mortality and excellent repair results.

C-13

Microplegia versus Cardioplexol® in coronary artery bypass surgery with minimal extracorporeal circulation: comparison of two cardioplegia concepts

Luca Koechlin[1], Bejtush Rrahmani[2], Urs Zenklusen[2], Thomas Doebele[2], Brigitta Gahl[2], Martin Grapow[2], Friedrich Eckstein[2], Oliver Reuthebuch[2]

[1]Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, Basel, Switzerland
[2]University Hospital Basel, Basel, Switzerland

Background: Aim was to compare the combined use of the Myocardial Protection System® and our refined microplegia with Cardioplexol® in coronary artery bypass grafting using the minimal extracorporeal circulation.

Methods: The analysis focussed on propensity-score matched pairs of patients in whom microplegia or Cardioplexol® was used. Primary efficacy endpoints were high-sensitivity cardiac troponin T on postoperative day 1 and peak values during hospitalization. Furthermore, we assessed creatine kinase and creatinine kinase-myocardial type as well as safety endpoints.

Results: 56 patients who received microplegia and 155 patients who received Cardioplexol® were included. The use of the microplegia was associated with significantly lower geometric mean (reference range) peak values of high-sensitivity cardiac troponin T (233 (194–280) ng/L vs. 362 (315–416) ng/L; $p=0.001$), creatinine kinase (539 (458–633) U/L vs. 719 (645–801) U/L; $p=0.011$), and creatinine kinase-myocardial type (13.8 (9.6–19.9) µg/L vs. 21.6 (18.9–24.6) µg/L; $p=0.026$); and a shorter length of stay on the intensive care unit (1.5 (1.2–1.8) days vs. 1.9 (1.7–2.1) days; $p=0.011$). Major adverse cardiac and cerebrovascular events occurred with roughly equal frequency (1.8% vs. 5.2%; $p=0.331$).

Conclusions: The use of our refined microplegia protocol was associated with lower peak values of high-sensitivity cardiac troponin T, creatinine kinase, and creatinine kinase-myocardial type and with a shorter length of stay on the intensive care unit, as compared to the use of Cardioplexol® in isolated coronary artery bypass surgery using minimal extracorporeal circulation.

C-14

Early diagnosis of myocardial infarction in patients with a history of coronary artery bypass grafting

Luca Koechlin[1], Jasper Boeddinghaus[1], Joan Elias Walter[1], Tobias Zimmermann[1], Ivo Strebel[1], Desiree Wussler[1], Jeanne Du Fay De Lavallaz[1], Thomas Nestelberger[1], Maria Rubini Gimenez[1], Patrick Badertscher[1], Karin Wildi[1], Tobias Reichlin[2], Danielle Menosi Gualandro[1], Raphael Twerenbold[1], Christian Mueller[1]

[1]Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, Basel, Switzerland
[2]University Hospital Bern, Bern, Switzerland

Background: The early diagnosis of acute myocardial infarction (AMI) can be particularly challenging in patients with a history of coronary artery bypass grafting (CABG) due to possibly altered chest pain sensation and pre-existing electrocardiographic abnormalities.

Methods: In this international multicenter study, final diagnoses were adjudicated by two independent cardiologists among patients presenting to the emergency department with symptoms suggestive of AMI. Thirty-four chest pain characteristics (CPC), four electrocardiographic (ECG) variables and hs-cTnT/I concentrations at presentation and after 1 h were compared against the adjudicated final diagnosis. Patients were stratified according to the presence or absence of previous CABG.

Results: Among 4015 patients (3686 without and 329 with previous CABG), incidence of AMI was significantly higher in patients with previous CABG (35% versus 18%; $p<0.001$). Three CPCs (9%) showed a different diagnostic performance (interaction $p<0.05$) with loss of diagnostic value in patients with previous CABG: chest pain aggravated by breathing (likelihood ratios [LR] 1.09 [95%CI, 0.73–1.65] versus 0.51 [95%CI, 0.43–0.61] in patients without CABG), chest pain aggravated by emotional stress (LR 1.40 [95%CI, 0.91–2.15] versus 0.68 [95%CI, 0.58–0.81]), and chest pain area > 3 cm (LR 0.93 [95%CI, 0.82–1.06] versus 1.07 [95%CI, 1.04–1.11]). Similarly, two (50%) electrocardiographic findings showed a different diagnostic performance (interaction $p<0.05$), again with loss of diagnostic value in patients with prior

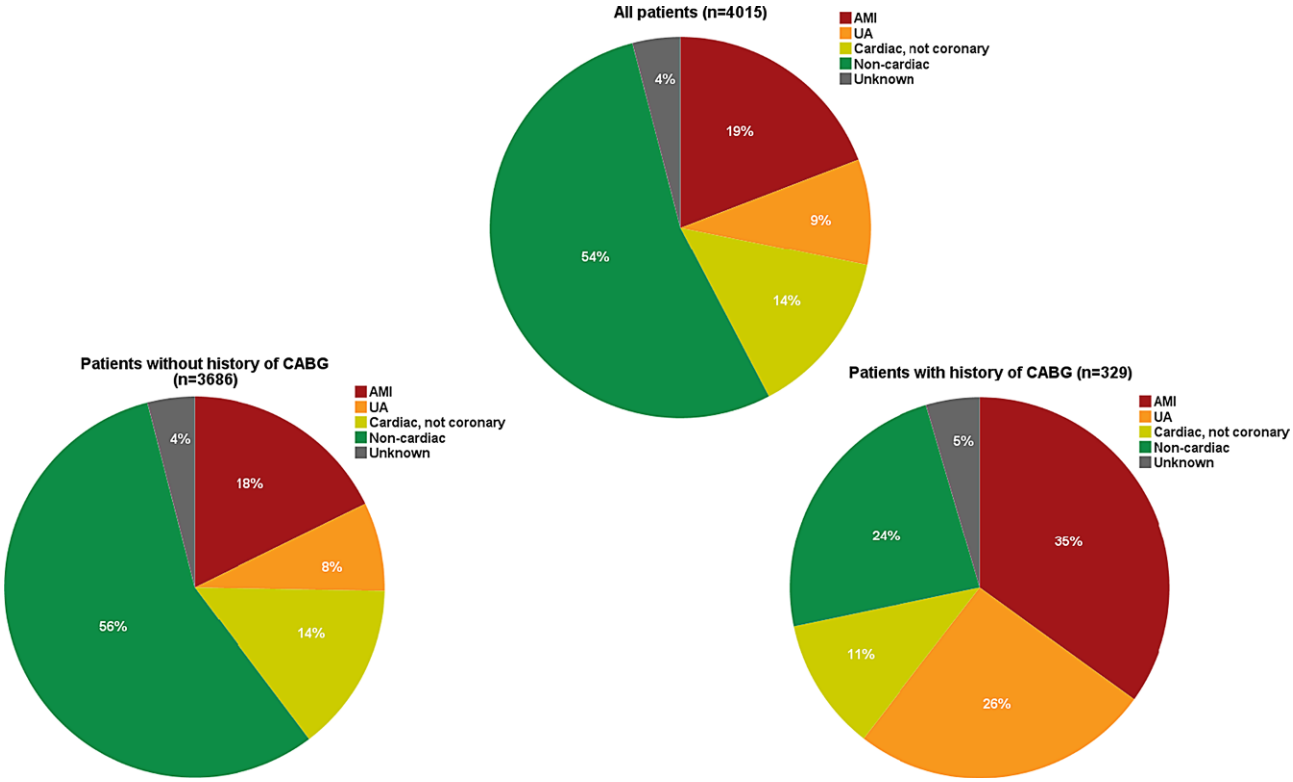


Fig. 1 | C-14 Differential diagnoses according to the presence or absence of previous CABG

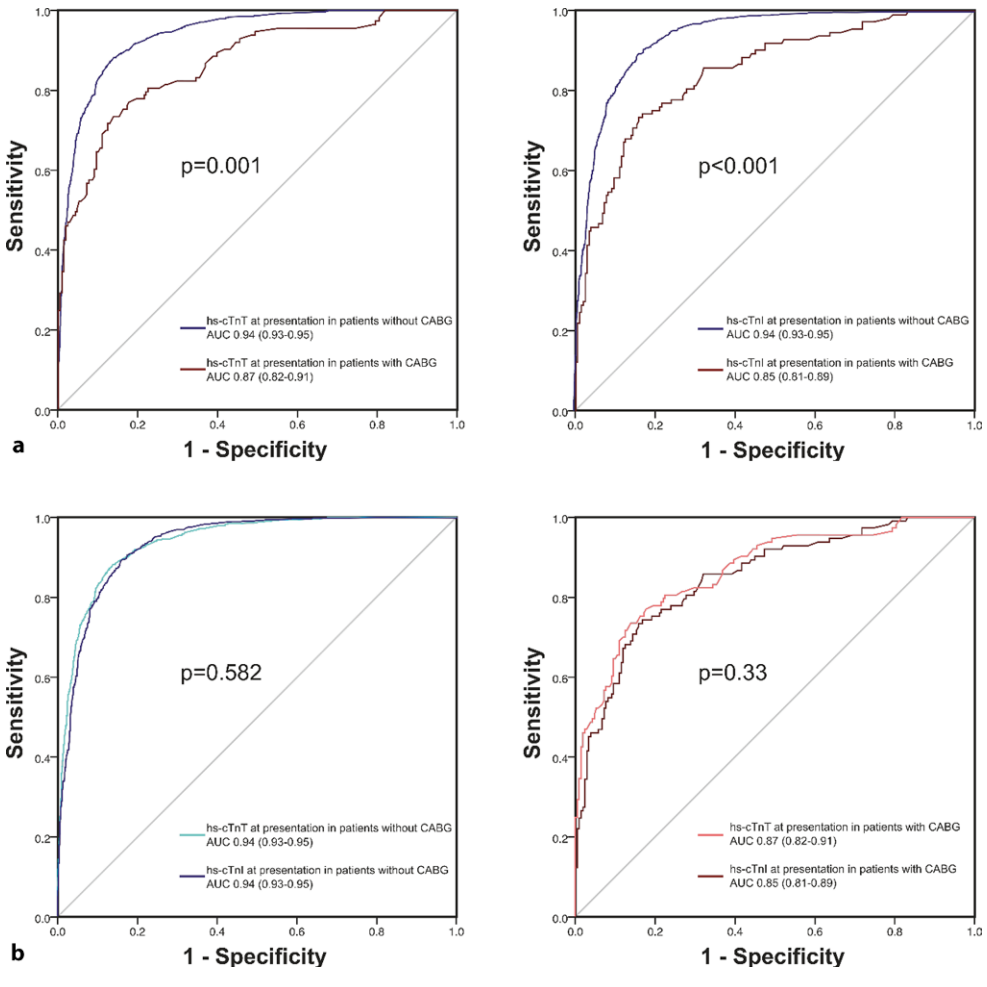


Fig. 2 | C-14 a Diagnostic accuracy of hs-cTnT and hs-cTnI concentrations at presentation for the diagnosis of AMI according to the presence or absence of history of CABG. b Diagnostic accuracy of hs-cTnT and hs-cTnI concentrations at presentation for the diagnosis of AMI in patients without and with a history of CABG. *hs-cTnT/I* High sensitivity cardiac troponin T/I, *AMI* Acute myocardial infarction, *CABG* Coronary artery bypass grafting

CABG (LR left bundle branch block 0.80 [95%CI, 0.34–1.86] versus 2.11 [95%CI, 1.44–3.10] in patients without CABG, T-inversions 1.25 [95%CI, 0.85–1.84] versus 2.82 [95%CI, 2.35–3.39]). The diagnostic accuracy of hs-cTnT/I was high in patients with prior CABG, but significantly lower compared to patients without prior CABG (hs-cTnT: AUC 0.87 [95%CI 0.82–0.91] versus AUC 0.94 [95%CI 0.93–0.95]; hs-cTnI: AUC 0.85 [95%CI 0.81–0.89] versus AUC 0.94 [95%CI 0.93–0.95]; $p<0.001$ for both). In patients with history of CABG, the hs-cTnT/I 0/1 h-algorithms maintained high negative and positive predictive value, but had lower efficacy with more patients remaining in the observe zone.

Conclusions: History of CABG substantially impacts on AMI incidence and the diagnostic performance of CPC, ECG and hs-cTnT/I. Attention to CABG-specific performances seems mandatory.

C-15

15 Jahre Erfahrung mit der En bloc-Rotation der Ausflusstrakte bei Kindern mit komplexer Transposition der großen Arterien oder ähnlichen Vitien

Michaela Kreuzer[1], Eva Sames-Dolzer[1], Roland Mair[1], Andreas Tulzer[2], Roland Gitter[3], Rudolf Mair[1]

[1]Department für Kinderherzchirurgie, Kepler Universitätsklinikum Linz, Linz, Österreich
[2]Med Campus IV, Kepler Universitätsklinikum Linz, Linz, Österreich
[3]Klinik für Kinderkardiologie, Kepler Universitätsklinikum Linz, Linz, Österreich

Grundlagen: Die komplexe Transposition der großen Arterien stellt eine große Herausforderung an die chirurgische Therapie dar. Traditionell werden die Kinder mittels einer Rastelli-Operation behandelt. Die Aortentranslokation ermöglicht eine anatomischere Korrektur dieses Vitiums. Bei der En bloc-Rotation der Ausflusstrakte kann zusätzlich in vielen Fällen die Pulmonalklappe erhalten werden. International sind die Erfahrungen mit dieser Operation gering. Diese retrospektive Single Center-Studie soll das Outcome nach 15-jähriger Anwendung der En bloc-Rotation zeigen.

Methodik: 27 Kinder mit Transposition der großen Arterien und linksventrikulärer Ausflusstraktstenose oder ähnlichen Fällen von Double Outlet Right Ventricle wurden seit 2003 einer En bloc-Rotation der Ausflusstrakte unterzogen, 13 davon waren weiblich. Das Alter der Patienten zum Operationszeitpunkt reichte von 4 Tagen bis 6,5 Jahren, im Median 0,28 [0,05; 1,84] Jahre. Das Gewicht lag zwischen 3,1 und 18,8 kg, im Median 5,2 [3,68; 8,35] kg. 6 Patienten hatten zwischen einer und vier Voroperationen. In 18 Fällen (66,7 %) konnte die Pulmonalklappe erhalten werden, 9 Patienten (33,3 %) bekamen einen transanulären Patch.

Ergebnisse: Eine Patientin verstarb an einem chronischen Linksherzversagen während des stationären Aufenthaltes, zu zwei weiteren Todesfällen kam es nach Entlassung: eine Aspiration nach Hirnblutung sowie ein plötzlicher Herztod. Eine Patientin befindet sich nicht in einem Follow Up-Programm. Das Follow Up-Intervall der somit 23 Patienten beträgt zwischen 132 Tage und 14,96 Jahre, im Median 7,28 [4,33; 9,37] Jahre. Sowohl Aorten- als auch Pulmonalklappen zeigten während der Follow up-Periode ein proportionales Wachstum. Die erhaltenen Pulmonalklappen blieben vergleichsweise klein, aber kompetent. An vier Patienten mussten insgesamt fünf Reoperationen vorgenommen werden: ein Re-VSD-Verschluss (Patient Nummer 5), eine Aortenklappenreparatur (Patient Nummer 6), eine Schrittmacherimplantation und eine Pulmonalarterienpatchplastik (Patient Nummer 7), ein Pulmonalarterienbanding (Patient Nummer 23). Ein weiterer Patient (Nummer 4) erhielt einen Stent in die linke Pulmonalarterie. Es war keine Reoperation aufgrund einer linksventrikulären Ausflusstraktstenose sowie kein Pulmonalklappenersatz notwendig.

Schlussfolgerungen: Die En bloc-Rotation der Ausflusstrakte ermöglicht eine anatomische Korrektur der komplexen Transposition der großen Arterien mit Wachstumspotenzial aller tubulären Strukturen. Die Reoperations- und Reinterventionsrate kann niedrig gehalten werden.

C-16

Short-term outcome and complications in veno-arterial extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock

Philipp Krombholz-Reindl[1], Andreas Winkler[1], Katja Gansterer[2], Johannes Steindl[1], Andreas Vötsch[1], Roman Gottardi[1], Christian Dinges[1], Rainald Seitelberger[1]

[1]Department of Cardiac Surgery, Paracelsus Private Medical University of Salzburg, Salzburg, Austria
[2]Paracelsus Private Medical University of Salzburg, Salzburg, Austria

Background: Veno-arterial extracorporeal membrane oxygenation (va-ECMO) as a temporary support in postcardiotomy heart failure is associated with severe morbidity and mortality. Aim of this study was to evaluate short-term outcome, and perioperative complications at our institution.

Methods: 90 patients who received perioperative va-ECMO for postcardiotomy heart failure between January 2012 and December 2018 were retrospectively analyzed. Successful (group 1, $n=52$) and unsuccessful ECMO weaning (death, bridge to device; group 2, $n=38$) was compared regarding demographic data, type and duration of surgery, cannulation strategy, operative risk scores, 30-day mortality, perioperative cardiac enzymes (Troponin-T, CK-MB), duration of ECMO therapy and complications.

Results: Mean age was 65.6 ± 10.7 years, surgeries included CABG only (19%), valve only (29%), CABG plus valve (28%) and other procedures (24%). 30-day mortality was 57%. Mean EuroScore II was 13.2 ± 15.5 for all patients and 12.2 ± 15.6 and 14.7 ± 15.5 for group 1 and 2, respectively. Mean duration of va-ECMO support was $6,8\pm4$ days, successful weaning was possible in 58%, 5.5% were transferred to a center for VAD- implantation. Arterial cannulation was performed via femoral artery (8.8%), ascending aorta (23.3%) and subclavian artery (66.6%). Vascular complications occurred in 37,5% of femoral cannulations. In group 2 significant more patients had CK-MB > 200 U/L at the first postoperative day ($p<0.01$). There was no difference in complications such as reoperation due to bleeding, acute kidney injury, major neurologic events and GI complications between the groups.

Conclusions: In our observation, there was no influence of cannulation strategies or postoperative complications on va-ECMO weaning rates. Early postoperative cardiac enzyme levels may have a predictive value on outcome.

C-17

ON-X Registry – preliminary results on mechanical AVR and target INR 1.5–2.0

Jakob Lichtenegger, Tandis Aref, Markus Reichl, Alfred Kocher, Günther Laufer, Martin Andreas

Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria

Background: Despite their longevity, long-term anticoagulant therapy remains the pivotal disadvantage of mechanical heart valves. In order to reduce bleeding complications, the On-X prosthesis was designed with low thrombogenic profile to optimize blood flow and fluid dynamics respectively and thus minimize blood damage. Aim of this study is to evaluate hazards focusing on the On-X mechanical prosthesis in the aortic position and observing their long-term survival, rate of re-operations and the occurrence of major adverse events within target INR range of 1.5–2.0.

Methods: An on-site registry enrolling 200 patients has been launched at our department. Preliminary results on 29 patients with implementation of the On-X mechanical prosthesis in the aortic position from January to December 2018 and completed 3 months follow up are reported. Patients characteristics, surgical specifics and valve-related complications were assessed. Primary endpoints concern thromboembolism, valve thrombosis, and bleedings after surgery as well as overall mortality. Secondary endpoints included any other adverse event observed with prosthetic valve replacement.

Results: A total of 29 patients were included in this preliminary analysis with a mean age of 45 ± 10 years and a mean EuroSCORE of 1.5 ± 1%. 72% of the study population were male. With regard to relevant comorbidities, 45% reported hypertension, 31% hypercholesterolemia and 21% coronary heart disease. 3.4% underwent previous cardiac surgery. Concomitant procedures were performed in 17%. 36% were operated on due to aortic valve insufficiency, 21% because of aortic valve stenosis, 45% suffered from combined valve disease. 66% of valvular anomalies were attributable to bicuspid aortic valve, 6.9% to an unicuspid aortic valve. Analyses of endpoints are depicted in Fig. 1; changes in medication at admission and after discharge are displayed in Fig. 2. All patients were alive at 3 months follow up. One patient was discontinued from the study due to the onset of de-novo atrial fibrillation.

Conclusions: Overall, the preliminary analyses suggest that the On-X aortic valve implementation and low target INR is safe and did not cause any relevant major adverse events 3 months after the operation. Neither stroke, thrombosis, or embolism occurred, all bleeding complications were minor so far.

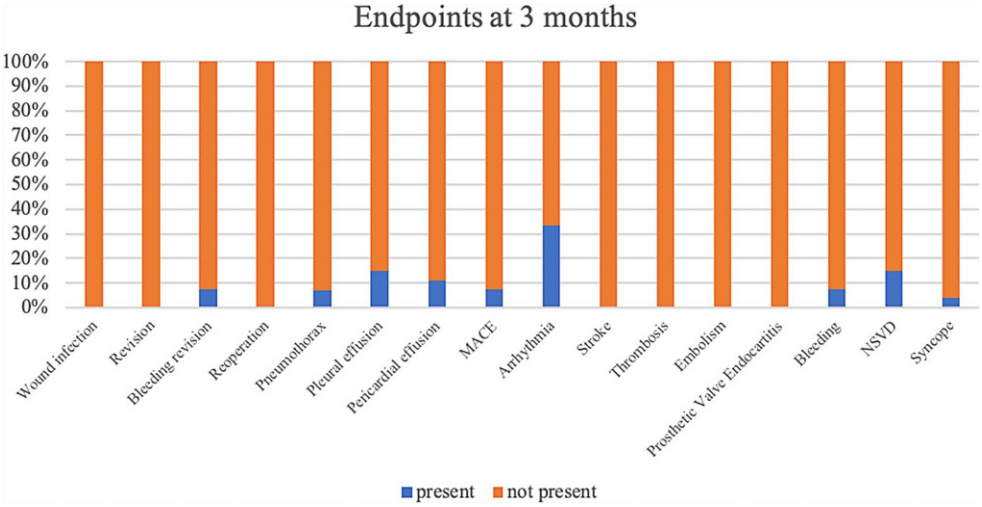


Fig. 1 | C-17

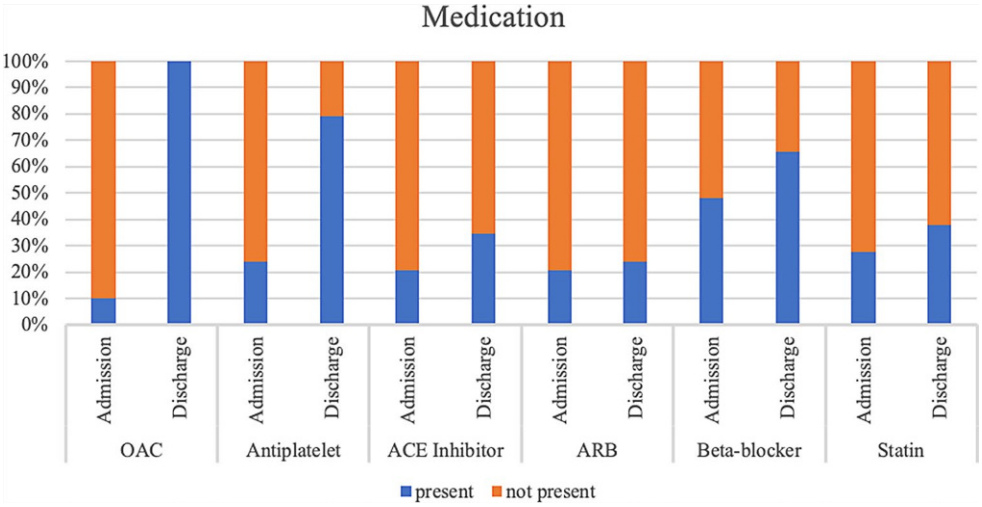


Fig. 2 | C-17

C-18

Case Report: Anatomische Korrektur einer Rezidiv-Aortenisthmusstenose mittels kombinierter Subclavian-Flap und Patchplastik

Roland Mair, Eva Sames-Dolzer, Michaela Kreuzer, Andreas Zierer, Rudolf Mair

Universitätsklinik für Herz-, Gefäß-, und Thoraxchirurgie, Med Campus III, Kepler Universitätsklinikum Linz, Linz, Österreich

Grundlagen: Die Re-Aortenisthmusstenose ist ein chirurgisch sehr anspruchsvolles Problem in der Kinderherzchirurgie. Die verbreitetste Behandlung ist die Ballondilatation. Diese ist aber besonders bei hypoplastischem Aortenbogen nicht immer möglich oder sinnvoll. Im Kindesalter sollte in jedem Fall eine anatomische Rekonstruktion angestrebt werden.

Methodik: Ein 6 Monate altes Mädchen mit Koarktation der Aorta, hypoplastischem Aortenbogen und bikuspider Aortenklappe, zeigte nach der Korrektur der Aortenisthmusstenose mittels Kunststoffinterponat in einem auswärtigen Zentrum, den gleichen Gradienten wie vor der Operation. In der präoperativen Herzkatheteruntersuchung zeigte sich der Aortenbogen verengt mit einem Durchmesser von 3,5 mm, der Aortenisthmus hochgradig stenotisch und in der Aorta descendens, an das Interponat anschließend, abermals eine Verengung auf zirka 2 mm. Im Zuge einer präoperativen Herzkatheteruntersuchung wurde die distale Stenose mittels Ballon dilatiert. Danach folgte die operative Sanierung des Bogens und der Aortenisthmusstenose, mittels Subclavian-Flap-Plastik (Waldhausen) kombiniert mit einer Patchplastik an der inneren Kurvatur. Wir wählten eine mediane Sternotomie als Zugang, um den Eingriff an der Herz-Lungen-Maschine durchführen zu können, da auch der komplette Aortenbogen operativ saniert werden musste. Jedoch zeigte sich während der Operation, dass wir von diesem Zugang aus nicht ausreichend über das Interponat hinauskamen, um es zu resezieren. Daher wurde die Patientin in Rechtsseitenlage gedreht und der Eingriff über eine laterale Thorakotomie fortgesetzt. Als Patchmaterial verwendeten wir die innere Kurvatur eines Aortenbogen Homografts. Intraoperativ zeigte sich in der Aorta descendens eine Dissektion. An dieser Stelle wurde postoperativ, in einem erneuten Herzkathetereingriff, ein Stent platziert.

Ergebnisse: Nach Vollendung der Therapie zeigte sich die Aorta in allen Abschnitten ohne jeglichen Gradienten. Außerdem zeigte sich der linke Arm in der Angiographie über A. vertebralis retrograd versorgt.

Schlussfolgerungen: Selbst nach fehlgeschlagener Rekonstruktion einer Isthmusstenose mittels eines langen Interponats ist trotz des ausgeprägten Substanzdefektes, eine anatomische Rekonstruktion des Aortenbogens mit Wachstumspotential möglich.

C-19

Postoperative Nachdosierung von Tranexamsäure als Ansatz zur Reduktion des Blutverlusts nach kardiochirurgischen Eingriffen

Florian Meissner[1], Katrin Plötze[2], Thomas Waldow[2]

[1]Klinik für Herzchirurgie, Universitätsspital Basel, Basel, Schweiz
[2]Klinik für Herzchirurgie, Herzzentrum Dresden, Dresden, Deutschland

Grundlagen: Das Ausmaß des Blutverlusts nach einer kardiochirurgischen Operation unter Einsatz der Herz-Lungen-Maschine (HLM) unterliegt patienten- und eingriffsbezogenen Faktoren. Neben lokalen chirurgischen Blutungsquellen, die durch eine Rethorakotomie identifiziert und versorgt werden können, sind Störungen der Hämostase als Folge des kardiopulmonalen Bypasses dafür ursächlich. Dazu zählen eine Hämodilution durch Gabe von kristalloiden Infusionslösungen und komplexe Thrombozytenfunktionsstörungen genauso wie die Überaktivierung des fibrinolytischen Systems. Um das Risiko klinisch relevanter Blutungen als Folge einer Hyperfibrinolyse zu minimieren, werden in der Kardiochirurgie prophylaktisch Antifibrinolytika wie Tranexamsäure (TXA) verabreicht. TXA hemmt die Fibrinolyse durch reversible Blockade der Lysin-Bindungsstelle von Plasminogen und Plasmin, wodurch der Abbau von Fibrin unterbunden wird. Während die Gabe von TXA vor Einsatz der HLM Gegenstand zahlreicher Studien ist und nachweislich zu einer signifikanten Reduktion von Blutverlust und Transfusionsbedarf führt, fehlen bislang Untersuchungen zum therapeutischen Nutzen der Nachdosierung von TXA bei postoperativen Blutungen.

Methodik: In einer retrospektiven Kohortenstudie wurden kardiochirurgische Patienten ohne und mit Nachdosierung von TXA, die sich bei elektiver oder dringender Indikation unter Einsatz der HLM einem koronaren Bypass-, Herzklappen- oder Aorteneingriff unterzogen, miteinander verglichen. Primärer Endpunkt war der postoperative Blutverlust innerhalb von 24 h. Sekundäre Endpunkte waren der Transfusionsbedarf, die Rate an Rethorakotomien, die Letalität und organbezogene Komplikationen.

Ergebnisse: Insgesamt wurden die Daten von 2.179 Patienten, die im Zeitraum vom 01.07.2013 bis 31.10.2014 an unserer Klinik operiert wurden, ausgewertet. Davon erhielten 92 bzw. ein Anteil von 4,2 % postoperativ TXA. Logistische Regressionsanalysen zeigten einen hoch signifikanten Zusammenhang zwischen dem frühen postoperativen Blutverlust und der Nachdosierung von TXA ($p < 0{,}00001$). Nach Coarsened Exact und Nearest Neighbor Matching mit Replacement zur Minimierung von Gruppenunterschieden wurden je 71 Patienten ohne bzw. mit Nachdosierung von TXA verglichen. Dabei ergaben sich keine signifikanten Unterschiede. Gegenüber Kontrollpatienten wiesen Patienten mit Nachdosierung von TXA einen statistisch nicht-signifikant höheren postoperativen Blutverlust auf (MWD 146,7 ml; $p = 0{,}064$), erhielten in ähnlicher Frequenz Bluttransfusionen (RR 0,98 [0,77–1,24]; $p > 0{,}99$) und hatten ein nicht-signifikant geringeres Risiko für eine Rethorakotomie (RR 0,70 [0,38–1,27]; $p = 0{,}325$). Einerseits ergaben sich postoperativ keine Hinweise auf ein signifikant erhöhtes Risiko thrombembolisch bedingter myokardialer (RR 1,00 [0,21–4,79]; $p = 1{,}000$) oder zerebrovaskulärer Ereignisse (RR 1,00 [0,14–6,90]; $p = 1{,}000$), eines Dialyse-pflichtigen Nierenversagens (RR 1,00 [0,26–3,84]; $p = 1{,}000$) oder einer erhöhten Letalität (RR 1,00 [0,26–3,84]; $p = 1{,}000$). Anderseits zeigte sich unter Nachdosie-

	vor Matching mit Replacement N = 2.179					nach Matching mit Replacement N = 142					
	Kontrolle N = 2.087		TXA N = 92		z	Kontrolle N = 71		TXA N = 71		z	Plot (z)
Demographische Daten											-3,5 0 3,5
Männer — n (%)	1.504	(72,1)	78	(84,8)	-3,285	56	(78,9)	58	(81,7)	-0,422	
Alter — a	68,4	± 9,6	69,7	± 8,2	-1,495	70,2	± 9,2	70,2	± 8,2	-0,048	
BMI — kg/m²	28,4	± 9,9	27,7	± 4,4	1,286	27,5	± 4,2	28,1	± 4,4	-0,908	
Kardiovaskulärer Status											
NYHA III/IV — n (%)	1.002	(48,0)	51	(55,4)	-1,402	43	(60,6)	41	(57,7)	0,342	
LVEF ≤ 30%	165	(7,9)	12	(13,0)	-1,443	6	(8,5)	8	(11,3)	-0,564	
KHK	1.532	(73,4)	75	(81,5)	-1,951	61	(85,9)	56	(78,9)	1,106	
rezenter Myokardinfarkt	415	(19,9)	22	(23,9)	-0,889	17	(23,9)	18	(25,4)	-0,195	
Nicht-kardiovaskuläre Risikofaktoren											
eGFR — ml/min. je 1,73 m²	70,5	± 19,8	66,0	± 20,5	2,087	69,6	± 17,3	67,0	± 20,6	0,818	
Niereninsuffizienz — n (%)	69	(3,3)	4	(4,3)	-0,482	1	(1,4)	2	(2,8)	-0,584	
Diabetes mellitus	810	(38,8)	30	(32,6)	1,240	24	(33,8)	24	(33,8)	0,000	
COPD	107	(5,1)	5	(5,4)	-0,128	5	(7,0)	2	(2,8)	1,168	
pulmonale Hypertonie	42	(2,0)	3	(3,3)	-0,665	6	(8,5)	2	(2,8)	1,467	
neurologisches Defizit	268	(12,8)	8	(8,7)	-1,369	10	(14,1)	5	(7,0)	1,374	
Operation											
EuroSCORE II	4,0	± 6,1	6,5	± 8,9	-2,571	5,7	± 7,1	6,0	± 8,3	-0,219	
Reoperation — n (%)	120	(5,7)	12	(13,0)	-2,056	8	(11,3)	7	(9,9)	0,273	
CABG	1.010	(48,4)	40	(43,5)	0,931	34	(47,9)	30	(42,3)	0,676	
Klappe	578	(27,7)	17	(18,5)	2,214	15	(21,1)	15	(21,1)	0,000	
CABG + Klappe	467	(22,4)	33	(35,9)	-2,655	21	(29,6)	25	(35,2)	-0,719	
LIMA	1.212	(58,1)	63	(68,5)	-2,096	47	(66,2)	48	(67,6)	-0,178	
OP-Dauer — min.	160,5	± 46,3	169,5	± 50,3	-1,686	180,2	± 64,1	169,5	± 48,6	1,116	

Abb. 1 | C19 Ergebnisse vor Nachdosierung von TXA vor/nach Matching mit Replacement

rung von TXA eine nicht-signifikant höhere Rate von Patienten mit eingeschränkter Nierenfunktion (RR 1,57 [1,01–2,43]; p).

Schlussfolgerungen: Die postoperative Nachdosierung von TXA zeigte keinen klinischen Zusatznutzen. Es wird empfohlen, die Anwendung von Antifibrinolytika nach Einsatz der HLM prospektiv in einer groß angelegten randomisierten kontrollierten Studie zu untersuchen. Dabei sollte der Fokus sowohl auf die Reduktion des perioperativen Blutverlusts und Transfusionsbedarfs als auch auf die Rate thrombembolischer Komplikationen gerichtet werden. In der klinischen Routine sollte die Nachdosierung von TXA bis zur Verfügbarkeit Evidenz-basierter Leitlinien primär Patienten mit massivem Blutverlust und präzise definierten diagnostischen Hinweisen auf eine Hyperfibrinolyse vorbehalten sein. Bei der Implementierung interner Protokolle zum Blutungsmanagement sollte eine die Therapie unterstützende, zeit- und patientennahe Diagnostik hyperfibrinolytischer Blutungen berücksichtigt werden.

C-20

Clinical comparative analysis of Bretschneider and St. Thomas cardioplegia solution in mitral valve repair via anterolateral right thoracotomy

Constantin Mork[1], Oliver Reuthebuch[1], Brigittta Gahl[1], Luca Koechlin[2], Lena Schoemig[1], Friedrich Eckstein[1], Martin Grapow[1]

[1]Department of Cardiac Surgery, University Hospital Basel, Basel, Switzerland
[2]University Hospital Basel, Basel, Switzerland

Background: Single dose Cardioplegia is preferred in minimal invasive mitral valve surgery to maintain preset visualization. The aim of our study is to compare two widely used crystalloid cardiopleagias Bretschneider (Custodiol®) versus St. Thomas crystalloid cardioplegia in patients who underwent mitral valve repair via small anterolateral right thoracotomy by performing a retrospective analysis.

Methods: From January 2012 until December 2018, 182 isolated mitral valve procedures for mitral valve repair via anterolateral right thoracotomy were performed. While 128 patients underwent myocardial protection with Bretschneider cardioplegia (Custodiol®), 54 patients received St. Thomas cardioplegia. Primary efficacy endpoint was peak postoperative high-sensitivity cardiac troponin (hs-cTnT) during hospitalization. Secondary endpoints were peak creatine kinase- myocardial type (CK-MB) and creatine kinase (CK) as well as safety outcomes. We used inverse probability of treatment weighting (IPTW) in order to adjust for confounding by indication, including age, female gender, logistic EuroSCORE and hypertension as covariates into the propensity model. We trimmed the tails of the propensity score, as the corresponding records are suspicious of residual confounding and calculated standardized differences to assess comparability of treatment groups after IPTW.

Results: Trimming did not cause substantial patient loss and treatment groups turned out comparable after IPTW with respect to patient characteristics such as age, female gender, body mass index (BMI) and comorbidities. The primary endpoint peak hs-cTnT showed a significant difference between Bretschneider (geometric mean 725 mg/L, reference range 613–858 mg/L) and St. Thomas (643 mg/L, reference range 538–768 mg/L, $p = .027$). Peak CK-MB (geometric mean after Bretschneider 45 µg/l, reference range 40–52, St. Thomas: 35 µg/l,

ml	Kontrolle N* = 71		TXA N = 71		MWD	95% KI	p
Blutverlust							
nach 24 h	1.383,7	± 596,5	1.530,4	± 598,8	146,7	[145,8–147,6]	0,064
nach 48 h	1.715,5	± 842,2	1.891,2	± 804,3	175,7	[174,8–176,6]	0,083
nach 120 h	2.002,7	± 1.357,2	2.083,5	± 1.078,6	80,7	[80,2–81,5]	0,132

n (%)	Kontrolle N* = 71		TXA N = 71		RR	95% KI	Plot (RR)	p
Transfusionsbedarf							0,1 1 10	
EK	47	(66,2)	46	(64,8)	0,98	[0,77–1,24]		> 0,99
FFP	15	(21,1)	21	(29,6)	1,40	[0,79–2,49]		0,335
TK	1	(1,4)	4	(5,6)	4,00	[0,46–34,91]		0,366
PPSB	8	(11,3)	6	(8,5)	0,75	[0,27–2,05]		0,778
Fibrinogen	11	(15,5)	11	(15,5)	1,00	[0,46–2,16]		1,000
Rethorakotomien nach Ursachen								
gesamt	20	(28,2)	14	(19,7)	0,70	[0,38–1,27]		0,325
chirurgisch	14	(19,7)	8	(11,3)	0,57	[0,27–1,28]		0,246
hämostatisch	2	(2,8)	3	(4,2)	1,50	[0,26–8,71]		> 0,99
Letalität und Komplikationen								
Letalität	4	(5,6)	4	(5,6)	1,00	[0,26–3,84]		1,000
Myokardinfarkt	3	(4,2)	3	(4,2)	1,00	[0,21–4,79]		1,000
Nierenversagen	21	(29,6)	33	(46,5)	1,57	[1,01–2,43]		0,057
Dialyse	4	(5,6)	4	(5,6)	1,00	[0,26–3,84]		1,000
zerebrovaskulär	2	(2,8)	2	(2,8)	1,00	[0,14–6,90]		1,000
Verlauf								
ITS ≥ 48 h	50	(70,4)	51	(71,8)	1,02	[0,83–1,26]		> 0,99
Hospital ≥ 14 d	23	(32,4)	25	(35,2)	1,09	[0,69–1,72]		0,859
Intubation ≥ 24 h	9	(12,7)	13	(18,3)	1,44	[0,66–3,16]		0,465
Reintubation	6	(8,5)	5	(7,0)	0,83	[0,27–2,61]		> 0,99
WHST	5	(7,0)	8	(11,3)	1,60	[0,55–4,65]		0,562

* nach Matching mit Replacement

Abb. 2 | C19 Primäre und sekundäre Endpunkte

reference range 30–42, $p = .028$) and CK (geometric mean after Bretschneider 1489U/l, reference range 1326–1671, St. Thomas: 1242 U/l, reference range 1043–1478, $p = .036$) showed the same pattern. We did not see any difference with respect to postoperative complications between treatment groups after IPTW.

Conclusions: Use of St. Thomas cardioplegia was associated with lower postoperative peak levels of all cardiac markers that reflect cardiac ischemia such as hs-cTnT, CK and CK-MB as compared to Bretschneider in propensity-weighted treatment groups.

C-21

Mitral valve surgery in octogenerians. Should we stay or should we go? A single center experience

Cenk Oezpeker, Daniel Höfer, Nikolaos Bonaros, Ludwig Müller, Michael Grimm

Medical University of Innsbruck, Innsbruck, Austria

Background: Mitral valve surgery (MVS) with predominately regurgitation is the second most frequent cause for valve surgery in the western countries. However in the octogenerians population MVS is, due to the patients fragility and higher prevelance of cormobidities resulting in higher mortality rates, not preferred. Many cardiologists prefer different conservative therapies instead of surgical interventions. The aim of this investigation is to present five years data in octogenarian patients with

isolated MVS or multivalve surgery with additionally coronary artery bypass grafting in some patients.

Methods: The data of 1814 patients, who underwent isolated or combined primary MVS in the department of cardiac surgery at the Medical University of Innsbruck between June 2004 and January 2018, were included in this retrospective study. 117 patients with the age ³ 80 years could be identified. Out of these, nine were excluded due to minor investigations on the mitral valve (e. g. Alfieri stitch, decalcification of the anterior leaflet). Finally 108 patients were included in the study cohort for further analyzes.

Results: Mean age of the patients was 82 years (maximum 89 years). 50% ($n=54$) were female patients. The median EuroScore II was 5.95% (IQR 3.74–9.7%). In addition the median NTproBNP level was 1507 ng/ml (IQR 896–2553 ng/ml). The main access was via full sternotomy with 61.1% ($n=66$) followed by the two minimally invasive approaches: minithoracotomy with 22.2% ($n=24$) and upper hemisternotomy(16.7%, $n=18$). In 64.8% ($n=70$) of patients a mitral valve repair was performed (35.2%, $n=38$ a MV-replacement). In 54,6% ($n=59$) of cases isolated MVS was performed, whereas in 15.8%, $n=17$ aortic valve replacement/repair and in 28.7% tricuspid valve repair and 1.9% triple valve surgery was performed. Furthermore additionally (single or multivessel) coronary-bypass grafting was considered in 23.1% ($n=25$). The 2000 days survival was achieved 68% of patients. However, a new onset of renal dialysis or hemofiltration was documented in 19.4% ($n=21$). Short term mechanical support (IABP or ECMO) was necessary in 6.2% ($n=7$) of patients. Periprocedural permanent pacemaker were implanted in 3.7% ($n=4$) of patients. A mediastinitis was documented in 2.8% ($n=3$) and a stroke in 1.9% ($n=2$) of patients.

Conclusions: MVS in octogenerians seems to have acceptable survival rates. However, it seems that the lesser the invasiveness of the MVS investigation for octogenerians are, the better are the clinical outcome paraemters. This might be achieved with different interventionally hybrid procedures reducing the investigation only to minimally invasive accesses.

C-22

Partial upper sternotomy versus mini-thoracotomy for isolated mitral valve surgery: a propensity-score matched analysis

Cenk Oezpeker, Daniel Höfer, Nikolaos Bonaros, Michael Grimm, Ludwig Müller

Medical University of Innsbruck, Innsbruck, Austria

Background: Minimally invasive mitral valve surgery through anterolateral mini-thoracotomy (MT) has become the standard therapy for isolated mitral valve disease in experienced centers. Multiple valve disease or other anatomical and certain clinical conditions, however, make this access not suitable for some patients and conventional full sternotomy is the mostly preferred approach. For those patients partial upper sternotomy (PS) can be used as a less invasive access. Whereas MT has been widely investigated, there are not enough insights to the PS approach for mitral valve surgery (MVS) in more morbid patients. Therefore we compared the data of both accesses.

Methods: This retrospective analysis includes data on 604 patients (MT $n=486$, PS $n=118$), who underwent either isolated or combined primary MVS via less invasive access at our department from May 2011 to September 2018. Out of the PS cohort, 24 patients were excluded due to additionally aortic valve or concomitant coronary bypass surgery leaving 94 patients who had been judged suitable for PS but also eligible for MT. To reduce the possibility of selection bias a 1:1 propensity-score matchmaking was performed which resulted in 71 pairs.

Results: During a median follow-up time of 1585 days (29–2832; PS 562 [29–2778 days], MT 2454 [30–2832 days]) all cause mortality was 7.1% ($n=5$). In the propensitiy-score paired model, there was no statistically significance between the two cohorts in the 30-days and 1-year mortality. Furthermore the 3-years survival showed a superiority in the MT-cohort (PS $n=4$, MT $n=0$; $p=0.011$). However in the secondary endpoints the cardiopulmonary bypass times (MT 208 vs PS 165 min, $p=<0.001$), the x-clamp times (MT112 vs PS 103 min, $p=0.045$) and the length of hospital stay (MT 13 vs PS 9 days, $p=0.014$) showed a statistically superiority of the PS access. All other secondary endpoints showed no statistically significance.

Conclusions: Despite higher morbidity of patients with PS, the mortality rates are minimally and comparable between both treatment cohorts. In addition shorter operative-times and similar perioperative outcomes in the PS-cohort may be a valid indication in high risk patients.

C-23

Partial upper sternotomy versus full sternotomy for mitral valve surgery: a propensity score matched analysis

Cenk Oezpeker, Daniel Höfer, Nikolaos Bonaros, Michael Grimm, Ludwig Müller

Medical University of Innsbruck, Innsbruck, Austria

Background: Minimally invasive mitral valve surgery (MIMVS) through anterolateral mini-thoracotomy (MT) has become the standard therapy for isolated mitral valve disease in experienced centers. Multiple valve disease or other anatomical and certain clinical conditions, however, make this access not suitable for some patients and conventional full sternotomy (FS) is the mostly preferred alternative approach. For those patients partial upper sternotomy (PS) can be used as a less invasive access. Whereas FS has been widely investigated, there are not enough insights to the PS approach for mitral valve surgery (MVS). Therefore we compared the data of both accesses.

Methods: This retrospective analysis includes data on 1639 patients, who underwent either isolated or combined primary MVS at our department from May 2011 to August 2017. Out of these, 1191 patients were excluded from this analysis due to MT access ($n=663$) and due to concomitant coronary artery bypass surgery but also because of re-do cases, concomitant aortic surgery or urgent/salvage MVS ($n=528$). Finally 99 patients who had been judged suitable for PS. In addition, 349 patients with FS for primary MVS were included in our study. To reduce the possibility of selection bias a 1:1 propensity-score matchmaking was performed which resulted in 98 pairs

Results: During a median follow-up time of 1491 days (478–2186; PS 1103 [331–1806 days], FS 2180 days [841–3054]) all-cause mortality was 15.90% (70 of 439 patients). In the propensitiy score paired model, PS showed statistically significant superior survival compared to FS at 30 days ($p=0.044$, hazard ratio (HR) 7.525, 95% confidence interval (CI) 1.06–53.56. Furthermore, 90- and 365 days survival after surgery showed a similiar trend, but without reaching statistical significance ($p=0.096$ and $p=0.077$). As secondary endpoints number of

second pump runs and hospital length of stay were significantly less ($p = 0.016$, $p < 0.001$) in PS patients.

Conclusions: The less invasive PS approach for MVS seems to have short- and long-term survival benefits. In patients who are not candidates for MT PS seem a favorable approach although prospective randomized-controlled trials are necessary for confirmation.

C-24

Ergebnisse der minimal invasiven Mitralklappenrekonstruktion bei degenerativer Mitralklappeninsuffizienz mit dem Neochord®-System aus dem Kepler Universitätsklinkum Linz

Martin Pilsl[1], Andreas Zierer[2]

[1]Kepler Universitätsklinikum Linz, Linz, Österreich
[2]Med Campus III, Kepler Universitätsklinikum Linz, Linz, Österreich

Grundlagen: Die transapikale off-pump Mitralklappenrekonstruktion mit Neochords® ist eine neue, minimal invasive chirurgische Therapiemethode bei degenerativer Mitralklappeninsuffizienz. Wir berichten über die Ergebnisse nach minimalinvasiver Mitralklappenrekonstruktion mittels Neochord-System aus dem Kepler Universitätsklinikum Linz.

Methodik und Ergebnisse: Zwischen Oktober 2017 und März 2019 wurde bei insgesamt 12 Patienten eine Neochord®-Implantation durchgeführt. Das mittlere Alter der Patienten betrug 74,7 Jahre (53–89 Jahre), 9 (75 %) davon waren männlich, 3 (25 %) weiblich. Bei 10 (83,3 %) Patienten wurde eine isolierte Neochord®-Implantation durchgeführt, 2 (16,6 %) wurden im Rahmen eines Kombinationseingriffes durchgeführt. Bei beiden Kombinationseingriffen erfolgte zusätzlich eine transapikale Aortenklappenimplantation. Bei 11 (91,6 %) Patienten wurden 3 Neochords® verwendet, bei 1 (8,3 %) Patienten waren 4 Neochords® erforderlich. Die ursächliche Pathologie an der Mitralklappe war bei allen 12 Patienten eine Carpentier Typ II Pathologie mit Prolaps isoliert am hinteren Segel.

Schlussfolgerungen: Insgesamt stellt die minimalinvasive Mitralklappenrekonstruktion mittels Neochord®-Implantation bei geeigneter Pathologie eine effiziente, sichere und wenig belastende Methode zur Mitralklappenrekonstruktion mit Erhalt der Anatomie der Mitralklappe dar. Aufgrund der noch geringen Fallzahl ist die vorgestellte Patientengruppe nicht repräsentativ. Da das System erst seit wenigen Jahren in klinischer Verwendung ist, sind auch entsprechende Langzeitergebnisse noch nicht verfügbar.

C-25

Bildgebung bei Mitralinsuffizienz – es ist nicht immer so wie es scheint

Leo Pölzl[1], Felix Nägele[1], Agne Adukauskaite[2], Silvana Müller[2], Nikolaos Bonaros[1], Florian Hintringer[2], Gerhard Pölzl[2], Daniel Höfer[1], Ludwig Müller[1]

[1]Universitätsklinik für Herzchirurgie Innsbruck, Medizinische Universität Innsbruck, Innsbruck, Österreich
[2]Universitätsklinik für Innere Medizin III (Kardiologie und Angiologie), Medizinische Universität Innsbruck, Innsbruck, Österreich

Grundlagen: Eine 75-jährige weibliche Patientin wird im September 2017 wegen wirksamer Mitralinsuffizienz und rezidivierender kardialer Dekompensationen zugewiesenen. Die Patientin präsentiert sich im NYHA Stadium III mit deutlicher Kongestion. Die transthorakale Echokardiographie bestätigte die Mitralinsuffizienz IV° bei weitgehend erhaltener systolischer LV Funktion und deutlicher Dilatation beider Vorhöfe. Die invasive Untersuchung ergab sekundäre pulmonale Hypertonie und einen reduzierten Cardiac Index. In der transösophagealen Echokardiographie (TEE) fanden sich keine relevanten Veränderungen an den Mitralklappensegeln. Der subvalvuläre Apparat stellte sich weitgehend unauffällig dar. Als zugrundeliegender Mechanismus der wirksamen Mitralklappeninsuffizienz (EROA 0,34 cm^2, RV 61 ml) wurde eine mäßige Restriktion des posterioren Segels sowie eine Ringdilatation mit zentrischem Regurgitationsjet identifiziert (Carpentier Typ IIIb).

Methodik: Aufgrund der Gebrechlichkeit der Patientin, eine chronische Niereninsuffizienz bei Z. n. akuten-auf-chronischem Nierenversagen wenige Monate zuvor sowie eine therapiebedürftige essentielle Thrombozythämie wurde im Heart Team die Indikation für einen edge-to-edge repair mittels MitraClip gestellt. Bei der komplikationslosen MitraClip-Implantation im Oktober 2017, konnte dir MI mit dem ersten Clip von IV° auf II° reduziert werden. Anlässlich der 3-Monatskontrolle berichtet die Patientin über eine deutliche Verbesserung der Leistungsfähigkeit (NYHA III auf II). Echokardiographisch zeigte sich eine Reduktion der MI auf I-II°. Bei der Einjahreskontrolle beklagte die Patientin eine erneute Abnahme ihrer Leistungsfähigkeit (NYHA III). In der TEE fand sich ein wirksames Rezidiv der MI, weiterhin ohne auffällige strukturelle Veränderungen an Klappe und subvalvulärem Apparat. Als zugrundeliegender Mechanismus für das Rezidiv wurde eine progrediente Ringdilatation postuliert. Im Heart-Team wurde eine chirurgische Intervention mit Explantation des MitraClips und Rekonstruktion von Mitralklappe festgelegt.

Ergebnisse: Bei dem mittels Minithorakotomie rechts vollendoskopisch durchgeführtem Eingriff ließ sich der MitraClip gut darstellen und konnte zur Gänze entfernt werden. Überraschenderweise fand sich eine massive Sklerosierung und Verdickung des subvalvulären Apparats, die in der vorausgehenden Bildgebung nicht ersichtlich war. Insgesamt zeigte sich das Bild einer postrheumatisch veränderten Klappe mit einem auffällig verdickten subvalvulären Apparat (Carpentier Typ IIIa). In der histologischen Aufarbeitung von Gewebeproben aus dem subvalvulären Apparat fand sich eine beträchtliche Myokardfibrose passend zu einem abgelaufenen Entzündungsprozess. Aufgrund der Gesamtsituation entschloss man sich zum biologischen Klappenersatz (33 mm Abbott Epic Bioprothese). Die zu jeder Zeit stabile Patientin konnte problemlos dekanüliert werden. Noch am OP Tag wurde die Patientin extubiert und am 8. postoperativen Tag ins Heimatkrankenhaus transferiert.

Schlussfolgerungen: Dieser Fall zeigt, dass trotz eingehender Evaluation von Mitralklappe und subvalvulärem Apparat in der TEE eine sichere morphologische Beurteilung der Klappe und des zugrundeliegenden Mechanismus der Mitralinsuffizenz nicht immer zweifelsfrei möglich ist. Die Möglichkeit von zusätzlichen, krankheitsrelevanten degenerativen Klappenveränderungen (Carpentier Typ IIIa) darf daher trotz vordergründig funktioneller Pathologie (Carpentier Typ IIIb) nicht außer Acht gelassen werden. Inwieweit die Klappenpathologie schließlich das interventionelle oder chirurgische Vorgehen beeinflusst, muss im Einzelfall im Heart Team entschieden werden.

C-26

The St Jude Prosthesis – An outdated gold standard for mechanical valve replacement?

Markus Reichl, Tandis Aref, Jakob Lichtenegger, Alfred Kocher, Günther Laufer, Martin Andreas

Medical University of Vienna, Vienna, Austria

Background: Mechanical prostheses evolved with the introduction of pyrolytic carbon. The St Jude prosthesis is the first bileaflet mechanical heart valve used as a gold standard in the treatment of young and middle-aged patients suffering from heart valve disease. Despite its low thrombogenic profile, this particular prosthesis has not yet been approved for lower target INR ranges than currently accepted by recommended guidelines in contrast to the On-X or Bicarbon prosthesis.

Methods: We have conducted a retrospective study including all patients undergoing aortic valve replacement with the St Jude prosthesis from its first implementation at our department until December 2010. A total of 132 patients were included for analysis. Main endpoint was survival. Secondary endpoints regarded valve-related hazards.

Results: 132 patients (30%: 70% = f: m) were enrolled with a mean age of 54 ± 15 years. 25% (N = 33) underwent previous cardiac surgery. Concomitant procedures were performed in 58% (N = 78) of the study population. 13% (N = 17) received MVR either prior to surgery or concomitantly. Overall mortality was 28% (N = 37) of which 9.8% (N = 13) were valve-related. Main death-cause was myocardial infarction (11%, N = 14). Other death causes included bleedings (2.3%, N = 3), stroke (0.8%, N = 1), endocarditis (0.8%, N = 1), cancer (3%, N = 4) and other reasons (8.3%, N = 11%). 14% (N = 18) experienced thromboembolic events of which 5.3% (N = 7) were strokes. 16% (N = 21) suffered from major bleedings due to long-term OAC. Prosthesis endocarditis was observed in 7.6% (N = 10). 6.1% (N = 8) demanded pacemaker implantation for postoperative arrhythmia within 14 days. 5.3% (N = 7) required Re-Do AVR for various reasons.

Conclusions: Thromboembolic events and major bleedings were rather balanced within our all-comer real-world population. We want to raise awareness for the high rate of complication rates after mechanical aortic valve replacement. Physician shall strive for novel prostheses or surgical techniques, especially in young and middle-aged patients with a higher life expectancy to avoid the long-term risks that occur with mechanical heart valves.

C-27

Three-dimensional transesophageal echocardiography reconstruction in acute mechanical mitral valve obstruction during pregnancy

Gregory Reid[1], Luca Köchlin[1], David Santer[1], Joachim Erb[1], Thomas Nestelberger[2], Martin Grapow[1], Freidrich Eckstein[1], Oliver Reuthebuch[1]

[1]University Hospital Basel, Basel, Switzerland
[2]University of Basel, Basel, Switzerland

Background: A 31-year-old patient admitted herself to our clinic in the 31 + 0 week of prima gravida pregnancy presenting initially with rapid onset dyspnea at rest, chest pain and hemoptysis over the course of the previous day. Patient history revealed only a mechanical mitral valve replacement (Sorin Bicarbon™ Bileaflet valve, 29 mm) 10 years earlier in Khartoum, Sudan because of post-rheumatic mitral valve stenosis. The patient was under phenprocoumon-therapy and had switched to low-molecular-weight heparin (LMWH) twice daily under frequent anti-XA activity monitoring, from the 6th week of pregnancy onwards. Transthoracic echocardiography showed a mean gradient of 29 mmHG over the mitral valve. Interdisciplinary setting of the indication for an emergency c-section, preceded by implantation of a veno-arterial Extracorporeal membrane oxygenation (ECMO) device. Intraoperative echography showed thecorrect orientation of the mechanical mitral valve and confirmed the pressure gradients. An immobile, anterior-medial wing with an adhering thrombus-like structure was seen. After successful delivery of a baby boy, intravenous lysis with Actilyse® (Alteplase) was initiated.

Methods: Three days later, the patient became hemodynamically unstable and an abdominal CT scan showed internal bleeding, requiring emergency intervention. Transesophageal controls showed complete regression of the adhering structure and a reduction of the trans-mitral valve gradient to a peak 15 mmHG and mean 9 mmHG but persistent immobile wing. The patient was discharged four weeks later, suffering from only light dyspnea. Transthoracic echocardiographic controls had shown little change in the mean gradient over the mitral valve (10 mmHg) and after three months the patient underwent elective mitral valve surgery. Intraoperatively, the immobile mitral valve wing was cleaned of an obstructing pannus both on the atrial and ventricular side. The original valve was found to be in perfect working order and was ultimately kept in place.

Results: The histological examination found the pannus to be consisting of fibrin and inflammatory cells, with no infec-

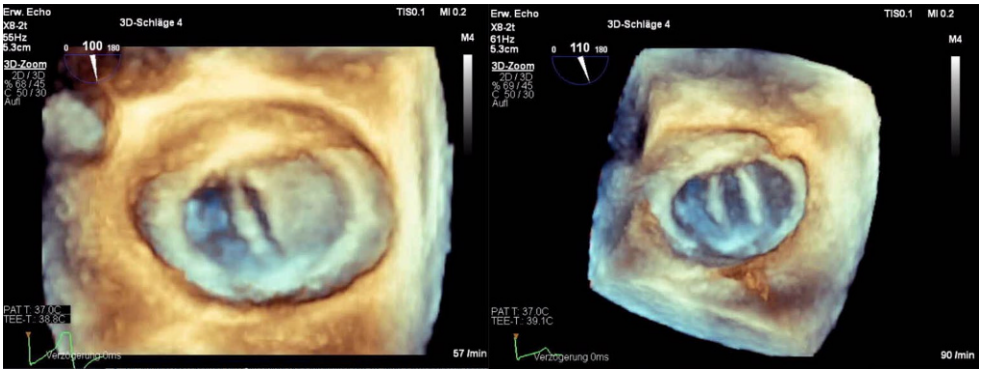


Fig. 1 | C-27 3D-Reconstruction of the mitral valve before (left) and after (right) the pannus removal

tious material. The patient was discharged on the eighth postoperative day.

Conclusions: This case highlights the benefits of three-dimensionally reconstructed ultrasound images in the management of complex, high risk patients.

C-28

Noninfective endocarditis ulceropolyposa of the aortic valve in a 28y old male

Gregory Reid, David Santer, Martin Grapow, Oliver Reuthebuch, Freidrich Eckstein, Arnheid Kessel, Sebastian Imhof, Maria Martinez, Hopfer Helmut, Florian Rüter

University Hospital Basel, Basel, Switzerland

Background: A 28y old male experienced fever and acute embolic closure of the left popliteal artery after a game of football, necessitating emergency intervention. Displaying splinter hemorrhages, but no signs of infection, empiric antibiotic treatment was initiated for 4 weeks, as well as phenprocoumon in a therapeutic dose. Diagnostic workup showed a visible vegetation on the aortic valve in echocardiography.

Methods: Six weeks later, due to sudden progressive growth and moderate aortic insufficiency, the indication for urgent aortic valve replacement was given by the interdisciplinary Heart Team. Intraoperatively, the valve was tricuspid with a large vegetation fusing two leaflets, creating a functionally bicuspid valve. A mechanical aortic valve was implanted (Medtronic Open Pivot™AP 360®, 28 mm). The histopathological workup showed no identification of pathogens or organisms. Light microscopy demonstrated a destructive, ulceropolyposis of the native valve combined with a florid inflammation. The patient recuperated well and was discharged after a short hospitalization. The hematological investigation revealed a hereditary heterozygous prothrombin-mutation (G20210A-Mutation).

Results: Seven months later the patient presented himself to the emergency ward with typical symptoms of unstable angina pectoris after cycling. High-sensitive Troponin T was elevated to a maximum value of 1521 ng/L (0–14 ng/L) and CK-MB to 76 µg/L (0–5 µg/L). The coronary angiogram showed multiple coronary embolisms with no signs of sclerosis. Echocardiography demonstrated the perfectly functioning mechanical valve without signs of adhering material. No intervention was performed and the patient was monitored on the intensive care unit. Reanalysis of the hematological-testing, bloodwork

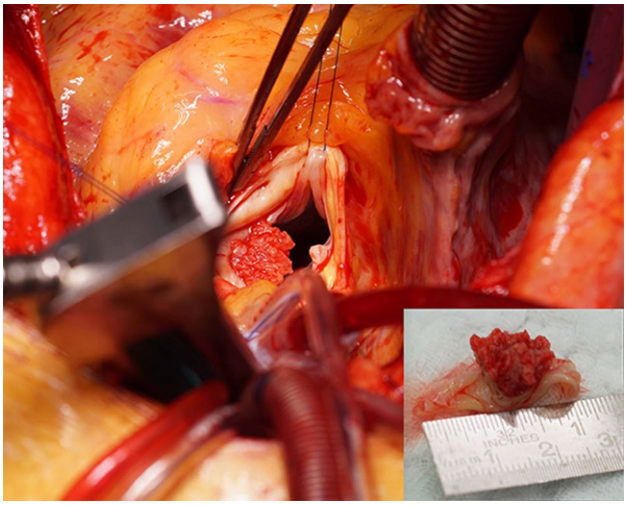


Fig. 1 | C-28 Intraoperative view of the aortic valve with visible vegetation. Inset: Magnified view with scale

and coagulation factors showed a Factor-VII deficiency leading to false high INR values. Anticoagulation monitoring was changed to daily Factor II-analysis with target values of 20–25%. The patient was discharged after a short hospitalization.

Conclusions: In Patients with rare hereditary coagulation disorders, anticoagulation therapy monitoring can be changed to Factor-II analysis in order to prevent possible complications.

C-29

Less invasive LVAD implantation reduces the perioperative blood product use at the time of heart transplantation

Julia Riebandt, Franziska Wittmann, Dominik Wiedemann, Arezu Aliabadi-Zuckermann, Angela Rajek, Andreas Zuckermann, Günther Laufer, Daniel Zimpfer

Medical University of Vienna, Vienna, Austria

Background: Less invasive (LIS) left ventricular assist device (LVAD) implantation may simplify subsequent cardiac transplantation by reducing adhesions and avoiding the need of a re-sternotomy. This study was performed to investigate the

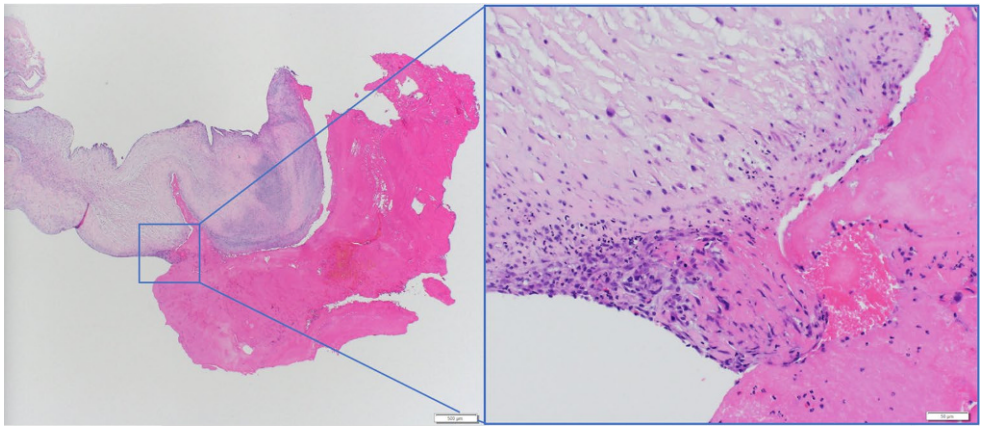


Fig. 2 | C-28 Histological analysis: a Valve leaflet. b Pannus. Magnified inset shows a non-specific inflammation and adhering fibrinous material

impact of LIS LVAD implantation on perioperative outcomes after cardiac transplantation.

Methods: A retrospective comparison of 44 patients after LIS or conventional (FS) LVAD implantation (LIS: $n=24$, conventional: $n=20$ patients) undergoing heart transplantation between 01/14 and 10/18 was performed. The groups were comparable with regard to preoperative patient characteristics (mean age 58 ± 11 years FS vs. 57 ± 8 years LIS, $p=0.559$; 85% male FS vs. 83% male LIS, $p=0.880$; MELD-XI Score 10 ± 5 FS vs. 10 ± 4 LIS, $p=0.917$).

Results: Early mortality rates did not differ between the two groups (0% 30-day mortality in both groups and 10% in-hospital mortality FS vs. 4% LIS). We observed a significant reduction in the perioperative use of packed red blood cells (PRBCs) in the LIS group (4.88 ± 2.88 Units vs. 8.55 ± 6.78 Units; $p=0.033$). Revision for bleeding was necessary in two patients of the FS group ($p=0.201$). There was a trend to a decrease of catecholamine dosage within the first 24 h after arrival on the ICU in the LIS group.

Conclusions: LIS LVAD implantation simplifies subsequent heart transplantation and reduces perioperative blood product use. In bigger cohorts, the observed differences might become significant.

C-30

Benefit of extracorporeal membrane oxygenation in myocardial infarction-induced cardiogenic shock

Elfriede Ruttmann-Ulmer[1], Julian Wagner[1], Hannes Abfalterer[1], Marion Dietl[2], Christina Tiller[3], Christoph Brenner[4], Grimm Michael[1], Peter Mair[4], Judith Martini[4], Hanno Ulmer[5]

[1]University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Plastic and Reconstructive Surgery, Landeskrankenhaus Feldkirch, Feldkirch, Austria
[3]University Hospital for Internal Medicine III (Kardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria
[4]University Hospital for Anaesthesia and Intensive Care, Medical University of Innsbruck, Innsbruck, Austria
[5]Department of Medical Statistics, Informatics and Health Economics, Innsbruck Medical University, Innsbruck, Austria

Background: Extracorporeal membrane oxygenation (ECMO) is frequently used for emergency support in patients with profound cardiogenic shock (CS) of all etiologies. However, no controlled study investigating ECMO in myocardial infarction-induced CS is available.

Methods: A total of 476 patients with AMI-induced CS (ICD codes: R57: cardiogenic shock; I21.9: acute myocardial infarction) were investigated. One hundred twenty seven patients (26.7%) received emergency veno-arterial ECMO support, 349 patients did not receive mechanical circulatory support. Patients were propensity score matched based on relevant clinical factors at admission such as age, gender, and the IABP shock II score at admission in the cath lab. Propensity score matching revealed 127 matched pairs.

Results: Mean age of patients was 65.0 ± 12.3 years and mean Syntax score was 25.9 ± 7.3 in the full unmatched patient population. Survival at 1, 3 and 5 years after CS was 45.6%, 43.5%, and 41.3% in the ECMO group and 17.4%, 15.8%, and 14.9% in the full unmatched control group (log-rank: $p<0.001$). After propensity score matching, 1, 3, and 5 year survival was 14.4%, 13.5%, and 11.2% in the matched control group ($p<0.001$). Cox regression analysis identified ECMO support (HR: 2.57; 95% CI: 1.89–3.50; $p<0.001$), completeness of revascularization (HR: 1.89; 95% CI: 1.74–2.34, $p=0.003$), previous CPR (HR: 0.67; 95% CI: 0.49–0.92, $p=0.013$), and high IABP-SHOCK II scores (HR: 0.74; 95% CI: 0.44–0.98, $p=0.005$) to be independent predictors for long term survival.

Conclusions: Extracorporeal life support by ECMO significantly increased survival in patients with AMI-induced CS. ECMO insertion increased survival probability 2.57 fold and should be considered as first line treatment in patients with AMI-induced CS.

C-31

Combined use of a semi-rigid mitral ring and a balloon expandable transcatheter valve for the treatment of mitral regurgitation in a patient with severe annular calcification

Adel Sakic, Can Gollmann-Tepeköylü, Johannes Holfeld, Michael Grimm, Nikolaos Bonaros, Ludwig Müller

University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background: A 76-year-old female patient presents with progressive dyspnea (NYHA III) and severe leg edema. The patient used to be physically very active in recent years. However, during the last 6 months symptoms have been progressive. Currently, she experiences angina and palpitations after 50 meters of walking. Besides that she presents in a good general condition. ECG shows normofrequent atrial fibrillation which has been present for several years. The patient is currently under coumarin therapy (CHA_2DS_2-VASc = 5, HASBLED = 2). In 2009, the patient underwent a biological aortic valve replacement (Carpentier Edwards Magna Ease 21 mm) plus single CABG procedure (vein graft to right coronary artery). In 2009 she had an endarterectomy procedure of the right carotid artery. The patient has a history of arterial hypertension, hypercholesterinemia and osteoporosis.

Methods: Transthoracic echocardiography showed severe mitral valve regurgitation with mild stenosis, mild tricuspid regurgitation and adequate function of the aortic valve prosthesis with preserved left ventricular function. Subsequent transesophageal echocardiography confirmed the mitral valve pathology with thickened valve leaflets, calcification of the mitral annulus, mild mitral stenosis (mean pressure gradient of 5 mmHg, mitral valve orifice area 2.4 cm^2) and a severe mitral regurgiation (Carpentier type IIIa/b, EROA 0.32 cm^2, RV 60 ml). The Tricuspid annulus measures 41 mm in diameter. Left ventricular dimensions are regular (LVEDD 49 mm) with ventricular ejection fraction of 54%. The left atrium is mildly dilated with 44 mm diameter, calculated systolic pulmonary arterial pressure is elevated to 60 mmHg. Coronary angiography showed perfect graft patency and no signs of coronary artery disease progression. For further diagnostic evaluation, the patient underwent a CT scan. It revealed massive calcifications of the mitral annulus with maximum intensity in the region of the posterior commissure (up to 1.3 cm thickness) expanding to A3 and A2 segments and the myocardium. Due to progressive symptoms and severe mitral regurgitation with preserved left

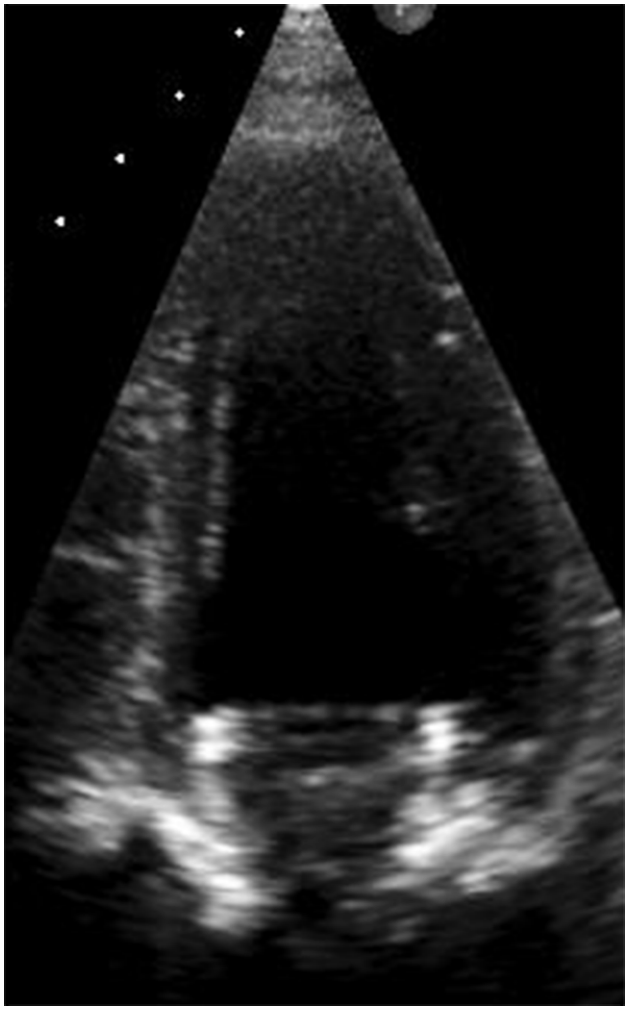


Fig. 1 | C-31 Transcatheter valve in a semi-rigid mitral ring in mitral position

ventricular ejection fraction and absence of significant comorbidities our heart team decided to perform surgical mitral valve replacement. We performed implantation of a semi-rigid ring (34 mm) with subsequent application of a transcatheter valve.

Results: We present a patient with severe mitral valve regurgitation and high perioperative risk for conventional mitral valve surgery. The massive calcification in the mitral annulus position as well as in the anterior mitral leaflet aggravates a conventional replacement. After prior aortic valve replacement, transcatheter mitral valve replacement is also contraindicated. A recent study showed that patient ineligible for TMVR and medical treatment have poor prognosis. Severe mitral annular calcification (MAC) is still an unsolved issue in patients with mitral regurgitation. The rates of atrioventricular rupture and severe paravalvular regurgitation in such cases are still very high and alternative options are limited. In this case, we present a new option for the treatment of MAC including the implantation of a semi-rigid mitral ring on the atrial side of the calcification. This creates a stable landing zone for a balloon expandable transcatheter valve. The latter can be implanted under direct view after excising the anterior mitral leaflet. Subsequently the risk of LVOT obstruction is minimized.

Conclusions: Implantation of a semi-rigid mitral valve ring and subsequent transcatheter valve implantation in mitral valve position reduces the risk of paravalvular leakage, outflow

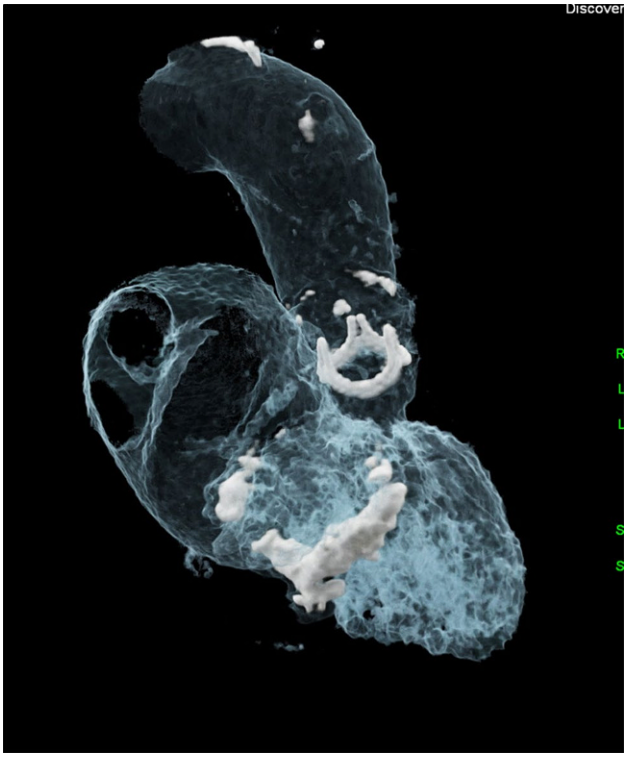


Fig. 2 | C-31 CT scan with severe mitral annular calcification

tract obstruction and atrioventricular rupture in patients with severe mitral annulus calcification.

C-32

St Thomas' Hospital Polarizing blood cardioplegia improves hemodynamic recovery in a porcine model of cardiopulmonary bypass

David Santer[1], Anne Kramer[1], Attila Kiss[1], Klaus Aumayr[2], Matthias Hackl[3], Stefan Heber[4], David J Chambers[5], Seth Hallström[6], Bruno K. Podesser[1]

[1]Ludwig Boltzmann Cluster for Cardiovascular Research at the Center for Biomedical Research, Medical University of Vienna, Vienna, Austria
[2]Clinical Institute for Pathology, AKH Wien, Medical University of Vienna, Vienna, Austria
[3]TAmiRNA GmbH, Vienna, Austria
[4]Institute of Physiology, Center for Physiology and Pharmacology, Medical University of Vienna, Vienna, Austria
[5]Cardiac Surgical Research, The Rayne Institute (King's College London), Guy's and St Thomas' NHS Foundation Trust, St Thomas' Hospital, London, United Kingdom
[6]Physiological Chemistry, Otto Loewi Research Center, Medical University of Graz, Graz, Austria

Background: Cardiac surgery demands highly effective cardioprotective regimens. We previously demonstrated improved cardioprotection with 'polarized' compared to 'depolarized' arrest. This study uses a clinically-relevant porcine model of cardiopulmonary bypass to compare the efficacy of blood-

based St Thomas' Hospital polarizing cardioplegia (STH-Pol-B) with blood-based St Thomas' Hospital hyperkalemic cardioplegia (STH2-B).

Methods: Pigs were monitored and subjected to normothermic cardiopulmonary bypass, cardiac arrest via antegrade cold (4 °C) blood cardioplegia (STH2-B, control group: $n=6$ or STH-Pol-B, study group: $n=7$), and global ischemia (60 min) followed by on-pump reperfusion (60 min) and subsequent off-pump reperfusion (90 min). At termination, tissue samples were taken for analysis of high-energy phosphates, ultrastructure and microRNAs. Primary endpoint of this study was CK-MB release during reperfusion.

Results: CK-MB was comparable in both groups. After weaning from cardiopulmonary bypass, hemodynamic parameters such as mean arterial pressure ($p=0.007$), left ventricular systolic pressure ($p<0.001$), external heart work ($p=0.012$), stroke volume ($p=0.015$) as well as dp/dtmax ($p=0.027$), were improved with polarizing cardioplegia. Wedge pressure was significantly lower in the study group ($p<0.01$). Energy charge was comparable between groups. MicroRNA-708–5p was significantly lower ($p=0.019$) and microRNA-122 expression significantly ($p=0.046$) higher in STH-Pol-B hearts.

Conclusions: Polarized cardiac arrest offers similar myocardial protection and enhances functional recovery in a porcine model of cardiopulmonary bypass. Differential expression of microRNAs may indicate possible new ischemia-reperfusion markers. These results confirm the non-inferiority and potential of polarized versus depolarized arrest.

C-33

Case Report: First description: Transapical aortic valve replacement (TAVR) after robot-assisted coronary artery bypass (RACABG)

Bruno Schachner, Peter Benedikt, Andreas Zierer

Department of Thoracic and Cardiovascular Surgery, Med Campus III, Johannes Kepler University Hospital, Linz, Austria

Background: We report the case of a 78-year-old patient suffering from severe aortic valve Stenosis. The patient also suffered from a coronary heart disease. Therefor he already received a robot-assisted coronary artery bypass procedure in April 2009. Due to cannulation transfemoral during the RACABG- procedure the patient wasn't suitable for a transfemoral access. In synopsis of the findings and after inter-disciplinary discussion in the Heart Team, the patient underwent a minimally invasive off pump aortic valve replacement.

Methods: After left anterolateral incision the situs showed adhesions due to the previous operation. After difficult preparation epicardial pacing wires were placed and tested. U-stitches with Teflon felt pledgets were placed at the apex of the left ventricle. Under guidance of transoesophageal echocardiography and fluoroscopy the aortic valve was passed with a guidewire. Then the stented valve (26 mm SAPIEN 3/XTTM (Edwards Lifescience, Irvine, CA, USA)) was deployed directly without previous balloon valvuloplasty and under rapid ventricular pacing. The intraoperatively function assessment with angio- and echocardiography showed a good placement of the valve. No paravalvular leak was detected. No insufficiency was shown.

Results: After surgery the patient underwent early weaning at the intensive care unit. The transfer to the normal ward was possible on the first post-operative day. The patient could

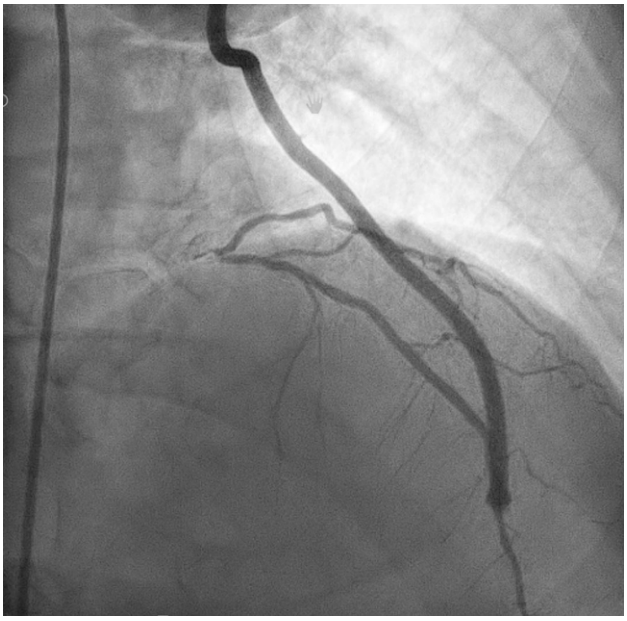


Fig. 1 | C-33

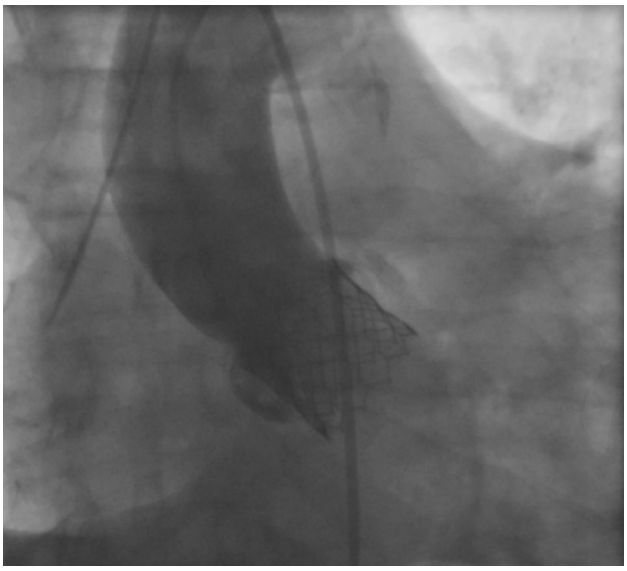


Fig. 2 | C-33

be mobilized quickly. The echocardiograph control showed an excellent result with no stenosis or paravalvular leak. The patient could be dismissed on the 7 post-operative day in good conditions.

Conclusions: This is to the best of our knowledge the first reported case of a patient receiving TAVR procedure after prior RACABG. Due to the patent bypass and the expected adhesion the transapical acess the risk of bypass injury is reduced. The minimal invasiv procedure also provides a fast recovery from the procedure.

C-34

Use of a pulmonary valved conduit in a growing long-term animal model – midterm results

Martin Schweiger[1], Walter Knirsch[2], Bernard Krüger[3], Alexandra Malbon[4], Thomas Frauenfelder[5], Thea Fleischmann[6], Mariam Lipiski[6], Frithjof Lemme[1], Michael Hübler[1]

[1]Pediatric Cardiovascular Surgery, Pediatric Heart Center, Department of Surgery, University Children's Hospital Zurich, Zurich, Switzerland
[2]Pediatric Cardiology, Pediatric Heart Center, Department of Surgery, University Children's Hospital Zurich, Zurich, Switzerland
[3]Department of Anesthesiology, University Hospital Zurich, Zurich, Switzerland
[4]Institute of Veterinary Pathology, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland
[5]Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, Zurich, Switzerland
[6]Division of Surgical Research, University Hospital Zurich, Zurich, Switzerland

Background: We established a chronic animal model to evaluate a tissue engineered valved conduit, connecting the right ventricular outflow tract to the bifurcation of the pulmonary arteries, during long-term follow up and growth up to 24 months.

Methods: 12 female Swiss white mountain lambs (27–38 kg BW at surgery) were operated, using left lateral thoracotomy and cardiopulmonary bypass (CPB) and survived the initial perioperative phase. The native pulmonary valve and the complete pulmonary trunk were resected. The conduit was constructed out of a de-cellularized porcine small intestinal submucosa extracellular matrix biologic scaffold and was implanted in orthotopic position. Follow-up transesophageal/-thoracic 2D echocardiography and laboratory values (LDH, Hb, HKT, WBC) were performed directly after surgery and after 1, 3, 6, 12, 18 and 24 months. Animals planned for scarification underwent CT scan prior to termination and the conduit was histologically examined.

Results: Mean follow-up time so far is 13 months (20 days–24 months). Four animals were sacrificed as planned at 24 months ($n=2$), 12 months ($n=1$) and 9 months ($n=1$). Two animals died due to infective endocarditis at day 20 (Germ: Enterobacta cloacae) and day 256 (Staphylococcus xylosus), postoperatively. One animal was found dead in the stable at day 23 post operation. Autopsy revealed aspiration pneumonia as reason for death. Five animals are still under follow up. Mean body weight at last follow up was 53.4 kg (28–67). Investigation of the conduit by echocardiography revealed no severe stenosis or calcifications [dp max 12.8; ± 8.5 (mean; SD) (5–31) and no greater than a mild regurgitation. Global heart function was uncompromised with a no greater than mild tricuspid, mitral and aortic valve regurgitation in all animals. LDH increased from a pre-operative mean 976 ± 78.2 (mean; SD) (889–1097) to 1100 ± 181.8 (mean; SD) (771–1369) [n. s.]. CT scan prior to termination (n: 4) revealed no calcification or dilatation of the conduit. Subsequent histologic evaluation revealed a variable degree of incorporation to native tissue between individual valve leaflets. Most were moderately populated by stromal cells and showed endothelialisation (confirmed by CD31 immunohistology) and little inflammation within the valve. Small foci of chondroid and osseous metaplasia were occasionally observed, predominantly at the suture sites rather than within the leaflets.

Conclusions: The implantation of a valved RV-PA-conduit in a growing animal model is feasible up to 2 years. The animals demonstrated, after the initial recovery phase from surgery, good physical development but remain at risk for endocarditis (16%). The function of the valved conduit was satisfactory up to a follow up of 24 months.

C-35

Experience of VV-ECMO in children with the Avalon®

Martin Schweiger[1], Anna Cavigelli-Brunner[2], Anna Valencia[1], Yvonne Kröger[3], Sebastian Bründler[3], Frithjof Lemme[1], Hitendu Dave[1], Tugba Erdil[1], Michael Hübler[1]

[1]Pediatric Cardiovascular Surgery, Pediatric Heart Center, Department of Surgery, University Children's Hospital Zurich, Zurich, Switzerland
[2]Pediatric Cardiology, Pediatric Heart Center, Department of Surgery, University Children's Hospital Zurich, Zurich, Switzerland
[3]Intensive Care Medicine and Neonatology, University Children's Hospital Zurich, Zurich, Switzerland

Background: The Avalon® bicaval double lumen cannula (Avalon®) represents an innovative concept for venovenous (vv) ECMO support in children with an easy and safe implantation. We report about our experience in different pediatric patients.

Methods: Retrospective analyses including all vvECMO Avalon® patients between 2014–2018. Primary endpoints: survival to hospital discharge, severe complications. Duration of vvECMO support, mechanical ventilation time and ICU stay were evaluated as well.

Results: In 18 patients, median weight 19 kg (range 4.2–50), Avalon® was implanted at a median age of 3.6 years (0.1–13). Respiratory failure pneumonia in 7, septicemia in 3, neoplastic disease 4, near drowning 2 and post heart-/chest- surgery 1. vvECMO was mainly installed at bedside under echocardiographic guidance. In 3 patients support was initiated as veno-arteriel (va)ECMO, which was successfully converted to vvECMO after a mean of 5 days. One patient needed a conversion to vaECMO after 12 days on vvECMO; in one patient a second vvECMO run was needed. Median ventilation time after vvECMO withdrawal was 3 days (1–32), median ICU stay 16 days (5–64). Eight severe complications occurred in 5 patients: 3 patients needed surgical repositioning of the cannula due to dislocation, including one patient with cannula perforation and subsequent haematopericardium needing sternotomy. One of these three patients underwent two explorative thoracotomies due to bleeding after lung biopsy on vvECMO. Additionally one patient developed haematopericardium due to therapeutic anticoagulation resulting in an explorative sternotomy without detecting a surgical bleeding site. Finally in patient n an exchange of the oxygenator was mandatory. Survival to discharge 83%. Successful weaning (16) after median support of 6 days (2–32). Median follow-up after vvECMO explantation was 166 days (0–1400) with an overall survival of 78% to present.

Conclusions: vvECMO with Avalon® cannula provides a simple, safe and successful respiratory support in the pediatric age group. Death is mostly related due to the underlying disease. Complication mainly account to cannula dislocation or

bleeding, jugular veinous thrombus formation ahs to be ruled out after explantation.

C-36

A new way to use transit-time flow measurement for CABG

Lukas Stastny, Markus Kofler, Julia Dumfarth, Simone Gasser, Elfriede Ruttmann, Adel Sakic, Alexandra Brix, Michael Grimm, Nikolaus Bonaros

University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background: This study aimed to assess the value of transit time flow measurement (TTFM) on in-situ IMA grafts during non-existing native coronary circulation and the relevance of collateral blood flow in target vessels.

Methods: Between 2014 and 2018, 134 patients undergoing on-pump CABG were evaluated using TTFM. We analyzed 111 single LIMA, and 57 single RIMA bypasses. Correlation between coronary relevant parameters was calculated using Spearman's ρ coefficient. Dependent and independent risk factors for decreased flow at arrested heart (FAH) <30 ml/min, increased pulsatility index (PI) > 3.0, as well as flow reduction > 30%, were calculated using univariate and multivariate analysis.

Results: FAH correlated with the diameter of the target vessel (Spearman's $\rho = 0.324$, $p < 0.001$) and the size of blood distribution (Spearman's $\rho = -0.342$, $p < 0.001$). The percentage of flow change was found to correlate the PI (Spearman's $\rho = -0.465$, $p < 0.0001$) and the degree of stenosis (Spearman's $\rho = 0.422$, $p < 0.001$). A small blood distribution area was the only risk factor for decreased FAH (OR 8.434, CI 95% [3.038–23.413], $p < 0.001$).

Conclusions: Flow measurement at the arrested heart provides additional information about the bypass graft, the quality of anastomosis and the physiology of coronary circulation.

C-37

What are the preoperative risk factors for heart failure after TAVI?

Lukas Stastny[1], Markus Kofler[1], Julia Dumfarth[1], Friedrich Guy[2], Bernhard Metzler[2], Michael Grimm[1], Nikolaus Bonaros[1]

[1]University Hospital for Cardiac Surgery, Department of Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]University Hospital for Internal Medicine III (Cardiology and Angiology), Medical University of Innsbruck, Innsbruck, Austria

Background: Acute heart failure is known to be the most frequent cause of hospital readmission after transcatheter aortic valve implantation (TAVI). Furthermore, it is associated with an increased risk of mortality. The study aimed to define independent predictors for acute heart failure after TAVI.

Methods: From 2008 to 2017, 298 patients with isolated aortic stenosis undergoing either transfemoral or transapical TAVI were included in this single-center study. The primary study endpoint was defined as hospital readmission due to acute heart failure. All analyses were performed as time-to-first-event analysis. Stepwise multivariable Cox regression analysis was used to determine independent predictors for acute heart failure.

Results: STS-Score > 4% (HR 2.900, 95% CI 1.001–8.398, $p = 0.05$), HS-Troponin T > 23.3 pg/ml (HR 2.570, 95% CI 1.073–6.156, $p = 0.034$) and stroke volume index < 35 ml/m^2 (HR 2.999, 95% CI 1.390–6.472, $p = 0.005$) were significant prognostic factors after multivariate Cox regression. NT-proBNP > 2762 pg/ml, mean gradient > 40 mmHg and EF< 30% were significant in univariate analysis, but not in multivariate regression analysis.

Conclusions: STS Score, high sensitive Troponin T, and stroke volume index are independent predictors for acute heart failure after TAVI. Special attention to these factors should be paid in identifying patients at risk for readmission.

C-38

Mastering the learning curve after implementation of an aortic valve repair program in a medium-volume center

Johannes Steindl[1], Andreas Vötsch[1], Roman Gottardi[1], Michael Kirnbauer[2], Apollonia Daburger[3], Rainald Seitelberger[1], Christian Dinges[1]

[1]Department of Cardiovascular and Endovascular Surgery, Paracelsus Private Medical University Salzburg, Salzburg, Austria
[2]Department of Anesthesiology, Perioperative Care and Intensive Care Medicine, Paracelsus Private Medical University Salzburg, Salzburg, Austria
[3]Department of Cardiology, Paracelsus Private Medical University Salzburg, Salzburg, Austria

Background: Aortic valve repair is the gold standard in surgery for aortic valve insufficiency (AI) in young patients. During the last decade continuous surgical developments decreased the learning curve of this complex procedure and lead to its broader use. In 2012 our institution launched an aortic valve repair program using both remodeling (Yacoub) and reimplantation (David) technique.

Methods: From September 2012 to February 2019, aortic valve repair was performed on 61 patients in our center. Indication for elective surgery was aortic root aneurysm ($n = 31$), isolated aortic valve insufficiency ($n = 11$) and valve insufficiency after Ross procedure ($n = 2$). Seventeen patients underwent surgery for acute aortic dissection. Valve cuspidity included tricuspid ($n = 33$), bicuspid ($n = 22$) and unicuspid ($n = 4$) valves. In 54 patients remodeling technique was used, 7 patients underwent reimplantation procedures. Effective height measurement was routinely performed. Leaflet plication and patch augmentation was done if necessary. In Yacoub procedures additional extraaortic subannular ring implantation ($n = 43$) was performed dependent on annular size. Concomitant procedures included partial ($n = 11$) or complete ($n = 12$) aortic arch replacement, mitral valve repair ($n = 2$), CABG ($n = 4$) and PFO-closure ($n = 1$).

Results: Successful valve repair was achieved in 58 patients (95.1%). Within the first two years of the program, conversion to aortic valve replacement was necessary due to remaining AI ≥ II° in 3 cases (4.9%). There was no perioperative death. Overall mortality was 1.6%. One patient died three months postoperatively from surgical complications. Mean aortic crossclamp time and time on extracorporeal circulation was 152 (± 56) and 215 (± 77) minutes respectively. There were two early repair fail-

ures before hospital discharge due to suture dehiscense. Both of them were successfully reoperated without need of valve replacement. Cumulative follow up was 1584 (1–72) months. Fifty-three patients (86.8%) presented with AI grade ≤ I at the latest follow up. Five patients (8.1%) showed AI ≥ II°. Two of them (3.2%) had to undergo consecutive valve replacement. There was no perioperative pacemaker implantation necessary.

Conclusions: Aortic valve repair can be safely performed in elective and acute settings in medium volume centers and offer excellent early- and midterm results. In our series, intraoperative repair failures occurred solely within the first two years of the program, which might indicate a learning curve concerning surgical technique and patient selection.

C-39

Pushing the limits too much? – Transcatheter mitral valve implantation: Midterm results of a case series of valve-in-valve, valve-in-ring and valve in native valve

Marie-Elisabeth Stelzmüller [1], Robert Zilberszac[2], Rüdiger Schernthaner[3], Bruno Mora[4], Günther Laufer[1], Wilfried Wisser[5]

[1]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
[2]Division of Cardiology, Department of Internal Medicine II, Medical Unversity of Vienna, Vienna, Austria
[3]Division of Cardiovascular and Interventional Radiology, Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria
[4]Division of Cardiothoracic and Vascular Anesthesia and Intensive Care Medicine, Medical University of Vienna, Vienna, Austria
[5]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria

Background: With an aging population the number of redo-surgeries for degenerated bioprosthesis and failed mitral repair as well as the morbidity and procedural complexity is increasing. This study presents short-term results of transcatheter mitral valve implantation (TMVI) as bail out strategy in otherwise inoperable patients.

Methods: From April 2011 to Juni 2018 14 patients (743 7 years), 64% female, with severe symptomatic mitral valve insufficiency underwent a transcatheter mitral valve implantation (mean Euroscore II 21% (5.5%–45.5%)). 5 underwent valve-in-valve (ViV) transapically ($n=6$) or transatrial ($n=4$) for degenerated bioprotheses, 1 valve-in-ring (ViR) transatrial for failed mitral repair, 3 valve-in-native valve (ViNV) transatrial for heavily calcified annulus which was infiltrating the myocardium. All patients were rejected for conventional mitral valve surgery based on their mitral valve pathology as well as their multiple comorbidities. Five patients underwent concomitant procedures such as additional tricuspid valve repair, left atrial thrombectomy, TAVI and aortic valve replacement.

Results: In 6 patients an Edwards Sapien XT valve size 26 mm, in 8 patients an Edwards Sapien 3 valve size 29 mm was used. The eight TMVI through a transatrial approach were performed with extracorporeal circulation, because of the concomitant procedures (left atrial thrombectomy, aortic valve replacement, tricuspid valve re-repair) via open approach. The remainingsix patients, the transcatheter valve was implanted during rapid pacing. Valve implantation was successful in all patients but one. In one patient undergoing ViNV, the prosthesis migrated after stopping extracorporeal circulation and needed to be fixed with additional sutures placed in the atrium. 1 patient died on day 8 (transapical ViV) and 2 patients on day 1 (transatrial ViNV) respectively due to multiple organ failure, one patient had a stroke. The postoperative survival was 71% at 6 months and 56% at 1 year, follow up.

Conclusions: The transcatheter mitral valve implantation seems to be a promising option for inoperable patients. The transcatheter valve could be placed safely in annuloplasty ring, as well as in bioprosthesis. Caution is indicated implanting the valves in the native annulus because of the higher likelihood for migration.

C-40

Fallbericht „Schrittmacher-assoziierte Infektion“

Philipp Sternbach, Claudia Stöllberger, Franz Weidinger

Krankenanstalt Rudolfstiftung, Wien, Österreich

Grundlagen: Infektionen stellen eine gefürchtete Komplikation nach Schrittmacher-implantationen dar. Wir berichten über einen Patienten, welcher neun Monate nach Implantation eines DDD-Schrittmachersystems wegen Perforation der Schrittmacher-Tasche bei uns in stationärer Behandlung war.

Methodik: Es handelt sich um den Fall eines 86-jährigen Patienten, welchem im April 2018 wegen eines Sick-Sinus-Syndroms (mit Sinus-Pausen von bis zu 4,5 Sekunden) ein DDD-Schrittmachersystem mit Aggregat im Bereich des rechten Brustkorbs implantiert worden war. Im Jänner 2019 spürte der Patient ein starkes Ziehen im Bereich des rechten Schlüsselbeins (mit Ausstrahlung zu Hals bzw. Fingerspitzen), welches am Folgetag verschwunden war. Dafür war jedoch eine Perforation von ca. 4 cm × 6 cm im Bereich der Schrittmacher-Tasche entstanden (siehe Abb. 1), durch welche ein Teil des Aggregats sichtbar war. Bei initialer Wundbegutachtung zeigten sich keinerlei Entzündungszeichen an oder um die perforierte Stelle; auch Fieber, Schüttelfrost und kardiale Beschwerden konnten nicht festgestellt werden. Es wurden mehrere Abstriche der Wunde und des sichtbaren Aggregat-Teils durchgeführt, sowie serielle Blutkulturen angelegt; außerdem wurde eine prophylaktische Antibiotika-Therapie mit Aminopenicillin und Sulbactam gestartet. Eine Echokardiographie hinsichtlich infektiöser Endokarditis fiel negativ aus. Das gesamte Schrittmacher-System wurde chirurgisch unter Lokalanästhesie explantiert, das Schrittmacher-Bett von überschüssigem Granulationsgewebe gereinigt (siehe Abb. 2). Im Zuge der Explantation wurden weitere Abstriche genommen, sowie eine bakterielle Untersuchung der Schrittmacher-Sonden durchgeführt.

Ergebnisse: Sämtliche Wundabstriche fielen negativ aus, es konnten also keine, für die Perforation verantwortlichen, Erreger gefunden werden. Auch die bakteriologischen Untersuchungen der Elektroden fielen negativ aus. Nach erfolgreicher Explantation wurde eine telemetrische Überwachung begonnen, um die Indikation eines neuen Schrittmachers zu prüfen. Da diese positiv ausfiel, wurde dem Patienten ein neues Schrittmacher-System implantiert, mit dem Schrittmacher-Bett kontralateral zur ursprünglichen Position. Abgesehen von einer minimalen Entzündung des Wundbereichs, zeigte sich der Patient im weiteren Verlauf komplikationslos, so dass er eine Woche nach Re-Implantation in gutem Allgemeinzustand nach Hause entlassen werden konnte.

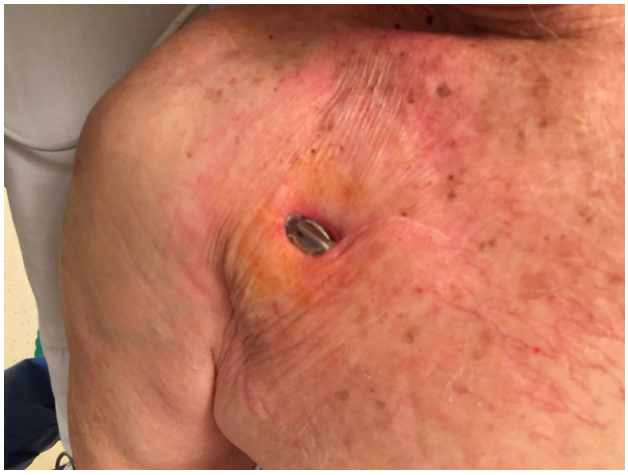


Fig. 1 | C-40 Perforierte Schrittmacher-Tasche mit sichtbarem Aggregat

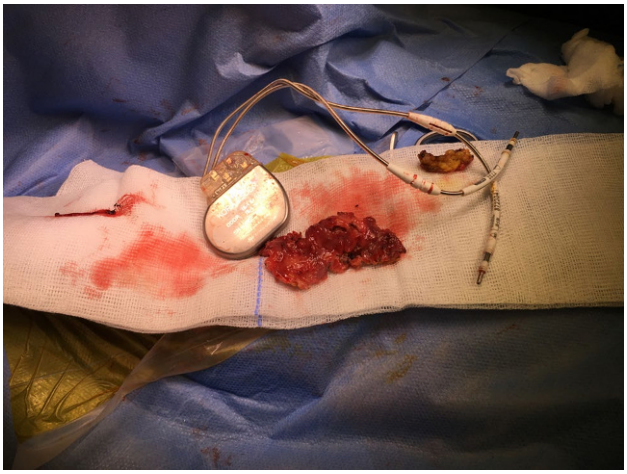


Abb. 2 | C-40 Explantiertes Aggregat, Sonden sowie das entfernte Granulationsgewebe

Schlussfolgerungen: Der lange Zeitraum zwischen Implantation und Perforation zeigt, dass auch nach Monaten bis Jahren eine Perforation möglich sein kann. Ein weiterer interessanter Aspekt dieses Falls ist die Tatsache, dass die Perforation der Schrittmacher-Tasche ohne nennenswerte Symptome (Schmerz, Schwellung, Rötung) passiert ist. Das therapeutische Vorgehen entspricht hierbei den Empfehlungen, welche 2018 im deutschen Ärzteblatt von Döring et al. publiziert wurden; Diese umfassen mehrfaches Prüfen auf potenzielle Erreger, Explantation des kompletten Schrittmacher-Systems und Re-Evaluation der Schrittmacher-Indikation vor etwaiger Implantation eines neuen Systems.

C-41

Der interdisziplinäre pädiatrische Fall: Agenesie des Ductus thoracicus und was nun?

Alissa Strugger[1], Igor Knez[1], Petra Filzmaier[1], Ayse Gürbüz[1], Martin Köstenberger[2], Larissa Krenn[3], Siegfried Rödl[3], Jakub Krumnikl[4], Andreas Gamillscheg[2], Otto Dapunt[1]

[1]Klinische Abteilung für Herzchirurgie, Universitätsklinik für Chirurgie, Medizinische Universität Graz, Graz, Österreich
[2]Klinische Abteilung für Pädiatrische Kardiologie, Universitätsklinik für Kinder- und Jugendheilkunde, Medizinische Universität Graz, Graz, Österreich
[3]Universitätsklink für Kinder-und Jugendheilkunde, Medizinische Universität Graz, Graz, Österreich
[4]Klinische Abteilung für Herz-, Thorax-, Gefäßchirurgische Anästhesiologie und Intensivmedizin, Universitätsklinik für Anästhesiologie und Intensivmedizin, Medizinische Universität Graz, Graz, Österreich

Grundlagen: Als CCLA, Central Conducting Lymphatic Anomaly, bezeichnet man ein Spektrum komplexer lymphatischer Anomalien welche aufgrund von Fehlfunktionen der Lymphgefäße zu Lymphleckagen und Proteinverlust führen können.

Methodik: Die hier vorgestellte Patientin ist ein Neugeborenes, bei welchem postpartal eine ca 5 × 4 × 4 cm große Zyste im Mediastinum ohne Handlungsbedarf diagnostiziert wurde. Als es am 16. Lebenstag zu einer Verschlechterung des Allgemeinzustandes kam, wurde sie stationär aufgenommen und es folgte eine Reihe von Interventionen wie Drainageanlagen, deren Wechsel sowie die Anlage eines transhiatalen Drains. Es wurde nun die Diagnose einer CCLA, wahrscheinlich einer Hypo-/Agenesie des Ductus Thoracicus gestellt. Trotz ausgedehnter medikamentöser und diätetischer Therapie kam es zu persistierend hohen Fördermengen aus sämtlichen Drainagen. Die Patientin wurde schließlich im Alter von einem Jahr operiert, dabei wurde eine Reduktionsplastik der Cysterna Chyli durchgeführt und eine Drainage in den verbleibenden Schlauch eingenäht, da der Druck im Venensystem zu hoch war und die Versuche einer Ableitung in den Venenwinkel frustran waren. In einem zweiten Eingriff wurde der Restschlauch in die Pleura parietalis eingenäht.

Ergebnisse: Es kam bei der Patientin nach der Entlassung einige Tage nach der Operation zu einer vollständigen Remission der Symptome. Es kam bei den Verlaufskontrollen zu keiner neuerlichen Volumszunahme der Cysterna chyli, zu keinen Pleuraergüsse und keinem Aszites. Die Patientin holte auch in Bezug auf Größe und Gewicht auf und zeigt sich nun in allen Bereichen innerhalb der 90. Perzentile.

Schlussfolgerungen: Der Ductus thoracicus ist das größte Lymphgefäß des Körpers und wird mit bis zu 190 ml Lymphe pro Stunde durchflossen. Kongenitale Anomalien desselben sind selten und der Umgang damit sowie die Behandlung der betroffenen Patienten sind nicht etabliert. Aufgrund der komplexen Natur dieser Malformationen sind häufig sowohl medikamentöse als auch operative Therapieansätze erfolglos. Zusammenfassend lässt sich sagen, dass solche komplexen Fälle immer in einem interdisziplinären Setting und unter Einbeziehung unkonventioneller Methoden und individuell auf den jeweiligen Fall bezogener Überlegungen behandelt werden sollten, um eine passende Lösung für jeden Patienten zu finden.

C-42

Early clinical outcomes of secondary endovascular repair versus open surgical replacement for thoracoabdominal aortic pathologies after frozen elephant trunk procedure

Philipp Szalkiewicz[1], Zsuzsanna Arnold[1], Daniela Geissler[1], Markus Mach[1], Bernhard Winkler[1], Gerard Mertikian[2], Gabriel Weiss[1], Martin Grabenwöger[1]

[1]Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Department of Interventional Radiology, Hospital Hietzing, Vienna, Austria

Background: Thoracoabdominal aortic (TAAA) pathology progression after aortic arch replacement with the Frozen Elephant Trunk (FET) technique is a challenging situation in cardiovascular surgery. Although, open thoracoabdominal aortic (TAAA) replacement (OPEN) and thoracic endovascular aortic repair (TEVAR) are standardized therapeutic approaches, comparison of their impact on the individual patient outcome is still lacking.

Methods: Between June 2006 and September 2018, 33 Patients underwent open TAAA replacement or TEVAR (TEVAR: 22 [66.7%]; female: 17 [51.5%]; aged 63 ± 11 years) for TAAA pathology after previous Frozen Elephant Trunk replacement. Fourteen patients with aortic dissection and 29 patients with aortic aneurysm, as well as 10 patients with both pathologies were included in the present study. In cases of elective intervention (TEVAR: 19 [86.4%]), custom made fenestrated stent grafts were designed according to the patients preoperative computed tomography angiography (CTA). TAAA replacement with a tubular aortic dacron prosthesis and left heart bypass was performed through posterolateral thoracotomy, followed by paramediane laparotomy.

Results: In the majority of cases ($n = 16$, 76%), the proximal landing zone of TEVAR stent grafts was in zone 4, whereas the distal end covered TH10 and TH12 in 50%. Neurological complications, such as paraparesis (TEVAR: 6 [27,3%]; $p = 0.077$), or spinal cord injury (TEVAR: 4 [18.2%] vs. OPEN: 1 [9.1%]; $p = 0.643$) occurred more frequently in the TEVAR group, although it did not reach statistical significance. In contrast, open TAAA replacement was significantly associated with visceral malperfusion (TEVAR: 1 [4.5%] vs. OPEN: 5 [45.5%]; $p = 0{,}01$). Accordingly, the OPEN group was at higher risk of renal malperfusion (TEVAR: 0 vs. OPEN: 2 [18.2%]; $p = 0{,}104$), contributing to renal failure (TEVAR: 3 [13.6%] vs. OPEN: 3 [27.3%]; $p = 0.375$) in this regard, however without any statistical significance. In hospital mortality occurred in one patient after TEVAR (4.5%). During the mean follow up period of 23 months, overall mortality was 23%, including three deaths from aortic related complications (TEVAR: 1 [4.5%] vs. OPEN: 2 [18.2%]; $p = 0.252$) and four deaths from non-aortic related complications (TEVAR: 2 [10.5%] vs. OPEN: 2 [18.2%]; $p = 0.611$).

Conclusions: Regarding the complexity of thoracoabdominal aortic pathologies, our results are acceptable for both procedures. Except malperfusion we could not highlight any significant differences between both methods. Limited due to the small sample size, more data is required for a final statement on the individual patient outcome.

C-43

The impact of device landing-zone morphology on the outcome after transcatheter aortic valve implantation

Philipp Szalkiewicz[1], Victoria Watzal[1], Thomas Poschner[1], Jong Hui Lee[1], Carina Cuhaj[1], Waseem Hasan[2], Fernando Frick[1], David Vesely[1], Ursula Slakov[1], Stephanie Wallner[1], Bernhard Winkler[1], Gabriel Weiss[1], Andreas Strouhal[3], Christopher Adlbrecht[3], Georg Delle-Karth[3], Martin Grabenwöger[4], Markus Mach[5]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Imperial College, London, UK, London, United Kingdom
[3]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Sigmund Freud University, Medical Faculty, Vienna, Austria
[5]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Austria, Graz, Austria

Background: The complex aortic root and left ventricular outflow tract geometry keeps transcatheter aortic valve implantation (TAVI) a challenging procedure. Paravalvular leakage and conduction disorders remain pressing issues to be addressed not only during preprocedural planning but also in ongoing device iterations. The present analysis aimed to evaluate the influence of landing-zone morphology (LZM) on the outcome after TAVI.

Methods: 532 patients underwent TAVI procedure (transapical access $n = 266$ [50%], female $n = 335$ [63%]) between June 2009 and December 2016. Preoperative MDCT-scans were analyzed by 3mensioValvesTM software, and the device landing zone geometry was measured at the annular level (A1) and 5 mm below (A2) and evaluated by non-tubular-index (NTI) calculation (A1-A2/(A1+A2+sqrt(A1*A2))). LZM was categorized as tubular (NTI > –6%) or frustum-shaped (NTI < –6%). Complete LZM measurement data were available for 168 patients. The primary endpoint was defined as the occurrence of paravalvular leak more than trace. The secondary endpoints were permanent pacemaker implantation after TAVI, 30-day mortality and a composite safety endpoint defined by the Valve Academic Research Consortium 2 (VARC-2).

Results: In our overall TAVI cohort of 168 patients, 73 (43.5%) patients presented a tubular LZM, whereas 95 (56.5%) patients showed a frustum-shaped LZM. In our analysis, LZM had no impact on the occurrence of postprocedural PVL more than trace (tubular LZM: 10 (14.3%) vs. frustum-shaped LZM: 14 (15.4%); $p = 0.514$), or any secondary endpoint. In a subgroup analysis differentiating between implanted balloon- and self-expandable valves our analysis showed a significant increase in 30-day mortality in patients with a frustum-shaped receiving a balloon-expandable valve (tubular LZM: 5 (7.7%) vs. frustum-shaped LZM: 0 (0%); $p = 0.024$) but not in patients treated with a self-expanding valve (tubular LZM: 5 (14.3%) vs. frustum-shaped LZM: 1 (2,7%); $p = 0.087$).

Conclusions: The present analysis suggests no impact of device landing zone morphology on structural interventional outcome parameters such as paravalvular leak or postprocedural pacemaker implantation irrespective of the chosen valve system. However, the significant increase in 30-day mortality in patients with frustum-shaped LZM treated with balloon-expandable valves warrants further investigation in a larger, sufficiently powered (multicenter) cohort.

C-44

Long-term conduction delay changes after transcatheter aortic valve implantation

David Vesely[1], Fernando Frick[1], Daniela Geisler[1], Victoria Watzal[1], Thomas Poschner[1], Philipp Szalkiewicz[1], Stephanie Wallner[1], Bernhard Winkler[1], Gabriel Weiss[1], Andreas Strouhal[2], Christopher Adlbrecht[2], Georg Delle-Karth[2], Martin Grabenwöger[3], Markus Mach[4]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[3]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Sigmund Freud University, Medical Faculty, Vienna, Austria
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Austria

Background: Conduction delay disorders are frequently observed after transcatheter aortic valve implantation and often require the implantation of a permanent pacemaker. While early recovery of conduction disorders has been postulated, long-term effects remain unknown. Therefore the aim of the study was to investigate changes in ventricular pacing patterns in patients with postprocedural permanent pacemaker implantations (PPI) after TAVI.

Methods: 532 patients underwent transfemoral or transapical TAVI between 2009 and 2016 at our institution. 68 Patients (81.7 ± 5.5 years) presented with postprocedural conduction delay disorders and received a permanent pacemaker. Pacemaker data has been analyzed on the first day after the implantation as well as 3 months, 12 months, and yearly thereafter.

Results: During the follow-up examination a net reduction of ventricular pacing percentage was observed in 10 (27%), 7 (39%) and 2 (25%) patients at 1, 2 and 3 years respectively, whereas a net reduction of at least 10% implantation in 4 patients (10.8%) at 1 year. All patients remained in the requirement for pacing prophylaxis. On the other hand, at 1 year 9 (24.3%; $p = 0.170$) patients experienced a percentage increase in ventricular pacing requirement of at least 10%, 10 (55.6%, $p = 0.120$) patients at 2 years, and 5 (62,5%; $p = 0.020$) at 3 years.

Conclusions: While our data support the hypothesis of conduction delay recovery after TAVI, these changes are minor and only observed within the first year after the valve implantation. Long-term changes in conduction delay disorders seem to progress over time underlining the importance of conceptual measures preventing the need for PPI after TAVI.

C-45

Which regimen is the best choice? The impact of antiplatelet and antithrombotic therapy on outcome and survival after transcatheter aortic valve implantation

Stephanie Wallner[1], Bernhard Winkler[1], Gabriel Weiss[1], Victoria Watzal[1], Carina Cuhaj[1], Thomas Poschner[1], Philipp Szalkiewicz[1], Waseem Hasan[2], Christopher Adlbrecht[3], Andreas Strouhal[3], Georg Delle-Karth[3], Martin Grabenwöger[4], Markus Mach[5]

[1]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Vienna, Austria
[2]Imperial College, London, UK, London, United Kingdom
[3]4th Medical Department and Karl Landsteiner Institute for Cardiovascular and Critical Care Research, Hietzing Hospital, Vienna, Austria
[4]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research, Sigmund Freud University, Medical Faculty, Vienna, Austria
[5]Heart Team Vienna, Department of Cardio-Vascular Surgery, Hospital Hietzing and Karl Landsteiner Institute for Cardio-Vascular Research; Division of Cardiac Surgery, Medical University Graz, Austria

Background: Thromboembolic complications and stroke are two of the main concerns of transcatheter aortic valve implantation (TAVI) when compared with surgical aortic valve replacement. Therefore the correct choice of antiplatelet or antithrombotic treatment is crucial. We compared procedural and follow-up outcomes and complications of our TAVI patients based on the preprocedural, discharge and long-term antiplatelet and antithrombotic treatment (single-antiplatelet [SAPT] vs. dual-antiplatelet [DAPT] vs. anticoagulation [OAC] vs. none [NT]).

Methods: Between June 2009 and December 2016, 532 patients underwent TAVI (transapical access $n = 266$ [50%], female $n = 335$ [63%]) in our institution. As main study endpoints for the preprocedural treatment, the VARC-2 defined bleeding and neurological complications were chosen as well as the VARC-2 composite early safety endpoint. For discharge and long-term treatment respectively, one-year and long-term survival with regard to cardio- and cerebrovascular events were evaluated. Mediator analysis was performed to adjust for confounders.

Results: Preprocedural antithrombotic or anticoagulation treatment had limited impact on VARC-2 defined postprocedural complications or 30-day mortality. There were no differences between the groups regarding the primary study endpoints bleeding ($p = 0.611$), stroke ($p = 0.771$) and composite early safety ($p = 0.385$), and for the secondary endpoint mortality at 30-days ($p = 0.490$). One-year survival differed significantly between the different postoperative regimens. While SAPT displayed significantly lower one-year survival compared to DAPT and OAC, patients under DAPT had a significantly higher one-year survival than patients under OAC (SAPT vs. DAPT $p < 0.001$; SAPT vs. OAC $p = 0.006$; DAPT vs. OAC $p = 0.003$). There was a strong trend towards improved two-year survival for patients in the OAC cohort treated with new oral anticoagulants compared to Vitamin K antagonists (NOACs vs. VKA; log-rank $p = 0.056$).

No difference was observed in long-term survival between the long-term treatment cohorts.

Conclusions: It is evident from the results that the preprocedural treatment regimens had a limited impact on the procedural outcome. The superior survival curves for DAPT within the first year and NOACs over VKA within the first two years warrant considerable attention in further recommendations of antithrombotic and anticoagulation regimens after TAVI.

C-46

Single center experience with the novel Carpentier Edwards Inspiris Resilia Aortic Valve Prosthesis

Stephanie Wallner, Niuscha Taheri, Zsuzsanna Arnold, Markus Mach, Daniela Geissler, Gabriel Weiss, Reinhard Moidl, Sandra Folkmann, Marie-Luise Harrer, Bernhard Winkler, Martin Grabenwöger

Hospital Hietzing, Vienna, Austria

Background: Aortic valve replacement is the second most common cardiac procedure. Population ageing is seen as the main driver for the increased incidence of aortic stenosis and need for biological valve replacement. Currently available biological prostheses have known limited durability but spare the use of warfarin as necessary for mechanical valves. Aim of this study was to report short term results and early experience of a novel biological resilient heart valve prostheses designed for improved durability.

Methods: Between 2017–2018, a total of 74 patients undergoing aortic valve surgery were treated with Inspiris Resilia Aortic Valve (Edwards Lifesciences Inc., Irvine, CA, United States of America) at our center. 68.9% of the patients were male, 31.1% were female with an overall median age of 62.09 ± 10.22 years. The patients population showed a typical risk profile (arterial hypertension 74.3%, hyperlipidemia 71.6%, current nicotine abuse 18.9%, ex-smoker 21.6%, IDDM 4.1%, NIDDM 16.2%). Mean valve size was 23.8 ± 2.31millimetres. 29 patients (39.2%) were treated because of a bicuspide degenerated aortic valve and 29.7% of the patients showed a concomitant cardiovascular disease (1-VD: 17.6%, 2-VD: 8.1%, 3-VD: 4.1%) with preoperative stenting in 8 cases.

Results: Overall survival was 95.9% with a median follow-up of 7.57 ± 4.96 months, postoperative period required a median of 12.69 ± 6.34 days (min. 6–max. 52). 54.1% of the procedures were combined procedures with overall aortic cross clamping time of 82.29 ± 24.46 minutes as well as extra corporeal circulation time of 116.22 ± 35.37 min. New onset of atrial fibrillation was detected in 14.9% of the patients postoperative. Haemodynamics of the aortic bioprosthesis were as follows with mean/max gradients of 12.95 ± 4.93 mmHg/23.70 ± 9.43 mmHg and a mean postoperative Vmax of 2.45 ± 1.8 m/s at the time of discharge.

Conclusions: Biological aortic valve replacement with the Carpentier Edwards Inspiris Resilia Aortic Valve showed good postoperative hemodynamic short-term results in the first series of patients after introduction of this novel resilient bovine pericardial valve prostheses. Long-term studies are warranted to gain more evidence on durability as well as hemodynamic performance of this novel prosthesis type.

C-47

10 year survival after surgical aortic valve replacement in octogenarians – a retrospective single centre study in 288 patients

Casey Zachariah[1], Christoph Anstötz[2], Wolfgang Dietl[1], Bruno K. Podesser[3], Christoph Holzinger[1], Karola Trescher[1]

[1]Department of Cardiac Surgery, University Hospital St. Poelten, St. Poelten, Austria
[2]General Surgery, Nordrhein-Westfalen, Germany
[3]Center for Biomedical Research; Department of Cardiac Surgery, University Hospital St. Poelten, St. Poelten, Austria

Background: Cardiovascular diseases impose a huge burden on our aging population. The incidence of aortic valve stenosis has been estimated to be 4% in patients above 85 years of age being the most frequent indication for aortic valve replacement in octogenarians. Having in mind that the majority of these patients are treated by transcatheter aortic valve implantation we were interested in long-term outcome of octogenarians after surgical aortic valve replacement.

Methods: The primary objective of this retrospective, non-randomized, single-centre comparative study was to determine and compare mortality rates of males and females above the age of 80 after surgical aortic valve replacement with a follow-up of 10 years. The secondary objective was to assess patients according to the New York Heart Association scale (NYHA) five and ten years after surgery. The data of 288 patients (mean age 82.5 +/– 2.3 years) who underwent surgical aortic valve replacement between 1st January 2007 and 31st December 2012 using a pericardial bioprosthesis were collected retrospectively. The current NYHA class was assessed via telephone call and compared to preoperative and five-year-postoperative status. Statistical analysis was performed using SPSS 25 for Windows

Results: The mean logistic EuroScore of the entire patient cohort was 13.5 +/– 7.9%. Cardiac and non-cardiac comorbidities were similar between males and females. 47,6% of the patients were in NYHA class III and IV before the operation.

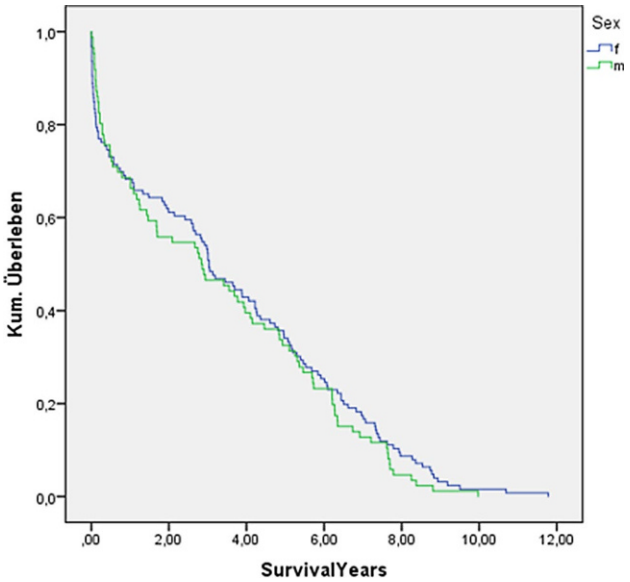


Fig. 1 | C-47 Cumulative survival of males and females over 10 years

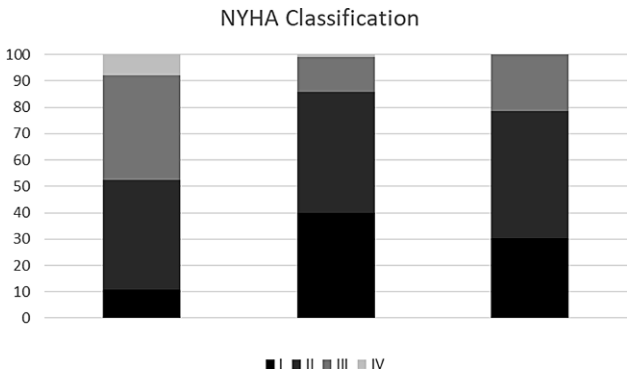


Fig. 2 | C-47 NYHA Classification

A Carpentier Edwards Perimount Magna Ease bioprosthesis was used in all 288 patients, the operation was performed via full sternotomy. 30-day mortality was 7.3% in total, with 10.3% it was significantly higher in females than in males with 3.3% ($p=0.017$). There was, however, no significant difference in cumulative survival between males and females ($p=0.396$) over 10 years (Fig. 1). The stratification of comorbidities showed that survival in patients with perioperative stroke was significantly worse than survival in patients without stroke ($p=0.001$). Chronic pulmonary disease at the time of surgery had no impact on long term survival ($p=0.397$). Postoperative NYHA class was significantly lower compared to preoperative NYHA class: 5 years after surgery 85.9% of the patients were in NYHA class I and II. This result remained stable over time in surviving patients with 78.6% of the patients still being classified as NYHA I and II 10 years after surgery (Fig. 2).

Conclusions: According to our data surgical aortic valve replacement in octogenarians can be performed with good and stable mid- and longterm results concerning mortality and quality of life in terms of NYHA classification. Nevertheless, patient selection is important to provide optimal longterm outcome for each patient especially as transcatheter valve implantation is a reasonable and justified treatment modality for patients with aortic stenosis.