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ABSTRACTS

Best Abstracts Sitzung

BA-1

Indications for and outcome in patients with the wearable cardioverter defibrillator (WCD) – results of the austrian WCD registry

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Background: The wearable cardioverter defibrillator (WCD) is an established treatment option for patients at high risk for ventricular tachycardia/ventricular fibrillation (VT/VF), either in whom this risk may only be temporarely present, or in patients at high risk for sudden cardiac death (SCD) or after VT/VF in whom an implantable cardioverter defibrillator (ICD is currently not possible for other reasons (infection, recent MI <40 days, recent PCI/CABG <3 months etc.) and in accordance with recent ESC guidelines.

Methods: Comprehensive registry including all patients in Austria who received a WCD in 2010–2015.

Results: Overall, 275 Austrian patients (59±14 years; 26 % female) received a WCD in 29 hospitals (range 1–61 patients/hospital) in Austria in 2010–2015. Left ventricular ejection fraction (LVEF) at the time of WCD initiation was 33±15 %, median CHA2DS2VASc-Score was 3 (2–5). 49 % of patients had VT/VF before the WCD initiation. Main indications for WCD therapy were: recent myocardial infarction with an LVEF<35 % (20 %), Newly diagnosed severe non-ischemic cardiomyopathy (25 %), severe ischemic cardiomyopathy with recent PCI/CABG (17 %), severe acute myocarditis (12 %), delay in ICD implantation due to infection, logistic reasons, or other (12 %), ICD-associated infection requiring temporal ICD explantation (9 %), VT planned to undergo ablation (1 %), inherited arrhythmic disease (1 %), post partum cardiomyopathy (1 %), or other (1 %).

The median WCD therapy duration was 60 (1–436) days per patient. There was no difference in WCD compliance between patients wearing the WCD <60 days vs. >60 days (23 (3–24) h/day vs. 22 (1–24) h/day; p=n.s.). 6 patients (2.2 %) received 8 adequate WCD shocks for VT/VF, with all shocks terminating VT/VF to sinus rhythm. All 6 patients who received WCD shocks subsequently received an ICD. No inadequate WCD shocks occured. During the WCD period, 4 patients suffered minor side effects (local skin irritation), whereas 2 patients had to terminate the WCD treatment prematurely due to skin pressure points and bruises. Main reasons for termination of the WCD therapy were ICD implantation (47 %), improvement of LVEF to >35 % with no subsequent need for ICD implantation (31 %), desire of the patient (4 %), terminal non cardiac disease (2 %), side effects of WCD therapy (1 %), non cardiac death (1 %), successful catheter ablation (1 %), whereas in the remaining patients the WCD is still in use.

Interestingly, of the 34 patients with severe myocarditis with an LVEF < 35 % and/or VT/VF who received a WCD for protection from SCD, only 5 patients (14 %) subsequently required an ICD after the WCD period, highlighting the clinical importance of the WCD use especially in this patient cohort.

Conclusions: The WCD is an effective treatment option in patients at temporal high risk for VT/VF and/or during a mandated waiting period for ICD implantation. Only 49 % of patients undergoing WCD therapy subsequently require ICD implantation.

BA-2

Pre-treatment with potent P2Y12 receptor inhibitors is associated with reduced in-hospital mortality in a real world setting of primary percutaneous coronary intervention

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Background: Pre-treatment with clopidogrel is associated with improved outcome in registry studies of primary PCI (pPCI). We aimed to investigate the effect of pre-treatment with oral P2Y12 receptor inhibitors in a real world setting of pPCI after the implementation of prasugrel and ticagrelor.

Methods and Results: We prospectively enrolled 6325 patients from the Austrian Acute PCI Registry undergoing pPCI between January 2011 and December 2014. Patients were grouped according to the start of P2Y12 inhibitor treatment into an early group (start before arrival at the PCI center, n=3538), an intermediate group (start after arrival at the PCI centre, but before catheterisation laboratory, n=1939) and a late group (start at the time of PCI or later, n=848). To investigate the effect of upstream treatment on in-hospital outcome we used multiple logistic regression analysis including major confounders and stratified by participating centres.

Tab. 1 Multivariable analysis

	OR	95 % CI
Age	1.07	1.06 to 1.09
Male sex	0.98	0.70 to 1.37
Cardiogenic shock	5.46	3.53 to 8.45
Resuscitation	4.25	2.87 to 6.31
Previous MI	1.58	1.06 to 2.34
ASA pretreatment	1.28	0.58 to 2.83
Heparin pretreatment	0.75	0.49 to 1.14
Secondary transfer	0.96	0.67 to 1.39
Delay (pain-PCI)	0.80	0.53 to 1.21
Diabetes mellitus	1.65	1.16 to 2.34
GP IIb/IIIa co-treatment	0.43	0.05 to 3.53
P2Y12 before PCI centre	0.62	0.41 to 0.95
P2Y12 at PCI centre	0.64	0.40 to 1.01
Cardiogenic shock * delay	4.39	2.29 to 8.40
stratified by centre, effect modification (cardigenic shock and delay)		

Tab. 2 In-hospital mortality, multivariable analysis

	OR	95 % CI
Age	1.07	1.06 to 1.09
Male sex	0.98	0.70 to 1.37
Cardiogenic shock	5.46	3.53 to 8.45
Resuscitation	4.25	2.87 to 6.31
Previous MI	1.58	1.06 to 2.34
ASA pretreatment	1.28	0.58 to 2.83
Heparin pretreatment	0.75	0.49 to 1.14
Secondary transfer	0.96	0.67 to 1.39
Delay (pain-PCI)	0.80	0.53 to 1.21
Diabetes mellitus	1.65	1.16 to 2.34
GP IIb/IIIa co-treatment	0.43	0.05 to 3.53
P2Y12 before PCI centre	0.62	0.41 to 0.95
P2Y12 at PCI centre	0.64	0.40 to 1.01
Cardiogenic shock * delay	4.39	2.29 to 8.40
stratified by centre, effect modification (cardigenic shock and delay)		

Regardless of the type of P2Y12 inhibitor used for upstream treatment (prasugrel 34 %, ticagrelor 17 %, clopidogrel 49 %), univariate analysis showed that early and intermediate treatment start were associated with reduced in-hospital mortality after pPCI compared to late start (4 % vs. 5 % vs. 12 %) Adjustment in multivariable analysis showed a strong association of early treatment start with reduced in-hospital mortality (OR 0.62 95 % CI 0.41 to 0.95). Intermediate treatment initiation was associated with comparable, borderline significant improvement (OR 0.64 95 % CI 0.40 to 1.01).

Conclusions: After the implementation of prasugrel and ticagrelor, early initiation of P2Y12 inhibitors remains associated with reduced in-hospital mortality in patients with STEMI in a large real-world setting of pPCI. These data support the recommendation of an early start with P2Y12 receptor inhibition in STEMI even when using more the potent and faster acting drugs prasugrel and ticagrelor.

BA-3

Extracellular volume by cardiac magnetic resonance T1 mapping in cardiac amyloidosis: validation with endomyocardial biopsy

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Background: Cardiac amyloidosis (CA) is caused by accumulation of amyloid fibrils in the myocardium, which leads to an increase in extracellular volume (ECV). Cardiac magnetic resonance (CMR) T1 mapping allows accurate non-invasive

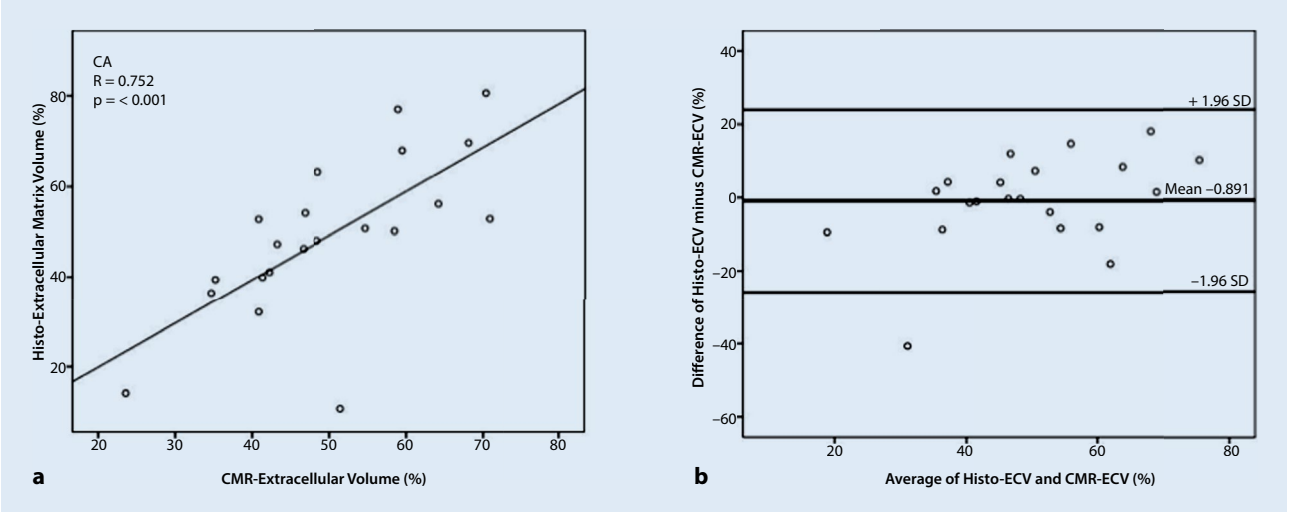

Fig. 1

ECV measurement. However, it has not been investigated weather CMR-ECV accurately quantifies ECV in CA.

Methods: Between July 2011 and November 2015 21 CA patients were enrolled. The study population consisted of 7 (33.3 %) wild-type transthyretin (TW-TTR) and 14 (66.6 %) light chain (AL) CA patients. All patients underwent endomyocardial biopsy (EMB) and CMR within 6 weeks. EMB specimens were stained with Modified Trichrome and ECV was quantified via ImageJ software using a color-threshold macro. CMR-ECV was quantified with T1 mapping using the Modified Look-Locker Inversion recovery (MOLLI) sequence. Spearman's correlation and Bland-Altman plots were used for correlation analysis and assessment of agreement between histological ECV (H-ECV) and CMR-ECV.

Results: Median ECV by CMR was of 48.5 % (23.6–71.0 %) and 50.2 % (10.7–80.6 %) by histology, the mean difference CMR-ECV and H-ECV was –0.376 (–40.7–18.1). CMR-ECV and H-ECV were highly correlated (R = 0.752; p = <0.001).

For WT-TTR-CA patients (N = 7) median CMR-ECV was 48.6 % (40.8–70.5 %), median H-ECV was 54.2 % (32.1–80.6 %), with a mean difference between CMR-ECV and H-ECV of 10.132 (-9.8–18.1). AL-CA patients (N = 14) showed a median CMR-ECV of 47.8 % (23.6–71.0 %), a median of H-ECV of 46.8 % (10.7–69.7 %), mean difference between CMR-ECV and H-ECV –0.746 (–40.7–8.4).

Conclusions: We are the first to histologically validate CMR-ECV in cardiac amyloidosis patients. Our results show excellent correlation and good agreement of CMR-ECV with H-ECV. ECV by T1 mapping accurately reflects extracellular matrix in cardiac amyloidosis patients. As many current phase II and phase III trials for treatment of CA are under way, ECV measurement via CMR may provide important information on weather CA therapies can indeed reduce ECV in CA.

BA-4

Ischemic postconditioning modulates focal adhesion signalling pathway in porcine model

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Background: Short repeated periods of occlusion/reperfusion after the reopening of the infarct-related artery represent ischemic postconditioning (IPostC). IPostC may induce cardioprotection preventing reperfusion injury thereby reducing infarct size. The mechanisms behind the cardioprotective effect of IpostC have been extensively studied, but still little is known. Here, we investigated the effect of IPostC on the gene expression response in ischemic and remote myocardium in porcine closed-chest reperfused acute myocardial infarction (AMI) model utilizing next generation sequencing (NGS).

Methods: Domestic pigs underwent induction of AMI by 90-min coronary balloon occlusion of the mid LAD followed by deflation of the balloon (reperfusion). The pigs were randomized to ischemic non-conditioning (group AMI; n = 12) and ischemic post-conditioning (group IpostC; n = 12) groups. IpostC was performed immediately after initiation of reperfusion by repeated 6×30sec coronary balloon inflation/deflation. Sham-operated pigs served as control (n = 6). Hearts were explanted after 3 hours (n = 6 of each group) and 3 days (n = 6 of each group) post/sham-AMI and transcriptomic analysis was performed in remote and infarcted area with NGS.

Gene Symbol	Gene Description	INFARCTED AREA				REMOTE AREA			
		3hours		3 days		3hours		3 days	
		AMI	IPostC	AMI	IPostC	AMI	IPostC	AMI	IPostC
		Log Fold Change				Log Fold Change			
ITGB1	Integrin β-1				0.70			-0.39	0.33
ITGB2	Integrin β-2				1.72				3.31
TLN1	Talin -1				0.90			1.90	
FLNC	Filamin C				0.82			0.72	0.57
ACTA1	Actin α-1	1.41	1.80		1.81	1.86	1.08	1.74	1.08
βACTIN	Actin β				0.99			-0.88	2.78
ACTN1	Actinin 1				1.22		2.43		
SRC	Non-receptor tyrosine kinase				0.78	-0.43		0.42	0.63
PTEN	Phosphatase and tensin homolog		0.61	0.96	1.04		0.80	1.10	1.01
PIP5K1	Phosphatidylinositol phosphate 5-kinase		0.64		0.48		1.69		1.65
PRKCA	Protein kinase C α		2.20	1.90	2.40		2.13	1.14	2.59
PIK3	Phosphatidylinositol bisphosphate 3-kinase		0.35	0.6	0.51		0.83	0.59	0.62
PIK3R5	Phosphoinositide-3-kinase, reg. subunit				1.02			2.23	
RHOA	Ras homolog family member A				1.57				1.21
ROCK1	Rho-associated, coiled-coil containing protein kinase 1	0.77	0.44	0.56	0.82	1.01	0.72	0.98	0.54
ROCK2	Rho-associated, coiled-coil containing protein kinase 2	0.85	1.42	1.2	1.32	1.04	1.66	1.05	1.29

Tab. 1 Significantly altered gene expression in group AMI and IPostC compared to group Control in remote and infarcted area after 3 hours and 3 days post reperfused AMI

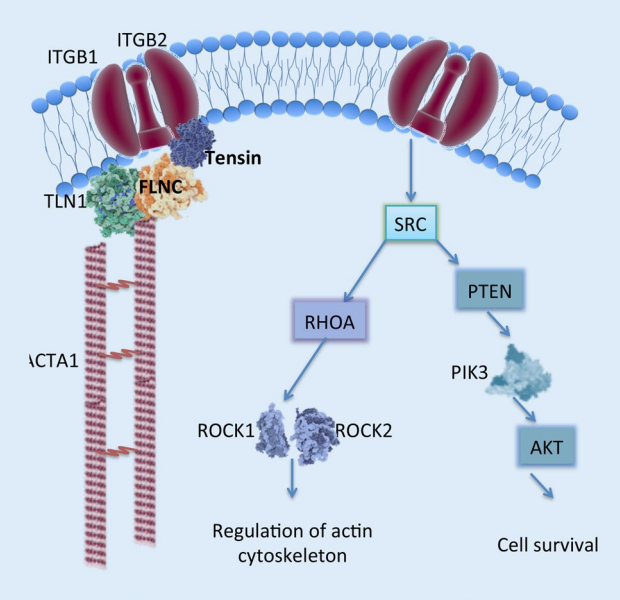

Fig. 1 Proposed schematic representation of the signaling pathways leading to cardioprotection by PostC of the porcine myocardium

Results: Gene ontology enrichment analysis showed significant overexpression of genes involved in focal adhesions (regulators of integrin-associated actin cytoskeleton and cell survival and maintenance of normal tissue morphology) in IPostC group (adjusted p value of 0.031) as compared to AMI group (Tab. 1). Upregulation of non-receptor tyrosine kinase and key receptors of focal adhesion signalling pathway (ITGB1, ITGB2) was pronounced in IPostC group in remote and infarction area at 3 days post-AMI. This led to further stimulation of PI3K/Akt survival signalling pathway. PTEN, PRKCA and PIK3 were overexpressed also in AMI group at 3 days post occlusion, whereas 3 hours post-occlusion animals showed non-significant regulation. This indicates earlier stimulation of PI3K/AKT by IPostC comparing to group AMI. Upregulation of RHOA protein induced increased expression of ROCK1/2, which has consequence in regulation of actin cytoskeleton and smooth muscle contraction. RHOA regulatory protein was overexpressed in infarcted and remote area only in group IPostC at 3 days post-AMI, whereas downstream kinases ROCK1 and ROCK2 were upregulated in all groups suggesting involvement of additional factors that control cytoskeleton.

Conclusions: We demonstrate first in a translational porcine model of iPostC that stimulation of focal adhesion signalling pathway leads to upregulation of cytoskeletal-based survival signalling. This may play a prominent role in protecting the myocardium from ischemia-reperfusion injury.

BA-5

Rho kinase inhibition protects from ischemia-reperfusion injury via a mechanism related to nitric oxide synthase and downregulation of arginase in diabetes

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Background: Activated RhoA/Rho associated kinase (ROCK) and arginase are implicated in vascular complication in diabetes. The present study investigated the cardioprotective effect of ROCK inhibition and its combination with remote ischemic perconditioning (RIPerc) in type 1 diabetes.

Methods: Anesthetized non-diabetic and streptozotocin-induced type 1 diabetic Sprague-Dawley rats were subjected to 30 min regional myocardial ischemia and 2 h reperfusion (IR) and allocated to (1) controls with no intervention during IR; (2) ROCK inhibition with hydroxyfasudil; (3) RIPerc (femoral artery occlusion for 15 min during the last 15 min of the myocardial ischemia); (4) ROCK inhibition+RIPerc, (5) NO synthase (NOS) inhibition by L-NMMA alone and (6) NOS inhibition combined with ROCK inhibition. Myocardial ROCK and arginase activity, arginase expression as well as infarct size (IS) were determined.

Results: Arginase activity and arginase 2 protein expression as well as ROCK activity were increased in type 1 diabetes ($P<0.05$). While RIPerc failed to induce cardioprotection in rats with diabetes, ROCK inhibition alone and in combination with RIPerc significantly reduced IS and arginase activity in both non-diabetic and diabetic rats by comparable magnitudes ($P<0.05$). The cardioprotective effect and the downregulation of arginase activity by ROCK inhibition in diabetes were abolished by NOS inhibition.

Conclusions: ROCK inhibition induces marked cardioprotective effects in rats with type 1 diabetes. The cardioprotective effect of ROCK inhibition in diabetes is mediated by a NOS-dependent signaling pathway associated with a decrease in arginase activity. This finding may be a potential therapeutic strategy to protect the diabetic heart against IR injury.

BA-6

A new experimental model of pulmonary arterial hypertension – KDR Knock out

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Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease characterized by obstruction of small pulmonary arteries leading to increased pulmonary vascular resistance. The key pathologic finding in this disease is a negative pulmonary vascular remodeling process with total vessel occlusion and a monoclonal expansion of collateral endothelial cells. It has been proposed that impaired vascular endothelial growth factor (VEGF) signaling plays a significant role in this process. Aim of our study was to investigate whether inhibition of VEGFR-2 (KDR) by direct gene manipulation may replicate classical pulmonary vasculopathy.

Methods: We utilized mice with conditional VEGFR-2/KDR knock-out in endothelial cells (KDR-/-). KDRflox/flox/Tie-2Cre and KDRflox/flox/Tie-2 mice were injected intraperitoneally with tamoxifen for three weeks to induce the knock-out. KDR-/- mice and wild type littermates were held in an environmental chamber with FiO2 of 10% or under normoxia for 2, 4, and 6 weeks. We investigated the effect of KDR deletion and chronic

normobaric hypoxia on pulmonary hemodynamics and right ventricular hypertrophy.

Results: There was no difference in mice might, heart weight and heart weight to body weight ratio between study and control mice. After KDR knockout mice revealed a significant increase in VEGF and BNP serum levels (Fig. 1). Real-time PCR indicated a significant downregulation of the BMP pathway as consequence of KDR knockout. KDR-/- mice showed significantly increased right ventricular pressures (RVSP's) and Fulton indices after 4, and 6 weeks under normoxic and hypoxic conditions conditions, compared with wild type controls, whereas there was no significant difference in systemic arterial pressure between both groups. Knockout mice showed a significant increase in pulmonary arterial wall thickness and significant increased α-SMC positive area measured by tissue FACS. Furthermore there we observed the loss of isolectin-4 positive microvessels in the knockout group. Most interestingly lung histologies demonstrated neointimal thickening and vessel occlusions in lungs of KDR-/- mice resembling human pulmonary arteriopathy.

Conclusions: Classical pulmonary arterial hypertension was induced in C57/BL6J mice by direct ablative gene manipulation of KDR.

Chirurgie Abstracts – Vortragssitzung 1

CA 1-1

Endocarditis-related stroke is not a contraindication for early cardiac surgery – an investigation among 395 patients with left-sided endocarditis

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Background: A treatment dilemma arises when surgery has to be performed in patients with infective endocarditis (IE) complicated by cardio-embolic stroke. Following a neurological event, the indication for cardiac surgery remains crucial due to the feared risk of intracerebral haemorrhage during extracorporeal circulation. Therefore, currently neurologists recommend surgery to be postponed for at least 1 month if possible.

Purpose: Aim of this study was to investigate the perioperative neurologic complication rate and the long-term neurologic recovery potential in patients with IE-related stroke and indication for cardiac surgery.

Methods: A total of 395 consecutive patients with left-sided IE undergoing urgent or emergent surgery was investigated. A preoperative CT scan or magnetic resonance imaging was performed in all patients with preoperative clinical signs of neurologic impairment. Postoperatively, a CT scan was performed in all patients with prolonged ventilation and before discharge. All survivors underwent frequent follow-up visits including echocardiographic controls and neurologic clinical examinations were performed in patients with previous stroke. Autopsies were performed in all non-survivors in order to evaluate perioperative neurologic complications such as ischemic exacerbation and new onset of cerebral haemorrhage.

During follow-up, neurologic recovery was assessed by the modified Rankin scale and the Barthel index. A Rankin scale of ≤1 and a Barthel index of 100 points was defined to indicate complete neurologic rehabilitation.

Mortality was assessed by regression models adjusting for age.

Results: Among stroke patients, the age-adjusted hospital mortality risk was 1.4 fold (95 % Confidence interval: 0.71–3.0; $p=0.3$) higher and the long-term mortality risk was 1.4 fold increased (95 % Confidence interval: 0.9–1.9; $p=0.09$) compared to IE patients without previous stroke.

Stroke, as the index clinical event, occurred in 99 patients (78.6 %), 21.4 % of cerebral embolism occurred while already being under antibiotic treatment. Cardiac surgery was performed within 72 hours after stroke onset in 38 % of IE patients and in 70 % within the first week.

Uncomplicated ischemic stroke was found in 87 patients (69 %) and 39 patients (31 %) presented with complicated cerebral lesions (concomitant abscess formation, secondary cerebral haemorrhage or meningitis). Hospital mortality was higher in patients with complicated stroke (23.1 % vs. 10.3 %; $p=0.06$), however, the observed risk for intraoperative haemorrhage was only 2.6 % among these patients.

In the long-term follow-up, full neurological recovery was observed in 82 survivors (71.3 %), partial recovery in 29 patients (25.2 %) and no clinical recovery in 4 patients (3.5 %).

Conclusions: Contrarily to common clinical practice and neurologic recommendations, early surgery in IE is safe and associated with a very low intraoperative neurologic complication rate. As hospital and long-term outcome was convincing together with the high neurological recovery potential we recommend early surgery in all patients with IE-related neurologic complications.

CA 1-2

3D Imaging – Experience in minimally invasive mitral valve surgery

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Background: Minimally invasive mitral valve surgery (MIMVS) through mini-thoracotomy is facilitated by video assistance. Due to difficult depth perception with 2D video systems most steps of the procedure by most surgeons are done under direct vision. We report our results of a 18 months period using 3D video-endoscopy.

Methods: A continuous series of 65 patients operated totally endoscopic with 3D imaging (Einstein Vision®) is included. Perioperative and short-term results are analyzed retrospectively. Crossclamping and CPB times for isolated MIMVS in 45 patients were compared with those from 275 MIMVS patients operated from 2001 to 2014 with 2D and direct vision. A total of 8 surgeons either operated self-responsible or were assisted by the MICS program director.

Results: From 06/2014 to 12/2015, 65 patients (median age 63 years), 37 (56.9 %) male underwent totally endoscopic MIMVS with 3D imaging. In 63 patients (96.9 %) transthoracic aortic clamping with cardioplegic arrest median ischemic and CPB times were 123 min (sd 32.2) and 222 (sd 65.1); in 2 patients

(3.1 %) a redo procedure was done under ventricular fibrillation. In 59 patients (90.8 %) MV repair was possible, 5 received planned MV replacement. Additional tricuspid valve repair, ASD/PFO closure and left atrial ablation were done in 8 (12.3 %), 13 (20 %) and 6 (9.2 %) cases. In 2 patients (3.1 %) conversion to median sternotomy was necessary: one due to bleeding and one due to unsuccessful reconstruction with final MV replacement. 30 days mortality was 0.

In 45 patients with isolated MIMVS CPB times were longer with 3D (221.0 min. sd 63.9) compared to 275 patients with 2D imaging (194.5 min. sd 64.6) $p=0.011$. Crossclamp times were comparable (121.9 sd 28.9 min. vs 110.4 sd 41.9 min., $p=0.082$).

Conclusions: Totally endoscopic MIMVS with 3D imaging is safe. Standard Carpentier techniques for repair or replacement can be performed without direct vision even in a training institution. Crossclamping times using 3D imaging are not different, however, total CPB times are longer, since preparative and final steps from pericardiotomy to crossclamping and vice versa were performed mostly by surgeons less experienced with the MICS approach.

CA 1-3

Acute type a dissection: impact of bicuspid aortic valve and bovine aortic arch on entry site location, surgical treatment and outcome

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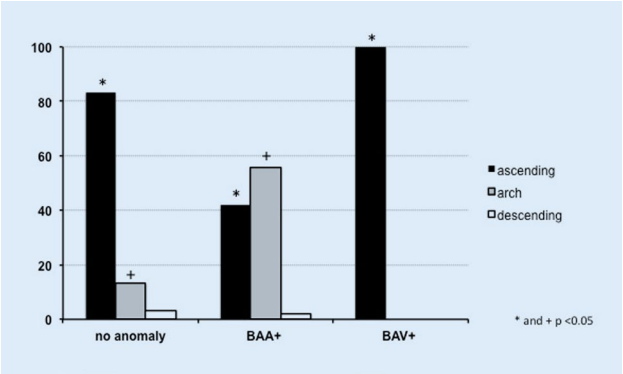
Background: To evaluate if a bovine aortic arch (BAA) or bicuspid aortic valve (BAV) influences location of the entry tear, surgical procedure and outcome of patients undergoing surgery for acute dissection type A (AADA).

Methods: 302 patients underwent surgery due to AADA (69.2 % male, mean age 60.6 ± 13.7) between 2002–2013. Imaging studies and operative reports were screened for presence of BAA or BAV and location of the primary tear. Dissection patterns, surgical treatment, risk factors for postoperative complications and long-term outcome were analyzed.

Results: Patients with AADA had concomitant BAA in 17.8 % ($n=50$) and BAV in 4.6 % ($n=13$). Location of the primary tear was predominantly in the aortic arch in patients with BAA (55.6 % vs. no anomaly 13 %, $p<0.001$). Multivariate analysis identified BAA as independent risk factor for a primary entry located in the arch (OR 7.588, 95 % CI 3.56–16.144, $p<0.001$). BAV emerged as independent risk factor for aortic root replacement (OR 14.08, 95 % CI 2.97–66.73, $p=0.001$), being performed more frequently in BAV patients (72.7 % vs. no anomaly 24.7 %, $p=0.002$). BAA had higher rates of postoperative neurologic injury (27.3 % vs. no anomaly 11.9 %, $p=0.017$); BAV underwent re-exploration due to bleeding more frequently (45 % vs. no anomaly 19 %, $p=0.045$). Long-term survival was comparable for patients with BAV and BAA and patients without congentital anomalies.

Conclusions: In AADA, congenital anomalies are associated with a distinctive location of the primary entry. In BAV patients, aortic root replacement is required more frequently, leading to higher rate of rethoracotomy for bleeding. BAA is associated with poor neurologic outcome.



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CA 1-4

Does CytoSorb adsorber therapy during extracorporeal circulation reduce postoperative inflammatory response?

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Background: Systemic inflammatory response syndrome (SIRS) after extracorporal circulation is a serious risk factor in cardiac surgery. The CytoSorb adsorber is integrated in the cardiopulmonary bypass (CPB) in order to extract inflammatory mediators such as IL-6 and therefore reduce the severity of postoperative inflammation. The aim of this retrospective study was to analyze whether CytoSorb application reduces SIRS during CPB in cardiac surgery.

Methods: From January to February 2016 seven patients (29 % females, 60 ± 6a) underwent cardiac surgery with CytoSorb (Valve + CABG: $n=3$, CABG only: $n=1$, valve + aortic procedure: $n=3$). After propensity score matching 11 patients (18 % females, 63 ± 3a) of the same observation period were included into the control group. Interleukin-6 (IL-6), c-reactive protein, fibrinogen and leukocytes were compared at three time points: preoperatively, one hour after surgery and on postoperative day one. Both groups were compared by student's t-test and ANOVA for repeated measurements. Data are given as means ±SEM.

Results: In total, 18 patients were included into the study. CPB time (CytoSorb vs. control: 152 ± 19 min vs. 120 ± 7 mins, n. s.), as well as aortic cross clamp time (CytoSorb vs. control: 86 ± 5 min vs. 107 ± 13 min, n. s.) were comparable in both groups. Postoperative ventilation time and ICU stay did not differ between the groups. The total volume demand during CPB was significantly higher in the CytoSorb group (6714 ± 535 ml vs. control group 4334 ± 382 ml; $p<0.01$). Leukocytes were significantly increased in the CytoSorb group on the first postoperative day (19 ± 2 vs. 13 ± 1 G/L; $p<0.05$). No statistical difference was observed for IL-6, c-reactive protein and fibrinogen.

Conclusions: No beneficial effects of the CytoSorb adsorber could be documented within the first 24 h postoperatively. Moreover, intraoperative volume demand and leucocytes were

even significantly increased in the CytoSorb group. IL-6 did not differ from the control group. Next step is a prospective randomized trial to confirm these preliminary results and to analyze further relevant inflammatory parameters.

CA 1-5

Complete revascularisation increases „bridge to recovery“ and survival in patients with acute myocardial infarction requiring emergency mechanical circulatory support

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Background: Approximately 5 % of patients with acute myocardial infarction develop cardiogenic shock (CS): Aim of this study was to investigate the prognostic outcome of patients with AMI and profound CS in patients receiving emergency mechanical circulatory support (MCS) using veno-arterial extracorporeal membrane oxygenation (va-ECMO).

Methods: A consecutive series of 81 patients with severe CS receiving va-ECMO in a “crash-and-burn” manner from 1997 to 2015 was investigated. Outcome evaluation regarding in-hospital mortality, “bridge to recovery” and long-term outcome in patients with successful weaning from va-ECMO was performed. Descriptive statistics and Kaplan-Meier survival analysis was performed to identify relevant prognostic parameters predicting successful weaning from va-ECMO and patient survival. Permission to perform this study was obtained from the local Institutional Reviw Board.

Results: Mean patient age was 58.8 ± 10.0 years and 77.8 % were male gender. Out-of-hospital mechanical cardiopulmonary resuscitation (CPR) was performed in 7 patients (8.9 %), within the cath-lab in 18 patients (24.1 %) and during surgical insertion of va-ECMO in 20 patients (25.3 %). Initial installation of intra-aortic-balloon counter-pulsation (IABP) was sustained in 33 patients (41.8 %). De novo AMI was responsible for 43 (53.1 %) of cases, acute stent thrombosis in 13 (16.0 %), and complications resulting from PCI were responsible for AMI in 30.9 %.

Mean SYNTAX score was 26.3 ± 6.2 and 71.6 % of patients had multivessel coronary artery disease. The left main was the culprid lesion for AMI in 19 patients (23.5 %) and the left anterior decending artery in 34 patients (42.0 %). Mean duration of va-ECMO support was 5.9 ± 5.4 days. Mean time from onset of AMI to dilatation/reperfusion was 5.4 ± 3.9 hours. Mean “door-to-balloon-time” was 1.35 ± 1.2 hours. Actuarial 30-day survival was 52.6 %, 43.8 % at 1 year and 36.4 % at 5 years. Restoration of spontaneous circulation enabling “bridge to recovery” and successful weaning from MCS was possible in 33 patients (40.7 %) and was significantly higher in patients receiving complete revascularization ($p = 0.026$). Bridge-to-recovery was significantly higher in patients with va-ECMO and consecutive acute coronary artery bypass grafting (CABG) vs. patients with culprid lesion PCI or conservative management only ($p = 0.011$).

Conclusions: AMI complicated by profound cardiogenic shock is still associated with a high in-hospital mortality even in patients undergoing MCS by va-ECMO. Complete revascularization significantly enhances “bridge to recovery” and long-term survival. Patients receiving CABG were more likely to undergo complete revascularization compared to patients with PCI or conservative management only.

CA 1-6

Long-term outcome of mitral valve repair versus replacement in a large series of patients with infective endocarditis

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Background: Infective endocarditis (IE) of the mitral valve remains a severe cardiac condition associated with high morbidity and mortality. Surgical management of IE includes reconstruction of cardiac morphology and total removal of infected tissues.

Purpose: Studies that investigate the surgical management of the mitral valve in IE are sparse. The ESC guidelines for IE do not clearly favour either mitral valve repair or mitral replacement. Aim of our study was to compare long-term results of mitral repair versus replacement in a large series of patients with IE.

Methods: Between 1990 and 2015, a consecutive series of 453 patients with IE presented at the Department of Cardiac Surgery of the Medical University of Innsbruck (Austria). Of these, 200 patients demonstrated with native (excluding prothesis infection), primary mitral valve endocarditis and were included into the study. Seventy-seven patients (38.5 %) received mitral valve repair (REPAIR) according to the technique of Carpentier, the remaining 123 patients (61.5 %) received mitral valve replacement (REPLACE). The two study groups were compared regarding demographic differences, extension of mitral valve destruction and concomitant comorbid factors. Long-term outcome defined as (1) cardiac death and as (2) a combined endpoint with freedom from valvular reoperation, recurrent endocarditis, and cardiac related death was evaluated using Kaplan-Meier survival analysis together with log-rank testing and multivariate Cox proportional hazards regression analysis. This study was approved by an independent Institutional Review Board.

Results: Mean age of patients in the REPAIR group was 51.9 ± 9.3 years versus 53.8 ± 10.5 years in the REPLACE group ($p = 0.68$). Patients were similar regarding other demographic differences and co-morbidities prior to surgery with the exception that patients in the REPAIR group suffered from a significantly higher rate of previous septic embolism (55.8 % vs. 37.4 %; $p = 0.01$), clinically manifest embolic stroke (45.5 % vs. 34.1 %; $p = 0.03$) and a significantly higher rate of multiple site embolism (31.2 % vs. 25.2 %; $p = 0.03$).

Despite the higher rate of preoperative neurological complications, univariate Kaplan Meier analysis showed a significantly increased overall survival in the REPAIR group compared to the REPLACE group ($p = 0.004$). Furthermore, there was a significantly increased event-free survival with freedom from valvular reoperations and recurrent endocarditis events in the REPAIR group ($p < 0.001$).

In the multivariate Cox regression analysis, long-term outcome regarding overall survival (Hazard Ratio: 0.54; 95 % Confidence Interval: 0.3–0.9; $p = 0.03$) and event-free survival (Hazard Ratio: 0.38; 95 % Confidence Interval: 0.23–0.64; $p < 0.001$)

remained significantly better in the REPAIR group, after adjusting for the most important confounding factors.

Conclusions: Data from a surgical center specialised on mitral valve repair procedures provide strong evidence in favour of mitral valve repair in native IE. Even when preoperative neurological complications are present mitral valve repair should be the surgical treatment of choice.

CA 1-7

Rapid-deployment aortic valve replacement: A single center experience of 300 implantations

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Background: Aortic valve replacement is still one of the most common procedures in cardiac surgery. Rapid-deployment valves were recently introduced to the market to facilitate valve implantation and reduce procedural time. We report our single center experience of the first 300 cases.

Methods: Patients received the Edwards INTUITY rapid-deployment valve during the pre-marked TRITON trial, the post-market FOUNDATION trial or thereafter as a standard biologic valve. Preoperative patient characteristics, procedural specifications and post-operative follow-up were recorded in the institutional database. The mean follow-up was 14±16 months.

Results: Three hundred patients (74 ± 9 years, 169 ± 9 cm, 79 ± 16 kg, 47 % female) were implanted between May 2010 and November 2015. The mean logistic EuroSCORE was 11.1 ± 12.4 % and the mean EuroSCORE II was 5.2 ± 8.3 %, respectively. The mean implanted valve size was 22.9 ± 2.2 mm. Operative mortality (30-day mortality) was 1 %. One, three and five year survival was 94 %, 88 % and 88 % respectively.

Conclusions: Implantation of a novel rapid-deployment biologic aortic valve was safe and feasible in an elderly patient population. Distinct differences to standard prostheses regarding valve-related adverse events and procedural details should be evaluated in further trials.

CA 1-8

Thoracic endovascular repair for acute complicated type B aortic dissections

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Background: To assess in hospital mortality and mid-term results in patients (pts) who underwent thoracic endovascular aortic repair (TEVAR) for acute complicated type B aortic dissections (acTBD).

Methods: Between March 2001 and November 2015, 51 patients (38 male, mean age 55 ±13) with an acTBD underwent TEVAR at our institution. Indications included aortic rupture in 8 (16 %) persisitng pain in 14 (27 %) and malperfusion in 29 (57 %) patients.

Results: Technical success (coverage of the primary tear site) was achieved in 46 patients (90.2 %). Overstenting of the left subclavian artery (LSA) was needed in 39 patients (complete overstenting in 21 pts; partial overstenting in 18 pts.). Overall hospital mortality rate was 6.3 % ($n=4$). Causes of death were rupture during the procedure in one patient and redissection with consequent aortic rupture after TEVAR in the remaining three. Permanent neurological dysfunction occurred in 2 patients. Eight patients needed early endovascular intervention due to a Type Ia or Ib endoleak and rapid progression of the aortic diameter ($n=3$ and $n=2$), persistent signs of ischemia ($n=2$), rupture ($n=1$). Furthermore, eighteen patients (35 %) developed early endoleaks (Type Ia $n=5$, Type Ib $n=11$, Type II $n=1$, Type Ib plus II $n=1$) and were observed throughout the postinterventional period. Out of these 6 pts needed secondary intervention ($n=2$) or surgery ($n=4$), (mean interval after procedure 92 month ± 56 month) due to aortic progression.

The actuarial survival was 89 %, 77 % and 67 % at 1.5 and 10 years, respectively. Freedom from treatment failure at 1 and 5 years (including reintervention, aortic rupture, device-related complications, aortic-related death, or sudden, unexplained late death) was 87.5 % and 82.0 %, respectively.

Conclusions: TEVAR in the treatment of acute complicated type B aortic dissection proves to be an excellent treatment modality in this high risk patient cohort. Refinements, especially in stent design and application, may further reduce the rate of endoleaks and improve the prognosis of patients in this life-threatening situation.

CA 1-9

Treatment of acute complicated type B aortic dissection with the frozen elephant trunk technique. A single centre experience

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Background: Effective treatment of acute complicated type B aortic dissection (AD) is challenging, especially when thoracic endovascular aortic repair (TEVAR) is contraindicated due to anatomic reasons. We present our early and midterm results of our single centre experience using the frozen elephant trunk technique (FET) for acute type B AD.

Methods: Between March 2008 and October 2015, 11 patients underwent surgery of the thoracic aorta for acute type B AD with the FET technique and were enrolled in the present case series study. The indication for surgery was a complicated type B AD which could not be treated with TEVAR due to the following reasons: inadequate proximal landing zone in four cases, retrograde dissection of the aortic arch in three cases, an enlarged diameter of the ascending aorta > 45 mm in two cases, and treatment failure of the TEVAR procedure in two cases. All operations were performed under circulatory arrest and bilateral antegrade cerebral perfusion. During follow-up, clinical examinations as well as evaluation of the aorta by computed tomography (CT) scans were performed after 6 months, 12 months and annually thereafter.

Results: Mean age of the patient cohort was 59 ± 13 years; 6 patients were male gender. The hospital mortality rate was 9 % (1/11), stroke occurred in one patient (9 %). During the follow up period of 28 ± 18 months, postoperative CT scans revealed perigraft thrombus formation and stable aortic dimensions in all surviving patients. No late aortic related event occurred.

Conclusions: Limited by the small sample size the FET technique seems to offer a feasible therapeutic option for complicated type B AD if TEVAR is contraindicated. In contrast to conventional aortic surgery via a lateral thoracotomy, the FET procedure can provide simultaneous treatment of the ascending aorta and aortic arch.

Chirurgie Abstracts – Vortragssitzung 2

CA 2-1

The change of tricuspid regurgitation severity and its impact on outcome in patients undergoing transfemoral vs. transapical transcatheter aortic valve implantation. Data from the VIenna transCaTheter aOrtic valve RegistrY (VICTORY)

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Background: Concomitant tricuspid regurgitation (TR) is frequently observed in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation.

Currently there is limited to no data on the change of TR after TAVI, thus the aim of this study was to investigate the importance of TR as a risk factor for adverse clinical outcomes and mortality in patients selected for either transapical (TA) or transfemoral (TF) TAVI.

Methods: TR changes were assessed in 279 patients before and after TAVI by comparing transthoracic echocardiography. The annulus diameter and the LVEF, peak and mean pressure gradients across the aortic valve were measured as well as the color flow Doppler signal was used to determine the presence and grade of aortic regurgitation. TR was assessed by visual inspection and color-flow Doppler. The patients qualified as TA-TAVI candidates as they had severe symptomatic aortic stenosis and were at high or prohibitive surgical risk and prohibitive iliac access vessels.

Results: After the procedure, the number of patients suffering from TR was reduced in both cohorts (TA 62.3 % to 57.2 %; TF 73.1 % to 66.4 %, in both cohorts not significant) even though patients with moderate to severe TR showed more improvement when treated transapically (TA 26.4 % to 17.6 %, $p=0.056$ vs. TF 26.8 % to 18.9 %, $p=0.568$). This improvement was not influenced procedural or baseline patients characteristics, by valve selection or the operative risk.

However, patients with moderate or severe TR were more prone to suffer from paravalvular leakage after TAVI (no/mild TR 43.4 % vs. moderate/severe TR 60.3 % $p=0.007$).

No significant differences were shown between both groups concerning the post-procedural complications defined according the VARC-2 Criteria and the 30-day mortality but longterm survival was significantly reduced in patients without improvement of concomitant TR (log rank $p=0.021$).

Conclusions: Patients with concomitant moderate to severe TR may benefit more likely from TA-TAVI as they feature better improvement than those patients treated transfemorally. Moreover, long term follow up showed a significant survival benefit in those patients with reduced TR after TAVI which also speaks in favour of transapical treatment. These findings, however, have to be confirmed in a larger multi-center study.

CA 2-2

Bail-out transcatheter aortic valve implantation in cardiac decompensated patients under ECLS support

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Background: Indications for transcatheter aortic valve implantations (TAVI) are mainly restricted to older patients with multiple comorbidities and who offer a high mortality risk by considering conventional surgery. Further limitations for this procedure are the economic burst. Therefore carefully patient selection is of prime importance. We wanted to report a case series of 4 patients who underwent TAVI under ECLS support due to cardiac decompensation.

Methods: Four male patients with reduced left ventricular ejection fraction (LV-EF) received ECLS either prior to the TAVI procedure in the theatre ($n=2$) or due to resuscitation ($n=2$). All patients showed low-flow low gradient aortic stenosis(AS) with LV-EF < 30 % and were cardiac decompensated needing inotropic support. Four patients showed high grades of renal insufficiency and two of them acute renal failure with dialysis prior to intervention. All patients received Edwards Sapien 3 (size 26 mm $n=2$; size 29 mm $n=2$) as TAVI via transapical ($n=3$) or transaortic approach. The patient with the transaortic approach needed additionally a single Bypass grafting to the LAD.

Results: Three patients survived the procedure with successfully weaning from the ECLS within few days. All of these three patients could be discharged home. One patient expired 6 days after TAVI due to failing myocardial recovery and multi organ failure.

Conclusions: Despite the very small number of patients TAVI under ECLS support seems to be a feasible strategy for decompensated heart failure or even resuscitated patients who otherwise have no interventional options for myocardial recovery due to the relevant AS.

CA 2-3

Impact of gradient and flow on perioperative renal function after transcatheter aortic valve implantation

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Background: Postoperative acute kidney injury (AKI) was shown to be associated with an increased mortality after transcatheter aortic valve implantation (TAVI). In this analysis, we aimed to investigate the impact of preoperative gradient and flow on kidney function after TAVI.

Methods: From 2008 to 2015, a total of 717 consecutive patients underwent TAVI for severe aortic stenosis (AS) in this two center study.

We divided our study population into 4 groups and compared patients with high gradient AS ($n=520$, mean gradient ≥40 mmHG; HG-AS) to those with low gradient AS ($n=197$, mean gradient <40 mmHG; LG-AS) and patients with high flow AS ($n=330$, stroke volume index >35 ml/m², HF-AS) to those with low flow AS ($n=314$, stroke volume index <35 ml/m², LF-AS)

Overall mean age was 81.7 (±5.6) years, and overall mean STS-score was 6.9 (±5.5) %.

VARC II- Criteria were used as clinical endpoint.

Results: Perioperative mortality did not differ between patients with low vs. high gradient AS (LG-AS 10.0 % vs. HG-AS 7.9 %, $p=0.368$). Device success, early safety and clinical efficacy were similar between the groups (all $p>0.05$). AKI ≥ stage 2 was detected significantly more often in the low gradient group (LG-AS 16.8 % vs. HG-AS 10.8 %, $p=0.032$).

With regard to the impact of flow, no difference was seen on mortality between patients with low vs. high flow AS $p=0.322$). Device success, early safety and clinical efficacy were also similar between the two groups (all $p>0.05$). The incidence of AKI ≥ stage 2 was higher in the low flow group (LF-AS 18.2 %), as compared to the high flow group (HF-AS 7.6 %, $p<0.001$).

Time-related valve safety was not different between all four groups.

Conclusions: Although we were able to show very good results regarding clinical outcome we identified low flow and low gradient to have an impact on renal function in patients undergoing TAVI.

CA 2-4

Perioperative outcome of low flow low gradient aortic stenosis in transcatheter aortic valve implantation. Insights from a two center study with more than 700 patients

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Background: Our aim was to investigate the outcome of low flow low gradient aortic stenosis (LFLG-AS) after transcatheter aortic valve implantation (TAVI). Further, we analyzed the impact of the ejection fraction (EF) on the outcome of patients with LFLG-AS after TAVI.

Methods: From 2008 to 2015, a total of 747 consecutive patients underwent TAVI for severe AS in this two center study.

We compared patients with LFLG-AS (stroke volume index >35 ml/m² and mean gradient <40 mmHG, $n=113$) with patients showing typical characteristics of severe aortic stenosis ($n=514$).

To further elucidate the impact of left ventricular ejection fraction on the perioperative outcome of patients with LFLG-AS, we divided LFLG patients into two subgroups according to the LVEF, with a cut off of 50 % to distinguish between reduced and preserved LVEF. Overall mean age 81.7 (±5.7) years, overall mean STS-score 7.0 (±5.5) %.

VARC II- Criteria were used do define clinical endpoints.

Results: Device success, early safety and clinical efficacy were not significantly different in patients with LFLG-AS (all $p>0.05$). The stroke rate (LFLG-AS 0.9 % vs. HG-AS 3.7 % $p=0.148$) was similar between the groups. Incidence of acute kidney injury ≥ stage 2 (LFLG-AS 20.4 % vs. HG-AS 11.5 % $p=0.012$) and renal replacement therapy (LFLG-AS 15.9 % vs. HG-AS 9.3 % $p=0.039$) were significantly higher in the LFLG-group. Perioperative mortality was significantly higher in LFLG-AS (LFLG-AS 13.3 % vs. HG-AS 7.4 % $p=0.042$).

The EF had no impact on perioperative mortality of patients with LFLG-AS (LFLG-reduced EF 10.9 % vs. LFLG-preserved EF 14.0 %, $p=0.765$).

Conclusions: Patients with LFLG-AS showed a worse outcome regarding VARC II endpoints. In our cohort, reduced ejection fraction did not impact the outcome of LFLG-AS patients undergoing transcatheter aortic valve implantation.

CA 2-5

Predictive factors for postoperative rethoracotomy in cardiac surgery

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Background: Postoperative bleeding and pericardial tamponade are one of the most common complications after cardiac surgery. Such complications demand fast diagnosis and consecutive treatment. Aim of this study was to identify predictors for patients having an increased risk of postoperative rethoracotomy.

Methods: By database research we analyzed all patients who underwent CABG, valve surgery or combined at our department in 2012. The patients were divided into two subgroups: elective and urgent. Groups were compared by student's t-test and $\chi 2$-test

Results: In total, 757 patients (68 ± 11 a; 34 % females) were included in the present study (CABG (48 %), valve surgery (38 %) or combined (14 %)). Eighty-eight percent of all patients were classified as elective and 13 % as urgent. Surgical revision rate due to postoperative bleeding was 3.4 % (elective vs. urgent: 3.5 vs. 3.2 %; n. s.). Rethoracotomy occured in 8.4 % (elective vs. urgent: 7.8. vs. 12.1 %; n. s.), while pericardial tamponade was documented only in 0.2 %. Patients who underwent rethoracotomy were significantly older than patients without reoperation (73 ± 9 vs. 68 ± 11a; $p<0.01$) On average 1.4 ± 2.0 red blood cell units were given intraoperatively (elective vs. urgent: 1.2 ± 0.7 vs. 2.3 ± 0.3; $p<0.001$) and 1.6 ± 3.7 postoperatively (elective vs. urgent: 1.5 ± 0.1 vs. 1.6 ± 0.2; n. s.). Patients with postoperative rethoracotomy had a significantly higher demand on intraoperative (2.0 ± 2.0 vs. 1.3 ± 2.0; $p<0.01$) and postoperative (4.4 ± 6.2 vs. 1.4 ± 3.6; $p<0.01$) blood transfusions. Furthermore, these patientes showed a significantly longer initial time of ventilation compared to patients without

rethoracotomy (81 ± 96 vs. 33 ± 70 h; $p < 0.001$). Finally, Rethoracotomy occurred significantly more frequently in combined procedures (CABG + valve surgery) than in single surgeries (15.9 vs. 7.6 %; $p < 0.01$).

Conclusions: Higher age, demand on blood transfusions and longer initial ventilation are potential predictors for postoperative rethoracotomy. Especially the intraoperative administration of blood transfusions must be taken into account for threatening postoperative complications. Further investigations need to expand the analysis period, define cut-off-levels and include other centers into the study.

CA 2-6

Topical application of intra-sternal Vancomycin and subcutaneous Gentamycin significantly reduces deep sternal wound infection after cardiac surgery

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Background: Deep sternal wound infection is still a major complication in patients undergoing cardiac surgery. We previously identified mammary artery harvesting as a risk factor for decreased antibiotic tissue penetration. In addition, other risk factors including diabetes may inhibit sufficient tissue penetration of perioperative antibiotic prophylaxis with Cefazolin. A novel closure protocol applying two topical antibiotics and further recommendations for sternal wiring was introduced at our department to decrease the number of sternal wound infections.

Methods: A twelve-months period prior to (March 2013–February 2014) and after (July 2014–June 2015) the introduction of a novel sternal closure protocol was studied. All deep sternal wound infections resulting from an operation during this period were analyzed. The closure protocol consisted of the intra-sternal application of Vancomycin and the subcutaneous application of Gentamycin. Furthermore, we increased the number of sternal wires to an average of 9–10 wires for more uniform distribution of lateral forces.

Results: Fifty-six out of 1103 patients operated prior to the protocol change developed an infection (5.1 %). The introduction of the novel sternal closure protocol reduced this number to 21 out of 1112 patients (1.9 %; $p < 0.001$). There was no difference between the age of infected patients (67 ± 11 vs. 64 ± 13 years; $p = 0.45$) or the time to infection (29 ± 55 vs. 24 ± 26 days; $p = 0.72$).

Conclusions: The topical application of two antibiotic agents significantly reduced deep sternal wound infection. We hypothesize that this protocol overcomes impaired tissue penetration as well as bacterial resistance.

CA 2-7

Transcatheter aortic valve implantation using transaortic access – experience from the multicentre, multinational, prospective ROUTE registry

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Background: Transcatheter aortic valve implantation (TAVI) represents an alternative to surgical valve replacement in high risk patients. Whereas the transfemoral access route is commonly used as the first line approach, the transapical access is an option for patients not suitable for transfemoral treatment mainly due to anatomical conditions. Transaortic (TAo)-TAVI has been shown to be a viable alternative surgical access route; however, only limited data on its effectiveness and safety has been published.

Objectives: The "Registry of the Utilization of the TAo-TAVI approach using the Edwards SAPIEN Valve" (ROUTE) was established to assess the effectiveness and safety of the use of transaortic access for TAVI procedures (NCT01991431).

Methods: ROUTE is a multicentre, international, prospective, observational registry where data was collected from 22 centres across Europe starting in February 2013. Patients having severe calcific aortic stenosis were documented if they were scheduled to undergo TAo-TAVI using an Edwards SAPIEN XT or a SAPIEN 3 valve. The primary endpoint was 30-day mortality. Secondary endpoints were intra-procedural/in-hospital and 30-day complication rates.

Results: In 301 patients included, valve success was documented in 96.7 %. The 30-day mortality was 6.1 % (18/293) (procedure-related mortality: 3.1 %; 9/293). The rate of vascular access complications (dissection, rupture, and/or major bleeding) was low at 2.0 %. In 3.3 % of patients paravalvular regurgitation was classified as moderate or severe (10/300). Other complications included myocardial infarction (1.0 %), stroke (1.0 %), transient ischaemic attack (0.3 %), major vascular complications (3.4 %), life threatening bleeding (3.4 %), and acute kidney injury (9.5 %). Twenty-six patients (8.8 %) required permanent pacemaker implantation.

Conclusions: Transaortic access for TAVI appears to be a safe alternative to the transapical procedure.

CA 2-8

Transcatheter mitral valve implantation with the Edwards Sapien XT in native mitral annulus: pushing the limits

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Background: Based on increasing life expectancy, the number of redo-surgeries for degenerated bioprosthesis is expected to increase. The transcatheter mitral valve implantation (TMVI) showed promising results in case of degenerative mitral valve

prosthesis or after mitral valve repair. We report about TMVI in native mitral valve annulus.

Methods: In march 2012 and january 2016 three frail female patients at the age of 66, 70 and 82 years old, with several comorbidities and severe mitral valve insufficiency and severe calcified mitral valve annulus. One patient had an aortic valve stenosis, mitral valve insufficiency and pulmonary hypertension, atrial fibrillation and diffuse liver damage. The other patient had a severe tricuspid – and mitral valve insufficiency. She had an aortic valve replacement and single bypass operation 6 month before TMV-surgery, atrial fibrillation, pacemaker-implantation, COPD Gold II, stroke, Billroth II 01/2012. The third patient present an additional aortic valve stenosis and tricuspid valve insufficiency, chronical atrial fibrillation and pacemaker-implantation. The TMVI was performed as an open heart-procedure and on-pump, the 29 mm Sapien XT prosthesis were implanted under direct view into the mitral valve annulus.

Results: The TMVI and the concomitant procedures (aortic valve replacement and tricuspid valve repair) were successful in all cases. The perioperative echo of the first patient showed two paravalvular leaks (PVL) resulting in a mitral valve insufficiency grade two. In the second case, the prosthesis was initially placed correctly, but half an hour after weaning from bypass, the TEE showed a prosthesis motion towards the left atrium. We decided to go on bypass and fix the prosthesis with sutures. Thereafter the mitral valve did not show any movement and only minimal PVL. The TMV-prosthesis of the third was fixed with nine sutures through the remaining leaflets of the stenotic mitral valve to prevent prosthesis migration. Postoperative echocardiography showed only a mild PVL. The first patient had a stroke perioperatively, which lead to a prolonged hospital stay and was discharged to rehab 21 days after surgery. Follow-up echocardiography after 1 and 1.5 years revealed two PVLs resulting in an mitral valve insufficiency grade two. The patient died 2 years and 3 month after surgery on progression of her liver cirrhosis. The second patient died on the first postoperative day because of her frailty on multiple organ failure.

The third patient left the hospital 30 days after surgery to a remobilisation ward.

Conclusions: The TMVI in degenerated mitral valve prosthesis or rings seems to be a promising option for surgically unmanagmentable patients, but implantation of TMV is challenging. The anatomical structure of the valve and the relationship between mitral valve and the interventiricular septum as well as the size of mitral valve annulus have to be addressed for successful implantation and to avoid device motion.

Chirurgie Abstracts – Vortragssitzung 3

CA 3-1

Klinische Signifikanz der frühzeitigen Koronarangiographie zur Kontrolle von perioperativen Ischämien nach herzchirurgischen Eingriffen

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Grundlagen: Die Literatur berichtet in 5 % der herzchirurgischen Fälle von perioperativen Ischämien. Die Hypothese der Studie war, dass zusätzlich zur Klinik (mit steigendem Katecholaminbedarf), pathologischen Laborparametern sowie Wandbewegungsstörungen (mit EKG-Veränderungen) eine frühzeitige Koronarangiographie bei der Entscheidungsfindung betreffend das weitere Vorgehen (Re-Eingriff, PCI, konservativ, ECMO) hilfreich sein kann.

Methodik: Zwischen August 2010 und Jänner 2016 wurde bei 63 konsekutiven Patienten (1,1 %), mittl. Alter 68,6 ± 11,1 Jahre (19,3–85,9 Jahre) (44 Männer (70 %), 19 Frauen (30 %)) im Hybrid-Op eine postoperative Akut-Koronarangiographie im Mittel am 2,6 ± 3,1 postop. Tag (unmittelbar postop.–11,4 Tag postop.) bei jedem Ischämie-Verdacht durchgeführt. Die Patienten wurden nach der Koronarangiographie in verschiedene Behandlungsstrategien unterteilt: Gruppe A: Re-Operation (Revision der CABG, Neuanlage CABG/Klappenersatz); Gruppe B: PCI; Gruppe C: keine Konsequenz (zu kleine Zielgefäße, technisch suboptimal machbar, blande Koronarien). Die Troponin T-Verläufe der ersten 72 postoperativen Stunden und zusätzlich nach der Angiographie wurden für diese Gruppen verglichen.

Ergebnisse: 34 Patienten mit einem St.p. CABG (54 %), einem St.p. Klappeneingriff ($n = 12$; 19 %), 7 Patienten nach einem Kombinationseingriff (11,1 %) und in 10 Fällen mit anderen Eingriffen (15,9 %) wurden akut nachkathetert. Es gab keinen signifikanten Unterschied hinsichtlich des Alters und des Geschlechts. Bei 19 dieser 63 Patienten handelte es sich beim primären herzchirurgischen Eingriff um einen Notfalleingriff. In der Gruppe A waren 31,7 %, in der Gruppe B 14,3 % und in der Gruppe C waren 54 % der Patienten. Postoperativ zeigten 44,4 % der Patienten ein Low Cardiac Output Syndrom (LCO), 39,7 % wurden reanimiert und 28,6 % zeigten ventrikuläre Rhythmusstörungen. Insgesamt 27 Patienten (42,9 %) benötigten eine intraaortale Ballonpumpe (IABP) (intraoperativ $n = 8$ (12,7 %); postoperativ $n = 10$ (15,9 %); nach Herzkatheter $n = 9$ (14,3 %)). Acht Patienten (2 aus der Gruppe A, 5 aus der Gruppe C; insgesamt 12,7 %) wurden mit einem ECMO-System versorgt ($n = 2$ intraoperativ, $n = 1$ postoperativ und 5 Patienten erhielten die ECMO nach der Koronarangiographie). Ein pathologisches EKG im Sinne von Ischämiezeichen hatten 20,6 % der Patienten, neu aufgetretene Wandbewegungsstörungen fanden sich bei 63,5 %. Hoch pathologische Troponin T Werte zeigten 19 Patienten (30,2 %), während 32 Patienten (50,8 %) einen massiven Anstieg im Verlauf zeigten. Hämodynamisch instabil waren 41 Patienten (65,1 %). Am OP Tag betrug das Troponin T durchschnittlich 3523 pg/ml, am Tag der Koronarangiographie 3075 pg/ml. Bei den chirurgisch sanierten Patienten fand sich im Vergleich zu den anderen Gruppen ein deutlicherer Troponin-Abfall ($p > 0{,}05$) 24–72 Stunden nach dem Zweiteingriff. Die Gesamt 30-Tages-Mortalität betrug 28,6 % ($n = 18$), ohne die ECMO Patienten betrug die 30-Tages-Mortalität in der Gruppe A 16,6 %, in der Gruppe B 25 % und 24,1 % in der Gruppe C, wobei in dieser Gruppe 5 der 8 ECMOs implantiert wurden.

Schlussfolgerungen: Kein einziger Patient kam durch die Koronarangiographie zu Schaden, in 46 % kam es zu einer Konsequenz, die 30-Tages-Mortalität bei der Re-Operation war niedriger ($p > 0{,}05$) gegenüber der PCI und dem konservativem Vorgehen. Patienten mit einer Re-Operation profierten durch einen schnelleren Abfall des Troponins nach der Intervention als Zeichen eines geringeren Myokardschadens.

CA 3-2

Einfluss von Hyperthermie und milder Hypothermie im Vergleich zu Dobutamin auf die myocardiale Funktion am gesunden Schweineherz

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Grundlagen: Die Körpertemperatur beeinflusst als wesentliche Determinate die cardiale Funktion. Welche Körpertemperatur nach cardiopulmonaler Reanimation zur Verbesserung des cardialen Outcome anzustreben ist, ist nach wie vor nicht ganz geklärt. Aufgrunddessen wurde in diesem Tiermodell am gesunden Schwein mittels Druck-Volumen-Messungen der Einfluss von Hyperthermie (HT, 40,5 °C), Normothermie (NT, 38 °C) und milder Hypothermie (MH, 33,0 °C) auf die systolische linksventrikuläre (LV) Funktion im Vergleich zu Dobutamin-Applikation analysiert.

Methodik: Im closed-chest-Setting wurden neun narkotisierte Schweine (67 ± 2 kg) mittels LV Druck-Volumen- sowie Swan-Ganz- und intravasalem Kühl-Katheter und einem Okklusionsballon in der Aorta descendens instrumentiert. Nach Baseline-Messungen bei HT erfolgte die titrierte intravenöse Dobutamin-Infusion (2,1 ± 0,1 µg/kg/min) um LV dP/dtmax zu verdoppeln. Anschließend erfolgte die sukzessive Kühlung auf Normothermie und Hypothermie und respektive die Wiederholung der Dobutamin-Infusion (1,8 ± 0,1 und 1,5 ± 0,1 µg/kg/min) bei jedem Temperaturschritt. Die Messung der LV-Funktion erfolgte währenddessen mittels endsystolischer und -diastolischer Druck-Volumen-Bestimmung während definierter kurzer Aortenokklusionen. Das extrahierte endsystolische LV-Volumen bei einem endsystolischen LV-Druck von 100 mmHg (LVV-Pes100) wurde als Parameter für die LV-Kontraktilität herangezogen.

Ergebnisse: Herzfrequenz (98 ± 4 vs 89 ± 4 vs 65 ± 2 bpm, $p < 0.05$) und Cardiac output (6,7 ± 0,3 vs 6,1 ± 0,3 vs 4,4 ± 0,2 l/min) sanken unter Kühlung von HT zu NT und MH, während ein Anstieg der LV-Kontraktilität beobachtet werden konnte (LVV-Pes100: 74 ± 5 at HT, 52 ± 4 at NT and 41 ± 3 ml at MH, $p < 0,05$). Der Effekt der Kühlung auf LVV-Pes100 (HT to NT: –22 ± 3 ml, NT to MH: –11±3 ml) war vergleichbar mit jenem von Dobutamin bei jeweiliger Temperatur (HT: –20 ± 3 ml, NT: –14 ± 3 ml, MH: –12 ± 4 ml). Zusätzlich erfolgte als Hinweis auf den Verlust der LV-Compliance bei niederer Temperatur ein stufenweiser Links-Shift der end-diastolischen Druck-Volumen-Beziehung von HT zu NT und MH. Dieser Effekt zeigte sich unter Dobutamin während MH partiell reversibel.

Schlussfolgerungen: Durch Kühlung von HT auf NT und folgend auf MH kann am gesunden Schweineherz ein Anstieg der LV-Kontraktilität ähnlich dem Effekt von niedrig-dosierter Dobutamin-Infusion erzielt werden. Daraus könnte geschlossen werden, dass durch Hypothermie der Bedarf an positiv wirkenden Substanzen reduziert werden könnte, sowie dass nach cardiopulmonaler Reanimation milde hypotherme Bedingungen für die myocardiale Funktion günstiger sein könnten.

CA 3-3

Cotinin-Untersuchung zeigt einen Dosis-abhängigen Effekt der Rauchexposition auf das Langzeitüberleben nach Herztransplantation

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Grundlagen: Rauchen ist ein Risikofaktor für kardiovaskuläre Erkrankungen. Bei Herztransplantation ist Rauchen ebenfalls ein Risikofaktor für das Überleben. Ziel der Analyse war es, zu untersuchen, ob der Biomarker Cotinin dazu verwendet werden kann, einen dosisabhängigen Einfluss auf das Langzeitüberleben nach Herztransplantation zu erkennen.

Methodik: 294 Herztransplantierte Patienten, die mindestens 1 Jahr überlebt haben, wurden in einer Querschnittsanalyse auf Cotinin im Harn getestet. Patienten wurden in folgende Kategorien eingeteilt: <10 ng/ml (Nicht-Raucher), 10–50 ng/ml (Passiv-Raucher), 50–100 ng/ml (leichter Raucher), 100–500 (mittelstarker Raucher) und >500 ng/ml (starker Raucher). Überlebensanalysen wurden mittels Kaplan-Meier-Analyse durchgeführt und mit dem Log-Rang-Test verglichen. Tod durch Tumor oder Graftvaskulopathie wurde in jeder Gruppe untersucht und mittels Chi2-Test verglichen.

Ergebnisse: 406 Cotinin-Testungen wurden in 294 Patienten durchgeführt. 14,3 % der Patienten wurden mehrmals getestet und zeigten immer gleiche Ergebnisse wie bei der ersten Testung. Mediane Zeit bis zur Testung waren 8,7 Jahre (0,25–0,75 %: 4,0–13,0 Jahre). Medianes Alter war 61,7 Jahre (25–75 %: 53,3–68,1) und 82,2 % waren männlich. Insgesamt 110 (38,7 %) Patienten waren aktive Raucher. Von den Nicht-Rauchern (NR) wurden 39,6 % ($n = 72$) als Passiv-Raucher (PR) definiert. Bei den aktiven Rauchern wurden 40,9 % ($n = 45$) als leichte (LR), 11,2 % ($n = 13$) als mittelschwere (MR) und 47,3 % ($n = 52$) als schwere Raucher (SR) definiert. Das 15 und 25 Jahres-Überleben zwischen Rauchern und Nicht-Rauchern war mit 78,0 % vs. 87,3 % und 35,9 % vs. 57,4 % knapp nicht signifikant unterschiedlich ($p = 0,051$). Nicht-Raucher und Passiv-Raucher hatten ein ähnliches Langzeitüberleben (15a: NR: 87,0 % PR: 87,9 %, 25a: NR: 58,8 % PR: 53,9 %, $p = 0,680$). Im Gegensatz dazu war das Langzeitüberleben bei den aktiven Rauchern signifikant unterschiedlich (15a: LR: 87,5 %, MR: 72,5 %, SR: 70,1 %, 25a: LR: 45,3 %, MR: 0 %, SR: 0 %; $p = 0,027$). Tod durch Tumor oder Graftvaskulopathie war zwischen Nicht-Rauchern und Rauchern signifikant unterschiedlich (NR 13/33: 39,4 % vs. Raucher 22/31: 70,9 %; $p = 0,011$)

Schlussfolgerungen: Cotinin-Testungen können eine gute Information über die Rauchexposition von transplantierten Patienten geben. Rauchen ist mit einem schlechtern Langzeitüberleben assoziiert, wobei eine Cotinin-abhängige Verschlechterung erkennbar ist. Aktive Raucher sterben häufiger an Tumoren und Graftvaskulopathie nach Herztransplantation.

CA 3-4

Herzoperation nach Herztransplantation – elektive Operation oder last-exit Strategie

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Grundlagen: Verbessertes Überleben nach einer Herztransplantation (HTX), aber auch die zunehmende Notwendigkeit der Transplantation marginaler Spenderorgane bei internationalem Organmangel machen eine herzchirurgische Intervention im Langzeitverlauf immer häufiger notwendig. Ziel dieser Arbeit ist die Aufarbeitung der Morbidität sowie Mortalität von PatientInnen mit herzchirurgischen Operationen nach einer HTX an unserem Zentrum.

Methodik: In dieser retrospektiven Studie wurden alle PatientInnen analysiert, die in unserem Zentrum herzchirurgischen Intervention nach einer Herztransplantation unterzogen wurden. Re-Transplantationen wurden nicht inkludiert.

Ergebnisse: Von März 1984 bis September 2014 wurden an der Herzchirurgie im AKH Wien insgesamt 17 (1.24 %) PatientInnen von 1369 PatientInnen nach einer Herztransplantation am Herzen reoperiert. Die Indikation zur herzchirurgischen Intervention war bei 5 Pat (29.4 %) eine Transplantat-Vaskulopathie, bei 7 Pat (41.2 %) ein Klappenvitium, und bei jeweils einem/einer Pat (5.9 %) ein infektiöses Pseudo-Aortenaneurysma, eine Aortendissektion, eine Ventrikuläre Herzunterstützungs-Implantation, Perikarditis constrictiva und eine iatrogene Koronar-Dissektion. 82 % waren männlich, 18 % weiblich. Die mediane Zeit zwischen der Transplantation und dem Re-Eingriff war 9.4 (2.7–11.3) Jahre. Der Krankenhausaufenthalt war im Median 31 (18–47) Tage. Die mediane Zeit zwischen HTx und der Re-Operation war 9,4 Jahre (2,7–11,3). Auf Grund von Nachblutung mussten 3 PatientInnen revidiert werden. Die Spitalsmortalität lag bei 11,8 % ($n=2$). Auf Grund einer chronischen Transplantat-Vaskulopathie mussten 2 PatientInnen (11,8 %) 3 und 9 Monate nach dem Folgeeingriff re-transplantiert werden. Das mediane Überleben war 506 Tage (242–2884), 47,1 % ($n=8$) leben derzeit noch. 17,6 % ($n=3$) waren Notoperationen, 82,4 %($n=14$) waren elektive Operationen. Die Spitalsmortalität war 66,7 % bei Notoperationen und 0 % bei selektiven Operationen.

Schlussfolgerungen: Geplante herzchirurgische Eingriffe nach einer Herztransplantation sind mit niedriger perioperativer Mortalität und Morbidität assoziiert. Akute Interventionen haben eine hohe Mortalität.

CA 3-5

Initiating repair in a porcine Ischemia/Reperfusion model by manipulating the blood flow with a Trans-Coronary sinus catheter intervention

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Background: We assessed the hypothesis that a coronary sinus catheter intervention (PICSO) substantiates angiogenesis and puts influence on protecting jeopardized myocardium in an ischemia/reperfusion model.

Methods: 32 open chest pigs received: sham-operation ($n=3$); Infarct and reperfusion without PICSO (control-group, $n=8$), PICSO without infarct and reperfusion (PICSO-A, $n=10$); PICSO with infarct and reperfusion (PICSO-B, $n=11$). LAD was occluded for 3 hours followed by 1 hour reperfusion. Duration of PICSO was 4 hours and was induced after 30 minutes ischemia continuing through reperfusion (3.5 hours). Specimen were taken from: LAD region (infarct), adjacent zones Border1 and 2, Circumflex region remote R and Right ventricle RV.

Results: VEGFR1 was significantly upregulated in arteries and veins in both interventional groups as compared to controls ($p<0.05$). VEGFR2 expression in arteries was significantly higher in PICSO-B as compared to controls and in arteries of both PICSO groups as compared to control ($p<0.05$). Significant upregulation of VEGFR2 could be found in veins of PICSO groups as compared to control and sham-operated animals ($p<0.05$). p53 was significantly downregulated in myocardial tissue of pigs from PICSO A group in comparison with control pigs ($p<0.05$). Ki67 was significantly upregulated in PICSO A in comparison with controls ($p<0.005$).

Conclusions: Significant upregulation of angiogenesis proteins in coronary vessels by activation of PICSO in arteries and veins seems to induce regenerative pathways leading to induction of angiogenesis and structural repair. The upregulation of the proliferating marker Ki67 suggests PICSO taking part in cell cycles whereas downregulation of p53 reflects inhibition of apoptosis as well as induction of cardiogenous repair mechanisms.

In conclusion, this study supports the notion that a simple trans-coronary sinus catheter intervention has beneficial effects on myocardial jeopardy by neoangiogenesis and cardioprotection leading to structural repair of the damaged heart.

CA 3-6

Institutional experience with a new fully magnetically levitated LVAD – analysis of the first 21 patients with the Thoratec Heartmate 3 device from the Vienna database

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Background: LVAD implantation has become a standard treatment option for terminal heart failure. We present our institutional experience with the Thoratec Heartmate 3 LVAS (HM3) in 21 patients.

Methods: Retrospective review of 21 patients receiving an HM3 between June 2015 and February 2016, regarding patient demographics, adverse events, length of support and outcomes.

Results: Mean age was 63 ± 8.7 years, ranging from 42 to 76 years. 86 % of the patients were male, 48 % suffered from ischemic cardiomyopathy. At the time of implantation, 5 % of the patients were in INTERMACS level 1, 10 % in INTERMACS level 2, 33 % in INTERMACS level 3 and 52 % in level 4–7. Two patients needed temporary right ventricular support; both could be successfully weaned from it. 14 % of the patients had previously undergone cardiac surgery, concomitant surgery was performed in 33 %. Duration of LVAD support ranged from 7 to 618 days with a mean of 215±205 days. No patient has been transplanted so far, two died on LVAD support (10 %) and 19 remain still on the device (90 %). Four patients (20 %) experienced at least one major bleeding event, including surgical bleedings in 50 %, gastrointestinal bleedings in 17 %, and intracranial bleedings in 33 %. One or more thromboembolic complications occurred in two patients (10 %) (one septic thrombus formation in the outflow graft after systemic infection, two ischemic strokes). No early or late right heart failure could be observed. 5 % of the adverse events had fatal consequences. 30-day and in-hospital mortality were low with 0 % and 5 %, respectively. One-year survival was 86 %. Causes of death were septic embolism stroke (POD 212) and Merkel cell carcinoma (POD 203).

Conclusions: Our initial results with the new HM3 LVAS are very promising with a very low incidence of bleeding or thromboembolic events and providing excellent mid-term outcomes. The pump can therefore be considered to be a safe and efficient therapy option in end-stage heart failure.

CA 3-7

Micro-embolic signals correlate with pump thrombus formation and non-thrombotic outflow graft occlusion in patients with left ventricular assist devices

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Background: Micro-emboli are detectable as high intensity transient signals (HITS) with Doppler ultrasound in different clinical conditions including patients with left ventricular assist devices (LVAD). In LVAD patients HITS represent micro-emboli of mostly gaseous nature. The cause of their formation, however, has not been determined.

Methods: From June 2014 to February 2016 LVAD patients were systematically screed for HITS in the LVAD outflow graft by transthoracic echocardiography. The occurrence of HITS was then correlated with pump thrombus formation (PT) and non-thrombotic outflow graft occlusion.

Results: HITS were detected in the outflow graft of 20 LVAD patients (Thoratec Heartmate II $n=12$, Heartware HVAD $n=8$). HITS correlated with PT in 14 patients (Heartmate II $n=7$, HVAD $n=7$) and non-thrombotic outflow graft stenosis in 6 patients (Heartmate II $n=5$, HVAD $n=1$). Patients with PT either underwent thrombolysis ($n=7$), pump exchange ($n=2$), LVAD weaning ($n=1$) or no treatment if no hard clinical treatment indication was present ($n=5$). In PT patients HITS disappeared after successful thrombolysis or pump exchange. Of note, pump thrombus formation or non-thrombotic outflow graft stenosis could be macroscopically assured at the time of transplant in the remaining patients.

Conclusions: HITS detection by transthoracic echocardiography identifies patients with pump thrombus formation and non-thrombotic outflow graft occlusion and might develop as a very sensitive screening tool for pump pathology and hypocoagulation monitoring.

CA 3-8

Temporary right heart support after LVAD implantation an initial single center report

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Background: Right ventricular failure after LVAD implantation is a serious complication. Herein we describe our initial experience with a novel temporary RVAD approach.

Methods: From february 2014 to september 2015 a total of 9 patients received implantation of a temporary RVAD System with cannulation of the pulmonary artery via a 8 mm prosthesis tunneled through the chest wall and a percutaneous venous drainage cannula inserted via the femoral vein. 7 patients (78 %) received the temporary RVAD system after implantation of a Heartware HVAD, 1 Patient received a Thoratec Heartmate II and in 1 Patient we used the temporary RVAD as stand alone therapy. Etiology of cardiomyopathy was ischemic in 2 patients and dilative in 6 patients.

56 % of the patients were Intermacs level I at time of implant.

Results: Median Duration of RVAD support was 9 (5–90) days. All patients survived 30 days and even after a median follow up of 60 (9–326) days all patients are alive. There were no strokes. We experienced 1 case of recurrent right heart failure. This patient underwent high urgent heart transplantation and is well thereafter.

Conclusions: Temporary RVAD support via this novel approach results in excellent outcome in this highly complex group of patients.

POSTER

Beste Poster

BP-1

Epicardial adipose tissue as a predictor of cardiovascular outcome in patients with acute coronary syndrome undergoing percutaneous coronary intervention

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Background: We sought to investigate the association between epicardial adipose tissue (EAT) and cardiovascular outcome in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).

Methods: Of 1198 patients undergoing PCI, 438 had a transthoracic echocardiography performed during index hospitalisation. EAT thickness was measured in the parasternal long-axis view, perpendicularly on the free wall of the right ventricle at end-systole in 3 independent cardiac cycles. Patients were stratified by EAT thickness. As primary endpoint, composite major adverse cardiovascular events (MACE), including cardiovascular death, non-fatal myocardial infarction (MI) and non-fatal stroke were investigated after 3 years of follow-up.

Results: Patients were included between 2004–2012, 33.1 % were female. Median EAT was 2.65 mm [IQR 2.00–3.00].

Concerning established risk factors patients suffering from diabetes ($p=0.049$) and patients with previous MI ($p=0.017$) had significantly higher EAT thickness. Additionally, EAT was moderately correlated with body-mass-index ($R=0.381$; $p<0.001$) and weight ($R=0.321$; $p<0.001$).

MACE occurred in 14.6 % after a mean follow-up of 2.76 ± 0.69 years, corresponding to 8.3 % with cardiovascular death, 4.6 % with MI and 1.8 % with stroke. In univariate Cox regression EAT had a significant predictive value for 3-year MACE (HR = 1.479 [95 % CI 1.192–1.953]; $p = 0.006$). After adjustment for established risk factors and confounders, EAT remained significantly associated with MACE (HR = 1.408 [95 % CI 1.015–1.953]; $p = 0.04$).

Conclusions: In a cohort of ACS patients all undergoing PCI, EAT was associated with established markers of cardiovascular death, namely BMI, weight, the presence of diabetes and previous MI. Moreover, EAT was an independent predictor for 3-year cardiovascular outcomes, also after adjustment for established cardiovascular risk factors.

BP-2

Association of smoking with myocardial injury and clinical outcome in patients undergoing mechanical reperfusion for ST-elevation myocardial infarction

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Background: There is evidence suggesting a positive effect of cigarette smoking on myocardial tissue reperfusion and clinical outcomes in patients with myocardial infarction ("smoker's paradox"). We aimed to evaluate the relationship of smoking with cardiac magnetic resonance (CMR)-determined myocardial salvage and damage as well as clinical outcome in patients undergoing primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI).

Methods: This multicenter study included 727 consecutive STEMI patients reperfused within 12 hours after symptom onset. CMR imaging parameters (area-at-risk [AAR], infarct size [IS], myocardial salvage index [MSI], microvascular obstruction [MVO]) and intramyocardial haemorrhage [IMH] were compared according to admission smoking status. Major adverse cardiac events (MACE) rates at 12 months after infarction were compared between groups.

Results: Three hundred and thirty-nine (46.6 %) patients were current smokers. There was no difference in the extent of AAR (35 [24–47] vs. 37 [27–49] % of left ventricular volume [LV], $p = 0.10$), IS (16 [8–25] vs. 17 [10–26] %LV, $p = 0.21$), MSI (53 [29–70] vs. 52 [34–71], $p = 0.47$), MVO (0 [0–1.7] vs. 0 [0–1.6] %LV, $p = 0.91$), or in the frequency of IMH (42 % vs. 39 %. $p = 0.58$) between smokers and non-smokers. Smokers had lower MACE (3.8 % vs. 8.2 %, $p = 0.01$) rate. However, adjustment for differences in baseline risk factors, attenuated the association of smoking with MACE markedly (HR = 0.71, 95 % CI 0.36 to 1.38, $p = 0.31$).

Conclusions: Smoking is not associated with PPCI efficacy (myocardial salvage) or irreversible myocardial damage in patients with STEMI. The lower MACE rate of smokers was entirely explained by differences in baseline risk characteristics, thus challenging the existence of a "smoker's paradox".

BP-3

IGF1R is a key-regulator of neonatal cardiac regeneration

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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. Of note, our group and others reported similar observations in newborn human babies suffering from neonatal MI.

The mechanisms of neonatal mammalian cardiac regeneration remain unclear. Here we show the crucial role of IGF1R, which was found in our time-course transcriptome analysis of neonatal mouse hearts.

Methods: IGF1R was specifically knocked-down (KD) in cardiomyocytes of murine postnatal day one (P0.5) pups using adeno-associated virus 9 (AAV9) delivered shRNAmirs (Igf1r.4971, $N = 12$) and compared to Renilla KD controls (Ren.713, $N = 8$). Viral transduction efficiency was tested on P4 hearts by immunofluorescence staining of the AAV9 containing GFP. On day two after birth (P1.5) mice underwent either SHAM ($N = 4$ in the IGF1R and the Renilla group) or LAD ($N = 8$ in the IGF1R and $N = 4$ in the Renilla group) surgery. Cardiac function and regeneration was subsequently assayed by echocardiography one day post injury (dpi) and 21 dpi followed by final histological analysis.

Results: LAD ligation resulted in significant MI in both experimental groups as shown by markedly reduced ejection fraction (EF) and fractional shortening (FS) on 1 dpi. Importantly, 21 days later both SHAM groups displayed comparable functional cardiac parameters. In contrast, IGF1R KD mice that underwent LAD ligation surgery presented significantly reduced EF and FS compared to the other three experimental groups (EF SHAM Igf1r.4971 52.54 ± 6.30 %, SHAM Ren.713 50.76 ± 5.64 %, LAD Ren.713 50.90 ± 6.18 %, and LAD Igf1r.4971 33.51 ± 1.54 %, 2way ANOVA $p < 0.0001$). Finally, histological analysis revealed significant fibrosis in the IGF1R LAD hearts compared to hearts of the other three groups, which did not differ from each other.

Conclusions: Whereas viral delivered IGF1R or control KD does not alter physiological cardiac development, IGF1R KD markedly impairs neonatal cardiac regeneration following hypoxic damage.

BP-4

Characterization of left ventricle function in a relevant experimental model for human rheumatoid arthritis

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Background: There is evidence that patients with rheumatoid arthritis (RA) have higher risk for cardiovascular disease as well as developed impaired left ventricle (LV) function. However, the mechanism behind the hemodynamic impairment is not completely understood. It is therefore an unmet need to characterize LV function in a relevant experimental model which ultimately give opportunity to develop treatment strategies that improve LV function in RA.

Aim: The present study was aimed to characterize LV function as well as inflammatory cytokines and chemokines in LV tissue samples in a TNF-driven inflammatory, erosive arthritis mouse model.

Methods: Anaesthetized and intubated male and female human TNF-alpha transgenic (hTNFg; $n=7$ in both sex) and their wild type littermates mice ($n=7$ in both sex) with age of 14–15 weeks were used. Hemodynamic function was evaluated by insert the catheter tip retrograde into LV. The mRNA levels of Interleukin 6 (IL-6), Interleukin-1β (IL-1β), Monocyte Chemoattractant Protein 1 (MCP-1), Macrophage Inflammatory Protein 2 (MIP2), Neutrophil Chemokine (KC) in LV samples were determined by reverse transcription-quantitative polymerase chain reaction (RT-qPCR).

Results: hTNFg mice showed severe clinical signs of arthritis such as severe paw swelling and almost complete loss of grip strength at week 14. In comparison to WT littermates, hTNFg mice significantly showed smaller body weight and heart weight ($P<0.01$, respectively). LV systolic pressure (hTNFg; male: 71 ± 16; female: 69 ± 8 vs. WT; male: 98±18; female: 89 ± 16 in mmHg) and the rate of LV pressure rise (+dP/dt; hTNFg; male: 5335 ± 1287; female: 4109 ± 910 vs. WT; male: 6816 ± 567; female: 5822 ± 1288 in mmHg/s) was markedly decline in hTNFg mice in comparison with WT littermates. There was a tendency in increase of left ventricle end-diastolic pressure and -dP/dt in hTNFg mice. However, there were no difference in mRNA expression of IL-6, IL-1β and MIP2 in heart tissue between the groups. In contrast relatives mRNA expression of MCP-1 (WT vs. hTNFg; male: 1.02 ± 0.21 vs. 1.65 ± 0.5; female: 1.44 ± 0.38 vs. 2.38 ± 0.43; $P<0.05$) and KC (WT vs. hTNFg; male: 1.05 ± 0.3 vs. 2.60 ± 0.81; females: 1.39 ± 0.53 vs. 2.09 ± 0.3 $P<0.05$) were significantly increased in hTNFg mice.

Conclusions: This is the first study to demonstrate that hTNFg mice showed significant impairment in LV systolic function in association with increase in tissue levels of MCP-1 and KC.

BP-5

Extracellular matrix remodelling precedes calcification in degenerative aortic valve stenosis

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Background: Aortic valve disease is the most frequent native valve disease in Europe, and the third most frequent cause of cardiovascular death. Calcification processes in degenerative aortic valve stenosis show strong similarities to atherosclerotic calcification. We investigated the role of extracellular matrix (ECM) molecules on the progression and calcification of degenerative aortic valve stenosis.

Methods: Aortic valves were collected at valve replacement surgeries or heart transplantations and prepared for RNA isolation and histology. RNA expression profiles of healthy controls, as well as sclerotic, mild, moderate and severe stenotic aortic valves were analyzed utilizing an Affymetrix Human Gene 1.0 ST Array and validated by real-time PCR.

Results: More than 60 ECM proteins and proteases were dysregulated in sclerotic and stenotic aortic valves compared to healthy controls. Matrix proteins including various collagens and proteoglycans showed a disease progression dependent increase of expression. Out of the ECM proteases cathepsins, MMPs and ADAMs showed also a significant correlation with stenosis progression. While sclerotic aortic valves showed high up regulation of ECM molecules, calcification markers like the osteoblast cadherin (CDH11), periostin and osteonectin were significantly upregulated at later disease stages.

Conclusions: Our data demonstrate a time-dependent change in ECM gene expression patterns over the spectrum of aortic valve degeneration leading to "bonification" of the ECM, followed by an increase of osteoblast like cells and overt calcification.

BP-6

Combined biomarker testing for the prediction of microvascular obstruction after primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction

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Background: Microvascular obstruction (MVO) as detected by cardiac magnetic resonance (CMR) imaging indicates microvascular destruction with subsequent adverse clinical outcome after reperfused ST-segment elevation myocardial infarction (STEMI). The predictive value of different biomarkers for the occurrence of MVO is insufficiently studied. This study compared the prognostic value of admission and peak concentrations of routinely available biomarkers for the detection of MVO after reperfused STEMI.

Methods: One hundred and twenty-eight STEMI patients undergoing primary percutaneous coronary intervention (PPCI) were enrolled in this single-center, prospective, observational study. CMR was performed within the first week after infarction to assess infarct characteristics, including MVO. Admission and peak concentrations of high-sensitivity cardiac troponin T (hs-cTnT), creatine kinase (CK), N-terminal pro-B-type natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hs-CRP), lactate dehydrogenase (LDH), aspartate transaminase (AST) and alanine transaminase (ALT) were measured.

Results: MVO was detected in 69 patients (54 %). Peak concentrations of hs-cTnT, CK, hs-CRP, LDH, AST and ALT showed similar prognostic value for the prediction of MVO (area under the curve (AUC) = 0.77, 0.77, 0.68, 0.79, 0.78 and 0.73, all $p>0.050$), whereas the prognostic utility of peak NT-proBNP was lower (AUC = 0.64). Combination of these biomarkers did not result in higher predictive value as compared to hs-cTnT alone ($p=0.349$).

Conclusions: hs-cTnT, CK, hs-CRP, LDH, AST and ALT peak concentrations provided similar prognostic value for the prediction of MVO, whereas the prognostic utility of NT-proBNP was lower. Combining these biomarkers could not further improve prognostic utility compared to hs-cTnT alone.

BP-7

Shock index as a predictor of myocardial damage and clinical outcome in ST-elevation myocardial infarction

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Background: Data on the prognostic value of the shock index in patients with ST-elevation myocardial infarction (STEMI) are scarce. Furthermore, the relationship of shock index with myocardial damage is unknown. Aim of this study was to evaluate the association of the shock index with markers of myocardial damage and clinical outcome in patients with STEMI.

Methods: This multicenter study analyzed 791 patients. Patients were categorized in 2 groups according to admission shock index (optimized cut-off = 0.62). Infarct severity was determined by magnetic resonance (CMR) imaging. Patients with cardiogenic shock that were unable to undergo CMR acquisition were excluded. Major adverse cardiac events (MACE) were defined as a composite of death, reinfarction and congestive heart failure within 12 months.

Results: Patients with elevated admission shock index ($n = 321$ [40.6 %]) had a significantly larger area-at-risk (37.6[27.8–50.4]% of left ventricular volume [LV] vs. 34.3[24.5–46.0]%LV, $p = 0.02$), larger infarct size (19.5[10.7–28.0]%LV vs. 14.9[7.7–22.3]%LV, $p < 0.001$), lower myocardial salvage index (46.2[27.9–64.5] vs. 53.5[36.5–75.2], $p < 0.001$), and a larger extent of microvascular obstruction (0.3[0.0–2.2]%LV vs. 0.0[0.0–1.4]%LV, $p = 0.01$). An elevated shock index was associated with reduced MACE-free survival ($p < 0.001$). Furthermore, admission shock index was identified as independent predictor of MACE (hazard ratio = 2.92[1.24–4.22], $p < 0.01$).

Conclusions: STEMI patients with an elevated admission shock index had more pronounced myocardial and microvascular damage. Moreover, shock index was independently associated with MACE at 12 months.

BP-8

Discriminatory power of intensive care unit scoring systems for outcome prediction in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery

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Background: Extracorporeal membrane oxygenation (ECMO) is an effective supportive treatment to ensure continuous organ perfusion and oxygenation in patients suffering from refractory heart or lung failure following cardiovascular surgery. Nevertheless, overall survival is still low and appropriate risk stratification challenging since established risk prediction models have not been validated for this high-risk critically ill patients. Therefore we investigated the significance of seven established risk prediction models and compared their accuracy for predicting the short and long-term outcome in patients undergoing ECMO-support therapy following cardiovascular surgery.

Methods: 205 patients treated with veno-arterial ECMO therapy following cardiovascular surgery at a university-affiliated tertiary care center were included into our single-center registry. SOFA, APACHE II, SAPS II, SAPS III, additive EuroSCORE, EuroSCORE II and the RIFLE classification were collected at time of ICU admission. All-cause 30-day mortality was defined as primary and 2-year long-term mortality as secondary study endpoint.

Results: During a median follow-up time of 35 months (IQR 19–69), 64 % of patients died. Median age was 65 years (IQR 56–71) and seventy-two percent of patients ($n = 148$) were male. ECMO support was initiated in 53 patients after valve surgery, in 21 after coronary artery bypass graft (CABG) surgery, in 46 after combined CABG-valve surgery, in 45 patients after cardiac transplantation, in 18 patients after ventricular assisting device implantation, in 15 after aortic reconstruction and in 7 after other cardiovascular surgeries. The respective median value of the study population for EuroSCORE (additive) was 10 (8–13), 10 (4–24) for EuroSCORE II 12 (10–14) for SOFA score, 43 (31–56)

Tab. 1

		30-day mortality			Long-term mortality		
	SD	HR per 1-SD (95 % CI)	*P* value	AUC (95 % CI)	HR per 1-SD (95 % CI)	*P* value	AUC (95 % CI)
EuroSCORE (additive)	3.68	1.09 (0.88–1.34)	0.447	0.54 (0.46–0.62)	1.25 (1.07–1.47)	0.005	0.61 (0.53–0.68)
EuroSCORE II	0.18	1.19 (0.98–1.45)	0.079	0.56 (0.49–0.64)	1.26 (1.09–1.45)	0.002	0.59 (0.51–0.66)
SOFAscore	2.69	1.05 (0.83–1.32)	0.699	0.51 (0.44–0.59)	1.06 (0.88–1.27)	0.55	0.50 (0.42–0.59)
SAPS II	17.45	1.34 (1.09–1.66)	0.007	0.58 (0.50–0.66)	1.40 (1.18–1.66)	<0.001	0.60 (0.52–0.68)
SAPS III	11.06	1.12 (0.90–1.38)	0.309	0.53 (0.45–0.60)	1.18 (1.00–1.39)	0.049	0.55 (0.47–0.62)
APACHE II	6.81	1.25 (0.99–1.08)	0.145	0.54 (0.46–0.63)	1.32 (0.99–1.09)	0.093	0.56 (0.48–0.65)
RIFLE categories	0.56	1.28 (0.93–1.75)	0.119	0.55 (0.47–0.63)	1.36 (1.06–1.74)	0.015	0.572 (0.50–0.65)

for SAPS II, 43 (36–51) for SAPS III, 16 (12–21) for APACHE II, respectively. RIFLE classification revealed a median of 36 (16 %) for patients at risk, 8 (4 %) for the injury category and 2 (1 %) for failure. Among all risk prediction models only SAPS II demonstrated a significant association with 30-day mortality in the univariable Cox-regression analysis with a HR per 1-SD of 1.34 (95 %CI 1.09–1.66; $P=0.007$) and an AUC of 0.58 (95 %CI 0.50–0.66). Detailed results of the survival analysis for all scoring systems as well as results of the ROC analysis are displayed in Tab. 1. Furthermore, SAPS II remained the strongest predictor for 2 year long-term mortality with a HR per 1-SD of 1.40 (95 % CI 1.18–1.66; $P<0.001$).

Conclusions: Seven well established risk prediction models for critically ill patients showed only limited discriminatory power for predicting outcome in patients undergoing ECMO-support therapy following cardiovascular surgery. Therefore, further improvement for better risk stratification in this vulnerable patient population is crucially needed.

BP-9

Accumulation of cardiac extracellular matrix is associated with adverse outcome in patients with chronic heart failure

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Background: We aimed to elucidate the influence of ECM area on outcome in various non-ischemic heart failure (HF) types.

Methods: A total of 73 HF patients who underwent left ventricular (LV) endomyocardial biopsy (EMB) were enrolled in our study. ECM area was quantified by TissueFAXS and ImageJ software. Patients were followed prospectively in 6-month intervals. The study endpoint was defined as hospitalization for cardiac reason and/or cardiac death. The prognostic relevance of ECM area was tested in multivariable Cox regression analyses. Furthermore, the influence of ECM area on invasively assessed hemodynamic parameters was tested.

Results: During a mean follow-up period of 14.0±13.9 months, 34 patients (46.6 %) reached the combined endpoint. Median ECM area was 30.5 %. Patients with ECM area ≥30.5 % experienced significantly more events (67.6 % vs. 25.0 %, $p<0.001$) in comparison to patients with ECM area <30.5 %. ECM area was independently associated with outcome in the total HF cohort ($p<0.001$, HR 1.040, 95 % CI 1.018–1.062) as well as in HF patients with preserved (HFpEF, $p=0.014$, HR 1.085, 95 % CI 1.017–1.158) and HF patients with reduced ejection fraction (HFrEF, $p=0.011$, HR 1.144, 95 % CI 1.031–1.269). Kaplan-Meier curves and respective Log-Rank tests show a worse event-free survival for patients with ECM area ≥ median in the entire cohort ($p<0.001$, Fig. 1a) as well as in the subgroups with HFpEF ($p=0.043$, Fig. 1b) and HFrEF ($p=0.002$, Fig. 1c).

Positive correlations were found between ECM area and pulmonary artery wedge pressure ($p=0.042$, R=0.249), mean pulmonary arterial pressure ($p=0.258$, R=0.035), as well as right atrial pressure ($p=0.353$, R=0.003), whereas stroke volume index ($p=0.045$, R=–0.247) was inversely correlated with ECM area.

Conclusions: ECM area within the LV myocardium is a determinant of left and right heart hemodynamics and crucially impacts clinical course in various non-ischemic HF types.

BP-10

The impact of fluid status and renal function on the outcome of patients with heart failure and preserved ejection fraction

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Background: Volume overload is a hallmark of acute and chronic heart failure (HF) and plays an important role in the pathogenesis of heart failure with preserved ejection fraction (HFpEF). Most HFpEF patients, at some point in their disease progression, will present acutely to an emergency department, where they will typically show symptoms of progressive volume overload. During the following hospitalization most patients respond well to standard diuretic therapy and are discharged with significantly improved symptoms, usually at the costs of impaired renal function. The study sought to define the prognostic significance of fluid status versus renal function in patients with a confirmed diagnosis of HFpEF.

Methods: Between December 2010 and July 2015, 162 consecutive HFpEF patients (69.3 % [$n=104$] female) without signs of overt decompensation, were enrolled in our prospective reg-

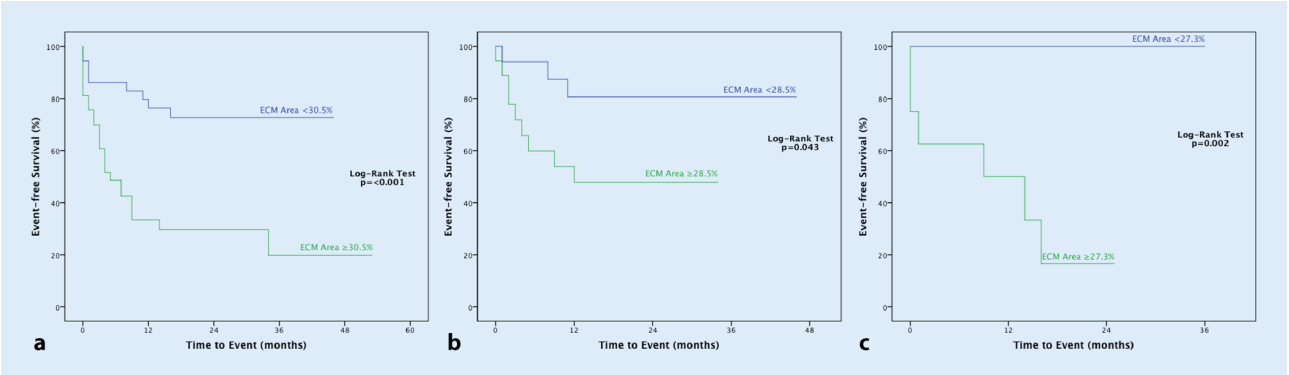

Fig. 1

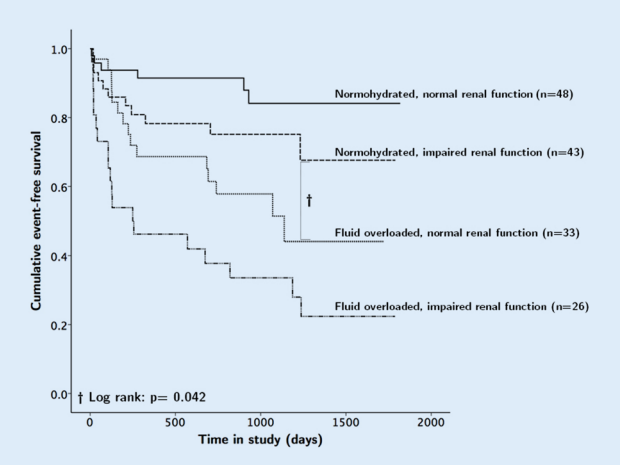

Abb. 1

istry. Fluid status at baseline was determined by bioelectrical impedance spectroscopy. Impaired renal function was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 determined by the modification of diet in renal disease study equation. The primary outcome measure was a combined endpoint consisting of hospitalization for HF and/or death for cardiac reason.

Results: During a median follow-up of 24.3 months (interquartile range (IQR): 19.8–33.2), 34.0 % ($n=59$) patients reached the combined endpoint. No patients were lost to follow-up. Of the 60.6 % ($n=91$) of patients who were hypo- or normovolemic (relative fluid overload [Rel. FO] in % mean -0.7 ± 5.7), 47.2 % ($n=43$) showed impaired renal function. 39.3 % ($n=59$) of all patients presented with fluid overload (mean Rel. FO % 11.5 ± 2.7) in the absence of clinically detectable edema. 44.0 % ($n=26$) of fluid-overloaded patients presented with impaired renal function. Multivariate Cox hazard analysis identified fluid overload (hazard ratio [HR]: 3.090; 95 % confidence interval [CI]: 1.68 to 5.68; $p<0.001$) as an independent predictor of adverse outcome. Most importantly, in a Kaplan-Meier analysis patients with fluid overload and normal renal function showed a significantly worse event-free survival compared to the subgroup with normohydration and impaired renal function (Log-rank: $p=0.042$).

Conclusions: Despite absence of clinically overt decompensation, HFpEF patients with measurable fluid overload face a dismal prognosis as compared to euvolemic patients. Patients with fluid overload may face a better outcome under continued fluid removal independent from changes in eGFR.

BP-11

Thrombusaspiration und GPIIb/IIIa Inhibitoren sind mit einem verbesserten postinterventionellen TIMI-Fluss bei Primär-PCI assoziiert

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Grundlagen: Zahlreiche Studien haben gezeigt, dass ein post-interventioneller TIMI-III-Fluss nach Primär-PCI (PPCI) die Kurz-und Langzeitüberlebensrate der Patienten erheblich verbessert. Über den Einfluss der antithrombotischen Therapie während der PPCI auf den post-interventionellen TIMI-Fluss ist hingegen noch wenig bekannt. Ziel der Studie war die Evaluation peri-interventioneller antithrombotischer Therapieoptionen hinsichtlich ihres Einflusses auf den Erfolg der PPCI bei Patienten mit ST-Strecken-Hebungsinfarkt (STEMI).

Methodik: Im Rahmen einer prospektiven multizentrischen Registerstudie wurden STEMI-Patienten erfasst, welche zwischen Jänner 2011 und Dezember 2013 einer PPCI unterzogen wurden und einen prä-interventionellen TIMI-Fluss von 0 oder I aufwiesen. Mittels multivariater Analyse wurden Anwendungsraten verschiedener peri-interventioneller antithrombotischer Therapieoptionen (GPIIb/IIIa-Inhibitoren, Thrombusaspiration, Bivalirudin) bei Patienten mit einem post-interventionellen TIMI-Fluss 0/I (PCI-Versager) im Vergleich zu Patienten mit TIMI-Fluss II/III (PCI-Erfolg) untersucht.

Ergebnisse: Ein PCI-Erfolg wurde bei 3254 (92,2 %) Patienten erreicht, 277 (7,8 %) Patienten waren PCI-Versager. Patienten mit PCI Erfolg wiesen höhere Raten an GPIIb/IIIa Inhibitoren ($n=1337$, OR 0.40, 95 % CI 0.31- 0.63, $p<0.01$) und Thrombusaspiration ($n=1238$, OR 0.31, 95 % CI 0.25–0.52, $p<0.01$) auf, als die Gruppe der PCI-Versager. Die Anwendung von Bivalirudin ± GPI ($n=250$) war im Vergleich zu UFH ± GPI ($n=3281$) nicht mit einer verbesserten Flussrate assoziiert (OR 0.71, 95 %CI 0.38–1.25, $p=0.2637$).

Schlussfolgerungen: In dieser „Real World"-Kohorte ist die Anwendung von GPIIb/IIIa Inhibitoren und der Thrombusaspiration bei STEMI-Patienten signifikant mit einem verbesserten post-interventionellen TIMI-Fluss assoziiert, während durch Bivalirudin keine signifikante Verbesserung der post-interventionellen Flussrate erreicht werden konnte.

BP-12

Absence of scaffold thrombosis after ABSORB implantation in 223 consecutive patients with personalised platelet inhibition at 365 days follow-up

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Background: Percutaneous coronary intervention (PCI) with implantation of complete bioabsorbable vascular scaffolds (BVS; ABSORB) might improve long-term outcome due to late lumen enlargement. However, recent meta-analyses are raising safety concerns by showing higher rates of scaffold thrombosis. The value of personalising dual antiplatelet therapy (DAPT) to overcome high on-treatment platelet reactivity (HPR) in regard to clinical outcome after BVS implantation is not known.

Methods and Results: Single-centre registry of 223 consecutive PCI patients with successful BVS implantation (from October 2012 to October 2014) and personalisation of DAPT guided by multiple electrode aggregometry (Multiplate). The cohort included 49 % patients with ACS (8 % STEMI, 41 % non-ST-elevation), with a mean age of 54±8 years and 17 % females and 28 % diabetics. A total of 476 BVS were implanted (mean 2.1 ± 1.4, range 1–7; total length 47±35 mm, range 12–168 mm). 84 % of patients showed a b2/c lesion morphology (incl. 9 % chronic total occlusion, 57 % bifurcations, 11 % thrombus containing). Complex bifurcation and multi vessel PCI was performed in 9 % and 28 %, respectively. HPR to adenosine diphosphate induced aggregation (≥50 U) occurred in 45 % of patients (69±14 U vs. 32±10 U; $p<0.001$) and was successfully treated with reloading (prasugrel or ticagrelor) in all cases (22±9 U; $p<0.001$). Follow up (FUP) at 30 days ($n=216$; 97 %) showed no (0 %) major adverse cardiac event (MACE). At one year FUP ($n=194$; 87 %) the cumulative incidence of MACE was 3.6 % ($n=7$), caused by 7 target lesion revascularizations (TLRs 3.6 %) including two myocardial infarctions (1.0 %). TLRs occurred at a median of 254 days (range 188–311 days) after PCI, without any death or scaffold thrombosis.

Conclusions: Implantation of BVS with personalisation of DAPT in routine clinical practice, including complex and long lesions, showed a very favourable early and long-term outcome at one year, without any scaffold thrombosis, in our single centre registry.

BP-13

High sensitivity troponin T Plasma levels predict postoperative survival in patients with severe aortic stenosis undergoing valve implantation

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Background: Optimal timing of aortic valve implantation in patients with severe aortic stenosis (AS) is under debate.1 Preprocedural biomarkers and/or depolarisation-repolarisation abnormalities may predict postoperative survival and therefore may be helpful in selecting high-risk but still asymptomatic patients for earlier valve implantation.

Methods and Results: The Tyrolean Aortic Stenosis Study II included consecutive patients ($n=666$) with severe AS undergoing valve implantation. During a mean follow up of 2.1 ± 1.4 years, 86 patients (12.9 %) died, among them 54 (8.1 %) due to cardiovascular causes.

Comparing preoperative high sensitivity troponin T (hsTnT) plasma levels and cardiac function, increased levels of hsTnT were correlated with a gradual decrease in left ventricular ejection fraction (LVEF). When comparing patients with undetectable hsTnT (< 5 ng/L) and hsTnT levels still within normal range (5–13.99 ng/L), no significant difference in mean LVEF was seen (57.76 ± 1.13 % versus 57.48 ± 0.62 %: $p=0.792$). Further mildly elevated hsTnT levels (14–50 ng/L) were already associated with a significant reduction in LVEF (52.38 ± 0.70 %) compared to patients with undetectable hsTnT ($p=0.001$) or values still within normal range ($p<0.001$).

HsTnT also showed highly statistical significance predicting both, cardiovascular ($p<0.001$) and all-cause mortality ($p<0.001$)

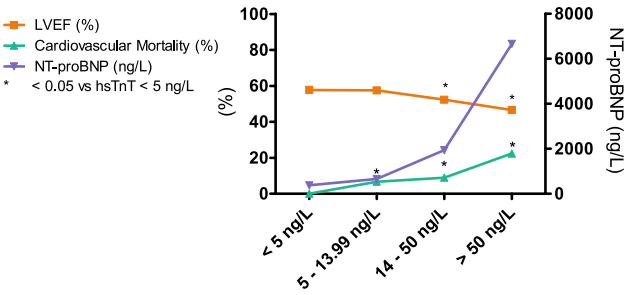
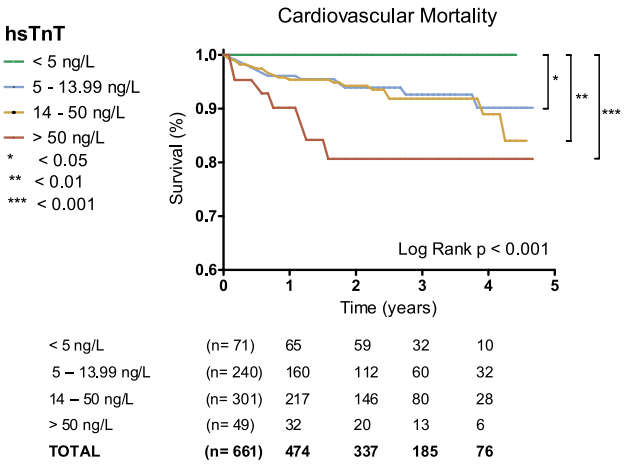
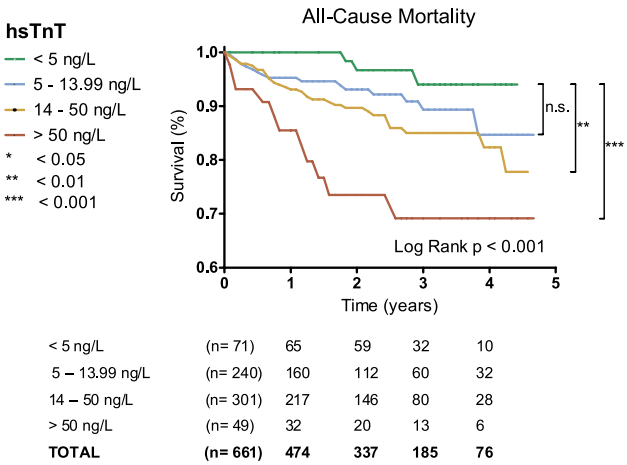


Fig. 1



a



b

Fig. 2

in univariate analysis. In patients with undetectable hsTnT plasma levels, there was no cardiovascular death during the follow-up period. Cardiovascular and all-cause mortality gradually increased with hsTnT elevation, reaching 22.5 % and 32.7 % in patients with hsTnT plasma levels above 50 ng/L, respectively.

Both hsTnT and N terminal pro brain natriuretic peptide (NT-proBNP) plasma levels also proved as the strongest independent risk factors for postoperative survival in Cox regression analysis including the known confounding factors age, renal function and concomitant significant coronary artery disease (hazard ratio [HR] per log unit 2.3, 95 % confidence interval [CI] 1.2 to 4.3; $p=0.012$ and HR per log unit 2.1, CI 1.3 to 3.5; $p=0.005$, respectively). These pre-procedural biomarkers also proved as independent risk factors in Cox regression analysis (HR per log unit 2.09, 95 % CI 1.09 to 4.02; $p=0.027$ and HR per log unit 1.77, CI 1.05 to 2.98; $p=0.033$, respectively), including the Thoracic Surgeons (STS) risk score (HR per log unit 3.47, CI 1.45 to 8.32; $p=0.005$). In contrast, electrocardiogram signs of left ventricular hypertrophy (Sokolow-Lyon voltage criteria) or fibrosis (strain) had no impact on postoperative outcome.

Conclusions: Postoperative survival in patients with severe AS undergoing valve implantation can be predicted by an integrated approach including hsTnT and NT-proBNP plasma levels, in addition to the well-established STS risk score. Further a decrease of LVEF caused by myocardial damage during the time to surgery may be predicted by previous raisings of hsTnT plasma levels.

Literature

1. Taniguchi T et al. Initial surgical versus conservative strategies in patients with asymptomatic severe aortic stenosis. J Am Coll Cardiol 2015; epub ahead of print.
2. Everett BM et al. Troponin and cardiac events in stable ischemic heart disease and diabetes. N Engl J Med 2015;373:610–620.

BP-14

Platelet hyper-reactivity following cessation of dual antiplatelet therapy

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Background: Clinical studies and registries have shown an increase of ischemic events soon after cessation of dual antiplatelet therapy (DAPT) in patients following percutaneous coronary intervention (PCI). Whether this can be attributed to temporary in vitro platelet hyper-reactivity, a potential platelet rebound effect, is an ongoing matter of debate. Aim of the study was to investigate if a platelet rebound effect occurs after cessation of modern DAPT including prasugrel and ticagrelor.

Methods: In total 52 patients with coronary artery diseases on DAPT following PCI with a planned and physician-driven cessation of $P2Y_{12}$ inhibition (clopidogrel: $n=16$, prasugrel: $n=17$, ticagrelor: $n=19$) were prospectively included. All patients were free from ischemic or bleeding events for at least 6 months. ADP-induced multiple electrode aggregometry (MEA) was assessed at 4 pre-specified time points: at baseline (BL, i. e. the last day of $P2Y_{12}$-inhibitor intake before cessation), as well as day 10, day 30 and day 180 following cessation of the $P2Y_{12}$-inhibitor, respectively.

Results: Within the first month following withdrawal of a $P2Y_{12}$-inhibitor (day 10 and day 30), ADP-induced platelet response was significantly increased, as compared to day 180 (d10 vs d180: $p=0.002$; d30 vs d180: $p=0.011$). History of hypertension ($p=0.012$), baseline platelet count ($p<0.001$), low HDL-cholesterol plasma levels ($p=0.004$), low glomerular filtration rate ($p=0.03$) and the kind of index event (acute coronary syndrome vs. stable angina, $p=0.042$) were independently associated with high off-treatment platelet reactivity on day 10.

Conclusions: In the present study, cessation of $P2Y_{12}$-inhibitors (clopidogrel, prasugrel, or ticagrelor) was associated with an increase of platelet reactivity between day 10 and day 30, as compared to day 180, and might account for an increase of ischemic events after $P2Y_{12}$-inhibitor withdrawal observed in clinical studies. These results are in line with previous data from studies on clopidogrel withdrawal, however, this has never been shown in the setting of modern ADP-blockers as prasugrel and ticagrelor. The identification of predictors of platelet hyperreactivity might help to decide which patient will benefit from prolonged or intensified platelet inhibition following PCI.

BP-15

Macitentan – treatment of pulmonary arterial hypertension

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Background: Macitentan (Opsumit®), a novel dual endothelin receptor antagonist (ERA), is approved for the treatment of pulmonary arterial hypertension (PAH) in patients with WHO functional class (FC) II and III, and may be used either as monotherapy or in combination. The approval of this substance was based on the results of the SERAPHIN-Study, a phase 3 outcome study conducted in 742 patients with symptomatic PAH.

Aim: To assess the efficacy and tolerability of macitentan as monotherapy or as combination therapy in patients with PAH who had been on treatment with bosentan, and as first-line therapy in newly diagnosed patients.

Methods: We followed PAH patients treated with macitentan 10 mg once daily by recording clinical and laborabory data, including the 6-minute walk distance, WHO FC, brain natriuretic peptide (NT-proBNP), liver function tests, and hemoglobin levels every 3 to 6 months in our outpatient clinic. Adverse events were recorded.

Results: In 2015 28 patients [23 female (82 %); 5 male (18 %), mean age of 58.1 ± 15.6 years] with group 1 pulmonary arterial hypertension were recorded. We treated 10 patients (35.8 %) with idiopathic PAH (IPAH), 12 patients (42.9 %) with PAH associated with connective-tissue disease, and 3 patients (10.8 %) with porto-pulmonary PAH. One patient each with heritable PAH (3.5.%), drug-induced PAH (3.5.%), and PAH associated to congenital heart disease (3.5 %) were observed.

During a mean treatment period of 10.2 ± 7.6 months 14 patients (50 %) received macitentan as monotherapy, and 14 patients (50 %) as combination therapy with either subcutaneous treprostinil sodium ($n=7$), soluble guanylate cyclase stimulator (sGC) ($n=5$), phosphodiesterase-5 inhibitors (PDE-5I) ($n=1$) or calcium channel blockers (CCBs) ($n=1$). The transition of bosentan to macitentan occurred in 12 patients (43 %), because of elevated liver function tests.

Six-minute walking distance improved by a mean distance of 41 m [CI (12–70.3), $p=0.020$]. A statistically significant decrease

of NT-pro BNP levels was present in patients receiving combination therapy ($n=14$, $p=0.001$).

Nasopharyngitis and headache were observed in 2 patients (7.1 %). None of the patients experienced a significant hemoglobin drop or elevation of liver function tests.

Conclusions: Macitentan is an efficacious, safe, tolerable and versatile new endothelin receptor antagonist.

BP-16

Reduction in inappropriate therapy through implantable defibrillator programming in primary and secondary prevention

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Background and objective: To assess the incidence, predictors, and outcome of inappropriate implantable cardioverter-defibrillator (ICD) therapy using different programming strategies.

Methods: From 1996 to 2016, all recipients of defibrillator devices were included in the current analysis. Individual ICD programming (IND) was used from 1996 until 2005, followed by standard (STD) 3 zone programming until 2009, and since 2010 a therapy reducing long arrhythmia detection time (RED) was established in all devices.

Results: A total of 1.811 patients implanted with an ICD for ischemic heart disease (55.5 %), dilative cardiomyopathy (19.4 %), hypertrophic cardiomyopathy (4.1 %), Long-QT and Brugada Syndrom (3.6 %) and for other reasons (17.4 %) were included in the analysis. For details see Table 1. ICDs were implanted for primary prevention in 39 % and for secondary prevention in 61 % of cases. During a mean follow-up of 3.9 ± 2.9 years, 3.1 ± 1.8 years and 2.5 ± 1.5 years in the IND, STD and RED phase, respectively, 20 %, 8.7 % and 4.9 % of patients experienced inappropriate ATP (anti-tachycardia pacing) therapy and 23.4 %, 6.9 % and 4.1 % of patients experienced inappropriate shock therapy. Poisson-Regression analysis using robust sandwich variance estimation revealed a significant reduction in inappropriate ATP and shock delivery in the RED phase compared to IND and STD phase (p <0.001), respectively. Kaplan Meier analysis revealed a significant reduction in time until inappropriate ATP and shock delivery in the RED phase compared to IND and STD phase (p <0.001). (Figs. 1 and 2) Mortality rates were independent from different programming strategies ($p=0.428$) or primary or secondary preventive reasons for ICD implantation ($p=0.597$, Fig. 3).

Conclusions: In a large cohort of ICD patients, inappropriate ATP and shock therapy were clearly dependent on device programming. A therapy reducing long arrhythmia detection time was found to be the best and a safe programming strategy. These data should encourage for an uniform approach in programming ICDs.

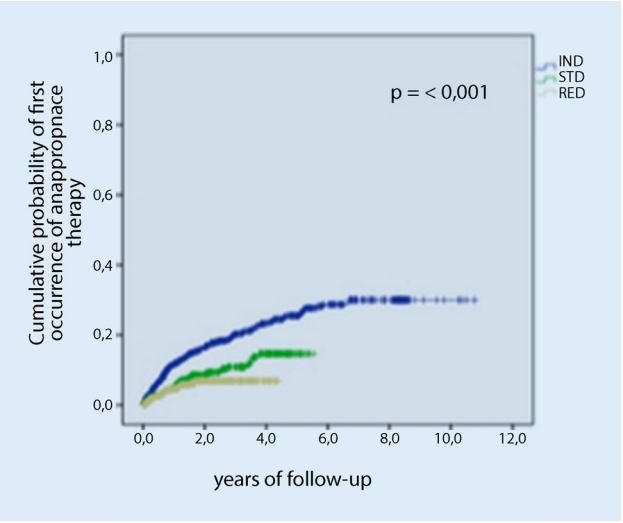

Fig. 1 Time until first Inappropriate ATP

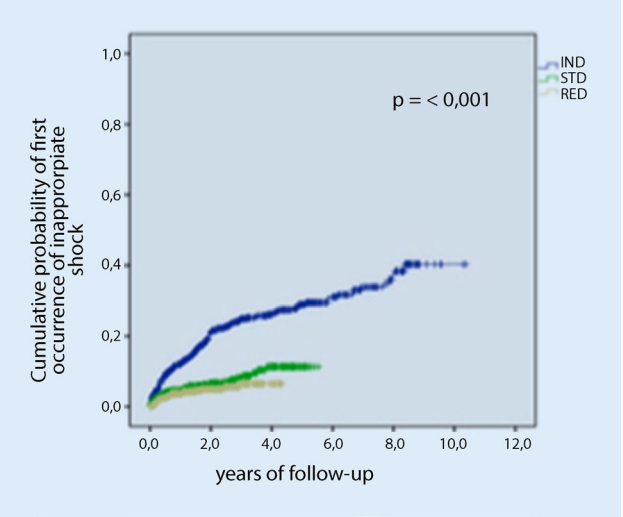

Fig. 2 Time until first Inappropriate Shock

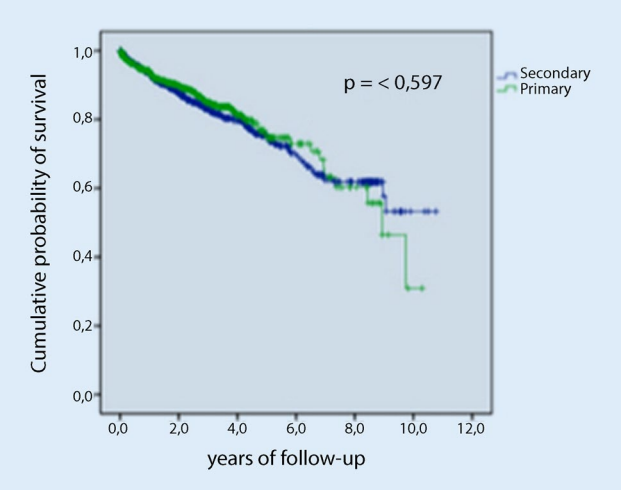

Fig. 3 Survival between Primary and Secondary Prevention

Tab. 1

	IND	STD	RED
Number of patients	730	508	573
Age (mean ± SD)	59.6 ± 13.3	59.9 ± 15.2	62.3 ± 14.1
Male (%)	80.1	82.30	81.80
Hypertension (*n*,%)	495 (67.8)	321 (63.2)	366 (63.9)
Hyperlipidemia (*n*,%)	223 (30.5)	148 (29.1)	174 (30.4)
Diabetes (*n*,%)	123 (16.8)	91 (17.9)	142 (24.8)
LVEF (*n* = 1665) (*n* / phase)	684	465	516
LVEF – normal (*n*,%)	128 (18.7)	86 (18.5)	88 (17.1)
LVEF – mild reduction (*n*,%)	82 (12.0)	50 (10.8)	59 (11.4)
LVEF – moderate reduction (*n*,%)	146 (21.3)	94 (20.2)	88 (17.1)
LVEF – severe reduction (*n*,%)	328 (48.0)	235 (50.5)	281 (54.5)

BP-17

Increased arrhythmia stability is associated with risk-factor specific structural remodelling in a porcine model of arterial hypertension and atrial fibrillation

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Background: Atrial fibrillation (AF) is the most common sustained arrhythmia in humans and is associated with an increased risk of stroke, morbidity and death. Arterial hypertension (HT) is found in 60–80 % of AF patients, is an independent predictor of new-onset AF and contributes to AF progression via unknown mechanisms.

We established a unique large animal model of rapid atrial pacing (RAP) induced AF combined with DOCA (desoxycorti-

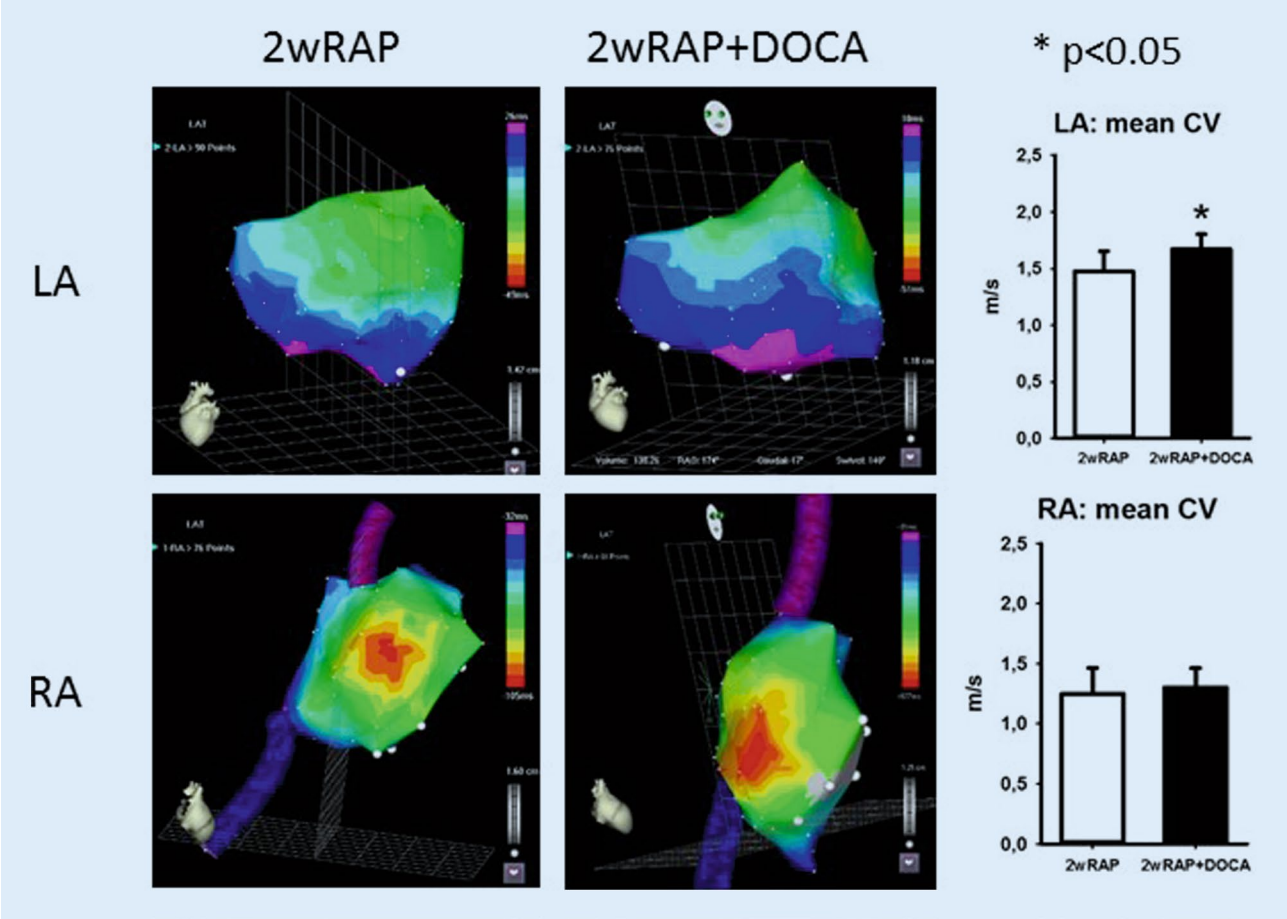

Fig. 1 Representative propagation maps (isochrones of 5 ms) of left and right atria in RAP vs. RAP+DOCA

costerone acetate) induced HT to investigate how HT affects the progression of AF.

Methods: 17 landrace pigs were implanted with custom made, telemetrically controllable pacemakers to induce AF. DOCA pellets were subcutaneously implanted in a subgroup of 9 animals (RAP+DOCA), the other 8 animals served as controls (RAP). Pacemakers were activated at a rate of 600/min two weeks prior to the final experiment which included transthoracic echocardiography, basic hemodynamic measurements, left and right atrial invasive electrophysiologic studies (measurement of atrial effective refractory periods – AERP), 3D electroanatomic mapping, high density epicardial multielectrode array mapping as well as histological analysis.

Results: Both groups had comparable body weight, cardiac output, pulmonary arterial pressure, left ventricular end diastolic pressure and left atrial pressure. Animals in the RAP+DOCA group had significant arterial hypertension (109.9 (100.137) vs. 82.8 (79.96) mmHg, $p<0.05$), concentric left ventricular hypertrophy (unchanged end-diastolic volume; end-diastolic diameter of the intraventricular septum: 17(15.18) vs. 11.5(10.13) mm, $p<0.01$), atrial dilatation (119.1±31.3 vs. 77.9±23.4 cm^2, $p<0.01$) and increased left (33.5±8.4 vs. 24.9±5.6 g, $p<0.05$) and right (23.7±2.9 vs. 19.4±3.1 g, $p<0.05$) atrial weights.

AF duration after pacemaker activation was significantly higher in RAP+DOCA animals, while left and right AERP at every measured S1 cycle length were unaltered. Epicardial multielectrode mapping showed increased conduction velocities on both atrial free walls. Enhanced conduction velocity during closed chest 3D electroanatomic mapping of the whole atria in DOCA+RAP animals could be confirmed for the left, but not for the right atrium (Fig. 1).

Multielectrode array recordings of both atria during AF revealed that this increased AF stability was not associated with increased AF complexity in both atria: mean AF cycle length, waves per cycle length, number of epicardial breakthroughs and mean conduction velocity during atrial fibrillation were unaltered.

HT was associated with severe structural remodelling. Histologic evaluation showed biatrial cardiomyocyte hypertrophy and interstitial fibrosis while distribution of Connexin 43 remained unchanged.

Conclusions: In this model of secondary hypertension, higher AF stability after two weeks of rapid atrial pacing is mainly driven by cardiomyocyte hypertrophy altering atrial conduction velocities. Since AF complexity in multielectrode array mapping as well as distribution of Connexin 43 were unaltered, fibrosis seems not to have a strong impact on AF stability in this model. Arterial hypertension triggers hypertrophic pathways which contribute to AF progression early in the disease which underlines the importance of strict blood pressure control in patients with arterial hypertension to prevent progression of the disease.

BP-18

Structural remodelling in a porcine model of rapid atrial pacing and arterial hypertension

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Background: Arterial hypertension (HT) is found in 60–80 % of patients with atrial fibrillation (AF), is an independent predictor of new-onset AF and triggers hypertrophic and profibrotic pathways resulting in structural remodelling potentially favouring the progression of the arrhythmia. Due to overlap of multiple possible risk factors and large heterogeneity in patients, risk-factor dependent structural remodelling remains incompletely understood. We previously established a

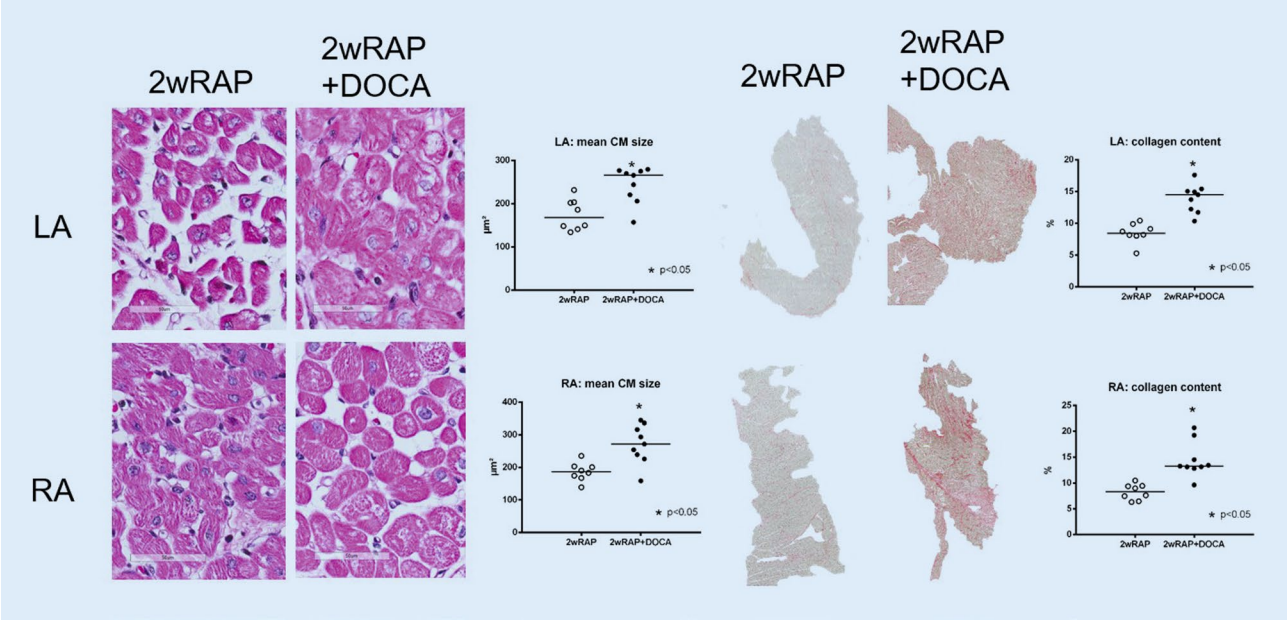

Fig. 1 Representative histological samples stained with HE (*left panel*) and PSR (*right panel*) showing hypertension-mediated cardiomyocyte hypertrophy and fibrosis in atrial fibrillation

unique large animal model of rapid atrial pacing (RAP) induced atrial fibrillation combined with DOCA-(desoxycorticosterone acetate)-induced HT giving the opportunity to elucidate risk-factor dependent mechanisms favouring the progression of atrial fibrillation.

In this study, we aimed to investigate the impact of arterial hypertension on structural remodelling during atrial fibrillation.

Methods: 17 landrace pigs were implanted with custom made, telemetrically controllable pacemakers to induce AF. DOCA pellets were subcutaneously implanted in a subgroup of 9 animals (RAP+DOCA), the other 8 animals served as controls (RAP). Pacemakers were activated at a rate of 600/min two weeks before histological samples of both atria were obtained for analysis of cardiomyocyte area (HE staining), atrial fibrosis (Picco-Sirius-Red staining) and distribution of Connexin 43 (Cx43 immunofluorescence for confocal microscopic analysis).

Results: Animals in the RAP+DOCA group had significant arterial hypertension and concentric left ventricular hypertrophy as compared to the RAP group. HT was associated with severe structural remodelling (Figure 1). Histologic evaluation showed biatrial cardiomyocyte hypertrophy (cross-section cardiomyocyte area: LA: 243.7±41.8 in RAP+DOCA vs. 174.4±36.0 μm^2 in RAP, $p<0.01$, RA: 271.6 (232,326) vs. 186.8(169,202) μm^2, $p<0.01$) as well as interstitial fibrosis (LA: 14.0±2.2 vs. 8.5±1.6 %, $p<0.001$; RA: 14.4±3.4 vs. 8.3±1.5 %, $p<0.001$) while distribution of Cx43 remained unchanged (0.37±0.1 vs. 0.39±0.1 ratio between Cx43 located on longitudinal sides and at intercalated disks, n. s.).

Conclusions: In this model of secondary hypertension, HT triggers hypertrophic and profibrotic pathways revealing a distinct form of risk-factor dependent structural remodelling in atrial fibrillation. These findings will help to understand mechanisms favouring the progression of atrial fibrillation in patients with arterial hypertension.

BP-19

Awareness, treatment and control of hypertension in Austria – A multicentre cross-sectional study

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Background: Although pharmacological treatment for hypertension (HTN) is available since the 1950s, less than half of all diagnosed and treated patients reach adequate blood pressure (BP) control in Europe today. There is no large, recent and properly conducted Austrian study available, with the last representative data being obtained in the 1990ies.

We sought to close this gap of evidence in Europe by providing information on HTN control in predominantly adherent patients.

Methods and Results: In October 2015, we enrolled 4303 patients with HTN who approached one of 158 participating pharmacies with a prescription filled for antihypertensive medication.

The recruitment was completed within 10 days. Patient's mean age was 68±12 years, 53 % were female. The mean systolic/diastolic BP was 144±20/84±12 mmHg.

On average, patients received 2.2±1.1 different antihypertensive substances, 45 % received a fixed-dose combination drug (FDC). Ninety-three percent were aware of their disease, 90 % claimed to have taken their medication prior to the survey, and 41 % had their BP controlled at a threshold of 140/90 mmHg. Predictors of HTN control were lower age (per decade increase OR 0.90, 95 %CI 0.85;0.96, $p<0.01$), female gender (OR 1.23, 95 %CI 1.07;1.41), the intake of medication on the day of the conduct of the survey (OR 2.15, 95 %CI 1.67;2.76), a university degree (OR 1.58, 95 %CI 1.19;2.08), and the consultation of a specialist for internal medicine/cardiology vs. a general practitioner (OR 1.20, 95 %CI 1.04;1.39). The use of FDCs vs. free drug combinations was not predictive of achieving HTN control, underlining that the included cohort was indeed adherent to therapy.

Conclusions: Despite a high degree of awareness and frequent use of FDCs, only 41 % of diagnosed, treated and adherent HTN patients had their BP controlled. Immediate action is required to improve BP control in Austria.

BP-20

Impaired high-density lipoprotein anti-oxidative function is associated with outcome in patients with congestive heart failure

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Background: Oxidative stress is mechanistically linked to the pathogenesis of congestive heart failure (CHF). Anti-oxidative functions of high-density lipoprotein (HDL) particles have been found impaired in patients with ischemic cardiomyopathy, however the impact of anti-oxidant HDL capacities on clinical outcome in CHF patients is unknown. We therefore investigated the predictive value of anti-oxidant HDL function on mortality in a representative cohort of patients with CHF.

Methods: We prospectively enrolled 320 consecutive patients (median age of 65 years, 81 % male gender, median NT-proBNP level of 1214 pg/ml, 46 % ischemic etiology) admitted to our outpatient department for heart failure and determined anti-oxidant HDL function using the HDL oxidant index (HOI). The HOI was determined by calculating the ratio of fluorescence in the presence of apo-B depleted patient samples divided by the fluorescence of oxidized LDL alone and log-transformed before analysis. Based on their HOI, the study population was stratified into patients with pro-oxidant serum activity (HOI ≥1) and patients with anti-oxidant serum HOI (HOI <1) capacity.

Results: During a median follow-up time of 2.8 years (IQR 1.8–4.9) 88 (27.5 %) patients reached the combined cardiovascular endpoint, defined as death due to cardiovascular events and heart transplantation (HTX). 116 (36.3 %) patients deceased due to all causes. An HOI ≥1 was significantly associated with survival free of cardiovascular mortality and HTX of patients in the Cox regression analysis with a hazard ratio (HR) of 2.28 (95 % CI: 1.48–3.51, $P<0.001$). This association remained significant after multivariable adjustment with an adjusted (adj.) HR of 1.69 (95 % CI: 1.07–2.67, $P=0.024$). Subgroup analysis revealed, that pro-oxidant HDL was an independent predictor of cardiovascular events in patients with ischemic etiology of CHF with an adj. HR of 2.65 (95 % CI: 1.37–5.11, $P=0.004$), while this was not the case for patients with non-ischemic CHF (adj. HR of 1.13 (95 %: 0.56–2.27, $P=0.733$). HOI ≥1 in ischemic

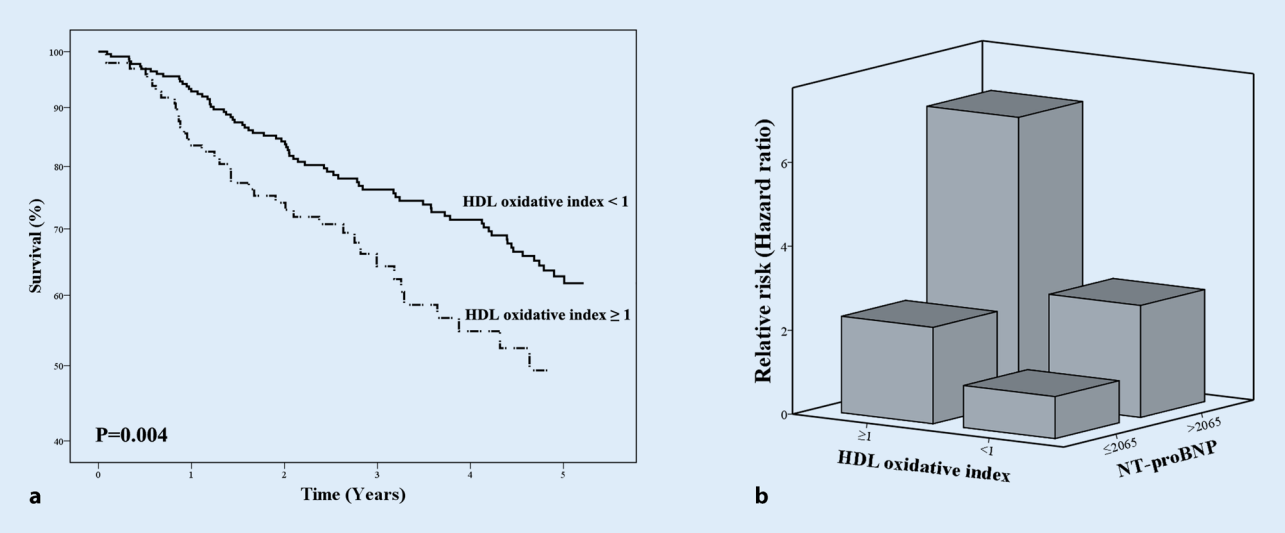

Fig. 1 a) Ischemic CHF, b) Ischemic CHF

CHF showed additional prognostic value beyond that achievable with NT-proBNP indicated by improvements in the category-free net reclassification index (NRI: 43.1 %, $P=0.02$) and integrated discrimination improvement (IDI: 0.0415, $P=0.02$) and even provided additional prognostic information over a comprehensive multivariable model comprising established parameters for risk prediction in CHF [NRI (46.2 %, $P=0.01$), IDI (0.0448, $P=0.02$)].

Conclusions: Impaired anti-oxidant HDL function represents a strong and independent predictor of mortality in patients with CHF. Implementation of HOI leads to a substantial improvement of risk prediction in patients with ischemic CHF.

Postersitzung 1 – Basic Science 1

1-1

APOSEC influcences expression of IL-6 and IL-18 in hypoxic porcine cardiomyocytes

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Background: In cardiovascular science the porcine heart is the suitable translational model for the investigation of several cardiovascular diseases. Nevertheless animal experiments have to be conducted following the 3R principle by Russel and Burch, which suggests to reduce and refine the animal testing and replace it with in vitro models. We previously described the successful establishment of a porcine cardiomyocyte cell culture model, which is currently not commercially available. The aim of this study was to investigate the cell behaviour after induction of hypoxia and in further consequence to analyze impacts of a paracrine factor APOSEC (secretom of apoptotic peripheral blood mononuclear cells) on cell morphology and factors IL-6 and IL-18, which are known to be up regulated due to hypoxic stress.

Methods: Porcine cardiomyocytes were isolated from pig heart muscle of the left ventricle and maintained in culture for one week (37 °C, 5 %CO_2; M199 supplemented with 10 %FBS and 1 %PenStrep). 5×104 cells per ml were seeded into ibidi slides (µ-slide 4 well) in 700 µl Medium199 per well and incubated over night in the incubator. Hypoxia was induced adding cobalt (II) chloride hexahydrate ($CoCl_2$) in different concentrations (50–800 µM) for two hours to the cells. Thereafter APOSEC was added after different time points (0 h, 2 h, 24 h) in different dilutions (1:2, 1:4, 1:8, 1:10) to the cells and cell morphology was observed via live cell imaging on Olympus fluorescense microscope. RNA was isolated from cell lysate and the expression of the proinflammatory cytokines IL-6 and IL-18 were measured after 24 h or 48 h of APOSEC treatment.

Results: Based on the changes in cell morphology, 100 µM $CoCl_2$ per reaction was chosen to be the optimal concentration for hypoxia induction. Hypoxia induction led to an increase of gene expression of IL-6 (by 1.95 fold) and IL-18 (by 1.32-fold) compared to normoxic cardiomyocytes. IL-6 expression of APOSEC treated cells was downregulated in all samples compared to hypoxic cells (Table 1). IL-18 expression was also down regulated in all of the APOSEC samples except in the samples in

Tab. 1

	Il-6 expression (log fold changes)	Il-18 expression (log fold changes)
normoxic cells	1.00	1.00
hypoxic cells 24 h incubtion	1.95	1.32
hypoxic cells 48 h incubation	0.68	0.69
aposec added after hypoxia + 24 h incubation	0.468	0.58
aposec added after hypoxia + 48 h incubation	0.470	0.56
Aposec added 2h after hypoxia + 24 h incubation	0.143	0.31
Aposec added 2h after hypoxia + 48 h incubation	0.206	0.43
aposec added 24h after hypoxia + 24 h incubation	0.0001	19.32
aposec added 24h after hypoxia + 48 h incubation	0.0002	34.31

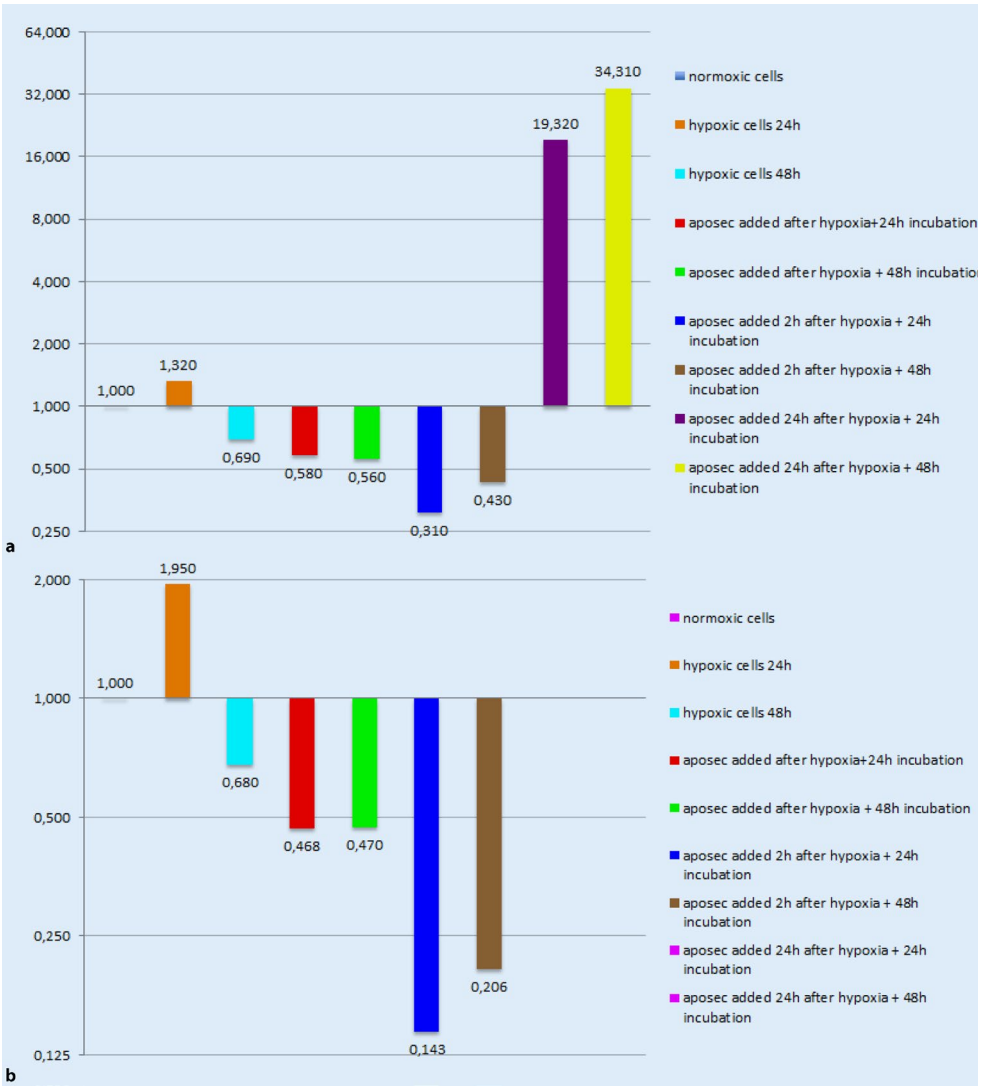

Fig 1. a) Il-18 expression (longfold changes), b) Il-6 expression (longfold changes)

which APOSEC was applied 24 hours after hypoxia induction, where IL-18 was extremely up regulated. (Table 1)

Conclusions: We successfully established a $CoCl_2$-induced hypoxia cell culture model, which was confirmed by up-regulation of IL-6 and IL-18 on RNA level. Furthermore we could observe a positive impact regarding cell morphology and down regulation of IL-6 and IL-18 in cells treated for 24 h with APOSEC which was added 2 hours after hypoxia.

1-2

Einfluss von Zellkulturbedingungen auf die Stammzelltherapie bei Myokardinfarkt am Beispiel von Interleukin-6

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Grundlagen: Große Hoffnungen wurden in den letzten Jahren wurden in die Stammzelltherapie nach Myokardinfarkt gesetzt. Mit Hilfe von aus dem Knochenmark von Patienten mit Herzinfarkt gewonnenen und kurzzeitig in Zellkultur gebrachten Stammzellen sollte der ischämiebedingte Schaden reduziert und die Pumpleistung des Herzens gebessert werden. Während hier die REPAIR-AMI Studie Erfolge verbuchen konnte, zeigten sich in einer anderen großen Studie (ASTAMI) keine signifikant besseren Ergebnisse. Weitere vorangegangene Studien konnten zeigen, dass beispielsweise Interleukin-6 (IL-6) über parakrines Signalling in Kardiomyozyten zu einer Aktivierung von zytoprotektiven Signalkaskaden (u. a. STAT3, ER1/2 und PI3K) führt. Wir wollten daher anhand von pro-inflammatorischen Faktoren wie IL-6 untersuchen ob Unterschiede zwischen den beiden Studienprotokollen gefunden werden können.

Methodik: Knochenmarkzellen wurden entsprechend der in der REPAIR-AMI und ASTAMI Studie verwendeten Protokollen prozessiert. Während in der ASTAMI-Studie die Stammzellen über Nacht bei 4° in NaCl-Lösung zusammen mit 20 % Heparin-Plasma gelagert wurden, wurde in der REPAIR-AMI

Studie X-Vivo 10 Medium verwendet. Des Weiteren wurde im REPAIR-AMI Protokoll 20 % autologes Serum zugesetzt und die Zellsuspensionen bei Raumtemperatur gelagert.

Ergebnisse: Mit unseren in vitro Daten konnten wir zeigen, dass Knochenmarkzellen, die nach dem REPAIR-AMI Protokoll gelagert wurden, tendenziell höhere Mengen an pro-inflammatorischen Faktoren sezernierten. Im Inkubator bei 37 Grad Celsius konnte dieser Effekt noch weiter deutlich gesteigert werden. Auch das Kulturmedium hatte einen Einfluss auf die Sekretionskapazität, X-Vivo 10 führte gegenüber NaCl ebenfalls zu einer gesteigerten Ausschüttung. Ein zusätzlicher Einflussfaktor war zudem die Hinzugabe von Serum anstatt von Plasma, dies löste eine weitere deutliche Steigerung der Sekretion an IL-6 aus.

Schlussfolgerungen: Das in der REPAIR-AMI Studie verwendete Protokoll bot deutlich bessere Umgebungsbedingen (höhere Temperatur, physiologischeres Medium und die Verwendung von Serum anstatt von Plasma) für die Produktion von parakrinen Faktoren wie beispielsweise von pro-inflammatorischen Zytokinen. Auch wenn ein länger bestehendes pro-inflammatorisches Milieu mit einer erhöhten Mortalität bei kardialen Erkrankungen assoziiert ist, könnte ein kurzer Peak dieser Faktoren Conditioning Mechanismen auslösen, die Kardiomyozyten resistenter gegenüber Hypoxie machen können. Dieser Umstand könnte erklären, weshalb die REPAIR-AMI Studie ein besseres Ergebnis als die ASTAMI-Studie erzielen konnte.

1-3

Effect of ischemic preconditioning and postconditioning on electrocardiac parameters in reperfused myocardial infarction

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Background: Brief repetitive ischemia called ischemic preconditioning (IPC), or postconditioning (PostC) are powerful protective conditions against myocardial infarction (AMI)-

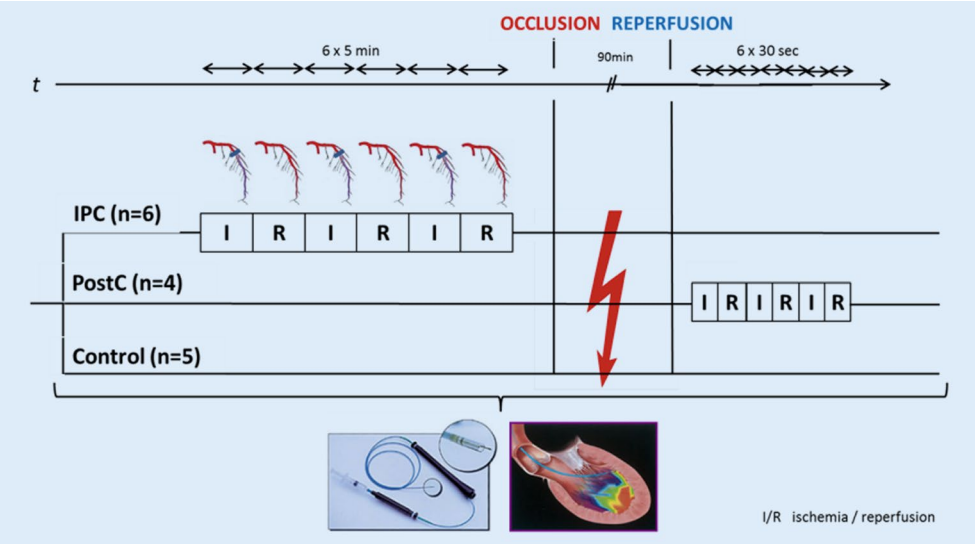

Fig. 1 Study design

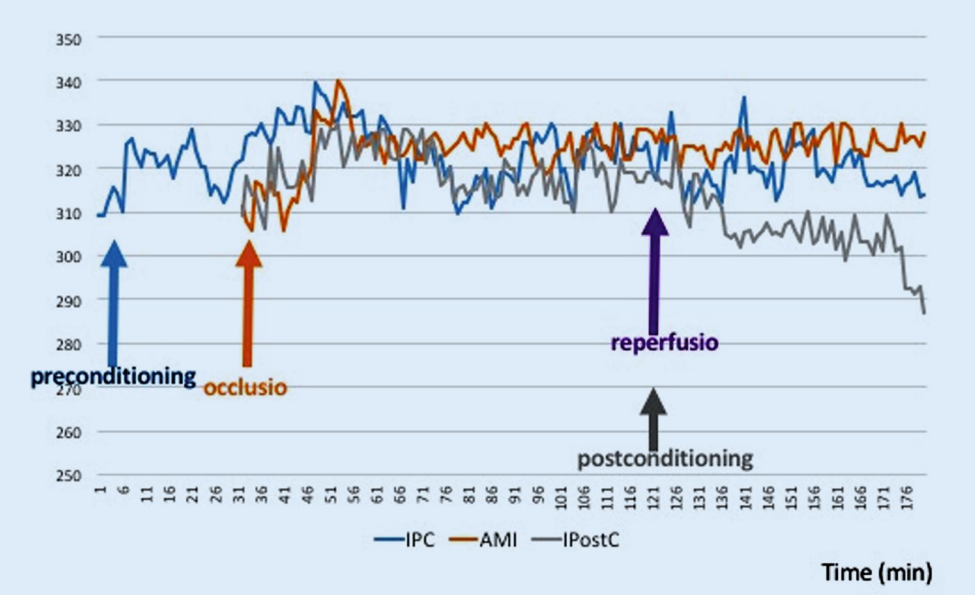

Fig. 2 Corrected QT time during ischemic preconditioning, myocardial ischemia, ischemic postconditioning and final reperfusion for the three groups AMI, IPC-AMI and AMI-PostC

related morbidity and mortality, yet the exact mechanisms are still unclear. We have investigated electrocardiac parameters using real-time detection of intracardiac electrocardiogram signal during IPC with subsequent infarction and infarction with/without PostC.

Methods: Domestic pigs underwent 90-min percutaneous occlusion of the mid LAD followed by reperfusion (I/R), with IPC (3×5 min I/R) before occlusion (group IPC-AMI, $n=9$), or with PostC (6×30 sec I/R) (group AMI-PostC, $n=3$) immediately after final reperfusion; group AMI served as control ($n=7$) (Fig. 1). NOGA endocardial mapping catheter was placed in the left ventricular (LV) cavity in a stable location, and displayed the intracardiac electrogram of a single ischemic LV distal anterior point during the entire procedure. LV function and infarct size were measured by cardiac MRI with late enhancement (LE) at the 1-month follow-up. Intracardiac QRS width, and QT time was measured in every minute, and the corrected QT time (QTc) was calculated according to the the Framingham Heart Study adjusted QT time method.

Results: Fig. 2 shows the intracardiac QTc time: IPC led to QTc prolongation. Shortly after start of the coronary occlusion, the QTc increased in all groups, and remained longer as compared with the baseline values. After reperfusion, the QTc time did not normalize. However, PostC reduced the AMI-induced prolonged QT time, in contrast with the AMI and IPC groups (Fig. 2). The QRS width did not changed in the 3 groups, indicating no intracardiac conduction abnormality. MRI+LE resulted in significantly better LV ejection fraction and smaller infarct size in group IPC-AMI as compared with groups AMI and AMI-PostC.

Conclusions: IPC but not PostC induce preservation of the myocardial function during reperfused myocardial infarction. PostC, but not IPC reduced the AMI-induced QTc time prolongation, which might explain the beneficial effect of PostC on AMI-induced cardiac arrhythmias.

1-4

Effect of the application of Aposec-pretreated- and native cardiosphere-derived cells on the myocardial expression of selected genes in a porcine model of myocardial infarction

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Background: Local cardiac delivery of cardiosphere-derived cells (CDCs) has been shown to induce moderate cardioprotective effects in animals and a clinical trial (CADUCEUS) in ischemic heart failure. In a closed chest reperfused acute myocardial infarction (AMI) animal model we have observed that pre-treatment of porcine CDCs with porcine APOSEC (secretome of apoptotic peripheral blood mononuclear cells, PBMCs) enhances the regenerative effect of the CDCs in pigs post-AMI. In order to investigate the molecular effects of CDCs pretreated with APOSEC (CDC-Apo), we examined heart tissues from pigs treated with intracoronary infusion of CDCs, CDC-Apo, or APOSEC in the reperfusion phase of AMI, for expression of molecular markers involved in myocardial infarct size and stem cell therapy.

Methods: Pigs underwent myocardial infarction (MI) by percutaneous balloon occlusion of the mid-LAD for 90 min followed by balloon deflation and intracoronary treatment with either CDC ($n=5$), CDC-Apo ($n=5$), or APOSEC ($n=5$), 5 animals served as sham-AMI control. One month after MI and cell treatments, pigs were sacrificed and heart tissues from the infarct, border and remote zones were collected and stored in RNA-Later. After tissue homogenization, RNA isolation, and transcription into cDNAs, myocardial expression of Connexin-43 (Cx43, regulates cell-to-cell connection, cell death and proliferation), CXCL12 (SDF-1a) (chemotactic factor), IL-6 (pro-inflammatory cytokine) and IL-8 (neutrophil chemotactic and angiogenetic factor) were determined by qPCR with normalization to housekeeping genes. Expression levels were expressed in % relative to control animals (100 %), which did not undergo AMI. The expression of the muscle-specific miRNA-1, linked to heart adaption after ischemia, arrhythmias, and hypertrophy was assessed.

Results: Cx43 showed reduced expression in the infarct zone of CDC and CDC-Apo treated animals compared to the APOSEC group (39.1±36.7 % and 31.8±31.9 % compared to 146.2±137.3 %). Myocardial CXCL12 (SDF-1) expression in the infarct area was reduced by treatment with CDC-Apo as compared to CDC and APOSEC (326.7±255.0 % vs. 980.6±574.4 % and 1053.2±367.7 %, respectively), and up regulated in the border and remote zones of all groups. The expression of inflammatory cytokines (IL-6, IL-8) was highly increased in all groups compared to healthy animals, and no significant differences in expression between the distinct treatment groups were observed. We detected reduced expression of miR-1 in the infarct zone of CDC-Apo treated pigs, while it was unchanged in the CDC group. Increased expression of miR-1 was found in the remote and border zones of all groups with no significant differences caused by treatments.

Conclusions: Analyses of gene expressions of selected markers for stem cell-based AMI therapy support the beneficial effects of APOSEC pretreatment of CDC for enhanced efficacy. Reduced expression of Cx43 and miR-1 after CDC-Apo treatment indicate attenuation of the ischemic injury.

1-5

Enhanced regenerative effect of cardiosphere-derived cells by pre-treatment with paracrine factor APOSEC in porcine closed-chest reperfused myocardial infarction proved by quantitative cardiac PET-MRI

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Background: In animal models and the clinical trial CADUCEUS, cardiosphere-derived cells (CDCs) have shown promise for treatment of ischemic left ventricular (LV) dysfunction after myocardial infarction (AMI). Recent data indicates that paracrine effects are important for the efficacy of cardiac cell-based therapy, due to limited engraftment of cells in the injured myocardium. APOSEC, the secretome of apoptotic peripheral

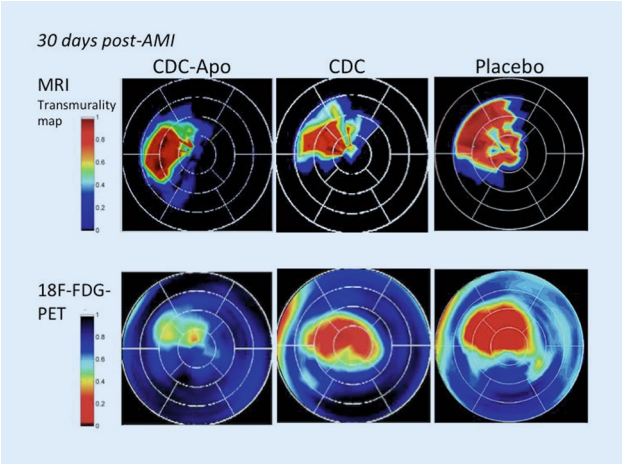

Fig. 1

blood mononuclear cells (PBMC) is a mixture of paracrine factors with cell protective, angiogenic and antiapoptotic effects. We hypothesized that pretreatment of CDCs with APOSEC enhances the paracrine cardiac regenerative effect of CDCs in a pig model of closed-chest AMI.

Methods: CDCs were isolated from porcine heart tissue. Allogeneic porcine CDCs were incubated in vitro with APOSEC in different doses and incubation times and the effects on CDC phenotype and transcriptome were assessed for selection of the optimal pre-treatment mode (CDC-Apo). Domestic pigs underwent AMI via percutaneous balloon occlusion of the mid-LAD for 90 min followed by balloon deflation. Fifteen min after reperfusion the pigs were randomized and received intracoronary infusion (3 ml/min, stop-flow technique) of either 10^7 CDCs ($n=5$) or 10^7 CDC-Apo ($n=5$) or phys. saline (placebo) ($n=4$). Cardiac 18F-FDG-PET-MRI with late enhancement was performed at 30-day follow-up. Quantitative comparative 17-segment analysis of PET-MRI of the groups was performed with in-house developed software.

Results: After selection of the optimal APOSEC dose (secretome derived from 10^7 PBMC) and incubation time (48 h) both VEGF secretion (63.0±11.7 vs 10.7±10.0 pg/mL) and SDF-1/CXCL12 expression of CDC-Apo (2.3±0.03 vs 1.0±0.1 fold relative expression) were significantly increased as compared to CDCs cultured in standard cell culture medium. Intracoronary infusion of CDC-Apo led to significant ($p<0.05$) increase in LV ejection fraction (43.6±6.1 % vs 37.8±4.4 % and 36.3±4.1 %), decrease in infarct scar (12.5±4.1 % vs 16.5±4.0 % and 22.7±2.2 % of the LV) as compared to CDC and placebo groups. Relative quantitative 18F-FDG-uptake of the MRI-derived infarcted area (transmurality over 50 %) was significantly higher in CDC-Apo vs CDC and placebo groups (67±2 % vs 53±3 %, and 55±7 %), indicating more preserved viability within the infarcted area in CDC-Apo group (Fig. 1).

Conclusions: In vitro treatment of CDCs with APOSEC induces enhanced expression of factors (SDF-1/CXCL12, VEGF) that have been shown to play a role in the regenerative effect of cell-based therapy. CDC-Apo-treated pigs suffered from less severe infarct scars. In total, pretreatment of CDCs with APOSEC enhanced the therapeutic potential of CDCs for treatment of ischemic LV dysfunction.

1-6

Histological analyses of paclitaxel coated cutting balloon treated in stent restenosis in pigs

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Background: Even though with the use of drug-eluting stents (DES) intracoronary stent restenosis (ISR) has become much less common, with the number of stents implanted it still displays a challenge. Reduction in lumen diameter in ISR is the result of neointima formation. Neointimal tissue proliferation occurs in association with macrophage accumulation and neovascularisation. Additionally fibrin, platelets and neutrophils were found at stent struts. Even though treating ISR with DES is a promising treatment option, a drug-eluting balloon (DEB) was considered another attractive treatment mode. Nevertheless no data on neointima composition in treatment of ISR with DEB exist. The aim of this study was to characterise neointimal tissue in ISR that has been treated with plain cutting-balloon or paclitaxel coated cutting-balloon.

Methods: Coronary arteries of 8 pigs were stented with bare metal stents (BMS) to induce high grade ISR. After one month ISR was treated with either plain cutting-balloon or paclitaxel (3 µg/balloon mm2) coated cutting-balloon. At one month follow-up coronary artery samples (LAD, LCX, RCA, OMA; proximal, medial, distal) were taken for histological analyses. Histomorphometric and histopathological analyses were performed and the presence of CD68+ macrophages was evaluated by immunofluorescence staining.

Results: Quantitative coronary angiography revealed a comparable degree of ISR in both groups one month after BMS implantation. %diameter stenosis (51±26 % vs. 51±36 %) and minimal lumen diameter (1.78±0.91 vs. 1.9±0.79 mm) were equal one month after BMS implantation in both groups before treatment with either plain cutting-balloon or paclitaxel coated cutting-balloon. Histomorphometry exhibited a significantly larger lumen area (2.15±0.63 vs. 1.76±0.44 mm^2, $p<0.05$) and

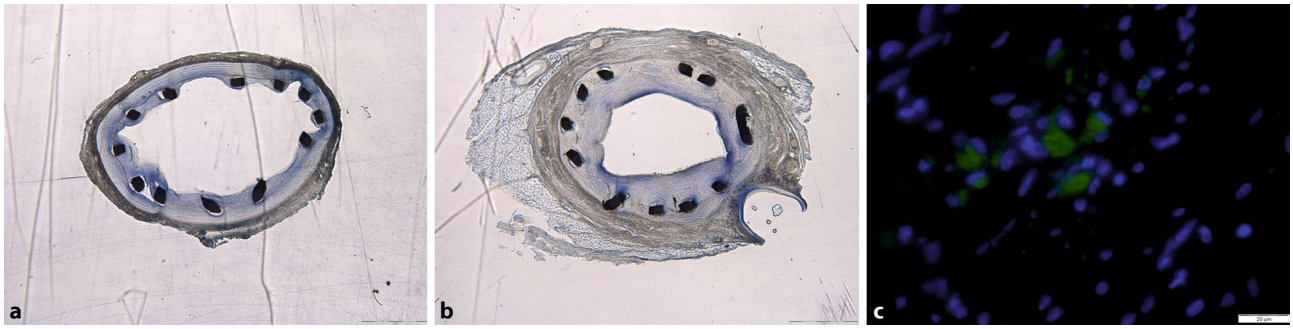

Fig. 1 a) paclitaxel coated cutting-balloon, b) plain cutting-balloon, c) $CD68^+$ macrophages

smaller neointima area (0.92±0.55 vs. 1.68±0.77 mm^2, $p<0.05$) in the paclitaxel cutting-balloon group. Histopathological analyses revealed less fibrin deposition (0.8±0.4 vs. 1.6±1.0, $p<0.05$) and adventitial inflammation (0.92±0.45 vs. 1.87±0.94, $p<0.05$) scores even though injury scores were similar (1.1±0.3 vs. 1.0±0.6, respectively). CD68+ macrophages have been found in 5 of 10 coronary artery samples (50 %) within the plain cutting-balloon group 11 of 20 coronary artery samples (55 %) within the paclitaxel coated cutting-balloon group.

Conclusions: This study highlights the successful treatment of ISR with paclitaxel coated cutting balloon and showed reduced formation of neointimal tissue, fibrin deposition and adventitial inflammation in the DEB group. Moreover, it describes the presence of CD68+ macrophages at a similar proportion within neointimal tissue in both groups.

1-7

Isolation and characterization of intramyocardially injected mesenchymal stem cells

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Background: Cardiac cell-based therapy is recognized as a promising therapeutic strategy in the protection and repair of damaged myocardium after infarction. However, the mechanism and also the significance of the cell-based effects are not clear and still discussed controversially. Previous studies confirmed the migration of the cardiac transplanted cells into the remote organs but little is known about the genetic response of the injected cells, the host myocardial cells, and the cells of the remote organs, if they come into contact with transplanted cells.

In this study, we aimed to re-gain the intracardiac transplanted porcine bone-marrow derived mesenchymal stem cells (pMSCs) from the heart and remote organs to investigate their transcriptome profile and the transcriptomes of the host myocardium and remote organs.

Methods: Calcein labeled pMSCs were injected into the border zone of infarction using 3D NOGA-guided percutaneous intramyocardial delivery one month after induction of acute myocardial infarction (MI). Cardiac and remote organ samples (liver, spleen, lung, lymph node, bone marrow, kidney) containing the labeled pMSCs and remote heart and remote tissue samples (as control) were harvested after 3 h, 12 h, 24 h, and 48 h follow-up.

Cell sorting: Harvested tissues were digested enzymatically with collagenase and homogenized in a gentleMACS Dissociator to obtain single cell followed by immediate storage of the samples in CellLater, in order to avoid RNA degradation. Using FACS-sorting on a FACSAria, the re-gained calcein-pMSCs were separated from the cardiac and remote organ cells.

Laser microdissection: Tissue samples were frozen in liquid nitrogen and cut into 10–14 µm sections. Calcein positive cells were determined on a fluorescent microscope and cells and surrounding tissue (as control) was isolated by laser microdissection.

mRNA and microRNA from both methods was isolated and the quality of RNA was monitored with an Agilent RNA 6000 Pico Chip and by real-time PCR. Representative samples were proceeded to Next Generation Sequencing (NGS).

Results: Green fluorescent calcein labeled pMSCS could be detected both in flow cytometry and in cryosections. For FACS sorting, the cells could be gated as own population and represented up to 5.2 % of the whole cell population (injection zone 12 h after injection). Also in most remote organs, labeled cells were detected: the highest amount of positive cells was found in the liver 48 h after injection (0.5 %). With laser microdissection, labeled MSCs could be cut out of the cryosections (Figure). The RNA integrity number (RIN) and the DV200 showed an RNA quality suitable for real-time PCR (RIN min 5) or NGS (RIN min 8; DV200 > 80 %).

Conclusions: Both methods are suitable for isolation of percutaneously intramyocardially injected pMSCs. The quality of RNA is suitable for further processing to analyse the transcriptome. FACS sorting can deliver higher amounts of labeled cells in a shorter isolation time but laser microdissection may be more precise. The results of NGS will show the changes of the transcriptomics of the transplanted and host organ cells in response to cell therapy.

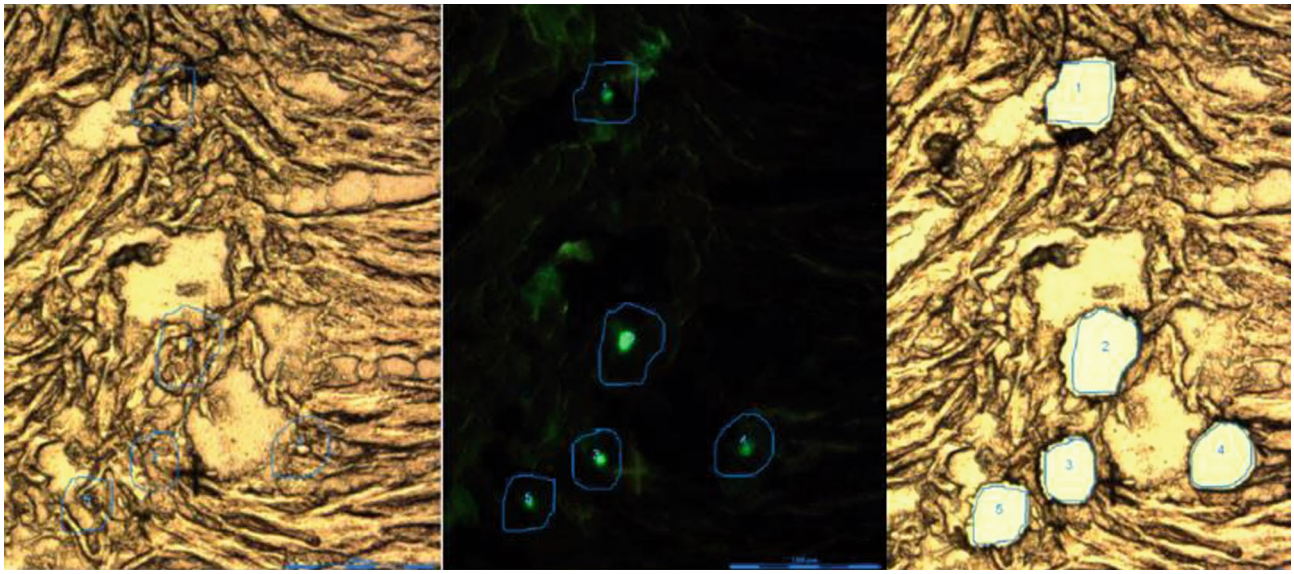

Fig. 1

1-8

Establishment of porcine cardiomyocyte cell culture for reducing large animal experiments

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Background: The development of in vitro models for the "3R" principle (Replacement, Reduction, Refinement of the animal models of human diseases) is a great challenge. Several cell culture models, of different species, have been proved to be acceptable for studying cardiovascular diseases as well as for preliminary testing of the pharmacological effect of various substances and therapies. Pigs are the suitable animals for several types of cardiovascular disease, interestingly, there is no pig cardiomyocyte cell culture commercially available. The main goal of this study was to set up the technique of isolating pig cardiomyocytes, maintaining them in culture, inducing hypoxia and preparing them for further investigations of effects of different substances in vitro.

Methods: After porcine heart explanation, heart tissue from the left ventricle was separated from epicardium, endocardium and the vessels to ensure using plain heart muscle tissue for cardiomyocyte isolation. Heart tissue was minced into small pieces (2 mm^2) and either used for collagenase II treatment or directly plated into petri dishes for the primary explant cell culture. Soon after the heart pieces adhere to the dish surface, petri dishes were filled with cardiomyocyte cell culture medium (M199, Sigma Aldrich, supplemented with 10 % FBS and 1 % PenStep) and incubated for about one week in a 5 % CO-Incubator at 37°C before checking cell outgrowth. The rest of heart tissue was used for collagenase II treatment, where the small pieces were added together with 0,2 % collagenase II in HBSS to gentle MACS dissociation C-tubes, and dissociated using preinstalled heart program two times, before incubating the solution 2×20 min at 37°C. After filtration of the cell solution using 100 µm cell strainers (BD) cells were cultivated with fresh culture medium in coated (0,1 % gelatine) T75 flasks. Cardiomyocytes were confirmed via microscopy and immunofluorescence staining for αSA, BNP, cardiac Troponin T, Connexin 43 and Vimentin. Mesenchymal stem cells (MSCs) cells were used as a control.

Results: Both methods of isolation of porcine cardiomyocytes were proven to be successful. The isolation with digestion media took about 3 hours, and the next day adherent cells could be observed. On the other hand, the isolation with the primary explant culture took approximately 1 hour but adhered cells were observed after 1–2 weeks. Isolated cardiomyocytes have the typical spindle-shaped morphology and showed positive immunofluorescent staining for αSA as well as BNP, cardiac Troponin T, Connexin 43 and negative for Vimentin (Figures and Table). Comparing these two isolation methods, concerning the yield and morphology of the cells, differences were not observed.

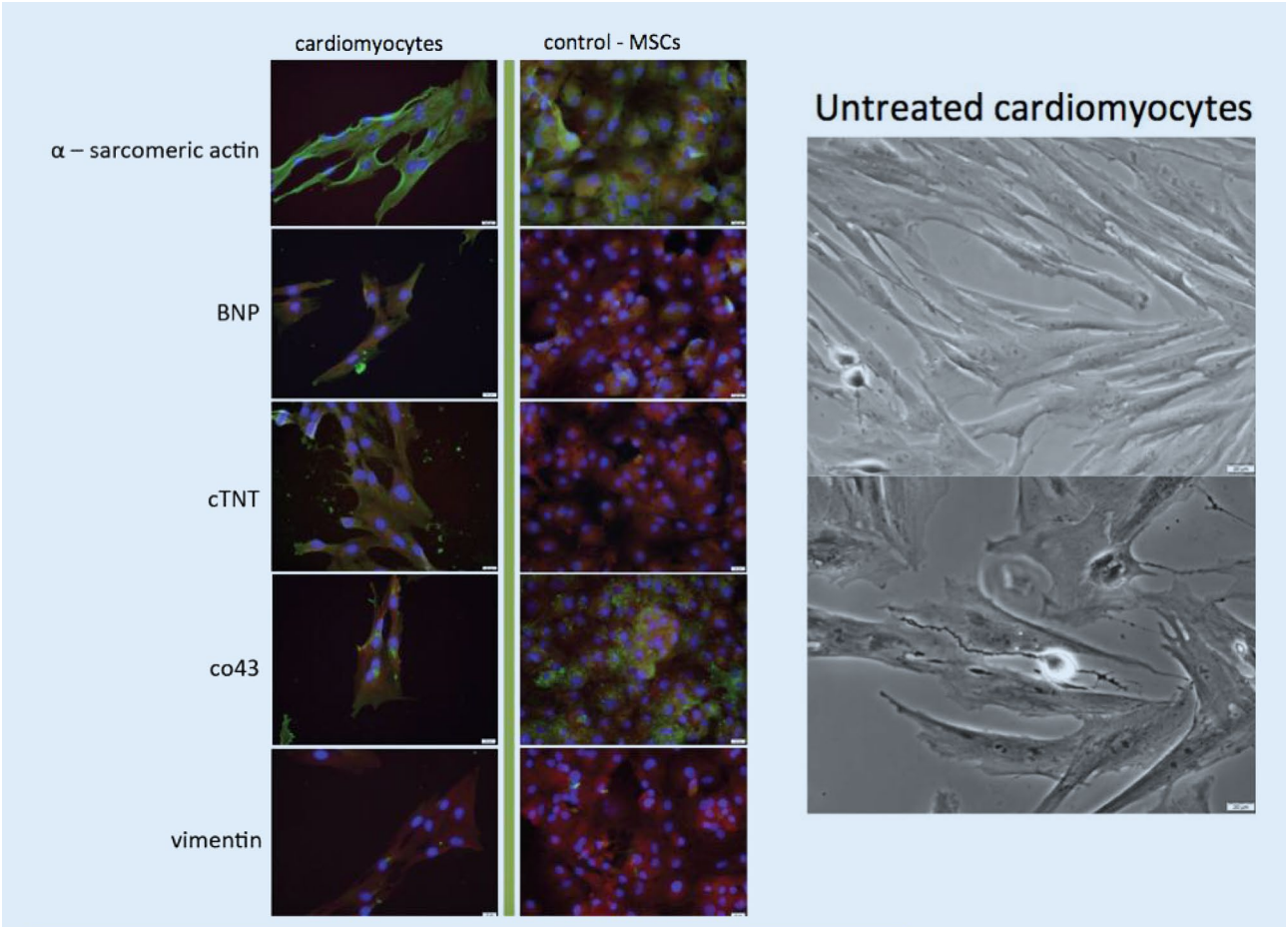

Fig. 1

Conclusions: This cell isolation and culture model is available for additional testing/screening of candidate substances and their impact on relevant target genes and miRNAs in normal or ischemic conditions before conducting the evaluation in pigs.

Tab. 1

marker	cardiomyocytes	MSC	fibroblasts
α – sarcomeric actin	+	+	-
BNP	+	-	-
cTNT	+	-	-
co43	+	+	+
vimentin	-	-	+

Postersitzung 2 – Rhythmologie 1

2-1

Qualität der von 2005–2014 vom BfArM für Herzschrittmacher bei Vorliegen von Produktproblemen veröffentlichten Kundeninformationen

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Grundlagen: Vermarktung und Marktüberwachung von Medizinprodukten und In-vitro Diagnostika 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 das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) für die meisten Medizinprodukte und In-vitro Diagnostika (IVD) bzw. das Paul Ehrlich-Institut (PEI) für ausgewählte IVD; in AU: BASG) melden und die Kunden über Kundeninformationen (Field safety notice, FSN) informieren, die auch den Behörden zur Verfügung gestellt werden. Ziel der Studie war die Untersuchung von FSN bei FSCA zu Herzschrittmachern, die von Anfang 2005 bis Ende 2014 auf der Homepage des BfArM veröffentlicht wurden.

Methodik: Für die in die Studie eingeschlossenen Produkte erfolgte eine Analyse der vom BfArM 2005 bis 2014 auf der Homepage (http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html) veröffentlichten FSCA und FSN in Hinblick auf die Anforderungen der MEDDEV 2.12-1 rev 8.

Ergebnisse: Für Herzschrittmacher fanden sich für den Untersuchungszeitraum 18 FSCA. Deutsche/englische FSN fanden sich in allen Fällen, die in 18/17 Fällen bzw. 7/10 Fällen eine klare Kennzeichnung als FSN bzw. eine entsprechende Angabe zum „Type of action" aufwiesen. In allen Fällen erfolgte die Angabe des Produktnamens. Eine Angabe von Lotnummern bzw. anderer Informationen zur Produktcharakterisierung erfolgte in 0/0 bzw. 13/14 Fällen. In allen Fällen fanden sich detaillierte Angaben zur FSCA bzw. zum meldepflichtigen Vorkommnis. Die meisten meldepflichtigen Vorkommnisse bezogen sich bei den Herzschrittmachern auf Komponentenfehler, wie z. B. defekte Kondensatoren oder fehlerhafte Isolierung bzw. Elektrodenbrüche sowie Softwarefehler, die in den meisten Fällen die Programmiergeräte der Implantate beeinträchtigten. Angaben zu produktbezogenen Risiken bei Gebrauch der betroffenen Produkte fanden sich ebenfalls in allen Fällen, wie z. B. Therapieausfall oder schwere Nebenwirkungen, wie z. B. Perikarderguss. In allen Fällen erfolgten außerdem Angaben der Hersteller zur Minimierung produktbezogener Risiken, die in den meisten Fällen aus zusätzlichen Verhaltensanweisungen, wie z. B. ein Softwareupdate zu installieren, bestanden. Eine Aufforderung, die FSN an weitere zu informierende Personen innerhalb der Organisation weiterzuleiten, fand sich in 8/5 Fällen. In allen Fällen erfolgte eine Angabe von Kontaktdaten des Herstellers. Eine Angabe darüber, dass die zuständige CA informiert war, fand sich in 12/9 Fällen und in 3/3 Fällen beinhaltete die FSN auch ein Bestätigungsformular für deren Erhalt.

Schlussfolgerungen: Die meisten FSN erfüllten die Vorgaben der MEDDEV. Zwischen deutschen und englischen FSN fanden sich typischerweise Unterschiede, z. B. in Hinblick auf die Weiterleitung der FSN an weitere zu informierende Personen, Vorliegen eines Hinweises darüber, dass die zuständige CA informiert wurde und das Vorliegen eines Formulars zum Bestätigen des Erhalts der FSN durch den Kunden. Aufgrund der Bedeutung der FSN zur Verminderung vom Produkt ausgehender Risiken im Falle einer FSCA sollten Form und Inhalt der FSN jedoch weiter verbessert werden.

2-2

Qualität der von 2005–2014 vom BfArM für kardiale Defibrillatoren bei Vorliegen von Produktproblemen veröffentlichten Kundeninformationen

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Grundlagen: Vermarktung und Marktüberwachung von Medizinprodukten und In-vitro Diagnostika 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 das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) für die meisten Medizinprodukte und In-vitro Diagnostika (IVD) bzw. das Paul Ehrlich-Institut (PEI) für ausgewählte IVD; in AU: BASG) melden und die Kunden über Kundeninformationen (Field safety notice, FSN) informieren, die auch den Behörden zur Verfügung gestellt werden. Ziel der Studie war die Untersuchung von FSN bei FSCA zu kardialen Defibrillatoren (ICD), die von Anfang 2005 bis Ende 2014 auf der Homepage des BfArM veröffentlicht wurden.

Methodik: Für die in die Studie eingeschlossenen Produkte erfolgte eine Analyse der vom BfArM 2005 bis 2014 auf der Homepage (http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html) veröffentlichten FSCA und FSN in Hinblick auf die Anforderungen der MEDDEV 2.12-1 rev 8.

Ergebnisse: Für Defibrilatoren fanden sich für den Untersuchungszeitraum 37 FSCA. Deutsche/englische FSN fanden sich in 37/35 Fällen, die in 36/33 Fällen bzw. 18/17 Fällen eine klare

Kennzeichnung als FSN bzw. eine entsprechende Angabe zum „Type of action" aufwiesen. In allen Fällen erfolgte die Angabe des Produktnamens. Eine Angabe von Lotnummern bzw. anderer Informationen zur Produktcharakterisierung erfolgte in 0/0 bzw. 30/28 Fällen. In allen Fällen fanden sich detaillierte Angaben zur FSCA bzw. zum meldepflichtigen Vorkommnis. Die meisten meldepflichtigen Vorkommnisse bezogen sich bei den Defibrilatoren auf Komponentenfehler, wie z. B. defekte Kondensatoren, sowie Softwarefehler, die in den meisten Fällen die Implantate beeinträchtigten. Angaben zu produktbezogenen Risiken, wie z. B. Ausfall oder Therapieeinschränkung bei Gebrauch der betroffenen Produkte fanden sich in 36/34 Fällen. In allen Fällen erfolgten Angaben der Hersteller zur Minimierung produktbezogener Risiken, die in den meisten Fällen aus zusätzlichen Verhaltensanweisungen, wie z. B. ein Softwareupdate zu installieren, bestanden. Eine Aufforderung, die FSN an weitere zu informierende Personen innerhalb der Organisation weiterzuleiten, fand sich in 14/8 Fällen. In 37/33 Fällen erfolgte eine Angabe von Kontaktdaten des Herstellers. Eine Angabe darüber, daß die zuständige CA informiert war, fand sich in 17/17 Fällen und in 1/0 Fällen beinhaltete die FSN auch ein Bestätigungsformular für deren Erhalt.

Schlussfolgerungen: Die meisten FSN erfüllten die Vorgaben der MEDDEV. Zwischen deutschen und englischen FSN fanden sich typischerweise Unterschiede, z. B. in Hinblick auf die Weiterleitung der FSN an weitere zu informierende Personen, Vorliegen eines Hinweises darüber, daß die zuständige CA informiert wurde und das Vorliegen eines Formulars zum Bestätigen des Erhalts der FSN durch den Kunden. Aufgrund der Bedeutung der FSN zur Verminderung vom Produkt ausgehender Risiken im Falle einer FSCA sollten Form und Inhalt der FSN jedoch weiter verbessert werden.

2-3

Septum hypertrophy as pre-procedural predictor of atrial fibrillation recurrence after circumferential pulmonary vein ablation

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Background: Atrial fibrillation (AF) recurrence rates after successful circumferential pulmonary vein ablation (CPVA) are still high, with success rates, ranging from 60 to 90 % depending on the series. The aim of this study was to evaluate, if septum hypertrophy is a pre-procedural predictor for AF recurrence after CPVA.

Methods: Echocardiographic examination was performed in 64 patients (35 men, mean age 60 ± 9 years, 65 % persistent AF, 12 patients with prior CPVA) who were going to receive CPVA procedure. Septum hypertrophy was seen as septal thickness more than 10 mm.

Results: During the mean follow up of 18 ± 13 months an AF recurrence was observed in 21 patients.

In the multivariate regression analysis including all baseline characteristics (Tab. 1), septum hypertrophy was associated with increased risk of AF recurrence (OR 1.78, CI 95 % 1.13–2.39, $p < 0.001$). Patients who suffered from recurrence had a mean septum thickness of 10.9 ± 1.5 vs. 9.3 ± 1.4 in AF free individuals.

Conclusions: These findings show that septum hypertrophy is an individual pre-procedural predictor of AF recurrence after CPVA. Consideration of this data may help professionals, estimating the risk of recurrence in patients undergoing ablation of AF.

2-4

Impact of surgical left atrial appendage exclusion on stroke prevention in patients with atrial fibrillation undergoing heart surgery

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Background: Surgical excision of the left atrial appendage (LAA) is currently a class IIb recommendation with the level of evidence class C according to the 2012 update of the ESC Guideline for the Management of Patients With Atrial Fibrillation (AF) and therefore may be considered in patients undergoing cardiac surgery. Due to the poor level of evidence we investigated the impact of surgical LAA exclusion in patients with AF undergoing heart surgery on stroke prevention.

Methods: We analyzed 150 patients with atrial fibrillation (71.9 % male, 66.9 ± 11.5 years), who underwent any kind of heart surgery at our affiliated department and divided them into two treatment arms. In 75 patients surgical removement by excision or ligation was performed.

Results: Baseline characteristics of both groups were similar, including CHA2¬¬DS2-VASc score. During a mean follow-up of 33.8 ± 18.2 months, a total of 3 strokes occurred, all in individuals who did not receive LAA exclusion (4.0 vs. 0.0 %). Log-rank test revealed significant difference in stroke free survival between the two treatment arms ($p = 0.022$).

Conclusions: Our results suggest the positive effect of LAA exclusion in patients with AF undergoing cardiac surgery due to any reason on the risk of developing stroke.

A large trial is needed to determine if surgical LAA exclusion prevents stroke.

2-5

ICD-Sondenperforation bei Patienten mit einer Noncompaction Kardiomyopathie

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Grundlagen: Die Noncompaction Kardiomyopathie (NCCM) ist charakterisiert durch eine Hypertrabekularisierung des linken Ventrikels mit schwammartig imponierender Myokardstruktur. Es liegt eine Zweischichtung der Wand mit einer kompaktierten Zone subepikardial und einer nichtkompaktierten Zone subendokardial vor. Der rechte Ventrikel (RV) kann ebenfalls betroffen sein. Im klinischen Verlauf können eine Herzinsuffizienz, Thrombembolien und maligne Arrhythmien auftreten. Guidelines für die Primärprävention des plötzlichen Herztodes (PHT), welche für die dilatative und die ischämische Kardiomyopathie entwickelt wurden, gelten auch für Patienten mit einer NCCM.

Die subakute Perforation der rechtsventrikulären freien Wand durch eine ICD-Elektrode ist eine seltene Komplikation und tritt bei Implantation moderner Elektroden in weniger als 1 % der Fälle auf. Bei Patienten mit einer NCCM ist über diese Komplikation bisher nicht systematisch berichtet worden.

Methodik: Innerhalb von 5 Jahren wurden bei 248 Patienten durch 2 erfahrene Rhythmologen ICD's zur Primär- und Sekundärprävention eines PHT implantiert. Die Häufigkeit einer subakuten RV Perforation bei Patienten mit einer NCCM (diagnostiziert mittels Echokardiographie und/oder kardialer MRT) wurde verglichen mit der Rate bei ICD-Patienten mit anderen kardialen Grunderkrankungen.

Ergebnisse: ICD-Elektroden wurden zur Primärprävention eines PHT bei 121 Patienten (49 %) und zur Sekundärprävention bei 127 Patienten (51 %) implantiert. Fünfundfünfzig dieser 248 Patienten (22 %) mit Linksschenkelblock und Zeichen der Herzinsuffizienz erhielten ein CRT-ICD System.

Bei insgesamt 8 Patienten mit einer NCCM wurden ICD-Elektroden implantiert (2 Frauen, 6 Männer, Alter 59±12 Jahre); 5 dieser Patienten (62 %) erhielten ein CRT-ICD-System. Bei allen NCCM-Patienten bestand die Indikation zur ICD-Implantation in einer Primärprävention des PHT. Eine RV-Beteiligung war bei diesen Patienten zuvor nicht diagnostiziert worden. Komplikationen traten bei 2/8 Patienten auf: eine Taschenninfektion und eine subakute Sondenperforation der freien rechtsventrikulären Wand nach 9 Tagen, die notfallmäßig chirurgisch versorgt wurde.

Eine subakute RV Perforation der ICD-Elektrode trat bei 1/8 Patienten mit einer NCCM (12.5 %) versus 0/240 Patienten mit anderweitigen kardialen Grunderkrankungen auf ($p=0{,}03$). Trotz normal erscheinender Morphologie des RV sowohl bei der kardialen MRT als auch bei der Echokardiographie können strukturelle Veränderungen des RV vorliegen, welche bei der NCCM eine Perforation der ICD-Elektrode begünstigen.

Schlussfolgerungen: Die subakute Perforation der rechtsventrikulären freien Wand durch eine ICD-Elektrode tritt häufiger bei Patienten mit einer NCCM auf. Eine septale Lokalisation der Elektrodenspitze sollte daher bevorzugt werden, weil das Interventrikularseptum selten in den Noncompaction-Prozess mit einbezogen ist. Alternativ kann in ausgewählten Fällen eine epikardiale Elektrodenimplantation oder ein subcutaner ICD in Frage kommen.

2-6

Interdisciplinary management of left ventricular noncompaction in pregnancy using a wearable defibrillator

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Background: Left ventricular hypertrabeculation/noncompaction (LVHT) is a cardiac abnormality of unknown etiology, characterized by extensive trabeculations of the left ventricular cavity and a two-layered structure of the left ventricular myocardium. LVHT is diagnosed in children and adults, mainly by echocardiography, and may be associated with heart failure, arrhythmias and embolic events. LVHT is no contraindication for pregnancy, however worsening of cardiac function and development of malignant arrhythmias has been described. Protection against malignant arrhythmias is provided by implanted defibrillators (ICDs) or wearable defibrillators (Lifevest). We present the first LVHT case with a lifevest during pregnancy.

Case report: A 27-years old woman with a diagnosis of LVHT since 2 years presented within the 16th week of pregnancy. She was free of cardiac symptoms. Echocardiography showed a left ventricular ejection fraction of 43 % (normal >60 %). The family history disclosed that her sister, also suffering from LVHT, had died at age 19 despite an implanted cardioverter-defibrillator (ICD) and the patient's father had died suddenly at age 34 years. Genetic testing was refused. She was on a medication with bisoprolol 10 mg/d. At completed 25 weeks of gestation betamethason was given for respiratory distress syndrom-prophylaxis. Since multiple ventricular ectopic beats and short ventricular ectopic runs were detected by 24-hour monitoring, and considering the family history, it was decided to provide her with a lifevest which she wore with high adherence. In the following weeks, the cardiac situation and brain-natriuretic peptide levels remained stable and no arrhythmias occurred. Within the 34th week of gestation she was hospitalized. Daily cardiotocograms and weekly Doppler-recordings of the umbilical cord detected no abnormalities. The primary Caesarean-section was scheduled at 37 weeks of gestation on a day when the medical staff of all involved departments was present in the operation room. The Caesarean-section was carried out without any problems in peridural anesthesia. The newborn girl had a weight of 2556 g and a length of 47 cm. Apgar score was 9/10/10. Postpartal development was excellent for mother and child. The child did not show any cardiac abnormalities. Clinical and cardiologic follow-up of mother and child 4 months postpartal showed a normal development of the child. The mother continues to take bisoprolol 10 mg/d, but has, so far, not consented to implantation of an ICD.

Conclusions: In view of the limited data and experience with the course of pregnancy in LVHT-patients, a close interdisciplinary monitoring between cardiologists, gynecologists, anaesthesiologists and neonatologists should be carried out. A wearable defibrillator is an alternative to protect against sudden death if a patient is at risk for malignant arrhythmias and an ICD is either unsuitable or undecided.

2-7

The HAS-BLED score for prediction of stroke and systemic embolism: Insights from the PREvention oF thromboembolic events – European Registry in Atrial Fibrillation (PREFER in AF)

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Background: A high bleeding risk remains the primary reason to withhold anticoagulation in AF patients. Since risk factors for stroke and bleeding overlap, such patients may also have an increased risk for thromboembolism, thus, potentially gaining greater benefit from anticoagulation. We therefore assessed the performance of the HAS-BLED score to identify patients at risk for stroke in a contemporary, largely anticoagulated AF cohort.

Methods and Results: We compared the performance of the HAS-BLED, $CHADS_2$, and CHA_2DS_2-VASc scores for the prediction of stroke or systemic embolism during one year follow-up in 7228 patients enrolled in 2012–2013 into the PREFER in AF registry.

The mean age was 72±11, mean HAS-BLED and CHA_2DS_2-VASc scores were 2.0±1.1 and 3.4±1.8, respectively. Anticoagulants were used in 83 % of patients, 25 % of the full cohort received antiplatelet therapy.

The primary endpoint occurred at an annual rate of 2.5 % (95 % CI; 2.1,2.9). Corresponding c-indices were 0.679 (95 % CI 0.631;0.728) for HAS-BLED, 0.667 (95 % CI 0.621;0.714) for $CHADS_2$ and 0.652 (95 % CI 0.606;0.699) for CHA_2DS_2-VASc (p = NS for the comparison of the scores).

A cluster of independent stroke risk factors (including heart failure, age ≥ 75 years, prior stroke or TIA, concomitant antiplatelet or non-steroidal anti-inflammatory drug treatment, labile INR and abnormal liver function) was identified outperforming the established scores (0.728, 95 % CI 0.681;0.776, $p < 0.01$ vs. established scores).

Conclusions: In a large cohort of anticoagulated AF patients, the HAS-BLED score performed similarly to $CHADS_2$ and CHA_2DS_2-VASc in predicting stroke, underlining that risk factors for bleeding and thromboembolism overlap substantially and cannot be separated by current algorithms.

2-8

Carvajal syndrome with oligodontia, hypoacusis, recurrent infections, and noncompaction in a patient with DSP gene mutation

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Background: Carvajal syndrome (CS) is characterized by dilated cardiomyopathy, wooly hair and palmoplantar keratosis. Mutations in the desmoplakin (DSP) gene are frequently found in patients with CS. CS with autosomal dominant inheritance associated with dental anomalies has been reported, so far, in the literature in 10 cases.

Case report: We report a 43-year-old Caucasian female with oligodontia, hypoakusis and recurrent infections since age 10 years. At age 15 her hair became wooly, and palmar and plantar hyperkeratosis developed. At age 20 recurrent syncopes started which were not further investigated but attributed to "psychogenic causes". Family history disclosed that her father and brother had also suffered from oligodontia, palmar and plantar hyperkeratosis and dilated cardiomyopathy. The father had died at age 60 and the brother at 41 years, both due to heart failure and ventricular tachycardia.

At the age of 43 she was referred for cardiologic examination. ECG showed a left bundle branch block. Coronary angiography was normal. Ventriculography, echocardiography and cardiac magnetic resonance imaging showed a moderately reduced systolic function with a left ventricular ejection fraction (EF) of 67 45–51 % and apical noncompaction. Telemetric monitoring disclosed episodes of unspecified tachycardia with a heart rate of 170/min, why bisoprolol was started. Regarding her complaints and the family history we recommended an ICD which she is currently considering. Meanwhile she was provided with a wearable cardioverter defibrillator. Genetic analysis disclosed a previously not described DSP gene mutation on position 1678 (c.1678A>T).

Conclusions: Dental and skin anomalies are frequently not registered by cardiologists. Similarly, skin anomalies and cardiac problems may be not recognized by dentists as well as dental anomalies and cardiac symptoms by dermatologists. Thus, the prevalence of CS with or without oligodontia may be higher than previously thought. Because of the frequent association of arrhythmias and sudden cardiac death with CS, recognition of CS is important and requires the cooperation of dentists, dermatologists, cardiologists and general practitioners.

2-9

Gender differences in patients receiving pacemaker; a single center large-scale cohort study

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Background: According to previous scientific reports, gender bias might exist in the choice of pacemaker (PM) device implantation or age of the patients at the first implantation. The aim of our large-scale cohort study was to evaluate the gender differences in patients receiving PM in the last 15 years, regarding indication of PM implantation, changes in the PM sensing and pacing thresholds and the intrinsic right atrial and ventricular electrical parameter.

Methods: The present study analyzed the implantation and follow-up data of 11,449 pacemaker (PM) implantations and controls between May 15th 2000 and May 14th 2015 in university hospital. Among all patients, 6907 had regular 12 months follow-up (FUP) controls with standardized documentation of all patient- and device-related parameter. Data acquisition related to the age, gender, indication for PM implantation (sinus node and/or AV-conduction disease, atrial or ventricular arrhythmia, bundle branch block), and type of PM devices, categorized as follows: AAI/R, VVI/R, VDD/R, or DDD/R. PM parameter (impedance of the atrial and ventricular leads, sensing or pacing thresholds) at the implantation and final FUP were recorded and changes were calculated. Differences between male and female gender were evaluated statistically using 2-sided t-test and chi-square test.

Results: Higher proportion of male patients received PM, than females (60.2 % vs 39.8 %). At the time of the first PM implantation, the mean age of male vs female patients were 69.8±14.8 vs 71.0±15.9 years ($p < 0.001$). Significant ($p < 0.01$) gender difference was found between males and females regarding the indication for PM implantation, as higher incidence of sinus node disease was detected in females as compared to males (25.7 % vs 20.6 %), in contrast with the diagno-

sis of AV blocks of any degree (27.8 % vs 30.8 %). No differences between male and female patients were recorded regarding type of all implanted PM. However, female patients with AV blocks received less frequently DDD/R PM as compared to males (65.7 % vs 71.2 %, $p < 0.05$). The median FUP time was longer in female patients (5.2±0–1 vs 4.8±0.1y, $p < 0.001$). No gender differences were found regarding baseline and FUP measured or programmed PM parameters (atrial and ventricular sensing and pacing thresholds, P and R-wave amplitudes). However, significant decrease in PM electrode lead impedance was found in male patients during over time both for atrial (–26±224 vs –4±359 ohm, $p = 0.05$) and ventricular (–31±183 vs –14±266 ohm, $p < 0.05$) electrodes, as compared to females, predicting pacing lead failure.

Conclusions: Our large-scale real-life patient cohort with primary PM implantation revealed important gender differences regarding rhythm disturbances requiring PM, and time-dependent changes in pacemaker lead impedances, but not in course of intrinsic right atrial and ventricular electrical parameters during FUP.

2-10

Therapy-resistant hypertension in atrial fibrillation – Can bradycardia be the cause?

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An 80-year-old female patient presented to our emergency department with worsening fatigue and weakness over the previous weeks. Co-morbidities included chronic kidney disease stage IV, osteoporosis, arterial hypertension and atrial fibrillation.

During 24-hour Holter monitoring, heart rate ranged between 30 and 73 beats per minute (bpm) and pauses up to 5 seconds were recorded. Telemonitoring revealed recurrent episodes of symptomatic bradycardia (fatigue, dizziness) during daytime with less than 30 bpm. The patient was scheduled for implantation of a cardiac single-chamber pacemaker.

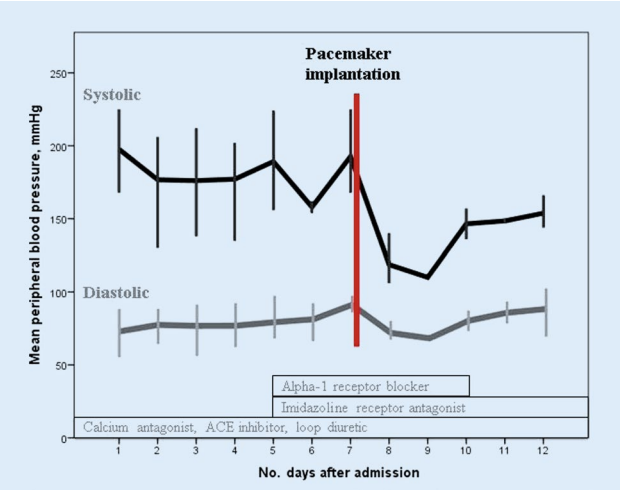

Fig. 1 Mean systolic and diastolic peripheral blood pressure during in-hospital stay. Whiskers indicate standard deviation

With her chronic medication (triple-therapy, including calcium antagonist, ACE inhibitor and loop diuretic) hypertension was poorly controlled: mean blood pressure (BP) was 198/71 ±24/10 mmHg on the day of admission. Improved control to 158/79 mmHg was achieved by adding imidazoline receptor antagonist and alpha-1 receptor blocker to the therapy.

After implantation (VVIR, 60 beats per minute lower pacing threshold, 78 % ventricular pacing rate) marked reduction was observed in BP: from 158/79 ±4/11 mmHg to 118/70 ±21/6 mmHg, over 24 hours before and after operation, respectively. Alpha-1 receptor blocker had to be terminated and imidazoline receptor antagonist was reduced. Overall, mean systolic BP declined from 182 ±26 mmHg (all measurements before operation) to 138 ±22 mmHg (all measurements after operation, see Figure 1). The patient was discharged under quadruple-therapy regimen (calcium antagonist, ACE inhibitor, loop diuretic and imidazoline receptor antagonist).

In this particular case improved blood pressure control after pacemaker implantation might be explained if chronotropic incompetence stood as secondary cause of uncontrollable hypertension. Future randomized controlled trials could address the question whether restoration of chronotropic competence by pacemaker implantation may facilitate BP control in therapy-resistant hypertension and bradycardia.

Postersitzung 3 – Herzinsuffizienz

3-1

Programmierung der quadripolaren LV-Elektrode nach optimalen Vektor-EKG und modifizierten Tei-Index

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Grundlagen: Trotz bestehender Leitlinien ist die Nonresponderrate (NR) unter kardialer Resynchronisationstherapie (CRT) mit bis zu 30 % immer noch hoch. Ein einfacher diagnostischer Test via EKG mit haemodynamischen Kontrollparametern in der transthorakalen Echokardiographie könnte hier Abhilfe schaffen. Die Analyse des Zeitintervalls (TI) im Vektor-EKG (VCG) bringt Aufschlüsse über die Erregungsausbreitungsstörung, da sich die spät depolarisierende Bereiche des linken Ventrikels zeitlich und örtlich in der Vektorschleife darstellen lassen. Eine Reduktion der elektrischen Ausbreitungsgeschwindigkeit in der isovolumetrischen Kontraktionszeit (ICT) verlängert diese und führt zu einer Abnahme der Kontraktilität. Der Beginnt der ICT koinzidiert mit dem maximalen Vektor im VCG. Die ICT lässt sich bei Patienten mit Linksschenkelblock echokardiographisch über den modifizierten Tei-Index messen. Die Firma St Jude Medical bietet eine vierpolige LV-Elektrode an, die damit durch eine größere Auswahl an Stimulationsvektoren besticht und zu einer geringeren NR führen soll.

Methodik: Ziel dieser Pilotstudie war es, zu überprüfen, ob eine Programmierung der quadripolaren LV- Elektrode nach dem optimalsten TI im VCG zu einer eine deutliche Verbesserung des Tei-Index und der LVEF führt. Zusätzlich wurde die NYHA-Klasse und ein 6 Minuten Gehtest (GMGT) evaluiert. Zwischen Juli 2014 und März 2015 wurden 6 Patienten in diese Pilotstudie

eingeschlossen (83 % Männer, 60 % DCM). Alle Patienten hatten im Rahmen einer leitlinienindizierten CRT-D-Implantation eine quadripolare linksventrikuläre Elektrode (QLVS) erhalten. Bei allen Patienten wurde das TI des VCG sowie die QRS-Breite ohne Stimulation, mit einer gleichzeitigen biventrikulären Stimulation (VV 0 ms) und einer vorzeitigen LV-Stimulation von 20 ms (VV-20 ms) für je 10 möglichen Vektoren der QLVS gemessen. Daneben wurde für jede Programmierung echokardiographisch der modifizierte TEI- Index bestimmt. Programmiert wurde der Vektor der QLVES mit der Kombination aus dem kürzesten TI und dem kürzesten QRS-Komplex. Das Follow-up erfolgte 3 Monate nach Einschluss. Ein Patient wurde bei den Einschlussmessungen bei signifikanter Verbreiterung des QRS-Komplexes unter biventrikulärer Stimulation – gleich welcher Programmierung- ausgeschlossen. Die mittlere QRS-Breite lag bei Einschluss vor der Device Therapie bei 150 ms, das TI bei 81,6ms und der modifizierte TEI-Index bei 0,81 bei einer mittleren LVEF von 28 %. Der 6MGT lag im Durchschnitt vor der Devicetherapie bei 315 Metern, die NYHA-Klasse bei II-III.

Ergebnisse: Insgesamt verbesserten sich 5 von 6 Patienten in ihrer LVEF um +17,3 % bei einer Verbesserung der Gehstrecke um +84 Meter. Alle Patienten berichteten subjektiv von einer deutlich gebesserten NYHA-Klasse. Das TI hatte sich unter biventrikulärer Stimulation deutlich von 81,5 ms auf 50 ms verkürzt, bei einer QRS-Breite von 121 ms. Der modifizierte Tei-Index verbesserte sich unter biventrikulärer Stimulation durchschnittlich um 0,2 Punkte gegenüber dem Ausgangswert, mit Ausnahme einer Patientin. Der Vektor D1-M2 wurde bei 2 von 5 Patienten programmiert, D1-RV, D1-P4, sowie P4-RV bei jeweils einem Patienten.

Schlussfolgerungen: Die Programmierung einer Quadripolaren Sonde nach dem kürzesten TI im VEK bietet eine gute Möglichkeit, die ICT, LVEF und damit die Klinik der Patienten unter CRT-Therapie zu verbessern. Mehr Patienten und ein verändertes Studiendesign sollten folgen.

3-2

The impact of regulatory T lymphocytes on long-term mortality in patients with chronic heart failure

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Background: Chronic heart failure (CHF) constitutes a global health issue representing a prevalent clinical syndrome. While pro-inflammatory cytokines proved to have a pivotal role in the development and progression of CHF, less attention has been paid to the cellular immunity. Regulatory T lymphocytes (Tregs) have an important role in the induction and maintenance of immune homeostasis. However recent evidence suggests a deregulation in Treg function causing abnormal immune responses leading to progression of pathology in inflammatory disease. Therefore we aimed to investigate the impact of Tregs on the outcome of patients presenting with CHF.

Methods: We prospectively enrolled 112 patients with CHF defined by New York Heart Association (NYHA) functional class > II and left ventricular ejection fraction (LVEF) <40 %. Cells from fresh heparinized blood were stained and analyzed using BD FACS Canto II flow cytometry. Cox regression hazard analysis was used to assess the influence of Tregs on survival. The multivariate model was adjusted for age, gender, type of CHF, LVEF and Nt-proBNP.

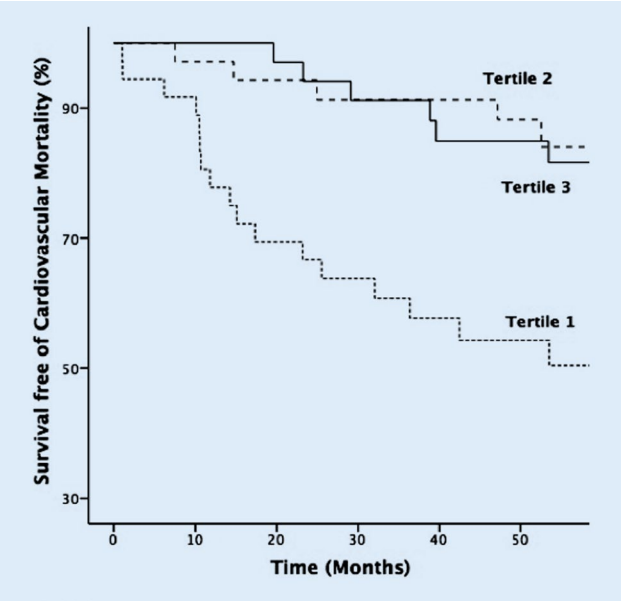

Fig. 1 Survival Curves of Cardiovascular Mortality. Kaplan-Meier plots showing cardiovascular mortality stratified by tertiles of Treg fraction among CD4+ cells. Tertiles were compared using log-rank test ($p<0.001$)

Results: After a mean follow-up time of 4.5 years 32 (28.6 %) patients died due to cardiovascular causes. Comparing survivors to non-survivors we found a significantly higher count of Tregs in surviving individuals ($p<0.001$). Interestingly we were able to show a higher total lymphocyte count ($p=0.004$) as well a significantly higher fraction of CD4+ cells ($p=0.042$) among survivors. More specifically, there was a significantly higher fraction of cytotoxic T cells characterized by the loss of CD28 within CD4 T cells ($p=0.032$) detectable in deceased individuals. Moreover Tregs were significantly associated with cardiovascular survival in in the entire study cohort with a crude HR per one standard deviation (1-SD) of 0.49 (95 % CI 0.33–0.72; $p<0.001$). Even after adjustment for potential cofounders Tregs remained independently associated with long-term survival with an adjusted HR per 1-SD of 0.59 (95 % CI 0.36–0.98; $p=0.043$).

Conclusions: Our results might indicate a potential influence of Tregs in the pathogenesis and progression of CHF, fostering the implication of cellular immunity in CHF pathophysiology and proving Tregs as a predictor for long-term survival among CHF-patients.

3-3

The impact of T-Lymphocytes on atrial fibrillation and mortality in patients with chronic heart failure

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Background: Atrial fibrillation (AF) represents the most common cardiac arrhythmia within the Western societies. Especially in patients with chronic heart failure (CHF) the development of AF represents a severe complication resulting in hemodynamic instability. However the exact pathophysiol-

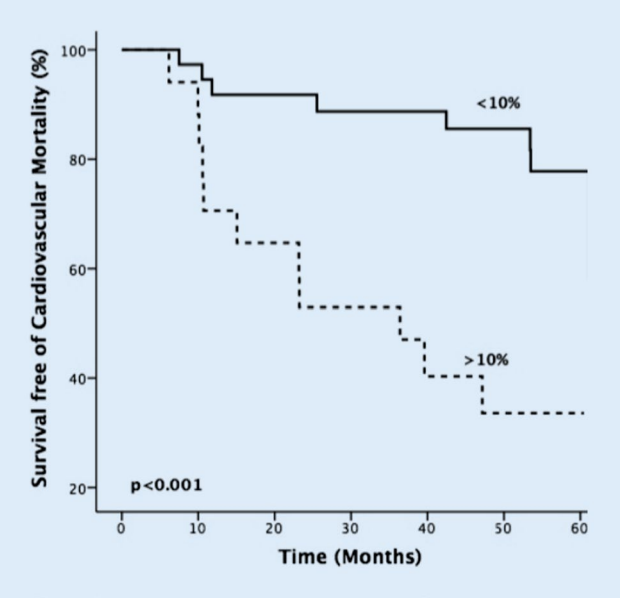

Fig. Survival Curves of Cardiovascular Mortality. Kaplan-Meier plots showing cardiovascular mortality in patients with atrial fibrillation according to CD4+CD28- frequencies in CD4+ cells, compared using log-rank test

ogy in the development of AF in this highly vulnerable patient collective is still incompletely understood. While a genetic predisposition is postulated as a trigger of AF, data on the immunological aspect in the development on AF and its impact on the patient outcome remain scarce.

Methods: Therefore we prospectively enrolled 112 patients with CHF defined by New York Heart Association (NYHA) functional class > II and left ventricular ejection fraction (LVEF) <40 %. Patients were stratified in two subgroups according to patients developing AF ($n=50$) and patients developing no AF ($n=62$). Cells from fresh heparinized blood were stained and analyzed using BD FACS Canto II flow cytometry. Cox regression hazard analysis was used to assess the influence of T Cells on survival. The multivariate model was adjusted for age, gender, type of CHF, LVEF and nt-proBNP.

Results: Comparing AF to non-AF patients we found a significantly higher total lymphocyte count ($p=0.005$), a significantly higher proportion of CD3+ T cells ($p=0.003$), and a higher fraction of CD4+ cells ($p=0.007$) in the AF subgroup. More specifically, there was a significantly higher number of cytotoxic T cells characterized by the loss of CD28 within CD4 T cells ($p=0.035$) detectable in individuals with AF. Interestingly we were able to demonstrate that the number of regulatory T cells was significantly lower ($p<0.001$) in patients with AF. After a mean follow-up time of 4.5 years 32 (28.6 %) patients died due to cardiovascular causes. The loss of CD28 within CD4 T cells was significantly associated with cardiovascular mortality in patients with AF, with an adjusted HR per one standard deviation (1-SD) of 1.59 (95 % CI 1.13–2.24; $p=0.008$), bot not in patients free of AF with an adjusted HR per 1-SD of 1.27 (95 % CI 0.86–1.87; $p=0.216$). Interaction analysis of the predictive value of CD4+CD28- T cells with AF showed borderline significance ($p=0.062$).

Conclusions: Our results might indicate a potential influence of T cells in the pathogenesis of atrial fibrillation. Specifically, cytotoxic CD4 T cells characterized by the loss of CD28 were associated with cardiovascular mortality in CHF-patients with AF.

3-4

Takotsubo Kardiomyopathie einer Patientin mit Morbus Addison infolge Überdosierung von Fludrocortison

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Grundlagen: Eine reversible linksventrikuläre Dysfunktion, auch Takotsubo-Kardiomyopathie (TTK) genannt, von Patienten mit Morbus Addison nach Einleitung einer Hormonersatz-Therapie ist selten. Die Pathogenese dieser Kardiomyopathie ist unbekannt.

Fallbericht: Eine 41-jährige Patientin mit einer Hashimoto Thyroiditis seit 3 Jahren and einer Nebennierenrindeninsuffizienz, die vor 4 Wochen diagnostiziert worden war, wurde wegen einer akuten Herzinsuffizienz im NYHA IV-Stadium aufgenommen. Die Symptome der Herzinsuffizienz hatten kurz nach Beginn der Hormonersatztherapie mit Hydrocortison 20 mg/Tag and Fludrocortison 0,3 mg/Tag begonnen. Neun Tage vor der Aufnahme war sie wegen Schwindel kollabiert und hatte sich eine Gehirnerschütterung und eine offene Nasenbeinfraktur zugezogen.

Bei der klinischen Untersuchung fanden sich Beinödeme, Tachykardie, Tachypnoe, beidseits Rasselgeräusche, und der Blutdruck betrug 110/70 mm Hg. Das Elektrokardiogramm zeigte eine Sinustachykardie, periphere Niederspannung, negative T-Wellen in V5 and V6 und ein verlängertes QT-Intervall mit einer QTc von 590 ms. Die Echokardiographie zeigte eine reduzierte systolische linksventrikuläre Funktion mit einer Auswurffraktion von 30 % und Akinesie des interventrikulären Septums und der Vorderwand. Bei der kardialen Magnetresonanz-Untersuchung (MR) fand sich ein relatives Enhancement von Gadolinium, hinweisend auf Hyperämie and kapilläre Leckage, und keine myokardialen Narben. MR-Untersuchungen der Sella und der Nieren zeigten keine Auffälligkeiten. Das Troponin T war gering erhöht. Eine neurohumorale Therapie mit Bisoprolol und Ramipril wurde begonnen. Die Dosis des Fludrocortisons wurde auf 0,05 mg/Tag reduziert. Unter dieser Therapie normalisierten sich innerhalb der folgenden 6 Monate sowohl das Elektrokardiogramm als auch die systolische Funktion, dokumentiert durch Echokardiographie and MR.

Schlussfolgerungen: Fludrocortison-Überdosierung und erhöhte myokardiale Vulnerabilität infolge Kortisol-Mangels sind als pathogenetische Faktoren für die TTK unserer Patientin in Erwägung zu ziehen. Angesichts der Anamnese und des MR ist eine Myocarditis unwahrscheinlich. Ein kardiales Monitoring mittels Elektrokardiogramm und Echokardiographie wird nach Einleitung einer Hormonersatztherapie bei Patienten mit Morbus Addison empfohlen.

3-5

Soluble urokinase-type plasminogen activator receptor improves risk prediction in patients with chronic heart failure

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Background: As chronic heart failure (CHF) represents a common clinical condition associated with poor prognosis, strategies to improve risk prediction are of major importance in this critical group of patients. Soluble urokinase-type plasminogen activator receptor (suPAR) originates from proteolytic cleavage and release of the membrane-bound receptor from activated immune cells and endothelial cells into the plasma and reflects the level of immune activation in various pathological conditions. As inflammation plays a crucial role in the complex pathophysiology of CHF, we hypothesized that suPAR may be a suitable prognostic biomarker in patients with CHF.

Methods: SuPAR levels were measured in 319 patients (median age: 64.6 years, 81.2 % male gender, median N-terminal pro B-type natriuretic peptide [NT-proBNP]: 1215 pg/ml, 46.7 % ischemic etiology) admitted to the outpatient department for heart failure of the Medical University of Vienna using a sandwich enzyme-linked immunosorbent assay kit.

Results: Patients were followed for a median time of 3.2 years (IQR: 2.0–4.9 years). During the follow up, 119 (37.3 %) patients deceased including 82 (25.7 %) patients, who died due to cardiovascular causes. Cox proportional hazard models were applied to assess the impact of suPAR on mortality. SuPAR was a strong predictor of mortality with a crude hazard ratio per one increase of standard deviation (HR per 1-SD) of 1.96 (95 % CI: 1.63–2.35; $P<0.001$) in univariate analysis and remained significant after adjustment for age, sex, body mass index, systolic blood pressure, New York Heart association functional classification, CHF etiology, NT-proBNP, left ventricular ejection fraction, estimated glomerular filtration rate, active smoking, diabetes mellitus, atrial fibrillation, hypertension, chronic obstructive pulmonary disease and C-reactive protein with an adj. HR per 1-SD of 1.38 (95 % CI:1.04–1.83, $P=0.026$). SuPAR added prognostic value beyond that achievable with the multivariable model indicated by improvements in C-statistics (area under the curve: 0.72 vs 0.74, $P=0.02$), the category-free net reclassification index (24.9 %, $P=0.032$) and integrated discrimination improvement (IDI: 0.011, $P=0.05$).

Conclusions: SuPAR is a strong and independent predictor of mortality in patients with CHF potentially suitable to refine risk assessment in this vulnerable group of patient. Our results emphasize the impact of immune activation on survival in patients with CHF.

3-6

Influences of a multi-modality cardiac rehabilitation program on quality of life, fitness, immune activation and depressive symptoms in heart failure patients – A pilot study

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Depression is a common co-morbidity in Heart Failure (HF) patients with incidences between 11–45 %, depending on HF severity according to the New York Heart Association (NYHA) class stages I–IV. Moreover, depressive symptoms among symptomatic HF patients are associated with significantly increased risk of cardiovascular hospitalization and mortality after controlling for HF severity and ejection fraction, hence effective treatments for depression in HF are required. HF and depression are both inflammatory states and share biological mechanisms such as sympathetic activation and elevated levels of pro-inflammatory cytokines. Among the available therapies, exercise training has been accepted to be safe and effective in tackling different aspects of HF symptoms and the patients' quality of life. Exercise training can lead to improvements in functional capacity, sympathetic activation and immune responses. Now, the aim of this study was the observation of potential changes regarding inflammatory cytokine levels, depressive symptoms and quality of life over the course of the 4-week inpatient reha-

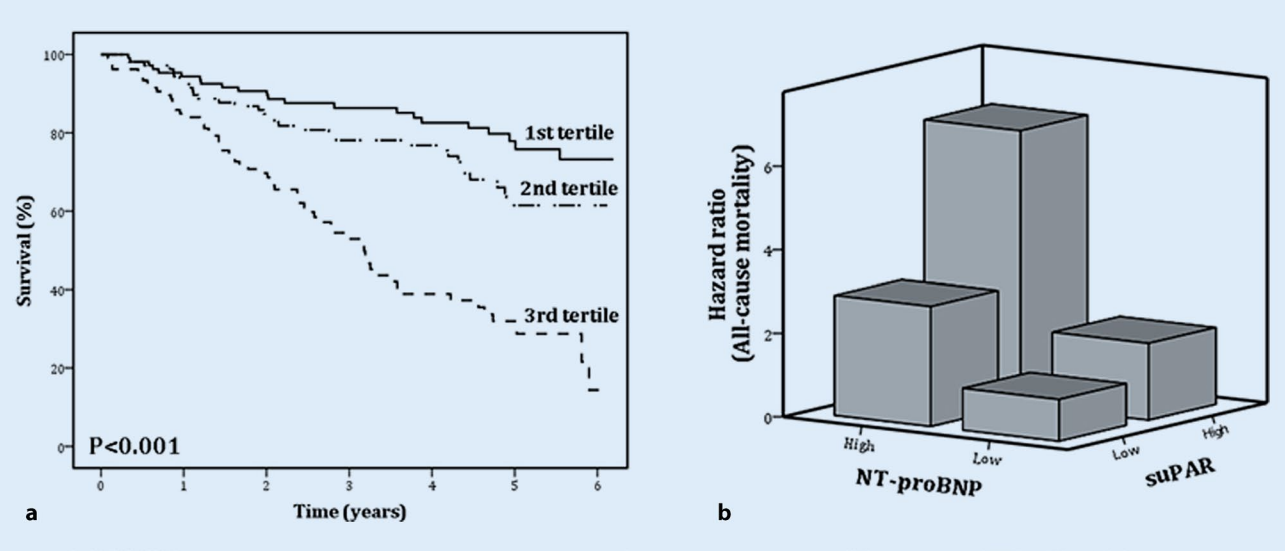

Fig. 1 a) Kaplan-Meier plot according to tertiles of suPAR, b) Combined assessment of NT-proBNP and suPAR

bilitation program which included a cassette of modalities such as counseling, psychosocial education, diet and supervised exercise training as a main pillar, and further the detection of correlations between changes in immune regulation, depressive symptoms and quality of life. The study was carried out in a within-subject design such that each study participant served as his own control and was followed 4-weeks prior to the start of the rehab program. 16 stable and optimal medically treated HF patients [mainly NYHA II; mean age 64 years; mean body mass index (BMI) 30.8 kg/m2; mean left ventricular ejection fraction (LVEF) 37 %] were assessed for their fitness, depressive symptoms, quality of life (QoL) and inflammatory markers. A paired-sample t-test was applied to detect significant differences between the control period and the rehabilitation period. Fitness improved significantly ($p=0.002$), as did QoL measures KCCQ (0.023), SF36 Physical Component Scale ($p=0.031$) and SF36 Mental Component Scale ($p=0.006$). With a few exceptions, these patients generally did not show elevated symptoms of depression and anxiety and no significant changes could be observed. sICAM-1, a marker for endothelial dysfunction was significantly decreased during the rehab program ($p=0.001$), whereas other inflammatory markers (TNF-α, IL-6, IL-1β) did not change or were not detectable. Significant negative bivariate correlation was observed between depressive mood and fitness, in such that patients with better mood showed better fitness at baseline assessment (–0,640; $p=0,008$) and after the rehab program (–0,575; $p=0,025$). Overall, despite the low subject number, it was found that a cardiac rehab-program for HF patients is effective in increasing QoL and physical function capacity alongside a decrease in sICAM-1 levels. Exercise training during the rehab program did not show to be effective in changing depressive symptoms and no correlations between biomarkers and depressive symptoms could be observed. Further research is necessary to establish whether exercise training can assist in ameliorating symptoms as a non-pharmacological alternative to treating depression in HF.

3-7

Circulating mitochondrial DNA predicts survival in patients with acute heart failure

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Background: Patients suffering from acute heart failure (AHF) requiring admission to an intensive care unit (ICU) have a poor prognosis. Activation of the innate immune system contributes to the pathogenesis of AHF. Mitochondrial DNA that shows similarities to bacterial DNA may be released after tissue damage and activates the innate immune system.

Purpose: The aim of this study was to analyze whether circulating levels of mtDNA predict 30-day survival in patients with AHF.

Methods: We included 90 consecutive patients with AHF admitted to our cardiovascular ICU (33 % with cardiogenic shock, 21 % with acutely decompensated HF and 46 % of patients suffered from AHF after cardiac arrest). Blood was taken at admission and mtDNA levels were measured by real-time PCR.

Results: Mean age was 62.1 ± 16.0, 76.7 % of patients were male and median NT-proBNP levels were 4986 (1525–23842) pg/mL. 30-day survival was 64.4 %. Median mitochondrial DNA levels at admission were significantly higher in non-survivors when compared with survivors (29.6 (12.1–70.7) ng/mL vs. 20.6 (7.3–37.1 ng/mL), $p<0.05$). Patients with plasma levels of mtDNA in the highest quartile had a 2.6-fold higher risk of dying after adjustment for age, gender, NT-proBNP levels and APACHE II score ($p<0.05$).

Conclusions: Circulating levels of mtDNA predict mortality in AHF patients requiring ICU admission.

3-8

Monocyte subset distribution predicts survival in patients with acute heart failure

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Background: Activation of the innate immune system contributes to the pathogenesis of acute heart failure (AHF). As key regulators of innate immunity, monocytes may play a crucial role in the development of this disease. Monocytes are a heterogenous cell population that can be divided into at least three cell populations: Classical monocytes (CM; CD14++CD16-), intermediate monocytes (IM; CD14++CD16+CCR2+) and non-classical monocytes (NCM; CD14+CD16++CCR2-).

Purpose: The aim of this study was to analyze whether monocyte subset distribution is associated with 30-day survival in patients with AHF.

Methods: We included 90 consecutive patients with AHF (33 % with cardiogenic shock, 21 % with acutely decompensated HF and 46 % of patients suffered from AHF after cardiac arrest). Blood was taken at admission and after 72 hours and monocyte subset distribution was analyzed.

Results: Mean age was 62.1 ± 16.0, 76.7 % of patients were male and median NT-proBNP levels were 4986 (1525–23,842) pg/mL. 30-day survival was 64.4 %. At admission, no association between monocyte subsets and outcome was seen. However on day 4, increased levels of IM (9.4 (4.0–13.8) % vs. 4.3 (2.1–7.9) %; $p=0.02$, respectively). and lower levels of CM were predictive of 30-day mortality (86.8 (77.5–88.9) % vs. 90.5 (84.3–92.9), $p=0.02$, respectively), while the NCM proportion was not associated with mortality. Risk of dying was increased 10.6-fold in the lowest tertile of CM and 9.5-fold in patients in the lowest IM tertile ($p<0.05$ for both).

Conclusions: Circulating monocyte subsets are associated with 30-day mortality in patients with AHF requiring ICU admission. Activation status of the innate immune system as reflected by monocyte subset distribution may play a major role in pathophysiology and outcome in this patient cohort.

3-9

Additive prognostic value of Copeptin and NT-proBNP in patients with acute heart failure

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Background: Patients suffering from acute heart failure (AHF) requiring admission to an intensive care unit (ICU) have a poor prognosis. The C-terminal portion of provasopressin (Copeptin) represents a surrogate parameter for vasopressin, has been described as a marker for endogenous stress. Besides its use as a rule-out marker in patients with NSTE-ACS it has been described as a prognostic biomarker in patients with acute illness.

Purpose: The aim of this study was to analyze whether admission levels of copeptin are associated with 30-day survival in patients with AHF admitted to a cardiac ICU.

Methods: We included 90 consecutive patients with AHF admitted to our cardiovascular ICU (33% with cardiogenic shock, 21% with acutely decompensated HF and 46% of patients suffered from AHF after cardiac arrest). Blood was taken at admission, mtDNA levels were measured by real-time PCR while copeptin was measured by an automated sandwich immunofluorescent assay

Results: Mean age was 62.1 ± 16.0, 76.7% of patients were male and median NT-proBNP levels were 4986 (1525–23,842) pg/mL. 30-day survival was 64.4%. Non-survivors had significantly higher values of both copeptin (139.8 (44.7–311.2) pmol/L vs. 31.4 (17–77.1) pmol/L, $p < 0.001$) and NT-proBNP (23,718 (2981–>35,000) pg/mL vs. 3262 (1000.3–8212.3) pg/mL). Interestingly, copeptin and NT-proBNP showed additive prognostic value. When patients were stratified according to the median of NT-proBNP and copeptin, those with both copeptin and NT-proBNP levels above the median had the highest risk of dying (HR 4.6, $p = 0.003$).

Conclusions: In a cohort of patients with AHF requiring ICU admission, copeptin levels measured at admission added prognostic value to NT-proBNP levels.

Postersitzung 4 – Akutes Koronarsyndrom 1

4-1

Catalytic iron in acute myocardial infarction complicated by cardiogenic shock – A biomarker substudy of the IABP-SHOCK II-Trial

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Background: Catalytic iron (CI) is unbound ferric iron with the potential to generate reactive oxygen species with further deleterious vascular effects. In acute coronary syndromes high levels of CI were linked to all-cause mortality. In cardiogenic shock (CS) the prognostic impact of CI and further iron metabolism is currently undetermined. Aim of this study was to investigate the prognostic impact of CI in patients with CS complicating acute myocardial infarction and to identify predictors of high CI levels.

Methods: The Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial randomized 600 patients with CS to either intraaortic balloon pump or control. In 185 of these patients, blood samples were collected at baseline and after two days. CI levels were measured using a modified bleomycin detectable iron assay. Furthermore, levels of free hemoglobin, total serum iron, transferrin, total iron binding capacity, ferritin, hepcidin and transferrin saturation were assessed.

Results: Patients with baseline CI levels in the highest quartile had a worse outcome in Kaplan-Meier-analysis in comparison to the other quartiles (day 1: HR 1.91 [1.11–3.31], $p = 0.005$; day 3: HR 2.15 [1.06–4.34], $p = 0.01$). In multivariable Cox-regression analysis baseline CI remained an independent predictor of 30-day mortality (HR per 10LOG 2.08 [1.25–3.47], $p = 0.005$) together with age, baseline serum lactate and reperfusion success. Predictors of CI levels on day 3 were baseline CI, bleeding events and baseline troponin T as marker for infarct size.

Conclusions: CI levels were associated with increased short-term mortality in CS complicating acute myocardial infarction. High levels of CI at day 3 were associated with bleeding and high troponin levels as marker of infarct size.

4-2

Culprit lesion location and outcome in patients with cardiogenic shock complicating myocardial infarction: A substudy of the IABP-SHOCK II-Trial

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Background: In myocardial infarction without CS the affected coronary vessel has significant influence on final infarct size and patient prognosis. For CS data on this relation are scarce. The objective of this study was to determine the prognostic relevance of the culprit lesion location in patients with cardiogenic shock (CS) complicating acute myocardial infarction.

Methods: In the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial patients with CS were randomized to therapy with intraaortic balloon pump or control. Additional CS patients not eligible for the randomized trial were included in a registry. We compared the location of the culprit lesions in these patients with regard to affected coronary vessel (left main [LM], left anterior descending [LAD], left circumflex [LCX] and right coronary artery [RCA]) and location within the vessel (proximal or mid/distal) regarding short- and long-term outcome.

Results: Of 758 patients the majority had the culprit lesion in the LAD (44 %) compared to RCA (27 %), LCX (19 %) or LM (10 %). Proximal lesions were more frequent than mid/distal culprit lesions (60 vs. 40 %, $p < 0.001$). No differences were observed for mortality with respect to either culprit vessel (log-rank-p-value = 0.54) or proximal vs. mid/distal location of the culprit lesion (log-rank-p-value = 0.45). This was also true after multivariable adjustment, independent predictors of outcome were serum lactate, success of revascularization, age, serum creatinine, prior stroke, known peripheral artery disease and left bundle branch block at admission.

Conclusions: For patients with CS complicating myocardial infarction, the culprit lesion localization seems to be unrelated with mortality.

4-3

Eine erhöhte maximale Blutglukosekonzentration ist mit einer erhöhten intra-ICU Mortalität von nichtdiabetischen Patienten assoziiert

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Grundlagen: Erhöhte Blutglukosewerte bei Aufnahme sind mit einer erhöhten Mortalität von Patienten mit akutem Myokardinfarkt assoziiert. Unklar ist jedoch ob erhöhte Glukosekonzentrationen per se einen Risikofaktor darstellen oder aber den Schweregrad der Grunderkrankung wiederspiegeln. Ziel unserer Studie war es daher zu untersuchen ob die maximale Blutglukosekonzentration im Zuge eines Intensivaufenthaltes die Mortalität beeinflussen.

Methodik: An der Universitätsklinik Jena wurden 2006 bis 2009 1712 Patienten, die mit ACS an einer Intensivstation hospitalisiert wurden, in dieser Studie untersucht. Das Follow-up wurde von Mai bis November 2013 durchgeführt. Die maximale Blutglukose im Zuge des Intensivaufenthaltes wurde neben klinischen Parametern sowie anderen Laborparametern dokumentiert. Das Langzeitüberleben wurde mittels Cox-Regressions-Analyse untersucht, die kurfristige (intra-ICU) Mortalität mittels Chi-Quadrat Test analysiert.

Ergebnisse: Eine ROC Kurve und die „area under the curve" wurden berechnet um den diagnostischen Effekt der maximalen Blutglukosekonzentration darzustellen (AUC 0,662 95 % CI 0,64–0,69; $p < 0{,}001$) und mit anderen Risikofaktoren wie Alter (AUC 0,71 95 % CI 0,69–0,73; $p < 0{,}001$) zu vergleichen. Mittels Youden Index wurde ein optimaler Cut-Off berechnet: 8,6 mmol/l. Jene Patienten die eine maximale Blutglukose oberhalb des Cut-Offs aufwiesen, zeigten eine deutliche Übersterblichkeit sowohl hinsichtlich Langzeit- (HR 2,82 95 % CI 2,08–3,83; $p < 0{,}001$) als auch Kurzzeitüberleben (3,4 % vs 12,5 %; $p < 0{,}01$). Eine maximale Blutglukosekonzentration über des Cut-Offs war jedoch nur bei nichtdiabetischen Patienten (3.1 % vs 14,7 %; $p < 0{,}01$) jedoch nicht bei Patienten mit bekanntem Typ 2 Diabets Mellitus (8,7 % vs 5,6 %; p = n.s.) mit erhöhter intra-ICU Mortalität assoziiert.

Der maximale Glukosewert (Veränderung pro Einheit in mmol/l) war mit einer erhöhten Langzeitmortalität assoziiert (HR 1,1 95 % CI 1,07–1,23; $p < 0{,}001$). Auch nach Korrektur für Alter bei Aufnahme, das Auftreten von Herzrhythmusstörungen, kardialer Dekompensation, Sepsis, Pneumonie und pektanginösen Beschwerden, dem Vorliegen von Niereninsuffizienz und Typ 2 Diabetes Mellitus sowie der maximalen Herzfrequenz und des höchsten Leukozyten- und Laktatwertes im Zuge des Intensivaufenthaltes blieb in einer multivariaten Cox Regressions Analyse ($n = 976$) der maximale Glukosewert im Zuge des Intensivaufenthalts ein unabhängiger Prädiktor für die Mortalität (HR 1,03 95 % CI 1,01–1,06; $p = 0{,}02$).

Schlussfolgerungen: Eine hyperglykäme Entgleisung im Zuge eines Myokardinfarktes ist mit einer erhöhten Mortalität assoziiert. Die maximale Blutglukose ist ein unabhängiger Prädiktor für Mortalität von Patienten mit akutem Myokardinfarkt. Der optimale Cut-Off, um Patienten mit erhöhtem Risiko zu identifizieren, ist mit 8,6 mmol/l niedrig. Diese Assoziation bleibt auch nach Korrektur für andere Risikofaktoren, klinische Parameter und relevanter Laborparameter bestehen. Weiters war eine erhöhte maximale Blutglukosekonzentration nur in nichtdiabetischen Patienten mit Myokardinfarkt mit erhöhter intra-ICU Mortalität assoziiert, was auf eine „protektive" Adaptation an hohe Blutglukosespiegel in diabetischen Patienten hinweisen könnte. Wir werten dies als Indizien dafür, dass erhöhte maximale Blutglukosekonzentrationen und somit eine hyperglykäme Entgleisung einen eigenständigen Risikofaktor für die Prognose von Patienten mit Myokardinfarkt darstellen.

4-4

Evaluation of the Manchester Triage System for patients with acute coronary syndrome and primary presentation in the emergency department

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Background: Chest pain is a frequent cause of presentation in emergency departments (ED). An early diagnosis of acute coronary syndrome (ACS), in particular in patients with ST-elevation myocardial infarction (STEMI), is crucial for treatment and prognosis. The Manchester Triage System (MTS) classifies patients based on their main symptoms into five different levels of urgency in terms of their need for assessment, irrespective of the eventual diagnosis. The aim of this study was to evaluate the MTS for patients with ACS and primary presentation in the ED.

Methods: Retrospective, single-center study of patients diagnosed with ACS (STEMI, non-STEMI, unstable angina pectoris (UAP)) and primary presentation in the ED between January 1st and December 31th, 2014.

Results: 282 patients (68.0 ± 14.6 years, female: 31.9 %) with ACS (STEMI 34.0 %, non-STEMI 61.7 %, UAP 4.3 %) were triaged by the MTS: MTS level 1 (immediate assessment) 0.4 %, MTS level 2 (very urgent) 51.4 %, MTS level 3 (urgent) 41.5 %, MTS

level 4 (standard) 6.7 %, MTS level 5 (non urgent) 0 %. While 195 patients (69.1 %) presented with chest pain, 87 patients had atypical symptoms (e. g. shortness of breath, palpitations, syncope). There was a significant difference between the mean MTS levels with respect to gender (male: 2.48, 95 % CI 2.40–2.57, female: 2.68, 95 % CI 2.53–2.82, $p = 0.022$) and age (age < 80 years: 2.50, 95 % CI 2.42–2.58, age ≥ 80 years: 2.70, 95 % CI 2.53–2.88, $p = 0.025$). We did not observe a significant difference in different types of ACS (STEMI: 2.46, 95 % CI 2.34–2.58, non-STEMI: 2.59, 95 % CI 2.49–2.68, STEMI vs non-STEMI: $p = 0.11$, UAP: 2.67, 95 % CI 2.25–3.08, STEMI vs UAP: $p = 0.26$) and diabetes (diabetic: 2.47, 95 % CI 2.35–2.58, non diabetic: 2.58, 95 % CI 2.49–2.68, $p = 0.13$). There was no correlation between MTS levels and infarct size measured by the maximum value of creatine kinase (MTS 1: 1707U/l, MTS 2: 891 ± 1229U/l; MTS 3: 889 ± 1436 U/l, MTS 4: 660 ± 1157 U/l, p = n. s.). Overall in-hospital mortality was 2.5 % ($n = 7$).

Conclusions: The majority of patients with ACS and primary presentation in the ED were classified as MTS levels 1 to 3 (immediate to urgent assessment). We observed significant lower MTS levels for males and patients younger than 80 years. As discrimination of different types of ACS is not possible with the MTS, we recommend to write an ECG in patients suspected for ACS within 10 minutes after first medical contact according to current guidelines in order to assure an early diagnosis of STEMI in the ED.

4-5

Myocardial infarction with proximal occlusion of the left anterior descending coronary artery in a 22-year old patient with polycythemia vera

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A 22-year old hemodynamically stable male patient was admitted due to recurrent chest pain since two days. The ECG showed discrete ST-elevations in the anterior leads (V1-V4) and a heart rate of 110 bpm. During echocardiography, contractility of the left ventricular anterior wall was impaired. Cardiac markers were significantly elevated with the maximum level of CK-MB of 92 U/l and hyTroponin of 0.73 ng/L at admission. In addition, increased levels of red blood cells, hemoglobin, hematocrit, white blood cells and platelets were found.

Medical treatment for ST-Elevation Myocardial Infarction including dual antiplatelet therapy was initiated according to current guidelines. Coronary angiography was performed within 30 minutes after admission and revealed an occlusion of the left anterior descending artery at its origin with visible collaterals from the normal circumflex and right coronary artery, indicating sub-acute occlusion. Therefore and due to the fact that a percutaneous coronary intervention would have involved the distal main stem and the proximal circumflex artery, revascularization was delayed. Cardiac magnetic resonance imaging was performed and showed more than 50 % viable myocardium within the anterior wall supporting the usefulness of revascularization. Considering the patient's age and coronary anatomy, elective coronary artery bypass grafting was performed.

Because of the polycythemia in the complete blood count (hemoglobin of 19.8 g/dl), the patient was tested for a mutation

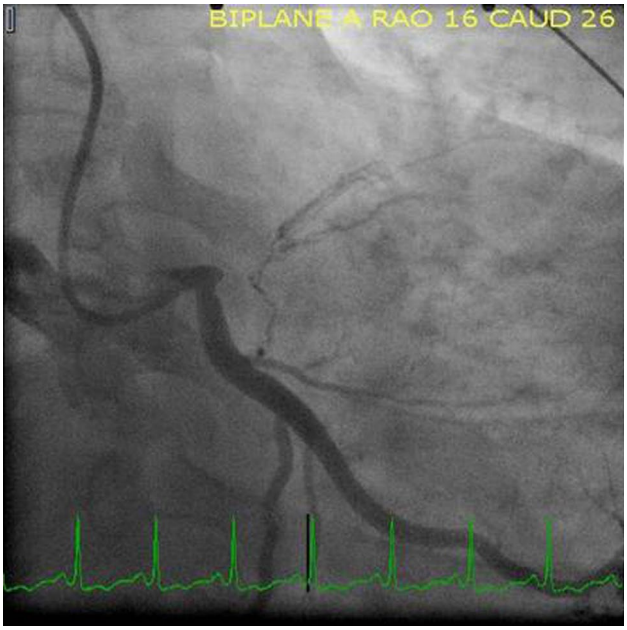

Fig. 1

of the Janus Kinase 2 gene (JAK2) which confirmed the diagnosis of polycythemia vera (PV) (EPO: 3mU/ml). Next to ongoing antiplatelet therapy, recurrent phlebotomy was started.

PV, a myeloproliferative disorder caused by mutations in the JAK2 Gene, is characterized by an overproduction of all blood cell lines leading to various complications including thromboembolic events (in 40 % of patients). The average age at the time of diagnosis is 60 years with only 7 % of patients being younger than 40 years. As potential causes for the development of coronary ischemia, hyperviscosity due to the increased hematocrit, intimal proliferation as well as increased platelet stimulation and aggregation are discussed.

The composed treatment of PV includes repeated phlebotomy and antiplatelet therapy amended by cytoreactive therapy with Hydroxyurea or Interferon-A.

This case reports may remind that in young patients with acute coronary syndromes even rare causes thrombus formation or embolization should be considered to allow an early and targeted therapy.

4-6

BMPRII signaling of fibrocytes, a mesenchymal progenitor cell population, is increased in STEMI and dyslipidemia

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Background: Inflammation is a hallmark of ST-elevation myocardial infarction (STEMI). Fibrocytes, a Collagen-I+CD34+CD45+ mesenchymal progenitor cell population accumulate in cardiac tissue of a murine ischemia/reperfusion model. In ACS, decreased levels of circulating fibrocytes were found, compared to healthy controls. Bone morphogenic protein receptor II (BMPRII) is involved in the vascular remodeling of lung and heart. Therefore, we studied BMPRII expression in fibrocytes at the culprit lesion site (CLS).

Methods: We sampled blood from the CLS and a femoral site in the course of primary percutaneous coronary intervention (pPCI) from STEMI patients ($n=50$, male = 78 %, mean age = 61±13y). Another sample was acquired 72 h after pPCI ($n=21$). A cohort of healthy controls ($n=20$, male 48 %, mean age = 51±8y) served as controls. Flow cytometry was employed to characterize fibrocytes.

Results: Fibrocytes were increased at the CLS compared to femoral blood (722 [276–1298] vs. 324 [180–589], $p=0.0001$). 72 h after STEMI, peripheral fibrocytes were decreased (246 [151–468] vs. 153 [102–252], $p=0.006$). Peripheral fibrocyte counts during pPCI were similar to those of controls.

No differences were found in BMPRII expression between coronary and femoral blood of STEMI patients; however, BMPRII expression was higher in patients than controls (MFI 22,106 [13,142–34,125] vs. 13,099 [8944–20,231], $p=0.014$). In patients suffering from dyslipidemia, BMPRII on fibrocytes was increased (MFI 26,056 [13,195–54,807] vs. 19,913 [13,635–22,965], $p=0.009$). 72 h after pPCI, BMPRII was significantly upregulated (MFI 22,294 [17,973–34,125] vs. 31,149 [27,722–45,724], $p=0.044$).

Conclusions: The two-fold increase of fibrocytes at the CLS and subsequent decrease 72 h after pPCI in peripheral blood supports the concept of an active process. BMPRII expression is increased in STEMI patients, particularly in patients with dyslipidemia, suggesting lipid-induced inflammation and activation of fibrotic vascular remodeling.

4-7

MicroRNA expression profiling to distinguish type 1 and type 2 myocardial infarction

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Background: A type 1 myocardial infarction (MI) is usually the result of atherosclerotic coronary artery disease, whereas myocardial necrosis in type 2 MI occurs because of an increase in myocardial oxygen demand or a decrease in myocardial blood flow. Clinical discrimination between type 1 and type 2 MI is often difficult. MicroRNAs (miRNAs) are short, non-coding RNAs with remarkable stability in circulation. miRNAs have emerged as a new group of potential biomarkers in several diseases, including prognosis in acute MI.

Aim: Here we aimed to investigate the value of circulating miRNAs as possible biomarkers to distinguish type 1 and type 2 MI.

Methods and Results: Expression profiling of 372 circulating miRNAs was performed in plasma samples of patients from 2 independent cohorts. First, 20 patients presenting with type 2 MI were randomly selected from cohort of 621 acute coronary syndrome patients. 20 age- and gender-matched type 1 MI patients were selected from same cohort. Patients with unstable angina and ST-elevation MI were excluded. Samples were pooled and miRNA arrays were performed in duplicates. miRNAs expression was normalized to C. elegans spike-in control as well as to average Ct value of expressed miRNAs (Ct < 30) within the group. Initial screening identified 29 differently expressed miRNAs between the 2 groups of patients. In order to reduce the number of candidate miRNAs, we have repeated the screening in 14 consecutive patients presenting with type 1 ($n=8$) and type 2 ($n=6$) MI. Again, patients with ST-elevation MI were excluded. We have observed 28 differently expressed miRNAs between the 2 groups. Among these, miRNA-1183 and -1207-5p demonstrated the highest difference between the two groups of patients with a 3-fold upregulation ($p<0.01$) in patients suffering from type 2 MI in both study cohorts.

Conclusions: Circulating miRNAs represent potential novel biomarkers to distinguish type 1 and type 2 MI. However, further analysis in a larger, prospective cohort is necessary to elucidate the diagnostic value of specific miRNA candidates in patients with type 1 and type 2 MI.

Postersitzung 5 – Basic Science 2

5-1

MicroRNA expression profiling in patients with symptomatic and asymptomatic carotid artery stenosis

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Background: Micro-RNAs (miRNAs) are small, non-coding RNAs, which seem to play an important role in atherosclerotic plaque formation, development and instability. miRNAs are detectable in circulation and have been proposed as biomarkers for coronary artery disease, myocardial infarction, heart failure and diabetes mellitus type II.

Aim: The aim of the present study was to characterize the miRNAs expression profiles in atherosclerotic plaque and plasma samples of patients with symptomatic and asymptomatic carotid artery stenosis.

Methods and Results: Sixteen patients, 8 asymptomatic and 8 symptomatic, were randomly chosen out of the pool of 238 prospectively enrolled patients who underwent carotid endarterectomy. Total RNA was isolated from the core and shoulder of carotid atherosclerotic plaques, as well as from plasma samples of each patient. In order to determine the specific miRNAs signature of patients with symptomatic and asymptomatic carotid artery stenosis, we profiled the expression of the 1008 most abundantly expressed and best characterized miRNAs in carotid atherosclerotic plaques, as well as the expression of 372 circulating miRNAs. We detected a significant over 2-fold upregulation of 6 miRNAs, and a downregulation of 15 miRNAs in symptomatic as compared to asymptomatic carotid atherosclerotic plaques. Out of 7 differently expressed circulating miRNAs, 2 were upregulated and 5 were downregulated in symptomatic patients. Expression of miRNA-370 was upregulated 3.5-fold ($p=0.006$) in plaque and 1.8-fold ($p=0.04$) in plasma of symptomatic patients. Conversely, miRNA-130b showed 1.9-fold ($p=0.006$) and 1.5-fold ($p=0.01$) downregulation in plaque and plasma of symptomatic patients, respectively. In order to validate the results, we will determine quantitative expression of differently expressed miRNAs in the whole study cohort.

Conclusions: The miRNAs expression profile differs significantly between symptomatic and asymptomatic carotid atherosclerotic plaques. We identified 2 miRNAs consistently up- (miRNA-370) and downregulated (miRNA-130b) in plaque and in circulation of symptomatic patients. Identification of a

specific miRNA signature in symptomatic carotid artery stenosis could improve our understanding of the pathophysiology and become a diagnostic tool for identification of unstable atherosclerotic plaques.

5-2

Macrophage M2 differentiation induces PAI-1 expression and reduces proteolytic capacity

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Background: Macrophages are myeloid cells representing a heterogeneous cell population. Depending on their local microenvironment they can polarize into proinflammatory M1 and anti-inflammatory M2 macrophages. In this study, we examined different proteolytic and migratory capacities via expression of plasminogen activator inhibitor-1 (PAI-1) and matrix-metalloproteinases (MMPs) among macrophage subsets.

Methods: Monocytes were cultivated for 7d with M-CSF to generate M0 macrophages. Macrophages were polarized for 48 h by LPS and interferon-gamma to generate M1 or by interleukin-4 (IL4) and IL13 to generate M2 macrophages.

Results: Macrophage polarization was determined by analysis of characteristic markers for macrophage differentiation. Macrophage subsets display distinct capabilities of matrix degradation, indicating different levels of proteolytic activity. Urokinase type 1 (uPA) is crucial for proteolytic activity. Despite highest uPA levels in M2 macrophages, uPA activity is comparable over all subsets. uPAR restricts plasminogen activation to the membrane. Overall uPAR expression is 9.3±2.7 fold higher in M1 than in M0 and M2 macrophages and distribution of uPAR on membrane protrusions is significantly higher in M1 macrophages. M1 macrophages have a 4.6±2.5 fold increase of gelatin matrix degradation capability compared to both M0 and M2 macrophages ($p = 0.01$). MMPs can be activated by uPA. MMP2 and MMP9 protein levels do not differ in macrophage subsets. uPA activity is tightly regulated by PAI-1. M2 display the highest PAI-1 levels compared to M1 and M0. Inhibiting PAI-1 by a specific nanobody lead to a significant increase in proteolytic activity of M2 macrophages without affecting M0 or M1 proteolytic capacities. After PAI-1 inhibition MMP9 activity in M2 macrophages was increased (1.8±0.2 fold, $p < 0{,}001$). Although MMP14 expression is comparable over all subsets, M1 macrophages display doubled MMP14 distribution on membrane protrusions compared to M0 and M2 macrophages. No differences in trans-migratory capacity were observed in all subsets.

Conclusions: Induction of PAI-1 expression reduces proteolytic but not trans-migratory capacity in M2 polarized macrophages.

5-3

Shift of ANG1/ANG2 balance causes reduced migration in aging endothelial cells

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Background: Aging is associated with a variety of cell type specific changes. Endothelial cells have been reported to have reduced angiogenetic capability upon aging. An important pathway for endothelial cell activation is the Angiopoietin (Ang) 1/2 pathway with its receptors Tie1 and Tie2. Whereas Ang1 is critical for vessel maturation and quiescence, Ang2 is an activating factor for endothelial cells promoting neovascularization.

Aim: The aim of our study was to identify a possible regulation of the Ang1/2 system upon endothelial cell aging.

Results: Aging endothelial cells (EC) were generated by passaging them at least 8 times. Aging endothelial cells were characterized by increased senescent associated cytokine expression (e.g. PAI-1, MCP1 and GMCSF) and reduced telomere length. Upon aging, endothelial cells showed increased levels of Ang1, both in mRNA (7.6-fold ± 4.3 versus young EC, $p = 0.05$) and secreted protein levels (573.3 pg ± 3.3 SD/ml young EC versus 687.5 pg ± 12.5/ml aging EC). In addition, Ang2 levels dropped significantly in both mRNA (0.13-fold ± 0.18 young EC, $p < 0.05$) as well as protein levels (2753.3 pg ± 373.4/ml young EC versus 549.4 pg ± 283.5/ml aging EC) resulting in a shifted ratio of Ang2/1 from 2.3 in young to 0.3 in aging endothelial cells. The Tie1/2 receptor system was not affected by aging and its expression remained stable. This change in Ang1/Ang2 relation was represented in a change in migration distance after 12 h in an in vitro scratch wound assay. Whereas young EC showed a mobility of 53,4553.3 ± 45,205.9 pixel, aging EC had a reduced migration of 390,780.2 ± 14,797.1 pixel ($p < 0.05$). Adding soluble Ang2 to aging cells in the scratch assay restored endothelial cell mobility after 24 h (940,679.6 ± 34,906.7 pixel, $p < 0.05$).

Conclusions: Aging induces a shift towards increased Ang1 expression in endothelial cells resulting in a reduced migration speed.

5-4

Tenascin-C and MMP-9 activation in the murine geriatric heart after myocardial infarction

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Background: Aging is associated with a higher incidence, mortality, and complication rate of myocardial infarction (MI). Tenascin-C (TNC) is a glycoprotein produced in the infarction border zone. Previous studies discussed TNC as prognostic marker for outcome after MI.

Methods: In male geriatric (OM, age: 18 months) and young (YM, age: 11 weeks) OF1 mice MI was induced by permanent LAD ligation. In SHAM groups the procedure was performed without LAD occlusion. 32 days after MI, cardiac MRI was used for hemodynamic evaluation. TNC plasma and septum tissue concentrations were assessed by ELISA (IBL 27767) and MMP-9 levels by QuickZyme Mouse MMP-9 activation assay.

Results: In a 2-way ANOVA MRI examination showed significant effects of age and of MI vs. SHAM on ejection fraction, stroke volume heart weight ratio, cardiac output heart weight ratio, end-systolic, and end-diastolic left ventricular volumes. Moreover, MI had a significant effect on stroke volume. No significant effects of age and of MI vs. SHAM were found on heart rate and cardiac output. Furthermore, no significant interactions between the two factors were found in any parameter.

TNC plasma concentration was significantly increased in mice with MI at all time points, and significantly decreased in geriatric mice 3 and 7 days after MI compared to young mice after MI (3 days: OM: 4.52±0.94 µg/ml, YM: 11.11±3.46 µg/ml; 7 days: OM: 4.22±1.92 µg/ml, YM: 9.03±4.09 µg/ml). Additionally, geriatric mice after MI showed decreased TNC septum tissue concentrations (7 days: OM: 0.114±0.043 ng/mg, YM: 0.217±0.064 ng/mg).

Moreover, geriatric mice after MI showed significant higher levels of active MMP-9 (OM: 0.041±0.013 ng/ml, YM: 0.006±0.010 ng/ml) in plasma 3 days after MI, although total MMP-9 levels did not differ.

Conclusions: We have successfully implemented a geriatric mouse model of MI with common signs of heart failure. Confirmed by MRI, we found significant hemodynamic differences between MI and SHAM groups, and also between OM and YM. We could find first evidence for age dependent differences in TNC production. These alterations should be respected in clinical studies examining the prognostic role of TNC in MI and heart failure. MMP-9 activation may play an important role in adverse post-infarction remodeling in the geriatric heart.

5-5

Differential expression of the plasminogen receptor Plg-RKT in monocyte and macrophage subsets – possible functional consequences in atherogenesis

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Background: Human monocytes can be divided into a classical (CM, CD14++CD16-), a non-classical (NCM, CD14+CD16++), and an intermediate subset (IM, CD14++CD16+) whereby CM are mainly phagocytes, NCM patrol along the endothelium and IM exhibit proinflammatory properties and are associated with inflammatory diseases such as atherosclerosis. Similar to monocytes, macrophages exhibit distinct heterogeneity. M1 macrophages secrete inflammatory cytokines, reactive oxygen species and matrixmetalloproteinases and are possibly involved in plaque vulnerability and destabilization whereas M2 macrophages are anti-inflammatory and linked to plaque stabilization. The plasminogen receptor Plg-RKT might contribute to plaque rupture as it is used together with the receptor of the urokinase plasminogen activator (uPA) uPAR by cells like monocytes and macrophages, to activate plasminogen to plasmin which is then used to degrade extracellular matrix. Here we aimed to analyse the expression of Plg-RKT on monocyte and macrophage subsets.

Methods: PMBCs were isolated from whole blood samples of healthy donors and were stained with fluorochrome-labelled antibodies against CD 14, CD 16, CD45 and Plg-RKT and uPAR and were analyzed with a flow cytometer. Cells were also incubated with FITC labelled plasminogen and stained and measured as described before via flow cytometry. The same experiments were performed with murine blood samples. However, to identify mouse monocyte subsets, CD11b and Ly6-C antibodies were used. Plg-RKT levels were also measured on macrophage subsets via flow cytometry.

Results: IM express the highest levels of Plg-RKT compared to CM ($p<0.0005$) and NCM ($p<0.005$). In addition, IM also bind the highest amounts of plasminogen indicating that they have a higher plasminogen activation capacity in comparison to the other two subsets. IM, in addition, have the highest amounts of uPAR compared to CM ($p<0.05$) and NCM ($p<0.05$). Interestingly, there seems to be a gender dependent difference in Plg-RKT levels with cells isolated from female donors having higher levels of Plg-RKT as compared to male cells. Ly6-C high expressing mouse monocytes are also able to bind higher amounts of plasminogen in comparison to Ly6-C low expressing monocytes ($p<0.05$). M1 macrophages express significantly more Plg-RKT compared to M0 ($p<0.00005$) and M2 ($p<0.005$).

Conclusions: Based on our data one might speculate that besides their inflammatory capacity IM as well as M1 macrophages might also be involved in processes requiring matrix degradation such as plaque destabilization in atherosclerosis.

5-6

The cardiovascular risk marker GDF-15 predicts cancer incidence in patients with type 2 diabetes

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Background: Epidemiologic studies suggest that diabetes is linked to increased cancer incidence and mortality. GDF-15, a biomarker that indicates the severity of cardiovascular diseases, is increased in patients with diabetes and has recently been linked to the occurrence of cancer. The aim of this study was to investigate whether circulating GDF-15 levels can predict the incidence of malignant diseases in a diabetic patient cohort already embracing an increased risk for cancer.

Methods: We prospectively enrolled a total of 919 patients with type 2 diabetes free from cardiac disease and no history of malignant disease, which were clinically followed-up for 60 months. GDF-15, NTproBNP, MR-proANP, MR-proADM, CT-proET-1, Copeptin and hsTnT were measured at baseline. Study

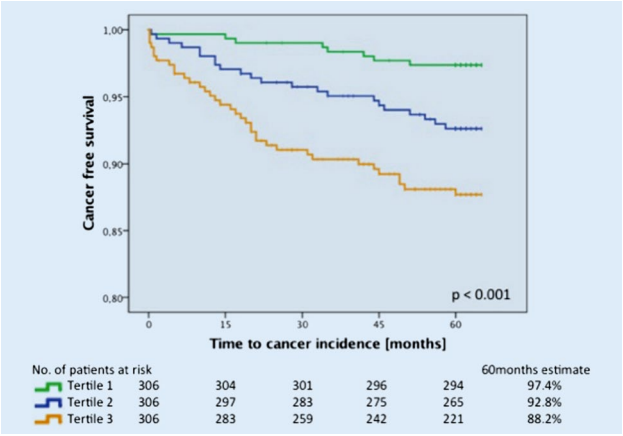

Fig. 1 Cancer free survival rates in patients with type 2 diabetes according to tertiles of GDF-15 levels ($p < 0.001$ between all groups, log-rank test)

endpoint was defined as the first diagnosis of any type of cancer during the follow-up period.

Results: During a median follow-up of 60 months, 66 patients (7.2 %) were diagnosed with cancer. Baseline circulating levels of GDF-15 were more elevated in patients that developed cancer over the follow-up period when compared to cancer-free patients. Elevated levels of GDF-15 were significantly associated with cancer incidence (crude HR per 1-IQR increase 2.13, 95 %CI 1.53–2.97, $p < 0.001$). This effect persisted after multivariate adjustment with an adj. HR of 1.86 (95 %CI 1.22–2.84; $p = 0.004$). Among the additionally tested cardiovascular markers in a subpopulation only CT-proET-1 showed a significant association with future cancer incidence with an unadj. HR of 1.68 (95 %CI 1.02–2.76, $p = 0.042$).

Conclusions: Elevated circulating levels of GDF-15 are associated with increased cancer incidence in patients with type 2 diabetes.

5-7

Attenuation of myocardial and vascular arginase activity by vagal nerve stimulation via a mechanism involving alpha-7 nicotinic receptor during cardiac ischemia and reperfusion

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Background: Electrical vagal nerve stimulation (VNS) protects from myocardial and vascular injury following cardiac ischemia/reperfusion (IR) via a mechanism involving activation of alpha-7 nicotinic acetylcholine receptors (α7 nAChRs) and reduced inflammation. Arginase has been proposed to be involved in development of IR injury and endothelial dysfunction after induction by pro-inflammatory mediators.

Purpose: The present study aimed to clarify (1) whether VNS attenuates IR-induced arginase upregulation in the myocardium as well as aorta and (2) whether this effect is mediated via a mechanism involving activation of the α7 nAChRs.

Methods: Anaesthetized Sprague-Dawley rats subjected to 30 min left coronary artery (LCA) ligation followed by 2 h reperfusion were randomly allocated to: (1) sham operation ($n = 5$); (2) control IR ($n = 10$); (3) VNS ($n = 13$, IR and intact right VNS 0.1–1 mA, 15 Hz throughout IR) and (4) methyllycaconitine ($n = 7$, MLA; 10 mg/kg ip, an α7 nAChRs antagonist) + VNS group. The stimulation was optimized to obtain a 10–20 % reduction in heart rate (HR) from baseline values. Infarct size was determined by triphenyltetrazolium chloride staining and expressed as % of the area at risk. Arginase activity was determined in the myocardium and aorta.

Results: VNS reduced infarct size compared to control IR (41 ± 3 % vs. 66 ± 3 %, $P < 0.001$). Myocardial IR increased arginase activity 1.6-fold ($P < 0.05$ vs. sham) in the myocardium at risk and 3.1-fold ($P < 0.001$ vs. sham) in aorta. VNS attenuated the increase in arginase activity compared to control IR both in the myocardium (1.2-fold vs. 1.6-fold of sham, $P < 0.05$) and in aorta (1.3fold vs. 3.1 fold of sham, $P < 0.001$). The administration of MLA partially abolished the infarct size limiting effect of VNS (55 ± 3 % vs. 66 ± 3 % in control, $P < 0.05$) and completely abrogated the effect of VNS on arginase activity (1.6-fold increase of sham in the myocardium and 2.5-fold increases in aorta), without affecting HR.

Conclusions: VNS reversed the upregulation of arginase not only in the affected organ, but also in the remote vasculature via a mechanism mediated through α7 nAChRs activation. This finding may represent a novel cardiovascular protective effect of VNS mediated via attenuated arginase activity.

5-8

Associations of estradiol, sex hormone-binding globulin and testosterone with circulating levels of amino-terminal pro-B-type natriuretic peptide in postmenopausal women: The Rotterdam study

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Background: Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) has a well-documented prognostic value for cardiovascular disease and sex-hormones are suggested to modulate NT-proBNP levels. However, little data is available on the association of sex-hormones with NT-proBNP in postmenopausal women. Furthermore, age and years since menopause may play a role on these associations, but have not yet been investigated.

Objectives: To assess the relationships between sex-hormones and NT-proBNP in postmenopausal women and whether these associations differ by age and years since menopause.

Methods: We measured estradiol, total testosterone (TT), sex hormone-binding globulin (SHBG) and NT-proBNP in 3139 postmenopausal women (free of cardiovascular disease), participating in the prospective population-based Rotterdam Study. Free androgen index (FAI) was calculated as ratio of TT to SHBG concentration. TT, SHBG, FAI and NT-proBNP were natural log transformed. Regression coefficients and 95 % Confidence Intervals (CI) were calculated using multivariable linear regression models adjusting for confounders

Results: After adjustment for age, body mass index, years since menopause, serum total cholesterol, hypertension, alcohol intake, physical activity, smoking and prevalent diabetes, higher levels of estradiol (per SD increase, β = 0.04; 95 %CI = 0.001 to 0.07) and SHBG (per SD increase, β = 0.17; 95 %CI = 0.13 to

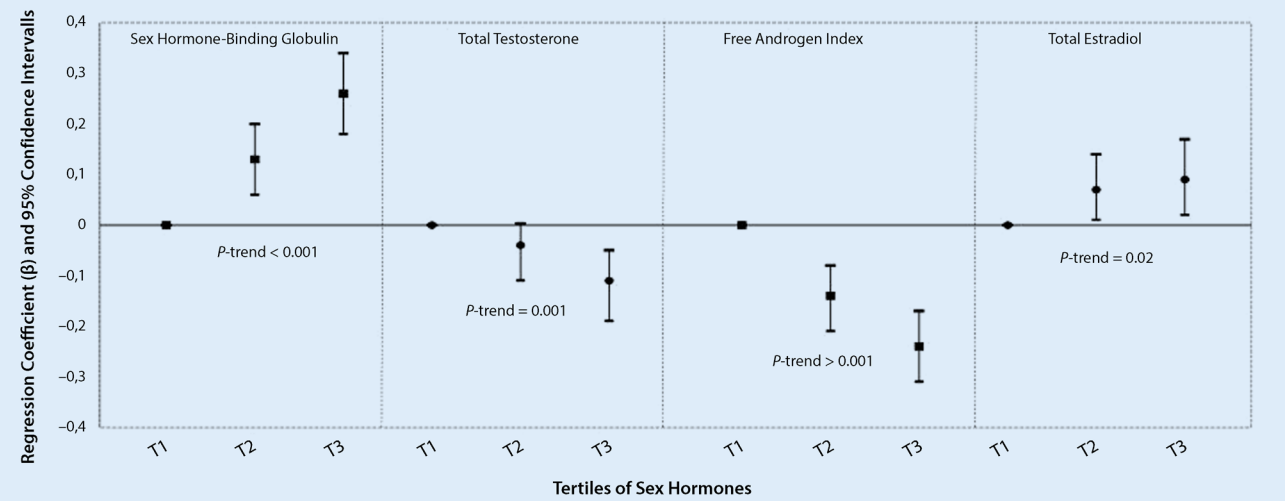

Fig. 1 Associations of sex hormone-binding globulin, testosterone, free androgen index and estradiol, with NT-pro-BNP levels in postmenopausal women, the Rotterdam Study

0.20) were positively associated with NT-proBNP concentrations. In contrast, TT (per SD increase, β = –0.06; 95 %CI = –0.08 to –0.03) and FAI (per SD increase, β = –0.13; 95 %CI = –0.16 to –0.10) were inversely associated with circulating NT-proBNP (both $p < 0.001$). These associations were independent of insulin resistance, C-reactive protein or fatty liver. However, significant interactions were found between estradiol, age (p-interaction = 0.002) and years since menopause (p-interaction = 0.01). After stratification by median-age (68,5 years), the positive association between estradiol and NT-proBNP was present in women 68,5 years or older (per SD increase, β = 0.10; 95 %CI = 0.04 to 0.16) whereas no association was observed in women younger than 68,5. Similarly, the stratification analysis by years since menopause (median) revealed that the positive association between estradiol and NT-proBNP was significant only in women 20 years or further from menopause (per SD increase, β = 0.06; 95 %CI = 0.01 to 0.11).

Conclusions: These findings suggest an association between estradiol, SHBG, and testosterone with circulating NT-proBNP levels among postmenopausal women. This association seems to be modified by age and years since menopause. Further studies are warranted to explore the mechanisms involved in these associations.

Postersitzung 6 – Bildgebung

6-1

A novel oscillometric technique compared with cardiac magnetic resonance for the assessment of aortic pulse wave velocity in ST-segment elevation myocardial infarction

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Background: Pulse wave velocity (PWV) is the proposed gold-standard for the assessment of aortic elastic properties. A recently developed oscillometric device, which allows for non-invasive and cost-effective measurement of aortic PWV, showed a moderate to good agreement with cardiac magnetic resonance imaging (CMR) in healthy volunteers. Now we compared the two methods in patients presenting with ST-segment elevation myocardial infarction (STEMI).

Methods: We assessed aortic PWV in 60 mechanically reperfused STEMI patients using two different methods. The oscillometric method (PWVOSC) is based on mathematical transformation of brachial pressure waveforms, oscillometrically determined using a common cuff (Mobil-O-Graph, I. E. M. Stolberg, Germany). Phase-contrast CMR imaging (1.5 Tesla scanner, Siemens, Erlangen, Germany) at the level of the ascending and abdominal aorta was performed to determine PWVCMR with the use of the transit time method.

Results: The mean age of the study population was 57 ± 11 years; 11 (19 %) were female. Median PWVOSC was 7.4 m/s (IQR 6.8–8.9 m/s) and median PWVCMR was 6.3 m/s (IQR 5.7–8.2 m/s) ($p < 0.001$). A strong correlation was detected between both methods (r = 0.724, $p < 0.001$). Bland-Altman analysis revealed a bias of 0.62 m/s (upper and lower limit of agreement: 3.84 m/s and -2.61 m/s). The coefficient of variation between both methods was 21 %.

Conclusions: In mechanically reperfused STEMI patients, aortic PWV assessed non-invasively by transformation of brachial pressure waveforms showed an acceptable agreement with the CMR-derived transit time method.

6-2

Changes of left ventricular filling and left atrial mechanics following long-distance triathlon

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Background: Maintenance of left ventricular (LV) diastolic filling is a prerequisite for keeping stroke volume (SV) up and to avoid exercise-induced cardiac fatigue during prolonged endurance exercise. So far, left atrial (LA) mechanics have raised little attention as a contributor of LV diastolic filling alterations during prolonged exercise. To this end, the purpose of this study was to assess LV diastolic filling and myocardial LA mechanics before and immediately after a simulated long-distance triathlon using comprehensive echocardiographic imaging.

Methods: Ten well-trained male triathletes (VO_{2peak} = 59 ± 6 $mL \cdot kg^{-1} \cdot min^{-1}$) participated in this study. Each participant completed a 60 min swim, 180 min bike exercise, and a 60 min all out run in a laboratory environment with special attention to adequate hydration matched to the individual sweat rate. All participants underwent echocardiographic analysis of established LV diastolic filling indices, as well as volumetric and largely load-independent speckle-tracking derived strain assessment of LA-reservoir, conduit and contractile function. In addition, laboratory analysis of cardiac enzymes (CK-MB, cTnT, proBNP) prior to and immediately after the exercise protocol was conducted.

Results: troke volume (pre: 108.0 ± 15.9 vs. post: 88.8 ± 19.0 mL; $p = 0.03$) was significantly reduced following the exercise protocol while indices of LV systolic function did not change. Doppler indices of early diastolic filling (E pre: 93.1 ± 9.7 cm/s vs. E post: 71.2 ± 17.9 cm/s; $p = 0.01$) decreased significantly postexercise whereas indices for late diastolic filling did not change. Among the volumetric LA indices only conduit volume (pre: 31.2 ± 7.5 mL vs. post: 22.4 ± 9.8 mL; $p = 0.05$) decreased. Among the speckle-tracking derived indices of LA- reservoir, conduit and contractile function there was a trend of enhanced contractile strain (pre: 15.0 ± 3.6% vs. post: 19.4 ± 4.8 mL; $p = 0.07$). Heart rate (53.1 ± 5.0 vs. 81.9 ± 16.9 beats per minute; $p = <0.0001$) was significantly higher and all cardiac enzymes significantly increased following the exercise protocol.

Conclusions: Comprehensive echocardiographic analysis depicts reduced conduit and compensatory increase in intrinsic myocardial LA contractile function following a long-distance triathlon protocol in well-trained and hydrated athletes. This data suggests that the decline in SV following prolonged exercise is not due to a fatiguing LA. Future studies are required to further understand the mechanisms of postexercise reduction in stroke volume as well as the mechanisms of cardiac enzyme release and thereby reshape the conflicting term exercise-induced cardiac fatigue.

6-3

Diastolic retrograde flow in the descending aorta by cardiovascular magnetic resonance imaging for the quantification of aortic regurgitation

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Background: Echocardiography is the standard method for quantification of aortic regurgitation (AR). However, accurate estimation of the severity of AR by echo may be challenging due to inherent limitations of applied methods. Cardiovascular magnetic resonance imaging (CMR) has recently been advertised as an accurate method for AR quantification, irrespective of acoustic windows.

The present prospective study sought to evaluate the usefulness of CMR for the quantification of AR.

Methods and Results: 2 06 consecutive patients (30% female, 55±21 years old) with varying degrees of AR by echocardiography (83 mild, 52 moderate, and 35 severe, 36 with inconclusive echocardiographic results – "moderate to severe" AR) were invited to undergo CMR within 4 weeks. CMR consisted of standard protocols including phase-contrast velocity-encoded imaging for measurement of regurgitant volume (RegV), and regurgitant fraction (RegF) at the sinutubular junction, and assessment of holodiastolic retrograde flow (HRF) in the descending aorta.

Severe AR was defined as the presence of HRF in the descending aorta by CMR.

Left ventricular (LV) volumes by CMR significantly increased with increasing AR severity by echo (LV end-diastolic volume/body surface area: mild: 77±24 ml/m^2, moderate: 96±28 ml/m^2, "moderate to severe": 106±43 ml/m^2, severe: 124±34 ml/m^2; $p < 0.001$), as did RegV (mild: 6±15 ml, moderate: 15±17 ml, "moderate to severe": 23±20 ml, severe: 48±27 ml; $p < 0.001$) and RegF at the sinutubular junction (mild: 7±15%, moderate: 14±15%, "moderate to severe": 22±17%, severe: 35±15%; $p < 0.001$).

Among the 135 patients with non-severe AR by echo, 11 (8%) had HRF by CMR, indicating severe AR.

Among the 35 patients with severe AR by echo, 12 (34%) did not show HRF by CMR, suggesting overestimation of AR severity in these patients.

In patients with inconclusive echo results, 42% had HRF in the descending aorta, indicative for severe AR.

Presence of HRF by CMR was associated with significantly higher RegF at the sinutubular junction (10±12% versus 37±19%, $p < 0.001$) and more dilated LVs (86±28 ml/m^2 versus 124±41 ml/m^2, $p < 0.001$).

Conclusions: Quantification of AR by CMR is feasible and highly reproducible. HRF in the descending aorta by CMR is an easy marker that helps to distinguish between severe and non-severe AR.

6-4

Prognostic relevance of the pulmonary artery diameter in relation to the ascending aorta

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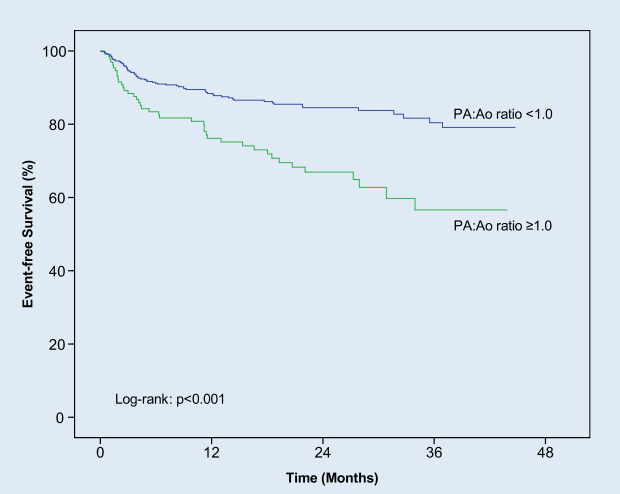
Background: The pulmonary artery (PA) diameter and its relation to the ascending aorta (PA:Ao ratio) by cardiovascular magnetic resonance (CMR) or computed tomography (CT) have been identified as non-invasive markers for pulmonary hypertension in heart and lung disease. However, the prognostic value of such measurements is largely unknown.

Methods and Results: 650 consecutive patients (47.2% female, mean age 56.1±17.1 years) referred to CMR were prospectively enrolled. Diameters of the great arteries were measured in axial black blood images. Based on previous results, a PA:Ao ratio ≥1.0 was chosen as cut-off for further analysis. The primary endpoint was defined as a composite of cardiovascular hospitalization and death.

131 (20.2%) patients presented with a PA:Ao ratio ≥1.0. These patients were more frequently female ($p = 0.010$), pre-



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sented with more atrial fibrillation ($p<0.001$), more diabetes ($p<0.001$), worse renal function ($p<0.001$), higher NT-proBNP levels ($p<0.001$), larger left ($p=0.023$) and right ventricles (RV, $p=0.002$), and worse RV function ($p<0.001$). Patients were followed for 17.8±12.9 months, during which 110 (16.9 %) experienced an event. Kaplan-Meier analysis revealed worse event-free survival rates in patients with a PA:Ao ratio ≥1.0 (log-rank, $p<0.001$). By multivariable Cox-regression analysis, a PA:Ao ratio ≥1.0 was independently associated with outcome, in addition to age, NT-proBNP serum levels, and RV size.

Conclusions: The PA:Ao ratio is an easily measurable parameter by CMR and CT. A ratio ≥1.0 identifies patients at risk, most likely due to elevated pulmonary artery pressures. Based on these results, the PA:Ao ratio should routinely be assessed in CMR and CT scans.

6-5

Impact of posteromedial papillary muscle infarction on mitral regurgitation after ST-segment elevation myocardial infarction

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Background: There is a growing interest in the role of papillary muscle infarction (PMI) as a cause of mitral valve regurgitation (MR) after ST-segment elevation myocardial infarction (STEMI). However, the results concerning the exact role of PMI location are still conflicting. Objectives: We hypothesized that infarction of the posteromedial papillary muscle as determined by cardiac magnetic resonance imaging (CMR) might be associated with an increased incidence of MR after STEMI.

Methods: 242 patients with first STEMI underwent a late-enhancement (LGE-) CMR within a median of 2 (IQR: 2-5) days and echocardiography within 3 (IQR: 2–5) days after primary angioplasty for the index event. PMI was scored based on short axis slices (AL-PMI: anterolateral PMI, PM-PMI: posteromedial PMI, AL/PM-PMI: AL- and PM-PMI).

Results: Patients with PM-PMI had significantly higher odds (OR: 2.62, $p<0.01$) for the occurrence of MR than patients with no-PMI, AL-PMI or AL/PM-PMI. Furthermore, advanced age, non-anterior infarct location and longer pain-to-balloon time were identified as risk factors for the occurrence of MR. Based on this results we established a new score for the risk estimation for MR after STEMI. This score successfully identifies a high risk for MR after STEMI (Chi-square: 30.1, $p<0.001$).

Conclusions: PM-PMI as determined by CMR significantly increases the odds for MR after STEMI. Our data, together with the established score, might help to identify patients at high risk for MR after STEMI and improve our understanding of the dynamic nature of functional MR.

6-6

Relation of inflammatory markers with myocardial and microvascular injury in patients with reperfused ST-elevation myocardial infarction

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Background: In patients with acute ST-elevation myocardial infarction (STEMI), elevated concentrations of inflammatory markers are correlated with worse clinical outcome. The aim of this study was to comprehensively investigate the relationship of circulating markers of inflammation with myocardial and microvascular damage after STEMI.

Methods: In 111 consecutive STEMI patients, blood samples were obtained on admission and from day 1 to day 4 after primary percutaneous coronary intervention (PPCI) and analyzed for high-sensitivity C-reactive protein (hs-CRP), white blood cell count (WBCc) and fibrinogen. Cardiac magnetic resonance imaging was performed within the first week and 4 months after PPCI for assessment of myocardial function and damage.

Results: Peak concentrations of hs-CRP (20.5 [9.6–44.4] mg/L), WBCc (12.4 [10.5–15.3] G/L) and fibrinogen (3640 [3150–4550] mg/L) showed significant correlations with both infarct size ($r=0.31$ to 0.41; $p<0.01$) and left ventricular (LV) ejection fraction ($r=-0.29$ to -0.39; $p<0.01$) assessed in the acute as well as chronic stage following STEMI. Furthermore, peak concentrations of these inflammatory markers were significantly higher in patients with microvascular obstruction (MVO) compared to patients without MVO ($p\leq0.01$). C-statistics revealed that the prognostic values of all three biomarkers for the prediction of large chronic infarct size (>8 % of LV myocardial mass) were moderate without significant differences (area under the curve (AUC): hs-CRP = 0.73 (95 %CI 0.63–0.82), WBCc = 0.67 (95 %CI 0.56–0.78) and fibrinogen = 0.70 (95 %CI 0.59–0.80); all $p>0.12$). Combination of inflammatory markers did not significantly increase the AUC ($p>0.05$).

Conclusions: In STEMI patients treated with PPCI, increased levels of hs-CRP, WBCc and fibrinogen are associated with decreased LV function and more pronounced myocardial damage at baseline and 4 months after infarction.

Tab. 1 Clinical and coronary computed tomography results in patients with angina pectoris an significant reversible ischemia, or possible reversible ischemia or no reversible ischemia on SPECT

	No ischemia in SPECT	Reversible ischemia in SPECT	Possible reversible ischemia in SPECT
Number of patients	*n*=101	*n*=42	*n*=38
Male gender	69 (68.3 %)	33 (78.6 %)	26 (61.9 %)
Age (year)	61 ± 10	64 ± 10	62 ± 13
St.p. AMI	37 (36.6 %)	32 (76.2 %)*	18 (42.9 %)
St. p. Bypass	6 (5.9 %)	0	2 (4.8 %)

6-7

Comparison of 201-Tl-persantin single photon emission computed tomography (SPECT) with contrast enhanced coronary computed tomography

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Background: A stepwise approach to diagnose coronary artery (CAD) disease including medical history and coronary computed tomography (CT) can identify patients with significant CAD but normal stress-test myocardial 201-Tl-Persantin single photon emission computed tomography (SPECT) who may benefit from invasive treatment. The aim of the present monocenter retrospective study was to compare the results of the two main non-invasive diagnostic tests, the SPECT with contrast-enhanced coronary computed tomography (CCTA), delivering functional or morphological information on suspected CAD, respectively.

Methods: Between 2010 and 2015, 181 patients with angina pectoris and suspicious CAD underwent both SPECT and CCTA. The mean time between the 2 investigations were 23±131 days; in most cases (60.2 %), the SPECT was the first investigation, followed by CCTA. Both investigations were performed in a standard manner. Coronary artery calcium score was determined according to the Agatston method. Solid, mixed or calcified plaques, as well as coronary artery occlusion were assessed visually.

Results: Totally, 42 patients (23.2 %) had significant reversible defect on SPECT, while 38 patients (21 %) showed a suspicted reversible defect on the SPECT and 101 patients did not have reversible ischemia. Table 1 lists the clinical characteristics and the results of the CCTA of these three groups of patients. Patients in the definitive reversible ischemia and possible reversible ischemia groups had similarly significantly higher Agatston score reflecting calcified plaques on the CCTA, as compared with the patients with no ischemia on SPECT. Surprisingly low number of patients with definitive reversible ischemia on SPECT (31 %) displayed any kind of plaque on the CCTA, while 21.8 % of patients with no ischemia on SPECT showed plaques on CCTA, in most cases in form of solid plaques; indicating the discordance between the morphological (CCTA) and functional (SPECT) diagnostics of the CAD.

Conclusions: SPECT and CCTA are valuable complimentary investigations for the more exact non-invasive diagnostic of CAD. Further investigations including the gold standard coronary angiography should estimate the predictive values of the combined non-invasive tests.

6-8

Influence of active and passive cardiac implants on CMR image quality

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Background: Cardiac magnetic resonance imaging of patient with active and passive cardiac implants has emerged as being feasible and safe despite previous contraindications. Artifacts caused by the systems containing ferromagnetic material can impair the diagnostic quality. We aimed to provided an overview over imaging quality depending on type of device and imaging sequence.

Material and Methods: 50 patients having been implanted with either a pacemaker, implantable cardiodefibrillator (ICD) or implantable loop recorder (ILR) were evaluated. Patients were scanned in a 1.5T MRI scanner and image quality was graded on a 4-point scale. Steady-state freeprecession and turbo field echo sequences were used to assess cardiac function. For myocardial late gadolinium-enhanced (LGE) imaging, 3D inversion prepared spoiled gradient-echo sequences were used.

Results: CMR was safe in all patients. There were no changes in pacing thresholds, sensing or lead impedance. Imaging artifacts were more prominent in SSFP then in TFE sequences. Devices implanted on the right side of the sternum did not impair image quality. ICD devices created larger artifacts then pacemakers and ILR did not impact imaging at all. Number of evaluable cardiac segments correlated with distance between device and heart.

Conclusions: When adhering to strict safety precautions CMR can be safe and feasible in patients carrying active and passive cardiac devices. While heavily depending on location and type of device imaging quality is generally good enough for diagnostic purposes.

6-9

Akute Herzinsuffizienz und plötzlicher Herztod durch ausgedehnte kardiale Sarkoidose – Ein case report

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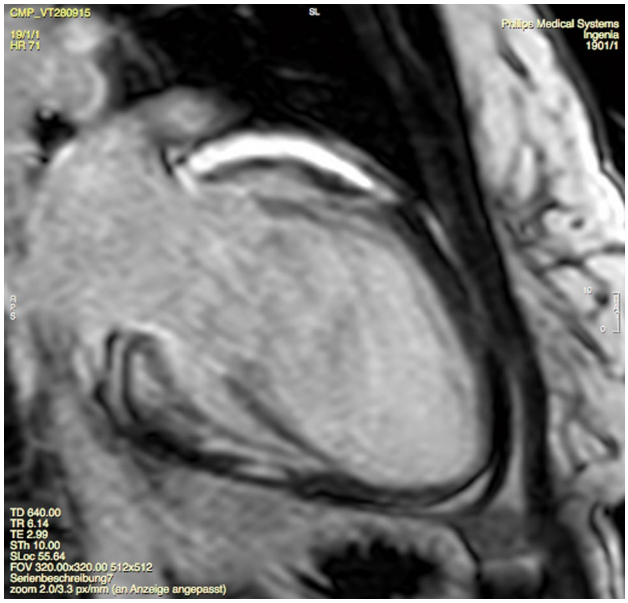
Grundlagen: Eine 50-jährige Frau gelangte aufgrund von seit 2 Wochen bestehender Dyspnoe zur Aufnahme. Als Ursache der Dyspnoe zeigte sich echokardiographisch eine höchst-

gradig reduzierte linksventrikuläre Pumpfunktion bei diffuser Hypokontraktilität. Die Anamnese hinsichtlich eines rezenten Infektes oder Angina pectoris war unauffällig. In der Koronarangiographie konnte eine relevante koronare Herzerkrankung ausgeschlossen werden. Unter Herzinsuffizienz- und Diuretikatherapie besserte sich der Zustand zunächst, nach 1 Woche entwickelte die Patientin allerdings rezidivierend ventrikuläre Tachykardien und musste mehrfach reanimiert werden. Zur weiteren Abklärung wurde sie dann an unser Zentrum transferiert und eine kardiale MRT durchgeführt.

MRT Protocol 1.5T Philips, Achieva scanner.

Sequenzen: T2 BB axial gesamter Thorax, SSFP cines 3 LA, SA Paket, RV 2CV, T2 STIR in 2 SA und 3 LA, Late Gadolinium Enhancement 15min nach KM Gabe.

MRT Befund: Die MRT Untersuchung ergab einen dilatierten LV mit hochgradig reduzierter Pumpfunktion. In den T2 STIR Aufnahmen konnten lediglich geringe v. a. septal betonte Ödemzonen dargestellt werden. Als auffälligster Befund zeigte sich ein ausgedehntes positives Late Gadolinium Enhancement, das sowohl subendokardial als auch subepikardial und intramural lokalisiert war. Insbesondere die basale Hälfte des gesamten Septums und der Vorderwand waren betroffen. Zusätzlich fand sich eine erhebliche RV Beteiligung. Das LGE zeigte eine sehr intensive Signalintensität, sodass aufgrund des diffusen Verteilungsmusters trotz fehlender nodulärer Anteile die Verdachtsdiagnose einer kardialen Sarkoidose gestellt und eine Myokardbiopsie angeschlossen wurde. Histologisch konnte eine granulomatöse aktive Inflammation dargestellt und damit die Verdachtsdiagnose einer kardialen Sarkoidose bestätigt werden. Differentialdiagnostisch kam noch eine Riesenzellmyokarditis in Frage. Diese konnte aber durch ein Referenzlabor histologisch weitgehend ausgeschlossen werden.



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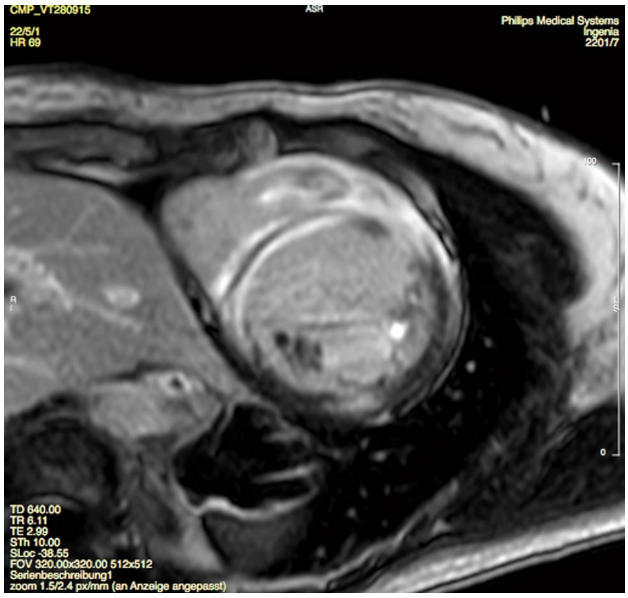

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Schlussfolgerungen: Bei Patienten mit akuter Herzinsuffizienz und malignen Rhythmusstörungen kann die kardiale MRT sinnvoll zur Differentialdiagnostik der zugrunde liegenden Pathologie eingesetzt werden. Anhand des LGE Befundes kann eine gezielte Biopsie erfolgen und hierdurch eine spezifische Therapie ermöglicht werden.

6-10

Vascular strain in Type 1 diabetics at different sites of the vascular tree

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Background: Diabetes mellitus is known to lead to vascular damage in the long-term. In healthy adults circumferential vascular strain differs between various vascular beds. Whether and to which extent these physiological differences still exist in diabetic subjects is not known. The aim of this project was to analyse vascular strain in different parts of the vascular tree in patients with type 1 diabetes mellitus without clinically manifest atherosclerosis.

Methods: In 33 patients with type 1 diabetes mellitus (21 females, 33±11.8 years) vascular strain was determined by speckle tracking. Therefore, the abdominal aorta (AA), the carotid arteries (CCA), femoral arteries (CFA) and popliteal arteries (POP) were assessed by vascular ultrasound. Three clips were recorded at each site for each patient. All investigations were performed in a fasting condition. Impairments in left ventricular ejection fraction were excluded by measuring the N-terminal pro-B-type natriuretic peptide and echocardiography. Hypertension was excluded by patients' history and 24-h-blood pressure investigation and peripheral arterial disease was excluded by ankle-brachial index measurements in all patients.

Results: In 33 patients with type 1 diabetes mellitus 613 of 693 available clips could be analysed. In patients with type 1 diabetes mellitus vascular strain varied between different parts of the vascular tree ($p<0.001$). In particular, vascular strain of elastic arteries (AA 5.6 % [4.15 < IQR < 7.95] and CCA 5.15 % [4.0 < IQR < 7.45]) was higher than vascular strain of muscular arteries (CFA 1.9 % [1.35 < IQR < 2.7] and POP 1.85 % [1.23 < IQR < 2.88], Fig. 1). In none of the arterial segments vascular strain was related to the glycated haemoglobin A1c.

Conclusions: In patients with type 1 diabetes mellitus vascular strain substantially varies along the vascular tree. Further analyses as well as a comparison with non-diabetic subjects are warranted to clarify the impact of these variations in vascular strain on the development of vascular damage in diabetes mellitus.

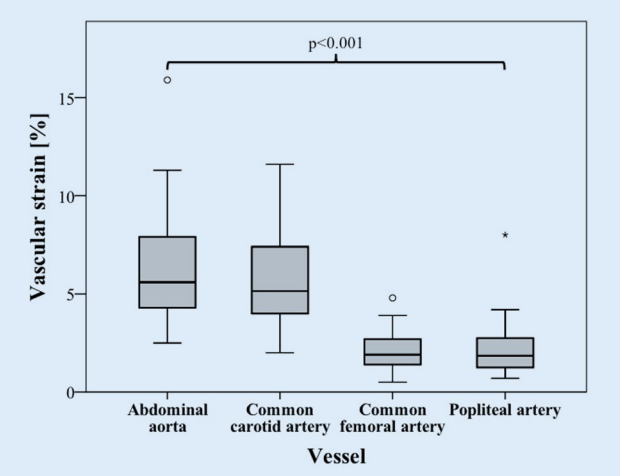

Fig. 1

Postersitzung 7 – Risikofaktoren/Stoffwechsel/Lipide 1

7-1

Non-alcoholic fatty liver disease strongly predicts incident diabetes in patients with coronary artery disease

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Background: Both coronary artery disease (CAD) and non-alcoholic fatty liver disease (NAFLD) are associated with type 2 diabetes. The purpose of this study was to investigate whether NAFLD predicts future diabetes in CAD patients who do not have diabetes.

Methods: We therefore prospectively recorded diabetes incidence in a large cohort of 1018 consecutive non-diabetic patients with angiographically proven CAD; for the diagnosis of NAFLD we used the validated fatty liver index (FLI); diabetes was diagnosed according to ADA criteria.

Results: At baseline, 44.3 % of our patients had impaired fasting glucose (IFG) and 55.2 % had an HbA1c of 5.7–6.4 % and thus were at risk of diabetes according to ADA categories. The prevalence of NAFLD was significantly higher in patients with IFG than in those with normal fasting glucose (46.8 vs. 34.0 %; $p<0.001$) but not between patients with an HbA1c of 5.7–6.4 % and those with an HbA1c <5.7 % (40.8 % vs. 38.5 %; $p=0.478$). Prospectively, 11.2 % of our patients newly developed diabetes during a follow-up period of 6.3±3.7 years; both IFG (OR 3.24 [2.03–3.32]; $p=0.001$) and an Hba1c of 5.7–6.4 % (OR 2.90 [1.50–5.61]; $p=0.002$) significantly predicted incident diabetes. Importantly, diabetes incidence was significantly higher in patients with NAFLD than in those who did not have NAFLD (18.4 vs. 8.5 %; $p<0.001$), and NAFLD strongly predicted incident diabetes both univariately (OR 2.41 [1.56–3.73]; $p<0.001$) and after multivariate adjustment including both baseline fasting glucose and HbA1c (OR 1.76 [1.11–2.79]; $p=0.017$).

Conclusions: We conclude that NAFLD in patients with CAD strongly predicts incident diabetes independently from the baseline glycemic state.

7-2

ProBNP strongly predicts future vascular events in angiographied coronary patients with as well as in those without the metabolic syndrome

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Background: Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker in various patient populations. The purpose of this study was to investigate whether proBNP is also a biomarker to predict cardiovascular events in metabolic syndrome (MetS) patients undergoing coronary angiography.

Methods: We therefore measured serum proBNP in 752 patients who underwent coronary angiography for the evaluation of suspected or established coronary artery disease (CAD). Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing ≥50 %. Presence of the MetS was defined according to the current harmonized consensus definition. Prospectively, we recorded vascular events over 5.1±2.4 years.

Results: ProBNP was significantly higher in patients with ($n=591$) than in subjects without significant CAD at baseline (715±1361 vs. 652±1842 pg/ml; $p=0.003$). Prospectively, we recorded 185 cardiovascular events. The incidence of vascular events significantly increased over tertiles of proBNP in patients with the MetS (15.8 %, 24.2 %, and 60.0 % respectively; $p=0.033$) as well as in subjects without the MetS (13.3 %, 22.2 %, and 64.4 %, respectively; $p=0.004$). Concordantly, serum proBNP significantly predicted the incidence of cardiovascular events after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol, HDL cholesterol and the eGFR both in patients with the MetS (standardized adjusted HR 1.34 [1.14–1.58]; $p<0.001$) and in subjects without the MetS (HR 1.24 [1.11–1.39]; $p<0.001$). These results were not attenuated after further adjustment for the angiographically determined baseline CAD state in patients with the MetS nor in subjects without the MetS (HRs 1.34 [1.14–1.57]; $p<0.001$ and 1.42 [1.24–1.63]; $p<0.001$, respectively).

Conclusions: We conclude that serum proBNP predicts cardiovascular events independently of established cardiovascular risk factors and of the baseline CAD state both in patients with and in subjects without the MetS.

7-3

ProBNP strongly predicts future vascular events in peripheral arterial disease patients with as well as in those without the metabolic syndrome

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Background: Pro B-type natriuretic peptide (proBNP) is an established prognostic biomarker in patients with heart failure. The purpose of this study was to investigate the power of proBNP to predict cardiovascular endoints in peripheral arterial disease (PAD) patients with the metabolic syndrome (MetS).

Methods: We prospectively recorded cardiovascular events over a mean follow-up period of 4.9±1.7 years in a consecutive series of 319 patients with sonographically proven PAD, including 144 subjects with the MetS and 175 without the MetS. Presence of the MetS was defined according to the current harmonized consensus definition.

Results: At baseline, proBNP did not differ significantly between PAD patients with the MetS ($n=144$) and those who did not have the MetS (1037±3386 pg/ml vs. 1027±3864 pg/ml; $p=0.759$). During follow-up, the incidence of cardiovascular events was 57.7 % among PAD patients with the MetS and 46.2 % among PAD subjects without the MetS ($p=0.042$). Serum proBNP significantly predicted the incidence of cardiovascular events after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol, HDL cholesterol and the eGFR both in patients with the MetS (standardized adjusted HR 1.68 [1.30–2.17]; $p<0.001$) and in subjects without the MetS (HR 1.40 [1.17–1.67]; $p<0.001$).

Conclusions: We conclude that proBNP strongly and independently from conventional risk factors predicts future vascular events in PAD patients with the MetS as well as in PAD patients without the MetS.

7-4

Remnant cholesterol predicts the development of type 2 diabetes mellitus in patients with established coronary artery disease

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Background: Remnant cholesterol recently has attracted interest as a marker of cardiovascular event risk and is associated with the metabolic syndrome as well as with type 2 diabetes (T2 DM). The purpose of this study was to investigate whether remnant cholesterol also predicts the development of diabetes in patients who do not have diabetes yet.

Methods: We prospectively recorded incident diabetes over 6.1±3.7 years in 861 consecutive non-diabetic Caucasian patients with angiographically proven coronary artery disease (CAD). Diabetes was diagnosed according to ADA criteria.

Results: At baseline, 41.3 % of our non-diabetic CAD patients had impaired fasting glucose (IFG); remnant cholesterol was significantly higher in IFG than in NFG patients (23±21 vs. 19±22 mg/dl; $p<0.001$). During follow-up, diabetes was newly diagnosed in 111 patients, i. e. in 12.9 % of the study population. Remnant cholesterol strongly predicted diabetes both univariately (OR 1.88 [1.56–2.27]; $p<0.001$) and after multivariate adjustment including both fasting glucose and HbA1c values (OR 1.40 [1.40–2.11]; $p<0.001$).

Conclusions: We conclude that the incidence of diabetes is high in patients with established CAD and that remnant cholesterol strongly and independently predicts the development of diabetes in this population.

7-5

Single and joint effects of obesity and of the metabolic syndrome on the development of diabetes in patients with coronary atherosclerosis

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Background: Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are non-obese. The purpose of this study was to investigate the single and joint effects of obesity and of the MetS on diabetes incidence in patients with angiographically proven coronary artery disease (CAD).

Methods: Diabetes incidence was recorded over 6.1±3.7 years in a large cohort of 1063 patients with angiographically proven CAD. Obesity was defined as a BMI ≥30 kg/m^2; presence of the MetS was defined according to the harmonized consensus definition.

Results: From our patients, 698 were non-obese and did not have the MetS, 62 were obese but did not have the MetS, 184 were non-obese but had the MetS, and 119 were obese and had MetS. During follow-up, the overall incidence of diabetes was 12.1 %, corresponding to 1.9 % per year. Diabetes incidence was 6.7 % in non-obese patients without the MetS. It was significantly higher in obese patients without the MetS (16.0 %; $p<0.001$), in non-obese patients with the MetS (22.3 %; $p=0.009$), and in obese patients with the MetS (24.4 %; $p<0.001$). Diabetes incidence however did not differ significantly between obese or non-obese MetS patients ($p=0.303$) or between obese patients with and obese patients without the MetS ($p=0.674$).

Conclusions: We conclude that the incidence of diabetes in patients with CAD is high, except among subjects who neither are obese nor have the MetS. Both obesity and the MetS increase diabetes risk; a metabolically healthy obese phenotype does not protect against the development of diabetes in this population.

7-6

The power of thyroid stimulating hormone to predict cardiovascular mortality in non-obese patients is significantly modulated by type 2 diabetes

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Background: Elevated thyroid stimulating hormone (TSH) is associated with cardiovascular risk factors, in particular with hypercholesterolemia, diabetes and obesity. The purpose of this study was to investigate the association between TSH and cardiovascular mortality in non-obese patients with or without type 2 diabetes (T2 DM).

Methods: We measured TSH in a high-risk cohort of 1741 non-obese patients undergoing coronary angiography for the evaluation of suspected coronary artery disease. Prospectively, the incidence of vascular events was recorded over 10 years.

Results: At baseline, TSH was not significantly different between patients with T2 DM ($n=502$) and those who did not have T2 DM (2.31±4.59 vs. 2.06±2.66 µU/ml; $p=0.446$). During follow-up, 553 patients suffered vascular events; the event rate was significantly higher in patients with T2 DM than in non-diabetic subjects (40 % vs. 29 %; $p<0.001$). TSH proved to be a strong and independent predictor of vascular events in non-obese patients without T2 DM (standardized adjusted HR 1.34 [1.03–1.66]; $p=0.013$), but not in those with T2 DM (HR 0.963 [0.894–1.037]; $p=0.315$). An interaction term TSH x T2 DM was significant ($p=0.026$), indicating that TSH was a significantly stronger predictor of vascular events in non-obese subjects without T2 DM than in those with T2 DM.

Conclusions: We conclude that the power of thyroid stimulating hormone to predict cardiovascular mortality in non-obese patients is significantly modulated by the presence of T2 DM.

7-7

The visceral adiposity index predicts cardiovascular events both in coronary artery disease patients with and in coronary artery disease patients without diabetes

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Background: The visceral adiposity index (VAI) is a validated tool for the evaluation of visceral adiposity, using waist circumference, serum triglycerides, age and gender to diagnose this metabolic abnormality. It has recently been associated with cardiovascular risk in primary care patients. The purpose of this study was to investigate the association of the VAI with mortality in patients with established CAD.

Methods: We therefore calculated the VAI in 1472 consecutive patients with angiographically proven stable CAD according to the Amato formula. T2 DM was defined according to the ADA definition. The incidence of vascular events was recorded over 10 years.

Results: At baseline, the VAI was significantly higher in CAD patients with T2 DM than in those without diabetes (362±330 vs. 247±224; $p<0.001$). Prospectively, 539 vascular events occurred; the event rate were significantly higher in patients with T2 DM than in those who did not have diabetes (44.8 % vs. 33.7 %; $p<0.001$). The VAI significantly predicted cardiovascular events in CAD patients with T2 DM (standardized adjusted hazard ratio (HR) 1.16 [1.01–1.33]; $p=0.037$) as well as in those without T2 DM (HR 1.14 [1.02- 1.27]; $p=0.018$).

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

7-8

Adiponectin and mortality in smokers and non-smokers of the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study

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Background: Cardiovascular diseases (CVD) are an important cause of morbidity and mortality worldwide. Decreased concentrations of adiponectin have been reported in smokers. Aim of our study was to analyze the effect of cigarette smoking on the concentration of adiponectin and potassium in active smokers (AS) and life-time non-smokers (NS) of the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study as well as their use for risk prediction.

Methods: Smoking status was assessed by a questionnaire and measurement of plasma cotinine concentration. Adiponectin serum concentrations were measured by ELISA. Adiponectin was binned into tertiles separately for AS and NS and Cox regression was used to assess the effect on mortality.

Results: 777 LURIC patients were AS and 1178 NS. Within 10 years (median) of follow-up 221 AS and 302 NS died. In unadjusted analyses AS had lower concentrations of adiponectin. However, after adjustment for age and gender there was no significant difference in adiponectin concentration anymore. In a Cox regression model adjusted for age and gender adiponectin was significantly associated with mortality only in AS with a HR (95 % CI) of 1.60 (1.14–2.24) comparing the 3rd with the 1st tertile, but not in NS. In a model additionally adjusted for the risk factors diabetes mellitus, hypertension, coronary artery disease, body mass index, LDL-cholesterol and HDL-cholesterol adiponectin was significantly associated with mortality with HR of 1.83 (1.28–2.62) and 1.56 (1.15–2.11) for AS and NS, respectively.

Conclusions: Increased adiponectin is a strong and independent predictor of mortality both in NS and AS and its determination could be used to identify individuals at increased risk.

7-9

The renin-angiotensin-aldosterone system in smokers and non-smokers of the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study

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Background: High concentrations of renin and aldosterone are risk factors for cardiovascular diseases (CVD) which are the leading cause of morbidity and mortality worldwide. Enhanced activation of the renin-angiotensin-aldosterone system (RAAS) by cigarette smoking has been reported. Aim of our study was to analyse the effect of cigarette smoking on parameters of the RAAS in active smokers (AS) and life-time non-smokers (NS) of the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study as well as the utility of RAAS parameter for risk prediction.

Methods: We determined the concentration of aldosterone, renin, angiotensin-I and angiotensin-II in participants of the LURIC study. Smoking status was assessed by a questionnaire and measurement of plasma cotinine concentration. Parameters were log transformed before entering analyses, where appropriate. We used a multivariate Cox regression analysis to assess the effect of parameters on mortality.

Results: From 3316 LURIC participants 777 were AS and 1178 NS. Within a median observation period of 10 years 221 (28.4 %) AS and 302 (25.6 %) NS died. After adjustment for age, gender and the use of anti-hypertensive medication only angiotensin-I was significantly different in AS compared to NS with an estimated marginal mean (95 % CI) of 1607 (1541–1673) ng/L and 1719 (1667–1772) ng/L, respectively. For both NS and AS renin and angiotensin-II were directly associated with mortality in the multivariate Cox regression analysis. Angiotensin-was only associated with an increased risk for mortality in NS (HR (95 % CI) of 0.66 (0.51–0.85)).

Conclusions: Increased renin and angiotensin-II are independent predictors of mortality in AS and NS while angiotensin-I was associated with reduced risk of death in NS only.

Postersitzung 8 – Interventionelle Kardiologie 1

8-1

Pre-interventional sST2 plasma concentration predicts one-year-mortality after transcatheter aortic valve implantation (TAVI)

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Background: Degenerative aortic valve stenosis is the leading valvular heart disease worldwide. Transcatheter aortic valve implantation (TAVI) is a relativly new procedure for valve replacement in high risk patients who are not suitbable for conventrional aortic valve replacement. sST2 has been introduced as a novel biomarker in patients suffering from heart failure for better risk stratification. We sought to investigate in our study whether sST2 can serve as a useful biomarker for the prediction of mortality of patients undergoing TAVI because of severe aortic stenosis.

Methods: 274 patients (149 female; age 80.50 ±0.51 SEM; EUROSCORE 23.83 ±1.65 SEM) that underwent TAVI procedure and were followed-up over 12 months were retrospectively investigated in this study. Plasma samples were evaluated for sST2 using commercially available ELISA kits.

Results: Plasma sST2 concentration correlated significantly with left ventricular ejection fraction (-0.21; $p=0.001$) and EUROSCORE (r = 0.18; $p=0.006$). Patients were divided in two groups: patients with sST2 plasma concentration below and above the cohort's median (6370 pg/ml): patients with sST2 plasma concentration above the median evidenced a significantly increased one-year-mortality rate after TAVI (22 % vs. 40 %, $p<0.05$). ROC and "area under the curve" calculation to evaluate sST2 for its prognostic relevance (AUC 0.67 95 % CI 0.59–0.75; $p<0.001$) and to compare it with other tools for risk assessment like the EUROSCORE (AUC 0.60 95 %CI 0.52–0.69; $p=0.02$) were performed. In a multivariate COX regression analysis and after correction for EUROSCORE, diabetes, mean aortic valve pressure gradient, CRP, renal function, coronary heart disease, arterial hypertension, besides pre-interventional left ventricular ejection fraction (RR 0.98 95 %CI 0.97- 0.99) and major vascular complications (RR 3,70 95 %CI 1,45–9,44) only a sST2 plasma-concentration above the median (RR 2.62 95 %CI (1.30–5.31); $p=0.007$) remained significantly associated with an elevated one-year-mortality after after TAVI.

Conclusions: Patients with a plasma sST2 concentration above the median (6370 pg/ml) evidenced a 2.6-fold increase of one-year-mortality after TAVI. sST2 plasma concentration remained predictive for mortality even after correction for relevant laboratory and echocardiographic parameters. We assume based on these results that sST2 could serve as very helpful indicator for assessing patients' risk before undergoing TAVI procedure. Measurements of pre-interventional biomarkers in patients undergoing TAVI could provide extra information. Comprehensive assessment of the patient's cardiovascular risk profile could be substantiated by measurement of plasma sST2 concentration.

8-2

TAVI leads to a peri-procedural increase of biomarker sST2 through hemodynamic stress but failed to alter sST2 concentration in the long term

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Background: Aortic valve stenosis due to calcification is the leading valvular heart disease in elderly patients. sST2 has been introduced as a novel biomarker in patients suffering from heart failure for better risk stratification. Here in this study we sought to investigate whether there are procedure related undulations in sST2 plasma concentration after TAVI and how aortic valve replacement does affect sST2 levels in the long term. Secondly we analyzed whether increases in ST2 plasma concentrations are associated with changes in circulatory levels of pro-inflammatory cytokines.

Methods: Plasma samples of 79 patients (30 female, age 80.5 ±0.5 years; EUROSCORE 23.83 ±1.65) undergoing TAVI were obtained before TAVI and after seven days, one, three and six months. Plasma levels of sST2, IL-33, IL-1beta and TNF-alpha were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit.

Results: TAVI significantly reduced mean aortic valve pressure gradient from 46.08 mmHg (±1.06 mmHg SEM) to 10.66 mmHg (±0.36 mmHg SEM) ($p<0.05$). sST2 plasma concentration before TAVI at baseline was 7235.66 pg/ml (±4015.36 pg/ml SEM) and significantly increased to 9479.91 pg/ml (±6685.90 pg/ml SEM, $p=0.01$) after seven days. After one month sST2 plasma concentration returned to baseline and remained there: One month after TAVI plasma ST2 levels declined to 7368.48 pg/ml (±3648.46 pg/ml SEM), to 7082.54 pg/ml (±3807.92 pg/ml SEM) after three months and to 7062.89 pg/ml (±3146.20 pg/ml SEM) after six months. Plasma concentration of IL-33 (235.81 pg/ml ±82.26 pg/ml SEM), IL-1beta (3.23 pg/ml ±1.04 pg/ml SEM) and TNA-alpha 3.85 pg/ml ±8.5 pg/ml SEM) remained unchanged by TAVI and stayed stable in the course.

Conclusions: TAVI is effective for aortic valve replacement in symptomatic patients suffering from severe aortic stenosis and is associated with a peri-procedural increase of sST2. As plasma levels of IL-33, IL-1beta and TNF-alpha remained stable throughout the entire follow-up period we speculate that this increase is caused by peri-interventional hemodynamic stress during TAVI.

Interestingly although the hemodynamic situation was significantly improved by TAVI, aortic valve replacement failed to decrease sST2 in the long-term. We speculate that additional factors and conditions, such as comorbidities, superimpose the hemodynamic improvement through TAVI.

8-3

Transcatheter aortic valve implantation without balloon valvuloplasty is not associated with transient left ventricular dysfunction

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Background: Aortic valve stenosis is the most common valvulopathy in developed countries. Transcatheter aortic valve implantation (TAVI) is an alternative for valve replacement even in patients not suitable for conventional open heart surgery. Balloon valvuloplasty under rapid ventricular pacing has been a routine part of TAVI. However, it carries substantial risks and therefore an increasing number of operators have started to refrain from it. A transient decrease of left ventricular function after TAVI with rapid pacing as well as myocardial injury was observed in previous studies. In our study we investigated if TAVI without prior balloon valvuloplasty ("direct TAVI") was associated with a similar increase in cardial biomarkers and decrease in ejection fraction.

Methods: A total of 164 consecutive patients (mean age 83 ± 0.43 SEM; 61 % female, pBNP 4522.12 pg/ml ± 535.50 SEM, Hb 12.30 mg/dl ± 0.14 SEM) undergoing transcatheter aortic valve implantation without balloon angioplasty at a single-centre between April 2013 and September 2014 were followed up for one year and were retrospectively analyzed regarding mortality, safety and efficacy endpoints as well as common laboratory and echocardiographic values.

Results: According to the VARC2 (Valve Academic Research Consortium) 89.1 % of patients remained free of a combined safety endpoint and technical success rate was 96.3 %. Mortality rates at 30 days ($n=114$) and 1 year were 3.0 % and 10.5 %, respectively.

TAVI without tachycardic pacing was highly effective in lowering aortic valve peak velocity from 4.36 m/sec (± 0.06 SEM) to 1.69 m/sec (±0.04 SEM). Left ventricular function remained unaltered four to eight hours after the intervention (50.64 % ± 0.80 SEM vs. 50.86 % ± 0.75 SEM) whereas high sensitive troponin T (ng/l) as a well established marker for myocardial injury increased significantly from 46.71 ± 7.65 SEM to 134.63 ± 6.73 ($p<0.05$) during this time. However, this rise in hs-troponin concentration was distinctly lower than the previously reported seven to fourteen fold increase in procedures with balloonvalvuloplasty.

Conclusions: TAVI using a self expanding system without prior balloon dilatation under tachycardic pacing is feasible, safe and effective for aortic valve replacement in symptomatic patients with severe aortic stenosis. Mortality and safety resulted in similar outcomes as the frequently used approach with tachycardic pacing. In contrast to a cohort of patients who underwent tachycardic pacing previously published by another center, our cohort did not suffer from transient impairment of left ventricular function. As marker of myocardial injury, hs-troponin, showed a less pronounced increase than reported previously which might lead to a prognostic benefit as troponin was shown to be a strong predictor of outcome. We therefore conclude that "direct TAVI" is a less invasive option involving less myocardial stress and might therefore be better suited for the elderly and multimorbid.

8-4

Einfluss der Transkatheter-Aortenklappen-Implantation (TAVI) auf endotheliale und thrombozytäre Mikropartikel bei Patienten mit hochgradiger Aortenklappenstenose

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Einleitung: Die degenerative, kalzifizierende Aortenklappenstenose (AS) ist die häufigste erworbene Herzklappenerkrankung weltweit. Unbehandelt ist sie mit einer hohen Mortalität verbunden. Es ist bekannt, dass eine AS mit einer vermehrten endothelialen Dysfunktion in Zusammenhang steht. Vorangegangene Studien haben gezeigt, dass die endotheliale Dysfunktion mit einer erhöhten Konzentration von endothelialen und thrombozytären Mikropartikelen (EMP und PMP; endothelial/platelet microparticles) einhergehen kann. Ziel dieser Studie war herauszufinden, inwiefern eine TAVI Prozedur einen Einfluss auf zirkulatorische Level von EMP und PMP hat und so möglicherweise zu einer Reduktion der endothelialen Dysfunktion während einer Follow-up Phase von 6 Monaten beiträgt.

Methodik: 92 Patient mit der Diagnose einer hochgradigen symptomatischen AS, die sich einer TAVI unterziehen sollten wurde in diese Studie eingeschlossen. Plasmaproben wurden von allen Patienten vor TAVI und zu jedem Kontrolltermin nach einer Woche, einem, drei und sechs Monaten gewonnen und mittels Durchflusszytometrie auf EMP und PMP untersucht.

Ergebnisse: Die Konzentration an CD62E+ EMP vor TAVI war 21,11 % (±6,6 % Standardabweichung, SD) und verringerte sich auf 20,99 % (±6,8 % SD) nach einer Woche, auf 16,63 % (±5,4 % SD, $p<0{,}0001$) nach einem Monat, auf 17,08 % (±4,6 % SD, $p<0{,}0001$) nach drei Monaten und auf 15,94 % (±5,4 % SD, $p<0{,}0001$) nach sechs Monaten. Die Durchführung der TAVI hatte keinen Einfluss auf CD31+/CD42b-, CD31+/Annexin+/- EMP ($p=$ns). Ein geringer, jedoch statistisch signifikanter Anstieg fand sich für CD31+/CD41b+ PMP nach der TAVI und während des gesamten Follow-ups.

Schlussfolgerungen: Neben einer Verbesserung der echokardiografischen Parameter durch die TAVI Prozedur, kam es zu einer Verringerung der endothelialen Dysfunktion in Zusammenhang mit einer damit einhergehenden Reduktion an CD62E+ EMP im Plasma der Patienten. Wir gehend davon aus, dass die Reduktion der trans-valvulären Gradienten durch die TAVI einen positiven Effekt auf Scherkräfte hatte und dies zu einer Abnahme der EMP führte.

8-5

Einfluss von linksventrikulärer Auswurffraktion und Diabetesstatus auf das Langzeit Outcome nach interventioneller ungeschützter Hauptstammintervention – ein retrospektives Langzeit Follow-up

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Grundlagen: Durch die demographische Entwicklung wird es in naher Zukunft zu einer deutlichen Zunahme der koronaren Herzkrankheit mit konsekutivem Anstieg von signifikanten Hauptstammstenosen kommen wird. Wenngleich ungeschützte Stenosen des linken Hauptstammes laut aktuellen Guidelines eine Domäne der chirurgischen Revaskularisation darstellen, ist es durch die technischen Entwicklungen der interventionellen Kardiologie dazu gekommen, dass immer häufiger Stenosen in dieser Lokalisation – gerade bei älteren oder multimorbiden Patienten – auch mittels Stentrevaskularisation saniert werden. In unserer Untersuchung evaluierten wir, ob Patienten unabhängig von ihrer linksventrikulären Auswurffraktion (LVEF) und ihrem Diabetesstatus von einem interventionellen Eingriff in gleichem Maße profitieren.

Methodik: Es wurden Patienten aus dem UNPROLEMA (UNPROtected LEft MAin disease) Register für ungeschützte Hauptstamminterventionen des Kepler Universitätsklinikums analysiert, die sich zwischen 11/2002 und 12/2013 einer ungeschützten Hauptstammintervention unterzogen hatten. Dabei wurden im Rahmen des Registers die Patientendaten durch Informationen aus Krankengeschichten sowie aus strukturierten Telefon-Interviews und Meldeamtsanfragen bzgl. Follow-up komplettiert. Die Patienten wurde gemäß ihrer LVEF und ihres Diabetesstatus (DM) in 4 Gruppen unterteilt: 1 = normale LVEF > 55 % ohne DM, 2 = eingeschränkte LVEF < 55 % ohne DM, 3 = DM mit LVEF > 55 %, 4 = DM mit LVEF < 55 %. Die Gesamtmortalität und das Auftreten von major adverse cardiac and cerebrovascular events (MACCE: definiert als STEMI, NSTEMI, 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 ermittelt. Schließlich wurde ein Cox Proportional Hazards (CPH) Model für das Auftreten von MACCE berechnet, in dem für potentielle Confounder wie Alter, Geschlecht, Nierenfunktion und kardiale Risikofaktoren adjustiert wurde.

Ergebnisse: Im genannten Zeitraum erhielten 256 Pat. eine ungeschützte Hauptstammintervention (Alter 71,0±10,4 Jahre, 30,9 % weiblich, 47 [18,4 %] nicht insulinpflichtige, 11 [4,3 %] insulinpflichtige Diabetiker), die sich auf die 4 Gruppen wie folgt aufteilten: 1 = 138 Pat., 2 = 60 Pat., 3 = 32 Pat., 4 = 26 Pat. Während einer medianen Follow-up Zeit von 4,1 Jahren (IQR: 2,0–7,0, Spannweite: 0–12) unterschieden sich die Kaplan-Meier Kurven für Tod jedweder Genese signifikant ($p<0{,}001$), wobei Pat. aus der Gruppe 1 ein besseres Überleben aufwiesen als die der Gruppen 3, und jene wiederum ein besseres Überleben als die der Gruppen 2 und 4. Von der Analyse der MACCE mussten 12 Pat. (4,7 %) ausgeschlossen werden, die am Leben waren, für die aber keine Follow-up Daten erhebbar waren. Auch die Wahrscheinlichkeit für das Auftreten von MACCE unterschied sich signifikant zwischen den Gruppen ($p=0{,}006$), wobei die Inzidenz in der Reihenfolge von Gruppe 1 zu 3 und nochmals zu 2 und 4 zunahm. In einem CPH Model zeigte sich entsprechend der zunehmend Risikokonstellation (von Gruppe 1 zu 3, 3 zu 2 und 2 zu 4) ein zunehmendes Risiko der Entwicklung von MACCE (HR 1,29, 95 % CI: 1,08–1,53, $p=0{,}004$).

Schlussfolgerungen: Eingeschränkte Linksventrikelfunktion und das Vorliegen eines Diabetes mellitus waren in unserer Kohorte von Patienten mit ungeschützter Hauptstammrevaskularisation mit einer erhöhten Mortalität sowie dem vermehrten Auftreten von MACCE assoziiert.

8-6

Bleeding and vascular complications after radial and femoral coronary catheterization in patients with acute coronary syndrome

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Background: The debate about the optimal vascular access for coronary catheterization in patients with acute coronary syndrome (ACS) is discussed controversially and the femoral approach remains the predominant access in many countries. Recent studies suggest lower bleeding and vascular complication rates with the radial technique. The aim of this study was to investigate the bleeding and vascular complication rates of the radial and femoral coronary catheterization technique in an unselected, all-comers study population with ACS.

Methods: Between January 1st, 2007 and December 31st, 2014, all consecutive patients with ACS (ST-segment elevation myocardial infarction (STEMI), non-STEMI, unstable angina pectoris (UAP)) undergoing diagnostic coronary catheterization and percutaneous coronary intervention (PCI) were enrolled in this retrospective, single-center, observational study. Vascular complications were defined as pseudoaneurysm, retroperitoneal haematoma, arteriovenous fistula and haematoma with a diameter >5 cm. Bleeding events were classified according to the TMI bleeding criteria as major and minor TIMI bleedings.

Results: 4506 patients with ACS (STEMI: 32.8 %, non-STEMI 35.2 %, UAP: 32.0 %) underwent coronary catheterization (femoral: 66.2 %, radial: 33.8 %) within the observation period. PCI was performed significantly more often in the femoral group compared to the radial group (75.4 % vs 70.2 %, $p<0.001$). Patients in the femoral group were older (67.3+/–12.3 vs 65.7+/–12.7 years, $p=0.04$) and the incidence of cardiogenic shock was significantly higher (5.1 % vs 2.0 %, $p<0.001$). We observed significantly fewer vascular complications with the radial coronary catheterization technique compared to the femoral technique (1.0 % vs 5.0 %, OR 0.20, 95 % CI 0.12–0.34, $p<0.001$), in particular fewer pseudoaneurysms (4 vs 77), retroperitoneal haematomas (0 vs 11), arteriovenous fistulas (0 vs 2) and haematomas with a diameter >5 cm (7 vs 52). While there occured 8 major TIMI bleeding events (0.27 %) in the femoral group, there were none in the radial group ($p=0.058$). The incidence of minor TIMI bleedings (0.1 % vs 1.6 %, OR 0.08, 95 % CI 0.02–0.35, $p<0.001$) and the in-hospital mortality (0.8 % vs 2.5 %, OR 0.31, 95 % CI 0.17–0.58, $p<0.001$) were significantly lower in the radial group.

Conclusions: Radial coronary catheterization may reduce severe bleeding and vascular complications in patients with ACS. However, the observed increased in-hospital mortality of patients with a femoral approach might be a consequence of a higher incidence of patients with cardiogenic shock in the femoral group.

8-7

Todesursachenanalyse von Patienten nach interventioneller ungeschützter Hauptstammintervention – ein retrospektives Langzeit-Follow-up

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Grundlagen: Gerade bei älteren Patienten mit einer Hauptstammstenose ist eine interventionelle Sanierung aufgrund meist zahlreicher Komorbiditäten und folglich erhöhtem perioperativen Risiko attraktiv. Das wird auch von den aktuellen Guidelines befürwortet. Wir evaluierten, ob alle Patienten, unabhängig vom Lebensalter, in gleicher Weise von diesem Eingriff profitieren und an welchen Erkrankungen die Patienten letztendlich versterben.

Methodik: Daten aus dem UNPROtected LEft Main (UNPROLEMA) Register des Kepleruniversitätsklinikums von Patienten, die sich zwischen 11/2002 und 12/2013 einer ungeschützten Hauptstammintervention unterzogen haben, wurden analysiert. Die Follow-up Daten wurden mittels Durchsicht der verfügbaren Krankengeschichten, eines strukturierten Telefon-Interviews sowie mittels Anfragen beim Meldeamt erhoben. Die Gesamtsterblichkeit und das Auftreten von Major Adverse Cardiac and Cerebrovascular Events (MACCE) wurde mittels Kaplan-Meier Analysen – stratifiziert für die Altersquartilen – evaluiert. Als MACCE wurden folgende Ereignisse klassifiziert: STEMI, NSTEMI, aortokoronare Bypassoperation, Re-Intervention im Zielgefäß, TIA/Insult und Tod jedweder Ursache. Der Log-rank Test wurde zur Evaluierung eines statistisch signifikanten Unterschiedes herangezogen. Die Todesfälle wurden nach Ursachen aufgeschlüsselt.

Ergebnisse: Von den 256 untersuchten Patienten mit ungeschützten Hauptstamminterventionen verstarben insgesamt 89 (34,8 %) im Beobachtungszeitraum von bis zu 10 Jahren. Das mittlere Alter war bei 71,0 ± 10,4 Jahre (Altersquartilen: Q1 bis 63,1, Q2 bis 73,3 Jahre, Q3 bis 79,0 und Q4 über 79,0 Jahre). Die Kaplan-Meier-Überlebensanalyse zeigte einen signifikanten Anstieg der Mortalität mit steigender Altersquartile ($p<0{,}001$).

Von den 256 Patienten konnten 12 Patienten nicht nachverfolgt werden, wobei anhand der Meldeamtsanfragen erhebbar war, dass diese nicht verstorben waren. Diese wurden von der Analyse der MACCE-Daten ausgeschlossen. Von den verbliebenen 244 Patienten betrug die mediane Follow-up-Zeit 4,1 Jahre (IQR: 2,0–7,0; Spannweite 0–12). Die Kaplan-Meier-Analyse konnte einen statistisch signifikanten Anstieg der MACCE-Rate mit steigender Altersquartile zeigen ($p=0{,}005$). In einem multivariaten Cox-Regressionsmodell zeigte sich nach Adjustierung für potentielle Confounder wie linksventrikuläre Auswurffraktion, Diabetes mellitus und glomeruläre Filtrationsrate eine Hazard Ratio von 1,3 für das Auftreten von MACCE pro Anstieg einer Altersquartile (95 % KI: 1,06–1,65; $p=0{,}014$).

Die Auswertung der Todesursachen ergab, dass 56 Patienten (62,9 %) an kardialer Erkrankungen verstorben sind und 33 (37,1 %) der Patienten an nicht kardialen Ursachen. 6 Patienten verstarben an einer malignen Erkankung (6,7 %), 4 an neurologischen Ursachen (4,5 %), 8 im Rahmen einer Infektion (9,0 %), 4 an einem Trauma (4,5 %) und 11 an anderen oder unbekannten Ursachen (12 %). Von den 7 Patienten (2,7 %), die im

Rahmen des Indexaufenthaltes verstarben, erfolgte bei 3 die Hauptstammrevaskularisation aufgrund eines STEMIs (einmal in kardiogenem Schock), ein Patient verstarb an einer dekompensierten Herzinsuffizienz und 3 an einer Stentthrombose.

Schlussfolgerungen: MACCE-Raten und Mortalitätsrisiko nach ungeschützter Hauptstamm-Intervention steigen in Abhängigkeit von dem Alter des Patienten trotz niedriger intraprozedurale Mortalität an. Etwa zwei Drittel aller Patienten verstarben nach Hauptstammintervention an kardialen Ursachen.

Postersitzung 9 – Akutes Koronarsyndrom 2

9-1

ATTAIN-Registry: Use of P2Y12-inhibitors in patients presenting with acute coronary syndrome in Austria

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Background: Both novel P2Y12-inhibitors (Prasugrel and Ticagrelor) have been shown to be superior compared to Clopidogrel. We sought to assess the prescription rate of the new P2Y12-inhibitors in patients presenting with ACS and its predictive parameters in Austrian PCI centres.

Methods: In this prospective multi-centre registry patients presenting with ACS at the emergency department at three Austrian hospitals were included. Platelet specific treatment strategies at admission and discharge were assessed in order to evaluate their guideline conform use.

Results: 601 patients were included from January until June 2015, 34.3 % were female. 298 (49.6 %) were diagnosed with ST-elevation myocardial infarction, 303 (50.4 %) with non-ST-elevation-ACS (NSTE-ACS).

87 (14.5 %) of all patients had either an absolute contraindication against Prasugrel or Ticagrelor or atrial fibrillation.

At discharge 189 (31.4 %) received Clopidogrel, 154 (25.6 %) Prasugrel, 193 (32.1 %) Ticagrelor and 31 (5.2 %) had no P2Y12-inhibitor. Of those who received Clopidogrel, 124 (20.6 % of all patients) had neither an absolute contraindication against a new P2Y12-inhibitor, nor atrial fibrillation. In multivariate logistic regression analysis predictive factors for use of Clopidogrel were NSTE-ACS (OR = 2.26 [1.40–3.64]; $p = 0.001$), hypertension (OR = 1.77 [1.06–2.95]; $p = 0.029$), prior stroke (OR = 8.91 [2.66–29.87]; $p < 0.001$), atrial fibrillation (OR = 30.40 [10.11–91.39]; $p < 0.001$), age > 75 years (OR = 2.38 [1.41–4.00]; $p = 0.001$) and coronary artery bypass graft vs. percutaneous coronary intervention (OR = 0.07 [0.02–0.26]; $p < 0.001$).

Conclusions: Despite very clear data on the superiority of the novel P2Y12 inhibitors, prescription of Clopidogrel remains high. Parameters associated with a presumably higher risk of bleeding were the most prominent factors for the prescription of Clopidogrel. Still, a quarter of all patients received Clopidogrel despite the lack of contra indications for the more powerful alternatives.

9-2

Impact of day and time of admission on short- and long-term mortality in the Vienna-STEMI-Registry

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Background: Several studies have shown contradictive findings regarding mortality and time or day of admission to tertiary hospitals. The aim of this study was to assess the impact of time or day of admission on short- and long-term mortality in the Vienna STEMI network (2003–2009).

Methods: The study population consisted of 2452 patients. Patients were stratified for weekend-admission (Saturday and Sunday) or weekday-admission (Monday until Friday) and for admission-time during official (Monday until Friday 07:00–14:00) or after official (weekdays 14:01–06:59 and weekends) working times of catheter laboratories. Outcome analysis was performed using univariate and multivariate Cox-regression analysis. As endpoint all-cause mortality was investigated after 30 days and 3 years of follow-up.

Results: Mean age was 61.25 ± 13.6 years, 70.9 % were male, 48.0 % presented with anterior wall infarction.

With respect to 30-day mortality, weekend-admission was correlated with a significantly better outcome compared to weekday-admission in multivariate Cox-regression analysis adjusting for established risk factors and confounders (HR 0.583 [95 % CI 0.419–0.802] $p = 0.001$). On Mondays, the trend for mortality was highest but did not reach statistical significance in multivariate analysis compared with the other weekdays ($p = 0.636$). As the most reliable explanation, computed with the Chi-quadrat test patients admitted on Mondays had a prolonged ischemic time (e. g. had the lowest rate of patients admitted within 120 minutes (12.0 % vs. 21.6 % $p < 0.001$) and the highest rate of patient admitted later than 12 hours after onset of pain (9.9 % vs. 6.3 % $p < 0.001$)), thus resulting in fewer immediate percutaneous coronary interventions (70.4 % vs. 80.0 %, $p < 0.001$) as patients admitted on other days of the week. Admission-time (HR 0.965 [95 % CI 0.660–1.410] $p = 0.854$) had no impact on 30-day mortality.

With respect to 3-year mortality, we did not detect significant differences for admission-time (HR 1.081 95 % CI 0.836–1.398] $p = 0.553$) or admission-day (HR 0.928 [95 % CI 0.742–1.161] $p = 0.513$) in univariate or multivariate Cox-regression analysis.

Conclusions: Admission-time had no significant effect on short and long-term mortality in the Vienna STEMI network. Interestingly, multivariate regression analysis revealed that

short-term mortality was higher on weekdays compared with weekends, while this difference was no more seen for long-term mortality.

9-3

Long-term clinical follow-up of patients with ST-segment elevation myocardial infarction receiving either Genous or Taxus stents. A retrospective data analysis

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Background: This study investigated the long-term (9 years) safety and efficacy of the primary percutaneous coronary intervention (pPCI) treatment of patients with ST-segment elevation myocardial infarction (STEMI) with Genous (endothelial progenitor capture passive coating stent) stent compared to Taxus (paclitaxel-coated drug-eluting stent, DES) stent.

Background: The Genous stent (bare metal stent with passive coating) has been proposed to implant in patients with STEMI, due to off-label use of DES for this indication in 2006–2007, and for the supposed rapid endothelialization of the stent. The comparison of the outcome of patients with de novo coronary lesions receiving either Genous or Taxus stent led to a non significant difference in target vessel failure rates (composite of cardiac death, myocardial infarction and target vessel revascularization) within 1 or 2 years (TRIAS study).

Methods and Results: A total of 203 patients with STEMI receiving either Genous (group G, $n=102$) or Taxus (group T, $n=101$) stent were retrospectively included. We assessed the annual cumulative incidence of major adverse cardiac and cerebrovascular events (MACCE) as a composite of death, reinfarction, stroke and target vessel revascularization from in-hospital up to 9-years follow-up.

The baseline characteristics of the patients (age, gender, presence of diabetes mellitus, hypertension, smoking, anterior wall infarction, previous infarction) did not differ between the groups. Significantly less patients had statin therapy before STEMI in the Genous group (G: 34.3 % vs T: 75.2 %), due to less incidence of hyperlipidaemia (G: 51 % vs T: 74.3 %), while the other medications were similar in the groups. The implanted stent size and lengths were similar in the groups.

Trend towards higher rates of in-hospital death (T: 2.0 % vs G: 7.8 %, $p=0.104$) was observed in the Genous group, while the non-target vessel revascularization was higher in the Taxus group at the 6-month FUP (T: 9.1 % vs. G 2.2 %, $p=0.04$). The cumulative incidence of MACCE showed significant ($p<0.05$) differences between the groups from the 3 years FUP (T: 19.8 % vs. G: 34.3 %), 5 years (T: 24.8 % vs. G: 38.2 %), 6 years (T: 25.7 % vs. G 392 %) and 7 years (T: 26.7 % vs. G: 40.2 %). Kaplan-Meier analysis resulted in significantly higher cumulative event-free survival rate in the Taxus group at the 9-year FUP, mainly due to the less TVR, as compared to the Genous group.

Conclusions: Against the expectations, that Genous stent might lead to more rapid endothelialization, implantation of Genous in patients with STEMI resulted in an unfavorable short-term and long-term clinical results. This, however, might partially be explained by the failure of the sufficient statin therapy prior to stenting.

9-4

Copeptin levels in patients with chest pain with type 1 and type 2 myocardial infarction

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Background: Copeptin, a C-terminal end of vasopressin, is used in emergency medicine as a stress biomarker for the early ruling out of acute coronary syndrome (ACS) (two marker strategy, ESC NSTEMI guidelines 2015). Whether Copeptin determination allows differentiation between type-1 and type-2 myocardial infarction (MI) or not, has not yet been investigated.

Objectives: This study evaluated whether there is a difference between Copeptin concentrations of type-1 and type-2 MI.

Methods: We examined 99 consecutive patients presenting with chest pain, at the emergency department of Wilhelminenhospital in Vienna. The subjects underwent a Troponin I and a Copeptin test at presentation and underwent further diagnostic measures to differentiate between type-1 and type-2 MIs. Furthermore, patients with a negative Troponin I at two consecutive blood samples (0, 3 hour strategy) were included into the group of no-MI.

Results: Median (25th; 75th percentile) Copeptin levels were 35.4 pmol/l (10.0; 132.6) in patients with type-1 MI, 23.3 pmol/l (8.7; 48.9) in patients with type-2 MI and 5.3 pmol/l (2.9; 11.7) in no-MI patients. There was a highly significant difference in Copeptin concentrations between both MI-types and no-MI subjects ($p<0.001$), while the difference between type-1 and type-2 MI was not significant ($p=0.68$). Using a cut-off of 10 pmol/l, 76.5 % of patients with type-1 MI, 69.2 % of patients with type-2 MI, but also 31.9 % of patients with no-MI showed elevated Copeptin level at presentation.

Conclusions: Copeptin as a stress biomarker has an equal increase in patients with type-1 and type-2 MI, which does not allow a differentiation between MI-types. Unspecific elevation in almost 1/3 of no-MI patients deserves further investigation.

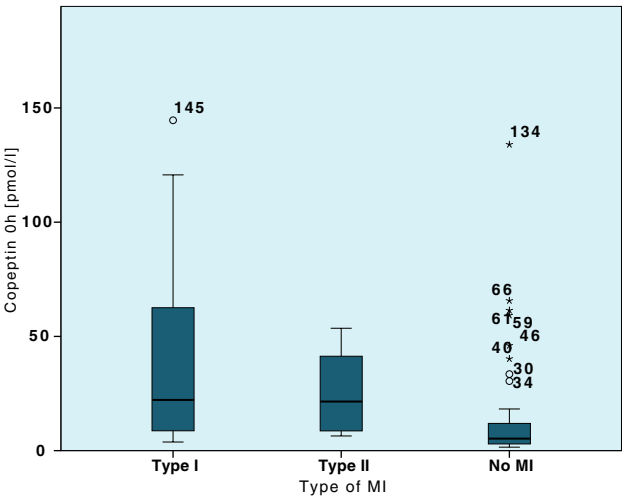

Fig. 1

9-5

Gender differences in short- and long-term mortality in the Vienna STEMI Registry

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Background: Data obtained from registries have shown that women diagnosed with STEMI are older, have more comorbidities and a worse clinical outcome. Aim of this study was to investigate potential gender differences in in-hospital and long-term mortality in patients from Vienna STEMI registry (2003–2009).

Methods: Data from 4593 patients who were enrolled from January 2003 until December 2009 into the Vienna STEMI registry were analyzed. Gender-related differences in patient characteristics, time delays, reperfusion therapy and short- and long-term mortality were compared. Data obtained from each gender were compared and rates for in-hospital and long-term mortality were plotted in Kaplan-Meier curves unadjusted and well as adjusted for confounders by use of multivariate Cox regression analysis. A landmark analysis was performed to assess the long term mortality in patients after discharge.

Results: Mean age, history of hypertension, diabetes mellitus, and shock at presentation were significantly higher compared to men, whereas men were more frequently smokers, had more frequently positive family history and a history of previous myocardial infarction, and received more often reperfusion therapy and GPIIb/IIIa inhibitors during PCI (Table 1). The only significant difference in time delay was found in the onset of pain-to first medical contact (FMC) time, which was significantly prolonged in women (Table 2). Unadjusted in-hospital mortality was statistically higher for women as was long-term mortality for all patients and long-term mortality for in-hospital survivors (Landmark analysis) (Table 3). After adjustment for confounders in-hospital mortality and long-term mortality (including the Landmark analysis) revealed no differences between men and women.

Conclusions: Although women had a prolonged onset of pain-to-FMC time as well as an increased cardiogenic shock rate at arrival and several differences in patient characteristics, no significant difference in in-hospital mortality and long-term mortality after adjustment for confounders could be demonstrated.

Tab. 1 Baseline characteristics. (SD) standard deviation, (MI) myocardial infarction, (ASA) acetyl salicyl acid, (PPCI) primary percutaneous coronary intervention, (TL) thrombolysis

Variables	Total ($N = 4582$)	Female ($n = 1326$)	Male ($n = 3256$)	p value
Age, yrs (mean ±SD)	61.3±13.7	67.2±14.0	58.9±12.8	**<0.001**
Diabetes Mellitus (%)	20.8	23.4	19.7	**0.008**
Hypertension (%)	51.9	58.9	49.1	**<0.001**
Hyperlipidemia (%)	39.5	39.0	39.7	0.670
Smoking (%)	42.0	34.0	45.1	**<0.001**
Positive family history (%)	17.1	15.3	17.9	0.061
History of previous MI (%)	17.6	15.3	18.5	**0.037**
Anterior MI (%)	48.6	48.2	48.7	0.775
GPIIB/IIIA (%)	14.9	12.7	15.8	**0.024**
ASA loading (%)	55.7	55.1	55.9	0.758
Reperfusion therapy				
PPCI (%)	82.4	81.2	82.9	0.216
TL (%)	13.0	12.0	13.4	0.243
No reperfusion (%)	4.6	6.8	3.8	**<0.001**
Shock (%)	8.7	10.9	7.8	**0.001**

Tab. 2 Time delays. (FMC) first medical contact, (IQR) interquartile range

Time delay	Total ($N = 4582$)	Female ($n = 1326$)	Male ($n = 3256$)	p value
Pain-to-FMC (min), median (IQR)	91 (53–180)	109 (60–202)	90 (50–180)	0.001
FMC-to-balloon (min), median (IQR)	111 (86–153)	112 (85–156)	110 (86–153)	0.797
Door-to-balloon (min), median (IQR)	60 (37–97)	63 (40–95)	60 (35–98)	0.678
Total ischemic time (min), median (IQR)	225 (146–364)	240 (148–378)	220 (146–360)	0.118

Tab. 3 Unadjusted and adjusted mortality hazard ratio (HR) for gender. (*only survivors of the hospital stay were calculated)

Mortality	Total n (%)	Female n (%)	Male n (%)	Unadjusted		Adjusted	
				HR (95% CI)	p value	HR (95% CI)	p value
In-hospital mortality	354 (7.7)	148 (11.2)	206 (6.3)	0.552 (0.447–0.681)	<0.001	0.965 (0.645–1.440)	0.860
Long-term mortality (all patients)	574 (12.5)	222 (16.7)	352 (10.8)	0.620 (0.524–0.734)	<0.001	1.069 (0.812–1.407)	0.636
Long-term mortality (landmark analysis*)	220 (5.2)	74 (6.3)	146 (4.8)	0.756 (0.571–0.999)	0.049	1.101 (0.754–1.607)	0.619

9-6

The impact of age and other risk factors at admission on short- and long-term mortality of patients in the Vienna STEMI network

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Background and Aim: Age is an important risk factor for patients with cardiovascular diseases. However, elderly patients are under-represented in most studies. The aim of this study was to investigate the influence of age and other risk factors on short- and long-term outcome in patients with ST-elevation myocardial infarction (STEMI) in the Vienna STEMI registry (2003–2009).

Methods: We included STEMI patients of the Vienna STEMI Registry, for which we had information on following characteristics evaluated at admission: age, gender, history of hypertension (HTN), hyperlipidemia (HLP), diabetes mellitus (DM), smoking habit, family history (FH), and previous infarction (previous MI), as well as about infarction location (anterior-wall vs. non-anterior) and shock, respectively. We excluded all patients with unknown reperfusion therapy and pharmacologic reperfusion (fibrinolytic therapy). Age and other risk factors at admission were associated with short- and long-term outcome. Short (30 days) and long-term (3 years) mortality was calculated with log-rank testing and is shown in Kaplan-Meier plots. Influence of patient characteristics on mortality was investigated with a backward eliminating Cox-regression model. In addition, a landmark analysis (only including hospital survivors after 30 days of the index event) for long-term mortality was performed.

Results: At total of 1996 patients fulfilled the criteria for further investigation. Mean age was 60.7 years. Overall 30-day and 3-years all-cause-mortality were 6.2 % and 13.3 %, respectively. Log-rank revealed significant differences between age cohorts for short and long-term mortality ($p < 0.0001$ for both). Cox-regression analysis for short-term mortality (Tab. 1) revealed an independent association for age ($p = 0.007$), HTN ($p = 0.017$) and shock ($p < 0.0001$). Long-term mortality (Table 2) was independently influenced by age ($p = 0.001$), DM ($p = 0.004$), HTN ($p = 0.033$), HLP ($p = 0.015$), positive FH ($p = 0.001$), previous MI ($p = 0.007$) and shock ($p < 0.001$). Landmark analysis (Tab. 3) showed independent association with long-term mortality for DM ($p = 0.002$), smoking ($p = 0.002$), HLP ($p = 0.006$), previous MI ($p = 0.001$) and shock ($p = 0.004$), but not for increasing age.

Conclusions: Age had substantial influence on short and long-term mortality, but elderly people showed a comparable good outcome to younger age cohorts if they survived the first 30 days. Admission in shock had the greatest negative impact on short- and long-term survival, followed by a previous myocardial infarction and diabetes. The "paradox" impact of smoking, hypertension, positive family history and hyperlipidemia on mortality might be explained by optimal secondary prevention measures after the index event and will be investigated in future attempts.

9-7

Influence of a public information campaign on patient-related delay time and total ischemic time in the Vienna STEMI registry

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Background and Aim: Patient related delay in STEMI is defined as time from onset of pain (OP) until first medical contact (FMC) conforming diagnosis by means of ECG. As such it represents a crucial determinant for infarct size and hence has tremendous influence on the patient's outcome and the likelihood to develop late clinical outcome. However, correct recognition of symptoms and call into the medical system requires sufficient awareness of the patient. One approach is to wage campaigns designed to disseminate information on signs and symptoms of STEMI. This was done in summer of 2006 for a 6-weeks time period by public information activities in radio and TV called "Schach dem Herztod". The aim of this study was to compare patient related delay and total ischemic time prior and over time after the campaign.

Methods: In Vienna, data of patients treated for STEMI were recorded in the VIENNA STEMI registry (2003–2009). All patients who for whom we had data on time from OP to FMC were included in the analysis as was total ischemic time (OP to start of reperfusion therapy). OP-to-FMC and total ischemic time (TIT) are shown as median and interquartile range (IQR) in minutes, TIT was furthermore treated as categorical variables (<240 min vs >=240 min). Delays were compared between following time periods: prior to campaign, start of campaign until 6 months after the end, 7th until 12th month after campaign and after 12th month after campaign. Delays are shown as median with IQR and categorical variables were compared with Qui2-test.

Results: In total, 1604 patients were included in the final analysis. Median time intervals for OP-to-FMC and for total

ischemic time prior and after the campaign are given in the table. The goal for the total ischemic time was reached by 49.9 % of patients prior to the campaign. Within the first six months this account raised to 61.1 %, followed by a decline until the end of one year (59.1 %) and afterwards (57 %; $p = 0.001$).

Conclusions: In our hands public campaigning is capable of shortening patient related delay time (OP-to-FMC) significantly over a long period, whereby the effect is more prominent in the first few months. Thereby, patient-related delay is the main determinant of total ischemic time.

9-8

Comparison of Prasugrel praehospital versus intrahospital in patients with ST-segment elevation myocardial infarction in terms of therapeutic outcome

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Background: Cornerstone of treatment to prevent thrombotic complications in ST-segment elevation myocardial infarction (STEMI) are P2Y12 antagonists, beside acetylsalicyl acid. After evaluation of the TRITON TIMI-38 and PLATO study, Prasugrel should be considered as drug of choice for patients presenting with STEMI.

Whether the time Prasugrel is given (praehospital or intrahospital) has an impact on the outcome is yet unknown.

Methods: We analyzed 147 patients presenting with STEMI in our study (76.9 % male, 58.5 ± 10.7 years), who underwent immediate percutaneous coronary intervention (PCI) and were given praehospital ($n = 50$) or intrahospital ($n = 97$) Prasugrel in two centres. Treatment was ESC guidelines 2012 conform. Mean Follow-up was 37.6 ± 12.1 months after PCI. Combined endpoint was defined as cardiovascular (CV) death, myocardial infarction or restenosis. For bleeding classification BARC score was used and significant bleeding was defined as any kind of bleeding BARC ≥ 2.

Results: Baseline characteristics of both groups were similar. Combined endpoint occurred 4 times (3 patients with intrahopsital administration). Endpoint free survival was not significant different ($p = 0.951$) between the intrahospital (44.0 ± 0.5 months) and praehospital (48.5 ± .1 months) group in Kaplan Meier analysis.

Actionable bleeding occurred 5 times, whereas 4 patients treated intrahospital suffered from it ($p = 0.533$).

Conclusions: In patients with STEMI, neither praehospital nor intrahospital Prasugrel administration was associated with significant differences in terms of actionable bleeding complications or combined endpoint of CV death, myocardial infarction and restenosis.

Postersitzung 10 – Rhythmologie 2

10-1

Leadless cardiac pacing after lead extraction in patients with severe device infection

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Background: Conventional pacemaker therapy is limited by short- and long-term complications, most notably device infection. Explantation of a pacemaker system and further management may be especially challenging in patients who are fully pacemaker dependent. Temporary pacemaker leads bear the risk of infection themselves, whereas epicardial lead placement requires chest surgery in these high risk patients. Leadless cardiac pacemakers (LCPs) may be beneficial in such cases as they eliminate the need for a device pocket and leads and thus may reduce the risk of re-infection.

Material and methods: We assessed a novel procedure in five patients with severe device infection who were pacemaker dependent. In a first step, leads were extracted using a mechanical rotation sheath as well as a lead locking device. Then, a single chamber LCP (Medtronic Micra®) was implanted into the right ventricle via a femoral vein access. We used a temporary pacemaker for bridging between step one and two in the first four patients. In the fifth patient the two steps were reversed eliminating the need for a temporary pacemaker. A follow-up PET scan of the heart and device pocket was performed 3 months after LCP implantation to detect ongoing or de-novo device infection in all patients.

Results: Five patients underwent system removals with lead extraction due to severe device infection at our institution between September and December 2015. Patients were between 56 and 88 years old, only one of them being female. All removed systems were single chamber pacemakers (VVI-R). Three were diagnosed with a pocket infection only, whereas the other two showed signs of both pocket and lead infection. The infected pacemaker systems had been implanted 8.0±4.3 years before removal on average. Successful lead extraction and LCP implantation could be accomplished in all patients. Mean procedure time for lead extraction and system removal was 41±15 minutes, while the mean time for LCP implantation was 35±12 minutes. The first four patients were bridged with a temporary pacemaker between two hours and three days after lead extraction. All patients stayed free of infection during the follow-up period of 151±42 days. PET CT confirmed absence of ongoing or de-novo infection 3 months after the procedure in all patients.

Conclusions: Leadless cardiac pacemaker implantation was safe and feasible in our five patients. It may be an option for patients with severe device infection, especially in those with blocked venous access paths and those who are pacemaker dependent. Direct implantation into the right heart chamber without any leads or a device pocket may reduce the risk of re-infection. Three months after lead extraction and LCP implantation our cohort of five patients stayed free from infection as confirmed by PET CT.

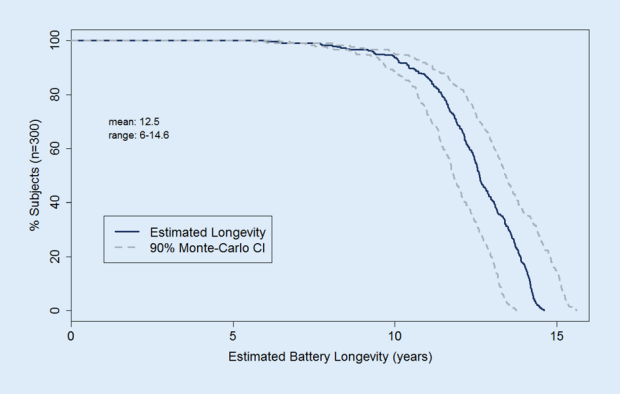

Fig. 1

10-2

Initial real world performance of a novel leadless pacemaker anticipates outstanding battery longevity – Data from the Micra Transcatheter Pacing Study

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Background: Battery longevity is especially important for leadless pacemakers designed to be endocardially abandoned at end-of-life. The Micra transcatheter pacemaker incorporates multiple features to prolong battery life. These include low power electronics driven by a high density battery (120 mA hr) and a Capture Management (CM) algorithm that measures the capture threshold daily, confirms it hourly, and adjusts the pacing safety margin to +0.5 V.

Methods: Factors relevant to battery longevity were evaluated in the first 300 patients to complete 6-month follow-up in the Micra clinical study. Battery longevity for each patient was projected based on use conditions.

Results: A low (≤2 V) and stable (≤1.5 V rise from implant) capture threshold was observed in 292 of 297 (98.3 %) patients with baseline and follow-up data. The CM threshold was accurate to within 0.5 V of the manual threshold in 279 of 280 (99.6 %) patients with paired test data. The pacing output was set using CM and the pulse width was held at 0.24ms in 298 of 300 (99.3 %) patients in whom programming was reported. Loss of capture was never observed in 27 patients who completed Holter monitoring, even for hourly confirmation test paces at the daily CM threshold +0.125 V. Mean pacing parameters included amplitude = 1.1 V, impedance = 594 Ω, rate 73 bpm, and pacing percentage = 50 %. Mean projected longevity was 12.5 years (Fig. 1).

Conclusions: Real world performance of the Micra transcatheter pacemaker through 6-month follow-up anticipates mean battery longevity of 12.5 years. Longevity is achieved with a high density battery and algorithms that reduce pacing current without risking reliable capture.

10-3

Is there a difference in outcome in patients undergoing ablation of paroxysmal atrial fibrillation as 1st vs 2nd line treatment?

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Background: Catheter ablation of paroxysmal atrial fibrillation (AF) is an established 2nd line therapy (after failed antiarrhythmic drug treatment) for patients with symptomatic paroxysmal atrial fibrillation (AF). According to the latest ESC guidelines, AF ablation may be considered in highly symptomatic, low-risk patients as a 1st line therapy option.

The fact that AF is steadily progressing over time indicates, that patients who receive catheter ablation as a consequence of failed antiarrhythmic drug treatment (and therefore at a later timepoint) might be potentially sicker compared to the 1st line therapy collective, which could result in a worse outcome of catheter ablation in the 2nd line therapy group. Our study

Tab. 1

Baseline characteristics	Over all	First-line group	Second-line group	*P* Value
Patients	100	45	55	–
Multiple procedure success rate off antiarrhythmic drugsdrugs	73 %	74 %	72 %	0.82
Single procedure success rate off antiarrhythmic drugsdrugs	76 %	75 %	76 %	1.00
Multiple procedure success rate with antiarrhythmic drugs	86 %	88 %	81 %	0.38
Single procedure success rate with antiarrhythmic drugs	76 %	81 %	71 %	0.12
Age (years)	53 ± 12	53 ± 13	54 ± 11	0.80
Female patients	23 %	27 %	21 %	0.05
Median FU time (days)	346 [91,1009]	352 [91,1009]	344 [93,730]	0.78
LA diameter 42 ± 6 mm	40 ± 6 mm	43 ± 6 mm	0.05	
Structural heart disease	12 %	6 %	16 %	0.15
LVEF	64 ± 6	64 ± 4	64 ± 7	0.38

investigated whether an earlier ablation approach may result in improved sinus rhythm maintenance after ablation.

Methods: A total of 100 patients with paroxysmal AF were included in the study (age 53±12; 23 % female) and were split up into a 1st- and a 2nd line ablation group. Success was defined as the absence of documented episodes of AF during the follow up time by means of serial ECG and Holter monitoring at 3, 6 and 12 months and at 6 months intervals thereafter. Statistical analysis was performed for single and multiple procedural success.

Results: Overall, 111 AF ablation procedures were performed in these 100 AF patients (1.2±0.5/patient). 45 patients received 1st line AF ablation and 55 patients underwent 2nd line AF ablation after a failed trial of antiarrhythmic drugs. There was no difference in baseline characteristics such as age, gender, structural heart disease, AF duration, LA size, or LVEF between groups (Table 1). The median follow up time was 352 [91; 1009] days in the first line group vs. 344 [93; 730] days in the second line group ($p = 0.78$).

There was no significant difference in arrhythmia-free survival between those patients who received AF ablation as a first- or those who received AF ablation as a second line therapy both in single procedure outcome (Table 1) and in multiple procedure outcome (success rate with antiarrhythmic drugs 88 % in the 1st line group vs. 81 % in the 2nd line ablation group; Log rank test $p = 0.38$; success rate off antiarrhythmic drugs 74 % in the 1st line group vs. 72 % in the 2nd line ablation group; Log rank test $p = 0.82$). In the 1st line ablation group 74 % of the patients in sinus rhythm were free from antiarrhythmic drugs at the time of last follow-up, compared to 72 % in the 2nd line ablation group ($p = 0.82$). In overall analysis for multiple procedural success a smaller left atrial diameter turned out to be a predictor of ablation success ($p = 0.039$).

Conclusions: Success of AF ablation does not seem to differ between patients who received AF ablation as a first line therapy and patients who received AF ablation as a second line therapy. Based on these data, a trial of antiarrhythmic drug therapy before AF ablation may be justified in the majority of patients with symptomatic paroxysmal AF eligible for rhythm control.

10-4

Katheterablation ventrikulärer Tachykardien bei struktureller Herzerkrankung und idiopathischem Kammerflimmern

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Grundlagen: Ventrikuläre Tachykardien (VT) stellen komplexe Krankheitsbilder dar, die für den Patienten eine hochgradige Einschränkung der Lebensqualität (zB Verkehrstauglichkeit, rezidivierende Schocks durch den implantierten Defibrillator, ICD) und potentiell lebensbedrohliche Situationen bedeuten. Die Behandlung umfasst die Therapie der Grunderkrankung (zB KHK), adäquate Medikation, Risiko-Beurteilung eines plötzlichen Herztodes, Device-Therapie sowie Möglichkeit einer Katheterablationsbehandlung.

Wir berichten über die Ablationsergebnisse unseres Zentrums aus den Jahren 2007 bis 2015.

Methodik: In den Jahren 2007 bis 2015 wurden im KH Elisabethinen Linz 227 VT-Ablationen durchgeführt [Abb. 1] und daraus die Gruppe der strukturellen Herzerkrankungen sowie Patienten mit idiopathischem Kammerflimmern (VF) retrospektiv analysiert. Erfasst wurden demographische, krankheitsspezifische, echokardiographische und ablationsbezogene Daten sowie Therapien durch implantierte Defibrillatoren. Die Verlaufskontrolle der Patienten erfolgte über Deviceabfragen, telefonische Kontaktaufnahme oder Krankenhausaufenthalte.

Ergebnisse: Eingeschlossen wurden 129 Patienten mit struktureller Herzerkrankung (ischämische Kardiomyopathie, CMP: 64 Patienten, idiopathisches VF: 28 Pat, dilatative CMP: 22 Pat, ARVC: 13 Pat, Myokarditis: 2 Pat), mit einem Alter von 58,4 ± 13 Jahren. 84,5 % waren männlich.

Die Krankheitsanamnese bis zur Ablation betrug 50,5 ± 53 Monate. Im Schnitt kamen in der Vorgeschichte 2 ± 0,67 Antiarrhythmika zum Einsatz (85,3 % Betablocker; 55,8 % Amiodaron; 14 % Sotalol; 5,4 % Klasse Ic). Die häufigsten Begleiterkrankungen waren Herzinsuffizienz (74,4 %), Dyslipidämie (68,2 %), KHK (55,8 %) und arterielle Hypertonie (45,7 %); die mittlere LVEF betrug 37 ± 13,9 %. 20 Patienten (15,5 %) wurden im VT-Sturm interveniert, 23 Patienten (17,8 %) kamen zu einer Zweit-Prozedur.

Die Dauer der in Sedoanalgesie (Propofol/Fentanyl) oder Intubationsnarkose erfolgten Eingriffe betrug 250,2 ± 67,4 Minuten, punktiert wurde wie folgt: femoralvenös (100 %), femoralarteriell (31,7 %), transseptal (38 %) und epicardial (14,7 %). Bei 7 Patienten (5,4 %) traten prozedurbezogene Komplikationen auf (4 × Hämopericard/Pigtail, je 1 × Hämopericard bzw Leistenblutung mit Notwendigkeit einer (herz)chirurgischen Sanierung, 1 hämodynamisch nicht tolerierte VT mit Notwendigkeit eines Prozedur-Abbruches). 1 Patient mit inzessanter VT bei ischämischer CMP verstarb 3 Tage nach frustranem Ablationsversuch im kardiogenen Schock.

Der Endpunkt einer fehlenden Auslösbarkeit der klinischen VT konnte in 73,6 % der Fälle (95 Patienten) erreicht werden, in 18,6 % (24 Pat) gelang eine Narbenhomogenisierung oder Substratmodifikation. In 2,3 % (3 Pat) musste komplikationsbezogen, bei 2 Prozeduren (1,6 %) aufgrund fehlenden Therapie-Erfolges und sehr langer Prozedurdauer abgebrochen werden. 57,4 % der Patienten waren im Follow-Up rezidivfrei, 76,1 % ohne antitachycardes Pacing und 87,3 % ohne ICD-Schock [Abb. 2].

Schlussfolgerungen: Die Katheter Ablation ventrikulärer Arrhythmien bei struktureller Herzerkrankung oder idiopathischem VF stellt eine komplexe Therapieoption für klinisch hochsymptomatischen Patienten dar und vermag Symptome und insbesondere ICD-Schocks zu reduzieren.

10-5

Leistenverschluss mittels ‚Double Purse-String Suture'-Technik bei sondenloser Schrittmacherimplantation – Erfahrungen mit dem Micra™ Transcatheter Pacing System

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Grundlagen: Sondenlose Schrittmachersysteme werden über einen femoralen Zugang und großkalibrige venöse Einführschleusen im rechten Ventrikel platziert. Die Schleuse des Micra™ Transcatheter Pacing Systems (Medtronic Inc., Minneapolis, MN, USA) hat einen Innendurchmesser von 23 French (F) und einen Außendurchmesser von 27 F. Die häufigsten

Komplikationen nach Punktion der Vena femoralis sind Hämatome, Pseudoaneurysmen und arterio-venöse Fisteln. Ein sicherer und vollständiger Verschluss des venösen Zugangs stellt einen entscheidenden Schritt am Ende der Prozedur dar.

Methodik: Nach Punktion der Vena femoralis und Hautinzision von 10 mm Länge und 5–10 mm Tiefe werden zwei subkutane Tabaksbeutelnähte für den abschließenden Leistenverschluss nach Entfernung der Einführschleuse vorgelegt. Mit Novosyn® 3.0 (B. Braun Melsungen AG, Melsungen, Deutschland) haben wir ein synthetisches, mittelfristig resorbierbares Nahtmaterial aus Polyglactin 910 verwendet, dessen vollständige Resorption 56–70 Tage dauert. Neben einer oberflächlichen Naht wird eine zweite, tiefer liegende Naht gesetzt, die durch die anatomische Nahebeziehung zur Punktionsstelle eine bessere mechanische Abdichtung und einen sicheren Verschluss gewährleisten soll. Diese ‚Double Purse-String Suture'-Technik wurde bei allen Patienten unseres Kollektivs angewendet und stellt eine Alternative zur gängigen ‚Figure of 8-Suture'-Technik dar. Die Beurteilung von Leistenkomplikationen erfolgte während des Indexaufenthaltes, nach 4 Wochen und 3 Monaten.

Ergebnisse: Im Zeitraum von Dezember 2013 bis Februar 2016 wurde bei 83 Patienten die Implantation eines Micra™ TPS durchgeführt. 23 (27,7 %) Patienten standen unter oraler Antikoagulation mit Marcoumar (INR 2,14 ± 0,41) und bekamen kein iv. unfraktioniertes Heparin (UFH) während der Implantation. 10 (12 %) Patienten standen unter oraler Antikoagulation mit Marcoumar (INR 1,84 ± 0,32) und bekamen zusätzlich iv. Heparin (UFH 3800 ± 1398 IE). 19 (22,9 %) Patienten standen unter oraler Antikoagulation mit einem DOAK, welches am Tag vor der Prozedur pausiert und am Tag nach der Prozedur fortgesetzt

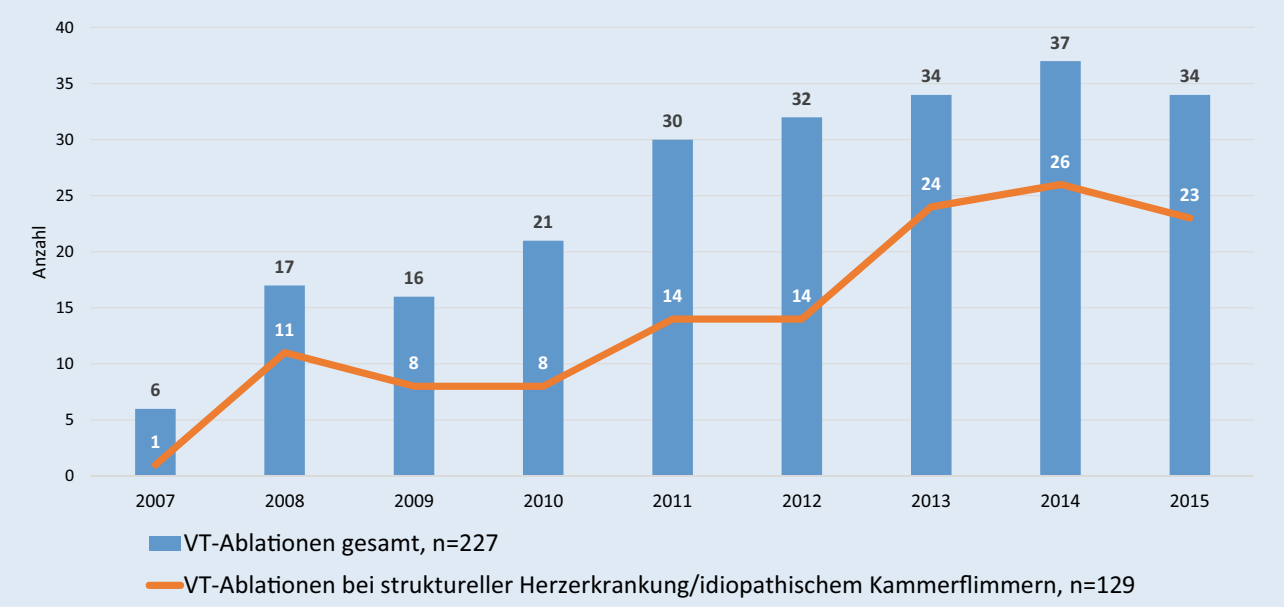

Abb. 1 VT-Ablationen KH Elisabethinen von 2007–2015

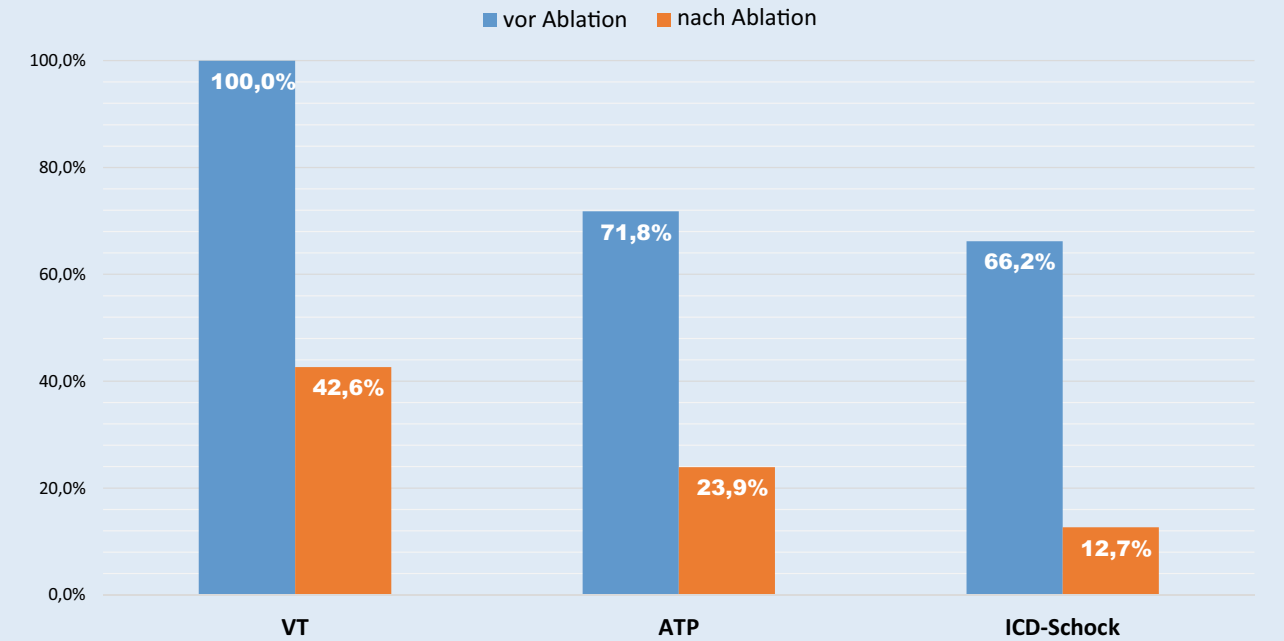

Abb. 2 Klinischer Verlauf VTs/ATP/Schock

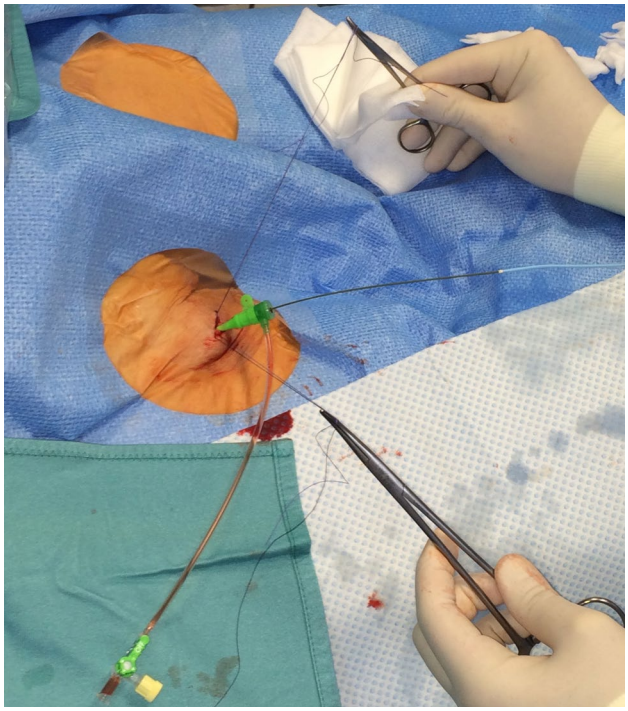

Fig. 1

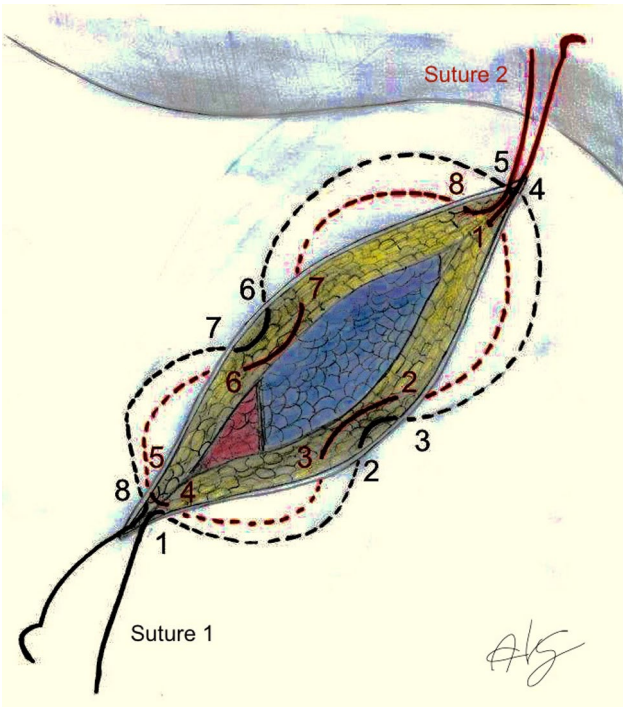

Fig. 2

wurde. Insgesamt bekamen 29 (34,9 %) Patienten während der Prozedur iv. Heparin (UFH 4362 ± 1109 IE). 21 (25,3 %) Patienten standen weder unter oraler Antikoagulation noch bekamen sie iv. Heparin während der Implantation. Bei drei (3,6 %) Patienten traten Leistenkomplikationen auf, zwei (2,4 %) Leistenhämatome und eine (1,2 %) arterio-venöse Fistel. Alle drei Fälle zeigten einen günstigen Spontanverlauf innerhalb der ersten 4 Wochen ohne Notwendigkeit einer chirurgischen Revision.

Schlussfolgerungen: Die ‚Double Purse-String Suture'-Technik stellt eine einfache, sichere und kostengünstige Methode zum Erlangen einer adäquaten Hämostase nach Entfernung großkalibriger venöser Einführschleusen, wie sie für die Implantation sondenloser Schrittmachersysteme verwendet werden, dar.

10-6

Implantationszeit, Durchleuchtungsdauer und Deployment-Rate mit dem Micra™ Transcatheter Pacing System – Zwei-Jahres-Ergebnisse eines High-volume Centers

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Grundlagen: Die Implantation sondenloser Schrittmacher stellt ein technisch neuartiges Konzept in der Schrittmachertherapie dar. Das betrifft einerseits den vaskulären Zugang mittels großkalibriger venöser Einführschleusen und andererseits das Handling mit dem Delivery-System und das abschließende Freisetzen (Deployment) des Schrittmachers am Implantationsort. Implantationszeit, Durchleuchtungsdauer und Deployment-Rate wurden als Parameter zur Beurteilung einer zu erwartenden Lernkurve im Verlauf des Beobachtungszeitraumes gewählt.

Methodik: Zwischen Dezember 2013 und Februar 2016 erhielten 84 Patienten an unserer Abteilung ein Micra™ Transcatheter Pacing System (Medtronic Inc., Minneapolis, MN, USA). Alle Implantationen wurden von zwei Implanteuren durchgeführt, dem Beginn des Programms mit der First-in-man-Implantation im Dezember 2013 ging ein Training am Tiermodell voraus. Das Patientenkollektiv wurde chronologisch in vier gleich große Gruppen zu 21 Patienten aufgeteilt und Implantationszeiten, Durchleuchtungsdauer und Deployment-Raten verglichen.

Ergebnisse: Die durchschnittliche Implantationszeit der vier Gruppen betrug 43,4 ± 16,1 (Gruppe 1), 35,2 ± 12,1 (Gruppe 2), 41,8 ± 22,9 (Gruppe 3) und 36,6 ± 14,8 (Gruppe 4) Minuten bei einer durchschnittlichen Durchleuchtungsdauer von 8,2 ± 6,4 (Gruppe 1), 6,0 ± 4,4 (Gruppe 2), 7,5 ± 6,0 (Gruppe 3) und 7,2 ± 4,4 (Gruppe 4) Minuten. Weder bei den Implantationszeiten ($p = 0{,}170$) noch bei der Durchleuchtungsdauer ($p = 0{,}243$) gibt es einen signifikanten Unterschied zwischen den vier Gruppen. Gleiches gilt auch für die Deployment-Rate, die allerdings einer großen interprozeduralen Schwankungsbreite von einem bis zu 20 Deployment-Versuchen unterlegen ist. Sie betrug 1,9 ± 1,9 (Gruppe 1), 2,0 ± 1,7 (Gruppe 2), 2,8 ± 4,1 (Gruppe 3) und 1,9 ± 1,8 (Gruppe 4) Deployment-Versuche ohne signifikanten Unterschied ($p = 0{,}756$) zwischen den vier Gruppen.

Schlussfolgerungen: Relativ konstante Implantations- und Durchleuchtungszeiten seit Beginn dieser neuen Implantationstechnik sprechen für ein technisch ausgereiftes und einfach zu handhabendes System. Die Deployment-Rate wird unter Berücksichtigung der bisher vorliegenden Erfahrungen als individuelle, nicht kalkulierbare und von den anatomischen Gegebenheiten abhängende Einflussgröße gesehen, die im Einzelfall einer großen Schwankungsbreite unterliegen kann und ihrerseits Implantationszeit und Durchleuchtungsdauer beein-

flusst. Eine initial hohe ‚operator experience' betreffend den Umgang mit venösen Schleusen, Nahttechniken für den Leistenverschluss und vorangegangenes Training am Tiermodell dürften zu den vorliegenden Ergebnissen beigetragen haben und werden als beeinflussbare Faktoren gesehen. Das Fehlen einer klassischen Lernkurve in unserem Patientenkollektiv scheint multifaktoriell bedingt zu sein, überwiegend getragen von der ‚operator experience' sowie dem technischen Konzept des Micra™ TPS und dessen Anwendbarkeit.

10-7

TENS and other forms of electrical stimulation therapy in patients with permanent pacemakers: An in vitro study

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Background: Among other forms of electric stimulation therapy, transcutaneous electrical nerve stimulation (TENS) is a currently used treatment modality for various pain conditions.

Apart from deep vein thrombosis, haemorrhagic conditions and pregnancy being absolute contraindications, there exists contradictory recommendation with regard to permanent pacemaker carriers.

With an average of 7853 pacemakers being implanted in Austria from 2009 to 2013 per year the number of permanent pacemakers carriers is continuously increasing. Respectively grows the number of patients requiring TENS after device implantation.

Previous reports show that TENS may safely be used in patients with permanent pacemakers. However there might be an association between the application of TENS and the occurance of significant bradycardia. This could be the result of inadvertently inhibited ventricular pacing during electric stimulation therapy. Accordingly Pacemaker manufacturers recommend heart rhythmn monitoring in the event of TENS.

Since TENS is commonly applied in an outpatient setting, this is hardly practicable.

Consequently we performed an in vitro study on the effects of electric stimulation therapy on artifical cardiac pacing.

Methods: A full size model for the human body was created out of towels soaked with sodium chloride solution (see picture). The concentration of the sodium chloride was chosen on the basis that the electrical impedance of the solution is similar to the human body.

Fig. 1

Tests were performed with 5 single-chamber devices pacemakers in VVI mode, from different manufacturers, currently being implanted in clinical routine.

The pacemakers and leads were placed in the model according to the position in vivo.

For electrical stimulation two devices were used. One commonly used for TENS therapy, the other device capable of applying various different modalities typically used in electric stimulation therapy. Each modality was tested in different configurations.

Electrodes simulating electrical stimulation were either both put on the same thigh or on different thighs contralaterally.

During the application of current, the pacemaker was connected to the programmer and intracardiac Electrograms were continuously recorded by the pacemaker and stored.

The inhibition of ventricular pacing was assessed during the application of current.

Results: Stimulation with modalities aS, GALV, FM, IG, HFT, LFT, BuT, EXPO, HV, MF, PS and TENS caused no ventricular inhibition of the pacemaker, if both electrodes were placed on one thigh (0 in 126 configurations, 0 %).

Stimulation with one electrode placed on each thigh (312 configurations in total) caused ventricular inhibition when applying EXPO (23 in 46 configurations, 50 %), IG30 (9 in 33, 27.3 %) and PS (99 in 119, 83.2 %). No ventricular inhibition occured when applying aS, GALV, FM, HFT, LFT, BuT, HV, MF, PS and TENS.

Conclusions: Electrical stimulation potentially interferes with pacemaker therapy. Stimulation on one single thigh is likely to be safe in patients with permanent pacemakers.

Some commonly applied modalities like TENS are generating waveforms that differ from native cardiac electric signal significantly. Consequently the pacemaker software is able to differentiate between intrinsic impulses and those generated by stimulation even if the electrodes are put on different thighs.

In vivo studies with a similar setup are mandatory to verfiy this result.

10-8

Nutzen- und Risikoabschätzung bei Einleitung einer oralen Antikoagulation bei nicht-valvulärem Vorhofflimmern: Ein Vergleich zwischen Selbsteinschätzung durch den Patienten und einer individuellen Risikobewertung durch CHA_2DS_2-VASc und HAS-BLED Scores

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Grundlagen: Patienten mit Vorhofflimmern (VHF) haben ein deutlich erhöhtes Thrombembolierisiko. Bei mittlerem bis hohem Schlaganfallrisiko ist die prophylaktische Einleitung einer oralen Antikoagulation (OAK) indiziert, allerdings auf

Kosten einer erhöhten Blutungsneigung. Ausreichendes Wissen um das Wesen und die Risiken dieser Erkrankung ist erforderlich, um den Willen und die Präferenzen des Patienten in die Behandlung einzubeziehen und damit die Akzeptanz und Adhärenz einer OAK zu verbessern. Ziel dieser Untersuchung ist ein Vergleich zwischen der Selbsteinschätzung von Nutzen und Risiko einer OAK durch den Patienten mit der individuellen Risikobewertung durch den behandelnden Arzt.

Methodik: Mittels eines standardisierten Fragebogens wurden Patienten um Abschätzung des eigenen Insult- und Blutungsrisikos gebeten und diese einer objektiven Bewertung durch den CHA_2DS_2-VASc und HAS-BLED Score gegenübergestellt.

Ergebnisse: Insgesamt wurden 91 Patienten (Alter 73±11 Jahre, 45 % weiblich) mit nicht-valvulärem VHF und Neueinleitung einer OAK in diese Multicenter-Studie inkludiert. Entsprechend den Empfehlungen der VHF-Leitlinien erhielten 75 (82,4 %) ein neues orales Antikoagulans. Der Großteil der befragten Patienten hatte größere Sorge, einen Schlaganfall als eine therapieassoziierte Blutungskomplikation zu erleiden. Zwischen der subjektiven Einschätzung und der objektiven Bewertung des Schlaganfall- bzw. Blutungsrisikos durch Patient und behandelnden Arzt fand sich kein signifikanter Zusammenhang ($p=0,08$; $p=0,47$ bzw. $n=90$, $p=0,01$; $p=0,91$). Patienten unterschätzten eher das eigene Schlaganfallrisiko, während das Blutungsrisiko durchwegs korrekter beurteilt wurde. Die Richtigkeit der eigenen Einschätzung korrelierte nicht mit dem Ausbildungsgrad ($n=75$; $p=-0,04$, $p=0,75$ für das Schlaganfallrisiko und $p=0,05$, $p=0,67$ für das Blutungsrisiko) und dem selbst angegebenen Informationsstand über VHF ($p=-0,17$, $p=0,12$ für das Schlaganfallrisiko und $p=-0,04$, $p=0,71$ für das Blutungsrisiko).

Schlussfolgerungen: Die subjektive Nutzen- und Risikoabschätzung hinsichtlich einer OAK durch den Patienten differiert deutlich von der individualisierten Bewertung durch den behandelnden Arzt. Die VHF-Leitlinien empfehlen neuerdings, die Patientenpräferenz in Therapieentscheidungen miteinzubeziehen. Eine partizipative Entscheidungsfindung und eine informierte Einwilligung vor Einleitung einer OAK erfordern eine noch umfassendere Information und Aufklärung des Patienten. Neue orale Antikoagulanzien werden heutzutage in der Behandlung von VHF vermehrt eingesetzt.

10-9

Predictors of new-onset atrial fibrillation and outcome in patients with pre-existing atrial fibrillation after TAVI

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Background: Rhythm disturbances after Transcatheter Aortic Valve Implantation (TAVI) are common. This study investigates risk factors for and outcomes of new onset of atrial fibrillation (NOAF) after TAVI compared to patients with pre-existent atrial fibrillation and those with sinus rhythm.

Methods: We performed a single-centre study of 398 consecutive patients undergoing TAVI with the Medtronic CoreValve prosthesis (94 % transfemoral, 6 % transaortic, 1 % transsubclavian) between May 2007 and May 2014. Median age was 82 (interquartile range 78–85) years, 63 % were female. EuroScore II predicted a median 30-day mortality of 5.9 %, German AV Score was 6.4 %. Patients were divided into a sinus rhythm group ($n=226$, 57 %) and baseline atrial fibrillation group ($n=172$, 43 %) according to clinical records and baseline electrocardiogram (ECG). Preprocedural pacemaker incidence was 5 % ($n=12$) in the sinus rhythm group and 16 % ($n=28$) in the baseline atrial fibrillation group. After the procedure, patients were monitored by telemetry during their stay and ECGs were made daily. NOAF was defined as any episode of atrial fibrillation before discharge from hospital in the SR group. All patients were followed up for one year.

Results: NOAF occurred in 7 % ($n=16$) of patients with prior sinus rhythm. Previous valve surgery was the only significant predictor of NOAF in multivariate analysis ($p=0.045$). Thirty-day mortality was 5.2 %, 0 %, 6.9 % in the sinus rhythm, NOAF and baseline atrial fibrillation groups ($p=0.629$), respectively. Pacemaker implantation rate in the first postprocedural year was 13.7 %, 25 % and 17 % in the sinus rhythm, NOAF and baseline atrial fibrillation groups ($p=0.550$). NOAF was not associated with a higher mortality or longer hospitalization, but rehospitalization rate was significantly higher ($p=0.03$). Baseline atrial fibrillation patients had a significant higher 1-year mortality (19.8 % vs. 6.3 % vs. 11.9 %, $p=0.024$) compared to NOAF or SR groups.

Conclusions: This study shows that NOAF is rare after TAVI, but is associated with a higher rehospitalisation rate after TAVI. Pre-existent AF, however, is associated with higher 1-year mortality. Therefore, it should be included in baseline risk evaluation of TAVI patients.

10-10

Supraventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy

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Background: Ventricular tachycardia (VT) and sudden cardiac death are common first manifestations of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC). Nevertheless, supraventricular tachycardia (SVT) is not rare and can lead to symptomatic palpitations, inappropriate ICD therapy and thromboembolic events. This study sought to assess the prevalence of SVT in a large cohort of patients with ARVC.

Methods: SVT occurrence has been interrogated in patients from our ARVC database (70 patients, 49 male, age 53.1±13.8 years, 45 patients (64.3 %) with previous VT ablation). ARVC/D diagnosis was confirmed using modified ARVC/D criteria. Rhythm monitoring has been done by 12 lead ECG, Holter ECG and device interrogations.

Results: 26 patients of 70 patients (37.1 %) have been diagnosed with SVT. In detail have been found: atrial fibrillation (16 patients, 22,9 %, ectopic atrial tachycardia (7 patients, 10.0 %), atrial flutter (6 patients, 8.9 %), frequent premature atrial contractions (2 patients, 2.9 %) and atrioventricular re-entrant tachycardia (1 patient, 1.4 %). The diagnosis of SVT was associated to VT recurrence in patients with previous VT ablation ($p=0.007$).

Conclusions: SVT frequently occur in patients with ARVC and may significantly contribute to morbidity and mortality. Diagnosis of SVT correlates with VT recurrence in patients with previous VT ablation. Thus, beside smart ICD programming, antiarrhythmic drug therapy and anticoagulation, ablation of SVT might be considered in ARVC patients with frequent VT.

Postersitzung 11 – Koronoare Herzkrankheit und Pulmonale Hypertension

11-1

Arterial hypertension is associated with the DNase I single nucleotide polymorphism Q222R and enhanced neutrophil extracellular trap formation

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Background: DNase I degrades neutrophil extracellular traps (NETs), an important effector mechanism of polymorphonuclear cells (PMNs). The Q222R single nucleotide polymorphism (SNP) in the DNase I gene impairs its function significantly. This SNP is associated with a higher incidence of myocardial infarction. In a model of spontaneously hypertensive rats, DNase I activity is decreased. We hypothesized that 1) Q222R is associated with hypertension and decreased NET degradation and 2) that high blood pressure (RR) leads to increased NET formation.

Methods: DNA ($n=274$, male=77%, age=59±13y) and PMNs ($n=18$, male=78%, age=64±10y) were isolated from STEMI patients at the Medical University of Vienna. Q222R SNP (ID rs 105384) was analyzed by reaction restriction fragment length PCR. PMNs were stimulated with 2.5 µM phorbol-12-myristate-13-acetate (PMA) and NET formation was measured using a fluorescence reader-based quantification assay.

Results: Hypertension was more common in patients with a homozygous Q222R SNP (84% vs. 62%, $p=0.046$). In patients with hypertension, both systolic and diastolic RR were positively correlated with NET formation after stimulation with PMA (systolic r=0.479, $p=0.044$; diastolic r=0.600, $p=0.008$, Figure 1).

Conclusions: Impaired DNase I activity leads to increased levels of extracellular DNA, a danger-associated molecular pattern (DAMP) which leads to chronic inflammation. This results in higher systemic blood pressure, which also fosters the proinflammatory milieu by ROS-mediated activation of PMNs.

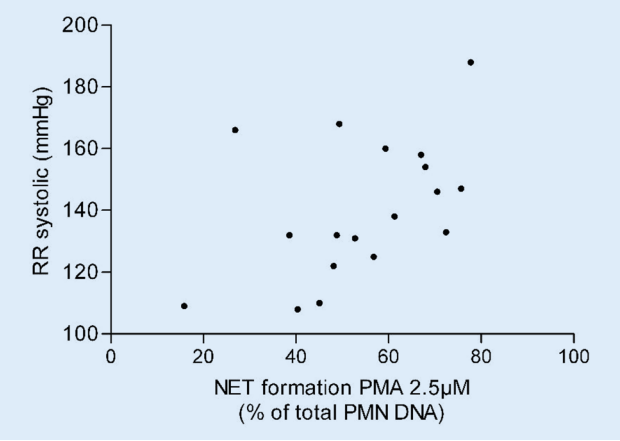

Fig. 1 Correlation of systolic RR with NET formation

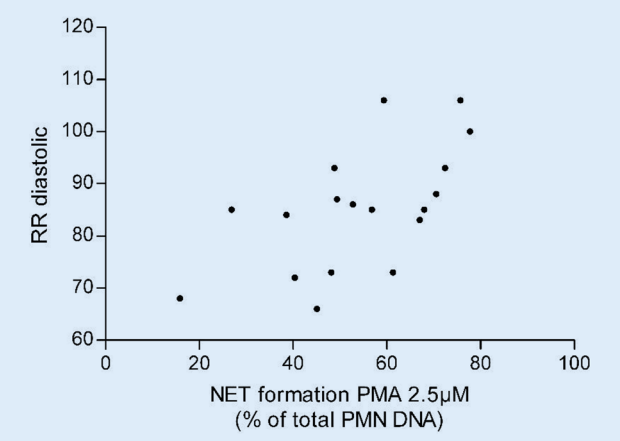

Fig. 2 Correlation of diastolic RR with NET formation

11-2

Evaluation of the creatinine uromodulin ratio as new serum marker for cardiovascular events

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Background: Uromodulin, a protein exclusively produced by the kidney, has recently been demonstrated to be lower in subjects with declined renal function and the ratio creatinine/uromodulin has been proposed as a novel and superior kidney biomarker in serum of healthy subjects. The purpose of this study was to investigate the prospective value of that new biomarker since it is thought to be of high clinical relevance given the link between kidney function and cardiovascular disease.

Methods: We thus evaluated the association between serum levels of uromodulin with the presence of CAD and the cardiovascular risk in 529 angiographically characterized patients. Cardiovascular events have been recorded up to 8 years.

Results: Serum uromodulin concentration did not significantly differ between patients with and without angiographically determined CAD (165.4±78.9 vs. 164.2±75.3 ng/ml ng/ml vs. $p=0.934$) but in patients with CAD, it correlated significantly and inversely with the extent of stenoses (r=–0.191, $p=0.001$). Apart from that, in the total population, there was a significant and inverse correlation with proBNP (r=–0.164, $p=0.002$). With respect to the full follow-up time of up to 8 years (6.6±1.8 years, mean±SD), first vascular events occurred in 27% of the study population. Applying the ratio creatinine/uromodulin in serum, we observed an adjusted HR of 1.27 [95%CI 1.10–1.47] and a $p=0.001$ with with age, sex, bmi, LDL- and HDL cholesterol, triglycerides, presence of CAD and hypertension, T2 DM, and smoking status as well as statin treatment as covariates.

Conclusions: We conclude, that serum uromodulin in combination with serum creatinine is a novel predictive tool for cardiovascular event risk.

11-3

HDL-Cholesterol serves as a powerful predictor of platelet activation in patients with coronary heart disease on dual anti-platelet therapy

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Background: The optimal duration of dual anti-platelet therapy (DAPT) following percutaneous coronary intervention (PCI) is a matter of debate. Biomarkers may help to identify patients who will benefit from extended or intensified DAPT. Aim of the study was to test the association between routine lipid parameters and platelet function in patients with coronary heart disease (CHD) on DAPT.

Methods: Overall, 58 patients on DAPT (clopidogrel: $n=18$, prasugrel: $n=17$, ticagrelor: $n=23$) were prospectively included following PCI. All patients were free from ischemic or bleeding events for at least 6 month. Fasting lipids, including HDL-Cholesterol (HDL-C), LDL-Cholesterol (LDL-C), total-Cholesterol (TC) and triglycerides (TG)), mean platelet volume (MPV, fl), platelet distribution width (PDW, fl), fraction of reticulated thrombocytes (RT) and ADP-induced multiple electrode aggregometry (MEA) were assessed 2–4 hours after intake of ASA (100 mg) and a P2Y12-Inhibitor.

Results: A significant inverse correlation was found for HDL-C levels and markers of platelet activation in univariable analysis: MPV (r = –0.351, $p=0.009$), PDW (r = –0.391, $p=0.003$), fraction of RT (r = –0.402, $p=0.003$) and ADP-induced MEA (r = –0.345, $p=0.011$). Only weak or no association was found between TG, TC, LDL-C and markers of platelet activation (table1). After adjusting for known and identified confounders of platelet activation and other lipid parameters in a linear regression model using backward elimination, HDL-C levels served as strong and significant predictors of MPV (95 % CI –0.009 to -0.039; $p=0.002$), PDW (95 % CI –0.034 to –0.094; $p<0.0001$), RT (95 % CI –0.031 to –0.107; $p=0.001$) and MEA (95 % CI –0.170 to –0.540; $p<0.0001$), while TG, LDL-C and TC were not significantly associated with platelet function.

Conclusions: In contrast to other routine lipid parameters, HDL-C levels highly correlate with different markers of platelet activation in patients with CHD on DAPT. Accordingly, patients with dyslipidemia might benefit from extended or prolonged antiplatelet therapy.

11-4

Non-alcoholic fatty liver disease in coronary artery disease patients – association with impaired glucose metabolism and with future cardiovascular event risk

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Background: Data on non-alcoholic fatty liver disease (NAFLD) in patients with the combination of both impaired glucose metabolism and established cardiovascular disease are scarce. The purpose of this study was to investigate the association of NAFLD with the glycemic state as well as its impact on cardiovascular event risk.

Methods: We enrolled a large series of 1791 patients with established cardiovascular disease (1472 patients with angiographically proven coronary artery disease and 319 patients with sonographically proven peripheral arterial disease) using the validated fatty liver index to diagnose NAFLD.

Results: At baseline, 42.5 %, 36.5 %, and 19.8 % of our patients had normal fasting glucose (NFG), impaired fasting glucose (IFG), and type 2 diabetes (T2 DM), respectively. The prevalence of NAFLD significantly increased from 34.2 % over 52.2 % to 62.7 % through these categories of the glycemic state ($p<0.001$). Prospectively, we recorded 701 cardiovascular events over a mean follow-up period of 5.6± 3.3 years. Cardiovascular event risk significantly ($p<0.001$) increased from 30.7 % in patients with NFG over 33.3 % in patients with IFG to 46.5 % in patients with T2 DM. NAFLD significantly predicted cardiovascular event risk both univariately and in age- and gender adjusted analyses (HRs 1.23 [1.05–1.45]; $p=0.012$ and 1.27 [1.08–1.50]; $p=0.005$, respectively), but not after additional adjustment for the glycemic state (HR 1.15 [0.97–1.37]; $p=0.098$).

Conclusions: We conclude that the prevalence of NAFLD in CAD patients is high and gradually increases with a worsening glycemic state; however, it does not predict cardiovascular events independently from impaired glucose metabolism in this patient population.

Tab. 1 Correlation of Lipid Parameters, HbA1c and Markers of Platelet Activation

		Mean Platelet Volume	Platelet Distribution Width	Reticulated Thrombocytes	Multiple Electrode Aggregometry
Total Cholesterin	Pearson Correlation	,022	,065	–,009	–,104
	P-value	,872	,632	,946	,448
HDL-C	Pearson Correlation	–,351	–,391	–,402	–,345
	P-value	,009	,003	,003	,011
LDL-C	Pearson Correlation	,183	,191	,017	–,038
	P-value	,191	,171	,904	,789
Triglicerides	Pearson Correlation	,126	,206	,231	,060
	P-value	,352	,125	,092	,666
Remnant-C	Pearson Correlation	–,099	–,043	,052	,059
	P-value	,466	,751	,708	,671
HbA1c	Pearson Correlation	,072	,120	,314	,138
	P-value	,600	,384	,024	,325

11-5

Critical evaluation – first assessment of surgical interventions of intravenous treprostinil administration with a gas driven implantable pump – long term follow up in a center with more than 36 pumps implanted

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Background: 2009 a gas driven implantable infusion pump was introduced for intravenous delivery of treprostinil for patients with pulmonary hypertension (PH). Since 2010 our center has acquired vast experience with this innovative treatment, as we consider parenteral treprostinil therapy without the frequent local side effects of subcutaneous infusion a major step forward. A fully implantable pump system minimizes the risk of rare but life-threatening line infections as compared to intravenous delivery with external pumps, but requires surgical intervention in case of drug delivery issues. Methods – At our specialized PH center data are documented in ELPHREG (Elisabethinen Linz Pulmonary Hypertension Registry).

Results: Between September 2010 and April 2015 more than 36 patients were implanted and followed up at our center. As previously reported no intraoperative complications were observed. During follow-up of more than 63 patient-years only 5 surgical interventions in 4 patients became necessary 2, 4, 8 and 28 months after implantation. Patient characteristics are shown in Table 1. While a catheter-kinking was managed with local anesthesia the other interventions required general anesthesia. One pump had to be refixed after rupture of fixation at the fascia, another patient was revised for possible catheter occlusion; the mechanically damaged part was replaced. A catheter loop due to non coaxial implantation required a complete catheter replacement in a second session. One pump had to be replaced as substantial weight loss led to rotation of the pump that made refill nearly impossible. Despite a seroma that resolved without surgical intervention after the pump replacement no complications were observed.

Conclusions: To the best of our knowledge this is the first report on surgical interventions in a large cohort of PH patients with the implanted pump. In our cohort intravenous delivery of treprostinil with this pump is effective. Necessary interventions were performed without complications.

Clinical implications: We recommend close patient monitoring at a specialized expert center and to renew the complete catheter right away in case of catheter alarm. If necessary, pumps can be replaced safely.

11-6

First highly promising experiences with implantations of a gas driven pump for prostacyclin therapy in patients even with severe pulmonary hypertension and concomitant hematologic malignancy

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Background: Pulmonary hypertension (PH) is a progressive fatal disease requiring aggressive specific therapy. As parenteral prostanoid administration with external pumps is associated with local side effects for subcutaneous treprostinil and rare but severe catheter-related infections for intravenous prostanoids, the availability of an implantable pump for intravenous treprostinil represents a significant progress. This surgical approach requires careful interdisciplinary interaction as PH patients carry significantly elevated anesthesia risks, especially with such relevant comorbidities.

Methods: At our specialized PH center data are documented in ELPHREG (Elisabethinen Linz Pulmonary Hypertension Registry).

Results: Between March 2012 and April 2015 three patients with severe PH and concomitant hematological malignancy were implanted at our center. Patient characteristics are shown in Table 1. According to our standard operating procedures all patients were uptitrated with subcutaneous treprostinil. Eligibility for anesthesia and pump implantation were independently assessed by the PH specialist, the anesthesiologist and the surgeon. All implantations at our center are performed by a dedicated surgical team. No perioperative complications were observed. In patient 3 a postoperative bleeding episode was managed during hospital stay. No other complications, especially no infections were observed. Patient 1 deceased 12 months after pump implantation due to the underlying malignancy. Currently a fourth patient, a 65 year old female with a diagnosis of post polycythemia vera myelofibrosis is on the waiting list for implantation as thrombocytopenia – a known side effect of ruxolitinib – is for now a contraindication for surgery.

Conclusions: The coincidence of life-threatening diseases provides an extraordinary challenge. Given intensive cooperation between all departments involved in the patient management and profound experience with the implantation procedure this treatment option can safely be offered even to patients with severe hematologic comorbidities as lymphomas. Implantation of an infusion pump for intravenous treprostinil in patients with severe hematologic comorbidity has not been reported before.

Clinical implications – The treatment of such patients has to be restricted to expert centers, implantations to surgically experienced specialised PH centers.

11-7

Einfluss von Endothelin-1 (ET-1) und einer ET-1 Rezeptor-Blockade auf endotheliale Micropartikel in vitro und in vivo

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Grundlagen: Es ist bekannt, dass die Konzentration von endothelialen Mikropartikeln (EMP) im Plasma mit der endothelialen Dysfunktion (ED) in direktem Zusammenhang steht.

Die ED tritt bereits in den frühesten Stadien der Atherosklerose auf und hat einen großen Einfluss auf vaskuläre Komplikationen bei Diabetes mellitus. Patienten mit Diabetes mellitus Typ II (DM II) weisen zudem eine erhöhte Expression von Endothelin-1 (ET-1) auf. Im Tiermodell hatte die Verabreichung eines ET-1 Blockers einen positiven Einfluss auf das Voranschreiten der Atherosklerose. Ziel dieser Studie war herauszufinden, ob die Blockade von ET-1 die Freisetzung von EMP in ET-1 stimulierten Endothelzellen reduzieren kann und ob dieser Effekt auch in vivo bei Patienten mit DM II nachzuweisen ist.

Methodik: Im in vitro Teil der Studie wurden humane Umbilikalvenen-Endothelzellen (HUVEC) entweder mit ET-1 alleine oder mit ET-1 und einem ET-1 Rezeptorantagonisten für 24 Stunden co-inkubiert. Anschließend wurden die Zellkulturüberstände gewonnen und abzentrifugiert. In die in vivo Studie wurden 36 Patienten mit DM II eingeschlossen und erhielten nach Randomisierung entweder Placebo oder Bosentan. Die Bosentandosis wurde von initial 62,5 mg zweimal täglich in den ersten zwei Wochen auf 2× 125 mg für weitere zwei Wochen gesteigert. Nach einer Gesamttherapiedauer von vier Wochen erfolgte ein Follow-up und Plasmaproben wurden gesammelt. Die Konzentration von EMP im Zellkulturüberstand und im Plasma der Patienten wurde mittels Durchflusszytometrie bestimmt.

Ergebnisse: Im Zellkulturüberstand von ET-1 stimulierten HUVECs konnte ein signifikanter Anstieg von CD31+/CD42b- EMP und von CD31+/Annexin+ und CD62E/Annexin+ EMP verzeichnet werden. Durch ET-1 Blockade konnte die EMP Konzentration wieder auf das Ausgangniveau reduziert werden. Im klinischen Teil dieser Studie hatte die Einnahme von Bosentan über einen vierwöchigen Beobachtungszeitraum keinen Einfluss auf die Plasmakonzentration von CD31+/Annexin-, CD62E+/Annexin+ und CD31+/CD42b- EMP bei Typ II Diabetikern (p = ns).

Schlussfolgerungen: Unsere in vitro Ergebnisse zeigen, dass ET-1 die Freisetzung von EMP in HUVEC Kulturen steigerte und durch Blockade des ET-1 Rezeptors wieder inhibiert werden konnte. In vivo hatte die Behandlung mit dem ET-1 Blocker Bosentan keinen Einfluss auf die Konzentration von EMP im Plasma von Patienten mit DM II. Wir vermuten, dass in unserem Kollektiv an älteren Typ II Diabetikern mögliche positive Effekte der ET-1 Blockade durch das gleichzeitige Vorliegen zahlreicher Komorbiditäten wie Hypertonie, Hyperlipidämie, Hyperglykämie und Nikotinabusus wieder abgeschwächt wurden. Es ist bekannt, dass multifaktorielle Trigger wie Inflammation, Scherkräfte, Hypoxie und Apoptose einen Einfluss auf die Freisetzung von EMP haben. Möglicherweise dürfte die Blockade eines einzigen Rezeptors, im Fall unserer Studie von ET-1, nicht ausgereicht haben um Plasmalevel von EMP in einem komplexen Krankheitsbild, wie es bei Typ II Diabetikern vorliegt, zu beeinflussen.

11-8

Einfluss von Hypoxie auf die Endothelfunktion: Eine Feldstudie auf 2978 m über Meeresspiegel

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Grundlagen: Die Atherosklerose ist die Ursache für die Entwicklung der meisten Erkrankungen des kardiovaskulären Systems und wird begleitet von der endothelialen Dysfunktion. Die Freisetzung von Mikropartikeln ist ein zentraler Bestandteil der endothelialen Dysfuntion.

Es ist bekannt, dass Hypoxie als Triggerfaktor für die Freisetzung von Mikropartikeln fungieren kann. Dennoch zeigten andere Studien in vivo, dass ein Aufenthalt in großen Höhen mit einer Reduktion an zirkulatorischen Level von Mikropartikeln verbunden war. Aufgrund dieser Datenlage wollten wir untersuchen wie sich ein Aufenthalt auf 2978 m auf Biomarker der endothelialen Dysfunktion, wie Mikropartikel und das sST2 Protein, bei gesunden Freiwilligen auswirkt.

Methodik und Ergebnisse: Achtzehn gesunde Freiwillige wurden im Rahmen eines Aufenthalts in Diavolezza (Schweiz) einer moderaten Hypoxie auf 2978 m ausgesetzt. Blutproben wurden auf mittels Durchflusszytometrie auf Mikropartikel und mittels ELISA auf sST2 hin evaluiert. Des Weiteren untersuchten wir den Einfluss einer Endothelin-Rezeptor Blockade durch Macitentan auf Mikropartikel, sST2 und echokardiografische Parameter in der Höhe und unter körperlicher Belastung. Ergebnisse: Während des Experiments fiel die O2-Sättigung auf 93 %. Ein signifikanter Abfall von endothelialen und thrombozytären Mikropartikeln (EMP und PMP) konnte auf 2978 m gefunden werden. Die Konzentration von CD31+/CD42b- EMP am Beginn lag bei 5,09 % (±1,26 % SEM). Nach Akklimatisierung auf 2978 m zeigten EMP Level einen signifikanten Abfall auf 1,19 % (±0,14 % SEM, p = 0,0005). Nach Rückkehr auf 143 m konnte ein signifikanter Wiederanstieg auf 2,88 % (±0,43 % SEM, p = 0,0007) verzeichnet werden. Diese Daten wurden durch einen parallelen Verlauf der sST2 Plasmawerte bestätigt. Eine Endothelin-Rezeptor Blockade durch Macitentan hatte nur einen marginalem auf EMP und sST2 Level, dennoch konnte eine Verbesserung der Rechtsherzfunktion in der Echokardiografie nachgewiesen werden.

Schlussfolgerungen: Diese experimentellen Daten zeigen, dass seine leichte Hypoxie zu einer Reduktion von Parametern der endothelialen Dysfunktion anhand von Mikropartikeln und sST2 führt.

Diese Ergebnisse unterstützen die Hypothese, dass ein Aufenthalt auf großer Höhe zu einer Reduktion des endothelialen Stresses und Dysfunktion führt. Große epidemiologische Studien konnten zeigen, dass Herzinsuffizienzpatienten, die auf

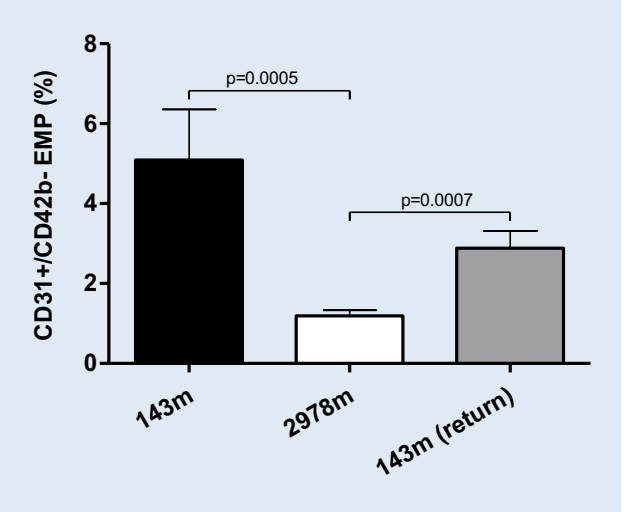

Fig. 1

größerer Höhe leben, eine signifikant reduzierte Mortalität haben. Als Ursache wurde bisher vermutet, dass körperliche Belastungen in größerer Höhe einen besseren Trainingseffekt hätte. In diesem Konzept könnte die Reduktion der endothelialen Dysfunktion ebenfalls einen wichtigen Einfluss haben.

11-9

Promising clinical experience with Riociguat in inoperable Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension patients in a real life setting

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Background: Pulmonary arterial hypertension PAH and chronic thromboembolic pulmonary hypertension (CTEPH) are severe and non curable diseases, which are nowadays treated with three substance classes (endothelin receptor antagonists, phosphodiesterase (PDE)5 inhibitors and prostanoids). Since 2014 Riociguat – a soluble guanylate cyclase stimulator – is also available in Austria.

Objectives: Data of 15 patients treated with Riociguat (12 CTEPH, 2 PAH, 1 patient PH) including 4 patients with additional permanent and 3 patients with paroxysmal atrial fibrillation were collected. Riociguat was used as an ad on therapy in 4 patients.

Reassessement of data was performed after 6 months of therapy.

Methods: After six months all 15 pts were evaluated in changes of NYHA functional class, 6 MWT, pro-BNP, renal function, hemoglobin, right ventricular function and sPAP estimated by echocardiography.

Results: All data were documented in the ELPHREG (Elisabethinen pulmonary hypertension registry).

Clinical Status, maximum tolerated dose of riociguat, WHO functional class, 6 minute walk test (6MWT), pro-BNP, renal function, hemoglobin, right ventricular function and sPAP estimated by echocardiography were revaluated after six months of riociguat therapy.

In all 15 patients we achieved the maximum dosage of 2.5 mg tid within 6 months. None of them experienced relevant side effects. The better 6 MWT (mean 6 MWT at beginning 224 m (14 patients, 1 immobile); after 6 months 324 m) correlated to the improvement of WHO functional class and reduction of pro-BNP (1978 pg/dl to 1242 pg/dl). The renal function was stable. Hemoglobin showed a decrease in 2 pts., as already shown in the CHEST 1.2 und PATENT 1.2 studies, but without any need of intervention. 6 patients showed an improvement of right ventricle function, no worsening was observed. The mean sPAP echo estimated was reduced from 80.5 mmHg to 63.5 mmHg.

Conclusions: In our cohort all patients reached the maximum dosage without relevant side effects. 2.5 mg tid were well tolerated, even in combination therapy with ERAs or prostanoids. All patients showed a clinical improvement in 6 MWT and WHO functional class reflecting the decrease of the pro-BNP value and sPAP. RV function kept stable or rather showed improvement in 6 pts. Hemoglobin values should be monitored closely.

Postersitzung 12 – Risikofaktoren/Stoffwechsel/Lipide 2

12-1

Cardiovascular safety of metformin and sulfonylureas in patients with different cardiac risk profiles

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Tab. 1 Demographics and clinical characteristics

	Analysis cohort (n = 2024)
Female – n (%)	902 (45 %)
Age (years)	63 (54–69)
BMI (kg/m^2)	28.4 (25.2–32.3)
Diabetes duration (years)	10 (5–20)
Medical history – n (%)	
Ischemic heart disease	223 (11%)
Hypertension	1407 (70%)
Albuminuria	332 (16%)
Atrial fibrillation	50 (3%)
Medical therapy – n (%)	
Metformin	980 (48%)
Sulfonylureas	515 (25%)
Insulin	1118 (55%)
ACE-I or ARB	1193 (59%)
Beta blocker	592 (29%)
Statin	908 (45%)
NT-proBNP (pg/ml)	105 (59–243)
HbA1c (%)	7.2 (6.5–7.9)
eGFR (ml/min/1.73 m^2)	73.18 ± 18.6
Total cholesterol (mg/dl)	187 (162–214)
LDL-cholesterol (mg/dl)	101 (82–121)
Treatment site – n (%)	
Centre 1	556 (28%)
Centre 2	1195 (59%)
Centre 3	193 (9%)
Centre 4	89 (4%)

Data is shown as number (percentage), median (interquartile range) or mean ± standard deviation. *BMI* body mass index; *ACE-I* angiotensin converting enzyme inhibitor; *ARB* angiotensin receptor blocker; *HbA1c* glycated haemoglobin; *eGFR* estimated glomerular filtration rate; *LDL* low density lipoprotein

Number of cases with missing data in order of appearance in the table (% relative to cohort size of 164): Sex – 0, age – 0, BMI – 1 (0.6%), duration of diabetes – 83 (51%), medical history – 71 (43%), medication – 35 (21%), NT-proBNP – 0; HbA1c – 58 (36%), eGFR – 8 (5%); total cholesterol – 8 (5%), LDL-cholesterol – 9 (6%), treatment site 2 (1%)

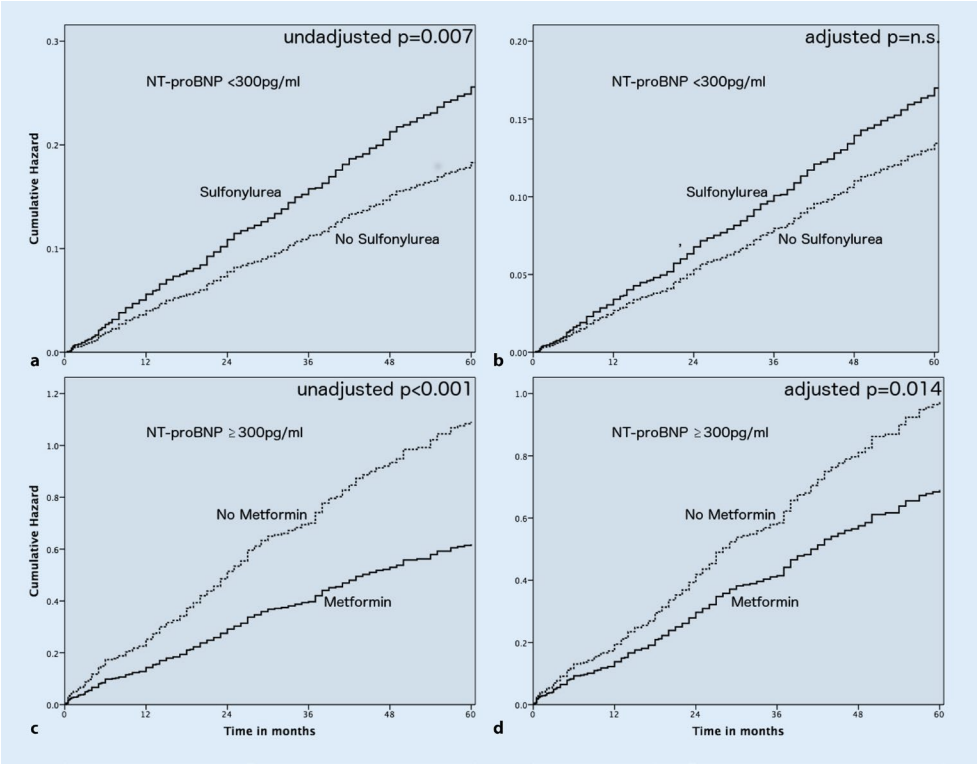

Fig. 1

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Background: Based on previous experiences, the FDA and the EMA recommend that clinical trials for novel anti-diabetic drugs are powered to detect increased cardiovascular risk. In this context, data concerning licensed drugs such as metformin and sulfonylureas are conflicting. The influence of baseline cardiovascular risk on any treatment effect appears obvious but has not been formally proven. We therefore evaluated association of metformin and sulfonylureas with cardiovascular events in patients with different cardiovascular risk profiles indicated by NT-proBNP levels.

Methods: 2024 patients with diabetes mellitus were included in this observational study. The primary endpoint was defined as a combination of cardiovascular events and death. Association of metformin and sulfonylureas were assessed using Cox regression models. Possible differences of these associations in patients with different NT-proBNP levels were studied by stratifying and through interaction analysis.

Results: During a median follow up of 60 months, the primary endpoint occurred in 522 (26%) of patients. The median age was 63 years. A Cox regression analysis was adjusted for site of treatment, concomitant medication, age, gender, BMI, HbA1c, duration of diabetes, glomerular filtration rate, cholesterol, and history of smoking and cardiac disease. Metformin was associated with a decreased risk in the cohort with elevated NT-proBNP ≥300 pg/ml (HR 0.70, $p=0.014$). There was no association with sulfonylureas. There was an interaction between metformin and NT-proBNP ($p=0.001$). This interaction was not significant for sulfonylureas and NT-proBNP.

Conclusions: Metformin is associated with beneficial cardiovascular outcomes in patients with diabetes only when (sub) clinical cardiovascular risk is present.

12-2

Die Graz Heart Study

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Grundlagen: Erkrankungen des Herz-Kreislauf-Systems wie Herzinfarkt und Schlaganfall sind verantwortlich für mehr als die Hälfte aller Todesfälle.

Ursächlich ist ein schleichender Umbauprozess im Bereich der Gefäße, der schließlich in Gefäßwandversteifung, Arteriosklerose, Herzinsuffizienz, Schlaganfall und Nierenschädigung mündet.

Im Rahmen der 2010 angelaufenen „Graz Heart Study“ (GHS), die Teil des Comet-Projektes (K-Projekt) „BioPersMed“ ist, ist die wichtigste Zielvorgabe, den vorhersagenden Wert bekannter und neuer Biomarker, Laborparameter, bildgebender Methoden und funktioneller Tests, für die Früherkennung kardiovaskulärer Erkrankungen zu evaluieren.

Methodik: In die GHS werden seit Dezember 2010 prospektiv Probanden mit kardiovaskulären Risikofaktoren, aber noch keinem arteriosklerotischen Ereignis, eingeschlossen und longitudinal nachbeobachtet. Es erfolgt eine Screening-Untersuchung, welche nach 2,4 und 6 Jahren wiederholt wird, dazwischen finden 3 Telefon–Visiten statt. In Kooperation mit der BioBank der Medizinischen Universität Graz werden Blut- und Urinproben, Speichel, sowie DNA für genetische Analysen asserviert. In einer detaillierten kardiovaskulären Phänotypisierung werden Routineparameter, die systolische und diastolische Ventrikelfunktion, kardiovaskuläres Remodeling sowie state-of-the-art echokardiographische Parameter (strain, strain-rate) erhoben. Die vaskuläre Funktion wird umfassend

u. a. durch Endothelfunktion, Pulswellenanalyse und Analyse der Intima/Media–Dicke an den Carotiden bestimmt. Die körperliche Leistungsfähigkeit wird nicht-invasiv mittels Spiroergometrie, Lungenfunktion und 6 Minuten Gehtest erhoben. Zusätzliche Untersuchungen in Subgruppen beziehen zerebrale arteriosklerotische Ereignisse (Schädel-MRT), Augenhintergrunduntersuchung (Fundus Kamera), ambulante 24Stunden-Blutdruckmessung und eine umfassende Analyse von soziodemographischen Parametern und der Lebensqualität ein.

Ergebnisse: Die primäre Auswertung des Basisdatensatzes der ersten 844 Probanden zeigte folgende Verteilungen. 466 Frauen, 378 Männer – Jüngster Proband 45 Jahre, Ältester 89 Jahre alt. Durchschnittliches Alter 57 Jahre, durchschnittlicher BMI 26 kg/m^2, durchschnittlicher Blutdruck 140/87 mmHg.

Bei den vorbekannten kardiovaskulären Risikofaktoren in dieser Kohorte sind die häufigsten Hyperlipidämie (52 %), arterielle Hypertonie (40 %) und Diabetes mellitus (7 %). 16 % sind aktive Raucher und 35 % Ex-Raucher.

Überraschend ist, dass einige Probanden bereits Symptome einer Herzinsuffizienz, wie z. B. eine Belastungsdyspnoe (26 %) und periphere Ödeme (13 %) aufweisen. 15 % berichten über eine typische AP-Symptomatik mindestens 1×/Monat. 60 % der untersuchten Probanden nehmen regelmäßig Medikamente ein, davon sind 66 % kardiovaskuläre Medikamente.

Schlussfolgerungen: Insgesamt zeigt sich, dass diese Kohorte eindeutig ein Risikokollektiv darstellt mit teilweise bereits pathologischen klinischen Parametern. Die weitere longitudinale Beobachtung dieser Kohorte ist Gegenstand aktueller Studien und soll die Risikostratifikation asymptomatischer Patienten mit erhöhtem kardiovaskulären Risiko verbessern.

12-3

Die Graz Heart Study – Teilauswertung des echokardiographischen Basisdatensatzes

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Grundlagen: Die Risikostratifikation asymptomatischer Patienten mit erhöhtem kardiovaskulären Risiko erfolgt heute auf dem Boden klassischer Risikofaktoren (wie z. B. arterielle Hypertonie, Hyperlipidämie, etc.) mit Hilfe von Score-Systemen (z. B. PROCAM-Score, EURO-Score). Allerdings sind die Zuverlässigkeit und der klinische Nutzen dieser Systeme unbefriedigend. Durch neue laborchemische und biophysikalische Biomarker könnte die Früherkennung und Risikostratifikation verbessert werden. Allerdings liegen derzeit keine Modelle vor, in denen die Kombination neuartiger Biomarker mit etablierten Risikomarkern untersucht wurde. Im Rahmen der 2010 angelaufenen „Graz Heart Study", die Teil des Comet-Projektes (K-Projekt) „BioPersMed" ist, ist die wichtigste Zielvorgabe, den vorhersagenden Wert bekannter und neuer Biomarker, Laborparameter, bildgebender Methoden und funktioneller Tests, für die Früherkennung kardiovaskulärer Erkrankungen zu evaluieren.

Methodik: In die GHS werden seit Dezember 2010 prospektiv Probanden mit kardiovaskulären Risikofaktoren, aber ohne manifeste kardiovaskuläre Erkrankung, eingeschlossen und longitudinal nachbeobachtet. Die Probanden werden alle 2 Jahre untersucht (Screening-Untersuchung), dazwischen finden Telefon-Visiten statt. In Kooperation mit der BioBank der Medizinischen Universität Graz werden Blut- und Urinproben, Speichel, sowie DNA für genetische Analysen asserviert. In einer detaillierten kardiovaskulären Phänotypisierung werden neben Routineparametern die systolische und diastolische Ventrikelfunktion, kardiovaskuläres Remodeling sowie state-of-the-art echokardiographische Parameter (strain, strain-rate) erhoben. Weiters werden u. a. eine Pulswellenanalyse und Analyse der Intima/Media-Dicke an den Carotiden durchgeführt zur Bestimmung der vaskulären Funktion. Die körperliche Leistungsfähigkeit wird nicht-invasiv mittels Spiroergometrie, Lungenfunktion und 6 Minuten Gehtest erhoben.

Zusätzlich erfolgen noch weitere Untersuchungen in Subgruppen. (Schädel-MRT, Augenhintergrunduntersuchung, ambulante 24Stunden-Blutdruckmessung, Analyse soziodemographischer Parameter und der Lebensqualität).

Ergebnisse: Die primäre Auswertung der Echokardiographien des Basisdatensatzes der ersten 844 Probanden (466 Frauen, 378 Männer) zeigte folgende Verteilungen. Alle Probanden zeigten eine normale LVEF ohne ein relevantes Klappenvitium. Bei ca. 30 % der Probanden konnte eine LV-Hypertrophie festgestellt werden. Ca. 50 % wiesen eine diastolische Ventrikelfunktionsstörung auf, davon ca. 5 % klinisch signifikant. In 25 % konnte ein leicht-mittelgradig dilatierter linker Vorhof vermessen werden.

Schlussfolgerungen: Die GHS Kohorte zeigt somit bereits deutliche Veränderungen am Herzen bei erhaltener systolischer Pumpfunktion, die für Remodeling und beginnende kardiovaskuläre Veränderungen sprechen.

12-4

Plasma parathyroid hormone is independently associated with atrial fibrillation – Insights from the LURIC study

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Background: Parathyroid hormone (PTH) influences the cardiac sympathomimetic system and calcium handling in cardiomyocytes. Furthermore, PTH is related to arterial hypertension. This led us to hypothesize that patients with atrial fibrillation (AF) show increased serum concentrations of PTH.

Methods: We enrolled data of blood samplings, ECG and coronary angiography of 3126 patients (age (mean ± SD) 63 ± 11 years, 30 % females) who participated in the LUdwigshafen RIsk and Cardiovascular health (LURIC) study. The diagnosis of AF was based on medical history and current ECG readings. We performed a multivariate binary logistic regression analysis with atrial fibrillation as the dependent variable in which we adjusted for age, sex, PTH, left ventricular ejection fraction, LDL cholesterol, mean pulse, thyroid stimulating hormone, type 2 diabetes, systolic office blood pressure, diastolic office blood pressure, history of myocardial infarction, coronary artery disease, valve disease, estimated glomerular filtration rate, 25-hydroxy-vitamin D3 and concomitant drug prescription.

Results: AF was diagnosed in 394 patients (14 %, age 66 ± 9 years, 28 % females). In the multivariate regression model PTH was significantly associated with AF (OR (95 % CI) 2.575 (1.457–

4.549), $P<0.001$). The association remained significant after further adjustment for concomitant drug intake.

Conclusions: Our study demonstrates that elevation of serum concentrations of PTH within the normal ranges are independently associated with AF. Whether elevated PTH predisposes for the development of AF and whether drugs lowering PTH might reduce the risk of AF remains to be elucidated in further studies.

12-5

Serum kynurenine, quinolinic acid and cardiac stiffness parameters: the eplerenone in primary hyperparathyroidism study

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Background: The essential amino acid tryptophan (TRYP) is metabolized via the kynurenine (KYN)-quinolinic acid (QUIN) pathway upon inflammatory stimulation. Experimental studies indicated a contribution of these derivatives to cardiac disease. Primary hyperparathyroidism (pHPT) is associated with low-grade inflammation and an increased prevalence of left ventricular (LV) hypertrophy and stiffness. We aimed to test the hypothesis that KYN and QUIN are related with echocardiogrpahic parameters of cardiac structure (LV mass index, left atrial volume index) and LV diastolic function (E/e' average) in a large cohort of pHPT patients.

Methods: Cross-sectional baseline data from 153 patients with pHPT were analyzed who participated in the "Eplerenone in Primary Hyperparathyroidism" Study. Tryptophan (TRYP), kynurenine (KYN) and quinolinic acid (QUIN) were determined in serum that had been frozen at -80°C immediately after blood sampling. QUIN was quantified by means of a novel liquid chromatography-mass spectrometry method that was recently developed and validated at our university.

Results: Mean age was 67 +/- 10 years and 121 (79%) were females. The prevalence of left ventricular hypertrophy was 46% and median E/e' (average) was 10.1 (8.1–12.9). CRP was correlated with LV mass index (Pearson r=0.202, $P=0.025$), left atrial volume index (r=0.273, $P=0.001$), serum KYN (r=0.210, $P=0.009$) and QUIN (r=0.312, $P<0.001$), but not with E/e'. Multivariate linear regression analyses (adjusted for age, sex, diabetes mellitus, mean nocturnal systolic blood pressure, antihypertensive drugs, estimated glomerular filtration rate (CKDEPI), body mass index, total serum cholesterol, smoking status, parathyroid hormone, adjusted calcium and CRP) with cardiac parameters as dependent variables revealed no association between TRYP and cardiac parameters. In contrast, KYN was independently related with E/e' (beta-coefficient 0.216, $P=0.028$) and left atrial volume index (beta=0.302, $P=0.001$). QUIN was independently related with E/e' (beta=0.300, $P=0.008$) and LV mass index (beta=0.222, $P=0.035$).

Conclusions: Circulating levels of KYN and QUIN, but not TRYP, are independently related with cardiac stiffness parameters in subjects with pHPT. These data add clinical evidence to previous experimental studies suggesting a direct contribution of an activated TRYP-KYN-QUIN pathway to myocardial disease.

12-6

Retinal vessel caliber, pulse wave velocity and intima-media thickness of the carotic artery as screening tools for early detection of cardiovascular diseases and cardiovascular risk factors

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Background: Vascular remodelling and functional impairment precede major complications of cardiovascular risk factors, such stroke or myocardial infarction. Novel non-invasive functional biomarkers tools, such as semi-automatic retina scanning, may improve early diagnosis of vascular impairment and may thereby improve risk stratification and management of patients at risk for cardiovascular diseases.

Methods: In $n=121$ consecutive participants of the Graz Heart Study within the Biopersmed Project, a prospective longitudinal study for probands at risk for cardiovascular disease (inclusion criteria: age >45 years, ≥1 cardiovascular risk factors), retinal vessel assessment was carried out in addition to an extensive cardiovascular phenotyping. The diameter of the retinal vessels was quantified by imaging the retina with a non-mydriatic fundus camera and the arteriolar-venular ratio (AVR) was calculated applying the Parr-Hubbard-Knudtson formula. Pulse wave velocity (PWV) was determined by a direct measurement of the time lag between electrical heart activity and arrival of the pulse wave in the carotid artery and in the iliac artery. Intima-medi-thickness (IMT) quantification followed standardized protocols.

Results: Compared to normotensive subjects the PWV was significantly higher in the hypertensive population (7.0±1.7 versus 8.0±1.9; $p=0.019$). Similarily, manifest type-2 diabetes showed an incresaed PWV (9.5±2.0 vs. 7.0±1.5; $p<0.001$). The AVR was significantly higher in the hyperlipidaemia group (0.66±0.05 vs. 0.63±0.05; $p=0.005$). The intima media thickness (IMT) did not differ significantly between and within the single risk factor groups, but it correlated with the systolic blood pressure (Pearson r=0 .415; $p<0.001$). The PWV was correlated

Tab. 1

Population characteristics (n = 108)	All patients	Fernale (n = 60)	Male (n=48)	p
Age (mean ± SD) [y]	59 ± 7.1	58 ± 7	59 ± 7	0.64
BMI (mean± SD) [kglml]	26.2 ± 4.8	24.9 ± 5.0	27.8 ± 4.1	0.002
Risk factors				
Hypertension [%] (n)	27.8	18.3 (11)	39.6 (19)	0.037
Diabetes Mellitus [%] (n)	12.0	6.7 (4)	18.8 (9)	0.078
Hyperlipidaemia [%] (n)	33.3	36.7 (22)	29.2 (14)	0.382
Positive Family History [%] (n)	97.2	100 (60)	93.8 (45)	0.050
Smoking, current [%] (n)	111	16.7 (10)	4.2 (2)	0.118
Ex-smoker [%] (n)	39.8	38.3 (23)	417 (20)	
Sleep apnoea [%] (n)	4.6 17 (1)	8.3 (4)	0.151	
Hyperuricemia [%] (n)	130	8.3 (5)	18.8 (9)	0.125
NYHA1 [n]	100	88.3 (53)	97.9 (47)	0.059
NYHA2 [n]	8	117 (7)	2.1 (1)	

with the systolic blood pressure (r = 0.398 $p < 0.001$), the HbA1c (r = 0.370, $p < 0.001$), and the IMT (r = 0.356; $p < 0.001$). The AVR was negatively correlated with the IMT (r = –0.261; $p = 0.006$). Interestingly, there was no correlation between AVR and PWV (r = –0.045, $p = 0.653$).

Conclusions: The PWV and retinal vessel calibers are promising screening parameters for early detection of cardiovascular diseases or existing risk factors since correlations for cardiovascular risk factors were identified. While the PWV aims at the evaluation of the stiffness of large arteries (aorta), the retinal vessel calibers reflect on the status of small vessels. This might explain the lack of a correlation between the PWV and the AVR. In summary, the PWV and the AVR provide additional information in the detection of cardiovascular diseases. To assess the clinical usefulness of the AVR and the PWV to guide therapeutic decision future interventional studies will be needed.

12-7

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

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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.

12-8

Reversal of premature aging markers after bariatric surgery

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Background: Obesity is considered to be a major risk factor in developing cardiac disease. In addition, obese patients suffer from a premature aging phenotype including increased secretion of senescence associated secretory proteins (SASP) and reduced telomere length compared to healthy controls.

Purpose: The aim of our study was to determine, if bariatric surgery and the resulting weight loss could reverse the previously observed premature aging phenotype.

Methods: We enrolled 76 patients undergoing bariatric surgery. Blood samples were taken before and 12 months after surgery. Markers of premature aging including the SASP IL6 and PAI-1 as well as telomere length and telomere oxidation were evaluated.

Results: Overall, patients showed a significant drop of body mass index (44.5 ± 4.2 before surgery versus 27.5 ± 3.6 after surgery, $p < 0.001$). In addition plasma levels for IL6 (3.1 ± 2.4 pg/ml before versus 1.7 ± 1.5 pg/ml after bariatric surgery, $p < 0.001$) and PAI-1 (98.4 ± 17.2 ng/ml before versus 83.8 ± 27.1 ng/ml after bariatric surgery, $p < 0.001$) were significantly reduced after surgery. In addition, telomere length on average increased by 58 % in the patient cohort (0.37 ± 0.28 a. u. before versus 0.59 ± 0.28 a. u. after bariatric surgery, $p < 0.001$). The telomere increase was accompanied by a reduction in the telomere oxidation index (2.86 ± 4.4 before versus 0.78 ± 0.56 after bariatric surgery, $p < 0.001$) indicating reduced oxidative stress for the telomeric region. This is further supported by an inverse correlation of telomere length with telomere oxidation at both time points (r = –0.376, $p < 0.001$ pre surgery and r = –0.705, $p < 0.001$ post surgery).

Conclusions: Our data indicate a significant reduction of the SASP IL6 and PAI-1 in plasma 12 months after bariatric surgery. In addition we observed an increase in telomere length in this setting. However, given the reduction in oxidative stress at telomeric regions we speculate that the increased telomere length is not due to active elongation but due to reduced breakage caused by telomere oxidation. Overall, bariatric surgery ameliorated the premature aging phenotype of previously morbidly obese patients.

Postersitzung 13 – Basic Science 3

13-1

The anti-cancer tyrosine kinase inhibitor sorafenib reduces cardiac contractile force by reducing cardiomyocyte calcium transient amplitude

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Background: Tyrosine-kinase inhibitors (TKIs) are widely used in cancer treatment. Although more targeted than conventional chemotherapy, TKIs exhibit substantial cardiotoxicity. Here, we aim to characterize underlying alterations of myocyte calcium homeostasis in order to identify potential protective co-treatments.

Methods: Human atrial muscle strips were isolated from right atrial appendages of patients undergoing heart surgery, placed in an organ bath, connected to a force-transducer, field stimulated (1 Hz), and exposed to increasing concentrations of sorafenib (1–30 mM). Cellular calcium transients (CaTs) were assessed at room temperature using confocal laser scanning microscopy in electrically stimulated (0.5 Hz), isolated murine C57BL/6 cardiomyocytes loaded with the calcium sensitive fluorescent dye Fluo-4/AM (1.5 uM). Myocytes were superfused with sorafenib (10 M) or vehicle control ($n=18$ and 10, respectively, 4 hearts/treatment). Isoproterenol (10 nM) and caffeine (30mM) responses were measured to assess beta-adrenergic reserve and sarcoplasmic reticulum (SR) calcium content, respectively. Custom-made R scripts were used for CaTs analysis and statistical testing (mixed 2-factor ANOVA or Welch t-test). Data are shown as mean ± S.E.M.

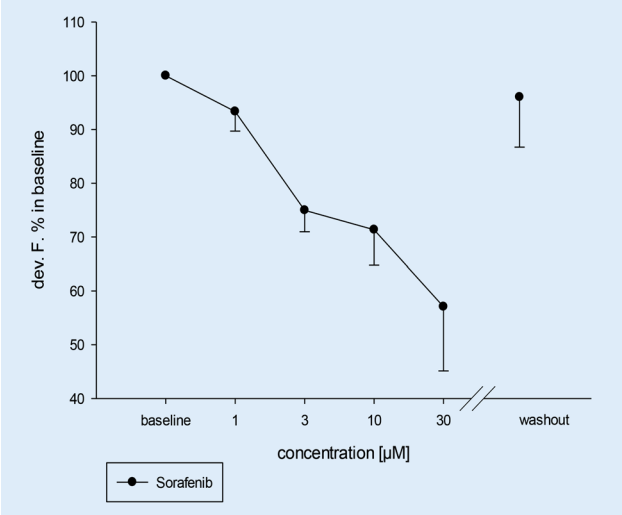

Fig. 1 Developed force in human muscle strips with different concentrations of sorafenib ($p<0.05$) vs baseline for 3–30 µM sorafenib

Results: Sorafenib dose-dependently and reversibly decreased contractile force in human atrial myocardium (3 µM: 75±4 %, 10 µM: 71±6.6 %, 30 µM: 57±11.9 %, all $p<0.05$ vs. ctrl, $n=13$, 5 hearts, Fig. 1). While sorafenib-superfused cardiomyocytes showed a progressive decrease in systolic calcium amplitude reaching 52±8,1 % of baseline at maximum drug effect ($p<0.001$), control cells did not show any significant difference over time ($p=0.93$, Fig. 2). Sorafenib decreased calcium release and re-uptake kinetics (RT50, Tau, and time to peak $p<0.05$). Beta-adrenergic stimulation with isoproterenol resulted in higher transient amplitude and calcium release velocity (dF/d^{tmax}) in control myocytes, which was attenuated in sorafenib-treated cells ($p<0.01$). In sorafenib treated cells SR calcium content was reduced compared to control cells (6.6±0.42 vs. 10.5±0.73 F/F0, $p=0.056$ – borderline significance).

Conclusions: Negative inotropy by sorafenib is caused by a decrease in intracellular CaT amplitude rather than (exclusive) myofilament calcium desensitization. SR calcium re-uptake is likely altered by sorafenib, as the SR calcium content is decreased and calcium re-uptake kinetics slowed. Further studies will identify underlying posttranslational modifications caused by TKIs and thus, potential targets for protective co-pharmacotherapy.

13-2

High levels of spermidine and spermine cause impaired force development, arrhythmias and negative inotropy in human atrial tissue

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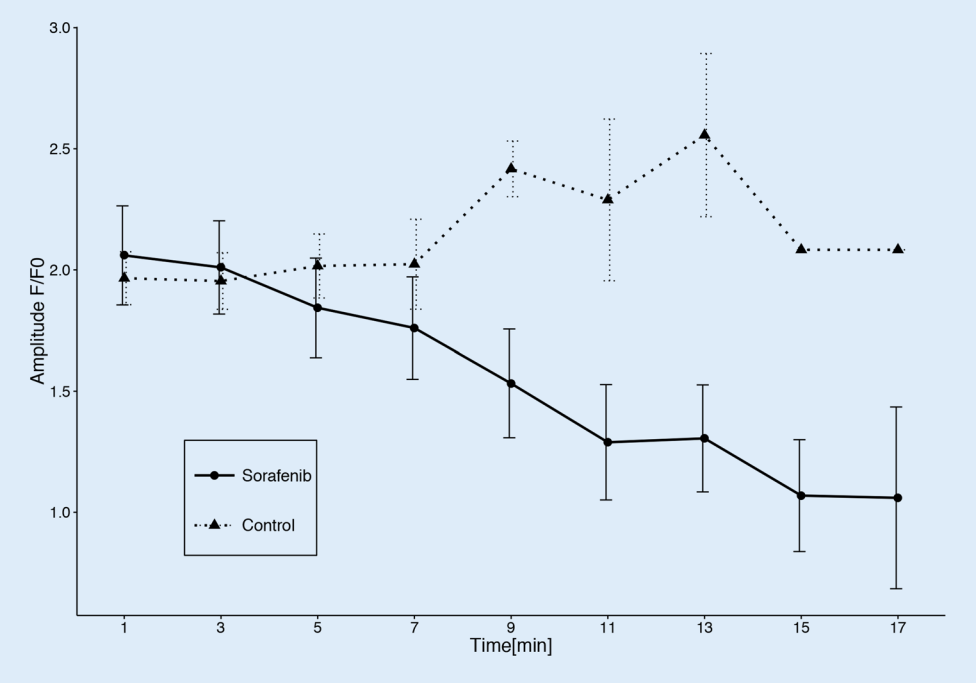

Fig. 2 Progressive decreases in calcium transient amplitudes in sorafenib treated cells over time ($p<0.001$)

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Background: The polyamines spermidine, spermine and putrescine are modulators of membrane excitability and cell contractility in experimental animal models. Binding of polyamines to several types of membrane ion channels is associated with altered ion homeostasis that may cause arrhythmias. Yet, the effect of polyamines on force development and arrhythmias in the intact human cardiac tissue remain unknown.

Methods: We used isolated muscle strips (trabeculae) of human atrial tissue from patients undergoing cardiac surgery (coronary artery bypass graft and/or aortic valve replacement). Trabeculae were perfused with a modified Tyrode's solution supplemented with increasing concentrations of spermidine, spermine or putrescine (100 nM, 1 mM, 10 mM, 100 mM and 1 mM; 20 min each concentration at 37 °C) and electrically stimulated at 1 Hz. Untreated muscle strips served as controls. Developed force and diastolic tension of trabeculae were measured using a force transducer. To elucidate spermidine-induced mechanisms underlying changes in the force development (1 mM), trabeculae were pre-incubated with ryanodine (1 µM) and phosphoinositol 3-kinase (PI3K) inhibitors, namely LY 294002 (5 µM) and A-66 (1 µM). Mixed ANOVA was employed to test for differences within groups (time/concentration) and between groups (treatment). Data are shown as mean ± SEM. Values of $P < 0.05$ were considered statistically significant.

Results: The administration of low concentrations (100 nM – 100 µM) of spermidine ($n = 14$ trabeculae), spermine ($n = 10$ trabeculae) and putrescine ($n = 7$ trabeculae) similarly reduced the force development compared to control ($n = 9$ trabeculae, n. s.). However, supraphysiological level of spermidine or spermine (1 mM) induced a significantly negative inotropic effect (figure 1). In addition, high concentrations (1 mM) of spermidine and spermine evoked proarrhythmogenic events (spermidine: 25 % of trabeculae, spermine: 50 % of trabeculae, control: 0 % of trabeculae) that were accompanied with impaired force development (figure 2). Interestingly, two spermidine-treated trabeculae developed sustained arrhythmias. On the other hand, putrescine-treated trabeculae did not show any arrhythmic events and had a comparable force development as controls.

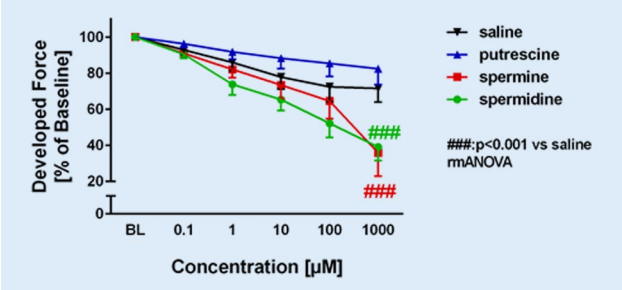

Fig. 1 Developed Force

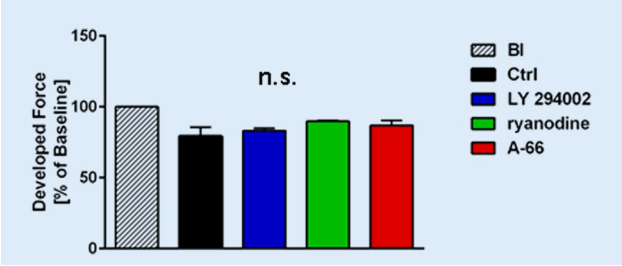

Fig. 3 Inhibitors + 1mM spermidine

The negative inotropic effect of spermidine was attenuated by ryanodine ($n = 2$ trabeculae), LY 294002 ($n = 3$ trabeculae) and A-66 ($n = 3$ trabeculae), but this effect did not reach statistical significance compared to control (figure 3).

Conclusions: Supraphysiological concentrations of the exogenous polyamines spermidine and spermine, but not putrescine, induced a negative inotropic effect and increased the arrhythmogenic potential of human atrial tissue. Pharmacological inhibition of cardiac ryanodine receptor and PI3K attenuated spermidine-induced negative inotropic effect, which might be due to decreased myocardial calcium. Our results suggest different mechanisms underlying the negative acute effects of polyamines at high concentrations on human cardiac tissue.

13-3

Measuring the „NET effect" – establishment of a NET quantification assay

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Background: Neutrophil extracellular traps (NETs) are a crucial effector mechanism of neutrophils implicated in thrombosis and inflammatory diseases. NETosis is induced by various stimuli, such as phorbol-12-myristate-13-acetate (PMA), ionomycin, interleukin-8 (IL-8) and lipopolysaccharide (LPS). Quantifying NETs remains challenging. Quantification by optical techniques is imprecise and unsuitable for larger sample numbers. We aimed to validate a fluorescence-based NET quantification assay (NQA).

Methods: PMNs were isolated and seeded into a 96-well culture plate. Respective stimuli were then added to the wells. PMNs were lysed using Triton X-100 as a positive control. After incubation for 2:45 min, 50 µM Sytox Green was added, which only stains extracellular DNA released from cells with disrupted cellular membranes, a hallmark feature of NETosis. After 15min of incubation, the plate was measured with a fluorescence reader. NET formation was expressed as fluorescence intensity percentage compared to positive control.

Results: After establishing suitable concentration ranges with PMNs of healthy controls, the NQA was used in a cohort of post-STEMI patients ($n = 27$, male = 63 %, age 64±12y). We

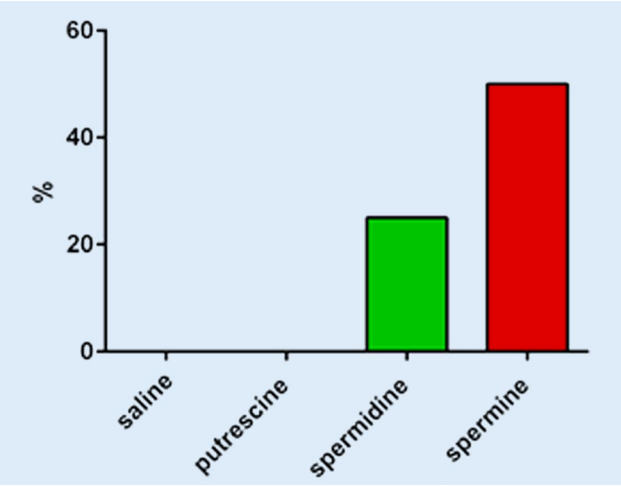

Fig. 2 % of trabecula with impaired contractility

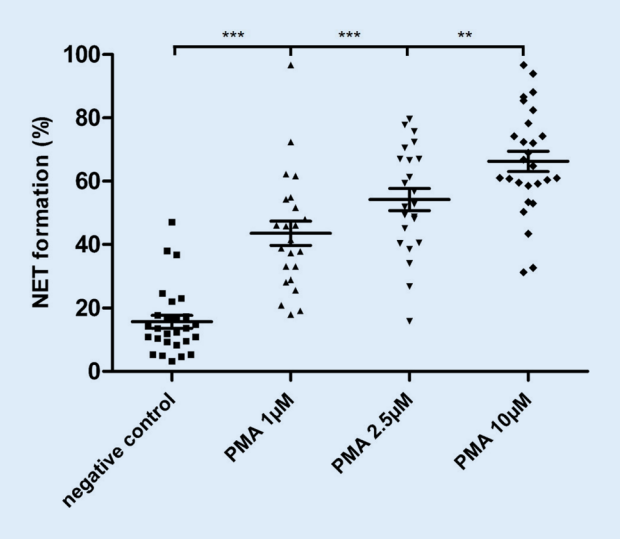

Fig. 1 NET Quantification – PMA ($n=27$)

observed a highly significant dose-dependent increase of NET formation in the presence of PMA (see figure) and ionomycin, LPS and IL-8.

Conclusions: The NQA is a robust and efficient assay allowing fast and reliable NET quantification. It can be used to investigate the NETotic potential of any stimulant and could provide further insights into NET formation.

13-4

Differential characteristics of hypertrophy induced by tachycardia, neurohumoral activation or stretch

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Background: Hypertrophy is established in stretch and in neurohumoral agonist stimulation models but not typically seen in chronic tachycardia models. The aim of this study was to characterize the very early remodeling events of tachycardia in comparison to stretch and angiotensin II.

Methods: Primary neonatal rat cell culture for cardiac fibroblasts or highly enriched ventricular cardiac myocytes (CM): Cyclic stretch (ST) was applied by a Flexcell 5000 tension system with 20 % elongation at a rate of 0.5 Hz. Tachycardia (TC) was generated by field stimulation with a C-Pace EP IonOptix cell stimulator with 4–8 Volts per cm with 5 Hz vs. 1 Hz. Angiotensin II (AT II, stabilized with a protease inhibitor) was applied in a concentration of 1 micromol/L. Cell size analysis was performed by Immuno staining with cell type specific antibodies for Desmin and Prolyl 4-hydroxylase and subsequent analysis by Image J software. Gene expression was investigated by realtime PCR using SYBR green. Signaling inhibitors were preincubated before trigger application in concentrations of 1 micromol/L for KN93 and 5 micromol/L for FK506.

Results: ST resulted in moderate hypertrophy with slow progression (maximum at 72 h), CM surface area (n of 1700 per group) increased by 12 % (3645 ± 99 µm² vs. 3255 ± 67 µm² in control; $p=0{,}001$). AT II increased cell size (n of 1700 per group) to a larger extend (by 27 %, 5359,7± 68 µm² vs 4208 ± 49 µm² in control, $p<0.001$) after 48 h. Interestingly, also sustained TC increased CM surface area (n of 300 per group), however, with an earlier maximum at 48 h (increase by 27 %; 3472 ± 78 µm² with 5 Hz vs. 2737 ± 78 µm² in control; $p<0{,}001$). The pattern of hypertrophy was more eccentric in TC than after ANG II or ST: Cellular long axis to short axis ratio was 5.4 after TC and 2.9 after ANG II (both $p<0.001$ vs. control) and 1.3 after ST. Furthermore, with sustained TC cells showed notable changes in cell orientation with clusters of alignment in series, which was not observable with ST. Pure fibroblasts did not show any effect on cell size neither after ST nor TC. Time dependent gene expression profiling showed a peak effect at 24 h after ST with upregulation of mRNA levels of the prohypertrophic genes ACTA1 (1.66-fold ± 0.23 $P=<0.001$, $n=9$), FHL1 (1.67-fold ± 0.08 $P=<0.001$, $n=9$), NppA (1.59 ± 0.07 $P=<0.001$, $n=9$), NppB (1.51 ± 0.17 $P=0.003$, $n=9$) but no significant upregulation in a pure fibroblast culture. The Calcineurin inhibitor FK506 decreased the upregulation of these genes, whereas the CaM-Kinase inhibitor KN93 had no significant effect. AT II stimulation ($n=6$ to 10) showed an earlier gene expression peak effect at 1 h up to 3 h for the selected marker genes ACTA1 (1.98 ± 0.40, $p=0.08$), RCAN1 (1.91 ± 0.23, $p=0.02$), ANF (2.26 ± 1.06, $p=0.81$), BNP (3.26 ± 1.68; $P=0.72$); TGFß (1.68 ± 0.78, $P=0.47$). Results of ongoing gene expression profiling and underlying signaling in TC will be presented in detail.

Conclusions: Our data give the first evidence that not only stretch and neurohumoral stimulation but also tachycardia results in hypertrophy as an early remodeling response and characterize the similarities and differences in pattern, gene expression profiling and signaling.

13-5

Serum uromodulin is associated with impaired glucose metabolism

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Background: Uromodulin is the most abundant urine protein under physiological conditions. It has recently been described as a serum marker of kidney disease. The purpose of this study was to investigate whether uromodulin also is associated with impaired glucose metabolism.

Methods: We therefore measured serum uromodulin in a series of 529 patients who were undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD); in patients without established diabetes oral glucose tolerance tests were performed. Prospectively, diabetes incidence was recorded over 4 years.

Results: Serum uromodulin was significantly and inversely correlated with fasting plasma glucose ($r=-0.158$; $p<0.001$), with plasma glucose 2 hours after an oral 75 g glucose challenge ($r=-0.144$; $p=0.002$), and with HbA1c ($r=-0.103$; $p=0.018$). From our patients 146 (27.6 %) had type 2 diabetes. Uromodulin was significantly lower in patients with T2 DM han among non-diabetic patients (147.7±69.9 vs. 171.4±78.9 ng/ml, $p=0.001$). Analysis of covariance confirmed that T2 DM was an independent determinant of serum uromodulin ($F=5.6$, $p=0.019$) after

multivariate adjustment including both the glomerular filtration rate and urinary albumin excretion. Prospectively, 21 patients of the initially non-diabetic subjects developed diabetes. Their uromodulin was intermediate (164±67 ng/ml) between those who did not develop diabetes and those who already at baseline had diabetes (p for trend over these three categories <0.001).

Conclusions: We conclude that serum uromodulin is significantly associated with impaired glucose metabolism; patients with T2 DM have significantly higher levels of uromodulin than non-diabetic subjects.

13-6

Shock waves induce angiogenesis via exosome release

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Background: Shock wave therapy (SWT) is developing a promising approach for the regeneration of ischemic myocardium by induction of angiogenesis. However, the mechanism of action remains unknown. Exosomes are released by mechanical shear stress and have been shown to induce angiogenic effects. We hypothesized that SWT induces exosome release and thus exerts its angiogenic effects.

Methods: Human umbilical vein endothelial cells (HUVECs) were treated with SWT. Subsequently, exosomes were isolated from the supernatant and analyzed by transmission electron microscopy (TEM) and nanoparticle tracking analysis. In a next step, exosomes were characterized and analyzed for their angiogenic potential in vitro. Exosome content was evaluated via a sequencing array. Finally, isolated exosomes were injected into subcutaneously implanted matrigel plugs in nude mice. Perfusion of the plugs was measured via Laser Doppler perfusion imaging (LDPI). Arterioles and capillaries were quantified histologically. In vivo imaging was performed to analyze functionality of the vessels.

Results: SWT caused exosome release in HUVECs. Supernatants of treated cells showed significantly higher concentrations of exosomes. Exosomes showed a characteristic cup-shaped morphology in TEM analysis. Treatment of HUVECs with exosomes induced phosphorylation of Akt and ERK, caused increased tube formation (CTR 19.5 ± 7.79 vs. SWT 178.5±31.14, $p = 0.004$) and endothelial cell proliferation (CTR 0.59 ± 0.02 vs. SWT 0.77 ± 0.04, $p = 0.011$). Pre-treatment with exosome-release inhibitor GW4869 abolished the angiogenic effects of SWT. Sequencing array showed the presence of angiogenic miRNAs in exosomes released after SWT. Injection of isolated exosomes into subcutaneously implanted matrigel plugs resulted in higher perfusion and increased number of capillaries (CTR 0.53 ± 0.19 vs. SWT 1.7 ± 0.26, $p = 0.0006$) and arterioles (CTR 0.8 ± 0.23 vs. SWT 4.5 ± 0.54, $p < 0.0001$). In vivo imaging of the matrigel plugs showed formation of functional vessels after exosome injection.

Conclusions: We show for the first time how the mechanical stimulus of SWT is translated into a biological response. SWT causes exosome release. Released exosomes show a very potent angiogenic effect. SWT might develop a potent therapeutic intervention for the treatment of ischemic heart disease.

13-7

Validation of a luminescence-based NET degradation assay

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Background: Formation of neutrophil extracellular traps (NETs), an effector mechanism of polymorphonuclear cells (PMNs), promotes thrombosis. Degradation of NETs is predominantly mediated via DNase 1. Impaired NET degradation is related to cardiovascular events and increased myocardial infarct size. Mechanisms influencing NET degradation are poorly understood. It is known that serine proteases like thrombin, plasmin and heparin support DNase 1 activity. We aimed to validate a luminescence-based NET degradation assay (NDA) to investigate mediators of NET degradation.

Methods: PMNs were stimulated with PMA to generate NETs in 48-well culture plates. Media containing DNase 1 and respective reagents were added. After degradation of NETs and release of double-stranded DNA (dsDNA) fragments supernatants from each well were transferred to a 96-well plate. PicoGreen (Thermo Fisher Scientific, P11496) was added to the wells. Lambda DNA served as a positive control and dsDNA levels were measured on a luminescence reader.

Results: In the presence of thrombin, NET degradation by DNase 1 was significantly enhanced in a dose-dependent manner (see figure), in the absence of serine proteases or heparin. Plasmin and heparin alone promoted NET degradation. EDTA completely inhibited DNase 1 activity.

Conclusions: The NDA is an efficient assay to evaluate the influence of any co-factor for DNase 1 activity and facilitates the analysis of the complex interplay between NET formation and degradation.

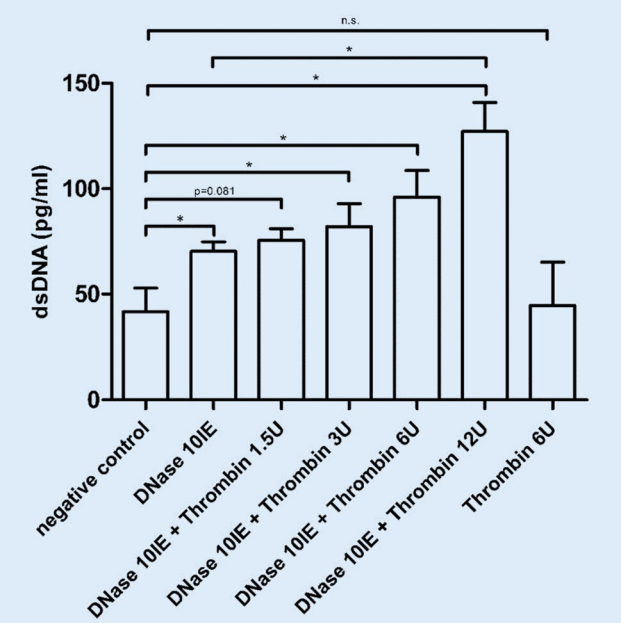

Fig. 1 Influence of thrombin on NET Degradation ($n = 5$)

13-8

Parathyroid hormone (1–34) has no direct effect on human atrial tissue

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Background: Increased levels of parathyroid hormone (PTH) have been associated with an increased prevalence of atrial fibrillation. Experimental data from small animal studies demonstrated that PTH directly modulates calcium levels in cardiomyocytes via PTH-receptors. We aimed to investigate possible direct effects of PTH on human atrial cardiac tissue.

Methods: Isolated human atrial trabeculae were electrically stimulated at 1 Hz and treated with increasing concentrations of PTH(1–34) (1 nM, 10 nM and 100 nM), a fragment of PTH and agonist on the PTH-receptor, for 2 hours. To elucidate the role of calcium, trabeculae were superfused either with a low (1.2 mM) or a high (3.5 mM) concentrated calcium tyrode solution. The latter mimics conditions of hyperparathyroidism. Developed force, diastolic tension and RT50 were recorded in treated and control trabeculae.

Results: PTH(1–34) did not cause any inotropic effects or alterations of RT50 in treated atrial trabeculae, neither at high ($n=5$; Fig. 1) nor at low ($n=5$; Fig. 5) calcium concentrations in comparison to control trabeculae from experiments performed at a calcium concentration of 2.5 mM. No arrhythmias could be detected under treatment of PTH(1–34). Overall, PTH (1–34) showed no acute direct effects in human atrial tissue.

Conclusions: Although recent studies provide evidence for the impact of PTH on cardiac tissue, no effect could be observed in our in-vitro experiments. We did not observe dose-dependent changes in contractility after PTH(1–34) administration. This finding indirectly showed that PTH(1–34) did not alter cellular calcium levels in human atrial tissue in the acute phase. Thus, the link between AF and high PTH remains unclear and is likely associated with chronic effects of PTH on cardiac tissue or a consequence of comorbidities associated with high levels of PTH, such as arterial hypertension.

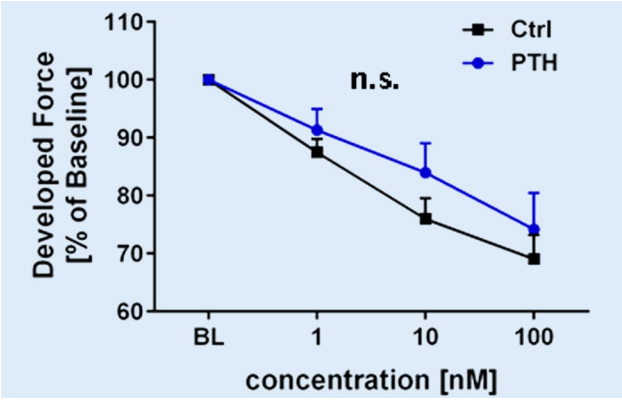

Fig. 1 Developed Force (3.5 mM Ca^{2+})

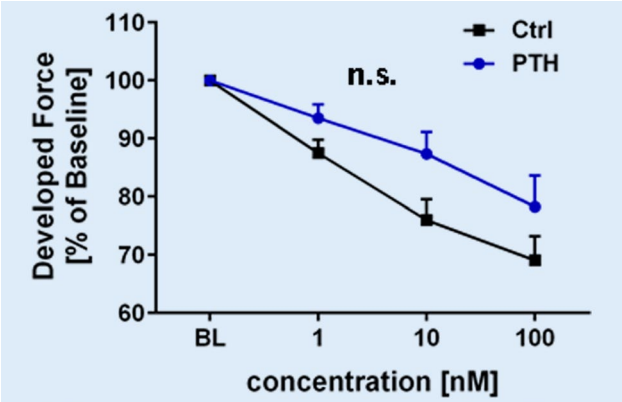

Fig. 2 Developed Force (1,2 mM Ca^{2+})

Postersitzung 14 – Diverse

14-1

Age-dependency of prescribing patterns of oral anticoagulant drugs in Austria between 2011–2014

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Background: Based on several randomized trials, non-vitamin K oral anticoagulants (NOACs) have been introduced within the last years as an alternative to vitamin K antagonists (VKAs) as oral anticoagulant drugs (OAC). The mean age of the patients included in the NOAC-investigating trials was 70–72 years. The age-pattern of patients to whom NOAC are prescribed in clinical settings is largely unknown. Thus, aim of the study was to assess the age-pattern of patients who received OAC in the years 2011–2014 in Austria.

Methods: The data analysis refers to the accounting data of the 13 major health insurance funds, covering more than 97 % of the Austrian population.

Results: The number of patients who received OAC in 2011–2014 increased by 43 % (182,464 to 261,347 patients). The number of patients who received NOACs increased nearly fivefold (20,927 to 96,247), whereas the number of patients who received VKAs increased by only 2 % (161,537 to 165,100). In 2011, the mean age of patients receiving VKAs was higher than of patients receiving NOACs (72 versus 68 years), whereas in 2014, the mean age of the patients receiving VKAs was lower than of patients receiving NOACs (73 versus 74 years). The proportion of patients ≥80 years who received VKAs declined from 26 % to 21 % of all OAC, and who received NOACs increased from 1 % to 12 %. Among nonagenarians, the proportion of patients receiving VKAs remained 2 % (3316 to 5858), whereas the proportion of patients receiving NOACs increased fourtyfold (91 to 4296).

Conclusions: NOACs are increasingly prescribed to patients aged over 80 years, although there are is a lack of data about efficacy and safety of OAC, about VKAs as well as about NOACs in octo-and nonagenarians. There is an urgent need for data about this patient group. The best solution would be to perform a randomized trial. In the meantime we suggest subgroup analyses about octo-and nonagenarians, in case they have been included in previously completed or still ongoing trials or registries for OAC in atrial fibrillation or venous thromboembolism.

14-2

Combination of D-Dimer and soluble endothelial cell adhesion molecule 1 in patients with suspected deep vein thrombosis

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Background: D-Dimer has a high diagnostic sensitivity but a low specificity in patients with suspected deep vein thrombosis (DVT) which limits its implementation as a general screening parameter and frequently results in unnecessary further imaging. Therefore novel biomarkers are needed that can be used in combination with D-Dimer to reduce false-positive laboratory results. The present study evaluates soluble platelet endothelial cell adhesion molecule 1 (sPECAM-1) as a novel biomarker for DVT. sPECAM-1 is a promising parameter, because it is generated at the site of thrombosis and is not affected by general inflammatory processes which are major confounders of D-Dimer.

Methods: 159 patients with suspected DVT were prospectively recruited. D-Dimer and sPECAM-1 levels were determined and subsequently manual compression ultrasonography (CCUS) was performed to confirm or exclude DVT.

Results: DVT was diagnosed in 27.7 % of all patients (44 out of 159). D-Dimer (cut-off >500 µg/L) had a diagnostic sensitivity of 97.7 % (95 % CI: 88.0 %-100 %) but a low specificity of 37.4 % (95 % CI: 28.6 %-46.0 %). Patients with false-positive D-Dimer values had higher levels of c-reactive protein (CRP) (2.6 ± 4.5 mg/dL versus 0.5 ± 0.78 mg/dL; $p < 0.001$) compared to patients with D-Dimer ≤0.500 µg/L and normal CCUS. sPECAM-1 was significantly higher in DVT positives compared to DVT negatives (85.9 [76.1/98.0] ng/mL versus 68.0 [50.1/86.0] ng/mL; $p < 0.001$) showing a sensitivity of 100 % (95 % CI: 92.0 %–100.0 %) and a specificity of 28.7 % (20.6 %–37.9 %) at the cut-off >50.2 ng/mL. In contrast to D-Dimer, sPECAM-1 did not correlate with inflammatory markers. The combination of sPECAM-1 and D-Dimer improved diagnostic specificity with a reduction of false-positive D-Dimer values Δ = –31.9 % resulting in a calculated sensitivity of 93.2 % (95 % CI: 81.3–98.6 %) and a specificity of 80.9 % (95 % CI: 72.5–87.6 %) in the logistic regression model.

Conclusions: The combination of D-Dimer and sPECAM-1 improves diagnostic accuracy and could avoid costly, unnecessary imaging in patients with suspected DVT. In particular, patients with an unspecific inflammatory background could benefit from the biomarker combination.

14-3

Concordance of glucose-based and of Hba1c-based diagnoses of diabetes in patients with peripheral arterial disease – a comparison between men and women

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Background: Concordance between glucose-based and HbA1c-based diagnoses of diabetes differs between populations. The purpose of this study was to investigate the concordance of glucose- and HbA1c-based diagnoses of diabetes in men and in women with peripheral arterial disease (PAD).

Methods: We measured fasting glucose as well as HbA1c and performed 75 g oral glucose tolerance tests in 282 consecutive patients, 197 men and 85 women, who had sonographically proven PAD but not previously diagnosed diabetes. Based on glucose values, diabetes was diagnosed with fasting plasma glucose (FPG) ≥126 mg/dl or post-challenge glucose ≥200 mg/dl 2 hours after the oral glucose load; based on HbA1c values diabetes was diagnosed with HbA1c ≥6.5 %.

Results: Among men, 25 had diabetes based on glucose criteria, of whom 13 also had diabetes according to the HbA1c criterion. Of the 172 men who did not have diabetes according to glucose criteria, 165 also did not have diabetes using HbA1c criteria; among women, 8 had diabetes based on glucose criteria, of whom 3 also had diabetes according to the HbA1c criterion. Of the 77 women who did not have diabetes based on glucose criteria, 74 also did not have diabetes according to HbA1c criteria. Concordance of glucose and HbA1c criteria was similar in men and women (90.6 % and 90.4 %; $p = 0.951$). Applying glucose criteria as a standard, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the HbA1c criterion for men were 52.0 %, 95.9 %, 65.0 %, and 93.2 %, respectively. For women, sensitivity, specificity, PPV and NPV of the HbA1c criterion were 37.5 %, 96.1 %, 50.0 %, and 93.7 %, respectively.

Conclusions: We conclude that the concordance of glucose and HbA1c criteria among patients with PAD is high and is similar in men and women. However, for both sexes the sensitivity of the HbA1c criterion is poor in this patient population.

14-4

Diabetes awareness among coronary artery disease patients differs significantly between men and women

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Background: Early screening for and treatment of diabetes mellitus is very important to prevent diabetes-related co-morbidities and premature deaths. Even slight changes in lifestyle and a moderate weight reduction help to decrease diabetes-related complications. Basically women are credited to have a better approach to health than men, e. g. demonstrated by more frequent medical check-ups or a healthier diet. The purpose of this study was to investigate diabetes awareness among men and women with established coronary artery disease (CAD).

Methods: We enrolled a total of 814 consecutive patients with angiographically proven CAD, 587 men and 227 women. Fasting glucose and HbA1c were measured and oral glucose tests were performed in all patients who did not report a history of diabetes.

Results: Overall, 74 men and 28 women (12.6 and 12.3 %, respectively) reported a history of diabetes. Based on glucose criteria only (fasting plasma glucose ≥126 mg/dl or glucose ≥200 mg/dl two hours after a 75 g oral glucose challenge), dia-

betes was newly diagnosed in 33 men and 3 women (5.6 and 1.3 %, respectively); when also HbA1c values ≥6.5 % were considered for diabetes diagnosis, diabetes was newly diagnosed in 67 men and 13 women (11.4 and 5.7 %, respectively). Thus, among those with diabetes, the proportion of newly diagnosed diabetes was higher in men than in women both when only glucose criteria and also when additionally the HbA1c criterion was applied for the diagnosis of diabetes (30.8 vs. 9.7 %; $p=0.007$ and 47.5 vs. 31.7 %; $p=0.014$; respectively).

Conclusions: We conclude that among CAD patients with diabetes significantly more women than men are aware of their condition.

14-5

Impact of age, weight and sex on motivation and interest on resuscitation training in 8–13-years-old schoolchildren: a randomized controlled trial

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Background: The World Health Organization, the American Heart Association and the European Resuscitation Council emphasize the importance of resuscitation training in school. However, since children younger than 13 years are not able to achieve a sufficient chest compression quality, concern has been raised that they become discouraged or disinterested. Due to the lack of evidence, practice of chest compression skills are limited to children who are 13 years or older. Therefore, we examined the impact of age, weight and sex on motivation and interest in resuscitation training in younger schoolchildren for the first time.

Methods: Children ($n=322$) between 8 and 13 years were included in a randomized, single-blind controlled trial. All children received 40 minutes basic life support training in small groups. We used two optically identical resuscitation manikins with different thoracic resistances: control group with standard resistance (45 kg), intervention group with lower resistance (30 kg). Children where not informed about the existence of two different resistances of the manikins and were told that the randomization is for uniform distribution, in order to prevent distraction from the actual training. After training, we assessed each child with a questionnaire and measured weight and height. The six-item questionnaire with four possible answers assessed the enjoyment and the interest in the training, if the training was easy for them, how well they judged their performance, if they wanted to repeat the training and if they thought resuscitation skills are important.

Results: Of 322 participants, 164 were assigned to the intervention group and 158 to the control group. The mean age was 10.1 (±1.4) years in the interventions group, respectively 10.5 (±1.5) years in the control group ($p=0.19$). The mean body weight was 40.1 (±11.5) kg in the intervention group, while it was 41.4 (±11.8) kg in the control group ($p=0.32$). 98 % of the participants in the intervention group and 99 % in the control group had fun or a lot of fun, ($p=0.32$). Glad or very glad to train resuscitation again in the future were 89 % of the participants in the intervention group and 91 % in the control group ($p=0.89$). 99 % of the participants in the intervention group and 98 % in the control group ($p=0.65$) were interested or very interested in the training. In the intervention group, 96 % believed to perform good or very good chest compression, while in the control group 93 % believed this ($p=023$). For 81 % of the participants in the intervention group, and 79 % in the control group, it was easy or very easy to perform chest compressions ($p=0.39$). For the whole sample independent of the group it was important to know how to help in case of emergency ($p=0.81$). There was no significant between-group difference in any of the items.

Conclusions: The results of this randomized trial show that school children experience a lot of fun when being trained for resuscitation and have a strong desire to practice it again in the future. The findings support the concept of an early resuscitation training and refute the view that children are discouraged or uninterested when receiving training/during CPR training.

14-6

Patterns of illness perception in patients with coronary artery disease

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Background: When faced with health threats such as symptoms or a new diagnosis, individuals actively create cognitive and mental representations of this threat. In recent years a series of studies have shown that it is important to pay attention to these individual representations, because the patients' models of illness are guiding coping strategies, are decisive for adherence to therapy and predict clinical outcome. Our study aimed to identify patterns of illness perception (IP) in patients with angiografically verified Coronary Artery Disease (CAD).

Methods: 166 patients (age: 64.4 ±12.1, 80.7 % male) were recruited after angiography at the cathlab of Hanusch hospital. Cluster analysis on the items of the Brief Illness Perception Questionnaire was used to identify distinct patterns of IP. The resulting groups were characterized with regard to Quality of Life (MacNew questionnaire), anxiety and depression (GAD-7 and PHQ-9) and resilience (RS-13).

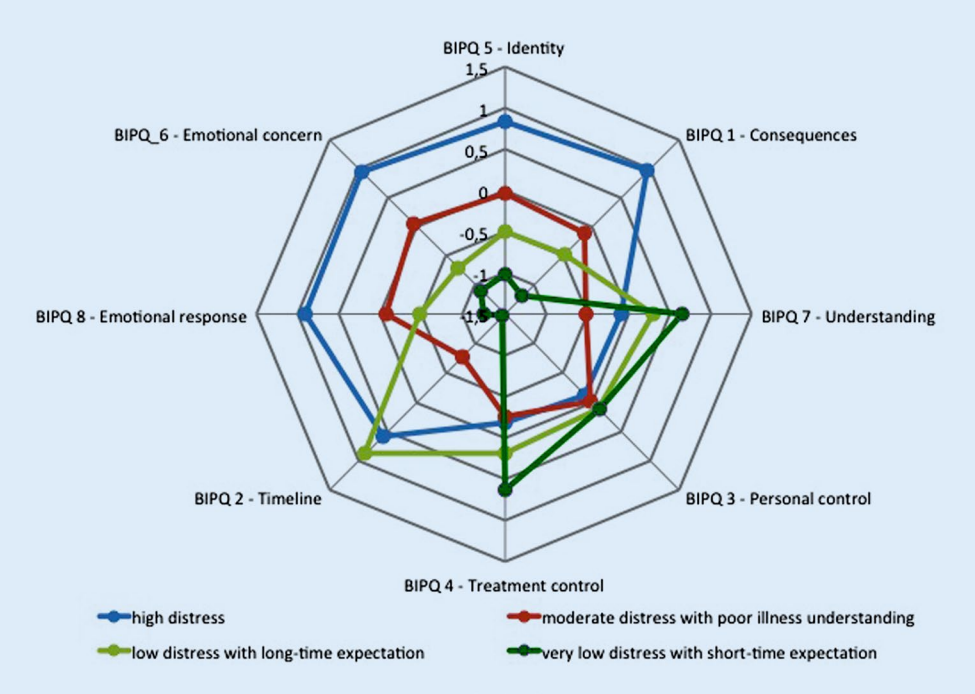
Results: Cluster analysis revealed 4 distinct groups. They differed significantly with regard to the items covering the perception of the physical (identity, consequences) and emotional impact of disease (emotional response and concern). Stronger perceptions in these domains were associated with lower Health Related Quality of Life and higher levels of emotional distress.

Group 1 included the patients with the strongest perceptions of the physical and emotional impact of disease. They expressed low treatment control, high chronic timeline and significantly higher levels of depression than the other groups. This pattern comprised 33.1 % of the sample and was labelled as "high distress".

Group 2 was characterized by more moderate perceptions of the emotional and physical impact of disease together with low scores on illness coherence and chronic timeline. The group included 27.7 % of the patients and was labelled as "moderate distress with poor illness understanding".

Groups 3 and 4 reported smaller physical and emotional impact of illness. The decisive difference existed with regard to chronic timeline: While patients of group 3 reported the highest, patients of group 4 showed the lowest scores in chronic timeline of all groups. The optimistic outlook on the course of disease of group 4 was associated with a significantly higher level of resilience compared to all other groups. Group 3, comprising 25.3 %, we labelled as "low distress with long-time expectation" and

Fig. 1



Group 4, comprising 13.9 %, as "very low distress with short-time expectation".

Conclusions: We identified 4 groups of CAD-patients sharing similar patterns of IP. Our result corresponds largely to recent findings in patients with COPD and chronic muscle disease thereby indicating parallels of IP in patients with different kinds of chronic illness. Further research is needed to explore if stratification of patients according patterns of IP can help to inform targeted psychosomatic interventions.

14-7

Predictors of low plasma levels of 25-Hydroxyvitamin D in cardiovascular rehabilitation patients

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Background: Low plasma concentrations of 25-hydroxyvitamin D [25(OH)D] are commonly accepted as an unfavourable condition. Although there is evidence that low or very low levels are associated with the risk of falls and fractures, with the likelihood of hypertension, metabolic syndrome and depression, the role of general supplementation is still matter of scientific discussion, despite proven benefit in selected populations (eg. advanced age or reduced sun exposure). Knowledge on this topic is neither new nor limited but there is still lack of awareness in specialized health care settings. Therefore this pilot study tried to identify predictors of decreased 25(OH)D plasma concentrations in in-hospital cardiovascular rehabilitation patients.

Methods: We examined the 25(OH)D plasma concentrations of 793 consecutive cardiovascular rehabilitation inpatients on admission at our institution. Age, sex, body-mass-index (BMI), preceding cardiac surgery (OP), ongoing supplementation and the living area (urban vs. rural) were defined as possible predictors and therefore examined using a regression model.

Results: Mean age of the population was 66 (±12) y, 69 % ($n=549$) were male ($p<0{,}05$). Mean 25(OH)D plasma concentration was 23.8 ng/ml. 43 % ($n=315$) had levels <20 ng/ml, which was considered as low and 16 % ($n=117$) <10 ng/ml (considered as very low). 34 % ($n=249$) of the patients had levels >30 ng/ml which was considered as optimal.

Age and living area did not correlate with plasma 25(OH)D levels, whereas the other mentioned variables did: Male sex, higher BMI (mean 29 ± 5,1) and preceding OP were correlated with lower plasma concentrations, ongoing 25(OH)D supplementation (12 %, $n=92$) and female sex with higher levels ($p<0.005$). Only 64 % ($n=59$) of those patients on supplementation had optimal levels >30 ng/ml. Sex differences regarding age (male 64 ±12 y, female 69 ± 12 y) and plasma 25(OH)D concentrations (male 22.6 ± 11.5 ng/ml; female 26.5 ± 14.7 ng/ml) were significant ($p<0.005$). Supplementation and preceding OP (33 %, $n=253$) had the strongest influence in the regression model and OP even kept a significant correlation when analysed for the subgroup with concentrations <20 ng/ml ($p<0.05$). None of the study patients was diagnosed 25(OH)D hypovitaminotic in the medical record on admission.

Conclusions: Low and very low plasma concentrations of 25(OH)D are frequent in cardiovascular rehabilitation patients and only very few are supplemented on admission and even those need further follow up. Particularly males with higher BMI and after cardiac surgery are at risk for low and very low plasma 25(OH)D concentrations. Therefore blood tests should be performed routinely and awareness of health professionals should be increased. Supplementation is likely to be beneficial, but more sufficiently powered outcome studies in cardiovascular patients (notably in heart failure) are needed.

14-8

Proposal for a novel definition of „Ideal Response“ to renal denervation and analysis of the optimal length of follow-up

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Background: Renal denervation (RDN) has shown to be an effective treatment option for patients suffering from resistant arterial hypertension in numerous unblinded clinical trials. However, as the randomized sham-controlled Symplicity HTN-3 trial had failed to achieve its primary efficacy endpoint, studies like the Spyral HTN Global Clinical Trial were designed to address possible confounding factors like drug changes and adherence as well as patient population and procedural variability.

In this regard, the definition of response to treatment is crucial for the evaluation of the effect of RDN. In previous clinical trials, adequate response was defined as a reduction of the mean systolic ambulatory blood pressure of more than 5 mmHg at merely a single follow-up point after six months.

As it was observed that patients fulfilling this criteria showed increased blood pressure levels at other time points of follow-up, this approach may not reflect sustained blood pressure reduction. Therefore, we redefined the criteria for ideal respondership and tried to evaluate the optimal duration of follow-up after RDN.

Methods: Patients with resistant hypertension, which was defined as a mean systolic office BP >160 mmHg after three measurements, were treated with RDN. All patients had to be on at least three antihypertensive drugs including one diuretic and secondary causes of hypertension were ruled out prior to the procedure. For RDN, the SymplicityTM RDN Catheter System (Medtronic Inc.) was used. Depending on renal artery anatomy, a maximum of 10 ablations were performed in each renal artery. The individual blood pressure course after RDN was monitored by scheduled follow-up visits after 3, 6, 12 and 24 months. At all visits including baseline, ambulatory blood pressure measurement (ABPM) was performed.

According to the assumption that an ideal responder should have lowered BP levels at every visit after RDN, ideal response was defined as a sustained reduction of the mean systolic blood pressure of at least 1 mmHg at each follow-up-visit compared to baseline levels. The number of patients fulfilling this definition was obtained by analyzation of their individual blood pressure course in order to evaluate the rate of sustained blood pressure reduction as well as to assess the optimal duration of follow-up necessary for the proposed novel definition of ideal respondership.

Results: We investigated the effects of RDN on blood pressure levels in 42 patients suffering from resistant hypertension. 11 of these patients were excluded after baseline ABPM had revealed pseudo-resistance with a mean systolic blood pressure <130 mmHg. By consideration of the proposed novel definition of “ideal response”, 12 of 31 patients (38,7 %) could be classified as ideal responders after 24 months. In this collective, there was a significant mean systolic blood pressure reduction at all follow-up points (3M: –21,4 mmHg, $p<0,01$; 6M: –15,8 mmHg, $p<0,01$;12M: –19,9 mmHg, $p<0,01$; 24M: –22,8 mmHg, $p<0,01$). Of the 13 patients that could be classified as ideal responders after 12 months, 12 patients (92,3 %) fulfilled the criteria with a sustained blood pressure reduction after 24 months.

Conclusions: As more than 90 % of all patients undergoing RDN that met the definition of “ideal response” after 12 months were also ideal responders after 24 months, a follow-up period of 12 months seems to be adequate to confirm sustained blood pressure reduction.

14-9

The association between negative stress coping strategies and Augmentation index75

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Background: According to the ESH-ESC guidelines for hypertension treatment Arterial stiffness (AS) plays a significant role in cardiovascular events (1). Augmentation index (AIx) is known as an indirect parameter of arterial stiffness (2). This parameter depends on heart rate (3), so it’s standardized to a heart rate of 75 bmp and named as AIx75. Furthermore there seems to be an association between the ability to cope with stress and the risk of atherosclerosis (4).

The aim was to evaluate if there is an association between stress coping strategies and parameters of arterial stiffness.

Methods: 40 volunteers (mean age 42.12 ± 11.62; 13 men, 27 women) underwent a test procedure consisting of a period of

Tab. 1

	Negative coping strategies		
	r	*p*	*N*
Heart frequency	.215	.182	40
Central systolic blood pressure	–.0062	.703	40
Central diastolic blood pressure	–.284	.075	40
Central pulse pressure	.099	.544	40
AIx75	.380	.016	40
Heart minute volume	–.040	.809	40
Augmentation pressure	.262	.102	40
PWV	–.273	.089	40

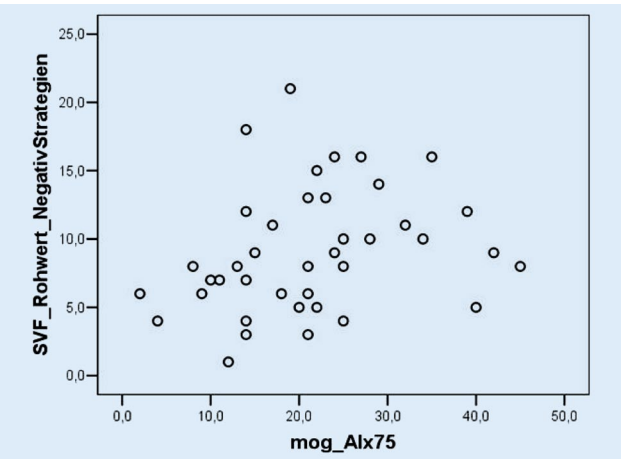

Fig. 1

rest and a standardized mental stress task (Determination test), during which cardiovascular parameters have been evaluated.

Besides others, arterial stiffness was evaluated oscillometrically using the Mobil-O-Graph® (I. E. M. Stolberg, GERMANY) by measuring pulse wave velocity (PWV) at the brachial artery. With the German stress coping questionnaire "Stressverarbeitungsfragebogen 120" it was possible to determine subjects' individual positive and negative stress coping strategies. Positive strategies result in efficient stress reduction and can be described as adequate coping strategies whereas negative strategies are associated with a stress-enhancing behaviour.

Results: Negative stress coping strategies correlated significantly (Spearman's correlation) with Augmentation Index 75 [90 %CI] (r = –.380, p = .016). There was no correlation between central blood pressure values, central pulse pressure values and pulse wave velocity.

Conclusions: Subjects with higher levels of negative stress coping strategies showed a significant correlation with AIx75. As AIx75 seemed to remain the only parameter which correlated significantly, the main statement has to be interpreted very critically. Nevertheless the thought itself seems to be promising as Lee et al. showed an inverse correlation between brachial-ankle pulse wave velocity (a direct parameter of arterial stiffness) and coping strategies, especially "seeking social support" (4).

14-10

The cardiovascular marker NT-proBNP reflects disease severity in patients with multiple myeloma

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Background: Elevated levels of cardiovascular markers including NT-proBNP have been shown to be associated with disease severity and mortality in an unselected population of cancer patients free from cardiac disease. The aim of this study was to investigate whether NT-proBNP levels are associated with disease severity in multiple myeloma specifically and how NT-proBNP levels are influenced by antineoplastic therapy.

Methods: We retrospectively analyzed data of a total of 119 patients with multiple myeloma free from cardiac disease, which were clinically followed-up (FUP) at the oncologic department for a median of 523 (IQR 443–648) days. NTproBNP, beta-2-microglobulin (B2M) and plasma levels of light chains were measured at baseline and FUP visits. The primary study endpoint was defined as a positive correlation between NTproBNP and disease severity reflected by B2M and paraprotein levels.

Results: During the FUP 22 patients (18 %) died. B2M was a significant predictor of death [crude HR of 2.36 (IQR 1.23–4.56), p = 0.010 for lnB2M]. NT-proBNP showed a highly significant positive correlation with beta-2-microglobulin at first presentation [r = 0.592 (Pearson), p < 0.001]. Additionally NT-proBNP correlated with paraprotein levels in patients with specific light chain disease [r = 0.376 (Spearman-Rho), p = 0.016 for IgG]. Characteristic curves showed a continuously increase of NT-proBNP in patients with multiple myeloma not fulfilling criteria for the initiation of a specific treatment, while patients on therapy displayed a decrease in NT-proBNP levels parallel to B2M decline reflecting therapy response.

Conclusions: Elevated levels of the cardiovascular marker NT-proBNP are associated with disease severity in patients with multiple myeloma.

Tab. 1 Baseline characteristics of patients with multiple myeloma (MM, n=119). Continuous variables are given as medians and inter-quartile ranges (IQR). Counts are given as numbers and percentages.

	MM patients (n=119)
Age, years (IQR)	65 (56-72)
Male gender, *n* (%)	67 (56%)
BMI kg/m2, (IQR)	25,6 (23–30)
Systolic BP, (IQR)	130 (120–141)
Diastolic BP, (IQR)	77 (69–83)
HR, (IQR)	72 (65–87)
Sinusrhythm, *n* (%)	53 (46%)
Atrial Fibrillation*n*	9 (8%)
Comorbidities	
Known CAD, *n* (%)	30 (25%)
Diabetes mellitus, *n* (%)	17 (14%)
Arterial Hypertension, *n* (%)	74 (62%)
Heart Failure, *n* (%)	19 (16%)
Valvular disease, *n* (%)	13 (11%)
Myocardial Infarction, *n* (%)	15 (13%)
Medication	
ACE , *n* (%)	44 (37%)
Beta-Blocker, *n* (%)	43 (36%)
ASS, *n* (%)	79 (66%)
Multiple myeloma parameters	
Receiving CHT since 2014, *n* (%)	72 (61%)
Bortezomib, *n* (%)	69 (58%)
Bendamustin, *n* (%)	14 (12%)
Cyclophosphamid, *n* (%)	42 (35%)
Doxorubicin, *n* (%)	13 (11%)
Thalidomid, *n* (%)	21 (18%) / Erhaltung 4 (3%)
Revlimid, *n* (%)	16 (13%) / Erhaltung 39 (32%)
Dexamethason, *n* (%)	69 (58%) / Erhaltung 30 (25%)
Gammopathy	
IgG Kappa, *n* (%)	46 (39%)
IgG Lambda, *n* (%)	23 (19%)
Free Light Chain Kappa, *n* (%)	16 (13%)
Free Light Chain Lambda, *n* (%)	10 (8%)
IgA Kappa, *n* (%)	12 (10%)
IgA Lambda, *n* (%)	9 (8%)
NT-proBNP, pg/ml (IQR)	198 (75–500)
ß2-Microglobulin (IQR)	2,62 (2–4,35)

IQR – interquartile range; *BMI* body mass index, *BP* blood pressure; *HR* heart rate; *CAD* coronary artery disease; *ACE* angiotensin converting enzyme; *ASS* acetyl salicylic acid; *NT*-proBNP N-terminal pro B-type natriuretic peptide; *CRP* C-reactive protein; *Hb* Hemoglobin; *ß2-Microglobulin* Beta-2-Microglobulin

Tab. 2a Laboratory parameters at baseline and following therapy in MM patients receiving CHT (n=XX). Variables are displayed as median and inter quartile range (IQR). Differences were calculated by the means of the Kruskal-Wallis-test

	baseline	1 months after CHT	3 months after CHT	6 months after CHT	*P*-value all	*p*-value pre vs post
NT-proBNP, pg/ml (IQR)	204 (127–546)	187 (151–232)	166 (94–570)	160 (41–230)	0.762	0.553
Beta-2-microglobulin, XX (IQR)	3.01 (2.46–3.42)	2.78 (2.30–3.41)	2.43 (2.20–3.25)	2.42 (2.11–2.82)	0.446	0.193
LDH, XXX (IQR)	XXX	XXX	XXX	XXX	0.798	0.774
Kreatinin, mg/dl (IQR)	1.00 (0.76–1.22)	0.86 (0.79–1.11)	0.90 (0.63–0.99)	0.97 (0.65–1.05)	0.550	0.339
Hämoglobin, g/dl (IQR)	11.3 (10.0–13.0)	11.5 (10.2–12.5)	11.0 (9.0–12.2)	11.9 (10.9–12.4)	0.779	0.659
Lambda LC, XX (IQR)*	26.4 (8.17–94.4)	24.0 (20.2–54.6)	20.0 (2.7–26.7)	18.8 (11.6–35.6)	0.452	0.526
Kappa LC, XX (IQR)*	16.6 (10.7–163.0)	14.0 (12.0–19.8)	12.2 (9.5–22.2)	11.8 (4.3–14.5)	0.324	0.322
IgA, XX (IQR)	XXX	XXX	XXX	XXX	0.562	0.267
IgG, XX (IQR)	XXX	XXX	XXX	XXX	0.918	0.526
IgM, XX (IQR)	XXX	XXX	XXX	XXX	0.868	0.968

* for patients with specific LC disease

Tab. 2b Laboratory parameters at baseline and following therapy in MM patients with conservative management (n=14). Variables are displayed as median and inter quartile range (IQR). Differences were calculated by the means of the Kruskal-Wallis-test

	baseline	1 months after CHT	3 months after CHT	6 months after CHT	*P*-value all
NT-proBNP, pg/ml (IQR)	204 (127–546)	187 (151–232)	166 (94–570)	160 (41–230)	0.956
Beta-2-microglobulin, XX (IQR)	3.01 (2.46–3.42)	2.78 (2.30–3.41)	2.43 (2.20–3.25)	2.42 (2.11–2.82)	0.871
LDH, XXX (IQR)	XXX	XXX	XXX	XXX	0.826
Kreatinin, mg/dl (IQR)	1.00 (0.76–1.22)	0.86 (0.79–1.11)	0.90 (0.63–0.99)	0.97 (0.65–1.05)	0.913
Hämoglobin, g/dl (IQR)	11.3 (10.0–13.0)	11.5 (10.2–12.5)	11.0 (9.0–12.2)	11.9 (10.9–12.4)	0.978
Lambda LC, XX (IQR)*	26.4 (8.17–94.4)	24.0 (20.2–54.6)	20.0 (2.7–26.7)	18.8 (11.6–35.6)	0.979
Kappa LC, XX (IQR)*	16.6 (10.7–163.0)	14.0 (12.0–19.8)	12.2 (9.5–22.2)	11.8 (4.3–14.5)	0.478
IgA, XX (IQR)	XXX	XXX	XXX	XXX	0.568
IgG, XX (IQR	XXX	XXX	XXX	XXX	0.477
IgM, XX (IQR)	XXX	XXX	XXX	XXX	0.279

* for patients with specific LC disease

Tab. 3 Laboratory parameters at baseline for MM patients with different outcome (n=97 survived vs. 22 dead). Variables are displayed as median and inter quartile range (IQR). Differences were calculated by the means of the Kruskal-Wallis-test

	TOD					
	0			1		
	Median	Perzentil 25	Perzentil 75	Median	Perzentil 25	Perzentil 75
proBNP	188.70	73.20	432.40	300.65	120.40	782.30
Beta2 Mikroglobul in	2.59	2.02	3.59	3.51	2.45	6.30
Hämoglobin	12.20	10.90	13.70	11.10	10.40	12.10
Kreatinin	.98	.80	1.37	.95	.75	1.41
LDH	174.00	151.00	208.00	180.50	168.00	204.00
IgA	137.00	58.70	319.00	86.40	65.30	152.00
IgG	904.50	531.50	1475.00	1240.00	684.00	2580.00
IgM	43.70	38.40	72.70	39.90	32.15	68.65
FreieKappaLK	14.90	9.67	45.00	34.10	14.70	251.00
FreieLambdaLK	20.90	10.50	51.60	15.90	11.40	39.20

	proBNP	Hämoglo-bin	Kreatinin	LDH	IgA	IgG	IgM	FreieKap-paL K	Freie Lambda LK	Beta2 Mikro-globulin
Mann-Whitney- U	896,000	521,000	391,500	332,000	119,000	278,000	80,000	256,000	332,000	234,000
Wilcoxon-W	5649,000	711,000	1822,500	1763,000	164,000	1454,000	116,000	1291,000	452,000	1362,000
Z	–1.171	–2.356	–.089	–.602	–1.315	–1.323	–.974	–1.391	–.337	–2.242
Asymptotische Signifikanz (2-seitig)	.242	.018	.929	.547	.188	.186	.330	.164	.736	.025
Exakte Signifikanz [2*(1-seitige Sig.)]					.197[b]		.347[b]			

Tab. 4 Korrelationen für specific light chain disease

			proBNP	Freie Lambda LK
Spearman-Rho	proBNP	Korrelationskoeffizient	1,000	,400
		Sig. (2-seitig)	.	,600
		N	10	4
	Freie LambdaLK	Korrelationskoeffizient	,400	1,000
		Sig. (2 -seitig)	,600	.
		N	4	4

			proBNP	Freie KappaL K
Spearman-Rho	proBNP	Korrelationskoeffizient	1,000	,429
		Sig. (2-seitig)	.	,337
		N	16	7
	Freie KappaLK	Korrelationskoeffizient	,429	1,000
		Sig. (2-seitig)	,337	.
		N	7	7

			proBNP	IgM
Spearman-Rho	proBNP	Korrelationskoeffizient	1,000	.
		Sig. (2-seitig)	.	.
		N	2	1
	IgM	Korrelationskoeffizient	.	.
		Sig. (2-seitig)	.	.
		N	1	1

			proBNP	IgG
Spearman-Rho	proBNP	Korrelationskoeffizient	1,000	,376*
		Sig. (2-seitig)	.	,016
		N	69	41
	IgG	Korrelationskoeffizient	,376*	1,000
		Sig. (2-seitig)	,016	.
		N	41	41

			proBNP	IgA
Spear-man-Rho	proBNP	Korrelationskoeffizient	1,000	,317
		Sig. (2-seitig)	.	,406
		N	21	9
	IgA	Korrelationskoeffizient	,317	1,000
		Sig. (2-seitig)	,406	.
		N	9	9

Postersitzung 15 – Herzinsuffizienz 2

15-1

Acute fulminant heart failure in a 32 year-old male due to an inherited Lamin A/C mutation

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Case report description: A 32 year-old male patient with unremarkable past medical history presented with acute-onset dyspnea, icterus, and massive leg, scrotum, and penis oedema. Echocardiography showed dilatation of both ventricles and atria, diffuse hypokinesia of the left ventricle (EF 16 %) with a wall-adherent apical thrombus, and reduced RV function. Chest X-ray and sonography demonstrated bilateral pleural effusions, dilatation of the inferior caval and hepatic veins, and ascites. Rhythm monitoring demonstrated atrial flutter and frequent polymorphic non-sustained VTs. NTproBNP was increased to 27,094 pg/ml (–88 pg/ml). Multiple cases of sudden cardiac death due to arrhythmic events or terminal heart failure at young ages were remarkable in the patient's family history.

We admitted the patient to our cardiac intensive care unit and initiated low-dose heart failure therapy including diuretics, low-dose norepinephrine, and levosimendan. The patient was heparinized and oral anticoagulation was initiated. Despite intensive therapy, the patient developed progressive anasarca and ascites and frequent non-sustained VTs with several morphologies as well as incipient renal and liver failure. Genetic testing had revealed a novel non-sense mutation in exon 3 of the LMNA gene causing a truncated Lamin A/C protein product. The patient was urgently listed for heart transplantation and successfully transplanted at day 28 after admission.

Conclusions: Lamins are intermediate filaments that polymerize and build a meshwork beneath the inner nuclear membrane; they are involved in maintaining nuclear structure, pore formation, heterochromatin organization, and transcriptional control. Lamin mutations cause multiple disparate diseases. If cardiomyopathy is present, it is often characterized by conduction disorders and arrhythmia, sudden cardiac death, and progressive heart failure with high mortality.

Our patient's extended family had been genetically tested prior to admission and the rate of sudden cardiac death was determined at approximately 30 % in over 60 studied subjects. Our patient had refused to be informed about the test result. Early diagnosis and initiation of heart failure therapy might have slowed disease progression. However, given the severity of the mutation with a short, largely non-functional protein product and the natural history of disease progression in family members, heart transplantation at a young age seemed unavoidable.

The main alternative to high-urgency transplant listing was implantation of a ventricular assist device as bridge-to-transplant/or recovery. Given prominent right heart failure, a biventricular device would have been necessary. Additionally, presence of left ventricular thrombus would have complicated

implantation. Given the natural history of this mutation, heart transplantation could have hardly been avoided.

Conclusions: In young patients, acute heart failure is frequently caused by myocarditis, however, a family history of heart failure and sudden cardiac death warrants monitoring of family members and genetic testing for underlying mutations. Cardiac laminopathies are often characterized by rapid progressive heart failure, rhythm disorders, and high mortality. Treatment of these patients, including organ replacement therapy, should not be delayed and is best achieved by a comprehensive heart team including cardiologists, cardiac/transplant surgeons, and anesthetists.

15-2

Adherence to current ESC Heart failure treatment guidelines in a Tertiary Referral Centre and University Teaching Hospital in Central Europe

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Background: The corner stones of modern heart failure (HF) treatment are angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB), a beta-blocker (BB) and a mineralocorticoid receptor antagonist (MRA). The European Society of Cardiology (ESC) HF treatment algorhythm published in 2012 introduced ivabradine as the next step of pharmacological intervention in patients with systolic HF. The aim of this study was to document the guideline adherence – or the lack of – in terms of OMT treatment for HF.

Methods: This is a prospective registry of patients admitted for worsening heart failure to our department. We used descriptive statistics to analyse the extent of guideline adherence and logistic regression to calculate possible predictors for receiving optimal medical treatment (OMT).

Results: To this day, 335 consecutive patients have been included, 39% female. 56% with ischaemic cardiomyopathy (CMP) and 43% with non-ischaemic CMP. Upon hospital admission 56% of all patients were on ACEIs/ARBs, 61% on BBs, 30% on MRAs and 0.4% on ivabradine. Upon discharge, 45% of patients were on ACEIs, 20% ARBs, 78% BBs, 49% MRAs and 1% ivabradine. In addition to the low number of patients on appropriate HF therapy, only 33%, 47% and 13% of the patients on ACEIs, ARBs and BBs had reached target doses of their respective medications upon admission. There was no difference between patients with first time or those with recurrent admission. Even though numbers are low in both groups, there was a significant difference between patients with OMT upon admission (18%) and discharge (27%). In univariate analysis, there was a tendency towards male gender for the prediction of OMT compared to female gender. The intrahospital mortality was 4.2%.

Conclusions: Despite very clear ESC recommendations and a well-documented benefit for our HF patients, very few of them are in fact treated accordingly. In comparison to international registry data, the percentage of heart failure patients with OMT was low.

15-3

Beneficial effects of levosimendan on survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery

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Background: The impact of levosimendan treatment on clinical outcome in patients undergoing extracorporeal membrane oxygenation (ECMO) support following cardiovascular surgery is unknown. It is tempting to speculate that the beneficial effects of levosimendan are more efficiently translated into improved survival, when adequate end-organ perfusion is ensured by concomitant ECMO therapy. We therefore analyzed the impact of levosimendan treatment on survival and ECMO weaning failure in ECMO patients following cardiovascular surgery.

Methods: We enrolled a total of 240 patients undergoing veno-arterial ECMO therapy following cardiovascular surgery at a university-affiliated tertiary care center in our registry.

Results: The median SAPS-3 score and median EuroSCORE of the study population were 43 (IQR 36–51) and 10 (IQR 8–13), respectively. ECMO support was initiated in 59 patients after valve surgery, in 24 after coronary artery bypass graft (CABG) surgery, in 56 after combined CABG-valve surgery, in 51 patients after cardiac transplantation, in 21 patients after ventricular assist device implantation, in 17 after aortic reconstruction and in 12 after other cardiovascular surgeries. Indications for ECMO implantation were weaning failure from cardiopulmonary bypass (60%), postoperative cardiogenic shock (20%), immediate post-transplant cardiac graft failure (6%), postoperative respiratory failure (4%), postoperative bleeding/tamponade with cardiogenic shock (4%), and miscellaneous conditions (6%).

In total 75% of patients received levosimendan during the first 24 hours following ECMO implantation. In brief, ECMO patients treated with levosimendan had a higher EuroSCORE ($P<0.001$) and SAPS III score ($P=0.02$), had a lower left ventricular ejection fraction ($P=0.04$), and required higher doses of noradrenaline ($P<0.001$) and dobutamine ($P=0.014$). Over a median follow-up of 37 months (IQR 19 to 67 months), 65% of patients died. Seventy-five percent of patients received levosimendan treatment within the first 24 hours after initiation of ECMO therapy. Cox regression analysis revealed a beneficial association between levosimendan treatment and successful ECMO weaning (adj. HR 0.41; 95%CI 0.22–0.80; $p=0.008$ Fig. 1a), 30-day mortality (adj. HR 0.52; 95%CI 0.30–0.89; $P=0.016$; Fig. 1b), and long-term mortality (adj. HR 0.64; 95%CI 0.42–0.98; $P=0.04$; figure 1C).

Conclusions: The present data suggest that an association between levosimendan treatment and improved short- and long-term survival in patients undergoing ECMO support following cardiovascular surgery. The current study advances the limited knowledge on the effects of levosimendan treatment in this specific patient population enabling a more individualized treatment decision-making.

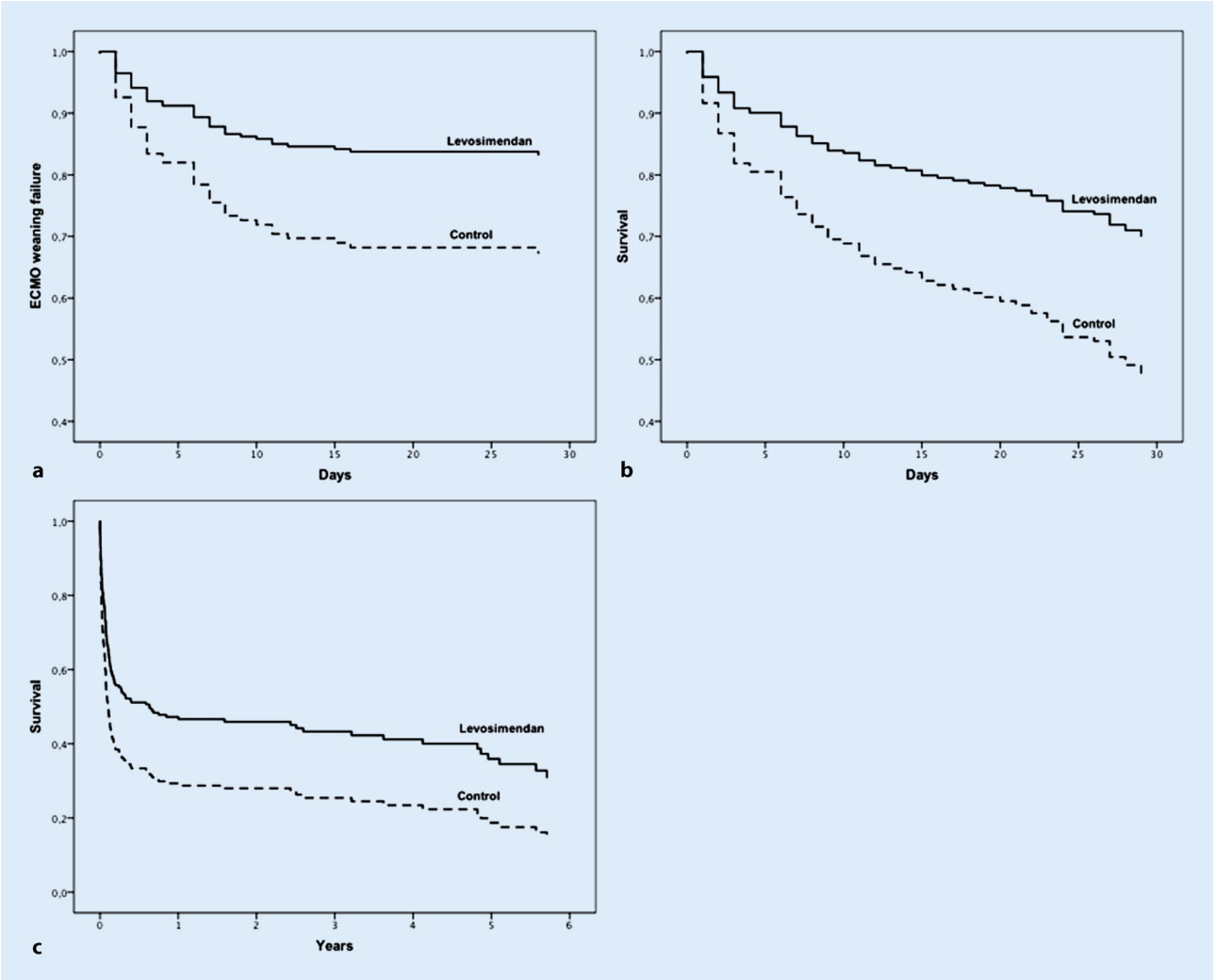

Abb. 1

15-4

Impact of hypoxic hepatitis on mortality in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery

K. Distelmaier, C. Roth, L. Schrutka, C. Binder, G. Heinz, I. Lang, G. Maurer, H. Koinig, D. Wiedemann, T. Fleck, B. Steinlechner, A. Niessner, G. Goliasch

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Background: Veno-arterial extracorporeal membrane oxygenation (ECMO) therapy aims to restore and maintain adequate end-organ perfusion in patients with severe heart or lung failure following cardiovascular surgery. However, despite hemodynamic support, ECMO patients are in a severely compromised hemodynamic condition and therefore vulnerable to ischemic events. Hypoxic hepatitis (HH) represents a form of hepatic injury following arterial hypoxemia, ischemia, and passive congestion of the liver that has been found associated with poor survival in critically ill patients. We investigated the incidence and the prognostic implications of HH in patients undergoing venoarterial ECMO support after cardiovascular surgery.

Methods: We included a total of 240 patients undergoing veno-arterial ECMO therapy following cardiovascular surgery at a university-affiliated tertiary care center into our single-center registry.

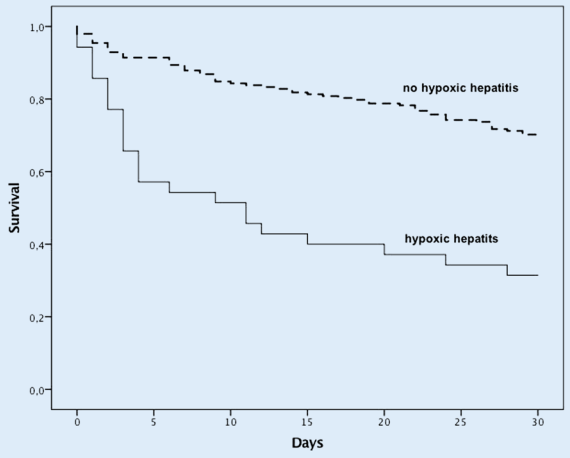

Fig. 1

Results: During a median follow-up time of 37 months (IQR 19 to 67 months) a total of 156 patients (65 %) died. Hypoxic hepatitis was diagnosed in 35 patients (15 %) within 72 hours following ECMO implantation. The occurrence of HH was identified as strong predictor for 30-day mortality with a crude HR of 3.47 [95 %CI 2.15–5.61, $P<0.001$] as well as for long-term mortality with a crude HR of 2.85 [95 %CI 1.91–4.25, $P<0.001$]. The observed associations persisted after adjustment for potential confounders with an adjusted HR of 4.02 [95 %CI 2.35–6.89, $P<0.001$] for 30-day mortality (Fig. 1) and an adjusted HR of 3.5 [95 %CI 2.08–5.09, $P<0.001$] for long-term mortality. There was no association between preoperative liver function parameters and the occurrence of hypoxic hepatitis.

Conclusions: HH occurs frequently in cardiovascular surgery patients undergoing venoarterial ECMO support and is strongly associated with poor short-term as well as long-term survival.

15-5

Right heart failure: The major cause of death in patients with heart failure and preserved ejection fraction

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Background: Recent studies show that right ventricular dysfunction with an ejection fraction below 45 % is an important predictor of hospitalization-related outcome in patients with heart failure and preserved ejection fraction (HFpEF). However, HFpEF patients suffer from a broad spectrum of non-cardiac co-morbidities. Therefore, it remains unclear whether affected patients die from right heart failure or other conditions.

Methods: Consecutive HFpEF patients in whom coronary artery disease has been excluded angiographically were prospectively registered. A diagnosis of terminal right heart failure was established, if the following criteria were met: 1. RVEF ≤ 45 % by cardiac magnetic resonance imaging and/or cardiac ultrasound, 2. clinical signs of right heart decompensation at the time of death, including dyspnea, ascites, liver enzyme elevation, leg oedema and jugular distension.

Results: Of the 230 patients registered, 38 patients (16.5 %) died after a mean follow-up of 30 ± 17 months. 60.5 % ($N=23$) of deaths were classified as cardiovascular and 29.0 % ($N=11$) as non-cardiovascular. In 4 (10.5 %) patients, the reason for death remained unknown. 20 (52.6 %) deaths were due to right heart failure, 6 (15.8 %) deaths due to major infections, such as necrotizing pancreatitis or bilateral pneumonia, and 1 (2.6 %) due to sudden cardiac arrest. 4 (10.5 %) deaths were related to cancer, other reasons for death included stroke, ileus and major bleeding (Fig. 1).

Conclusions: In our well- characterised HFpEF cohort, nearly half of all death cases could be attributed to right heart failure, which should therefore be considered as a main therapeutic target in affected patients.

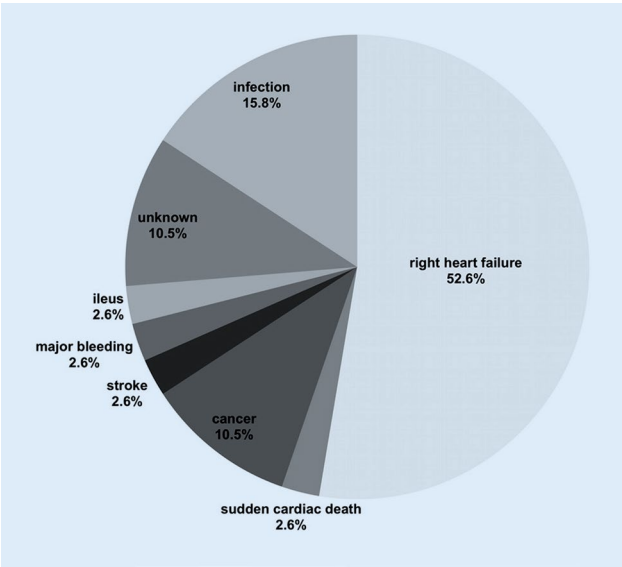

Fig. 1 Causes of death in heart failure with preserved ejection fraction. A total of 38 total deaths had occurred within an observation period of 30 ± 17 months

15-6

Fingerprint of the Renin-Angiotensin-System during ARNI therapy in patients with systolic heart failure

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Background: Angiotensin-receptor-neprilysin-inhibition (ARNI), which combines angiotensin receptor blockade (ARB) and neprilysin inhibition (NEPi), has been shown to reduce hospitalization and all-cause mortality in patients with heart failure with reduced ejection fraction (HFrEF) compared to angiotensin-converting-enzyme-inhibitor (ACE-I) therapy. NEPi was also hypothesized to exert favorable effects on systemic renin-angiotensin-system (RAS) components, however, the effect of ARNI on the alternate RAS axis has not been studied in details.

Methods: In our exploratory study, we investigated 6 patients with HFrEF eligible for ARNI therapy in line with the PARADIGM enrollment criteria. Blood samples were collected

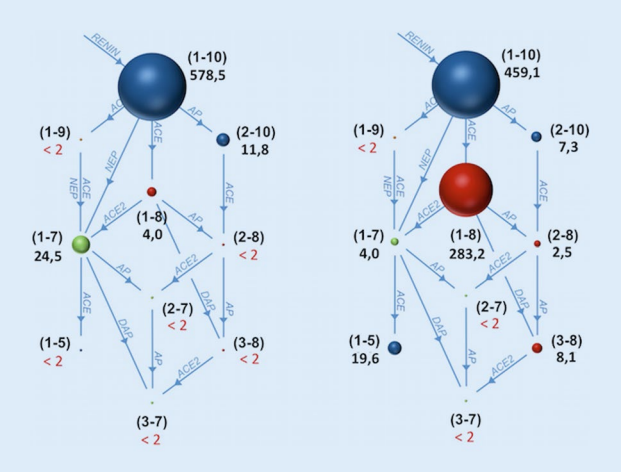

Fig. 1

under ACE-I therapy and 4 weeks after switching to ARNI therapy. The full spectrum of circulating plasma angiotensin metabolites were stabilized with protease inhibitors and subsequently quantified by mass spectrometry.

Results: (Fig. 1)

As expected, ACE-I therapy led to suppressed Ang1-8 (AngII) levels associated with elevated levels of Ang1-10 (AngI). Switching to ARNI therapy resulted in a marked increase of Ang1-8 levels (ACE-I: 4.0 pg/ml vs. ARNI: 283.2 pg/ml) and lower Ang1-10 levels (ACE-I: 578.5 pg/ml vs. ARNI: 459.1 pg/ml) due to recovered ACE activity and the onset of the ARB effect. However, the levels of the putatively beneficial Ang1-7, a member of the alternate RAS axis and counter player of Ang1-8, were higher on ACE-I therapy (ACE-I: 24.5 pg/ml vs. ARNI: 4.0 pg/ml). This could be caused by the concomitant formation of Ang1-7 from excess Ang1-10 by NEP and reduced degradation to Ang1-5 by inhibited ACE. ARNI therapy on the other hand consisting of ARB and NEPi, leaving ACE activity largely unaffected, seems to go along with low Ang1-7 levels as a net effect on the enzymatic interplay.

Conclusions: Ang1-7 levels seem to be reduced on ARNI therapy compared to ACE-I. This suggests that the alternate RAS axis may not play an important role in mechanisms responsible for the therapeutical benefits of ARNI.

15-7

Soluble neprilysin predicts outcome in patients with heart failure with reduced ejection fraction

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Background: The combination of angiotensin receptor blockade and neprilysin inhibition (NEPi) has been shown to reduce hospitalization and all-cause mortality in patients with heart failure with reduced ejection fraction (HFrEF) compared to angiotensin converting enzyme inhibition. The possible impact of soluble neprilysin (sNEP) on outcome has been discussed controversially in recent studies.

Methods: We prospectively enrolled 109 consecutive patients with HFrEF. Plasma concentrations of B-type natriuretic peptide (BNP), N-terminal proBNP (NT-proBNP) and sNEP were measured with specific ELISA assays. All-cause mortality was defined as primary endpoint.

Results: During a median follow-up of 26 (IQR 24–28) months 21 (19 %) patients died. sNEP levels were 1362 pg/ml (IQR 882–2006) and correlated inversely with BNP (–0.207, $p=0.034$) and NT-proBNP (–0.251, $p=0.010$). sNEP was a significant predictor of all-cause mortality with a hazard ratio per IQR of 0.34 (95 %CI 0.15–0.76; $p=0.010$) and of 0.41 (95 %CI 0.17–0.95; $p=0.037$) after adjustment for age, gender and GFR. Stratification of the cohort after both NT-proBNP and sNEP levels pointed towards a benefit for patients with high sNEP levels irrespective of the NT-proBNP category with a significant survival difference over all groups in the log-rank-test ($p=0.04$, Fig. 1). Most remarkably, sNEP showed significant additional prognostic value beyond that achievable with the sole assessment of NT-proBNP indicated by improvements in the category-free net reclassification index for mortality (NRI 58 %, $P=0.02$).

Conclusions: Circulating levels of soluble NEP show an inverse correlation with NT-proBNP and BNP and are independenly associated with all-cause mortality in HFrEF.

15-8

Riociguat – new therapeutic approach in the management of cardiac amyloidosis

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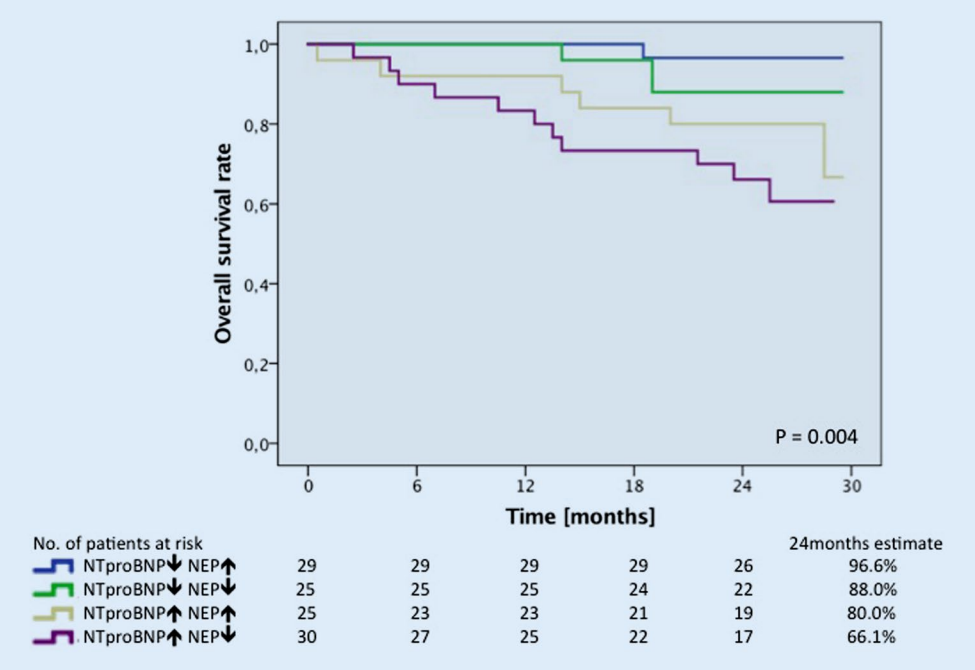

Fig. 1

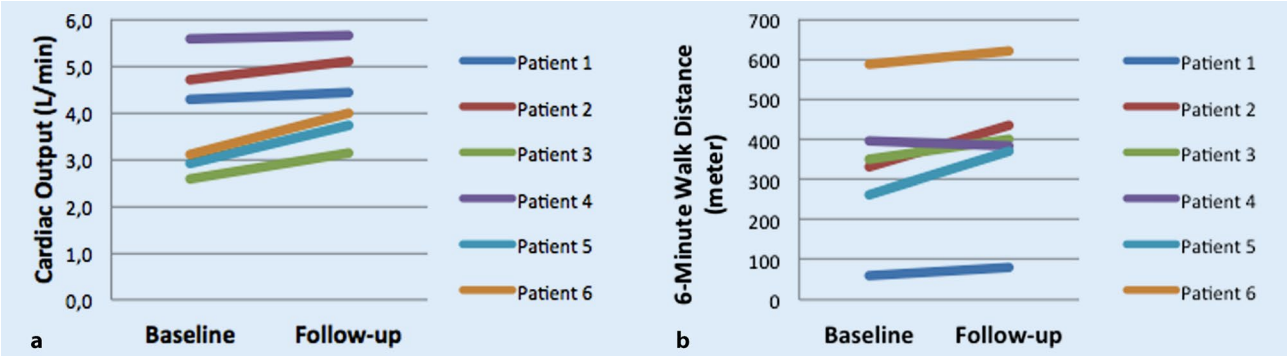

Fig. 1

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

The solouble guanylate cyclase (sGC) – stimulator riociguat, already approved for the treatment of precapillary pulmonary hypertension, has also been shown to have favorable hemodynamic effects in heart failure.

We aimed to test the safety and efficacy of riociguat in patients with cardiac amyloidosis.

Methods: CA was diagnosed based on cardiac magnetic resonance imaging and myocardial biopsy. Baseline work-up of patients and re-evaluation under therapy included the assessment of blood pressure, NYHA functional class, exercise capacity as measured by the 6-minute walk test (6MWT), serum NT-proBNP and invasively measured hemodynamic parameters.

Results: Six participants with wild-type transthyretin amyloidosis (83.3 % male, 16.7 % female, mean age 80.3 ± 7.0 years) were included in our national named-patient use program. Follow-up was performed after a median of 5.3 ± 2.6 months.

Systolic (131 ± 19.1 mmHg versus 119 ± 8.5 mmHg, $p = 0.345$) and diastolic (85.2 ± 6.1 mmHg versus 73.5 ± 9.5 mmHg, $p = 0.058$) blood pressure basically remained unchanged from baseline values. With respect to efficacy parameters, 6-minute walk distance (6-MWD) improved from 330 ± 172 m to 381 ± 174 m ($p = 0.046$). In parallel, cardiac output increased from 3.9 ± 1.2 l/min to 4.3 ± 0.9 l/min ($p = 0.028$), while left and right heart filling pressures did not significantly change (mean pulmonary arterial pressure: 33.7 ± 8.7 mmHg versus 32.3 ± 7.6 mmHg. $p = 0.917$) and pulmonary artery wedge pressure: 23.5 ± 8.1 mmHg versus 22.7 ± 6.7 mmHg, $p = 0.752$) under treatment.

Conclusions: In this first report from a national named patient use program we could demonstrate that riociguat treatment is safe and effective in patients with CA. Further studies are warranted to support the evidence that riociguat may relieve the burden of disease associated with CA.

Postersitzung 16 – Interventionelle Kardiologie 2 und Vitien

16-1

Assessment of hemodynamic effects of TAVR in severe aortic stenosis by pulse wave analysis

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Tab. 1 Parameters for the calculated central pressure curves before and after TA VR obtained from carotid measurements. Variables are displayed as median and inter quartile range (IQR). Differences were calculated by the means ofthe Mann-Whitney-U-test

	Severe aortic stenosis	AfterTAVR	*p*-value
max dP/dt, mmHg/ms (IQR)	626.9 (432.5–835.2)	959.7 (790.3–1263.7)	<0.001
SVI, - (IQR)	134.1 (115.2–144.8)	146.6 (123.9–178.3)	0.014
Duration of diastole, ms (IQR)	560.9 (472.8–647.5)	576.3 (542.9–723.9)	0.271
Ejection duration per period, - (IQR)	36.3 (34.5–40.1)	32.9 (28.9–36.7)	0.003
AI, - (IQR)	154.6 (141.4–169.0)	139.5 (131.7–156.5)	0.017
AGPH, - (IQR)	32.1 (28.6–38.5)	28 (23.5–35.9)	0.063
TI, ms (IQR)	105.8 (95.1–146.1)	87.6 (82.5–97 .8)	<0.001
T2, ms (IQR)	229.3 (214.0–253.4)	197.3 (192.9–217.4)	0.001
PI, mmHg (IQR)	114.8 (101.5–123.1)	118.1 (100.3–129.2)	0.230
P2, mmHg (IQR)	133 (119.5–148.8)	133 (119.5–149.5)	0.530

max dP I dt - peripheral maximal pulse height dP I dt; *SVI* subendocardial viability index/ratio (Buckberg index; ratio of diastolic area/min and systolic area/min); *AI* augmentation index; *AGPH* augmentation per pulse height; *TI* time to first peak; *T2* time to second peak; *PI* pressure at TI; *P2* pressure at T2.

Background: Pulse wave analysis (PWA) is a useful tool for non-invasive assessment of hemodynamic changes. The diagnostic information measured by PWA in the setting of transfemoral transcatheter aortic valve replacement (TF-TAVR) has not been investigated yet.

Methods: We prospectively enrolled 25 consecutive patients with severe aortic stenosis selected for a TF-TAVR procedure. Peripheral radial and carotid pressure curves were measured directly before and up to 7 days after the procedure. The characteristics of the calculated central (aortic) pressure curves were compared. The change in the subendocardial viability index (SVI), an indicator of reverse subendocardial ischemia, was defined as primary endpoint.

Results: Fig. 1 shows characteristic pressure curves before and after TAVR. All parameters of the calculated central aortic pressure curves yielded comparable results obtained from radial or carotid measurements sites (e. g. Pearson correlation coefficient for delta (SVI): r = 0.97, $p < 0.001$). The maximum velocity over the aortic valves (AV_{max}) was reduced by TAVR procedure from 4.9 m/s (IQR 4.2–5.1) to 2.2 m/s (IQR 2.0–2.7) ($p < 0.001$) as expected. As a result the SVI increased significantly [134 (IQR 115–145) vs. 147 (IQR 124–178), $p = 0.014$]. Additionally dP/dt, a measure of left ventricular contractility, and the augmentation index (AI) changed significantly before and after the procedure [627 (IQR 433–835) vs. 960 (IQR 790–1264); $p < 0.001$ for max dP/dt and 155 (IQR 141–169) vs. 140 (IQR 132–157); $p = 0.017$ for AI], confirming the beneficial hemodynamic effects of replacing the stenotic valve. Table1 shows the results of the parameters of the central curves for the carotid measurements.

Conclusions: PWA is a simple and non-invasive tool to assess hemodynamic changes in the setting of TAVR, irrespective of measurement site. TAVR results in a significant improvement of markers of subendocardial viability and left ventricular contractility. Further follow-up repeated measurements will aim to analyze the PWA parameters in case of developing aortic insufficiency post-TF-TAVR and the predictive values of these parameters assessing long-term clinical outcome.

16-2

Long-term outcome data of the bioabsorbable everolimus-eluting coronary stent system (ABSORB) – Preliminary results from a single centre registry

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Background: It was shown that the bioabsorbable everolimus-eluting ABSORB stent (Abbott Vascular, USA) has a similar safety profile in terms of target lesion revascularisation, stent thrombosis and restenosis compared to third generation drug eluting stents, but there are also controversial data in the literture. We assessed long-term outcomes using optical coherence tomography in patients who received an ABSORB stent in order to compare our own experience with this device with international data.

Methods and Results: Between January 2013 and December 2015, 49 patients received an ABSORB stent, of whom 43 % initially presented with stable or unstable angina (no troponin elevations) and 57 % with an acute coronary syndrome (ACS).

Mean age of our patients was 53 ± 10 years, 94 % were male and 63 % had one-vessel disease. In total, 1.7 ± 0.9 ABSORB stents were implanted per intervention and patient. Thirty-eight patients (78 %) did not experience recurrent symptoms and/or a cardiovascular events until December 2015, of whom 14 % ($n = 7$) had an angiographic follow-up at two years without any significant restenosis. Three patients (6 %) experienced a coronary event not related to the ABSORB-stented lesion. In 8 (16 %) patients target lesion failure was diagnosed, which was a composite of ischemia-driven target lesion revascularization (ID-TLR), Non-ID-TLR, including also the angiographic detection of in-stent restenosis (ISR) of >50 %.

ID-TLR occurred in 4 (8 %), of which 3 events were definit stent thromboses and 1 was a high grad ISR accompanied with troponin elevation. Non-ID-TLR occurred in 4 (8 %) patients, of which 2 events were due to high-degree ISR, while, one was a

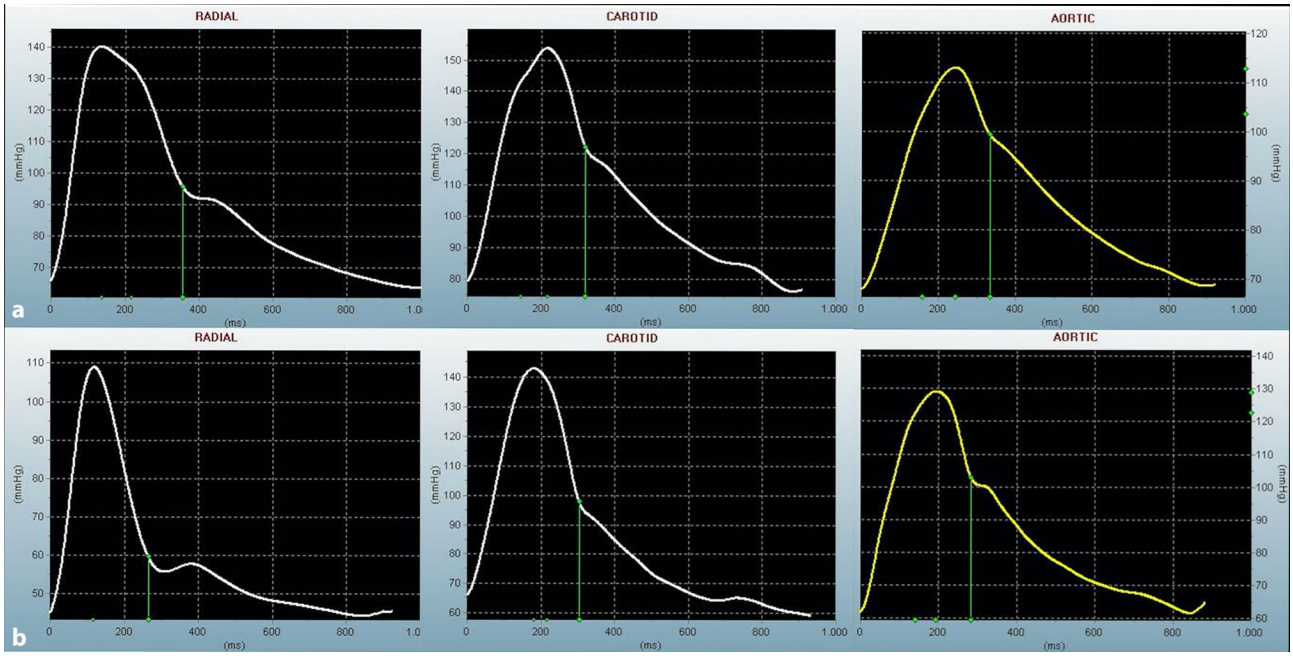

Fig. 1 Characteristic pressure curves for the radial an carotid measurement sites as well as for the calculated central curves. a. Measurements in severe aortic stenosis. b. Measurements after TAVR

de-novo, lipid rich thin-cap atheroma, and one an ISR of >50% not suitable for revascularization. Events occurred primarily in patients implanted in the first year of experience (2013, time to event 11.8±7.1 months), while only 1 of 8 events occurred in a patients implanted later.

Conclusions: In contrast to previously published findings, target lesion failure was frequent (16%) in patients undergoing implantation of ABSORB stents in our hands with main problems in the first year of experience with this stent at a time when the optimal implantation technique was not known or not made accessible for the user. After improvement of clinical routine by stepwise optimization of the implantation technique the ABSORB bioresorbable scaffold behaved comparable to second generation drug-eluting stents when used in the correct indication.

16-3

One-year mortality after transcatheter aortic valve implantation (TAVI) compared to surgical aortic valve replacement (SAVR): A systematic literature review and meta-analysis

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Background: Transcatheter aortic valve replacement (TAVI) has become an alternative treatment option also in patients eligible for surgical aortic valve replacement (SAVR), but with an increased peri-operative risk. Supplementary to data from randomized controlled trials (RCTs) comparing TAVI with SAVR, the body of evidence from non-randomized trials is constantly growing. While these real-world cohorts better reflect clinical reality, they are often small-sized and significant effects might only be visible upon pooling in a meta-analysis. Therefore, we performed a systematic review and meta-analysis to compare the effects of TAVI and SAVR on one-year mortality including both randomized and non-randomized studies.

Methods: A systematic literature search was performed to identify studies comparing TAVI in at least 20 patients to alternative treatment strategies and reporting mortality as outcome. For the purpose of this presentation, only comparisons of one-year mortality between TAVI and SAVR are reported. Six electronic databases were searched between 1st of January 2002 and 15th of January 2015, updates were screened until 15th of June 2015. In addition, hand searching was performed. Two reviewers independently performed eligibility assessment, study selection, data extraction and quality assessment. Meta-analysis of relative risks and 95% confidence intervals were calculated using fixed (Mantel-Haenszel) or random-effects

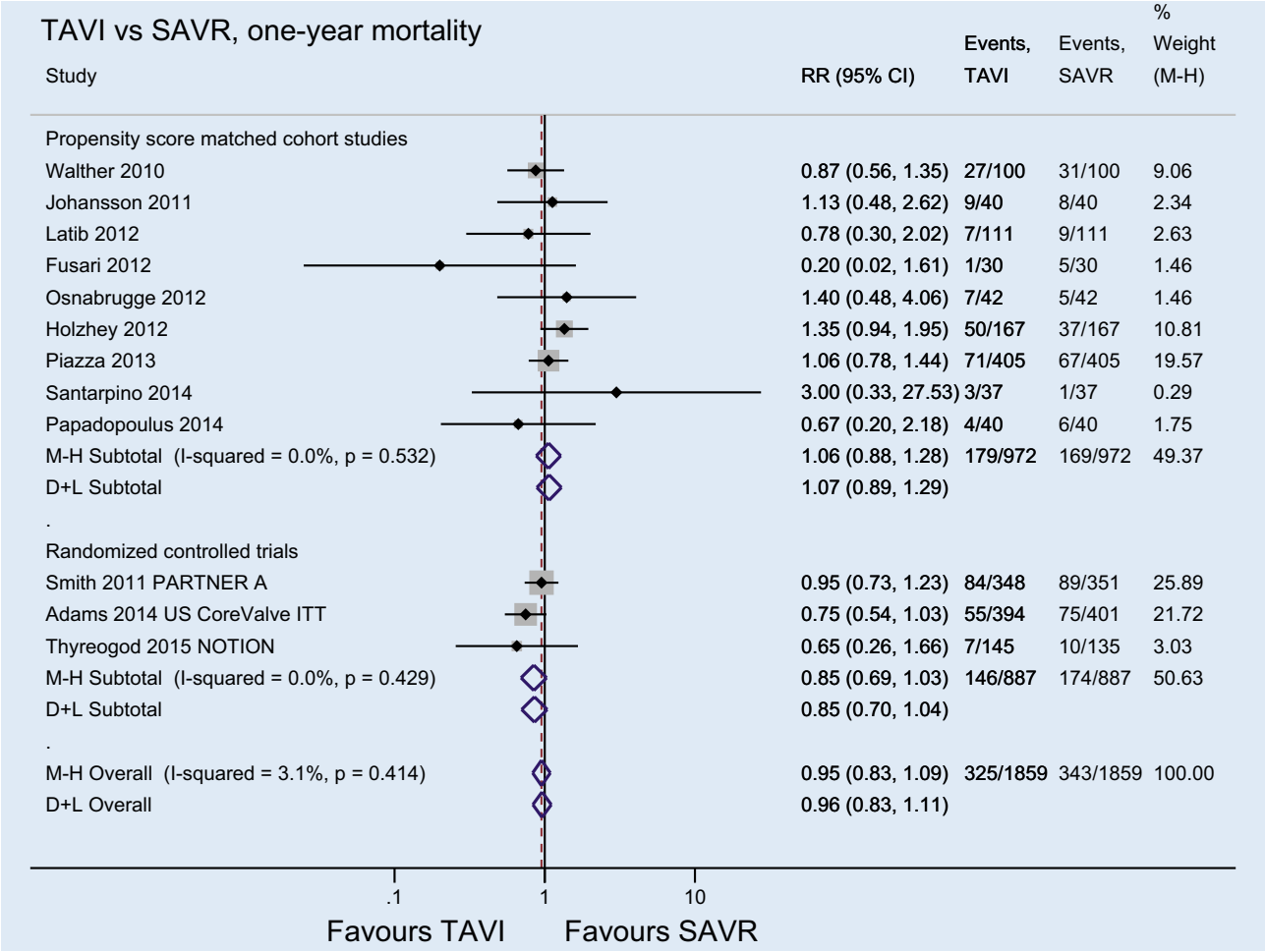

Fig. 1

models (DerSimonian and Laird, in case of high heterogeneity [I2 >50 %]).

Results: After screening of 5747 abstracts data were extracted from 65 publications, of which 32 reported one-year mortality of TAVI versus SAVR. These comprised 3 randomized controlled trials and 29 cohort studies (9 with propensity score matching) comparing TAVI with SAVR. Pooled analysis showed no difference in one-year mortality between TAVI and SAVR in both the complete study sample (32 studies, 21152 patients, RR 1.09, 95 % CI 0.84–1.41, $p = 0.523$, I2 = 88.1 %) and in a subgroup including only RCTs and propensity score matched studies (12 studies, 3718 patients, RR 0.95, 95 % CI 0.83–1.09, $p = 0.414$, I2 = 3.1 %, Fig. 1).

Conclusions: Our meta-analysis showed no difference for one-year mortality between TAVI and SAVR. This not only confirms previous data from randomized controlled trials but also supports the establishment of heart teams in order to make recommendations for either approach on an individual basis.

16-4

Procedural outcomes of chronic total occlusion percutaneous coronary intervention – insights from the Medical University of Vienna

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Background: Reopening a chronic total occlusion (CTO) of a major coronary artery remains a challenging procedure in percutaneous coronary intervention (PCI). We sought to evaluate whether procedural characteristics and outcomes vary according to antegrade or retrograde approach and according to CTO target vessel (left anterior descending artery (LAD), left circumflex artery (CX), right coronary artery (RCA), ramus intermedius (RI)).

Methods: 69 patients who underwent PCI of 70 CTO lesions in a native coronary artery between December 2014 and January 2016 were analyzed according to clinical and procedural characteristics. Procedural success was defined as < 50 % residual stenosis with thrombolysis in myocardial infarction (TIMI) flow 3 antegrade. Major complications included severe bleeding, coronary perforation, pericardial tamponade and contrast induced nephropathy.

Results: Mean age was 65±12 years and 20 % were female. Overall procedural success rate was 81 %. Procedures with antegrade ($n = 40$) or retrograde ($n = 11$) approach had higher success rates compared to PCIs, where a combined approach was used ($n = 19$; 90 % vs. 91 % vs. 59 %, $p = 0.005$, respectively). Combined procedures had longer fluoroscopy times (71 [IQR, 53–107] minutes vs. 40 [IQR, 29–46] minutes for antegrade and 68 [IQR, 46–79] minutes for retrograde; $p = 0.002$) and required more contrast (353 [IQR, 307–457] mL vs. 243 [IQR, 189–318] mL for antegrade and 270 [IQR, 197–362] mL for retrograde; $p = 0.001$). Major complications occurred in 7 cases (10 %) without any differences regarding procedure approach ($p = 0.338$).

RCA was the target vessel in 40 cases (57 %), LAD in 23 (33 %), CX in 5 (7 %) and RI in 2 cases (3 %). Stenting was performed in 33 (83 %) of all RCA CTOs, in 18 (78 %) of LAD, in 5 (100 %) of CX and in 2 (100 %) of RI CTOs ($p = 0.470$). More stents per vessel were implanted after RCA-PCI (2.2±1.4) compared with other vessels (1.4±1.0 for LAD vs. 1.8±0.8 for CX vs. 1.0±0.0 for RI,; $p = 0.093$) and metallic drug-eluting stents were more frequently used than bioresorbable vascular scaffolds ($p = 0.062$). Success rate was lower in LAD (78 %), followed by RCA (80 %), CX (100 %) and RI (100 %) CTOs ($p = 0.361$). Longer fluoroscopy times were required in LAD CTOs (59 [IQR, 39–75] minutes vs. 45 [IQR, 38–68] minutes for RCA and 44 [IQR, 39–100] minutes for CX; $p = 0.899$). CX CTOs required more contrast (461 [IQR, 315–499] mL vs. 250 [IQR, 185–330] mL for RCA and 320 [IQR, 230–400] mL for LAD; $p = 0.013$). There were no vessel specific differences in major complications ($p = 0.484$).

Conclusions: This contemporary analysis of a high-volume CTO center indicates acceptable rates of procedural success. The lowest success rate is found in procedures using a combined antegrade and retrograde approach, whereas no difference in outcome can be reported regarding CTO target vessel.

16-5

Ultrasound-assisted catheter-directed thrombolysis followed by post-procedural an with rivaroxaban in patients with intermediate high-risk pulmonary embolism- a case series

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Background: Intermediate-high risk pulmonary embolism, which is characterized by echocardiographic and laboratory signs of right heart dysfunction carries a significant risk of short term mortality (up to15 % within the first 3 months). Recently, a randomized trial comparing ultrasound-assisted catheter-directed thrombolysis (USAT) with anticoagulation alone (ULTIMA trial) in patients with intermediate-high risk pulmonary embolism has provided evidence for the feasibility and safety of this treatment(1).

Case series: Between October 2013 and October 2015, five consecutive patients (3 males, 2 females) with intermediate-high risk pulmonary embolism were admitted to our coronary care unit. The mean age of the patients was 73 years (range 51–82 years). The PESI class was in all cases >III (mean 125 points). After initial treatment with low-molecular weight heparin, therapy was switched to unfractioned heparin and USAT with recombinant tissue plasminogen activator (rtPA) was performed. The doses ranged between 10 mg and 20 mg, depending on the individual characteristics (body weight, extension of pulmonary emboli). After a mean of 16 hours (range 14–20 hours) the catheter was removed and heparinisation was continued for a total of at least 48 hours. With the exception of a major bleeding episode and a transient rise in creatinine in one patient after the procedure, no adverse events were observed. All patients recovered well and symptoms were markedly improved shortly after the procedure. Thrombolysis resulted in a significant reduction of the RV/LV rate (RV/LV ratio decreased from a median of [1,22 range 1,07–1,24] at baseline to a median of 0,87 [range 0,76–1,07] after 3 days and to a median value of 0,69 [range 0,65–0,81] after follow-up). After a mean time of 2.4 days (range 2–4 days) treatment with rivaroxaban was initiated as post-procedural anticoagulation therapy in each patient with a dose of 15 mg twice per day for the first 3 weeks. After 3 weeks the dose was changed to 20 mg once daily.

After a mean time of 112 days (range 86–181 days), follow-up visits including echocardiography were performed. No detect-

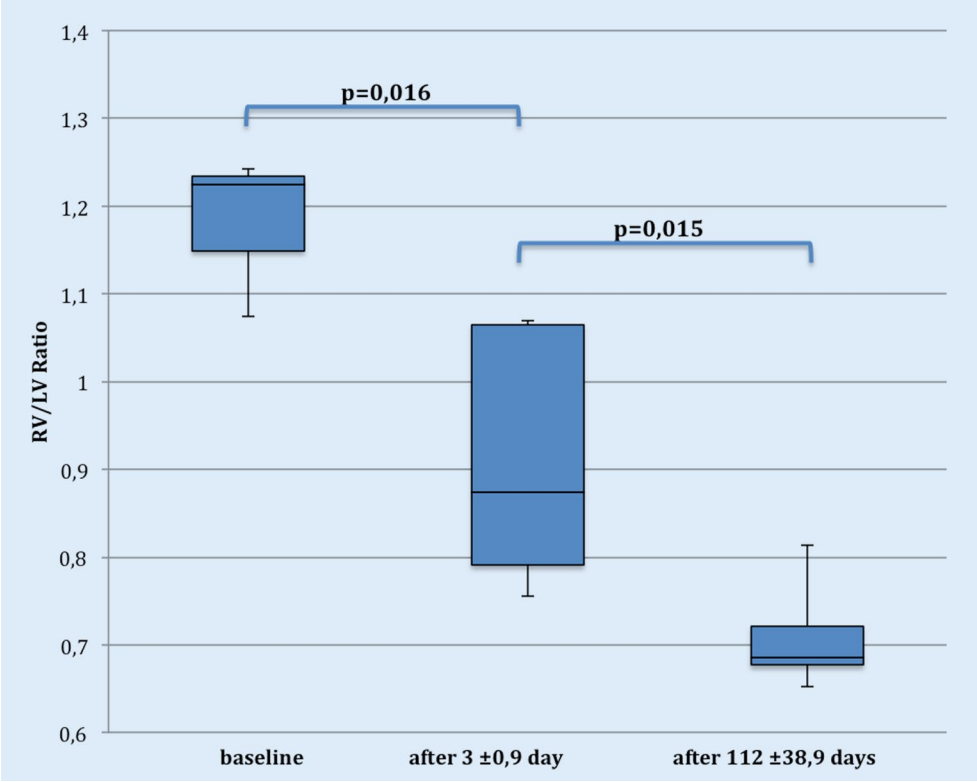

Fig. 1

able signs of right ventricular dysfunction and in addition, no recurrent VTE events or bleeding episodes were observed. Continuation of anticoagulation treatment was recommended for all patients.

Conclusions: USAT appears to be a promising new therapy for intermediate-high risk pulmonary embolism with immediate clinical improvement in all patients. With the initiation of rivaroxaban therapy shortly after USAT, we observed a favourable outcome during hospitalization as well was during the follow-up period.

Literature

1. Kucher N, Boekstegers P, Müller OJ, Kupatt C, Beyer-Westendorf J, Heitzer T, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014 Jan 28;129(4):479–86.

16-6

Balloon aortic valvuloplasty as a bridge therapy to transcatheter aortic valve implantation (TAVI) in a patient with Heyde syndrome

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Background: Morbus Heyde is a clincial syndrome characterized by gastrointestinal (GI) bleeding from angiodysplasia in the presence of severe aortic stenosis. Passage through the stenosed aortic valve induces a sheer-stress dependent structural molecular change of von Willebrand Factor (vWF) which makes the molecule sensitive for proteolytic cleavage and subsequent degradation which leads to a loss of high molecular multimers of vWF and a consecutive primary hemostatic disorder.

Case: A 81 year-old male patient with severe symptomatic aortic valve stenosis (AVA: 0,8 cm^2, max./mean transvalvular gradient: 134/86 mmHg) was referred to our department for transfemoral aortic valve implantation (TAVI) evaluation. The patient's past medical history was significant for recurrent episodes of major GI bleedings with a demand for red blood cell transfusions and argon laser coagulation of the intestinal angiodysplasia. Plasma protein gel electrophoresis revealed a remarkable high molecular vWF multimer deficiency (FIGURE 1). Hence, the diagnosis of morbus Heyde with acquired von Willebrand Factor syndrome type 2 was made. Antiaggregatory treatment (a conditio sine qua non for TAVI) had to be withdrawn because of recurrent severe anemia due to persistent excessive GI bleeding. Consequently, we decided to perform an interventional ballon aortic valvuloplasty to reduce local sheer-stress and restore primary hemostasis. Postinterventional complete correction of high molecular vWF multimer deficiency (Fig. 1) was accompanied by hemoglobin level stabilization. Thus, it was possible to initiate dual antiaggregatory Treatment. Successful TAVI procedure was performed 2 month later without further GI bleeding complications.

Conclusions: Balloon valvuloplasty can be used successfully as a bridge therapy to TAVI in patients with Heyde syndrome and severe GI bleeding to restore primary hemostasis.

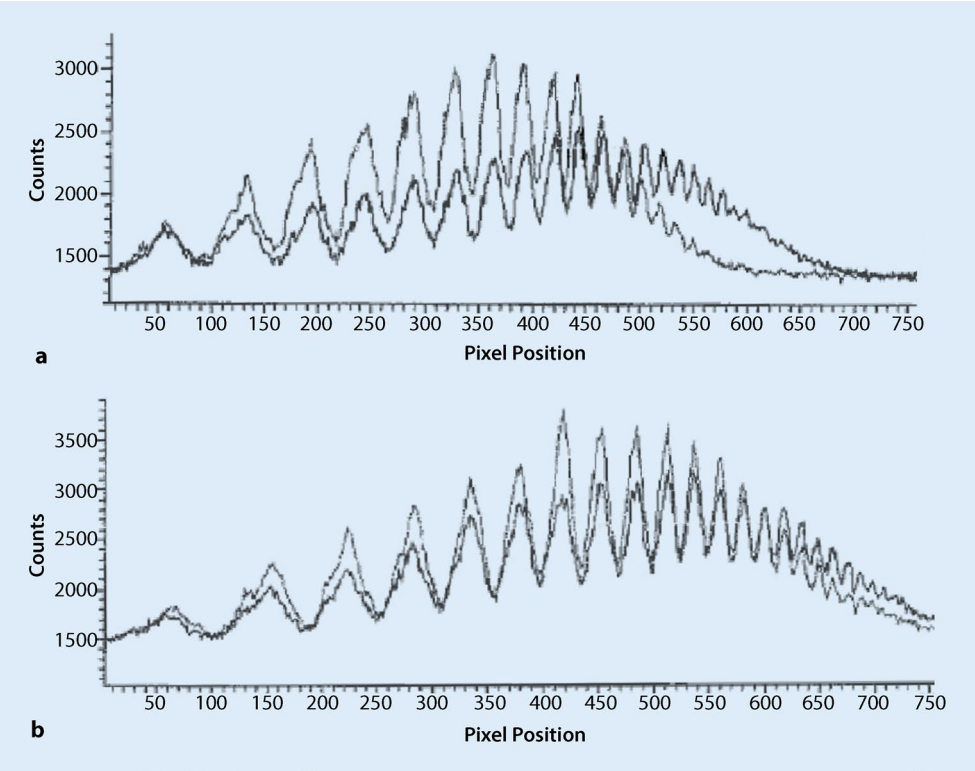

Fig 1 Densitometrical quantification of von Willebrand Factor (vWF) multimer electrophoresis bands shows vWF multimer deficiency prior ballon valvuloplasty in comparison to control (a) and complete norrmalization after ballon valvuloplasty (b)

16-7

Severe mitral valve insufficiency in a patient rejected for conventional mitral valve repair: Is NeoChord the solution?

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Background: Surgical mitral valve repair with artificial chords is an established concept with excellent results. NeoChord is a new off- pump development in mitral valve repair, for patients with mitral valve prolapse. Through a transapical approach, artificial neo-chords are implanted and fixed on mitral valve leaflets, avoiding the cardio pulmonary bypass. This case reports a patient with a prolapse of the posterior leaflet, who was rejected for conventional mitral valve repair and scheduled for NeoChord-implantation.

Methods: A 88 years old female patient (log Euroscore 45.24 %, Euroscore II 13.91 %) with severe mitral valve insufficiency, based on a prolapse of the P 2 segment of posterior leaflet and moderate reduced left ventricular ejection fraction. The patient presented with decompensation and acute lung edema. Additionally she had an acute renal insufficiency (cardiorenal syndrome), CAVD and pulmonary artery pressure of 48 mmHg. Because of her comorbidities and frailty the patients was considered as too high risk for conventional surgery and therefore underwent a NeoChord-Implantation. Introduction of the NeoChord -System through the apex via a left sided thoracotomy. Four NeoChords were implanted under 3D echocardiography guidance, to repair the posterior leaflet prolapse

Results: The NeoChord-Implantation was successful. Postoperative echocardiography showed only mild central mitral valve regurgitation. The patient was transferred to the ICU and extubated the same day. 5 days later the patient could be transferred to IMC and a few days later, the patient was recompensated and transferred to general ward. The patient could be discharged to home. The patient died of a severe gastrointestinal and urogenital infection 4 month after surgery.

Conclusions: NeoChord-Implantation seems to be a feasible and promising technique for stable patients with structural mitral valve insufficiency. In this case of acute decompensation and lung edema because of severe mitral insufficiency, a surgical option was not reasonable due to the calculated high perioperative risk. Even in this situation, NeoChord implantation could dramatically reduce mitral valve insufficiency. Despite of the frailty of the patient, the NeoChord-System showed satisfying results. Collecting mid-and longterm results is inevitable to investigate the patients who benefits most and enlarge the inclusion criteria.

Chirurgie e-Poster-Sitzung

CeP-1

Acute type A dissection in octogenarians: Does emergency surgery impact long-term survival?

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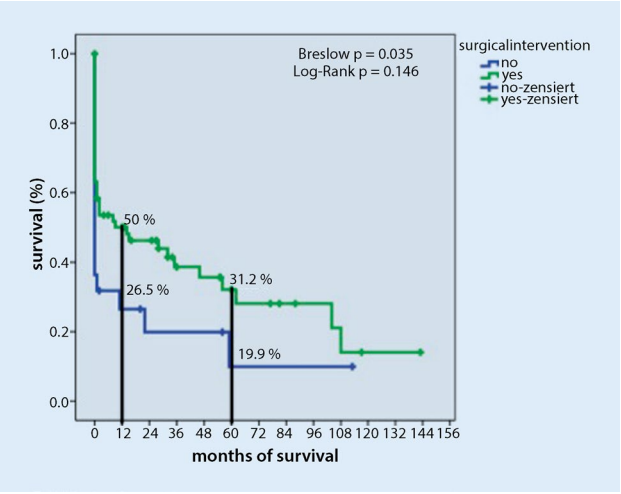

Fig. 1 Survival: surgical vs. medical treatment

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Background: Surgical therapy for acute aortic dissection type A (AADA) in octogenarians carries high morbidity and mortality. The role of medical treatment in this setting is discussed controversially. Aim of this study was to determine if risk of surgery for AADA outweighs risk of death from medical treatment only

Methods: From 2002–2015 a total of 90 consecutive octogenarians (mean age, 83.5±3 years) were treated for AADA at three different international institutions. Patients were divided into two groups: 67 patients underwent surgery, 23 patients received medical treatment. Analysis of early and late outcome in the different treatment groups was performed.

Results: Patients in the medical treatment group were significantly older than in the surgical group (84.9±3.7 vs. 83±2.5 years, $p=0.008$) and in a more critically ill state at admission. Out of 67 patients deemed for surgical therapy, 3 patients (4.5 %) died from aortic rupture. preoperatively. Perioperative mortality was 14.9 % ($n=10$). In patients undergoing surgical repair, rate of prolonged ventilation (63.2 % vs. 5.9 %; $p<0.001$) and renal failure (35.1 % vs. 5.9 %, $p=0.029$) was significantly higher. 30-day survival was impaired in the medical treatment group (34.8 % vs. 61.2 % in the surgical group; $p=0.032$). Multivariate analysis identified coronary artery disease and complicated dissections – composite variable of preoperative resuscitation, neurologic injury and malperfusion syndrome – as independent risk factors for 30-day mortality in the surgical group (OR: 3.925, 95 %-CI: 1.2–12.8, $p=0.024$). There was no difference in long-term survival between the two treatment groups.

Conclusions: Emergency surgery for AADAs in octogenarians is associated with high intraoperative mortality and postoperative morbidity. Due to the devastating results of medical therapy in octogenarians, surgery should be performed for uncomplicated dissections. Despite better immediate survival after surgery, aortic repair does not impact long-term survival.

CeP-2

Surgical treatment for acute type A aortic dissection: Benefit of female gender not confirmed

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Background: Outcome of women suffering from acute type A aortic dissection (AAD) has been discussed controversially. This study investigates impact of gender on outcome in surgically treated patients with AAD.

Methods: From 2002–2015 250 men and 110 women underwent surgery for AAD in two international centers. Preoperative characteristics, surgical therapy and outcome were compared.

Results: Women were older (64.6±13.8 vs. 58±13.4 years, $p<0.001$) and had smaller body surface areas (1.8±0.2 vs. 2.1±0.2 m^2, $p<0.001$). Preoperatively, women had higher rates of cardiopulmonary resuscitation (CPR) (14.9 % vs. 6.4 %, $p=0.028$) and pericardial effusion (59.1 % vs. 45.7 %, $p=0.022$). Surgical therapy differed in terms of higher rates of root replacement in men (29.9 % vs. 19.3 % in women, $p=0.038$). Multivariate analysis revealed different predictors for in hospital mortality – peripheral vascular disease (odds ratio [OR] 10.6, 95 % confidence interval [CI] 2.4–47.1, $p=0.002$) and preoperative malperfusion (OR 6.4, 95 % CI 1.4–29.9, $p=0.019$) in women, coronary artery disease (OR 4.1, 95 % CI 1.8–9.5, $p=0.001$) and preoperative CPR (OR 6.8, 95 % CI 1.8–25.6, $p=0.005$) in men. There was no difference in early outcome or long-term survival.

Conclusions: Despite higher age and the more critical state of women suffering from AAD, there are no differences in early and long-term outcome

CeP-3

Case report: 26-year-old asymptomatic patient with cor triatriatrum sinister with singular communication < 5 mm within a calcified membrane in the left atrium

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Background: Cor triatriatum is a very rare congenital heart failure (0,1–0,4 %), which mostly becomes symptomatic in the early childhood.

Case presentation: A 26-year old patient without previous medical history presented with dyspnoea and atrial fibrillation. A cor triatriatum was diagnosed and excision of the septum was done.

Conclusions: From literature we know that the severity of symptoms is correlating with size and number of fenestrations. In our case communication was <5 mm. Histopathologic analysis showed many calcium deposits.

Conclusions: or triatriatum sometimes first becomes symptomatic in the adulthood. The reason for this delayed but sudden appearance of symptoms might be the increase of calcification or fibrosis of the intraatrial septum.

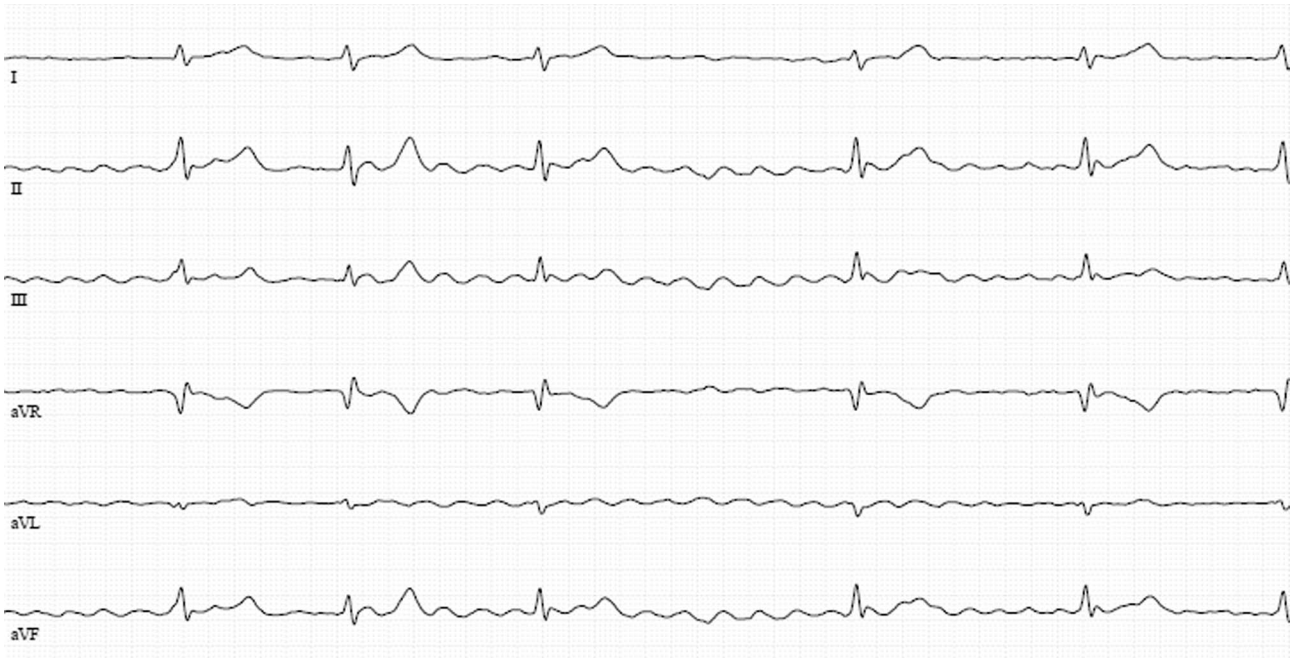

Fig. 1 Preoperative ECG: Atrial fibrillation, 74/min, vertical heart position, QRS = 86 ms

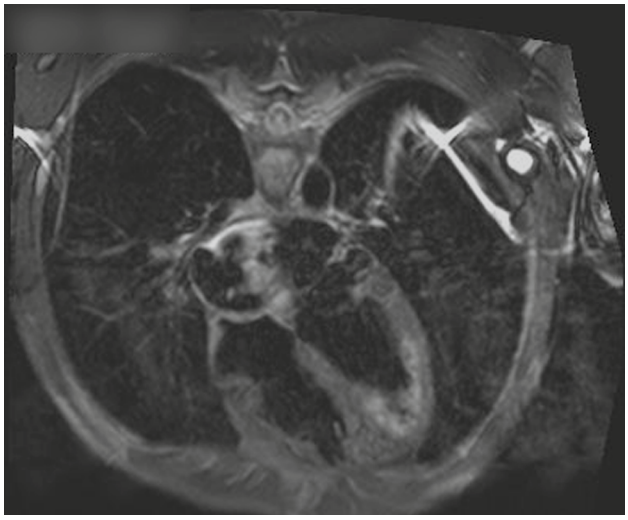

Fig. 2 preoperative Cardiac-MR

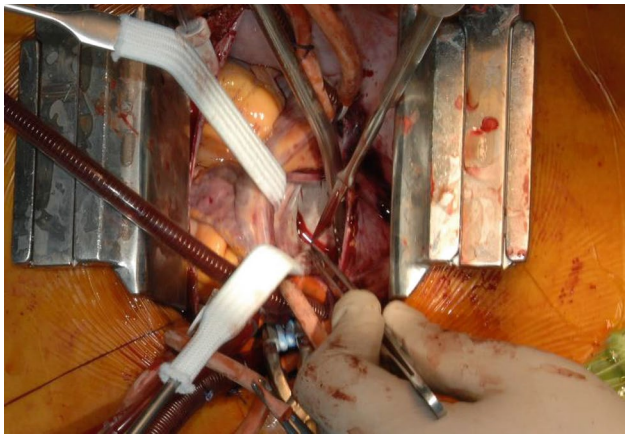

Fig. 3 Excision of the membrane/septum (*red arrow*), opening of the mitral valve appears (*black arrow*)

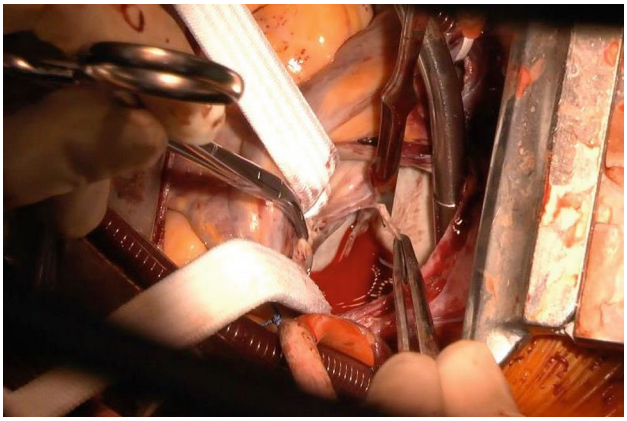

Fig. 4 intraoperative, after opening the upper chamber of the left atrium, just before excision of the subsepted membrane/septum (*red arrow*)

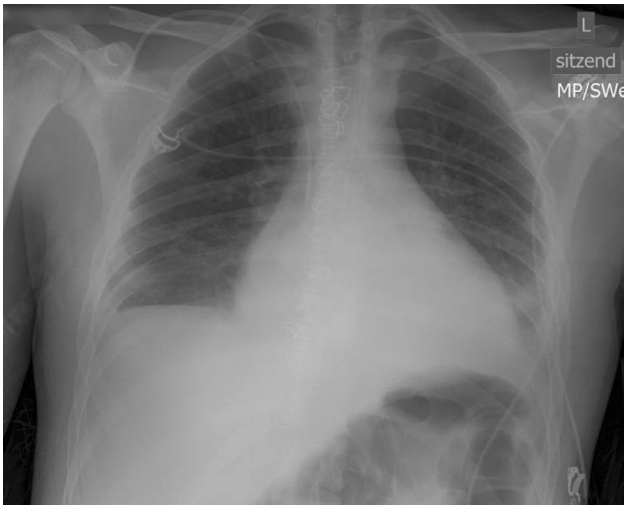

Fig. 5 chest X-ray, 2nd postoperative day

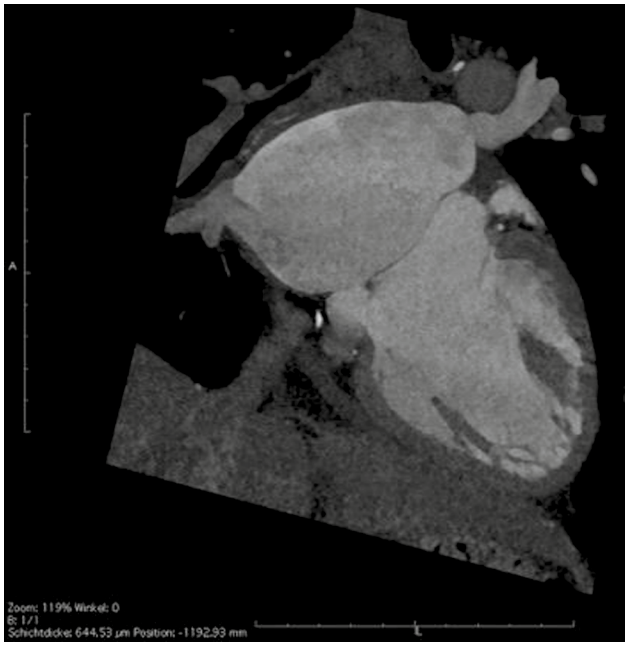

Fig. 6 Coronary plane of the preoperative Cardiac-MRT, communication between the upper and lower chamber of the left atrium (*red*)

CeP-4

Case report: Transcatheter aortic valve implantation in a patient with severe aortic valve stenosis, concomitant aortic root aneurysm and aortic coarctation

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Aortic root aneurysm is currently considered an exclusion criterion for transcatheter aortic valve implantation (TAVI). There is limited to no experience with transcatheter aortic valves in the setting of concomitant aortic root aneurysm and to our knowledge, this is the first case of a successfully implanted transcatheter heart valve in the presence of aortic root aneurysm. Up to date there is no data in the form of randomized clinical studies to prove the safety or efficacy of TAVI in patients with aortic root aneurysm.

Therefore many concerns must be taken into account when planning such a procedure. In such a setting device malpositioning and migration due to large annular size are major risk factors for unsuccessful TAVI implantation alongside the known common complications such as paravalvular leaks, AV-block and stroke.

We hereby report the case of a very frail 87-year-old gentleman who had been treated successfully with TAVI in the setting of severe aortic stenosis accompanied with aortic root aneurysm. Accurate preoperative planning and device selection were crucial and challenging in this case notably because retrograde access of any kind other than the right subclavian site was not achievable as the patient received surgery for aortic coarctation in the past and presented with severe kinking and narrowing of the proximal descending aorta. The applied strategy was to obtain retrograde access from the right subclavian artery for pressure measurement and pigtail insertion. Transapical TAVI was then performed uneventfully under fluoroscopic and transesophageal echocardiography (TEE) guidance. A multidetector computed tomography (MDCT) evaluation at 6 month did not show device dislodgement or any other complications. We conclude that TAVI in patients with aortic root aneurysm is feasible in highly selected cases after comprehensive preoperative evaluation.

CeP-5

Schrittmacherperforation ohne Perikarderguß – ein Case report

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Grundlagen: Ventrikelperforationen nach Schrittmacherimplantation sind nicht so selten, in einer Untersuchung konnten bei 100 Implantationen im CT in 15 % atriale und in 6 % ventrikuläre Perforationen nachgewiesen werden (Hirschl Pace 2007). Symptome können oft erst spät nach der Implantation auftreten. Das klinische Bild ist meist geprägt von einem Perikarderguss, andere Symptome sind Reizschwellenanstieg, Exitblock, Undersening, Thoraxschmerzen oder Perikarditis.

Methodik und Ergebnisse: Einer 75 jähriger Frau wurde im Jänner 2015 wegen Sick-Sinus Syndrom mit Vorhofflimmern ein bifokaler Schrittmacher Biotronik Epyra DR implantiert. Der initiale Verlauf war komplikationslos. 10 Monate nach Implantation kam die Patientin mit akuten Thoraxschmerzen links zur Aufnahme. In der Abklärung fand sich eine normale Schrittmacherfunktion, im Thoraxrötgen etwas atypische Sondenlage

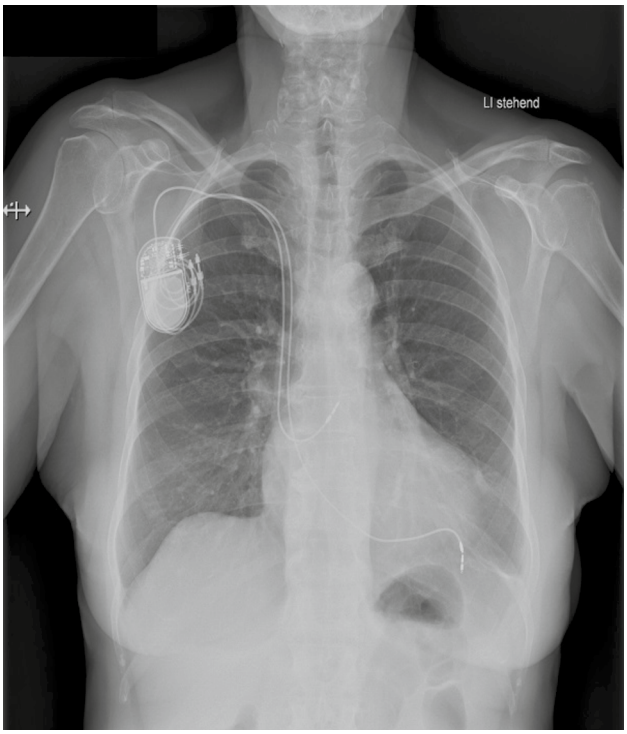

Fig. 1

(s.Abb), im Echo kein Perikarderguss, als Differentialdiagnose wurde ein akutes Koronarsyndrom ausgeschlossen und die Patientin wieder entlassen. Erst 3 Monate später, im Februar 2016, wurde die Sondenperforation im Echo diagnostiziert, weiterhin ohne Perikarderguss, jedoch nun fehlerhafter SM-Funktion (Exitblock und Undersensing). Bei der Revision wurde die Sonde entfernt und es bildete sich intraoperativ ein Erguss mit Tamponadezeichen, der akut drainiert werden musste.

Schlussfolgerungen: Ein fehlender Perikarderguss nach Schrittmacherimplantation schließt eine Sondenperforation nicht aus. Auch Monate nach Schrittmacherimplantation ist die Entfernung einer perforierten Schrittmachersonde nicht gefahrlos und sollte unter Echo Kontrolle durchgeführt werden.

CeP-6

The mechanism of guide wire perforation during transcatheter aortic valve implantation – Insights by intracardiac echocardiography

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We present the case of a 67 years old patient with low flow -low gradient severe aortic stenosis (gradient 68/46 mmHg, SVI <35 ml/m^2 BSA) with preserved ejection fraction and severe chronic obstructive pulmonary disease (GOLD IV) with long-term oxygen therapy, who underwent transcatheter aortic valve implantation via transfemoral access in sedation. A 29 mm Sapien prosthesis was successfully implanted. Echocardiography after implantation revealed no signs of periprosthetic regurgitation but a minimal pericardial effusion. Four hours after the intervention, the patient became slightly unstable. A new echocardiographic evaluation revealed a progression of the pericardial effusion, which was surgically drained. The hemodynamic deterioration continued despite adequate drainage. A non-treatable ventricular rupture was noted after immediate sternotomy and the patient expired on the operating table. Post mortem examination revealed a ventricular perforation at the base of the left ventricle (at the vicinity of the anterolateral commissure of the mitral valve which led to a diffuse intramyocardial bleeding exiting at the lateral wall of the left ventricle). A post mortem analysis of the intracardiac echocardiography revealed a penetration into the left ventricular myocardium by

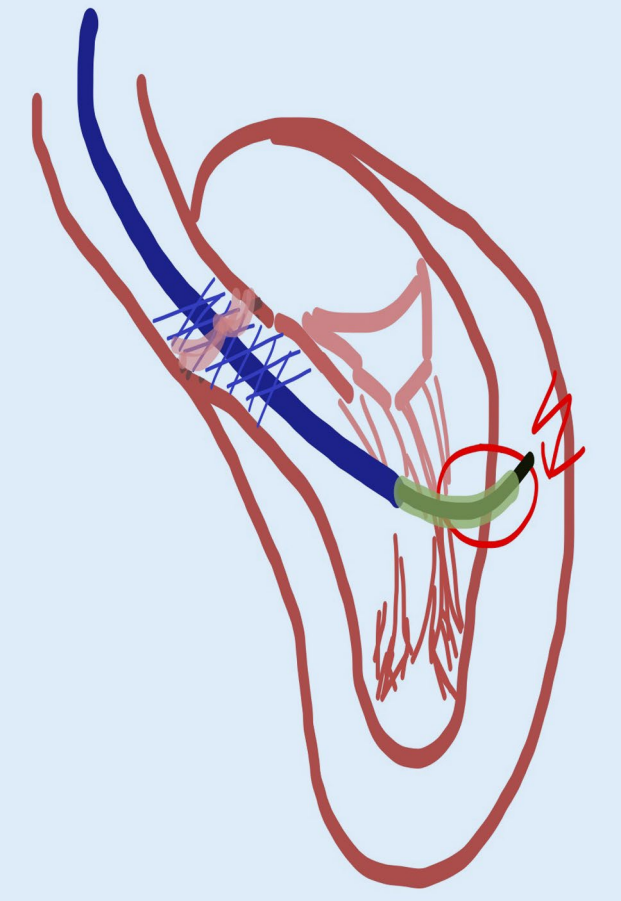

Fig. 1

the soft wire used for retrograde passing of the aortic valve. A pig-tail catheter was used to change to an extra-stiff guide wire for valve implantation. During rapid pacing for balloon valvuloplasty and valve implantation, the extra-stiff wire progressively penetrated the left ventricular myocardium, which inevitably led to ventricular rupture (illustration 1). After this incidence, we changed our technique to a blunt advancement of the pig tail catheter into the left ventricle, in order to avoid impingement of the left ventricular trabecles or the papillary muscles.

This case shows us the importance echocardiographic imaging in routine technical steps of transcatheter procedures. Avoiding high risk maneuvers in fragile tissue of high-risk patients can contribute to further risk reduction of transcatheter valve implantation.