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Abstracts**

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Österreichische Kardiologische Gesellschaft Annual Conference

May 25–28, 2011, Salzburg

Abstracts

In alphabetical order: session / first author

Best Abstracts I (BAI) and Best Abstracts II (BAII) are highlighted in red.

■ Akutes Koronarsyndrom/Acute Coronary Syndrome

Potential Arrhythmogenic Effects of Endothelin – A Receptor Blockade in ST-Elevation Acute Coronary Syndrome | – 1

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Background Ventricular arrhythmias are the most common complication after acute myocardial infarction (AMI). Endothelin (ET), a mediator of microvascular dysfunction and cardiac remodeling, has been demonstrated to have arrhythmic potential. The present electrocardiographic study, designed to assess the pro- or anti-arrhythmogenic effects of ET-A receptor blockade in AMI is based on a randomized protocol.

Methods Patients with posterior-wall ST-elevation acute coronary syndrome (STE-ACS) were randomly assigned to receive intravenous BQ-123 at 400nmol/minute or placebo over 60 minutes, starting immediately prior to primary percutaneous coronary intervention (PCI) (n = 54). 24-hour Holter recordings (Del Mar Avionics, Del Mar Medical Systems, Irvine, CA) were performed at 2 (IQR 1–3) days (n = 29) and at 45 (IQR 33–62) days (n = 26) to assess standard Holter parameters. The predefined primary endpoint of

the study was the presence of ventricular tachycardia and/or late potentials. Patient characteristics with or without available 24h ECG were similar (Table 1).

Results There was no significant difference in the predefined combined primary endpoint after 45 days (0 [0%] in the BQ-123 vs 1 [10%] in the placebo group; p = 0.435).

At 2 days, an increase in the total number of supraventricular extrasystoles (SVES) in patients randomized to BQ-123 (45 [IQR 17–165] beats vs 11 [IQR 5–73] beats in placebo treated patients; p = 0.023) occurred. There was no significant difference regarding ventricular arrhythmias (extrasystoly [VES] and non-sustained ventricular arrhythmias [NSVT]) and heart rate variability (HRV) values.

Furthermore at 45 days, an increase in the total number of SVES (105 [IQR 33–226] beats in BQ-123 vs 11 [IQR 3–98] beats in placebo; p = 0.033) and thus an increase in mean SVES per hour (4.7 [IQR 1.7–10.3]/h vs 0.5 [IQR 0.1–3.5]/h; p = 0.011) was observed. As at baseline, the total number of VES and NSVT and HRV values were not significantly different between the 2 treatment groups. No patients treated with BQ-123 and one patient treated with placebo developed late potentials (p = 0.244). Beta-blocker medication was not associated with SVES in regression analysis (standardized beta 0.084; p = 0.690).

Conclusion Overall, short-term administration of BQ-123 after AMI was safe. However, SVES increased.

Proteomic Profiling of Acute Coronary Thrombosis Reveals a Local Decrease of Pigment Epithelial Derived Factor PEDF | – 2

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Aims Thrombotic occlusion of an epicardial coronary artery upon atherosclerotic plaque rupture is considered the ultimate and key step in acute myocardial infarction (AMI). The pathophysiological mechanisms of coronary thrombus formation in AMI are still not fully deciphered.

Methods and Results We have analyzed soluble and particulate thrombus material aspirated from the ruptured plaque site of non-diabetic patients with ST-elevation myocardial infarction using proteomic techniques. Label-free quantitation of MS/MS data revealed an accumulation of platelet and polymorphonuclear cell specific proteins but also the presence of proteins specifically expressed in activated monocytes, T-cells, endothelial cells and dendritic cells. When culprit site derived plasma was compared to systemic plasma we observed a prominent differential regulation of complement cascade components and a decrease of anti-thrombotic pigment epithelial derived factor (PEDF). ELISA showed PEDF, which is known to have a protective role in atherothrombosis to be relatively decreased at the culprit site with a level of expression that is inversely correlated with local matrix metalloproteinase 9 (MMP-9) activities. In vitro, culprit site plasma displayed enhanced proteolytic activity towards PEDF.

Table 1: C. Adlbrecht et al.

	Patients with 24h ECG available (n = 26)	Patients with no 24h ECG available (n = 28)	p-value
Age (years)	59.5 (51.8–74.3)	58.0 (52.0–68.0)	0.802
Male n (%)	19 (73%)	24 (86%)	0.249
Randomized to active treatment group n (%)	13 (50%)	15 (54%)	0.408
Ischemic time (hours)	4.0 (2.5–5.5)	4.0 (2.0–6.9)	1
IRA			0.568
RCA n (%)	22 (85%)	22 (79%)	
LCX n (%)	4 (15%)	6 (21%)	
CKmax (U/L)	1795 (1101–3057)	1665 (787–2596)	0.382
Hypertension n (%)	19 (73%)	15 (54%)	0.138
Hyperlipidemia n (%)	22 (85%)	22 (79%)	0.568
Diabetes mellitus n (%)	3 (12%)	3 (11%)	0.923
Current smoker n (%)	13 (50%)	18 (64%)	0.289
On beta-blocker n (%)	25 (96%)	25 (89%)	0.336

IRA: Infarct related artery; RCA: Right coronary artery; LCX: Left circumflex coronary artery; CKmax: Peak creatine phosphokinase level

Conclusion Given the importance of PEDF in atherosclerosis and thrombosis it is tempting to speculate that local administration of PEDF may become a novel strategy for the treatment of coronary thrombosis.

Clopidogrel Pre-Treatment is Associated with Reduced In-hospital Mortality in Primary Percutaneous Coronary Intervention for Acute ST-Elevation Myocardial Infarction **BAIL**

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Aims Pre-treatment with clopidogrel results in a reduction of ischemic events in elective coronary interventions. Data on upstream clopidogrel in the setting of primary percutaneous coronary intervention (PCI) is limited. The aim of this study was to investigate whether clopidogrel loading before arrival at the PCI centre may result in an improved outcome of primary PCI for ST-elevation myocardial infarction (STEMI).

Methods and Results In a multicentre registry of acute PCI 5955 patients undergoing primary PCI in Austria between January 2005 and December 2009 were prospectively enrolled. Patients were stratified into 2 groups, a clopidogrel pre-treatment group (n = 1635 patients) receiving clopidogrel before arrival at the PCI centre and a peri-interventional clopidogrel group (n = 4320 patients) receiving clopidogrel at a later stage. Multiple logistic regression analysis including major confounding factors and stratified for the participating centres was performed to investigate the independent effect of pre-treatment with clopidogrel on in-hospital mortality.

On univariate analysis, clopidogrel pre-treatment was associated with a reduced in-hospital mortality (3.4% vs 6.1%, $p < 0.01$) after primary PCI. After adjustment for major confounders in multivariate analysis, clopidogrel pre-treatment remained a strong and independent predictor of in-hospital mortality (OR 0.59, 95%-CI: 0.38–0.91; $p = 0.02$; **Table 2**).

Conclusion Clopidogrel pre-treatment before arrival at the PCI centre is associated with reduced in-hospital mortality compared with peri-interventional treatment in a real world setting of primary PCI. These results strongly support the recommendation of clopidogrel treatment “as soon as possible” in the setting of primary PCI.

Table 2: J. Dörler et al.

Variable	Odds ratio	95%-CI	p-value
Clopidogrel pre-treatment (yes vs no)	0.59	0.38–0.91	0.02
Cardiogenic shock (yes vs no)	20.3	14.3–28.9	< 0.01
Resuscitation (yes vs no)	2.02	1.33–3.07	< 0.01
Previous myocardial infarction (yes vs no)	1.57	1.02–2.42	0.04
Year (2005–2007 vs 2008–2009)	1.10	0.78–1.56	0.59
Gender (male vs female)	1.06	0.74–1.52	0.77
Age (per year)	1.05	1.04–1.07	< 0.01
ASA/Heparin pre-treatment (yes vs no)	0.75	0.49–1.15	0.19
Gp IIb/IIIa-Antagonist pre-treatment (yes vs no)	1.09	0.67–1.76	0.74
Secondary transfer (yes vs no)	0.72	0.49–1.06	0.09

The Prevalence and Distribution of Culprit Artery Occlusion in Non-ST-Elevation Myocardial Infarction: “Pseudo-NSTEMI” **BAIL**

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Purpose Non-ST-segment elevation myocardial infarction (NSTEMI) may be associated with total occlusion of the culprit artery, which is frequently not diagnosed on the standard 12-lead ECG. This may lead to missed opportunities for prompt reperfusion therapy. We sought to determine the prevalence of acute artery occlusion and location of culprit lesions involved in NSTEMI.

Methods We examined 2219 consecutive patients with NSTEMI enrolled in a multicentre registry of acute percutaneous coronary intervention (PCI). The inclusion criteria were definite myocardial infarction (elevated troponin and/or CKMB with either symptoms and/or ST-segment depression) and invasive strategy within 72 hours of symptom onset. The patients were divided into 2 groups according to the initial TIMI flow (TIMI 0/I, “occluded”; vs TIMI II/III, “patent”). Baseline characteristics, treatment, culprit artery distribution and in-hospital outcome were compared.

Results The prevalence of total occlusion was 33.9% in the entire cohort. In patients with total occlusion, the culprit lesion was more frequently located in the arteries supplying the infero-lateral territory (circumflex, CX; right coronary artery, RCA) compared to patients with patent arteries (CX: 31.2% vs 18.8%, $p < 0.01$; RCA: 31.2% vs 22.6%, $p < 0.01$; LAD: 26.6% vs 38.2%, $p < 0.01$). Patients with total occlusion had significantly shorter delays to PCI (pain to PCI: 951 [460–1730] min. vs 1302 [582–2221] min., $p < 0.01$; door to PCI: 360 [125–1138] min. vs 180 [791–1483] min., $p < 0.01$). In-hospital mortality, however, was similar in both groups (TIMI I vs TIMI II/III 2.7 vs 1.8; $p = n.s.$).

Conclusion Totally occluded culprit lesions occur in one third of patients with NSTEMI in a real world setting and are more frequently located in CX and RCA, but may also be seen in LAD territories. Early risk stratification needs to be enhanced to improve identification of “Pseudo-NSTEMIs” that would benefit from urgent reperfusion as in STEMI.

Cardiogenic Shock Complicating Myocardial Infarction – Patients at Risk and Differences to Patients with ST-Elevation Myocardial Infarction? **| – 3**

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Background Development of cardiogenic shock (CS) in acute myocardial infarction (AMI) is a severe and life-threatening compli-

Table 3: G. Färnau et al.

	Shock	No shock	Odds ratio	CI	p-value
Male sex (%)	70.5	74.6	0.87	0.68–1.1	0.24
Prior AMI (%)	17.8	9.0	0.60	0.46–0.78	0.001
Prior PCI (%)	18.0	8.8	0.59	0.45–0.77	< 0.001
Prior CABG (%)	6.9	1.4	0.41	0.30–0.57	< 0.001
Smoking (%)	38.3	43.2	1.16	0.91–1.47	0.22
Hypertension (%)	68.9	69.8	1.03	0.81–1.32	0.81
Hyperlipidemia (%)	41.7	35.3	0.82	0.65–1.04	0.98
Diabetes (%)	34.6	29.1	0.84	0.66–1.06	0.14
Sinusrhythm (%)	69.6	92.0	2.57	2.10–3.14	< 0.001
Anterior wall infarction (%)	54.4	48.7	0.84	0.63–1.12	0.22
3 vessel disease (%)	57.1	21.3	0.34	0.27–0.42	< 0.001

cation and CS remains the leading cause of mortality in AMI. Currently, the risk factors for development of CS are poorly determined.

Methods We analyzed a cohort of 224 patients presenting with CS in AMI and compared them to 557 patients with acute AMI without CS in history and baseline characteristics.

Results Patients in CS were significantly older (67.0 ± 12.4 vs 63.9 ± 12.3 years; $p = 0.002$), but there was no difference in weight, height and body mass index (83.0 ± 15.6 vs 81.4 ± 14.7 kg; $p = 0.17$; 172.0 ± 10.6 vs. 171.1 ± 9.0 cm; $p = 0.24$; 27.8 ± 4.5 vs 27.7 ± 4.3 ; $p = 0.96$, respectively). Neither smoking, nor the presence of hypertension, hyperlipidemia, diabetes or anterior wall infarctions showed higher risk for CS, but patients with CS had higher rates of prior AMI, percutaneous coronary intervention and coronary artery bypass grafts, had higher degrees of multi vessel disease and showed less rates of sinus rhythm at presentation (Table 3).

Conclusion The most relevant risk factors for development of CS are age, history of previous AMI, evidence of prior coronary revascularization and multivessel disease compared to AMI patients without CS.

The Influence of CYBA (P22-PHOX) Polymorphisms in Young Myocardial Infarction Survivors (≤ 40 Years of Age) | 4

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Background Acute myocardial infarction at a young age is associated with high morbidity and long-term mortality. The NADPH oxidase system as a main source of reactive oxygen species in vascular cells has been implicated in development and progression of coronary artery disease. In our study, we investigated the effect of polymorphisms in the p22-PHOX (CYBA) gene on coronary artery disease in young patients (≤ 40 years).

Methods and Results We prospectively recruited 302 subjects into our multi-center case control study, including 102 young myocardial infarction patients (≤ 40 years) from 2 high volume cardiac catheterization hospitals and frequency-matched them on age, gender, and center to 200 hospital controls in an approximate 2:1 ratio per case patient. The homozygote c.-930A > G promoter polymorphism was significantly more prevalent in the controls than in the infarction patients. In the adjusted logistic regression analysis, we detected a protective effect of the c.-930A > G promoter polymorphism against premature myocardial infarction. Using a log-additive/per-allele model, we detected an unadjusted OR of 0.63 (95%-CI: 0.45–0.9; p-value: 0.011). In the adjusted model the association was more pronounced with an odds ratio of 0.5 (95%-CI: 0.3–0.81; p-value: 0.005). The C242T polymorphism and the 640A > G polymorphism did not differ significantly between the study groups. Furthermore we could not detect a significant effect for these polymorphisms in the logistic regression analysis.

Discussion The present study suggests a protective association between the c.-930A > G promoter polymorphism in the p22-PHOX (CYBA) gene and the development of myocardial infarction in young individuals (≤ 40 years).

Impact of Baseline BNP Level on Early and Late Clinical Outcomes After STEMI: 2-Year Results of the HORIZONS-AMI Study | 5

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Background B-type natriuretic peptides (BNP) are well-established predictors of outcome in ST-elevation myocardial infarction (STEMI). However, limited data are available on the association of initial BNP concentrations with frequent co-morbidities (left ven-

tricular function, anemia, renal dysfunction) observed in patients with acute STEMI. Furthermore, the bleeding risk of patients with high admission BNP levels has also not been investigated yet.

Methods A total of 839 STEMI patients enrolled in the HORIZONS-AMI trial had baseline BNP levels measured in the emergency room as part of the study protocol. We compared the 2-year clinical outcomes between the low ($n = 421$, $\text{BNP} \leq 0.71$ mg/dl) and high ($n = 418$, $\text{BNP} > 0.71$ mg/dl) BNP groups according to the median cut-off-value.

Results Patients with higher initial BNP levels had significantly longer time from symptom onset to first balloon inflation (225 min vs 194 min) and significantly longer door-to-balloon times (100 min vs 89 min). Surprisingly, LVEF was not significantly different among patients with low or high concentrations of BNP (50% vs 51%; $p = 0.758$) but the incidence of anemia (8% vs 12%; $p = 0.026$) and reduced renal function ($\text{eGFR} < 60$ ml/min/1.73 m²: 11% vs 25%; $p < 0.001$) was significantly higher among patients with higher admission BNP. No differences was observed in procedure related variables, ACT value, GP IIb/IIIa or stent use or in antiplatelet compliance. In multivariate survival analysis high concentrations of BNP were strong predictors of major bleeding, as well as early and late mortality and stroke but not of ischemic endpoints (TVR, reinfarction or stent thrombosis). Furthermore, higher concentrations of BNP were also predictive of worsening renal function after index PCI.

Conclusions In the present study we could show that high admission concentrations of BNP are associated with anemia and reduced renal function at admission to the hospital with STEMI but are not related to left ventricular function. According to the present results, patients with high admission concentrations of BNP are at significantly higher risk of worsening renal function after primary PCI. The significant association of high BNP levels with bleeding-risk should be evaluated by future studies.

Vasospastic Angina in a Patient Presenting with Recurrent STEMI

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Introduction Coronary artery vasospasm, or smooth muscle constriction of the coronary artery, is an important cause of chest pain syndromes that can lead to myocardial infarction, ventricular arrhythmias, and sudden death. If minimal or no angiographic evidence of coronary artery disease is found in a patient who has recently had angina at rest with transient ST-segment elevation, vasospastic angina is the more likely diagnosis. Once the diagnosis of coronary artery vasospasm is made, calcium channel blockers and long-acting nitrates may be used for long-term prophylaxis and treatment.

Case Report We report on a 50 year old male patient presenting to the emergency department with acute coronary syndrome a total of 6 times within a 4 month period. At first presentation ECG showed a prior undiagnosed left bundle branch block. Laboratory testing showed slightly elevated cardiac enzymes. Coronary angiography revealed small vessel disease without significant stenosis. Angiographic imaging of the right coronary artery showed vasospasm of the proximal RCA. The patient was treated with aspirin, clopidogrel, statins and amlodipin. One week later the patient was readmitted to our department with acute resting chest pain and significant ST-elevation in the posterior leads. Angiographic imaging showed no significant stenosis or coronary spasm. CKMB was measured 10 times above normal. With the assumption of the patient having vasospastic angina he was started on diltiazem 90 mg twice daily. One week after discharge the patient was again (3rd time) admitted with acute STEMI, this time with ST-elevation in the anterior leads. Angiographic imaging showed vasospasm in the proximal LAD and serial spasms of the RCA. After application of intracoronary nitrate the spasms dissolved with ST-segment resolution. Diltiazem was increased to 180 mg twice daily. Six weeks later the patient was readmitted with acute coronary syndrome without ST-segment changes and slightly elevated cardiac enzymes. Because of

the known vasospastic angina the patient was treated with intravenous nitrates with resolution of symptoms. Diltiazem was increased to 90 mg, 5-times daily and nitrates p.o. were added (Isosorbit-5-mononitrat, 40 mg, twice daily). One month later the patient presented with STEMI (posterior leads). After intravenous nitrates were given, he was treated with diltiazem (180 mg, 3-times daily) and nitrates (40 mg, twice daily). The last episode of resting angina was documented one month later. Since then (a 12 month period) the patient is symptom-free with maximum medical therapy consisting of calcium channel blockers and long-acting nitrates.

Discussion In patients presenting with acute coronary syndrome and haemodynamic stability initial medical treatment should include sublingual, topical, or intravenous nitrate therapy. Until atherosclerotic coronary disease (a much more frequent cause of chest pain) is excluded, standard therapies, including antiplatelet/antithrombotic, statins, and beta-blocking treatments, should be administered. Once the diagnosis of coronary artery vasospasm is made, calcium channel blockers and long-acting nitrates may be used for long-term prophylaxis. Maximum dose vasospastic medical therapy, as shown in our case, may be necessary until the patient achieves long term pain free intervals.

Typ II Variant of Kounis Syndrome Due to Ibuprofen Use | – 6

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Introduction Kounis Syndrome is the coincidental occurrence of acute coronary syndromes with allergic or hypersensitivity reactions. Two types of Kounis syndrome have been described.

We report a case of 2 stepped life threatening Typ II Kounis syndrome leading to acute myocardial infarction following a first time intake of Ibuprofen and recurrence under acetylsalicylic acid (ASS) therapy.

Case Report A 53 year-old male presented because of acute shortness of breath and severe chest pain. ECG reveals ST-elevation in diaphragmal leads. Angiography showed diffuse arteriosclerotic plaques and severe spasms in both coronary arteries. After intracoronary Nitroglycerin administration spasms resolved and symptoms improved. He received antiplatelet (GPIIb/IIIa Blocker, clopidogrel, ASS) and betablocker therapy. Laboratory findings showed elevated levels of CK (479 U/l) and CK-MB (67 U/l). Allergic asthma bronchiale was known for 3 yrs and the patient was on inhalative steroid therapy. Furthermore he suffered from chronic sinusitis and nasal polyps.

Chest pain and dyspnoe occurred 1,5 hours after intake of Ibuprofen (400 mg) because of headache. In the meanwhile, while recovering from STEMI, 2 episodes of severe chest pain, hypotension and ST-elevation in the inferior leads occurred. The patient was treated with Morphine, Hydrocortisone 250 mg and Diltiazem. Symptoms and ECG changes resolved within 30 minutes.

Serum tryptase level and Urinary-Serotonin and 5-HIES were in normal range. No hint of inflammatory vasculitis, IgE was raised to a level of 201 U/ml. We stopped ASS and Diltiazem and Clopidogrel was chosen for maintenance therapy. After 7 days the patient was discharged free of symptoms.

Discussion In this patient we postulate a Typ II Kounis syndrome and aspirin sensitive asthma.

NSAIDs, like Ibuprofen, inhibiting Cyclooxygenase 1 are able to cross react with ASS, and inhibit vasodilatory prostaglandins and cause a predisposition to coronary spasms. ASS can precipitate asthmatic attacks, and provoke coronary artery spasm. Most cells located in the shoulder region of coronary arteriosclerotic plaques, play an important role in the pathophysiology of acute coronary syndrome and myocardial infarction due to allergic plaque rupture like in Kounis II syndromes.

The recurrence of ST-elevation on low dose ASS is probably an effect of the slow process of mast cell degranulation based on the massive reaction due to the Ibuprofen related allergic event.

Conclusion Numerous animal venoms, substances/drugs including drug eluting stents are capable to induce an allergic myocardial infarction. Currently treatment for mast cell stabilisation is used to avoid mast cell degranulation. In this case ASS seems to play an important role to adhere the allergic reaction, on the other hand prescription of ASS is a Class I Indication for patients suffering myocardial infarction. Trials have shown ASS desensitization to be feasible. Nevertheless with regard to the massive coronary spasm in this case a provocation test with ASS was not performed for ethical reasons. We decided to maintain a clopidogrel alone regimen. An important, maybe life saving issue, is to instruct the patient to avoid Ibuprofen in the future.

High-Sensitive Cardiac Troponin T (hs-cTnT) Assay is not Superior to a Previous cTnT Assay Generation for the Diagnosis of Acute Myocardial Infarctions in a Real-World Emergency Department | – 7

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Introduction High-sensitive troponin T (hs-cTnT) has been recently demonstrated to have an increased sensitivity for the early diagnosis of acute myocardial infarctions (AMI) in preselected patient populations. We compared the diagnostic performances of hs-cTnT with the 4th generation cTnT assay during a period of 2 months in a real world emergency department (ED) treating mainly adults with medical or neurological emergencies to evaluate potential benefits for routine diagnosis.

Methods cTnT was measured on request of the attending physicians in 2438 patients (60 ± 21 years, 52% females). It was only ordered in patients treated by internists or neurologists and measured by assays from Roche Diagnostics.

Results There were 451 patients with the chief complaint of chest pain and 292 with dyspnea. These patients included 69 AMIs (delay from onset to admission 1–25 hours, median 2.5 hours). 540 patients had neurological diseases, such as stroke. The remaining patients suffered from various internal diseases. 785 patients of the whole study population had acute or chronic cardiac diseases. Using the 99th percentile cut-off the sensitivities and specificities for AMI diagnosis on admission in the whole study population were 88 and 74% (hs-TnT) and 84 and 80% (4th generation cTnT, cut-off 0.01 µg/L), and using the 10% coefficient of variation cut-off (0.03 µg/L) for the 4th assay generation 70% and 93%, respectively. The overall diagnostic performances for AMI diagnosis of both assay generations were comparable (area under receiver operating characteristics curves [AUC] 0.89 ± 0.03 vs 0.87 ± 0.03; p = 0.30). However, hs-cTnT detected significantly more patients with acute or chronic cardiac diseases (AUC: 0.78 ± 0.01 vs 0.68 ± 0.01; p < 0.001).

Conclusions In unselected ED patients hs-cTnT assay is not superior to the previous cTnT assay for AMI diagnosis. If for both assays the 99th percentile cut-off limit is used also the early sensitivities on admission are comparable, but the 4th cTnT assay generation loses AMI specificity at 0.01 µg/L as well. However, with the endpoint detection of any acute or chronic cardiac diseases hs-cTnT is significantly superior to the previous cTnT assay due to its better assay precision at the low measuring range, which cannot be outweighed by lowering the cut-off value of the 4th cTnT assay generation to 0.01 µg/L.

Low Prevalence of the Acetylsalicylic Acid and Clopidogrel Resistance in Patients with Acute Coronary Syndromes in Patients under Pantoprazole Treatment | – 8

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Background Acetylsalicylic acid (ASA) and clopidogrel combined with prophylactic proton pump inhibitor (PPI) treatment has been standard therapy of patients with acute coronary syndromes (ACS) until the recent warning of the US Food and Drug Administration because of possible interactions of PPIs with clopidogrel metabolism. We therefore investigated the prevalence of ASA and clopidogrel low- or no responders in ACS patients with stent implantation on day 2 of coronary care unit (CCU) stay with pantoprazole treatment (40 mg per day).

Methods We investigated 135 patients (95 males, 40 females) aged between 35 and 88 (62 ± 11) years with ST segment elevation myocardial infarction (STEMI) ($n = 110$) and non-STEMI ACS ($n = 25$). In 89 patients drug-eluting and in the remaining patients bare metal stents were implanted. All patients were loaded with 250–500 mg ASA on the first day of hospital stay and received 100 mg ASA as maintenance dose per day. Patients received 600 mg clopidogrel as a loading dose on the first day of hospital stay and 75 mg clopidogrel as maintenance dose per day. Platelet function in the morning of day 2 of CCU stay was assessed by multiple electrode platelet aggregometry (Multiplate®, Dynabyte, Munich, Germany) in hirudin anticoagulated whole blood. Based on the published literature ASA non-responders were classified as patients with > 75 U and low-responders with values between 31 and 74 U in the ASPItest®. Patients with > 47 U in the ADPtest® were classified as clopidogrel low- or non-responders.

Results The platelet reactivity in the ASPItest® ranged from 0–79 U (mean 8 ± 10 U) with 4 low-responders (35 U, 35 U, 65 U, 68 U) and 1 non-responder (79 U). The platelet reactivity in the ADP test ranged from 0–87 U (mean 16 ± 19 U) with 9 low-responders (48 U, 49 U, 50 U, 50 U, 51 U, 58 U, 69 U, 72 U, 87 U).

Conclusions Given the low prevalence of clopidogrel (6.7%) and ASA low- or no-responders (3.7%) in our real-world ACS patients with 600 mg clopidogrel loading dose and concomitant pantoprazole treatment routine platelet function testing does not seem to be necessary in this patient group.

Aufnahmeblutdruck und Mortalität bei Patienten mit akutem Myokardinfarkt XI – 1

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Einleitung Die ischämische Herzkrankheit gilt als weltweit führende Todesursache, der arterielle Hypertonus als einer der bekanntesten Risikofaktoren kardiovaskulärer Erkrankungen. Einer rezenten Studie zufolge könnte in der Akutsituation des Myokardinfarktes allerdings ein indirekt proportionaler Zusammenhang zwischen Mortalität und systolischem Blutdruck bestehen, mit dem niedrigsten Risiko bei Werten > 163 mmHg. Diese Studie beinhaltete allerdings nur Patienten, die in weiterer Folge an Intensivstationen behandelt wurden. Aus diesem Grund soll der Effekt von systolischem Blutdruck bei Aufnahme bzw. diastolischem Blutdruck und Pulsamplitude auf die 1-Jahres-Mortalität an einem breiten Kollektiv von Infarktpatienten untersucht werden.

Material und Methode Retrospektive Analyse des MCI-Registers der UK für Notfallmedizin (1991–2009). Patienten nach kardiopulmonaler Reanimation oder Sekundärtransport wurden ausgeschlossen. Logistisches Regressionsmodell für 1-Jahres-Mortalität als Outcome, Blutdruck stratifiziert in Quartilen als Hauptprädiktor, Adjustierung für demographische Faktoren, Risikofaktoren und Therapie.

Ergebnisse Bei 2917 Patienten mit akutem Herzinfarkt war die adjustierte Odds Ratio für systolischen Blutdruck auf die 1-Jahres-

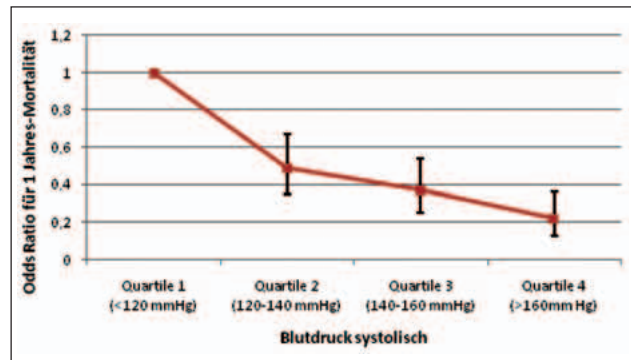


Abbildung 1: D. Roth et al.

Mortalität im Vergleich zur niedrigsten Quartile (< 120 mmHg) für die 2. Quartile (120–140 mmHg) 0,49 (95 %-CI: 0,35–0,67), für die 3. Quartile (140–160 mmHg) 0,37 (0,25–0,54) und für die 4. Quartile (> 160 mmHg) 0,22 (0,13–0,38); für diastolischen Blutdruck im Vergleich zur 1. Quartile (< 60 mmHg) für die 2. Quartile (60–80 mmHg) 0,46 (0,31–0,68), für die 3. Quartile (80–85 mmHg) 0,35 (0,22–0,54) und für die 4. Quartile (> 85 mmHg) 0,29 (0,18–0,46); für die Pulsamplitude im Vergleich zur 1. Quartile (< 50 mmHg) für die 2. Quartile (50–60 mmHg) 0,62 (0,41–0,93), für die 3. Quartile (60–75 mmHg) 0,38 (0,27–0,54) und für die 4. Quartile (> 75 mmHg) 0,23 (0,15–0,34).

Diskussion Es konnte ein indirekt proportionaler Zusammenhang zwischen Aufnahmeblutdruck und 1-Jahres-Mortalität gezeigt werden. Die Wahrscheinlichkeit, innerhalb eines Jahr zu versterben, ist demnach für Patienten mit einem systolischen Blutdruck > 160 mmHg am geringsten. Übernormal hoher Blutdruck ist in dieser Akutsituation demnach möglicherweise als Zeichen eines intakten physiologischen Reaktionsmechanismus zu sehen (Abbildung 1).

Akute Koronarsyndrome bei Migranten: Risikoprofil und angiographische Befunde XI – 4

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Einleitung Da bei den Akut-Koronarangiographien eine Häufung von jungen Patienten mit Migrationshintergrund aufgefallen ist, wurden retrospektiv demographische und klinische Daten unserer Patienten ausgewertet.

Methode Eingeschlossen wurden alle Patienten, die im Jahr 2010 an unserer Abteilung akut koronarangiographiert wurden. Aus den Entlassungsbrieffen wurden Alter, Geschlecht, Befund der Koronarangiographie, Hypertonie, Diabetes mellitus, Hypercholesterinämie, Nikotinabusus und ethnische Herkunft erhoben, und Vergleiche zwischen Patienten mit österreichischer und nicht-österreichischer Herkunft vorgenommen. Aus dem Bevölkerungsregister wurden Informationen über die Wiener Bevölkerung entnommen.

Ergebnis Es wurden 157 Patienten (25 % weiblich) mit einem mittleren Alter von 60 ± 14 (35–93) Jahren akut angiographiert. Die Koronarangiographie zeigte eine Eingefäßerkrankung bei 36 %, eine Zweigefäßerkrankung bei 25 %, eine Drei- oder Mehrgefäßerkrankung bei 35 % und keine Koronarstenosen bei 5 %. Eine Hypertonie fand sich bei 68 %, Hypercholesterinämie bei 66 %, Nikotinabusus bei 57 % und Diabetes mellitus bei 24 %. 51 Patienten (33 %) waren Migranten: 22 kamen aus dem ehemaligen Jugoslawien, 12 aus der Türkei, 7 aus dem arabischen Raum, 5 aus Nordosteuropa, 4 aus Zentraleuropa und einer aus Guinea-Bissau. Migranten waren jünger als Patienten mit österreichischer Herkunft (53 vs. 64 Jahre; $p = 0,0000$). Keine signifikanten Unterschiede zwischen Migranten und Österreichern gab es in der Häufigkeit von Nikotinabusus (62 vs. 54 %), Hypercholesterinämie (63 vs. 67 %), Hypertonie (67 vs. 69 %), Diabetes mellitus (24 vs. 25 %) und in der Geschlechtsverteilung (Migrantinnen 24 % vs. Österreicherinnen 26 %). Sowohl eine koronare Eingefäßerkrankung als auch eine Zweigefäßerkrankung fand

sich bei Österreichern etwas häufiger als bei Migranten (37 vs. 33 %) bzw. (28 vs. 18 %). Eine Drei- oder Mehrgefäßerkrankung hatten mehr Migranten als Österreicher (43 vs. 30 %), allerdings waren die Unterschiede erst oberhalb eines Alters von 60 Jahren signifikant (73 vs. 37 %; $p = 0,0189$).

Laut Bevölkerungsregister lebten 2008 in Wien 1.674.909 Menschen, 323.415 davon Migranten. Unter den akut angiographierten Patienten war der Anteil von Migranten höher als in der Gesamtbevölkerung (33 vs. 19 %; $p < 0,0001$). Überrepräsentiert unter den akut angiographierten Patienten waren Migranten aus dem ehemaligen Jugoslawien (14 vs. 7 %; $p = 0,0032$), aus der Türkei (8 vs. 3 %; $p = 0,0007$) und aus dem arabischen Raum (5 vs. 1 %; $p = 0,0004$).

Konklusion Migranten, die akut koronarangiographiert werden, sind jünger als Patienten, die aus Österreich stammen, unterschieden sich aber kaum in Hinblick auf die klassischen Risikofaktoren. Dieses Phänomen weist auf ein höheres kardiovaskuläres, möglicherweise auch genetisches, Risiko von Migranten hin, das einer weiteren prospektiven Untersuchung bedarf.

Die Versorgung des NSTEMI-ACS in der Steiermark – Eine Subgruppenanalyse des steirischen ACS-Registers

XI – 2

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Einleitung Seit 2006 werden sämtliche in der Steiermark behandelten ACS-Patienten im steirischen ACS-Register erfasst. Im Rahmen der Datenerhebung werden sowohl Informationen bezüglich der zeitlichen Versorgungsqualität als auch Details bezüglich der demographischen Verteilung registriert. Eine Subgruppenanalyse der einzelnen Entitäten (STE-ACS, NSTEMI-ACS) wird ebenfalls durchgeführt. Hierbei handelt es sich um die Subgruppenanalyse des NSTEMI-ACS Patientenkollektivs aus den Jahren 2006–2009.

Material und Methode Die Datenerfassung erfolgt standardisiert in den 3 steirischen Herzkatheterzentren. Der Datensatz wird im Sinne eines zentral geführten und verwalteten ACS-Registers in Graz bearbeitet und aktualisiert. Die statistische Auswertung erfolgt über das Institut für Medizinische Informatik, Statistik und Dokumentation der Medizinischen Universität Graz. Es handelt sich hierbei um eine retrospektive Analyse der erhobenen Daten.

Ergebnisse Der gesamte Datensatz aus den Jahren 2006–2009 besteht aus einem Patientenkollektiv, welches insgesamt 6812 ACS-Patienten enthält. Die Entitätenverteilung aller ACS-Patienten über den Beobachtungszeitraum 2006–2008 zeigt 32 % STE-ACS-Patienten sowie 68 % NSTEMI-ACS-Patienten. Diese Verteilung lässt sich in ähnlichem Ausmaß in allen steirischen Bezirken nachweisen. Das durchschnittliche Patientenalter des NSTEMI-ACS Patienten beträgt 70,5 Jahre, geschlechtsspezifisch erkrankten Frauen durchschnittlich mit 74 und Männer mit 68 Jahren an einem NSTEMI-ACS. Das Auftreten der STE-ACS- sowie NSTEMI-ACS-Fälle über die Jahre ergibt keinen signifikanten Unterschied (χ^2 -Test: $p = 0,102$).

Die Entität NSTEMI-ACS kann in die beiden klassischen Subgruppen NSTEMI sowie IAP aufgesplittet werden. Es zeigen sich somit in der Steiermark über den Beobachtungszeitraum 49,9 % NSTEMI-Patienten sowie 18,1 % IAP-Patienten in Bezug auf das Gesamtkollektiv. Das Männer-Frauen-Verhältnis in der NSTEMI-ACS-Subgruppe beträgt ca. 60 % zu 40 %.

Diskussion Die Erfassung und konsequente Auswertung sämtlicher steirischer ACS-Patienten bildet die Grundlage jeglicher Evidenz in der steirischen Akutversorgung des ACS. Die gewonnenen Ergebnisse werden im Sinne eines Qualitätsmanagements mit anderen nationalen sowie internationalen ACS-Registern verglichen.

Die Subgruppenanalyse des NSTEMI-ACS zeigt hinsichtlich der demographischen Verteilung (Geschlechterverteilung, Entitätenverteilung innerhalb des NSTEMI-ACS etc.) Parallelen zu Datensätzen anderer Register. Seit Einführung des steirischen ACS-Registers im Jahr 2006 besteht die Möglichkeit, das Patientenkollektiv hinsicht-

lich Unterschiede in der Akutversorgung, geographischer Besonderheiten etc. zu bewerten.

Prognostic Value of Presentation with STE-ACS vs NSTEMI-ACS in Patients with Acute Occlusion of the Left Circumflex Artery

XI – 3

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Purpose Acute coronary syndromes (ACS) due to acute occlusion of the left circumflex artery (LCX) may present as ST-elevation myocardial infarction (STEMI) or non ST-elevation myocardial infarction (NSTEMI) in the 12-lead ECG depending on the dominance of the LCX. Aim of this study was to evaluate the prognostic value of ST-segment changes in electrocardiogram in patients with ACS and occluded LCX.

Methods In total, 1,490 consecutive patients, who underwent elective or acute PCI, were included in a prospective registry from January 2003 until December 2006. Forty nine patients had an angiographically proven acute occlusion of the LCX. Patients were divided retrospectively into 2 groups, those with STEMI and those with NSTEMI at presentation. Time from presentation to 1st diagnostic angiogram, all-cause mortality and the combined endpoint all-cause death and target vessel revascularisation were evaluated during a mean follow-up period of 24.56 ± 12.5 months (range 6–52 months).

Results Twenty four of the 49 patients with an occluded LCX at the first diagnostic angiogram (49%) patients a NSTEMI and 25 (51%) patients presented with STEMI. Clinical and angiographic characteristics such as age, gender, arterial hypertension, diabetes mellitus, hyperlipidaemia, previous myocardial infarction, renal dysfunction, heart failure, drug eluting stent implantation, stent length and stent diameter, respectively, were not significantly different between the 2 groups. Time from presentation to angiogram was 842.6 ± 985.5 minutes for NSTEMI and 104.4 ± 59.5 minutes for STEMI patients ($p = 0,001$). Four (16.7%) patients of the NSTEMI and 3 (12%) patients of the STEMI group died during the follow-up (HR 1.2; 95%-CI: 0.2–5.7; $p = 0,7$). Seven (29.2%) patients of the NSTEMI group and 3 (12%) patients of the STEMI group reached the combined endpoint of all-cause death and target vessel revascularisation (HR 2.4; 95%-CI: 0.6–9.3; $p = 0,2$).

Conclusion In this small series in 1,490 consecutive unselected “real world” patients who underwent PCI and stent implantation 49 (3.3%) had an occluded LCX, of which about half presented with STEMI or NSTEMI, respectively. For both groups clinical long-term outcome was statistically comparable but showed a trend to higher all-cause mortality in patients presenting with NSTEMI, in which diagnostic and therapeutic angiograms were performed delayed. Patients with ACS and occluded LCX without ST-segment elevation might have a benefit of early revascularisation and should therefore be diagnosed earlier e.g. by use of 17-lead ECGs as reported elsewhere and/or by immediate diagnostic angiography when symptoms and risk constellation suspect occlusion of an epicardial coronary artery.

iFMC-to-ECG-Time from Intrahospital First Medical Contact to ECG – How to Improve Delays in an Emergency Department – A Randomised Clustered Interventional Trial

XI – 6

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Background The European Society of Cardiology-Guidelines for Acute Coronary Syndrome (ACS) emphasize that the assessment (including the electrocardiogram [ECG]) of patients with suspected

ACS should be obtained within 10 minutes after first medical contact (FMC) upon arrival in the Emergency Department (ED). Former studies reported that this challenging goal usually requires high efforts.

Aim of the Study The aim of this study was to investigate the effect of a dedicated ECG technician (ET) on intrahospital First Medical Contact to ECG time (iFMC-to-ECG).

Materials and Methods All patients with the chief complaint of “chest pain” presenting to the out-patient-clinic (OPC) at the ED of the Medical University Vienna were included. The study was conducted from August, 23rd to September, 20th, 2010. The intervention was the availability of a dedicated ET. In the control group no ET was available. The availability of the ET was randomized to three equally distributed shifts per day (morning, day, night). The ET rotas were concealed for clinical staff. Information about availability of ETs was marked with an alert sign at triage point and registration counter. Primary outcome was previously defined as iFMC-to-ECG in ET rotas vs non dedicated resident nurses. iFMC-to-ECG delays are presented as median and interquartile ranges 25–75%. To compare delay times we used a Mann-Whitney-U-test.

Results During the study period, in total 908 patients received an ECG recording for different reasons. 353 (38.8%) out of these patients had chest pain as chief complaint. 635 (69%) of all patients met inclusion criteria's for analysis. 179 (28.2%) of these patients arrived during intervention. In the interventional group 129 patients (72.1%) received their ECG within 10 minutes versus 59 patients (12.94%) in the control group ($p = 0.001$). The median iFMC-to-ECG time during intervention was 8 (IQR 6–10) minutes versus 32 (IQR 16–52) minutes in the control group minutes ($p = 0.0001$). This represents a Risk Ratio of 5.6 (95%-CI: 4.2–7.4) in the interventional group.

Conclusion Implementing an ECG technician in the ED is feasible to reach a higher percentage of patients within the recommended 10 minutes benchmark of guideline requirements compared to business as usual.

„Schach dem Herztod!“ Auswirkungen einer Massenmedienkampagne auf das Patientendelay: Eine Single-Center-Kohorten-Beobachtungsstudie

XI – 5

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Hintergrund Öffentliche Aufklärung ist ein wichtiges Instrument zur frühzeitigen Beeinflussung wichtiger Zeitabläufe in der Herzinfarktversorgung. Ein wichtiges Zeitfenster stellt in dieser Hinsicht das Patientendelay dar, welches die Zeit zwischen Beginn des Brustschmerzes und Alarmierung des Rettungsdienstes zeigt. Durch Massenmedienkampagnen kann das Patientendelay positiv beeinflusst werden. In Österreich versuchte die Kampagne „Schach dem Herztod!“, zwischen 24. Juli 2006 und 19. August 2006 mittels TV- und Radiowerbespots sowie 2000 Plakaten die Öffentlichkeit dafür zu sensibilisieren.

Ziel Primäres Outcome dieser retrospektiven Kohortenbeobachtungsstudie ist es, den Effekt der Kampagne „Schach dem Herztod!“ in einer retrospektiven Analyse des lokalen ACS-Registers im Vorher-/Nachher-Design anhand der Verbesserung des Patientendelays zu analysieren.

Material und Methodik Im lokalen ACS-Register der Universitätsklinik für Notfallmedizin Wien werden alle Patienten mit Myokardinfarkt, die an unserer Abteilung hospitalisiert werden, registriert. Anhand dieser wurde das Patientendelay des Jahres 2006 analysiert. Inkludiert wurden alle Patienten, die in diesem Zeitraum ambulant oder durch den Rettungsdienst zugewiesen und mit Myokardinfarkt an unserer Abteilung vorstellig wurden. Exkludiert wurden Sekundärzuweisungen, Patienten, bei denen das Patientendelay nicht rekonstruiert werden konnte, sowie Patienten die während der Interventionsphase zwischen 24. Juli 2006 und 19. August 2006 hospitalisiert wurden.

Tabelle 4: R. van Tulder et al.

	Vorher	Nachher
n	105	84
Alter	60 ± 13	57 ± 13
Weiblich	26 (24,8 %)	18 (21,4 %)
Diabetiker	18 (17,1 %)	15 (17,8 %)
Hypertonie	51 (54,6 %)	45 (53,6 %)
Raucher	41 (39,0 %)	36 (42,8 %)
Hyperlipidämie	28 (26,6 %)	28 (33,3 %)
Familienanamnese	23 (21,9 %)	12 (14,3 %)
Frühere PCI	8 (7,6 %)	7 (8,3 %)
VWI	42 (40,0 %)	28 (33,3 %)
HWI	28 (26,6 %)	21 (25,0 %)
NAH	11 (10,5 %)	7 (8,3 %)
NAW	61 (58,1 %)	52 (61,9 %)
RTW	10 (9,5 %)	3 (3,6 %)
Ambulant	17 (16,2 %)	21 (25,0 %)
STEMI	70 (66,6 %)	51 (60,7 %)

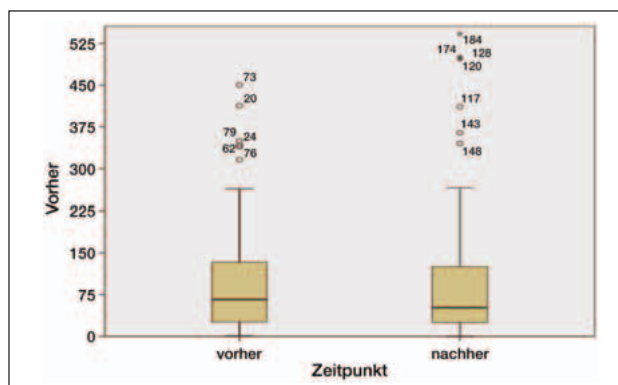


Abbildung 2: R. van Tulder et al.

Ergebnisse Der Beobachtungszeitraum beinhaltet Patienten des Registers im Jahr 2006. 209 Patienten konnten für die Analyse identifiziert werden. Anhand der Einschlusskriterien konnten 105 (50,2 %) Patienten in der Präinterventionsphase und 84 (40,2 %) Patienten in der Postinterventionsphase analysiert werden. 20 (9,6 %) Patienten der Interventionsphase wurden exkludiert. Die demographische Daten zeigt **Tabelle 4**. Für folgende Daten wurden der Median und die Interquartilen-Ränge (IQR) 25–75 % berechnet. Wir analysierten das Patientendelay mit einem Mann-Whitney-U-Test (**Abbildung 2**).

In der Präinterventionsphase betrug das Patientendelay im Median 66 (IQR 26–133) Minuten vs. 52 (IQR 25–122,5) ($p = 0,983$) in der Postinterventionsphase.

Konklusion Für die Massenmedienkampagne „Schach dem Herztod!“ konnte keine signifikante Verbesserung des Patientendelays in unserem Register festgestellt werden.

Impact of Elevated Glucose Levels in Patient Hospitalized with Non-ST-segment Elevation Acute Coronary Syndrome (NSTEMI-ACS) on Long-Term Mortality

XI – 7

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Background and Aim Due to the fact that there is only few data on long-term mortality in patients with hyperglycemia hospitalized with acute coronary syndrome, this study aimed to show the impact of elevated admission glucose on 4-year mortality in patients with NSTEMI-ACS.

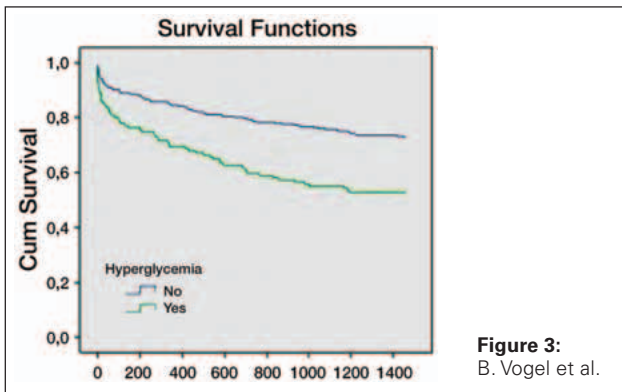


Figure 3:
B. Vogel et al.

Table 5: B. Vogel et al.

	Sig.	HR	95%-CI
Age	< 0.001	1.071	1.047–1.095
Female gender	0.122	1.312	0.930–1.851
Pos Trop I	0.006	1.609	1.147–2.255
ST-deviation	0.212	1.232	0.888–1.710
Crcl < 60	0.044	1.697	1.014–2.842
Admission glucose	0.039	1.004	1.000–1.008
Hyperlipidemia	0.207	1.263	0.879–1.814
Adipositas	0.866	1.029	0.736–1.440
Smoking	0.110	1.615	0.897–2.907
Invasive treatment	0.002	0.460	0.284–0.743

Methods This data is derived from a registry with 813 consecutive patients admitted to the cardiology department with the diagnosis of non NSTEMI-ACS between Jan 2001 and Dec 2004. Hyperglycemia is defined as a glucose level of > 140 mg/dL on hospital arrival. In 110 patients the glucose level at admission was missing, another 211 patients had evident diabetes and were excluded from the analyses. A follow-up concerning all-cause mortality up to four years was obtained.

Results Patient with hyperglycemia were older (75.5 years SD $\pm$ 12.2 vs 68.2 years SD $\pm$ 14.8; $p < 0.001$) and less frequently received coronary revascularization during first hospital stay (22.8% vs 36.9%; $p = 0.007$) than patients with normal admission glucose levels. In-hospital mortality, as well as four-year mortality was higher in patients with hyperglycemia (10.7% vs 5.3%; $p = 0.034$; HR 2.15 95%-CI: 1.0–4.4 and 46.3% vs 27.3%, $p < 0.001$; HR 2.51 1.66–3.81, respectively) than in those without elevated admission glucose levels (Figure 3). In a Cox proportional hazard model the admission glucose level was an independent predictor for 4-year mortality (Table 5).

Conclusion An elevated glucose level in patients hospitalized with acute coronary syndrome without ST-segment elevation is associated with worse long-term outcome.

Prozessorientierte Umsetzung von Leitlinien für den ST-Hebungsmyokardinfarkt im Krankenhaus Schwarzach

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Innere Medizin, Kardiologie, Krankenhaus Schwarzach

Einleitung In der Europäischen Union sind Herz-Kreislauf-Erkrankungen die bedeutendste Todesursache und verantwortlich für 43 % der Gesamtsterblichkeit (Bundesanstalt Statistik Österreich, 2009). Ein wesentlicher Anteil dieser kardiovaskulären Sterblichkeit fällt auf den akuten ST-Hebungsmyokardinfarkt (STEMI). Von internationalen kardiologischen Fachgesellschaften (ESC, ACC/AHA) wurden Leitlinien zur Behandlung des STEMI verfasst, in

denen die diagnostischen und therapeutischen Möglichkeiten evaluiert werden. Durch entsprechende standardisierte Empfehlungen soll die Behandlung effizienter gestaltet und konsekutiv die Mortalität gesenkt werden [Antman et al. 2004, Hamm et al. 2004, van de Werf et al. 2003]. Besondere Bedeutung für die Prognose gewinnt der Zeitfaktor [Steg, 2003] von der Diagnosestellung zur Therapie.

Material und Methode Die Darstellung der jeweiligen Leitlinie als erweiterte ereignisgesteuerte Prozesskette (eEPK) ist der beste Weg zu einer prozessorientierten Sichtweise mit potenziell vielfältigen Möglichkeiten [Vollert, 2008], die Leitlinien in nachfolgenden Schritten in IT-Anwendungen einzubinden. Übersichtsmodelle in Form von Wertschöpfungskettendiagrammen können dabei einen wertvollen Anhalt liefern, welche Kernprozesse nachfolgend in einer eEPK modelliert werden sollten.

Die Leitlinie zum Vorgehen bei STEMI wurde in einer eEPK umgesetzt. Ein wesentliches primäres Ziel stellte dabei die Idee dar, übergeordnete als auch einzelne Arbeitsabläufe (z. B. Ablauf im Herzkatheterlabor) in praxisnahen Flow-Charts abzubilden. Bei der Erstellung der eEPKs wird aus Gründen der Übersichtlichkeit, zusätzlich zur Definition der Elemente durch ihre Form, eine farbliche Gestaltung benützt. Dies folgt dem Ampelprinzip, wobei Ereignisse immer rot und Funktionen immer grün dargestellt werden.

Diskussion Die Arbeit stellt einen Vorschlag zur Diskussion, die Leitlinien der ESC mit schon bestehenden Verfahren zu einer prozessorientierten Sichtweise zu verknüpfen.

Durch die standardisierte Modellierung der Abläufe können Prozesse umfassend dargestellt und transparent gemacht werden. Dies ist für Zertifizierungsprogramme ein wertvolles Hilfsmittel. Darüber hinaus wird das Potenzial geschaffen, die einzelnen modellierten Sachverhalte in einer weiteren Ebene auch an andere IT-Systeme wie ein Krankenhausinformationssystem (KIS) anzubinden. Somit wären einzelne Prozessschritte auch hinsichtlich einer Qualitätskontrolle mess- und auswertbar (Abbildung 4).

Basic Science

Secretion of Cytokines and Chemokines by Peripheral Blood Mononuclear Cells is Triggered by Coagulation Products

III – 3

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Background Chemokines are multifunctional mediators that are involved in development and homeostatic, stem-cell survival, wound healing and immune responses, as well as triggering chemotaxis and angiogenesis. Their production and release is partly controlled by cytokines such as Interleukin 1 beta (IL-1 β), Interleukin 6 (IL-6) or Tumor necrosis factor alpha (TNF- α). Diagnostic analysis of cytokines and chemokines in serum or plasma has become an important issue in several disease conditions. Studies confirmed the involvement of these mediators systemic immune activation/sepsis, wound healing, autoimmune-diseases, arteriosclerosis and myocardial infarction. However, cytokines and chemokines are usually not considered to be very stable after blood collection, which might therefore alter test results. Thus, the aim of the pilot study was to obtain better knowledge about stability of these mediators in blood samples for interpretation of test results.

Materials and Methods Venous blood was taken from healthy probands ($n = 7$) using different blood tubes (serum, heparin plasma and EDTA plasma). Blood tubes were either centrifuged initially within 20 minutes after venipuncture and kept frozen at -80° until further testing or were stored at 4°C , at room temperature (RT) or at 37° for up to 24 hours. Samples were evaluated for IL-1 β , IL-6, TNF- α and for selected chemokines such as Interleukin-8, Epithelial neutrophil-activating protein 78 (ENA-78) and Granulocyte chemoattractant peptide-2 (GCP-2) using commercially available Enzyme-linked immunosorbent assay (ELISA) kits.

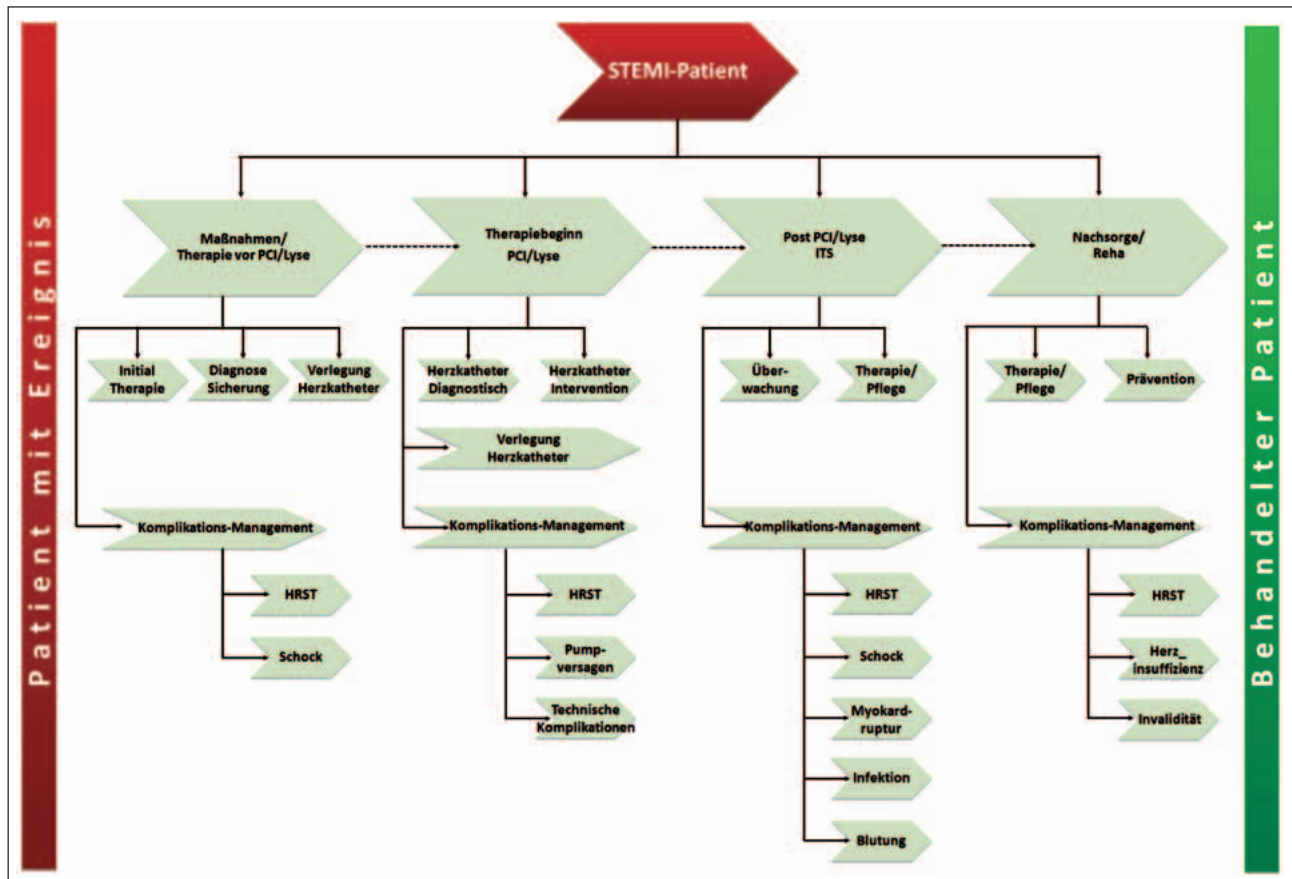


Abbildung 4: H. Wallner et al.

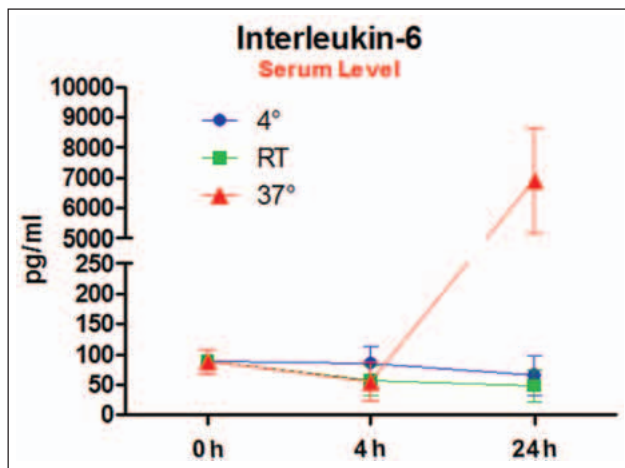


Figure 5: L. Beer et al.

Results Interestingly all examined mediators rise when samples were stored above room temperature for more than 4 hours in serum tubes. The rise of serum cytokine and chemokine levels culminated in a 79-fold increase for IL-6 ($p < 0.0081$) (Figure 5), a 22-fold increase for ENA-78 ($p < 0.0006$) and a 17-fold increase for GCP-2 ($p < 0.0026$) compared to basic values. Serum levels of IL-1 β and TNF- α where not detectable at base line but rise up to 1157 pg/ml (IL-1 β ; $p < 0,03$) and 488 pg/ml (TNF- α ; $p < 0,03$).

Conclusions These data indicate that most cytokine and chemokine levels remain stable when analyzed within a short interval after venipuncture. When tubes were exposed to temperatures higher than 24° (RT), levels of measured factors increased dramatically. EDTA plasma seems to be the most suitable for stability reasons and should be used for analysis of these mediators. We hypothesize that initia-

tion of the blood clotting cascade in serum tubes, strongly mediated by the elevated levels of fibrin, concurrent with higher temperatures induce a pro-inflammatory microenvironment which triggers release of cytokines and chemokines from cellular compartments.

Regulation of Specific Glycolytic Pathways by Beta-Blockers in Normoxia and Hypoxia II – 2

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Introduction Pyruvate dehydrogenase kinase inhibits pyruvate dehydrogenase, which constitutes an important step in glucose metabolism. Cardiac metabolism of glucose is very tightly regulated to maintain the variable energy demand that is required by cardiac tissue. Energy metabolism of the cardiac myocyte can be regulated within seconds up to a few minutes or chronically regulated within the time frame of hours to days. Glucose metabolism is activated in early myocardial ischemia – a sensitive response to increased need of high-energy-phosphate in the healthy heart during extreme physical activity. However, in coronary heart disease, this activation becomes deleterious. In myocardial ischemia, inhibition or decreased gene expression of pyruvate dehydrogenase kinase is necessary in order to shift myocardial metabolism towards the fetal phenotype, thus metabolising more glucose than fat in order to preserve myocardial integrity.

Methods Myocardial tissue probes derive from the right auricle of patients undergoing cardiac surgery. A small part of the right auricle is removed when the heart is put on extra-corporeal circulation. This sample is then placed in cooled Tyrode solution and hypoxia is brought about by switching 100% oxygen to 100% nitrogen (hypoxia) in one of the two chambers. By doing so, we are able to compare ischemic and non-ischemic tissue of the same patient. Snap frozen samples are stored at -70°C until RNA isolation. Quality of isolated RNA is analyzed by Agilent's Bioanalyzer 2100 system. Ar-

rays are scanned with the AB1700 Chemiluminescence Array Reader and images, data are processed by PANTHER software.

Results In our microarray experiments, we find that, in particular, pyruvate dehydrogenase kinase isoform 4 is significantly less expressed under nebivolol both during O₂ perfusion and simulated ischemia, an effect practically negligible under atenolol. Here, nebivolol also exhibits a unique cardio-protective property, different from standard beta-blockers. We find that, without the influence of beta-blockers, there is no significant regulation of pyruvate dehydrogenase kinase-expression during myocardial ischemia. There is just a trend towards a decrease in pyruvate dehydrogenase kinase-Gene expression. There is, however a significant difference between the expression of PDK during myocardial ischemia in the presence of atenolol (3.62 ± 0.18) and nebivolol (1.97 ± 0.06 ; $\pm$ SEM; $p < 0.05$): pyruvate dehydrogenase kinase-expression is decreased during normoxia (trend) and ischemia (significant) in the presence of nebivolol.

Conclusion Here, confirmed by real time PCR, the finding that pyruvate dehydrogenase kinase gene expression is down-regulated by nebivolol compared to atenolol in normoxia (trend, not statistically significant) and simulated ischemia/hypoxia (statistically significant) may argue for a higher protective, anti-ischemic but also anti-anginal potential of nebivolol compared to standard beta-blockers like atenolol. Especially patients with angina may profit from this particular property of nebivolol over atenolol.

Der Multikinaseinhibitor Sunitinib hat akute Auswirkungen auf die kardiale Kontraktilität II – 3

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Hintergrund Multikinase-Inhibitoren weisen teilweise ein beträchtliches kardiotoxisches Potenzial auf. In klinischen Phase-III-Studien sind unter Sunitinib in rund 10 % der Fälle kardiale Probleme beobachtet worden, vor allem bei lang andauernder Therapie.

Wir haben uns zum Ziel gesetzt, die akuten Effekte von Sunitinib auf die kardiale Kontraktilität an isoliertem humanen Myokard zu untersuchen. Mithilfe von micro-RNA-Expressions-Analysen wurde einem möglichen Effekt von Sunitinib auf das Expressionsmuster nachgegangen.

Methoden Humane endokardiale Trabekel ($n = 26$) aus dem rechten Vorhofohr ($n = 6$) wurden in modifizierter Tyrode im Organbad bei 37°C, pH 7,4 und 2mM Ca²⁺ mit 1 Hz stimuliert. Die entwickelte Kraft (in % der Kraft bei optimaler Vordehnung, $L_{max} = 100\%$), diastolische Spannung und Kontraktionskinetik nach Applikation von Sunitinib (0,1–10 μ M) oder Vehikel (DMSO 0,1 %) wurden nach 5, 10, 20 und 30 min ermittelt.

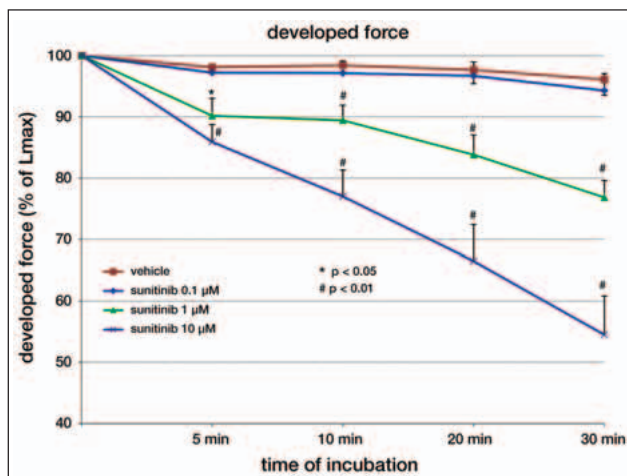


Abbildung 6: B. Doleschal et al.

Die HL-1-Zell-Linie (atriale Mauscardiomyozyten) wurde für 24h mit Sunitinib (0,1–1 μ M) inkubiert. Affymetrix-Microarrays wurden verwendet, um mehr als 600 microRNAs zu analysieren. RT-PCR wurden zur Bestätigung der Microarrays durchgeführt.

Ergebnisse Bei 0,1 μ M (entspricht dem normalen therapeutischen Level) hatte Sunitinib keinen akuten Effekt auf die entwickelte Kraft. Vorbehandlung mit 1 μ M bzw. 10 μ M Sunitinib (30 min) reduzierte die entwickelte Kraft auf $76,9 \pm 2,8\%$ bzw. $54,5 \pm 6,3\%$ verglichen mit einer Reduktion auf $96,1 \pm 2,6\%$ in Kontrolltrabekeln ($p < 0,05$ bzw. $p < 0,001$) (Abbildung 6). Die diastolische Spannung und die Kontraktionskinetik blieben von Sunitinib unbeeinflusst.

Im Expressionsmuster der analysierten microRNAs zeigte sich nach 24h kein Unterschied zwischen unbehandelten und mit Sunitinib inkubierten Kardiomyozyten.

Diskussion Die Ergebnisse zeigen, dass Sunitinib neben der bekannten langfristigen negativen Auswirkung auf die Herzfunktion auch einen dosisabhängigen akut negativ-inotropen Effekt auf humanes Myokard zeigt. Dieser zeigt sich insbesondere bei höheren Dosen, was klinisch bei eingeschränkter Clearance (z. B. eingeschränkte Leberfunktion) der Patienten berücksichtigt werden sollte. Eine Veränderung des Expressionsmusters von micro-RNAs wurde nicht beobachtet.

Impact of Reperfusion Times on Myocardial Infarct Size and Hemodynamic Function in Rat Hearts II – 4

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Introduction Mortality for emergency bypass surgery after Acute Coronary Syndrome still accounts for up to 46.7%. Aim of this study is to establish an acute Ischemia/Reperfusion-model in the rat to evaluate Ischemia/Reperfusion (I/R) damage depending on a change in reperfusion time, and to improve intraoperative myocardial protection.

Methods Following temporary LAD ligation (60'), male Sprague Dawley rats were randomly assigned to 60' (group 1; $n = 11$) or 120' (group 2; $n = 12$) in vivo reperfusion. Subsequently, 3 hearts in each group were randomly assigned to TTC and Evans Blue staining to measure infarct size (IS) and area at risk (AAR). IS and AAR were expressed as percentage of the left ventricle. The remaining hearts were used for evaluation of hemodynamic parameters in an erythrocyte perfused isolated working heart during 45' baseline measurements, 60' of Custodiol-protected ice cold ischemia and 45' of postischemic reperfusion.

Results In both groups, global ex vivo ischemia significantly reduced postischemic external heart work (group 1: $70 \pm 20\%$; group 2: $82 \pm 13\%$; $p < 0,01$) and cardiac output (group 1: $74 \pm 17\%$; group 2: $83 \pm 11\%$; $p < 0,01$) compared to preischemic baseline. Coronary flow (CF) was significantly reduced only after 2h of reperfusion (group 1: $102 \pm 16\%$, n. s.; group 2: $85 \pm 16\%$; $p < 0,05$). Between the groups there was a significant difference in the recovery of CF with better recovery after 1h reperfusion ($p < 0,05$). Similar IS and AAR were measured in both groups (group 1: IS = 39.1%, AAR = 56.7%; group 2: IS = 35.9%, AAR = 67.91, n. s.). However, viable myocardium in the ischemic area (AAR-IS) was significantly larger in group 2 (group 1: 17.5%; group 2: 32.0%, $p < 0,05$).

Diskussion We were able to establish a standardized, reproducible in vivo I/R-model in the rat. In this model, protective effects of different cardioplegic solutions can be evaluated. Additionally, the decrease of CF after 2h of reperfusion suggests that damage of vital myocardium is further enhanced after a longer reperfusion time. This might be due to endothelial dysfunction induced by metabolites of I/R injury. Thus, improvement of endothelial protection might be an interesting therapeutic target to gain better outcome in these high-risk patients.

Experimental Acute Type B Aortic Dissection – Different Sites of Primary Entry Tears Cause Different Ways of Propagation

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Objectives Many dissections seem to also have a retrograde component. The aim of the study was to evaluate different sites of primary entry tears and the propagation of the dissecting membrane, ante- and retrograde, in an experimental model of acute type B aortic dissection.

Methods The entire thoracic aortic aorta including the supraaortic branches was harvested from 26 adult pigs. An intimal tear of 15 mm was created via contralateral incisions sites 20 mm downstream the origin of the left subclavian artery. In 13 cases the dissection was created at the concavity and in 13 cases at the convexity. The aortic annulus was then sewn into a silicon ring of a driving chamber. The distal aorta was connected to a tubing with adjustable resistance elements. The circulation was driven by the pneumatically driven Vienna heart to mimic aortic flow and pressure.

Results Mean circulation time was 64 ± 45 min. A mean pressure of 152 ± 43 mmHg and a mean flow of 4.5 ± 1.0 L/min were reached. The median antegrade propagation length of the dissecting membrane was 65 mm. The median retrograde propagation length in primary entry tears at the convexity was 20 mm and was stopped by the left subclavian artery. In aortas with the primary entry tear at the concavity, median retrograde propagation length was 21 mm extending up to the ascending aorta in 16%.

Conclusions In this experimental model of acute type B aortic dissection, we confirmed that many type B dissections do also have a retrograde component. At the convexity, this component is stopped by the left subclavian artery as an anatomic barrier. At the concavity, the propagation of the dissecting membrane may extend up to the ascending aorta and may therefore cause retrograde type A dissection. These findings may substantiate clinical need for treatment of type B dissections with a primary entry tear at the concavity.

MPO (Myeloperoxidase) Expression is Up-regulated in Simulated Myocardial Ischemia in the Presence of Beta-Blockers

|| – 7

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Experimental evidence suggests a crucial role of immune reaction in the pathophysiology of atherosclerosis and acute myocardial infarction. For example, a few regulatory T-cells control a wide spectrum of the inflammatory cascade. In ischemia, a pro-inflammatory imbalance with damaging effects in terms of left ventricular performance and patient outcome is the result of this uncontrolled immune response [Am Heart J 2008; 156: 1065–73]. Ischemic injury leads to left ventricular remodelling and oxidative stress and inflammation are key elements in this context. Leukocyte-derived markers such as myeloperoxidase (MPO) correlates with outcome in ischemic heart disease.

In our present work using microarray technique, we have found that, in T-cell mediated immunity generally, a noteworthy down-regulation is brought about by beta-blockers. From our investigations we suspect that most important, unique pleiotropic effects of nebivolol may be centered around favourable effects upon T-cell mediated response to ischemia. In our microarray experiments we found an up-regulation of MPO expression in the presence of nebivolol as well as in the presence of atenolol both in hypoxic as well as in well oxygenated conditions, as can be seen below. Using PCR for validation, we find that during experimental ischemia, there is an up-regulation of MPO-expression. There is a differential regulation between different beta-blockers during myocardial ischemia, which warrant further investigation.

MPO is 1,3x up-regulated in nebivolol under hypoxia and 4x under normoxia. MPO is 350x up-regulated in atenolol under hypoxia and 1,5x under in nebivolol.

Using PCR for validation, we find that during experimental ischemia, there is an up-regulation of MPO-expression. There is a differential regulation between different beta-blockers during myocardial ischemia, which warrant further investigation. We believe that there are complex pleiotropic effects of beta-blockers on immunity. Such pleiotropic effects have received more attention recently. For example, in the JUPITER trial, in apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events by unfolding pleiotropic anti-inflammatory actions [JUPITER Study, N Engl J Med, 2008]. Our preliminary results show that beta-blockers inhibit the expression of T-cell immunity related genes during experimental hypoxia and we find that during experimental ischemia, there is an up-regulation of MPO-expression. There is a differential regulation between different beta-blockers during myocardial ischemia, which warrant further investigation. In the light of JUPITER and other recent publications on modulating inflammation by pleiotropic effects of cardiovascular drugs, the specific property of immune modulation by beta-blockers in myocardial ischemia may warrant further attention. However, a further detailed exploration on both expression and molecular level is certainly needed.

New Insight into the Regulation of PAK4 (p21[CDKN1A]-Activated Kinase 4) in Human Atrial Tissue during Myocardial Ischemia from In Vitro Measurements in Human Atrial Tissue

|| – 5

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Introduction Serine/threonine-protein kinase PAK 4 is an enzyme that, in humans, is encoded by the PAK4 gene. Members of the PAK family of serine/threonine kinases serve as targets for the small GTP-binding proteins Cdc42 and Rac and have been implicated in a wide range of biological activities. Some exciting developments help elaborate the regulation of PAK activity and identify downstream signalling targets. These include the discovery of the Cool/Pix and Cat proteins, which modulate PAK signalling, and downstream kinases that modulate the organization of the actin cytoskeleton or gene expression. Considering these recent findings, we investigate their regulation during experimental myocardial ischemia.

Methods Myocardial tissue probes derive from the right auricle of patients undergoing cardiac surgery. A small part of the right auricle is removed when the heart is put on extra-corporal circulation. This sample is then be placed in cooled Tyrode solution and hypoxia is brought about by switching 100% oxygen to 100% nitrogen (hypoxia) in one of the two chambers. By doing so, we are able to compare ischemic and non-ischemic tissue of the same patient. Snap frozen samples are stored at -70°C until RNA isolation. Quality of isolated RNA is analyzed by Agilent's Bioanalyzer 2100 system. Arrays are scanned with the AB1700 Chemiluminescence Array Reader and images, data are processed by PANTHER software.

Results After 30 minutes of myocardial hypoxia we find that there is no significant regulation of PDK-expression during myocardial ischemia. There is just a trend towards a decrease in PAK4-Gene expression. There is, however, a significant difference between the expression of PAK4 during myocardial ischemia in the presence of nebivolol (0.75 ± 0.04) and control ischemia experiments (1.2 ± 0.06 ; $\pm$ SEM; $p < 0.05$): PAK4-expression is decreased during normoxia (trend) and ischemia (significant) in the presence of nebivolol (Figure 7).

In this figure, the results from real-time PCR measurements of PAK4 experiments are illustrated (O_2ko = well oxygenated, no ischemia, no drug; N_2ko = experimental ischemia, no drug; O_2at = well oxygenated, no ischemia, atenolol present; N_2at = experimental ischemia, atenolol present; O_2neb = well oxygenated, nebivolol present; N_2neb = experimental ischemia, nebivolol present).

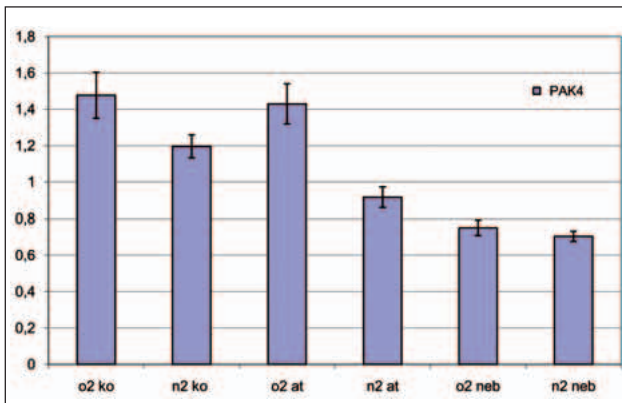


Figure 7: R. Gasser et al.

Summary While we found just a trend towards a decrease in PAK-4 expression during experimental ischemia, beta-blockers led to a significant decrease in PAK-4 expression. The recent advances in understanding these new regulators (PAK family) and their targets could explain some of the cellular cardioprotective effects that have been attributed to beta-blockers during myocardial ischemia. Specific cardioprotection of beta-blockers may thus (at least) partially be explained by PAKs decisive role played in myocardial integrity.

Regulation of Gene Expression associated with NOS Inhibition during Experimental Ischemia III – 6

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Introduction Methylation of arginine residues in proteins and subsequent proteolysis results in the liberation of free methyl-arginines, including asymmetric dimethylarginine (ADMA; R-Me₂), an inhibitor of nitric oxide synthetases (NOS). ADMA is metabolised by dimethylarginine dimethylaminohydrolase (DDAH) to citrulline (CIT) and dimethylamine (MA). ADMA is recognised as a plasma marker of increased cardiovascular risk but it is unclear whether it ever accumulates to sufficient levels to affect NO pathways. However, it has been shown by chemical biology and gene deletion techniques that loss of DDAH function elevates plasma and tissue ADMA levels. On the other hand it is possible that a feed back mechanism exists which regulates DDAH expression upon the availability of NO. In this context, it has to be mentioned that nebulivol can stimulate an increase of endothelial NO, which becomes available at the vascular smooth muscle and induces vaso-relaxation. Nebivolivol seems to interact with the endothelial NO pathway in two complementary ways: it increases NOS activity and reduces the NO-scavenging radical superoxide anion, by re-directing deranged NOS activity.

Methods Myocardial tissue probes derive from the right auricle of patients undergoing cardiac surgery. A small part of the right auricle is removed when the heart is put on extra-corporal circulation. This sample is then placed in cooled Tyrode solution and hypoxia is brought about by switching 100% oxygen to 100% nitrogen (hypoxia) in one of the two chambers. By doing so, we are able to compare ischemic and non-ischemic tissue of the same patient. Snap frozen samples are stored at -70°C until RNA isolation. Quality of isolated RNA is analyzed by Agilent's Bioanalyzer 2100 system. Arrays are scanned with the AB1700 Chemiluminescence Array Reader and images, data are processed by PANTHER software.

Results In the microarray preliminary analyzes we found that DDAH gene expression is significantly down-regulated by nebulivol compared to atenolol both in O₂-perfused preparations and simulated ischemia/hypoxia (N₂-perfused) preparations. Using real-time PCR, we were able to confirm that DDAH gene expression is significantly down-regulated by nebulivol compared to atenolol in simulated ischemia/hypoxia (N₂-perfused) preparations: It could be shown that, without beta-blockers, there is no significant regulation

of DDAH-expression during myocardial ischemia. There is, however a significant difference between the expression of DDAH during myocardial ischemia in the presence of atenolol (33.2 ± 4.2) and nebulivol (6.7 ± 0.7 ; $\pm$ SEM; $p < 0.05$).

Conclusion In the present study we find that the myocardial expression of DDAH is reduced in the presence of nebulivol in both normoxia as well as hypoxia. The measured decrease of DDAH seen under nebulivol but not with atenolol both during normoxia and hypoxia could be a measure for the increased availability of NO brought about by nebulivol as a feed back control. This is of interest since several steps in the pathways of interaction have remained unclear as yet. It is certainly promising to investigate further into this interrelation of NO, DDAH and nebulivol.

Increased Matrix-Metalloproteinase-2 Expression of Infarcted Myocardium Attenuates Homing of Mesenchymal Stem Cells III – 1

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Background Matrix-metalloproteinase 2 (MMP2) has been shown to cleave the stromal derived factor 1, interrupting the SDF-1/CXCR4 axis of stem cell homing in the ischemic injured myocardium. We have previously shown the immediate decrease of the myocardial blood flow after intracoronary mesenchymal stem cell (MSC) delivery. The present study investigated the myocardial expression of MMP2 and CXCR4 after intracoronary or intramyocardially injected MSC in porcine closed-chest reperfused acute myocardial infarction (AMI).

Methods Farm pigs were subjected to 90-min occlusion of the mid left anterior descending coronary artery followed by reperfusion. Allogeneous porcine MSC were transiently transfected with Ad-GFP and Ad-Luc (GFP-Luc-MSC), and were injected either intracoronarily using stop-flow technique, or percutaneous intramyocardially 1-week post-AMI. Myocardial blood flow (MBF) was measured by combination of pressure wire and special designed infusion catheter under maximal hyperemia caused by adenosine. Myocardial expression of MMP2 (index of ischemic/oxidative stress) and CXCR4 receptor (index of homing signal) were measured from the infarcted tissue and border zone of infarction 1-day post GFP-Luc-MSC delivery. The global left ventricular ejection fraction (EF) was measured 1-month post cell therapy by using magnet resonance imaging (MRI). MicroCT of the infarcted hearts were performed using cast preparation method to visualize the microvascularization 1 month after MSC delivery.

Results The baseline parameter, such as number of delivered cells, heart rate, blood pressure and weight were similar in the two groups. MBF decreased immediately after intracoronary delivery, while no significant change in tissue perfusion could be detected using the percutaneous intramyocardial delivery mode. Intracoronary delivery of GFP-Luc-MSC increased in the expression of MMP2 (75 kD isoform) in the infarcted myocardium (300 ± 135 vs 166 ± 49 intensity $\times$ mm²; $p = 0.029$), and at the border zone (338 ± 81 vs 185 ± 38 intensity $\times$ mm², $p < 0.001$), with parallel decrease in expression of CXCR4 (0.058 ± 0.05 vs 0.71 ± 0.05 ng/tissue/ml; $p = 0.008$), as compared with intramyocardial cell transfer. Fluorescence immunohistochemistry indicated higher level of myocardial expression of different homing (tenascin, cadherin and integrin) and angiogenic factors (FGF-2 and VEGF) in the infarcted area and at the border zone, in the intramyocardial group. Increase in EF was significantly higher in the intramyocardial group, as compared to the animals in the intracoronary delivery group (0.8 ± 8.4 vs $5.3 \pm 5.2\%$; $p = 0.046$). A significant, negative correlation was found between the decrease in MBF and increased MMP2 myocardial expression ($r = -0.943$) and reduced myocardial CXCR-4 expression ($r = 0.631$), indicating a

direct, unfavorable influence of microvascular obstruction on homing signal. As a consequence, MBF at day 1 correlated significantly with FUP ejection fraction ($r = -0.854$). MicroCT presented a higher capillary density in the infarcted area in the intramyocardial group as compared to a heart of intracoronary delivery group.

Conclusions Intracoronary stem cell delivery led to increased myocardial expression of MMP2 and reduced CXCR4 expression with attenuated functional recovery of the infarcted heart.

Inhibition of IL-1-beta Convertase and Caspase-1 Reduces Intimal Apoptosis Paralleled with Inhibition of Inflammation and Neointimal Hyperplasia After Balloon Injury and Stenting of the Porcine Coronary Arteries

III – 2

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Introduction Intracoronary administration of the IL-1 β convertase and caspase-1 inhibitor acetyl-tyrosinyl-valylalanyl-aspartylchloromethyl-ketone (Ac-YVAD-cmk) significantly decreases the coronary arterial tissue concentration of the proinflammatory cytokine IL-1 β , the rate of apoptosis in the intima after coronary artery stenting in pigs. The aim of the present study was to evaluate the association between intimal inflammation and intimal apoptosis in relation to neointimal development after intracoronary administration of Ac-YVAD-cmk before coronary intervention (stenting or percutaneous coronary balloon dilatation [PTCA]).

Methods Eight pigs received intracoronary infusion of 25 and 25 mg Ac-YVAD-cmk (solved in 2% DMSO and PBS solution, 1mg/min) selectively into the left anterior descending (LAD) or the left circumflex coronary arteries (LCx) before implantation of bare metal stent (BMS) (group BMS-Inhibitor) or balloon dilatation with oversizing (1.3:1 balloon:artery ratio) injury (group PTCA-Inhibitor). The LAD and LCx were randomly selected for stenting or PTCA. The next 8 animals served as controls with implantation of either BMS (group BMS) or solely PTCA randomly chosen of LAD or LCx. After 4 weeks, the amount of neointimal hyperplasia (neointimal area, expressed as mm²), and degree of intimal inflammation (score 0–3), fibrin deposition (0–3), haemorrhagia (0–3) and the injury score have been assessed by means of histopathology, in accordance with relevant guidelines for preclinical experiments involving coronary stenting. Terminal transferase-mediated dUTP nick end labeling (TUNEL) was carried out to calculate the percentage of the number of apoptotic cells in relation to the total number of intimal cells.

Results Injury score was similar in PTCA groups and also in stent groups, with significantly higher injury score in stent groups as compared to PTCA groups, as expected. Intracoronary infusion of Ac-YVAD-cmk resulted in a significantly less intimal apoptosis in PTCA-Inhibitor ($3.5 \pm 2.7\%$ vs $13.1 \pm 6.7\%$; $p < 0.001$), as well as in BMS-Inhibitor groups ($3.5 \pm 3.8\%$ vs $14.8 \pm 7.7\%$; $p = 0.001$) as compared to control groups, respectively. Significantly smaller neointimal area was found both in PTCA-Inhibitor (0.5 ± 0.35 vs 1.2 ± 0.44 mm², $p = 0.001$) and BMS-Inhibitor groups (0.68 ± 0.21 vs 1.7 ± 0.71 mm²; $p = 0.001$) as compared to control groups. Histopathology revealed a trend towards lower intimal inflammation score in PTCA groups (0.22 ± 0.44 vs 0.5 ± 0.52 in PTCA-Inhibitor and PTCA-Control, $p = 0.214$) but significant difference between the stent groups (0.33 ± 0.5 vs 1.22 ± 0.67 , BMS-Inhibitor vs BMS groups, $p = 0.006$). Fibrin deposition, haemorrhagia and necrosis were similar in the PTCA groups, as well as in BMS groups. Intracoronary administration of Ac-YVAD-cmk did not affect the endothelialisation. Pooling the data of the 4 groups, higher apoptosis index was associated with higher neointimal area ($r = 0.501$; $p = 0.022$) and neointimal inflammation score ($r = 0.675$; $p < 0.001$).

Discussion Short exposure of coronary arteries to IL-1-beta convertase and apoptosis inhibitor results in a significant decrease in

intimal apoptosis paralleled with a significant inhibition of neointimal inflammation and neointimal hyperplasia, suggesting a direct role of apoptosis-induced releases of different mediators (such as IL-1 β) which promote neointimal development after coronary interventions.

Subzelluläre Unterschiede in der Kinetik der zytosolischen Ca-Entfernung in Kardiomyozyten

II – 8

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Die zytosolische Kalziumentfernung geschieht in Kardiomyozyten vor allem durch die sarkoplasmatische Ca-ATPase (SERCA) und den sarkolemmalen Na/Ca-Austauscher (NCX), in geringerem Maße auch durch die plasmalemmale Kalzium-ATPase und Mitochondrien. Wir quantifizieren erstmals räumliche und zeitliche Inhomogenitäten in der zytosolischen Kalziumentfernung in ventrikulären Kardiomyozyten.

Die Herzmuskelzellen wurden aus dem linken Ventrikel von Mäusen und Schweinen isoliert und anschließend elektrisch stimuliert (1 Hz). Die zytosolischen Kalziumtransienten wurden konfokal gemessen (Fluo-4 AM, 1,5 ms/scan Linie). Forskolin (Forsk, 10 μ M) wurde zur Stimulation, Cyclopiazonic acid (CPA, 1 μ M) zur Hemmung der SERCA verwendet. SEA0400 (0,3 μ M) kam zur Inaktivierung des NCX zum Einsatz. Zur Hemmung der Zellkontraktion wurden Blebbistatin (10 μ M) oder 2,3-Butanedione-Monoxime (10 mM) verwendet. Die Zeit bis zur halbmaximalen Kalziumfreisetzung (TF50), die Ca-Amplitude (Fpeak F/F0) und die Zeitkonstante des Kalziumabfalls (τ) wurde für lokale Ca-Transienten (1 μ m Intervalle entlang der Scanlinie, local) und den Gesamt-Transienten der Zelle (global) berechnet. Der Variabilitätskoeffizient des lokalen Taus innerhalb einer Zelle ($CV = \text{Standardabweichung/Mittelwert}$) wurde zur Messung der örtlichen Inhomogenität der Kalziumentfernung aus dem Zytosol verwendet. Weiters wurden Zellregionen mit schneller (fastCaR, local $\tau < \text{global } \tau$) bzw. langsamer (slowCaR, local $\tau > \text{global } \tau$) Kalziumentfernung klassifiziert.

Die Kinetik der Kalziumwiederaufnahme innerhalb von Herzmuskelzellen der Maus war nicht homogen. Die maximale Differenz der lokalen taus entlang der Scanlinie bei 1 Hz Stimulation betrug 237 ± 29 ms (Mittelwert $\pm$ S.E.M., $n = 10$ Zellen), entsprechend einem CVtau innerhalb einer Zelle von $14 \pm 7\%$. Die Ausdehnung abgrenzbarer inhomogenen Regionen betrug $4,6 \pm 0,5$ μ m (fastCaR) und $5,1 \pm 1,4$ μ m (slowCaR). In Kardiomyozyten des Schweins waren die Inhomogenitäten in der Kalziumentfernung wesentlich ausgeprägter ($CV\tau = 25 \pm 5\%$; $p < 0,01$ vs. Maus; $n = 10/\text{Spezies}$). Die räumliche Variation in der Kalziumwiederaufnahme war nicht durch Unterschiede in der Kinetik der Ca-Freisetzung oder die Höhe der lokalen Ca-Transienten zu erklären. Forskolin führte zu einer signifikanten Beschleunigung des globalen Taus (85 ± 8 vs. 116 ± 22 ms bei Ausgangsbedingungen, „Baseline“ BSL). Forsk beschleunigte die Ca-Wiederaufnahme in slowCaR stärker (τ auf $72 \pm 4\%$ der BSL) als in fastCaR (τ auf $78 \pm 5\%$ der BSL); $p < 0,05$, $n = 7$). SERCA-Inhibierung durch CPA führte ebenfalls zu einer stärkeren Änderung der lokalen taus in slowCaR als in fastCaR ($164 \pm 5\%$ vs. $134 \pm 6\%$ von BSL; $p < 0,05$, $n = 7$) und damit zu einem signifikanten Anstieg der Inhomogenität der Kalziumentfernung ($CV\tau$ auf $19 \pm 5\%$ vs. $15 \pm 7\%$ bei BSL; $p < 0,001$). Hemmung des sarkolemmalen NCX durch SEA0400 führte zu einer Steigerung des globalen taus ohne signifikanten Unterschied zwischen fastCaR und slowCaR ($108 \pm 1\%$ vs. $112 \pm 1\%$ von BSL).

Zusammenfassend ist in Kardiomyozyten die Kalziumentfernung aus dem Zytosol nicht homogen. Im Großtier Schwein finden sich ausgeprägtere Inhomogenitäten als bei Mäusen. Intrazelluläre Regionen mit langsamer zytosolischer Kalziumentfernung lassen sich eher durch Modulation der SERCA-Aktivität beeinflussen. Unsere Ergebnisse sprechen dafür, dass in verschiedenen Regionen der Zelle die SERCA-Aktivität in unterschiedlichem Ausmaß zur zytosolischen Ca-Entfernung beiträgt.

Direct Epicardial Shock Wave Therapy for Myocardial Regeneration in Ischemic Heart Disease || – 1

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Introduction Recently shock waves are well known to induce tissue regenerative effects. Transthoracic cardiac shock wave therapy (SWT) could be shown to augment myocardial vascularization in a porcine model of myocardial infarction. SWT even improves myocardial perfusion and causes relief of angina symptoms in humans with severe coronary artery disease. Nevertheless the underlying mechanism remains largely unknown.

Materials and Methods Adult Sprague-Dawley rats were subdivided in 3 groups: sham-operated (sham), infarcted myocardium with epicardial SWT (SWT group) and infarcted myocardium without epicardial SWT (control). Four weeks following myocardial infarction (MI), SWT (100 impulses at 0.15 mJ/m²) was applied directly to the infarcted region in the SWT-group, control animals were left untreated. Cardiac function was evaluated using echocardiography. Angiogenesis was evaluated by analysis of several RNA and protein expressions.

Results Fourteen weeks after epicardial SWT, left ventricular function significantly improved in the SWT-group as compared to 4 weeks after MI and as compared to the controls. Quantitative histology revealed more vital cells and more endothelial cells in the SWT group.

SDF-1 and its receptor CXCR-4 were both upregulated in the treatment group as shown by immunohistochemistry. In peripheral blood higher numbers of circulating endothelial progenitor cells could be detected in the treatment group.

Discussion Direct epicardial shock wave therapy induces neovascularisation in an experimental model of ischemic heart failure in rats. High numbers of circulating endothelial progenitor cells can be found in the peripheral blood. At the same time SDF-1 and its receptor CXCR-4 were upregulated in the myocardium. These findings indicate that one of the main mechanisms of SWT may be recruitment of vessel forming cells.

Anti-Thymocyte Globulin (ATG) Reduces Damage Caused by Ischaemia and Preserves Cardiac Function after Experimental Myocardial Infarction III – 5

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Introduction Acute myocardial infarction (AMI) followed by cardiac remodeling is a major cause of congestive heart failure and death. Over the last decades research has focused on finding therapies to reduce inflammatory reactions after an ischaemic event. Of relevance are reports showing that infusion of apoptotic leucocytes or anti-lymphocyte serum after AMI can reduce myocardial necrosis and preserves cardiac function. In order to corroborate this therapeutic mechanism, the utilisation of immunosuppressive agents with a comparable mechanism such as anti-thymocyte globulin (ATG) was evaluated in this study.

Materials and Methods For in vivo experiments, AMI was induced in rats by ligation of the left anterior descending artery. Initially after the onset of ischaemia, rabbit ATG (10 mg/rat) was injected intravenously. Untreated and sham operated animals served as controls. Histological evaluations were performed 3 days after AMI in order to analyze angiogenic cell populations in the infarcted myocardium. Cardiac function was analyzed by echocardiography six weeks after induction of MI. Determination of infarction size was conducted by planimetry.

Results Rats that were injected with ATG evidenced higher numbers of CD68+ macrophages and c-kit+ endothelial progenitor cells (EPC) in the ischaemic myocardium 72 hours after AMI as compared to controls. Animals injected with ATG evidenced less myo-

cardial necrosis, showed a significant reduction of infarct dimension and an improvement of post AMI remodeling after six weeks (infarct dimension 26% vs 12%, $p < 0.01$). Furthermore, echocardiography revealed an improved functional recovery in treated animals as evidenced by a reduced loss of ejection fraction (EF, 43% in controls vs. 52% in treated animals, $p < 0.01$, $n = 13$ per group).

Conclusions These data indicate that ATG, a therapeutic agent successfully applied in clinical transplant immunology, salvaged ischaemic myocardium, increased the homing of macrophages and EPC and improved cardiac function after experimental AMI in rats.

Intravenous and Intramyocardial Injection of Irradiated Apoptotic Peripheral Blood Mononuclear Cells (PBMC) Preserves Ventricular Function after Myocardial Infarction III – 6

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Background Congestive heart failure developing after acute myocardial infarction (AMI) is a major cause of morbidity and mortality. Clinical trials of cell based therapy after AMI evidenced only a moderate benefit. Of clinical relevance are reports that demonstrated that infusion of apoptotic cells lead to an initiation of immunosuppressive mechanisms. Based on these reports, we hypothesized that injection of apoptotic cells into ischaemic myocardium reduces inflammatory reactions after AMI.

Material and Methods Cell suspensions of apoptotic cells were injected intravenously (IV) or intramyocardially (IM) in an experimental rat model of AMI. Sham operated animals and rats injected with control medium or viable cells served as controls. Tissue specimens were obtained 72 hours after induction of AMI to analyze the cellular infiltrate within the ischaemic myocardium. Cardiac function was analyzed by echocardiography and infarction size was determined by planimetry after 6 weeks.

Results Rats that were injected with irradiated apoptotic PBMC showed enhanced homing of macrophages and endothelial progenitor cells (EPC) within 72 hours as compared to controls. Planimetric analysis showed a significant reduction of infarction size and improvement of post AMI remodelling with less signs of dilation (infarct dimension 5% in IV injected animals, 9% in IM injected rats, 25% in controls, $p < 0.001$, respectively) (**Figure 8**). Rats that were injected with viable non-irradiated PBMC or fresh culture medium

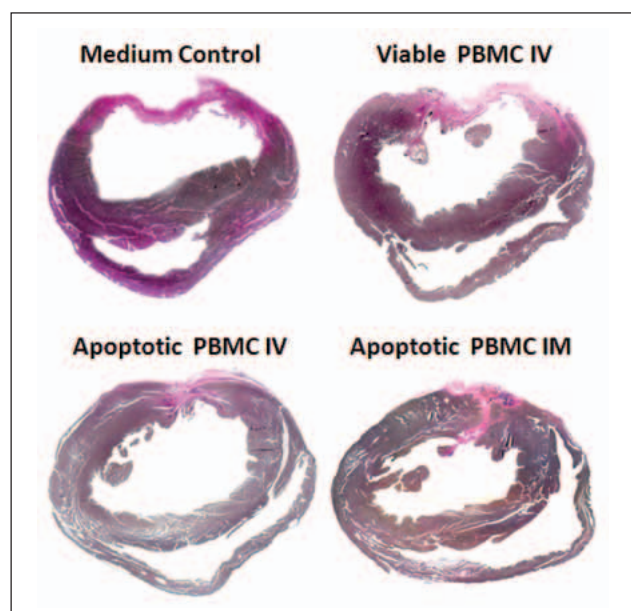


Figure 8: M. Lichtenauer et al.

showed signs of dilation which were accompanied by a considerable loss of ventricular function. Echocardiography revealed that ventricular function was almost preserved in the treatment groups with EF values of 53% and 55% vs. 42% in untreated controls compared to 61% in sham operated rats (n = 13 per group, p < 0.01).

Conclusions Based on these data we conclude that apoptotic cells induce the expression of pro-angiogenic factors necessary for attraction of regenerative cells to sites of ischaemia. Intravenous and intramyocardial injection of apoptotic cell suspensions results in attenuation of myocardial remodelling after experimental AMI, preserves left ventricular function and increases homing of regenerative cells.

Secretome of Apoptotic Peripheral Blood Cells (APOSEC) Confers Cytoprotection to Cardiomyocytes and Inhibits Tissue Remodeling after Acute Myocardial Infarction

III – 4

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Background Heart failure following acute myocardial infarction (AMI) is a major cause of morbidity and mortality. Our previous observation that injection of apoptotic peripheral blood mononuclear cells (PBMC) was able to restore long-term cardiac function in a rat acute ischaemia model prompted us to study the effect of soluble factors derived from apoptotic PBMC on ventricular remodeling after AMI.

Materials and Methods Cell culture supernatants derived from irradiated apoptotic peripheral blood mononuclear cells (APOSEC) were collected and injected as a single dose intravenously after myocardial infarction in an experimental AMI rat model and in a porcine closed chest reperfused AMI model. Magnetic resonance imaging (MRI) and echocardiography were used to quantitate cardiac function. Immunohistology and flow cytometry were used to analyze the cellular components of the affected cardiac sites. Analysis of soluble factors present in APOSEC was performed with proteome membrane arrays and activation of signalling cascades in human cardiomyocytes by APOSEC in vitro was studied by immunoblot analysis.

Results Intravenous administration of a single dose of APOSEC resulted in a reduction of scar tissue formation in both AMI models (Figure 9). Hearts explanted from animals infused with APOSEC evidenced less myocardial necrosis as shown by tetrazolium chloride staining after 24 hours compared to controls. Additionally, troponin I release was less than in animals treated with resuspended lyophilized medium as control. In the porcine reperfused AMI model APOSEC led to higher values of ejection fraction (57.0% vs 40.5%; p < 0.01), a better cardiac output (4.0 vs 2.4 l/min.; p < 0.001) and a reduced extent of infarction size (12.6% vs 6.9%; p < 0.02) as determined by MRI. Administration of APOSEC in the rat AMI model caused increased presence of CD68+ macrophages and c-kit+ endothelial progenitor cells (EPC) in the infarcted myocardium within 72 hours. Exposure of primary human cardiac myocytes with APOSEC in vitro triggered the activation of pro-survival signalling-cascades (AKT, p38 MAPK, Erk1/2, CREB, c-Jun) and increased anti-apoptotic gene products (Bcl-2, BAG1).

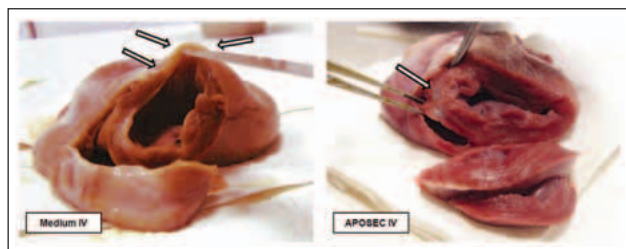


Figure 9: M. Lichtenauer et al.

Conclusions Intravenous infusion of culture supernatant of apoptotic PBMC attenuated myocardial remodelling in both models of experimental AMI. This effect seems to be due to the activation of pro-survival signalling cascades in the affected cardiomyocytes and to a higher presence of regenerative cells (EPC and macrophages) within the ischaemic tissue. Thus APOSEC would appear to represent a “biological” which prevents experimental myocardial infarction by causing peri-infarct conditioning and stimulation of regenerative effects in the hypoxic myocardium.

Evaluation of the Association between Common Variants at the GCK, GCKR, MTNR1B, and G6PC2 Loci with Angiographically Characterized Coronary Atherosclerosis

III – 7

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Single nucleotide polymorphisms in the genes encoding glucokinase (GCK), glucokinase regulatory gene (GCKR), melatonin receptor 1B (MTNR1B), and islet-specific glucose 6 phosphatase catalytic subunit-related protein (G6PC2) have been associated with altered glucose metabolism. Potential links between these polymorphisms and coronary artery disease (CAD) are unclear and are addressed in the present study.

We genotyped variants GCK rs1799884, GCKR rs780094, MTNR1B rs10830963, and G6PC2 rs560887 in a large cohort of 1663 consecutive Caucasian patients undergoing coronary angiography for the evaluation of established or suspected stable CAD. Significant CAD was diagnosed in the presence of coronary stenoses $\geq 50\%$.

Coronary angiography revealed significant CAD in 57.8% of our patients. No significant associations of variants GCK rs1799884, MTNR1B rs10830963, and G6PC2 rs560887 with angiographically determined CAD were observed. However, variant GCKR rs780094 was significantly associated with a reduced risk of coronary atherosclerosis both univariately (allelic OR 0.84 [0.73–0.96]; p = 0.013) and after adjustment for potential confounders including fasting glucose (adjusted, allelic OR = 0.84 [0.74–0.97]; p = 0.015).

We conclude that variant GCKR rs780094 is significantly associated with angiographically determined CAD. Because this association is independent from fasting glucose, the polymorphism appears to be linked to CAD via non-glucose mechanisms.

Intracardiac Delivery of Mesenchymal Stem Cells Promotes Recruitment of Haematopoietic Progenitors at the Site of Ischemic Injury in Experimental Myocardial Infarction

III – 8

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Background Bone marrow-derived mesenchymal stem cells (MSCs) are prominent candidates for cell-based cardiac repair based on their immune tolerance and paracrine effects, secreting various cytokines and growth factors, resulting angiogenesis and improved microvascular function. In our present experiment we have investigated the chemotactic signal of MSC for hematopoietic stem and progenitor cell (HPC) recruitment.

Methods Closed chest reperfused acute myocardial infarction (AMI) was induced by 90-min occlusion of the middle portion of the left anterior descending coronary artery, followed by reperfusion in domestic pigs (n = 11). The allogeneic MSCs (CD34⁺, CD45⁺, CD44⁺, CD90⁺) were transfected transiently with Ad-Luc plasmid vector. Two weeks post-AMI, the animals were randomized, and received either $11.6 \pm 2.1 \times 10^6$ transfected Luc-MSCs in 12 sites intramyocardially using the NOGA three-dimensional technology (n = 5, group Luc-MSC), or served as controls (n = 6, group C). One

day after MSC delivery, the hearts were explanted, and in vitro bioluminescence imaging were performed to visualize the injections sites loaded with Luc-MSCs. The bioluminescent positive myocardial areas of group Luc-MSC and the myocardial sites with the similar localizations of group C were cut and homogenized for measurement of myocardial CXCR4 expression (homing signal for recruitment of stem cells in the host tissue) and for flow cytometry, for quantify the presence of CD34⁺, CD31⁺ and CD34⁺CD31⁺ HPCs.

Results No differences were found between the Luc-MSC and control groups regarding the weight, gender, location of coronary artery occlusion. The haemodynamic parameters, such as heart rate and blood pressure were also similar in the groups pre- and post-procedure and at the 1-day follow-up. In vitro bioluminescent images displayed 8 ± 3 sites of MSC delivery. Myocardial expression of CXCR4 was significantly elevated at the injections site of infarction (0.71 ± 0.05 vs 0.59 ± 0.05 ng/mL tissue homogenate; $p = 0.008$) and in the plasma (5.11 ± 1.87 vs 2.62 ± 1.17 ng/mL; $p = 0.006$) 1 day post Luc-MSC delivery, as compared with controls. Significantly higher number of CD34⁺ HPC (150 ± 29 vs 110 ± 35 cells/uL tissue; $p = 0.001$), CD31⁺ HPC (700 ± 675 vs 480 ± 255 cells/uL tissue; $p = 0.007$) were found at the border zone of infarction in pigs with Luc-MSC injections. Trend to higher density of CD31⁺ cells were found in Luc-MSC group, as compared to controls ($p = 0.057$). There was no differences between the groups regarding the absolute number of CD34⁺, CD31⁺ and CD34⁺CD31⁺ HPCs in the myocardial infarcted (scar) area.

Conclusion Intracardially injected MSC contribute to recruitment and homing of the autologous hematopoietic stem and progenitor cells, probably due to their paracrine effect, expressing chemotactic signals for cardiac accumulation of HSC.

Selective Mobilization of Different Endothelial Progenitors in Experimental Closed-Chest Reperfused Myocardial Infarction

XII – 1

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Background Increase in circulating various stem and progenitor cells in the peripheral blood (PB) in response to myocardial ischemia is a well-understood process in rodents. In humans, comparison of patient cohorts with acute ST-elevation myocardial infarction (STEMI) or chronic myocardial ischemia revealed an elevated number of circulating stem and progenitor cells in patients with STEMI. We have previously reported the increased mobilization and homing of CD31⁺CD90⁺CD45⁺ endothelial mature progenitor cells from bone marrow (BM) after ischemic preconditioning. However, no data exist on the mobilization of different early endothelial stem (CD34⁺) and progenitor cell subtypes (EPS, such as CD34⁺CD31⁺ and CD31⁺) in experimental closed-chest reperfused AMI (most similar to human STEMI with primary percutaneous coronary intervention).

Methods Under general anaesthesia, closed chest reperfused STEMI was induced in 22 domestic pigs by 90-min occlusion of the mid left anterior descending coronary artery (LAD), followed by balloon deflation inducing reperfusion. The pigs were then allowed to recover. Peripheral blood samples were collected pre-STEMI, after 1h reperfusion and at the day 4 post-STEMI. The total number of circulating leukocytes were measured, and the percentage proportion of the mononuclear cells were calculated by qualitative differential blood analysis. The absolute number of circulating CD34⁺, CD34⁺CD31⁺ and CD31⁺ cells were determined by fluorescence activated cell sorting (FACS).

Results The number of PB leukocytes increased from pre-STEMI to day 4 follow-up. Similarly, the absolute number of PB mononuclear cells increased too. FACS analysis revealed elevated number of mobilized CD34⁺ cells immediately post reperfusion (from 347 ± 199 to 346 ± 202 /uL), with further increase at day 4 (575 ± 335 /uL; $p < 0.05$). However, no change could be observed in circulating number of CD34⁺CD31⁺ (from 251 ± 214 to 160 ± 153 and 188 ± 217 /uL from pre- to post-STEMI and at 4 day) or CD31⁺ cells (from

181 ± 94 to 233 ± 208 and 194 ± 142 /uL, from pre- to post-STEMI and at 4 day) during the 4-day follow-up.

Conclusions Differential subtypes of early BM origin stem and progenitor cells are mobilized as a response to the stimulating factor of myocardial ischemia/reperfusion within 4 days of STEMI. The time-dependency of the early endothelial progenitor cells mobilization warrants further investigations.

Gallensäuren-induzierte Arrhythmien am menschlichen Vorhofmyokard: Einfluss der Konjugation und mögliche Wirkungsmechanismen

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Einleitung Klinische Befunde legen nahe, dass hohe systemische Gallensäurespiegel – wie sie zum Beispiel bei der Intrahepatischen Schwangerschaftscholestase vorkommen – zu Arrhythmien führen können. Die arrhythmogenen Effekte der Gallensäuren konnten bereits in In-vitro-Studien an neonatalen Rattenkardiomyozyten nachgewiesen werden. Die Auswirkungen von erhöhten Gallensäurekonzentrationen auf das menschliche Herzen und die zugrunde liegenden zellulären Mechanismen sind allerdings noch weitgehend ungeklärt.

Methoden Isolierte humane atriale Herzmuskeltrabekel; modifizierte bikarbonathaltige Tyrode-Lösung, 11,2 mM Glukose, 2,5 mM Ca²⁺, 37°C, pH 7,4; Elektrische Stimulation mit 1 Hz und 0,5 Hz. Es wurde das Auftreten von Arrhythmien (AEC) nach Verabreichung von den beim Menschen dominierenden primären Gallensäuren (Taurin- und Glyzin-konjugierte Cholsäure und Chenodeoxycholsäure) und der therapeutisch genutzten Ursodeoxycholsäure in steigenden Konzentrationen (10 µM–1 mM, $n = 49$) analysiert. Des Weiteren wurde der L-Typ Ca²⁺-Kanals mit Diltiazem gehemmt und mit BayK8644 aktiviert (1 µM, $n = 8, 10$). Außerdem bestimmte man die absoluten Refraktärzeiten durch Ankoppelungsversuche mit stetig abnehmendem Stimulationsintervall nach Inkubation mit Taurocholsäure ($n = 16$).

Ergebnisse Es konnten keine Arrhythmien bei Konzentrationen ≤ 30 µM und 1 Hz Stimulation beobachtet werden. Steigende Gallensäure-Konzentrationen führten zu Arrhythmien, insbesondere bei 0,5 Hz Stimulation ($11 \pm 2,85$ AECs/min vs. keine AECs bei der Kontrolle; $p < 0,01$). Betreffend den verschiedenen Konjugationen konnte kein statistisch signifikanter Unterschied bezüglich der arrhythmogenen Potenz der Gallensäuren gezeigt werden. Nach einer Auswaschphase der Gallensäure konnte die Rückbildung der Arrhythmien gezeigt werden.

Die Blockade des L-Typ Ca²⁺-Kanals mit Diltiazem führte zu einer Erhöhung der Arrhythmie-Inzidenz während die Aktivierung mit BayK8644 Arrhythmien vollständig unterdrücken konnte.

Die absoluten Refraktärzeiten in Anwesenheit von 0,3 mM und 1 mM Taurocholsäure nahmen auf 165 ± 9 ms und 174 ± 12 ms im Vergleich zur Kontrolle 157 ± 11 ms zu ($p < 0,05$ und $p < 0,01$).

Diskussion Das menschliche Vorhofmyokard entwickelt nach Zugabe von Gallensäuren dosis- und frequenzabhängige Arrhythmien, welche allerdings unabhängig von der jeweiligen Konjugation der Gallensäure auftreten. Der therapeutisch protektive Effekt von Ursodeoxycholsäure in vivo konnte am isolierten Myokard nicht nachgewiesen werden. Die Zunahme der absoluten Refraktärzeiten nach TCA-Inkubation weisen auf eine Verlängerung des Aktionspotenzials hin, welche gemeinsam mit der Frequenzabhängigkeit für „Early Afterdepolarizations“ als Ursache der Arrhythmien sprechen. Die Aktivität des L-Typ Ca²⁺-Kanals korreliert invers mit der Arrhythmie-Inzidenz, was für eine Rolle von Ca²⁺ als „second messenger“ und nicht für eine direkte Wirkung auf die Elektromechanische Koppelung spricht.

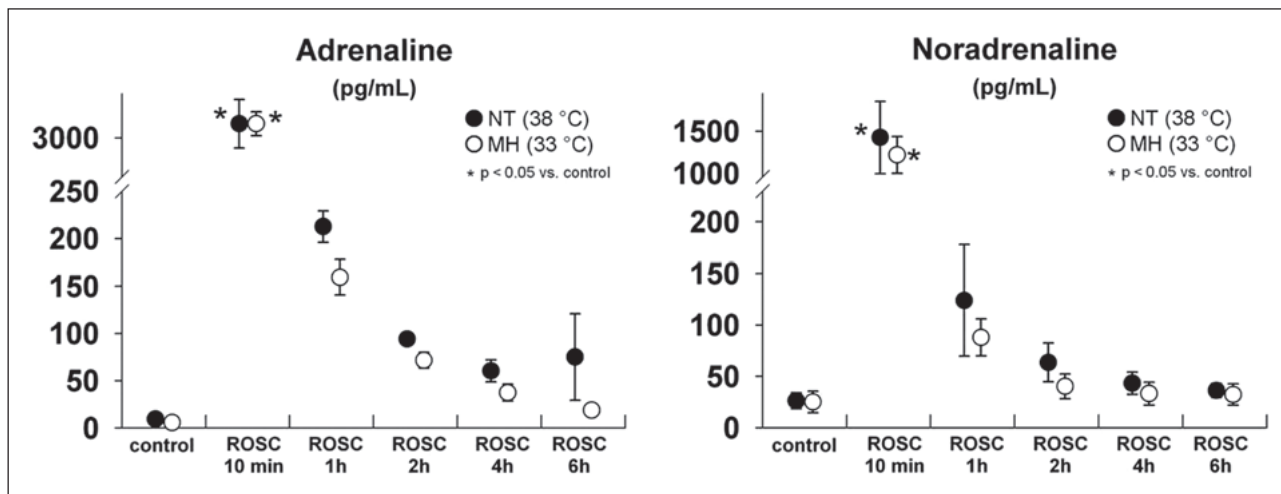


Figure 10: M. Schwarzl et al.

Mild Hypothermia Does Not Further Excite Sympathetic Activation after Cardiac Arrest in Pigs

XII – 3

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Background Mild hypothermia (MH, 32–34 °C) is induced after cardiac arrest to attenuate hypoxic brain injury. Experimental data also indicate a positive inotropic effect of MH. However, increased noradrenalin levels and shivering in awake and anaesthetized patients might reflect sympathetic activation, which would be an adverse side effect of MH after cardiac arrest. We aimed to study, whether or not MH further excites sympathetic activation after resuscitation.

Methods In 16 anaesthetized pigs (64 ± 2 kg), ventricular fibrillation (VF, 5 min) was induced electrically. After resuscitation including a single bolus of adrenaline (1 mg), pigs were assigned to either normothermia (38 °C, n = 8, NT) or MH (33 °C, n = 8, intravascular cooling device). At control conditions and at 10 min, 1 h, 2 h, 4 h, and 6 h after return of spontaneous circulation (ROSC), the heart rate variability (HRV) of a 15-min-ECG-sample was analyzed, and blood samples were drawn. The high-frequency-fraction (HF, 0.07–0.5 Hz) of HRV represented parasympathetic tone, the ratio between low-frequency-fraction (LF, 0.01–0.07 Hz) and HF represented sympathetic tone. Adrenaline, noradrenaline and dopamine levels were measured via commercial RIA-kits.

Results HF decreased in both groups at 10 min after ROSC (MH: 41 ± 6 vs 68 ± 5; p < 0.05; NT: 29 ± 4 vs 64 ± 7; p < 0.05). At 2 h after ROSC, HF was already higher in MH than in NT (76 ± 3 vs 37 ± 5; p < 0.05), and LF/HF was already lower in MH than in NT (0.21 ± 0.05 vs 1.75 ± 0.43; p < 0.05). At 6 h after ROSC, HF and LF/HF were back to control values in both groups. Catecholamine levels were not different between both groups at any time point (Figure 10).

Conclusion Both HRV and catecholamine levels returned to control values in both groups again, indicating that the induction of MH does not add further sympathetic stress to resuscitated hearts. Thus, beneficial effects of MH on cardiac function do not rely on an increased sympathetic tone.

The Induction of Mild Hypothermia Improves Oxygen Supply-Demand Balance in a Model of Acute Ischemic Heart Failure in Pigs

XII – 2

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Background The induction of mild hypothermia (MH, 32–34 °C) is guideline therapy after cardiac arrest. In normal and resuscitated porcine hearts, MH exerts a positive inotropic effect and reduces whole body oxygen demand.

Hypothesis The induction of MH is a beneficial intervention in acute ischemic heart failure.

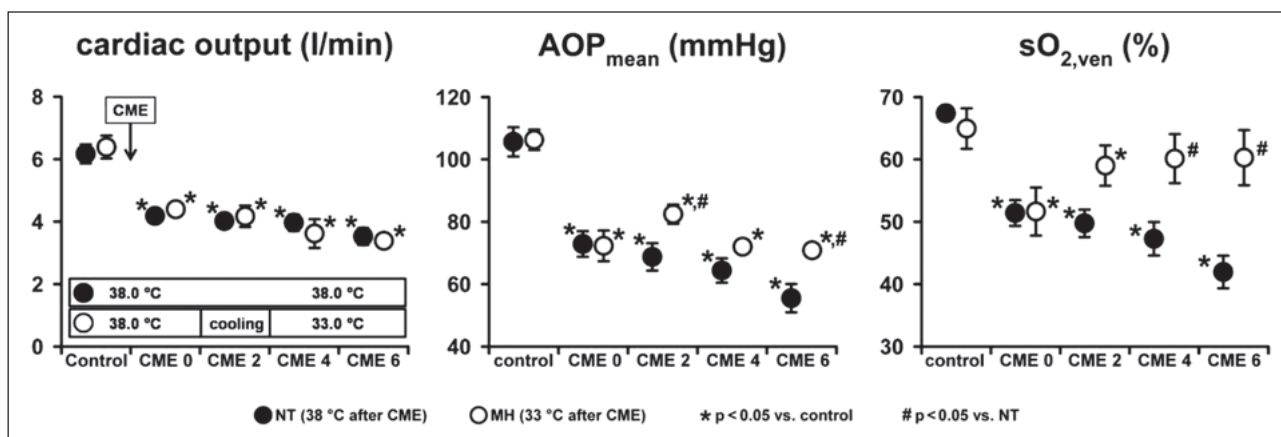


Figure 11: M. Schwarzl et al.

Methods In a closed chest preparation, 15 anesthetized pigs (70 ± 1 kg) were acutely instrumented with a Swan-Ganz catheter, a left ventricular (LV) pressure-volume catheter, a right atrial pacing probe, an intraaortic balloon catheter and an intravascular cooling device. $45 \mu\text{m}$ polystyrene microspheres were infused repeatedly into the left circumflex coronary artery (coronary microembolisation, CME) until cardiac power output decreased by $> 40\%$. Pigs were then assigned to either normothermia (NT, 38°C , $n = 8$) or MH (33°C , $n = 7$). Data are reported at 6 h after CME (CME 6) vs control.

Results The target temperature of 33.0°C was reached at 193 ± 13 min after CME. Heart rate (bpm) increased during NT ($99 \pm 6^*$ vs. 86 ± 4), but decreased during MH ($65 \pm 4^{*,*}$ vs. 86 ± 4). Cardiac output was reduced to a similar degree in both groups, but mean aortic pressure (AOP) was less decreased in MH due to increased systemic vascular resistance (mmHg/l/min, MH: $20 \pm 1^{*,*}$ vs. 16 ± 1 , NT: 14 ± 1 vs. 17 ± 1) (**Figure 11**). Also, LV dP/dtmax was less decreased vs. control in MH ($-31 \pm 4\%$) than in NT ($-45 \pm 2\%$). Central venous oxygen saturation (%) was markedly higher in MH than in NT due to reduced whole body oxygen consumption during MH (ml/min, MH: $193 \pm 8^{*,*}$ vs 332 ± 18 , NT: 274 ± 13 vs 311 ± 10).

Conclusion The induction of MH in acute ischemic heart failure markedly improves systemic oxygen supply-demand balance by reducing systemic oxygen demand and further exerts a slight positive inotropic effect. These data warrant clinical studies of MH as a rescue intervention in acute heart failure and cardiogenic shock.

Interleukin-33 Induces Urokinase-Type Plasminogen Activator and Plasminogen Activator Inhibitor Type-1 in Human Endothelial Cells In Vitro XII – 4

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Background The plasminogen system comprises an inactive proenzyme, plasminogen, which can be converted to the active enzyme, plasmin, which degrades fibrin to fibrin degradation products. Two physiological plasminogen activators (PA) have been identified: tissue-type PA (t-PA) and urokinase-type PA (u-PA). t-PA is primarily involved in maintaining fibrin homeostasis, while u-PA plays a pivotal role in proteolysis of extracellular matrix, tissue remodeling and angiogenesis, as well as in atherosclerosis progression, plaque instability and restenosis. Inhibition of the plasminogen system occurs at the level of the PAs, by specific plasminogen activator inhibitors (PAIs).

It is thought that IL-33, a recently described member of IL-1 cytokine family, plays a role in the pathogenesis of atherosclerosis and was shown to induce vascular permeability and the production of inflammatory cytokines in endothelial cells and to stimulate angiogenesis. IL-33 is a ligand for its specific ST2 receptor, and its signaling is negatively regulated by a soluble form of ST2 that lacks the transmembrane domain and presumably acts as a decoy receptor. Here we aimed to study a possible regulation of u-PA and PAI-1 by IL-33 in human endothelial cells (EC) in vitro.

Methods Human umbilical vein EC (HUVEC) and human coronary artery EC (HCAEC) were treated with recombinant human IL-33 alone or with soluble ST2 fusion-protein (sST2 Fc). Specific mRNA levels for u-PA and PAI-1 were determined by RT-PCR and u-PA and PAI-1 antigen was measured by specific ELISAs.

Results u-PA mRNA was up-regulated up to 5-fold in HUVEC and up to 2.4-fold in HCAEC when these cells were treated with 100ng/ml IL-33 for 9 hours whereas PAI-1 mRNA increased up to 2.5-fold and up to 2-fold, respectively. u-PA antigen increased up to 30-fold, and PAI-1 antigen increased up to 2-fold after 48 hours of incubation with 100 ng/ml IL-33 in HUVEC. The increase in u-PA and PAI-1 antigen was concentration-dependent when the cells were incubated with IL-33 at concentrations ranging from 1 to 100ng/ml . sST2 Fc abrogated the IL-33-induced increase in u-PA and PAI-1 antigen, which suggests that these effects of IL-33 are ST2 receptor mediated.

Conclusion Via induction of u-PA and PAI-1 in endothelial cells, IL-33 could contribute to the modulation of endothelial cell-mediated extravascular proteolysis in processes such as neovascularization and vascular remodeling. By modulating these processes IL-33 could affect plaque angiogenesis thereby impacting on the stability of these vascular lesions in atherosclerosis.

Injection of Apoptotic Peripheral Blood Mononuclear Blood Cells (PBMC) Increases Elastin Expression in Cardiac Scar Tissue after Myocardial Infarction XII – 5

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Background Within the last decades early reperfusion therapy significantly reduced mortality following acute myocardial infarction (AMI) and also improved survival and prognosis of patients. However, the development of chronic ischaemic heart disease and congestive heart failure represents one of the most frequent causes of hospitalization in developed countries. We have previously shown that injection of apoptotic cells improves left ventricular function after acute experimental myocardial infarction in rats. In this study we sought to investigate changes in the composition of the fibrotic scar tissue after AMI.

Materials and Methods Cell suspensions of apoptotic cells were injected intravenously or intramyocardially after experimental AMI induced by coronary artery ligation in rats. Sham operated animals and rats injected with control medium or viable cells served as controls. Immunohistological analysis was performed to analyze the cellular infiltrate in the ischaemic myocardium. Six weeks after induction of AMI the scar tissue was examined for the ratio of collagenous and elastic fibres. Cardiac function was quantified by echocardiography. Moreover, the expression of transcripts for elastin and collagen was analyzed using RT-PCR.

Results Hearts of treated animals evidenced enhanced homing of macrophages and cells staining positive for IGF-I and FGF-2 as compared to controls. Six weeks after AMI animals treated with intravenous or intramyocardial administration of irradiated apoptotic PBMC presented a remarkable accumulation of elastic fibers, culminating in the border zone between viable myocardium and scar tissue (**Figure 12**). A planimetric analysis revealed that the fibrotic scar in apoptotic cell (IV and IM) injected rats was composed by $5.5\% \pm 1.1$ and $8.9\% \pm 2.2$ of elastic fibres compared to $0.2\% \pm 0.1$ in controls

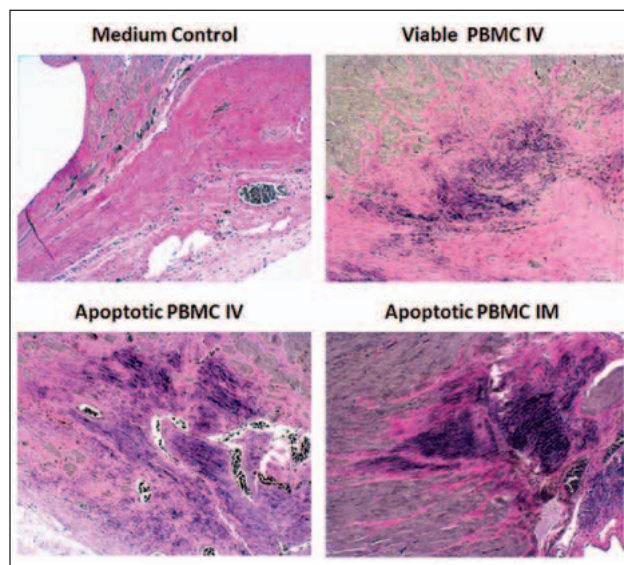


Figure 12: G. Werba et al.

and $2.9\% \pm 0.2$ in viable injected animals ($p < 0.001$ vs control, $n = 10-12$ per group).

Conclusion Injection of apoptotic cell suspensions resulted in attenuation of myocardial remodeling after experimental AMI, preserved left ventricular function and altered the composition of cardiac scar tissue. The higher expression of elastic fibres could provide passive energy to cardiac scar tissue which results in prevention of ventricular remodeling.

■ Bildgebung/Imaging

Vitalitätsdiagnostik in hochgradig wandverdünnten Myokardabschnitten mittels kardialer Magnetresonanztomographie IV – 1

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Einleitung Eine Wanddicke von < 6 mm in Verbindung mit Akinésie gilt im Allgemeinen als myokardiale Narbe und als Zeichen fehlender Vitalität. In der kardialen Magnetresonanztomographie (CMR) stehen routinemäßig 2 Verfahren zur Verfügung, um das Ausmaß des „late gadolinium enhancement“ (LGE) als Ausdruck der myokardialen Narbe zu quantifizieren: eine Gradientenecho-Inversion-Recovery- (GE-IR-) Sequenz und eine Phase-Sensitive-Inversion-Recovery- (PSIR-) Sequenz. In einer Fallserie von Patienten mit extrem verdünntem Myokard wurden beide Verfahren herangezogen, um den Zusammenhang zwischen Wanddicke und Vitalität zu evaluieren.

Material und Methode Bei 5 Patienten mit ischämischer Kardiomyopathie und einer EF $< 40\%$, wo bereits im Echo eine verdünnte Narbe beschrieben war, wurde eine CMR durchgeführt. Alle Patienten waren männlich und hatten eine Infarkt-anamnese (4 Vorderwand, 1 Vorder- und Hinterwand). Mit Steady-State-Free-Precession- (SSFP-) Techniken wurden dynamische Aufnahmen der Herzaktion vorgenommen und die linksventrikuläre Masse (LVM) und Auswurf-fraktion (EF) sowie das linksventrikuläre enddiastolische Volumen (LVEDV) bestimmt. Zehn Minuten nach Verabreichung von $0,1$ mmol Gadolinium/kg KG wurden das LGE mittels GE-IR sowie PSIR untersucht.

Ergebnisse Das mittlere LVEDV war deutlich erhöht ($279,4 \pm 36,7$ ml; $223-316$ ml), die LVM im Verhältnis dazu nur gering erhöht ($194,6 \pm 30,6$ g; $160-235$ g). Die EF betrug im Mittel $25,7 \pm 11,0\%$; $12-40\%$. Bei 4 Patienten fand sich im wandverdünnten akinetischen Bereich eine transmurale Narbe/Fibrose sowohl im GE-IF als auch in der PSIR; beim verbleibenden Patienten zeigte sich erhaltene Myokardvitalität in den wandverdünnten akinetischen Arealen in beiden Verfahren.

Diskussion Der Nachweis einer extremen Wandverdünnung Myokardabschnitten mit Wandbewegungsstörungen kann nicht *a priori* als fehlende Vitalität gewertet werden, sondern erfordert eine weitere Abklärung.

Value of 2D-Strain Dobutamine Stress Echocardiography Compared with 18FDG-PET for Evaluation of Viability and Scar in Patients with Low Flow – Low Gradient Aortic Stenosis. A Sub-Study of the TOPAS Study BAI

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Purpose In patients with low flow-low gradient aortic stenosis (LFAS) dobutamine stress echocardiography allows discrimination

Table 6: P. E. Bartko et al.

	N	Rest	LDD	PDD
Viable	234	$6.5 \pm 6.8^*$	$7.6 \pm 7.1^+$	$7.3 \pm 6.9^{\#}$
Reduced viability	72	$4.5 \pm 6.4^*$	$3.7 \pm 8.0^+$	$4.1 \pm 7.5^{\#}$

* $p = 0.023$ viable vs reduced viability at rest

+ $p = 0.000$ viable vs reduced viability at LDD

$p = 0.000$ viable vs reduced viability at PDD

	N	Rest	LDD	PDD
Normal	262	$6.5 \pm 6.8^*$	$7.8 \pm 7.2^+$	$7.6 \pm 6.9^{\#}$
Scar	22	$3.1 \pm 6.0^*$	$1.3 \pm 7.0^+$	$3.8 \pm 6.5^{\#}$

* $p = 0.025$ normal vs reduced scar at rest

+ $p = 0.000$ normal vs reduced scar at LDD

$p = 0.014$ normal vs reduced scar at PDD

between true and pseudo severe aortic stenosis as well as the assessment of functional myocardial reserve, which is a strong predictor for post-operative outcome. Reduced left ventricular contractility needs further evaluation of the amount of residual viability (as revealed by 18FDG-PET) to estimate the potential of functional improvement. We investigated the value of peak systolic longitudinal 2-D strain (PLS) for discrimination between different viability states in comparison to 18FDG-PET.

Methods We consecutively enrolled 22 patients with LFAS, which was defined by aortic valve area (AVA) $\leq 1.2\text{cm}^2$ (indexed AVA $\leq 0.6\text{cm}^2/\text{m}^2$), LVEF $\leq 40\%$ and mean pressure gradient ≤ 40 mmHg. All patients underwent N-13 ammonia (perfusion scan)

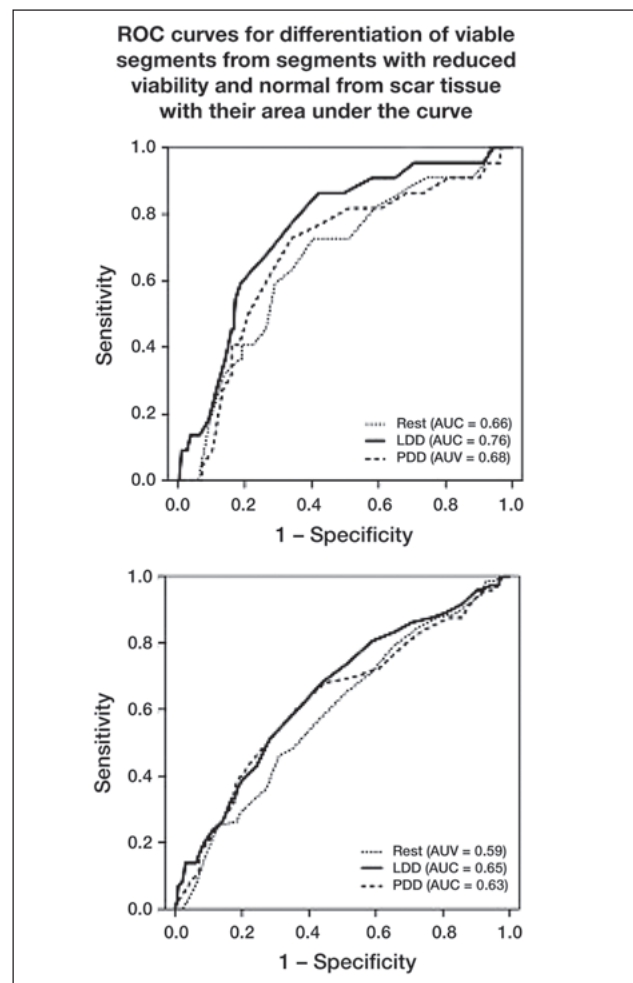


Figure 13: P. E. Bartko et al.

Table 7: P. E. Bartko et al.**PLS cut-off values for differentiation between viable/reduced viability and normal/scar**

	Rest	LDD	PDD
Cut-off viable/reduced viability	-6.8	-7	-6.8
Sensitivity/specificity	56%	62%	62%
Cut-off scar/normal	-5.6	-6	-6
Sensitivity/specificity	65%	70%	68%

and 18FDG-PET (metabolism scan) and were thus classified as follows: Normal (N-13 ammonia uptake > 70%), perfusion/metabolism mismatch (N-13 ammonia uptake ≤ 70% and 18FDG uptake > 70%), perfusion/metabolism match (N-13 ammonia uptake ≤ 70% and 18FDG uptake < 70%) and scarred segments (N-13 ammonia uptake ≤ 70% and 18FDG uptake < 50%). Subsequently we arranged segments into groups: viable (normal and mismatch) versus reduced viability (match and scar) and normal versus scar. PLS analysis was performed offline in the apical 4,3, and 2 chamber views by a blinded observer for each step: echocardiography at rest, 10mcg/kg/h (LDD) and peak dose (PDD) dobutamine. We used bull's eye analysis with an 18 segment model to compare 18FDG-PET with speckle tracking echocardiography.

Results 16 male and 6 female patients, age 70 ± 12 years (mean $\pm$ SD) were examined. LVEF was $29 \pm 11\%$, AVA-index $0,4 \pm 0,1 \text{ cm}^2/\text{m}^2$. Segmental classification by 18FDG-PET: We found 324 viable segments and 72 segments with reduced viability. Sub-analysis showed 262 normal segments and 22 scarred segments. PLS values for different viability states are shown in **Table 6**. ROC curves with corresponding areas under the curves for differentiation of viable from segments with reduced viability as well as normal from scar tissue are shown in **Figure 13**. PLS cut-off values and sensitivity/specificity are shown in **Table 7**.

Conclusions In patients with LFAS PLS is significantly impaired in segments with reduced viability compared to viable segments and even more impaired in scar compared to normal tissue. Dobutamine administration improves differentiation of viable from segments with reduced viability by PLS with best performance at LDD levels. PLS in the setting of DSE in patients with LFAS may provide a new tool to discriminate different states of viability, especially to differentiate scar from normal myocardial tissue.

Nicht-invasive Darstellung der elektroanatomischen Aktivierung des Herzens (NICE) in einem CRT-Patienten mit einer quadripolaren Linksventrikel-Elektrode

IV – 2

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Hintergrund Häufige Probleme der kardialen Resynchronisationstherapie (CRT) sind die hohe Rate an Non-Respondern sowie die Phrenikusstimulation. Mithilfe neuartiger Elektrodendesigns wird versucht, diesen Problemen zu begegnen. Mittels NICE wird in diesem Fallbericht der Einfluss verschiedener Linksventrikel-Stimulationsorte bzw. unterschiedlicher Stimulationsvektoren (VectSelect™) auf die elektroanatomische Aktivierung des Herzens in einem Patienten mit quadripolarer Linksventrikel-Elektrode untersucht.

Methode NICE erfolgte in einem Patienten (männlich, 62 Jahre, QRS-Dauer 184 ms, LVEF = 21 %), nach Implantation eines CRT-Systems mit quadripolarer Linksventrikel-Elektrode (Quartet™ 1458Q; St. Jude Medical Inc.). Es wurde die elektroanatomische endo/epikardiale Aktivierung der Ventrikel während unterschiedlicher Stimulationspfade (VectSelect™) dargestellt. NICE arbeitet durch Fusion der Daten eines individuellen anatomischen Modells

Tabelle 8: T. Berger et al. Einfluss der unterschiedlichen Stimulationsvektoren auf die QRS-Dauer während LV- und BiV-Stimulation (3,5 V/0,5 ms)

Vektor	QRS-Dauer (ms)	
	LV only	BiV
Distal1–Mid2	135	133
Distal1–Proximal4	122	142
Distal1–RV coil	122	139
Mid2–Proximal4	141	122
Mid2–RV coil	153	137
Mid3–Mid2	170	120
Mid3–Proximal4	175	136
Mid3–RV coil	180	128
Proximal4–Mid2	178	121
Proximal4–RV coil	197	124

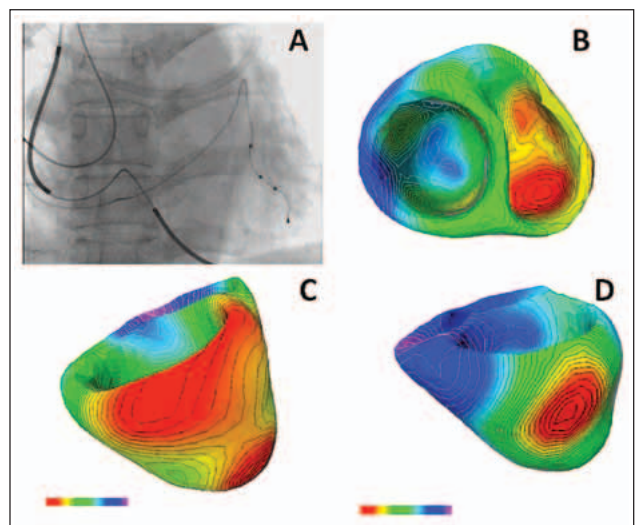


Abbildung 14: T. Berger et al. (A) Lage der Elektroden in der Durchleuchtung (RAO); NICE-Darstellung der elektroanatomischen Aktivierungssequenz während RV-Stimulation (B), während BiV-Stimulation mit distal1/proximal4 (C) und mid2/prox4 (D) Stimpfad-Programmierung (Isochrone in Millisekunden).

des Torso (mittels MRI generiert) mit der Information eines hochauflösenden 65-Elektroden-Oberflächen-EKGs. Daraus erfolgt mittels eines inversen Algorithmus – basierend auf dem biophysikalischen Bidomain-Modell – die Berechnung der zeitlichen und räumlichen Ausbreitung der elektrischen Aktivierung der Ventrikel.

Resultate Während RV-Stimulation zeigte sich eine geringgradige Verlängerung der QRS-Dauer im Vergleich zum intrinsischen Sinusrhythmus (190 vs. 183 ms) während LV als auch BiV-Stimulation (beide: Stimulationspfad distal 1/proximal 4; 3.5V/0,5 ms) in einer Verkürzung der QRS-Dauer (122 und 142 ms) resultierte. Es zeigte sich eine große Variabilität hinsichtlich der QRS-Dauer während unterschiedlicher Stimulationspfade bei gleicher Stimulations-elektrode (**Tabelle 8**). Die endo-/epikardiale elektroanatomische Aktivierung des Ventrikels während RV, LV und BiV-Stimulation ist in **Abbildung 14** dargestellt.

Zusammenfassung NICE ermöglicht die nicht-invasive Visualisierung der unterschiedlichen ventrikulären Aktivierungssequenzen während unterschiedlicher Stimulationsmodi. NICE ermöglicht somit eine individuelle elektroanatomisch-gestützte Optimierung der CRT-Programmierung. In Kombination mit den MRI-Daten sollte in Zukunft bereits präoperativ die optimale Platzierung der linksventrikulären Elektrode (abhängig von evtl. Narbenarealen und der CS Anatomie) planbar sein.

Simultane 64-Zeiler-Spiral-CT-Koronarangiographie bei kardialer CT-Untersuchung vor geplanter Katheterablation von Vorhofflimmern – Ergebnisse eines prospektiven Registers

IV – 3

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Hintergrund Durch zunehmende technische Verbesserungen hat sich die CT-Koronarangiographie (CT-KA) mittels hochauflösender Spiral-Computertomographie (CT) als zuverlässige Methode zum Ausschluss einer koronaren Herzkrankheit (KHK) etabliert. Spiral-CT-Untersuchungen werden jedoch auch zunehmend zur Erfassung anatomischer Informationen, die für eine integrative Bildgebung bei der Ablation von Vorhofflimmern (VHF) verwendet werden, durchgeführt. Da VHF in gewissem Ausmaß mit einer zugrunde liegenden KHK assoziiert ist, erscheint eine simultane CT-KA bei Patienten (P) mit Herz-CT vor geplanter VHF-Ablation sinnvoll.

Wir untersuchten Machbarkeit, Qualität und Aussagekraft der simultanen CT-KA bei kardialer CT-Untersuchung von P mit VHF und fehlender KHK-Anamnese.

Methodik Patienten mit paroxysmalem VHF und niedriger bis mittlerer Prätestwahrscheinlichkeit für KHK, bei denen zur Evaluierung hinsichtlich einer VHF-Ablation eine Herz-CT-Untersuchung geplant war, wurden in das Register aufgenommen. Nicht eingeschlossen wurden P mit bekannter KHK, nach Koronarinterventionen oder aortokoronarer Bypassoperation.

Die Erfassung der kardialen Anatomie und der CT-KA erfolgte mit demselben Scan nach intravenöser Kontrastmittelinjektion. Die Untersuchung erfolgte im Sinusrhythmus. P mit einer Herzfrequenz über 70/min erhielten Betablocker und Sedativa. Die technische Durchführung im Spiralmodus beinhaltete eine Rotationszeit von 330 ms, retrospektives Gating und eine Kollimation von $64 \times 0,6$ mm. Zusätzlich erfolgte ein Kalzium-Scoring (Agatston-Score-Äquivalent, ASÄ).

Die Auswertung erfolgte unmittelbar nach Ende der Untersuchung. Es wurde der Ausschluss einer KHK oder Nachweis einer nicht signifikant stenosierenden Sklerose (NSS) beziehungsweise von signifikanten Koronarstenosen ($> 70\%$, SST) evaluiert. Die Qualifizierung der CT-KA als unauffällig (ASÄ = 0 und normales Angiogramm), nicht NSS und SST erfolgte ebenso wie die Beurteilung der Bildqualität in gut, mittel und schlecht im Konsens zweier Untersucher.

Ergebnisse Es wurden 244 P (172 männlich) mit einem mittleren Alter von 62 ± 7 Jahren untersucht. Die mittlere Scan-Zeit betrug $13,9 \pm 0,7$ Sekunden. Der statistische Medianwert des ASÄ lag bei 9,5 (Interquartilsabstand 0–187,5).

Bei 243 P erlaubte die Bildqualität eine Untersuchung aller Gefäße (gut bei 182, mittel bei 61 P), bei 1 P machten hochgradige zirkuläre Gefäßverkalkungen eine valide Befundung unmöglich. Eine koronare Herzerkrankung konnte bei 106 P (43 %) ausgeschlossen werden, weitere 116 P (48 %) wiesen eine NSS auf, während bei 22 P (9 %) zumindest eine signifikante Stenose suspekt wurde. Bei diesen P wurde eine konventionelle Koronarangiographie durchgeführt, in der sich signifikante Stenosen in 7 Fällen zeigten. Hier erfolgte eine perkutane Koronarintervention.

Schlussfolgerung Im Rahmen einer kardialen CT-Untersuchung für geplante VHF-Ablationen kann simultan eine CT-KA mit hoher Bildqualität erfasst werden. Bei P mit VHF und geplanter Ablation ist auch ohne typische KHK-Anamnese eine Atherosklerose der Koronararterien in über 50 % zu erwarten.

Erhaltene Vitalität in hochgradig wandverdünnten Myokardabschnitten: Eine multidisziplinäre Fallstudie

IV – 4

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Einleitung Eine Wanddicke von < 6 mm in Verbindung mit Akinésie gilt im Allgemeinen als myokardiale Narbe und als Zeichen fehlender Vitalität. Oft wird aus diesem Grund von Revaskularisationsmaßnahmen Abstand genommen. Die klinische Beobachtung pektanginöser Beschwerden trotz der beschriebenen Morphologie gibt Anlass zu der Vermutung, dass auch bei wandverdünntem Myokard vitales Gewebe vorliegen kann.

Fallbericht Ein 61-jähriger Mann wurde mit einem akuten Koronarsyndrom stationär aufgenommen. Troponin T war mit $0,26$ ng/ml erhöht, die CK lag im Normbereich, das EKG war unauffällig. Echokardiographisch fand sich ein dilatierter linker Ventrikel mit hochgradig reduzierter systolischer Funktion und diffusen Wandbewegungsstörungen. Die Koronarangiographie zeigte eine höhergradige Hauptstammstenose, mehrfache komplexe Stenosen der LAD, eine verschlossene A. circumflexa und eine proximal verschlossene rechte Koronararterie. Es wurde ein Vitalitätsnachweis mittels MR durchgeführt, wobei sich eine Wandverdünnung auf ca. 5 mm im Bereich der akinetischen mittleren und apikalen Vorderwand zeigte; in diesen Abschnitten fand sich überraschenderweise kein Nachweis eines transmuralen „late enhancements“ (LE) nach KM-Gabe. Es bestand jedoch ein umschriebenes transmuraleres Fibroseareal in der normaldicken basalen Diaphragmalwand. Auch eine Thallium-Ruhe-Myokardszintigraphie erbrachte einen Vitalitätsnachweis in der Vorderwand. Eine Bypassoperation wurde geplant, allerdings verstarb der Patient nach einem neuerlichen Myokardinfarkt im kardiogenen Schock. Die Obduktion zeigte in der verdünnten Vorderwand ebenfalls lediglich den rezenten, letalen Myokardinfarkt ohne ausgedehnte, alte Narbe, diese zeigte sich in der basalen Diaphragmalwand entsprechend dem LE des MRT.

Diskussion Auch in akinetischen, wandverdünnten Myokardabschnitten kann Vitalität noch erhalten sein. Das kardiale MR ist hier in guter Korrelation mit szintigraphischen Verfahren und mit der tatsächlichen pathoanatomischen Morphologie.

Myocardium at Risk in ST-Elevation Myocardial Infarction: Comparison of T2-Weighted Edema Imaging with the Endocardial Surface Area Assessed by Magnetic Resonance and Validation Against Angiographic Scoring

XIII – 1

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Objectives The objective of this study was to assess the area at risk (AAR) in ST-elevation myocardial infarction (STEMI) with 2 different magnetic resonance imaging (MRI) methods and to compare them to the validated angiographic APPROACH-score in a large consecutive patient cohort.

Background Edema imaging with T2-weighted MRI and the endocardial surface area (ESA) assessed by late gadolinium enhancement (LGE) have been introduced as relatively new methods for AAR assessment in STEMI. However, data on the utility and validation of these techniques are limited.

Methods One-hundred-ninety-seven patients undergoing primary percutaneous coronary intervention in acute STEMI were included. AAR (assessed with T2-weighted edema imaging and the ESA method), infarct size and myocardial salvage (AAR minus infarct size) were determined by MRI 2–4 days after primary angioplasty. Angiographic AAR scoring was performed by use of the APPROACH score. All measurements were done offline by blinded observers.

Results The AAR assessed by T2-weighted imaging showed good correlation with the angiographic AAR ($r = 0.87$; $p < 0.001$), where-

as the ESA showed only a moderate correlation either to T2-weighted imaging ($r = 0.56$; $p < 0.001$) or the APPROACH-score ($r = 0.44$; $p < 0.001$). Mean AAR by ESA ($20.0 \pm 11.7\%$ of left ventricular mass) was significantly ($p < 0.001$) smaller than the AAR assessed by T2-weighted imaging ($35.6 \pm 10.9\%$ of left ventricular mass) or the APPROACH-score ($27.9 \pm 10.5\%$ of left ventricular mass) and showed a significant negative dependence on myocardial salvage index. In contrast, no dependence of T2-weighted edema imaging or the APPROACH-score on myocardial salvage index was seen.

Conclusions The AAR can be reliably assessed by T2-weighted MRI, whereas assessment of the AAR by ESA seems to be dependent on the degree of myocardial salvage, thereby underestimating the AAR in patients with high myocardial salvage such as aborted infarction. Thus, assessment of the AAR with the ESA method cannot be recommended.

Welche Rolle hat das koronare Multislice-CT vor Rekanalisationen chronischer Koronarverschlüsse?

IV – 6

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Einleitung Die katheterinterventionelle Rekanalisation chronischer Koronarverschlüsse (CTO) ist eine sehr aufwendige und komplikationsreiche Prozedur. Die Indikationsstellung muss daher sehr streng erfolgen. Jede Möglichkeit zur Optimierung von Interventionsstrategie und Erfolgsquote sowie Reduktion von Strahlung, Kontrastmitteldosis und Komplikationen sollte ausgeschöpft werden. Die koronare Multislice-CT (kMSCT) bietet hierfür interessante Ansatzpunkte.

Daraus ergibt sich die Fragestellung, ob mithilfe der kMSCT Aussagen über den Gefäßverlauf, die Verschlusslänge und -charakteristik, die Gefäßperipherie und Kollateralisierungswege getroffen werden können.

Methode Retrospektive Analyse der klinischen und radiographischen Daten aus einem monozentrischen CTO-Register.

Ergebnisse Insgesamt wurden im Zeitraum von 4/07–2/11 90 Patienten mit einem CTO katheterinterventionell behandelt. Davon erhielten 31 zuvor ein Koronar-CT (34,4 %). Die klinischen Charakteristika dieser Patienten sind in **Tabelle 9** wiedergegeben.

Das CTO-Gefäß wurde durch die kMSCT bei 22/31 Patienten eindeutig und artefaktfrei dargestellt (70,9 %). Die Verschlusslänge konnte bei 21/31 Patienten (67,7 %) exakt berechnet werden und betrug im Median 25 mm (8–88 mm). Die Verschlussmorphologie wurde bei 20/31 gut, bei 7/31 mäßig und bei 4/31 unzureichend beschrieben. Die Peripherie des verschlossenen Gefäßes wurde in 24/31 Untersuchungen beschrieben, ein Kollateralkreislauf nur bei 12/31. Insgesamt war das kMSCT in 25/31 Fällen technisch ausreichend und die spezifische Fragestellung konnte beantwortet werden (80,6 %). Bei 6/31 wurde der CT-Datensatz exportiert und bei der CTO-Rekanalisation im Herzkatheterlabor als Pathfinder verwendet („CT-true cath lab planning“).

Tabelle 9: C. Granitz et al.

Männer/Frauen	27/4
Mittleres Alter	60,61 $\pm$ 9,13
anamnest. Myokardinfarkt	9 (29 %)
anamnest. PCI	17 (54,8 %)
anamnest. CABG	4 (12,9 %)
Diabetes mellitus	6 (19,3 %)
Art. Hypertonus	24 (77,4 %)
Hyperlipidämie	30 (96,7 %)
Rauchen	15 (48,4 %)
Niereninsuffizienz (GFR < 30 ml/min)	1 (3,2 %)
betroffenes CTO-Gefäß (LM, LAD, RCX, RCA)	1/8/6/16
1/2/3 Gefäß-Erkrankung	7/13/11
Führendes Symptom CCS 1/2/3/4 NYHA $\geq$ 2	3/12/11/2/3
Vitalitätsnachweis: Szintigramm/MRI/keiner/andere	19/5/7

Um kumulative Strahlendosis zu sparen, wurde bei 17/31 ein strahlensparender Algorithmus verwendet („step and shoot“).

Der mittlere Kontrastmittelverbrauch bei der kMSCT betrug 88 ml.

Diskussion Wenn die kMSCT technisch gelingt, kann die Charakteristik des Koronarverschlusses mit ausreichender Qualität dargestellt werden. Dies ermöglicht eine bessere Planung der Therapie-strategie im Herzkatheterlabor. Ein besonderes Augenmerk sollte zukünftig auf die Darstellung des Kollateralkreislaufs gelegt werden, weil sich aus diesen Informationen wichtige Implikationen bezüglich eines retrograden Zugangsweges ergeben.

Ascending Aortic Distensibility Coefficients Rather than Local Aortic Pulse Wave Velocities Discriminate Healthy Volunteers From Patients with Coronary Artery Disease

IV – 7

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Background Cardiac Magnetic Resonance (CMR) is a unique method to determine regional and local aortic elastic parameters. So far no study has compared the use of local distensibility coefficients (DC, $10 - 3 \times \text{mmHg}$) and local ascending aortic pulse wave velocities (PWV, m/s), determined by CMR in patients with coronary artery disease. This study investigates the use of local (ascending) aortic DC ascending in healthy volunteers and patients with CAD and compares the results to regional and local pulse wave velocities. This is of clinical importance since we showed previously the limitations of local PWV determination in a diseased population.

Methods We performed velocity encoded, phase contrast CMR (retrospectively ECG-gated, temporal resolution: 20 ms) in 18 healthy volunteers as well as in 26 patients with coronary artery disease (CAD) ($n = 42$, mean age 46.6 ± 20.3 years, 11 female).

Measurements were performed at the levels of the ascending and descending thoracic, as well as the abdominal aorta. Flow-volume curves and cross-sectional area changes were determined during early systole. Regional PWVTT was determined by the established transit-time method and served as a reference standard. DC ascending was determined as the product of the relative area change during systole and the pulse pressure (mmHg). Local PWVQA was determined as the ratio between the flow (Q) and area (A) variations.

Results Healthy volunteers differed significantly from CAD patients in regional PWVTT (4.93 ± 0.59 vs 9.16 ± 3.57 [m/s]; $p < 0.001$) and DC ascending (23.07 ± 8.47 vs 6.80 ± 4.34 [$10 - 3 \times \text{mmHg}$]; $p < 0.001$). Local ascending aortic PWVQA, however, failed to detect differences between healthy volunteers and CAD patients (3.48 ± 1.79 vs 2.46 ± 3.49 [m/s]; $p = 0.267$).

Furthermore DC ascending correlated inversely with age ($r: -0.739$; $p < 0.001$) and PWVTT ($r: -0.538$; $p < 0.005$). Local PWVQA did not correlate with age ($p = 0.374$) or regional PWVTT ($p = n.s.$).

Conclusion This pilot-study indicates that local aortic DC ascending is a robust method for the assessment of CAD patients. Local PWVQA, however, failed to detect differences in local aortic stiffness between the 2 studygroups. For the assessment of local ascending aortic elasticity in CAD patients with CMR, DC ascending should be preferred to local PWVQA.

Early Microvascular Obstruction After Acute Myocardial Infarction Predicts Clinical Long-Term Outcome: Data From a 5 Year Follow-Up

BAI

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Aims Early and late microvascular obstruction (MVO) assessed by cardiac magnetic resonance imaging (CMR) are prognostic markers for combined clinical endpoints after acute myocardial infarction (AMI). However, there is a lack of studies with long-term follow-up periods (> 24 months).

Methods AMI patients reperfused by primary angioplasty (n = 129) underwent MRI at a median of 2 days after the index event. Early MVO was determined on dynamic Gd-first-pass Images directly after the administration of 0.2 mmol/kg bodyweight Gd-contrast agent. Furthermore ejection fraction (EF, %), left ventricular myocardial mass (LVMM, g) and total infarct size (% of LVMM) were determined with CMR. Clinical follow-up was conducted after a median of 52 months. 26 patients were lost to follow-up. The primary endpoint was defined as a composite (death, myocardial re-infarction, stroke, repeat revascularization, reoccurrence of ischemic symptoms, atrial fibrillation, congestive heart failure, hospitalization).

Results 52 pre-defined events occurred during follow-up. Initially 65 patients showed early MVO. Median event free survival was 1176 days in patients presenting without early MVO and 785 days in patients with early MVO (p = 0.02). Patients with early MVO had larger infarcts (22% of LVMM vs 13%; p = 0.002) and a lower EF (39% vs 46%; p = 0.006). Early MVO was independently associated with the composite primary endpoint in the multivariable Cox regression analysis adjusting for age, ejection fraction and infarct size. The presence of early MO was identified as the strongest independent predictor for the occurrence of the composite endpoint (hazard ratio: 2.79; 95%-CI: 1.25–6.25; p = 0.012).

Conclusion Early MVO, as assessed by first-pass CMR is an independent long-term prognosticator for morbidity after AMI.

The Role of Coronary Artery Calcium Scoring Via SPECT-CT in Patients With Normal Myocardial Perfusion Imaging for Diagnosis of Suspected Coronary Artery Disease

IV – 8

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Aim The aim of this study was to evaluate the impact of a combined evaluation of the coronary artery calcification (CAC) score with normal Single Photon Emission Computed Tomography (SPECT) imaging in the diagnostic process in patients with suspected coronary artery disease (CAD). As a pharmacological stress imaging by SPECT does not detect hemodynamically relevant stenoses under 50%, moderate CAD can never be totally excluded despite normal MPI results.

Methods In a prospective study we measured CAC of 74 patients (29 m, 45 f, mean age 58,7 [m] and 64,4 [f]) with suspected CAD and normal SPECT imaging. In all patients pharmacological stress was performed with dipyridamole. Both, SPECT and CAC score were performed on the same machine, a T6 Symbia gamma camera (Siemens, Knoxville, USA). Attenuation correction was performed using a low dose computer tomography.

Results The mean total CAC score was 182.6 ± 435.7 and ranged from 0–2309. Twenty-one of 29 male patients (72%) and 17/45 female patients (38%) had an elevated Agatston score of > 10. There were 9 cases (5 m, 4 f) with a calcium score of > 400 and 3 cases (2 m, 1 f) with a calcium score of > 1000. No single cardiac events were noted in these patients during a mean follow up time of 10.3 months (range 7–13 months, median 11 months) except one cardiac death in a patient with total Agatston score of 278.

Conclusion Increased CAC score is a known risk marker for future cardiac events. Our results showed that massively elevated CAC scores can be detected despite normal SPECT stress imaging. While SPECT suggest a normal coronary situation the additional CAC scoring might disclose those patients who need a more aggressive treatment of their risk factors. A combination of SPECT and CAC can be achieved on a one-day basis on one machine and would lead to a faster and more convenient management of patients with suspected CAD.

Focal and Non-Focal Irreversible Injury in Patients with Symptomatic Myocarditis

XIII – 2

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Background The use of late-enhancement (LE) CMR imaging offers a high specificity for the detection of myocardial injury in myocarditis. Nevertheless, it was shown to be insensitive for the detection of symptomatic myocarditis with limited or nonfocal irreversible injury. We aimed to identify focal as well as diffuse, visually not detectable regions of necrotic myocytes by a pixel-based volumetry (PBV) assessment of LE sequences and compared it with CMR acquired functional parameters.

Methods Cardiac MRI was performed in 51 patients, 23 female, aged 40 ± 17 years within the first week after onset of symptoms of acute myocarditis. PBV of LE areas were calculated using an individual signal intensity cut-off value of the myocardium in each patient. Parameters of global left ventricular function were determined from short-axis cine cardiac magnetic resonance sequences.

Results LE was detected in 40 patients (79%) and comprised at mean $5.6 \pm 7.8\%$ (0.5–36.3%) of overall myocardial pixel. Extent of LE did not correlate with left ventricular ejection fraction (LV-EF) (p = 0.4) nor with end-diastolic-volume (EDV) (p = 0.3). However, LV-EF of patients with a focal extent of LE (15/40 patients, 37.5%) was significantly lower (p < 0.03) than global LV function of patients with diffuse LE (25/40 patients; 62.5%) detected by PBV.

Conclusion Left ventricular ejection fraction was significantly higher in patients with diffuse myocarditis than in patients with focal myocarditis. Our approach of using a pixel-based volumetry of CMR late enhancement images based on individual signal intensity cut-off values offers an accurate quantitative assessment of disseminated myocarditis.

Size Matters! Impact of Gender, Age, Height, Weight and Overweight on Heart Dimensions

XIII – 3

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Background Many diseases cause changes of the size of the heart. The judgment whether a heart is normally sized or enlarged is important, particularly when heart dimensions determine patient management as for example in patients with valvular heart disease. However, the impact of overweight on heart dimensions and potential gender differences are unclear.

Methods We prospectively included 516 outpatients (women: n = 316, age 15–91 years, height 143–183 cm, weight 32–128 kg; men: n = 200; age 16–82 years, height 156–200 cm, weight 54–240 kg) without known cardiac disease and with unremarkable clinical status who underwent a standard echocardiographic evaluation. Multiple linear regressions on the impact of height, weight, age, gender, body mass index (BMI), and body surface area (BSA) on heart dimensions were performed.

Results Women had significantly smaller hearts: left ventricular end-diastolic diameter (EDD) 41.4 ± 3.4 vs 46.0 ± 3.8 mm; p = 0.0007; right ventricular EDD 28.0 ± 3.3 vs 32.2 ± 3.5 mm; p < 0.0001; left atrial area 14.2 ± 3.2 vs 16.3 ± 3.7 cm²; p < 0.0001; right atrial area 12.5 ± 2.9 vs 15.6 ± 3.9 cm²; p < 0.0001.

By multivariable analysis left ventricular dimensions were independently influenced by gender, height, BMI, and age (all p < 0.0001) while only gender and BSA had an independent impact on right ventricular size (all p < 0.0001). Both left and right atrium size, were independently influenced by BSA, gender, and age (all p < 0.0001).

Conclusions Women have smaller hearts than men, independent from height and weight. Furthermore, age, height, weight, and consequently BMI and BSA determine heart dimensions. These results are important as patient management in many cases depends on dis-

crepancies of heart dimensions from “normal values”. Normal values and cut-offs should therefore account for gender, age, and body size.

Refinement of Echocardiographic Criteria for Left Ventricular Non-Compaction XIII – 5

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Background and Aim Left ventricular noncompaction (LVNC) is a cardiac abnormality of unknown etiology whose echocardiographic criteria are still controversial. Cooperation between echocardiographic laboratories may contribute to uniformly accepted criteria.

Methods and Results Echocardiograms from patients proposed for inclusion into a registry were jointly reviewed. Three experts with 17–26 years experience with LVNC agreed on a common definition of LVNC: 1.) > 3 prominent trabeculous formations along the left ventricular endocardial border visible in end-diastole, distinct from papillary muscles, false tendons or aberrant bands; 2.) trabeculations move synchronously with and have the same echogenicity as the myocardium, 3.) trabeculations form the noncompacted part of a 2-layered myocardial structure, best visible at end-systole; 4.) perfusion of the intertrabecular spaces from the ventricular cavity is present at end-diastole on Color-Doppler echocardiography or contrast echocardiography, and 5.) absence of other cardiac anomalies. During 3 sessions 115 cases (37 % females, aged 18–87, mean 57 years) were reviewed. Eleven patients (18 % females, age 47–77, mean 60 years) were excluded because of < 4 trabeculations (n = 5), lack of a 2-layered myocardial structure (n = 1) and poor image quality (n = 5). The observers agreed on inclusion or exclusion in all cases. Consensus was achieved that measurements of the thickness of the myocardial layers, and calculation of the non-compacted:compacted ratio is investigator-dependent, and standards for measurements were impossible to achieve.

Conclusions When diagnosing LVNC, end-systolic as well as end-diastolic images have to be considered. > 3 trabeculations as well as a 2-layered myocardium are required for diagnosing LVNC. Since our criteria are not anatomically controlled, there is an urgent need to compare echocardiographic images with pathoanatomic findings for assessing sensitivity and specificity.

Anwendung der Stressechokardiographie in Österreich IV – 5

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Einleitung Unter den nicht-invasiven diagnostischen Untersuchungsmethoden in der Kardiologie ist die Stressechokardiographie (SE) ein kostengünstiges, sensitives Verfahren ohne Strahlenbelastung. Ziel unserer Studie war, die Anwendung der SE in Österreich zu erfassen.

Material und Methode Die Datenerhebung erfolgte mittels strukturiertem Fragebogen in Österreichs Spitälern mit internen bzw. spezifisch kardiologischen Abteilungen. Erhoben wurden die Häufigkeit der Anwendung, die Indikation, die Anzahl der Untersuchungen pro Abteilung, die Art der verwendeten Geräte und angewandten Techniken, der Zeitaufwand für die Untersuchung sowie auftretende Komplikationen.

Ergebnisse Es wurden nahezu alle Krankenhäuser mit internistischen Abteilungen erfasst. Im Zeitraum 2008/09 wurde in 66 von 132 Spitälern die SE angewendet. Kärnten hat die höchste, Steiermark die geringste Dichte an Abteilungen mit SE-Angebot. Die Untersuchungsfrequenzen über die Jahre seien rückgängig, gaben 48 % an. Pro Jahr führten 43 % der Abteilungen maximal 10 Untersuchungen durch, in nur 4 Abteilungen waren es mehr als 100 pro Jahr (Abbildung 15). Ein bis 13 Ärzte führten pro Krankenhaus die

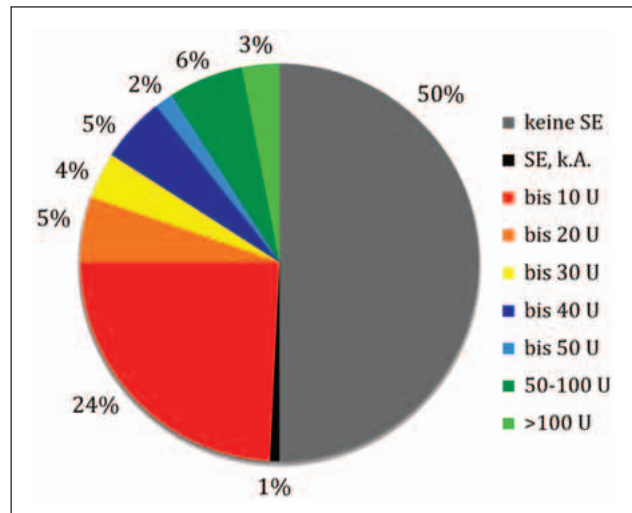


Abbildung 15: D. Weidenauer et al.

Untersuchung durch. In 75 % der Spitäler wurde die SE zur Evaluierung einer Low-Flow-Aortenstenose, in 74 % zur Ischämiediagnostik und in 54 % zur Vitalitätsdiagnostik angewendet. Im Beobachtungszeitraum wurden in Österreich insgesamt 1249 SE-Untersuchungen zur Ischämiediagnostik durchgeführt. Kontrastmittel kamen in 70 % der Abteilungen, in 20 % sowohl für die Endo- als auch für die Myokarddarstellung zur Anwendung. Die häufigste Belastungsform war die Dobutamin-SE. Tissue Doppler wurde in 56 %, „strain rate imaging“ in 20 % und 3D-Echo in 6 % der Krankenhäuser angewendet.

Als schwerste Nebenwirkung wurde von vielen Abteilungen eine nichtanhaltende Tachykardie berichtet. Hämodynamisch relevante Arrhythmien traten in 7 Fällen auf: 3× Kammerflimmern, 4× VT, in 2 Fällen kam es zu einem tödlichen Ausgang. Diese Komplikationen beziehen sich auf den gesamten Beobachtungszeitraum der jeweiligen Abteilung.

Diskussion Da 74 % aller internistischen Abteilungen Österreichs die SE nicht oder maximal 10× pro Jahr nutzen und in nur 4 Abteilungen die in Qualitätsrichtlinien empfohlene Untersuchungszahl (100 Untersuchungen/Jahr) erreicht wird, ergeben sich mehrere Fragen: Warum wird die SE in Österreich so selten angewendet? Können die Qualitätsanforderungen von den Untersuchern bei geringen Fallzahlen erfüllt werden? Erklärt die fehlende Verrechnbarkeit den *Status quo*? Mit welchen Strategien könnte die Situation verbessert werden? Bei steigenden Spitalskosten und Patientenzahlen sollte man nicht zuletzt aus ökonomischer Sicht überlegen, ob man einen seiner „besten Spieler“ (hohe Spezifität, hohe Sensitivität, fehlende Strahlenbelastung, kostengünstig) auf der „Ersatzbank“ lässt?

Projekt „CQI Echo“ – Systematisches Qualitätsmanagement im Echolabor XIII – 4

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Einleitung In einem 2009 publizierten Positionspapier der European Association of Echocardiography (EAE) wird ein systematisches Qualitätsmanagement in den Referenzzentren für Echokardiographie empfohlen. Folgende Bereiche des Untersuchungsprozesses sollen dabei regelmäßig evaluiert werden: Patientenselektion, Durchführung der Untersuchung, Interpretation der Ergebnisse und Befunderstellung. Auf Basis dieser Empfehlungen war das Ziel der vorliegenden Untersuchung, den Qualitätsstandard der echokardiographischen Befunde zu analysieren und durch gezielte Maßnahmen zu verbessern. Die Grundvoraussetzungen wie die Kenntnis der wichtigsten Kennzahlen des Echolabors sowie ein schriftlich festgelegter standardisierter Ablauf der Untersuchung

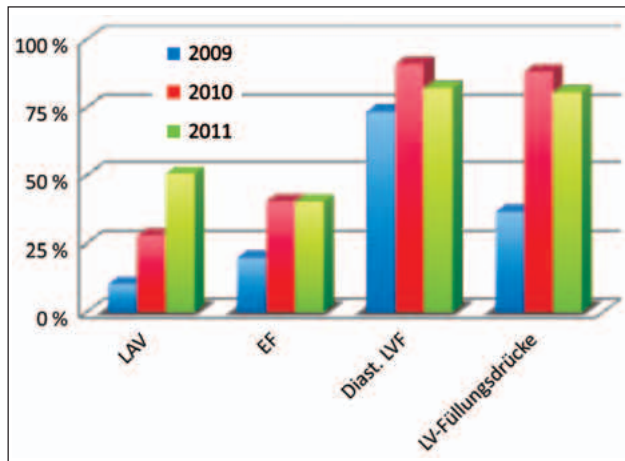


Abbildung 16: W. Weihs et al.

und Befunderstellung sind bereits seit mehreren Jahren etabliert. Die Untersuchung ist ein Teil des Projektes „CQI Echo“ (Continuous Quality Improvement of Echocardiography).

Methoden Die Echokardiographien werden von insgesamt 10 erfahrenen Untersuchern vorgenommen und in einer digitalen Datenbank (EchoPAC®) gespeichert. Einmal jährlich werden die Befunde aller Mitarbeiter stichprobenartig nach folgenden Kriterien überprüft: Befund vorhanden und komplett (Empfehlungen der EAE), Anteil der Normalbefunde (Ziel: $< 1/3$), Anzahl der Bilder/Loops pro Untersuchung, Messung des linksatrialen Volumens (LAV) und der linksventrikulären Volumina/EF nach der Simpson-Methode, Beurteilung der diastolischen Linksventrikelfunktion und der Füllungsdrücke entsprechend den aktuellen Empfehlungen der EAE. Zur Optimierung der Qualitätskriterien wurden folgende Maßnahmen ergriffen: gemeinsame Besprechungen der Ergebnisse, Schulungen, Anpassung der Software und Hardware an die Arbeitsabläufe (Erweiterung der Befundkonsolen).

Ergebnisse Es wurden 3 Analysen (2009, 2010, 2011) an insgesamt 810 echokardiographischen Befunden durchgeführt. Der Anteil fehlender Befunde wurde von 5,6 % auf 0,7 %, jener der inkompletten Befunde von 8,9 % auf 1,5 % reduziert. Der Anteil an Normalbefunden lag in allen 3 Analysen < 25 %. Die Anzahl der Standbilder/Loops pro Untersuchung nahm von 17 auf 21 zu. Die Messungen des linksatrialen Volumens (10 % vs. 40 %), der linksventrikulären Volumina/EF (20 % vs. 34 %), der LV-Füllungsdrücke (41 % vs. 80 %) konnten deutlich gesteigert werden (Abbildung 16). Die Beurteilung der diastolischen Linksventrikelfunktion lag in allen Analysen gleichbleibend > 75 %. Bei den pathologischen Echokardiographien (= alle außer den Normalbefunden) lagen die Werte mit 51 %, 40 % und 82 % noch höher.

Schlussfolgerung Eine systematische Evaluierung der echokardiographischen Untersuchungen nach definierten Qualitätskriterien ist neben der Kenntnis der wichtigsten Kennzahlen eine entscheidende Maßnahme zur Qualitätssteigerung im Echolabor. Standardisierte Abläufe der echokardiographischen Untersuchung sowie Befunderstellung, welche sich an aktuellen internationalen Empfehlungen orientieren sollten, sind dabei die Grundvoraussetzungen.

■ Chirurgie/Surgery

Angiographic Evaluation of Robotically Assisted Coronary Anastomoses Using Conventional and CT-Angiography

V – 2

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Objectives Robotic technology enables totally endoscopic coronary artery bypass grafting on the arrested or on the beating heart. The aim of the study was to investigate the short-term quality of robotically sutured anastomoses by means of invasive graft angiography and multi-detector CT angiography.

Methods Two hundred seventy-six patients received robotically sutured coronary anastomoses using the da Vinci telemanipulation system. 140 (51%) and 264 (96%) underwent postoperative conventional graft angiography and CT angiography respectively. The vast majority of the patients underwent single or double arrested heart TECAB (207/276), 21 patients had a BH TECAB, 12 and 3 patients received a sequential or Y-grafting respectively. 48 patients underwent robotically sutured anastomosis through conventional sternotomy.

Results The median interval from surgery to coronary angiography was 3 months (0.25–72 months). The median interval to CT angiography was also 3 months (0.25–8 months). 160/319 (50%) robotically sutured anastomoses were evaluated by conventional graft angiography. There were 3 anastomoses with a non-significant angiographic stenosis, 2 anastomoses with a relevant stenosis > 50 %, 1 anastomotic occlusion, and 1 anastomosis to an incorrect target vessel. CT angiography revealed 1 anastomotic stenosis, 2 grafts with a string phenomenon as a result of competitive flow, 3 graft occlusions and one incorrect grafting site. In 153/160 (96%) anastomoses evaluated by invasive angiography a perfect result was detected. Accordingly CT angiography revealed a perfect postoperative result in 298/305 evaluated anastomoses (98%). CT angiography could very well detect relevant angiographic stenosis, graft occlusion and incorrect target vessel anastomosis in all cases.

Conclusion Robotically sutured anastomosis on the arrested or on the beating heart, as well as robotically-assisted composite grafting can be performed with satisfying angiographic results. CT angiography can be used as an alternative for postoperative evaluation of relevant anastomotic dysfunction.

Mid-Term Results after Robotically Assisted Totally Endoscopic Repair of Intraatrial Communications

V – 1

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Objectives Repair of atrial septal defects is increasingly performed via mini-thoracotomy or in a totally endoscopic fashion using robotic technology. Perioperative results of small series of totally endoscopic ASD-repair have been reported in the literature but the long-term results of the procedure are still unknown.

Methods Seventy two patients (21 male, 51 females, median age 38 [16–62]) were operated at 2 institutions using the da Vinci robotic system. Pathology of interatrial communication included an atrial septal defect II in 56 patients, a patent foramen ovale in 15 patients and a sinus venosus defect in 1 patient. Nine of the patients had a malpositioning of an atrial septal occluder which had to be surgically removed. Twenty nine patients received a patch reconstruction and 43 of the patients had a direct closure. The major perioperative and mid-term results were evaluated by echocardiography as well as clinical follow-up.

Results Median operation time was 310 min (186–650), cardiopulmonary bypass time was 135 min (55–269), and aortic cross clamp time was 70 min (33–164). One conversion to mini-thorac-

otomy was needed. Two patients had to be reoperated due to residual shunt detected before discharge. The mean follow-up was 29 months (0.25–94). No stroke, or other major cardiac event was reported during follow-up. The median NYHA classification was 1 (1–3) during follow-up and the median ejection fraction was 70% (65–80). No additional residual shunt was detected after discharge.

Conclusion The midterm results of robotically assisted totally endoscopic atrial septal defect repair are very satisfactory and well comparable with conventional and mini-thoracotomy approaches. Complex defects including removal of malpositioned occluders can be repaired using endoscopic methods.

Mechanisms of Symptomatic Spinal Cord Ischemia after TEVAR-Insights from the European Registry of Endovascular Aortic Repair Complications (EuREC)

V – 3

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Background Mechanisms of symptomatic spinal cord ischemia after thoracic endovascular aortic repair (TEVAR) are not sufficiently identified. We hypothesized that a simultaneous closure of two independent vascular territories or the combination with prolonged hypotension may be associated with symptomatic spinal cord ischemia.

Methods and Results We developed a risk model including prolonged intraoperative hypotension or simultaneous closure of at least two spinal cord blood supplying territories for development of symptomatic spinal cord ischemia with a positive predictive value 0.75 (CI: 0.38–0.75) and negative predictive value of 1.00 (CI: 0.98–1.00). This risk model was applied to the European Registry on Endovascular Aortic Repair Complications (EuREC) registry; between 2002 and 2010, 19 participating centers reported a total of 38 patients with symptomatic spinal cord ischemia (1.7%). A substantial to almost perfect correlation between the proposed risk model and the occurrence of symptomatic spinal cord ischemia could be observed (Kappa 0.77; CI: 0.65–0.90). Bootstrapping underlined the robustness of the proposed risk prediction model of prolonged intraoperative hypotension or simultaneous closure of at least two spinal cord blood supplying territories in the development of symptomatic spinal cord ischemia after TEVAR (CI: 0.63–0.88).

Conclusions Extensive coverage of intercostal arteries by TEVAR alone is not associated with symptomatic spinal cord ischemia as sacrifice of one spinal cord blood supplying vascular territory is irrelevant. Simultaneous closure of at least two supplying vascular territories is highly relevant, especially in the combination with prolonged intraoperative hypotension. As such, these results further emphasize preservation of the left subclavian artery.

Mortality and Neurologic Injury After Surgical Repair with Hypothermic Circulatory Arrest in Acute and Chronic Proximal Thoracic Aortic Pathology – Analysis of Different Age Groups

BAI

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Aims To determine incidence and risk factors for mortality and neurologic injury in patients undergoing surgical repair with hypothermic circulatory arrest (HCA) in acute and chronic thoracic aortic pathology in different age groups.

Methods and Results We analyzed 523 consecutive patients undergoing repair of acute and chronic thoracic aortic pathology between 2005 and 2010. Acute type A aortic dissection was the underlying pathology in 206 patients (13.6% $\geq$ 75a) and chronic ascending aortic aneurysm in 317 patients (16.8% $\geq$ 75a). Pre- and intraoperative factors were evaluated by means of stepwise logistic regression analysis to determine risk factors of mortality and neurologic injury. In acute type A aortic dissection, overall mortality was 9.7% (< 75 years, 8.8%; $\geq$ 75 years, 17.9%; $p = 0.169$) whereas over-

all mortality in chronic ascending aortic aneurysms was 2.2% (< 75 years, 1.5%; $\geq$ 75 years, 5.9%; $p = 0.089$). In acute type A aortic dissection, overall neurologic injury was 8% (< 75 years, 7.3%; $\geq$ 75 years, 14.3%; $p = 0.260$) whereas overall neurologic injury in chronic ascending aortic aneurysms was 2.8% (< 75 years, 2.7%; $\geq$ 75 years, 3.8%; $p = 0.650$). Stepwise logistic regression analysis revealed duration of surgery (OR 1.009; CI: 1.005–1.012; $p = 0.000$), duration of HCA (OR 1.016; CI: 1.001–1.031; $p = 0.037$), logistic EuroSCORE levels (OR 1.035; CI: 1.010–1.060; $p = 0.005$), but not age $\geq$ 75 years (OR 1.096; CI: 0.314–3.825; $p = 0.886$) as independent predictors of mortality. Duration of HCA (OR 1.014; CI: 1.002–1.027; $p = 0.027$), logistic EuroSCORE levels (OR 1.028; CI: 1.005–1.052; $p = 0.019$), but not age $\geq$ 75 years (OR 1.019; CI: 0.307–3.383; $p = 0.976$) were independent predictors of neurologic injury.

Conclusions Age $\geq$ 75 years is not associated with prohibitively increased risk for mortality and neurologic injury in patients undergoing surgical repair for acute and chronic thoracic aortic pathology using HCA. Duration of surgery and duration of HCA as well as logistic EuroSCORE levels, reflecting the extent and severity of the underlying disease, are independent risk factors for adverse outcome. As such, advanced age alone should no longer be considered as a contraindication for surgery in these patients.

The Influence of Gender on Mortality in Patients After Thoracic Endovascular Aortic Repair

V – 4

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Aims The aim of this study was to determine if gender affects mortality in patients after thoracic endovascular aortic repair (TEVAR).

Methods We retrospectively analyzed 286 consecutive patients undergoing TEVAR at our institution during a 12-year period (female 29%, median age 69a). Chronic health conditions, risk factors as well as early and long-term outcome were assessed. Follow-up data were available in all patients.

Results For female gender, 1-year survival and 5-year survival was 84% and 56% vs 83% and 60% for male gender. No significant gender influence was observed (OR 0.96; 95%-CI: 0.59–1.56). Furthermore, no significant gender influence could be observed according to the individual indication atherosclerotic aneurysms (OR 0.78; 95%-CI: 0.41–1.47), acute type B dissections (OR 0.78; 95%-CI: 0.21–2.83), penetrating ulcers/intramural hematoma (OR 1.48; 95%-CI: 0.53–4.19) as well as traumatic aortic lesions (OR 1.48; 95%-CI: 0.53–4.19). Age (OR 3.6; 95%-CI: 1.24–10.45) as well as COPD (OR 3.09; 95%-CI: 0.98–9.73) were independent predictors of mortality in females.

Conclusions Gender does not affect mortality in patients after TEVAR irrespective of the underlying indication, atherosclerotic aneurysms, acute type B dissections, penetrating ulcers/intramural hematoma as well as traumatic aortic lesions. Classical risk factors such as age and the presence of COPD at the time of TEVAR remain the most important risk factors in females.

Minimally Invasive Mitral Valve Surgery – Technique and Perioperative Results in 341 Patients

V – 5

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Objective Minimally invasive intracardiac surgery through a lateral minithoracotomy was introduced in the mid 1990s with a then prohibitive complication and mortality rate. Diffusion of the technique is still limited although results are now excellent in specialized centers. The results of Austria's first minimally invasive mitral valve surgery program are analyzed.

Methods From 03/2001 to 01/2011 341 patients underwent minimally invasive mitral valve surgery at our institution. Additional tricuspid annuloplasty (TVP) was indicated for severe tricuspid regurgitation or tricuspid annular dilatation > 40 mm. Left atrial ablation (RF-Maze) was performed using unipolar radiofrequency for chronic AF.

Results Perioperative mortality was 0.6% (2 patients). After implementation of the minimally invasive valve program TVP or Maze procedure in addition to MVP or MVR was added after 54 successful isolated MV procedures. 295 patients had mitral valve repair, in 46 elective prosthetic mitral valve replacement was performed. 4 patients (1,2%) had intraoperative conversion to valve replacement for failed repair, 9 patients (2,6%) needed conversion to median sternotomy for intraoperative complications. All pathologies amenable to valve repair were addressed by the minimally invasive technique, annuloplasty ring sizes ranged from 24–40 mm (mean 32,7 mm). Repair techniques included predominantly leaflet resection, sliding leaflet plasty, PTFE chordae insertion, papillary muscle splitting, papillary muscle transposition, chordal transfer, pericardial patch plasty, prosthetic ring annuloplasty and prosthetic valve replacement.

Conclusions Minimally invasive mitral valve surgery can be performed safely with excellent results if the classic repair techniques are employed. If required, additional procedures like TVP, RF-Maze and others can be performed by the same approach. The minimally invasive access is the procedure of choice in our institution for most mitral valve procedures excluding valves with severe annular calcification.

Wahrnehmungsstörungen und kognitive Residuen nach kardiochirurgischen Eingriffen

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Einleitung Das postoperative Delir und die kognitiven Residuen sind fundierte und gut bekannte Komplikationen nach kardiochirurgischen Eingriffen. Wahrnehmungsstörungen und vor allem Alpträume als Symptome des Delirs wurden jedoch bislang als Ausdruck für die emotionale Belastung nicht speziell beachtet. Ziel der Studie war es, die Inzidenzrate und den Typus von Wahrnehmungsstörungen zu evaluieren.

Material und Methode Bei 28 Patienten (67,9 % Männer, Alter: 74,18 Jahre $\pm$ 5,62, Intervention: 57 % CABG, 43 % AKE) wurde das Ausmaß kognitiver Residuen mittels Mini-Mental-State-Examination (MMSE) zu 5 Messzeitpunkten (prä-, postoperativ, 1. und 4. Woche des Anschlussheilverfahrens [AHV], 3-Monats-Follow-up) erfasst.

Ergebnisse 42,9 % der Patienten berichteten retrospektiv im AHV von Wahrnehmungsstörungen mit verschiedener Intensität (akustische, optische Halluzinationen, Zönanthesien, Mikro-, Makropsien, Metamorphopsien, Veränderungen der Wahrnehmungsintensität). Es bestand kein signifikanter Zusammenhang zwischen der Intervention und der Wahrnehmungsstörungen. 7,1 % der Patienten hatten ein Delir mit der Notwendigkeit zur psychopharmakologischen Behandlung. Patienten nach einem AKE ($26,44 \pm 2,29$) zeigten geringere postoperative MMSE-Werte als CABG-Patienten ($28,57 \pm 1,01$, $t[21] = 3,05$; $p < 0,01$), während präoperativ kein Unterschied bestand. Es zeigten sich keine signifikanten Veränderungen im MMSE-Punktwert in den weiteren Testreihen. Wahrnehmungsstörungen waren mit einer geringeren Operationsdauer assoziiert ($t[19] = 4,47$; $p < 0,01$). EKZ und AKZ zeigten keine signifikanten Effekte hinsichtlich der Wahrnehmungssymptomatik.

Diskussion Kognitive Residuen nach kardiochirurgischen Eingriffen sind aus der Literatur gut bekannte Komplikationen und beeinträchtigen den Patienten ohne Bewusstseinsveränderung. Die Ursachen für den Patienten belastende Wahrnehmungsstörungen sind weitgehend unbekannt. Die extrakorporale Zirkulation wird eher für das Auftreten von kognitiven Residuen verantwortlich gemacht. Mögliche Auswirkungen durch die medikamentöse Behandlung (Narkotika, Morphin-Derivate) sowie die Elimination orientierungsfördernder Maßnahmen in den Intensiv- und Überwachungs-Stationen sind hinsichtlich der Ätiologie von Wahrnehmungsstörungen und auch von kognitiven Residuen in diesem Zusammenhang zu diskutieren.

Hybrid Treatment of Aortic Stenosis and Coronary Artery Disease by Transcatheter Aortic Valve Replacement and Percutaneous Coronary Intervention

V – 7

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Background The presence of coronary artery disease (CAD) is a significant risk factor for increased mortality in patients undergoing aortic valve replacement for severe aortic stenosis (AS). Transcatheter aortic valve replacement shows promising results. The aim of the study was to analyze the short and mid-term outcome of hybrid treatment of patients with AS and CAD by percutaneous coronary intervention (PCI) and transcatheter aortic valve implantation (TAVI).

Methods From February 2008 till December 2010, 11 patients with severe AS and CAD were treated with TAVI and PCI; the male:female ratio was 8:3. The median age was 82 years (range 79–88) and median logistic EURO Score 29.64% (range 8.1–74.5%). The follow up period was 262 days (range 43–564 days).

Results All 10 patients received successfully a biological aortic valve implantation. Twelve bare metal coronary stents were implanted (2 patients received 2 stents). Median interval between PCI and TAVI was 29 days (range 2–210 days). We observed no perioperative mortality (30-days). Three patients died during follow up (between 43–84 days post-operative). No coronary or valvular re-intervention was required.

Conclusion Combined treatment of concomitant CAD and AS by transcatheter procedures for high risk patients provides satisfactory peri-operative and 1-year results.

Intraoperative and Intermediate-Term Results of an Interdisciplinary Transcatheter Aortic Valve Implantation (TAVI) Program

V – 6

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Background The aim of the study was to evaluate results of first 3 years of our institutional TAVI program in high risk patients, who were excluded from conventional surgical therapy due to an increased operative risk.

Methods From February 2008 till December 2010, 52 cases with severe aortic stenosis were included in our TAVI-program by a cardiosurgical-cardiological team. The access-rate was transapical in 26 patients, in 18 transfemoral and in 3 transaxillary. The median age was 82 years (range 58–94) and median EURO Score 29.6% (range 6.2–74.5%). 14/51 patients have had previous cardiac surgery. The median follow up period was 304 days (range 1–1058 days).

Results 48 patients had successful TAVI, 2 needed to be converted from initial TAVI to conventional replacement, 2 had balloon valvuloplasty only and 11 patients needed PCI before TAVI. The perioperative mortality (30 days) was 5.88% (3 patients) and during follow up 13.73% (7 patients). No patient suffered myocardial infarction, 2 had peri-operative stroke and 2 during follow up. In 9 patients peri-operative renal failure needing hemofiltrations was observed.

Conclusion Due to interdisciplinary cooperation of cardiac-surgery and cardiology our TAVI program implying transfemoral, transapical and transaxillary excess could be established with low complication- and mortality-rate.

Minimally Invasive Double Valve Surgery Can Safely be Combined with Additional Procedures V – 9

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Objective Although minimally invasive cardiac surgery is well established, diffusion of the technique is limited. Contraindications are not only conditional on the disease but also on the surgeon's experience and attitude. To evaluate disease related contraindications we investigated our patients receiving minimally invasive double valve surgery with or without additional procedures.

Methods 331 patients undergoing minimally invasive mitral valve surgery between 2001 and 2010 were analyzed. Additional tricuspid annuloplasty (TVP) was indicated for severe tricuspid regurgitation or tricuspid annular dilatation > 40 mm. Left atrial ablation (RF-maze) was performed using unipolar radiofrequency.

Results After implementation of the minimally invasive valve program, TVP was added after 54 successful isolated MV-procedures. 70 patients (25.3%) had combined mitral and tricuspid surgery. TV surgery was always performed as ring annuloplasty. 17 double valve patients had additional RF-maze. 12 patients underwent closure of the left atrial appendage (LAA), 13 patients underwent additional PFO closure. Mortality in the double valve group was 1.4% and 0.45% in the MV only group ($p = n.s.$).

Conclusions Minimally invasive TVP can be added safely to MV surgery. Further procedures like RF-maze, LAA- or PFO-closure can also safely be performed. Neither mortality nor major complications related to the combined procedures were increased.

Minimally Invasive Mitral Valve Reconstruction on the Fibrillating Heart – An Attractive Surgical Strategy for High-risk Patients V – 8

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Objective Reoperative mitral valve surgery is associated with high operative risk. An aortic valve prosthesis (AVP) can severely impair visualization to the mitral valve, so that these patients are often denied surgery. Furthermore, patients with severely calcified aorta are usually considered inoperable.

Mitral valve repair without aortic crossclamping on the fibrillating heart may be an attractive surgical option for these extremely high-risk patients.

Methods We report the series of 7 patients undergoing mitral valve surgery via a right-sided minithoracotomy without aortic crossclamping on the fibrillating heart. Three patients had an AVP in situ, 3 patients underwent CABG before, 2 patients presented with porcelain aorta. Reconstruction was possible in 6 patients, 1 patient, who underwent mitral valve repair plus CABG before, received mitral valve replacement. Cannulation for cardiopulmonary bypass was performed femorally in 3 and via the axillary artery in 4 patients.

Results No fatalities were observed. One patient required thoracotomy for bleeding. One patient suffered from ischemic embolism to the leg due to the arterial pressure line. The postoperative course was uneventful in all other cases. No patient presented with significant residual mitral insufficiency in control echocardiography.

Conclusion Mitral valve reconstruction via a right-sided minithoracotomy is an attractive surgical option in high-risk reoperative settings.

Minimally Invasive Repair of Atrial Septal Defects – Ten Years of Experience V – 10

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Introduction Atrial Septal Defects (ASD) apply for 5–10% of congenital heart disease. The extent of the defect rises from a persistent foramen ovale to the sinus venosus defect and anomalous drainage of one or more pulmonary veins (PAPVC). We reviewed our experience on the minimally invasive surgical technique.

Methods We reviewed all patients undergoing minimally invasive ASD-closure at our institution from 2001–2010. Analysis was performed concerning ASD-pathology, patient characteristics and operative variables.

Results From 01/2001 through 12/2010, 38 patients underwent minimally invasive ASD-closure. 20 defects were closed directly, 18 by patch. Since 2007, also Sinus Venosus Defects are successfully treated minimally invasive ($n = 10$). Intraatrial baffle correction of PAPVC and reconstruction of vena cava superior is feasible ($n = 4$). The mean age was 40.7 years, mean weight was 70.2 kg. Mean aortic crossclamp time was 53.7 min. There was no fatality and no severe perioperative complications. One patient experienced occlusion of femoral artery late postoperatively (2.6%).

Conclusion Minimally invasive correction of defects of the intraatrial septum has successfully been introduced into clinical routine at our institution. Operative morbidity is very low and even complex reconstructions can be performed with good results. Median sternotomy is only performed in smaller children any longer at our institution.

Sorin Freedom SOLO: Häodynamisches Outcome nach operativem Aortenklappenersatz mit einer Stentless-Perikardprothese – Eine retrospektive Analyse

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Hintergrund Der operative Aortenklappenersatz gilt als Standardtherapie der symptomatischen und schweren Aortenklappenstenose. Mit der Einführung biologischer Substitute konnte die bei der Implantation mechanischer Prothesen notwendige lebenslange Antikoagulation umgangen werden. Vor allem Patienten zwischen 65 und 75 J. profitieren vom Einsatz biologischer Prothesen. Unter ihnen zeigen gerüstlose Modelle, wie die Freedom-SOLO-Perikardprothese, eine ausgezeichnete Häodynamik mit niedrigen transvalvulären Druckgradienten, einer optimalen Flussgeschwindigkeit sowie einer Zunahme der effektiven Klappenöffnungsfläche. Ziel dieser Studie war die Erfassung des häodynamischen Outcomes nach Implantation der Sorin-Freedom-SOLO-Prothese.

Methoden Die Studie wurde als retrospektive Datenanalyse durchgeführt. Eingeschlossen wurden konsekutiv alle Patienten, welche im Zeitraum zwischen Jänner 2006 bis einschließlich September 2009 an der Herzchirurgie des Krankenhauses Hietzing einen AKE mit Implantation der Freedom-SOLO-Prothese erhielten. Zur Beurteilung wurden die postoperativen und Follow-up-transthorakalechokardiographischen Untersuchungen herangezogen.

Resultate 74 Patienten (42 Frauen, 32 Männer, mittleres Alter $74,6 \pm 7,6$ Jahre) erhielten eine Freedom-SOLO-Prothese in Aortenposition, jeweils 50 % isolierter bzw. kombinierter AKE. Der durchschnittliche „logistic EuroScore“ betrug $11,0 \pm 7,6$. Die durchschnittliche EKZ bzw. AKZ lag bei $117,4 \pm 29,6$ bzw. $78,3 \pm 22,3$ Minuten. Das FU erfolgte durchschnittlich nach $14,3 \pm 8,2$ Monaten. Der maximale bzw. mittlere Druckgradient betrug früh-postoperativ $19,0 \pm 8,8$ bzw. $10,9 \pm 5,4$ mmHg PO und $19,9 \pm 12,2$ bzw. $11,22 \pm 7,8$ im FU. Kein Patient verstarb während des Eingriffs. Die 30-Tages-Mortalität lag bei 6,8 %. Mit 36 % und 30 % waren Pleuraerguss und vorübergehendes VHF die häufigsten Komplikationen. Nur 2 Patienten musste wegen eines paravalvulären Leaks reoperiert werden.

Konklusion Die Sorin-Freedom-SOLO-Prothese zeichnet sich durch ein gutes hämodynamisches Profil mit niedrigen transvalvulären Druckgradienten bzw. Flussgeschwindigkeiten aus. Die durch die vereinfachte Implantation relativ kurze Aortenklammzeit und extrakorporale Zirkulationszeit wie auch die niedrigen, postoperativen Druckgradienten stellen die Freedom-SOLO-Prothese als eine sichere und effektive Alternative zu konventionellen Bioprothesen dar.

■ Kardiomyopathie/Cardiomyopathy (CMP)

Seizure-Associated Tako-Tsubo-Cardiomyopathy

XIII – 7

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Background Tako-Tsubo-cardiomyopathy (TTC) is characterized by chest pain, dyspnoea, electrocardiographic changes resembling an acute coronary syndrome, and transient wall-motion abnormalities in the absence of coronary artery obstruction. TTC occurs frequently after emotional or physical stress. Seizures have been reported as triggers of TTC. It is unknown if seizure-associated TTC differs from TTC associated with other triggers. Aim of the review was to compare seizure-associated TTC with TTC-series comprising > 30 patients.

Methods and Results Own observations and literature search identified 36 seizure-associated TTC cases (6 male, mean-age 61.5 years). Seizure-type were tonic-clonic (n = 13), generalized (n = 5), status epilepticus (n = 6), grand mal (n = 2) or not reported (n = 13). Twelve patients had a history of epilepsy, in 15 patients TTC-associated seizure was the first or the information was not given (n = 9). In 17 patients TTC occurred immediately after the seizure, in 9 patients 1–72 hours postictally, and in 10 patients, the interval was not reported. In 20 patients neurologic, in 14 psychiatric disorders were reported. Seventeen patients suffered from medical comorbidities like arterial hypertension (n = 11), hyponatremia (n = 2) or cancer (n = 2). Compared with 974 patients reported in TTC-series, patients with seizure-associated TTC were younger (61.5 vs 68.5 years; $p < 0.0001$), more frequently males (17 vs 9%; $p = 0.004$), had less frequently chest pain (6 vs 76%; $p < 0.005$), cardiogenic shock (25 vs. 8%; $p = 0.003$) and recurrence (14 vs 3%; $p = 0.004$).

Interpretation Seizure-associated TTC manifests frequently as sudden hemodynamic deterioration which could result in patient's death in the absence of adequate help. Probably, some cases of sudden unexpected death in epilepsy are attributable to TTC.

Prognostic Significance of Family History in Cardiomyopathy

XIII – 8

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Aims Family history plays an important role in ischemic cardiomyopathy (ICM) as well as in non-ischemic cardiomyopathies (NICM). Familial screening of patients with dilated cardiomyopathy has been shown to allow for an early diagnosis of the disease in family members and thus can improve survival in these patients. However, it is unclear if a positive family history and hence a higher propensity for a genetic background of the disease has an influence on survival in unselected patients with cardiomyopathy (CM). Our aim was to compare the prognosis of ICM and NICM patients with positive and negative family history in order to assess the influence of family history on survival.

Methods and Results From 2000 to 2009 clinical and laboratory variables of 1223 consecutive outdoor patients with heart failure were evaluated. Follow-up (mean 39.4 months) and information on family history of CM and aetiology of CM were available in 1098 patients. The end point was defined as death from any cause or heart

transplantation. NICM patients (n = 767) had a positive family history in 24.8%, with no significant difference in age at presentation between groups. Patients with ICM (n = 331) had a positive family history in 24.2%; those with positive family history were younger at presentation (61.7 vs 65 years; $p = 0.009$). There were no significant differences in NYHA classes between patients with or without family history in either group. Sex-stratified bivariate Cox regression analysis showed a significant association of positive family history with reduced transplant-free survival in NICM patients (HR 1.36 [SD 1.01–1.82; $p = 0.041$]) but not in ICM patients (HR 0.86 [SD 0.6–1.24; $p = 0.432$]).

Conclusion In this cohort of unselected patients with CM the propensity for a genetic background was comparable high in ICM and NICM. In NICM patients a positive family history was associated with worse prognosis. These results further highlight the importance of a meticulous family history in particular in NICM patients not least in view of evolving prospects in genetic testing.

Immunosuppressive Therapy in Biopsy-proven Virus-negative Inflammatory Cardiomyopathy

XIII – 9

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Introduction The role of immunosuppression in the treatment of myocarditis is still debated. Hence it was the aim of our single center study to investigate the response to immunosuppressive therapy in patients with virus-negative inflammatory myocarditis (autoreactive virus-negative inflammatory cardiomyopathy).

Methods and Materials From 2001 to February 2011, 416 patients with suspected myocarditis were subjected to left ventricular endomyocardial biopsy and right cardiac catheterization.

Inflammatory, virus-negative myocarditis was diagnosed in 69 patients, defined by immunohistochemical analysis quantifying the number of infiltrating activated lymphocytes ($> 7/\text{mm}^2$) and leucocytes ($> 14/\text{mm}^2$) and with conventional histological criteria (WHO Task force/Dallas Criteria). The presence of persisting viral genome was excluded by polymerase chain reaction analysis. Patients were tested for CMV, EBV, PVB19, HHV6,8, HSV1,2 using qualitative PCR in endomyocardial biopsy and in whole blood.

In addition serological antibody screening was applied for all above viruses and for antimyocardial antibodies.

57 patients were treated with azathioprine and prednisone for 6 months in addition to conventional therapy for heart failure.

Up to now clinical follow-up, control endomyocardial biopsy, and right heart catheter results after 6 month therapy are available in 31 patients. Clinical 6-month follow-up only is available in 9 patients.

Results Mean age at study entry was 47 (range 18–68, 33% female). Immunosuppression was well tolerated and resulted in an improvement of LV-ejection fraction ($26.7 \pm 14.0\%$ – $39.0 \pm 13.6\%$; $p < 0.0001$), and NYHA class (2.4 ± 0.09 – 1.5 ± 0.6 ; $p < 0.0001$), and a decrease of NTproBNP (995 ng/l [IQR 249–2460]–294 ng/l [IQR 89.7–764.2]; $p = 0.009$). Cardiac output increased from $3.8 \pm 0.9\text{ l/min}$ – $4.5 \pm 0.9\text{ l/min}$ ($p = 0.013$); PCWP decreased from $19.5 \pm 9.9\text{ mmHg}$ – $12.5 \pm 4.8\text{ mmHg}$ ($p = 0.001$).

Conclusion Patients with evidence of inflammatory, virus-negative myocarditis/inflammatory cardiomyopathy clearly benefit from immunosuppressive therapy on top of conventional HF therapy.

An Unusual Manifestation of Tako-Tsubo-Cardiomyopathy

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Introduction Tako-Tsubo-cardiomyopathy is characterized by typical symptoms of cardiac ischemia and transient abnormalities of left ventricular wall motion (usually “apical ballooning”) in absence of significant coronary heart disease.

We report the case of a 79-year-old man with a recent manifestation of cardiogenic syncope, presenting an unusual “inverted” pattern of Tako-Tsubo.

Methods We evaluated our patient by 12-lead ECG, Holter monitoring, echocardiography and coronary angiography. A periodical follow-up has been performed.

Results We present a 79-year-old man, recently suffering from recurrent cardiogenic syncope without any other cardiac symptoms. During the Holter monitoring a symptomatic episode of non-sustained ventricular tachycardia was detected. In coronary angiography vascular morphology was normal; ventriculography showed an akinesis of the basal left ventricular segments. We suspected an “inverted Tako-Tsubo”, although detailed medical history could not clearly identify any stress factors. Wall motion abnormalities disappeared during a follow-up period of four weeks, since then syncopal events have not occurred any more.

Discussion Tako-Tsubo-Cardiomyopathy is a rather variable entity. Besides the common clinical and morphologic presentation, atypical manifestations have to be mentioned. Life-threatening arrhythmia is a feared complication concerning all variants of Tako-Tsubo.

Cardiac Devices and Neuromuscular Disorders in Left Ventricular Non-Compaction XIII – 6

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Background Left ventricular hypertrabeculation/noncompaction (LVHT) is associated with arrhythmias and neuromuscular disorders (NMD). Cardiac implantable electronic devices (CIED) like anti-bradycardic pacemakers (PM), implantable cardioverters/defibrillators (ICD) and cardiac resynchronization therapy (CRT) are beneficial but have also disadvantages and complications. Aim of the study was to assess outcome of LVHT-patients with and without CIED and the association with NMD.

Methods Included were patients with LVHT diagnosed echocardiographically between 1995 and 2010. All patients underwent a baseline cardiologic examination and were invited for a neurological investigation. During May 2010, the patients were screened for CIED.

Results In 154 LVHT-patients (28% female, age 53 ± 16 , 14–94 years) during a mean observation time of 65 months, the annual mortality was 4.81%. Twenty-four patients had CIED implanted: ICD $n = 5$, CRT $n = 3$, ICD/CRT $n = 9$, PM $n = 6$ and PM/ICD/CRT $n = 1$. Patients with CIED had more often heart failure (96 vs 38%; $p < 0.001$), left bundle-branch-block (58 vs 12%; $p < 0.001$), valvular abnormalities (88 vs 53%; $p < 0.01$), LVHT affecting the lateral wall (75 vs 44%; $p < 0.01$), larger left ventricular diameters (72 vs 60 mm; $p < 0.001$), a poorer left ventricular function (16 vs 25 % fractional shortening; $p < 0.001$) and tended to suffer more from NMD than patients without CIED (75 vs 57%). ICD-discharges occurred in 20% during 47 months. LVHT-patients in sinus rhythm with left-bundle-branch-block responded well to CRT whereas patients with atrial fibrillation did not. In PM-patients heart failure developed due to inadequate rate control but not induced by right apical pacing.

Conclusion CIED in LVHT should be implanted according to current guidelines.

Stress-Induced Cardiomyopathy (Tako-Tsubo-Syndrome) in Austria: A Retrospective Analysis BAI

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Wien; Linz; Wels; Graz; Salzburg; Innsbruck

Background Tako-Tsubo-Syndrome (TS) is a still infrequently diagnosed clinical syndrome characterized by transient cardiac dysfunction with (usually) reversible wall motion abnormalities (WMA).

Aim To investigate the type of TS, the causative triggers, underlying risk factors, as well as clinical complications in the short and long-term follow-up of TS patients (pts), we performed a multicenter retrospective analysis. Eleven Austrian interventional cardiology departments, which prospectively have collected data of TS pts between 2004 and 2010 agreed to participate in this registry.

Methods Type of TS, causative triggers, clinical characteristics as well as outcome of 179 consecutive pts with proven diagnosis of TS were analyzed retrospectively. Pts were included into the registry if they were admitted to the hospital with chest pain characteristic for acute myocardial infarction (MI) accompanied by new ECG changes consistent with acute myocardial ischemia, elevated biomarkers (troponin, creatine kinase, CK-MB), transient left ventricular WMA and after angiographic exclusion of a $\geq 50\%$ stenosis of epicardial coronary arteries by coronary angiography, respectively.

Results Of the 179 pts, 168 (94%) were women and 11 (6%) were men. Mean age was 69.2 ± 11.5 years (range 35–88 years). Cardinal symptoms of TS were acute chest pain (82%) and dyspnea (32%). All pts demonstrated typical WMA, of which 3 different types could be defined: 1) the more common apical form of TS ($n = 71$; 40%); 2) a combined apical and mid-ventricular form of TS ($n = 30$; 17%) and 3) a less frequent pattern of an isolated midventricular TS ($n = 8$; 5%), respectively. In retrospect, only in 101 pts (57%) a causative trigger for onset of symptoms could be identified: physical stress was present in 52 pts (51%), emotional stress in 41 pts (41%) and a combined emotional/physical trigger in 8 pts (8%), respectively. During hospital stay cardiovascular complications were found in 22 pts (12%): These consisted of cardiac arrhythmias in 10 pts (46%), cardiogenic shock in 6 pts (27%) and cardiac decompensation in 8 pts (36%), respectively. Control of left ventricular function was available in 124 pts (69.3%), whereby 46 pts (25.7%) underwent a control echocardiography prior to discharge, within 7.2 ± 4.8 days and 78 pts (43.6%) had an examination of regional WMA at a later occasion, after 186.4 ± 316.7 days. Control echocardiography showed complete recovery of WMA in 75 pts (60.5%) and persistent WMA in 49 pts (39.5%). Recurrences of TS events were only seen in 4 pts.

Conclusions This study represents to date the largest series of pts suffering from TS in Austria. As confirmed by our study the prevalence of TS in women was significantly higher than in men and the apical type of TS was detected most frequently. The clinical presentation was similar to the clinical picture of acute MI and TS could only be differentiated from acute MI by coronary angiography demonstrating no or non-significant plaque formations in epicardial coronary arteries. Emotional and physical triggers were involved in about half the pts each. In contrast to international reports, only 60% of TS pts showed a complete recovery of the initial WMA.

■ Diverse/Sundry

NT-ProBNP for Detection of Sunitinib-Induced Cardiac Toxicity in Renal Cell Carcinoma VI – 2

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Aim Metastatic renal cell carcinoma (mRCC), the most common form of kidney cancer, is associated with a poor 5-year survival rate. Targeted treatment with the tyrosine kinase inhibitor sunitinib has recently been shown to significantly improve the outcome in this disease. However, sunitinib has been shown to induce cardiac toxicities, especially hypertension and left ventricular dysfunction may occur, as well as myocardial ischemia or arrhythmias. Therefore, frequent assessment of cardiac function and close clinical observation has been considered essential in these patients. However, frequent echocardiograms might not be feasible in every patient in the routine clinical practice. Similarly, electrocardiograms (ECG) may show a variety of changes, often requiring interdisciplinary cardiology and oncology work up to interpret the findings within the clinical con-

text. Easily available biomarkers for cardiac toxicity are desirable to detect cardiac damages and support the decision of treatment continuation. N-terminal-pro-B-type natriuretic peptide (NT-proBNP) has been shown to increase in chemotherapy-induced cardiotoxicity. The aim of this prospective analysis was to investigate the role of NT-proBNP as possible early indicator for sunitinib-induced cardiac toxicity.

Patients and Methods All patients with mRCC assigned for first-line treatment with sunitinib were analyzed for history or evidence of cardiac diseases. Monitoring included assessment of clinical symptoms, electrocardiograms, echocardiograms and biochemical markers of cardiac damage NT-proBNP and cardiac Troponin T (TnT). Echocardiograms and electrocardiograms were obtained at baseline, every 3 months and at increase of biochemical markers. NT-proBNP (Roche Elecsys) and TnT were assessed at baseline and then every 4 weeks, as well as routine laboratory parameters. A significant clinical finding indicating cardiac damage was defined as a newly pathological echocardiogram, development of cardiac clinical symptoms, new changes in the ECG or increased TnT.

Results Forty-five patients with a median age of 66 years (range 40–82 years) were included in this analysis, 98% of pts had undergone nephrectomy. After a median treatment period of 15 weeks (2–101), 34 (76%) patients experienced an increase of NT-proBNP when compared to their baseline values. New changes in ECG and echocardiograms were observed in 7 (21%) and 6 (18%) patients, respectively. Echocardiography detected regional wall motion disturbances ($n = 4$), progression of diastolic dysfunction ($n = 2$) and severe congestive heart failure in 1 patient. NT-proBNP levels without increase from baseline were always associated with the complete absence of clinical findings for cardiac toxicity. Higher NT-proBNP levels during treatment were significantly more often associated with the presence of a cardiac event ($p = 0.001$). A wide range of NT-proBNP was observed during sunitinib-treatment, with events occurring mainly in pts with NT-proBNP levels above 1000 pg/ml.

Conclusion Our observations indicate that increased NT-proBNP plasma levels might serve as an easily assessable marker for cardiac toxicity. An increase of NT-proBNP during treatment may indicate overt or subclinical cardiac damage. An interdisciplinary approach between cardiologists and oncologists is essential to allow continuation of tumor-treatment under cardiac therapy for optimal outcome of these patients.

Metabolic Benefits of Eccentric Endurance Exercise in Overweight and Obese Individuals VI – 3

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The interplay of muscle contraction with an external force can result in one of 3 types of muscle activity: shortening or “concentric” when muscle contraction is stronger than the external force; lengthening or “eccentric” when the external force is stronger; and isometric when both forces are equal. Eccentric endurance exercise (e. g. hiking downwards) is less strenuous than concentric exercise (e. g. hiking upwards) but its metabolic effects are largely unknown; no data exist in overweight and obese individuals.

We allocated 43 overweight and obese sedentary individuals to an exercise intervention program, consisting of hiking downwards a pre-defined route in the Austrian Alps over 2 months. For the opposite way, a cable car was used where compliance was recorded electronically. The difference in altitude was 540 meters; the distance was covered 3–5 times a week. Fasting and postprandial metabolic profiles were obtained at baseline and after the 2 months period.

Compared with baseline, eccentric exercise significantly lowered fasting glucose (98 ± 11 vs 96 ± 14 mg/dl; $p = 0.042$) and improved glucose tolerance (242 ± 48 vs 219 ± 60 mg $\times$ dl $^{-1} \times$ h; $p = 0.001$). Furthermore, eccentric exercise significantly improved triglyceride tolerance (1841 ± 893 vs 1468 ± 656 mg $\times$ dl $^{-1} \times$ h; $p = 0.001$) and the postprandial leukocyte count (69.4 ± 11.7 vs 67.0 ± 13.0 G $\times$ L $^{-1} \times$ h; $p = 0.044$).

We conclude that eccentric exercise is a promising new exercise modality with favourable metabolic effects. This little strenuous exercise could become especially important, as a large proportion of patients suffer from comorbidities that confer a low tolerance for higher-intensity training protocols.

OAK-Therapieeffizienz bei Patienten mit Vorhofflimmern VI – 4

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Einleitung Die orale Antikoagulation (OAK) bei Patienten mit Vorhofflimmern ist ein viel diskutiertes Thema. Ziel der Studie war, die Therapieeinstellungsqualität zu überprüfen und jene Patienten mit erhöhtem Risiko für Komplikationen aufgrund einer unzureichenden Therapieeinstellung zu eruieren.

Methoden Eingeschlossen wurden 212 Patienten mit permanentem oder paroxysmalem Vorhofflimmern, welche sich im Zeitraum von August 2008 bis Jänner 2011 in der allgemeinen Herzambulanz zur Einstellung mit Vitamin-K-Antagonisten in Behandlung befanden.

Es wurden die vorliegenden INR-Werte und Kontrollintervalle im besagten Zeitraum sowie mittels Patientenfragebogen Begleiterkrankungen sowie etwaige Komplikationen unter der Therapie erhoben (125 Patienten). Die Therapieeinstellung unter OAK-Therapie wurde von August 2008 bis November 2010 erhoben. Die Patienten wurden anhand der vorliegenden Therapiedauer in 3 Gruppen unterteilt (≤ 365 Tage, $365 < x < 770$ Tage und ≥ 770 Tage).

Die erhobenen INR-Werte wurden definierten Wertbereichen zugeordnet.

Ergebnisse Das durchschnittliche Alter betrug 76,04 Jahre. **Tabelle 10** zeigt die Verteilung der erhobenen INR-Werte im Beobachtungszeitraum.

Es zeigte sich eine Abnahme der INR-Werte außerhalb des therapeutischen Bereiches, umso länger die Patienten in Kontrolle waren. Als häufigste Komplikation sind Hämatoeme zu nennen, die bei 26,4% ($n = 33$) der Patienten vorkamen. In allen 3 Beobachtungszeiträumen wurden Unterdosierungen häufiger verzeichnet als Überdosierungen.

Bei 4,72% der Patienten waren mehr als 50 % der erhobenen INR-Werte außerhalb des therapeutischen Bereiches und somit die Therapie als insuffizient zu werten. Auffallend war hier, dass die Patienten von Therapiebeginn an nicht zufriedenstellend einzustellen waren.

Bei allen 212 Patienten konnten keine ischämischen Insulte oder zerebralen Blutungen unter OAK beobachtet werden, es ist jedoch davon auszugehen, dass hierfür ein weit größeres Patientenkollektiv notwendig ist.

Diskussion Von insgesamt 212 Patienten hatten lediglich 4,72 % ($n = 10$) der Patienten mehr als 50 % der erhobenen INR-Werte außerhalb des therapeutischen Bereiches und haben somit unter der OAK-Therapie keinen adäquaten Schutz vor hämorrhagischen als auch ischämischen Ereignissen. Für diese Patienten stellt sich die

Tabelle 10: R. Breier et al.

Follow-up	≤ 365 d (n = 594)	366–769d (n = 2443)	≥ 770 d (n = 1858)	Insgesamt (n = 4895)
INR 2–3	58,92 % (n = 350)	68,11 % (n = 1664)	72,98 % (n = 1356)	68,85 % (n = 3370)
INR 3–4	11,62 % (n = 69)	13,79 % (n = 337)	11,03 % (n = 205)	12,48 % (n = 611)
INR $x < 2$ und > 4	29,46 % (n = 175)	18,09 % (n = 442)	15,99 % (n = 297)	18,67 % n = 1119
INR > 4	5,39 % (n = 32)	3,60 % (n = 88)	2,91 % (n = 54)	3,55 % (n = 174)
INR < 2	24,07 % (n = 143)	14,49 % (n = 354)	13,08 % (n = 243)	15,12 % (n = 740)

Frage, ob eine Therapieumstellung auf ein Ersatzpräparat einen Vorteil bringen würde. Hier muss aber auch erwähnt werden, dass zumeist als Ursache eine Incompliance von Therapiebeginn an vorlag und somit ein Therapieerfolg unter anderen Medikamenten ebenso nicht zu erwarten wäre.

Neue Biomarker zur Früherkennung und Risikostratifikation kardiovaskulärer Ereignisse – die „Graz Heart Study“ (Comet-Projekt „BioPersMed“)

VI – 5

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Hintergrund Die Risikostratifikation asymptomatischer Patienten mit erhöhtem kardiovaskulären Risiko erfolgt heute auf dem Boden klassischer Risikofaktoren mithilfe von Score-Systemen (z. B. EuroSCORE). Allerdings ist die Zuverlässigkeit dieser Systeme ungenügend. Durch neue laborchemische und biophysikalische Biomarker könnten 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 über das Comet-Projekt (K-Projekt) „BioPersMed“ finanziert ist, wird diese Fragestellung untersucht.

Methodik In der „Graz Heart Study“ werden seit Ende 2010 prospektiv 1000 Probanden mit kardiovaskulärem Risikofaktoren, aber noch keinem atherosklerotischen Ereignis eingeschlossen und longitudinal nachbeobachtet. In Kooperation mit der Biobank der Medizinischen Universität Graz werden Blut- und Urinproben, Speichel, sowie DNA für genetische Analysen aserviert. In einer detaillierten kardiovaskulären Phänotypisierung werden neben Routineparametern die systolische und diastolische Ventrikelfunktion, kardiales Remodelling sowie moderne echokardiographische Parameter (strain, strain-rate) erhoben. Die vaskuläre Funktion wird umfassend u. a. durch Endothelfunktion, Pulswellenanalyse und Analyse der Mikrozirkulation (Endopad und Endothelfunktionsprüfung) bestimmt. Die körperliche Leistungsfähigkeit wird mittels Spiroergometrie und 6-Minuten-Gehtest erhoben. Zusätzliche Untersuchungen in Subgruppen beziehen zerebrale atherosklerotische Ereignisse (Schädel-MRT), Augenhintergrunduntersuchung und eine umfassende Analyse von soziodemographischen Parametern und der Lebensqualität ein. Die Rekrutierung erfolgt in enger Kooperation mit dem niedergelassenen Bereich.

Erste Ergebnisse In einer Pilotstudie zu Zeitaufwand, Untersuchungsablauf und Compliance wurden seit Ende 2010 19 Probanden eingeschlossen. Die Teilnehmer wiesen mindestens einen klassischen kardiovaskulären Risikofaktor auf: Arterielle Hypertonie (100 %), Dyslipoproteinämie (93 %), Adipositas (BMI > 25 kg/m²: 79 %). 26 % der Patienten hatten ein manifesten Diabetes, 32 % einen HbA_{1c} ≥ 6 %. 58 % der asymptomatischen, subjektiv gesunden Probanden zeigten bei normaler linksventrikulärer Funktion ein NTproBNP > 100 pg/ml. 58 % zeigten erhöhte Hinweise auf diastolische Dysfunktion mit E/E'-Wert > 10.

Schlussfolgerung In der „Graz Heart Study“ wird in einem großpopulationsbasierten Ansatz an subjektiv gesunden Patienten mit erhöhtem kardiovaskulären Risiko die Bedeutung neuer biophysikalischer und biochemischer Biomarker für Risikostratifikation und Prädiktion kardiovaskulärer Komplikationen analysiert. In unserem Probedurchlauf konnten wir die Machbarkeit des diagnostischen Phänotypisierungsansatzes nachweisen. Die Compliance lag bei 100 %, alle Patienten durchliefen in weniger als 4 Stunden das Standarduntersuchungsprogramm.

Es zeigte sich, dass asymptomatische, bisher als gesund klassifizierte Probanden mit kardiovaskulärem Risiko bereits in erheblichem Umfang erhöhte NTproBNP-Werte und ein pathologisches E/E' als mögliches Korrelat für subklinisches kardiovaskuläres Remodelling aufwiesen. Dieser erste Befund belegt die klinische Relevanz dieses Forschungsprojektes.

P-Glycoprotein-Affecting Food in the Diet of Hospitalized Patients

VI – 6

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Introduction Dabigatran, apixaban and rivaroxaban are new antithrombotic drugs (NAD) which had in clinical trials a similar effect as Vitamin-K-antagonists (VKA) for stroke prevention but a lower complication rate. NAD are claimed to have less food-interactions than VKA. However, NAD-absorption is dependent on the intestinal P-glycoprotein- (P-gp-) system which is influenced by drugs and food components. Aim of the cross-sectional study was to screen the diet of hospitalized patients for P-gp-affecting food.

Methods From the literature P-gp-affecting food components like phenolic acids and analogs, flavonoids, tannins, stilbenes, curcuminoids, coumarins, lignans and quinines were identified. The weekly order for food supply of a 214-beds community hospital in Vienna in November 2010 was analyzed regarding the frequency of P-gp-affecting food components.

Results The following P-gp-affecting foods were identified: Coffee, black tea, peppermint tea, orange juice, apple juice, chocolate powder, red wine, oranges, lemons, tangerines, kiwi, apples, rapeseed oil, tomatoes, cabbage, red cabbage, leek, onions, root vegetables, bell peppers, lettuce, carrot, cauliflower, broccoli, rutabaga, romain lettuce, spinach, peas, string beans, celery root, strawberries, raspberries, raisins, chocolate cake, mustard, black pepper, and curry powder. These food compounds are frequently associated with beneficial health effects.

Conclusions P-gp-affecting food is frequently ordered for hospitalized patients. We suggest to investigate the influence of P-gp-affecting food on serum-levels of NAD and coagulation parameters, and to re-analyze bleeding and embolic events in NAD-investigating trials considering the patients' diet. Since drugs like clopidogrel are also substrates of the P-gp-system, more attention should be directed to drug-drug and drug-food-interactions due to influences on the P-gp-system.

Spezielle Induktionstechniken im Kontext ärztlicher Hypnose für den kardiovaskulären Patienten

VI – 1

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Einleitung Hypnose ist eines der ältesten bekannten Heilverfahren. In den vergangenen Jahrzehnten erlebte sie besonders im anglo-amerikanischen Raum eine Renaissance, die sich auch immer mehr auf Europa erstreckt. Durch eine Literaturrecherche wird hier eine Darstellung spezieller Induktionstechniken, insbesondere von Schnellinduktionstechniken im Kontext von Einsatz- und Anwendungsmöglichkeiten in der Kardiologie dargestellt.

Methodik 1.) Literaturrecherche: Da es sich bei der klinischen Hypnose um ein ausgesprochen individuelles und dynamisches Heilverfahren handelt, finden sich in der einschlägigen Fachliteratur hauptsächlich Fallbeschreibungen, in die diverse Techniken etc. eingebettet wurden. Diese veröffentlichten Fallbeispiele wurden im Rahmen der Diplomarbeit analysiert und ausgewertet.

2.) Ausbildungs- und Selbsterfahrungen: Die Wahl dieser Methode beruht auf der Tatsache, dass sich die Techniken und Methoden der klinischen Hypnose nach Erickson am effizientesten durch Selbsterfahrung und Übung in Kombination mit ausgedehnten Literaturrecherchen erlernen lassen. Die Beschreibung von Selbsterfahrung stellt eine klassische Methode im Bereich der Hypnotherapie dar.

Ergebnisse Es gibt auch in Zeiten der „5-Minuten-Medizin“ Methoden der medizinischen Hypnose und vertieften Kommunikation, die das Erreichen der Therapieziele für Patienten und Ärzte verbessern können. Es ist möglich, eine Erhöhung der Compliance bei gleichzeitiger Reduktion der Wirkstoffdosis zu erreichen. Dies ist zum einen wegen der immer größer werdenden Nachfrage seitens der Patienten nach komplementären und additiven Behandlungs-

methoden und zum anderen aufgrund der heute schon weit verbreiteten Anwendung derartiger Verfahren im angloamerikanischen, aber auch im europäischen Raum von Bedeutung. Ein Thema in diesem Zusammenhang ist der Einsatz von Hypnose, speziell im Sinne von Angst- und Schmerzbeherrschung vor, während und nach interventionellen Eingriffen. Aber auch in der Arbeit mit Angstpatienten oder zur Vorbereitung von kardiochirurgischen Eingriffen sowie im Rahmen des Weanings (CCU) kann Hypnose zur Anwendung kommen. Des Weiteren kann jedes ärztliche Gespräch durch den Einsatz hypnotischer Sprachmuster und Kommunikationstechniken effizienter und entspannter gestaltet werden. Durch den zusätzlichen Einsatz ärztlicher Hypnose im therapeutischen Geschehen können Behandlungen für den Patienten in physischer und psychischer Hinsicht schonender und angenehmer vorgenommen werden. Im Rahmen dieser Arbeit werden aus den zahlreichen Methoden, Techniken und Taktiken, die die klinische Hypnose bietet, diejenigen herausgearbeitet, deren Relevanz und Durchführbarkeit in einem ärztlich-klinischen Kontext von Bedeutung sind. Der theoretische Kern der Arbeit besteht somit in der Beschreibung und Darstellung von Hypnosetechniken und deren Adaptierung auf eine klinische Entscheidung, wobei vor allem auf diejenigen Techniken eingegangen wurde, die sich leicht erlernen und mit minimalem Zeitaufwand bei gleichzeitig maximalem Outcome durchführen lassen (vgl. „Schnell-induktionen“). Ein weiterer Schwerpunkt wurde auch auf die Neuerarbeitung von klinisch relevanten Techniken gelegt.

Schlussfolgerung Der Neuigkeitswert der Arbeit besteht darin, besonders diejenigen Werkzeuge und Methoden aufzuzeigen und zusammenzufassen, die besonders rasch und einfach im alltäglichen kardiologisch-ärztlichen Bereich Anwendung finden können.

Entwicklung der ergometrischen Leistungsfähigkeit bei Sportstudenten und -studentinnen von 1986–2009

VI – 7

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Einleitung Um an der Universität Graz ein Sportstudium beginnen zu können, werden die Studierenden einem Auswahlverfahren unterzogen. Nach den sportmotorischen Tests folgt eine ergometrische Untersuchung, welche die Leistungsfähigkeit der zukünftigen Studentinnen und Studenten zum Ausdruck bringt. Ziel dieser Arbeit war es, die Leistungsfähigkeit der Grazer Sportstudierenden darzustellen und über den Zeitraum der vergangenen 24 Jahre zu verfolgen. Weiters wird versucht, Vergleiche mit altersentsprechenden Normwerten und dem Durchschnitt der österreichischen Gesamtbevölkerung herzustellen.

Methoden Alle Sportstudenten müssen sich vor Beginn des Studiums einer leistungsdiagnostischen Untersuchung unterziehen. Die Daten der vergangenen 24 Jahre wurden hinsichtlich Veränderungen über die Zeit ausgewertet. Zur Beurteilung der Leistungsfähigkeit wurden die maximal erbrachte Leistung (Pmax), die maximale erbrachte Leistung pro kg Körpergewicht (Pmax/kg) und die maximale Sauerstoffaufnahme auf das Körpergewicht bezogen (VO₂max/kg) herangezogen.

Ergebnisse Die anthropometrische Auswertung ergab für die 1307 Sportstudenten einen Größenzuwachs von 2 cm und eine Gewichtssteigerung von 2 kg. Bei den 592 Sportstudentinnen war weder eine Größen- noch eine Gewichtssteigerung zu erkennen.

Die maximale Leistungsfähigkeit eines männlichen Sportstudenten beträgt im Durchschnitt der vergangenen 24 Jahre 311 Watt, das sind 4,21 Watt/kg. Die maximale Sauerstoffaufnahme beträgt 3,6 l/min, das sind 49 ml/kg/min. Es zeigte sich ein Verlauf der maximalen Leistung pro kg Körpergewicht von 3,9 Watt/kg in den 1980er-Jahren und 4,3 Watt/kg in den 1990er-Jahren sowie von 2000 bis heute. Über die Zeit zeigte sich bei den Studenten eine Veränderung der VO₂max/kg von 46 ml/kg/min in den 1980er-Jahren über 49 ml/kg/min in den 1990er-Jahren bis hin zu 50 ml/kg/min nach dem Jahr 2000.

Bei weiblichen Sportstudenten beträgt der Durchschnitt der vergangenen 24 Jahre eine maximal erbrachte Leistung von 211 Watt, das sind 3,48 Watt/kg. Die maximale Sauerstoffaufnahme beträgt 2,24 l/min bzw. 33,5 ml/kg/min. Bei den Studentinnen stieg die Pmax/kg von 3,2 Watt/kg in den 1980er-Jahren über 3,5 Watt/kg in den 1990er-Jahren bis hin zu 3,6 Watt/kg ab dem Jahr 2000. Auch hier zeigte sich eine Veränderung der VO₂max/kg von 35 ml/kg/min in den 1980er-Jahren ein Maximum von 38 ml/kg/min in den 1990er-Jahren und ein Rückgang auf das Ausgangsniveau von 35 ml/kg/min nach dem Jahr 2000.

Diskussion Unsere Langzeituntersuchung zeigt, dass die Sportstudenten größer und schwerer geworden sind, wohingegen die Studentinnen auf gleichem Niveau geblieben sind. Die Leistungsfähigkeit stieg bei den Studenten leicht an, bei den Studentinnen hingegen blieb sie auf einem konstanten Niveau.

Health Related Quality of Life, Anxiety and Depression after PCI in NSTEMI Patients

VI – 8

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Purpose Our study sets out to examine the correlation between changes in Health Related Quality of Life, anxiety and depression after PCI.

Methods 308 NSTEMI PCI patients (71.8% men; age: 63.3, SD: 9.3) at 6 centers in Austria completed the HADS depression/anxiety and the MacNew HRQoL questionnaire before discharge and 1, 6 and 12 months after discharge.

Results MacNew-HRQoL-Score increased significantly during the 12 months follow up period in all 3 subscales (emotional, physical, social). The MacNew-Global mean value increased from 5.1 ± 10–5.5 ± 1.0. Clinically relevant increase of MacNew-Global of 0.5 or more was found in 45 %–54 %, clinically significant decrease of 0.5 or more in 12 %–14 % of the patients.

Change in MacNew-HRQoL was significantly correlated to changes in HAD anxiety and depression score: Clinically relevant decrease of MacNew-HRQoL was associated with a pronounced increase in mean HAD score (anxiety: 3.1–4.9, depression: 3.2–4.7), whereas clinically relevant increase of MacNew-HRQoL was correlated to a more moderate decrease (anxiety: 1.7–2.5, depression: 1.3–1.7).

At the baseline before discharge probable caseness of anxiety disorder (HADS anxiety ≥ 11) was found in 11,6 % of the patients, probable caseness of depression disorder (HADS depression ≥ 11) in 5%. During the 12 months follow up period this status maintained in 3.6–4.4% (anxiety) and 2.5–3.6% (depression) of the cases. With respect

Table 11: H. Sipötz et al.

		Baseline	1-Month-Follow-up	6-Months-Follow-up	12-Months-Follow-up
MacNew Global	Clinically significant increase (≥ 0,5)	–	45.1%	53.8%	47.1%
	Clinically significant decrease (≥ 0,5)	–	14.0%	11.7%	13.9%
HADS-anxiety	Probable caseness of mood disorder (≥ 11)	11.6%	9.6%	12.0%	10.5%
HADS-depression	Probable caseness of mood disorder (≥ 11)	5.0%	8.5%	10.4% *	9.7% *

* indicates a significant increase of probable caseness of depression disorder

to probable anxiety disorder improvement (7.6–8.8%) and deterioration (5.2–8.4%) balance each other leading to the result that the percentage of mood disorder remains relatively stable during the follow up period (9.6%–12%). In the case of probable depression disorder deterioration (4.8–7.2%) exceeds improvement (1.6–2.9%) by far. Therefore the percentage of probable depression disorder increased significantly from 5% to 10% after 6 and 12 months, respectively.

Discussion Overall, change of HRQoL after PCI is closely associated with changes to both HADS anxiety and HADS depression in a very similar fashion. Clinically relevant decrease of HRQoL is correlated to a pronounced deterioration of anxiety and depression symptomatology. Conversely clinically relevant increase of HRQoL is not as strongly linked to improvement of signs of anxiety and depression.

However, anxiety and depression differ distinctly with respect to the percentage of cases with probable mood disorder in the follow up period. Whereas we found a doubling of cases with probable depression disorder the number of cases with probable anxiety disorder remains stable. Interestingly this is not due to a greater number of patients deteriorating to the level of probable mood disorder but to the fact that only very few patients with probable depression disorder at the baseline improve their status.

Our findings show that the evaluation of anxiety and depression provides important additional information for a better understanding of HRQoL outcome in PCI-patients.

The clinically relevant change in MacNew Global score, HADS anxiety and depression during the 12 months follow up period after PCI shows **Table 11**.

■ Gefäßbiologie/Vascular Biology

Association between Inflammation and Atherosclerosis in Metabolic Syndrome Patients: The Same in all Arterial Beds? XII – 6

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While inflammatory markers are firmly established as predictors of clinical atherothrombotic events, data on their association with directly visualized atherosclerosis are controversial. We aimed at investigating the association of C-reactive protein and of leukocytes with atherosclerosis in different arterial beds.

We enrolled 405 consecutive Caucasian patients with the Metabolic Syndrome (MetS) who were referred to coronary angiography for the evaluation of stable coronary artery disease (CAD) and who did not have a history of peripheral arterial disease (PAD). Significant CAD was diagnosed in patients with significant coronary artery lumen narrowing $\geq 50\%$ ($n = 232$); subjects without such lesions served as controls ($n = 173$). Additionally, we enrolled 200 MetS patients who underwent routine duplex sonography for the evaluation of suspected or established PAD and in whom PAD was verified sonographically.

The inflammatory markers CRP and leukocytes did not differ significantly between patients with stable CAD and controls (0.47 ± 0.71 vs 0.43 ± 0.48 mg/dl; $p = 0.472$; 6.9 ± 1.7 vs 6.9 ± 1.8 G/L; $p = 0.856$, respectively). In contrast, CRP as well as leukocytes were significantly higher in PAD patients compared to both, patients with stable CAD (0.94 ± 1.88 vs 0.47 ± 0.71 mg/dl; $p = 0.001$ and 7.6 ± 2.3 vs 6.9 ± 1.7 G/L; $p = 0.003$, respectively) and controls (0.94 ± 1.88 vs 0.43 ± 0.48 mg/dl; $p = 0.008$; 7.6 ± 2.3 vs 6.9 ± 1.8 G/L; $p = 0.005$, respectively).

In conclusion, CRP and leukocytes do not differ between MetS patients with or without stable CAD but are significantly elevated in MetS patients with PAD. This is well in line with the extremely high cardiovascular event risk of PAD patients.

Effect of Drug-eluting Stent and Drug-Eluting Balloon On Endothel-Dependent and -Independent Vasomotion of the Coronary Arteries XII – 7

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Background The 1st generation drug-eluting stent (DES) implantation has been shown to result in long-term endothelial dysfunction and vasoconstriction; both phenomena have been suggested to be in association with delayed healing and late thrombosis. In contrast, human coronary arteries showed a relatively preserved endothelium-dependent coronary vasomotion after 2nd generation DES implantation or use of drug-eluting balloon (DEB). The aim of the present study was to investigate the endothelium-dependent and independent vascular response of coronary arteries after use of different intracoronary devices, such as DEB, plain balloon, bare metal stents (BMS) and DES.

Methods Domestic pigs underwent coronary artery balloon dilatation with DEB (size of 3 mm, length of 15 mm, inflation time of 2 × 30 sec) or plain balloon (3/15 mm, 30 sec), or stent implantation with BMS or DES (both 3.0/15 mm, 30 sec). The dilated segments of DEB and plain balloon, and the proximal reference segments of the stented arteries (without stent) have been prepared 5 ± 1 h after percutaneous coronary intervention (PCI) for in vitro measurements of endothelium-dependent and -independent vasomotor reaction. Isometric circular wall tension (contractile response) and maximal vasodilation of the arterial segments were determined after bolus application of sodium-nitroprussid (endothelium-independent reaction) and substance-P (endothelium-dependent vasomotion) directly into the organ bath solution, and expressed in wall tension development (mN).

Results The endothelium-dependent vasomotor response is shifted to vasoconstriction after implantation of DES or BMS, but only partially after DEB or plain balloon, indicating a severe or mild dysfunction of the endothelium, as compared to control (non-instrumented) arteries (23.4 ± 6.7 , 24.3 ± 4.7 , 17.2 ± 6.3 , 10.6 ± 3.5 and 10.4 ± 3.9 mN, respectively), with significant difference between control arteries and DES or BMS ($p < 0.005$) and DEB ($p = 0.028$). Sensitivity of vascular smooth muscle to sodium-nitroprussid was impaired in DES or BMS-treated arteries, but in less extent in DEB or plain balloon-dilated segments (0.05 ± 0.02 , 0.06 ± 0.05 , 0.10 ± 0.1 , 0.1 ± 0.05 and 0.25 ± 0.1 mN, respectively) with significant differences between non-PCI arteries and DES ($p = 0.002$), BMS ($p = 0.008$), DEB ($p = 0.026$) or plain balloon ($p = 0.047$), indicating less media (muscular) damage of balloon intervention when compared to stenting.

Conclusion Coronary arteries treated with plain balloon, DEB, BMS and DES showed partial loss of endothelial-dependent and -independent vasodilator response, in increasing order of magnitude, which might influence the long-term outcome of PCI, regarding restenosis, vessel remodeling and thrombosis. The presented in-vitro experiments have a potential guidance for engineering of new intracoronary devices.

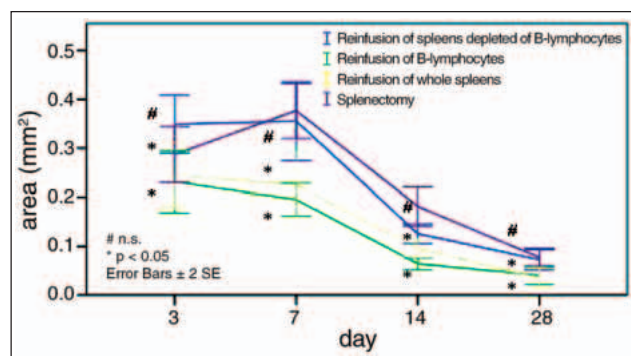


Figure 17: M. K. Renner et al. Cross-sectional thrombus areas.

The Role of B-lymphocytes in Thrombus Resolution XII – 8

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Purpose Splenectomy is associated with complex venous thromboembolism such as recurrent deep venous thrombosis, portal vein thrombosis, and chronic thromboembolic pulmonary hypertension (CTEPH). The spleen serves not only as a red blood cell filter but also constitutes an immunological organ. The aim of our study was to decipher the population of spleen cells responsible for misguided thrombus resolution after splenectomy.

Methods We utilized a mouse model of stagnant flow venous thrombosis to characterize thrombus resolution. Splenectomy was performed one month before vena cava ligation. In defined groups, whole spleens, spleens depleted of B-lymphocytes or B-lymphocytes alone were reinfused intraperitoneally. On days 3, 7, 14 and 28 after vena cava ligation thrombi were harvested for histology.

Results Thrombus areas of splenectomized mice were significantly larger than those of controls at all time points (ANOVA, $n = 8$; $p < 0.05$). Reinfusion of autologous whole spleen-homogenates reconstituted a normal pattern of thrombus organisation. Reinfusion of spleen tissue depleted of B-lymphocytes could not accelerate thrombus resolution significantly. However, reinfusion of autologous splenic B-lymphocytes in previously splenectomized mice normalized thrombus resolution (**Figure 17**).

Discussion Reinfusion of spleen cells can restore the normal process of venous thrombus organisation in a mouse model. Our data demonstrate that spleen B-lymphocytes play a role in thrombus resolution.

Fatal Basilar Artery Occlusion Shortly After Initiation of Dabigatran

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Objective Concerns about initiation and monitoring of dabigatran after surgery and about the overlap with low-molecular-weight heparin are strengthened by the case of a male with atrial fibrillation (AF) for 30 years.

Case Report After an embolic stroke 27 years previously, phenprocoumon was started, but resumed after 7 years for unknown reasons. In the following years he was without any drugs. At age 78 years, he suffered from acute pain of his right leg leading to right-sided embolectomy. Antithrombotic therapy comprised enoxaparin 60 mg/bid, on the 5th postoperative day phenprocoumon 9 mg/d and on the 6th postoperative day 6mg/d. Because the discharge-INR was only 1.18, enoxaparin was recommended until the INR was > 2.0 . The patient's son, a general practitioner, changed phenprocoumon to dabigatran 110 mg/bid on the 8th postoperative day. No blood tests were performed thereafter. Sudden pain in his left calf induced re-admission on the 13th postoperative day. Blood tests showed gamma-glutamyltransferase 126 U/l, prothrombin time 33 sec, fibrinogen 359 mg/dl, antithrombin 87%, INR 2.5 and D-dimer 20 µg/ml. No surgery was indicated but dabigatran was resumed, dalteparin 5000 IE/bid and 40 µg alprostadil-infusion were started. After 8 hours he was found comatose. Computed tomography showed a pulmonary lesion suggestive of malignoma and basilar artery occlusion. Partial mechanical recanalisation was achieved but a steady perfusion could not be achieved even after application of 5 mg alteplase into the basilar artery, and the patient eventually died.

Conclusion In postoperative AF-patients dabigatran should be avoided. Drug-interactions of dabigatran should be studied, and vitamin-K-antagonists with their easily measurable effect should be used in postoperative AF-patients.

■ Herzinsuffizienz/Heart Failure

Die Prognose der akuten Herzinsuffizienz anhand der Daten des EuroHeart Failure Survey am LKH-Universitätsklinikum Graz VII – 1

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Einleitung Die Prognose der akuten Herzinsuffizienz ist weiterhin besorgniserregend. Die Daten zur 1-Jahres-Mortalität variieren von 10–50 %. Um realitätsnahe Information zu bekommen, wurde von der European Society of Cardiology (ESC) das EuroHeart Failure Survey III etabliert.

Patienten und Methodik Im 8-monatigen Zeitraum zwischen Oktober 2009 und Mai 2010 wurden an 136 Krankenhäusern europaweit Patienten mit akuter Herzinsuffizienz in das Survey aufgenommen. Der Einschluss war nur an einem Tag der Woche möglich, der frei wählbar war und konstant bleiben musste. Nach 3, 6 und 12 Monaten (jeweils ± 1 Monat) war ein Follow-up geplant. Hier werden die lokalen Daten des größten österreichischen Zentrums präsentiert.

Ergebnisse Bisher konnte von 28 Personen (14 männlich, 14 weiblich; mittleres Alter 77 ± 13 Jahre) ein 12-Monate-Follow-up erhoben werden. 10 Patienten (4 männlich, 6 weiblich; 36 %) waren verstorben, ein Patient war nicht zu erreichen und wurde als Lost-to-Follow-up klassifiziert (4 %). 4 Patienten (40 %) sind in den ersten 3 Monaten nach Hospitalisierung verstorben, weitere 2 (20 %) in den Monaten 3–6 nach Krankenhausaufnahme und schließlich weitere 4 (40 %) in den letzten 6 Monaten des Beobachtungszeitraums. Das Mortalitätsrisiko ist für Frauen mit 43 % höher als für Männer mit 29 %. Sieben der 10 Todesfälle sind auf eine kardiale Genese zurückzuführen, wobei in 6 Fällen ein Pumpversagen, und in 1 Fall ein plötzlicher Herztod identifiziert werden konnte. 2 (20 %) Patienten verstarben an einer nicht-kardiovaskulären Genese, in einem Fall (10 %) war die Todesursache nicht zu erheben. Von den 17 überlebenden Patienten waren 2 Patienten (12 %) im NYHA-Stadium-1, 1 Patient im Stadium 2 (6 %), 10 (58 %) im NYHA-Stadium-3 sowie 2 Patienten (12 %) im Stadium 4. In 2 Fällen (12 %) war keine Zuordnung möglich. 12 Monate nach einer Episode von akuter Herzinsuffizienz waren 15 Patienten (88 %) mit einem Betablocker therapiert, 7 Patienten mit einem ACE-Hemmer (41 %), 6 mit einem Angiotensin-Rezeptor-Blocker (35 %), 5 mit einem Aldosteron-Antagonisten (29 %) und 11 mit einem Diuretikum (65 %).

Schlussfolgerung Unsere Daten zeigen, dass die Mortalität nach einer Episode mit akuter Herzinsuffizienz weiterhin hoch ist. Verbesserungspotenzial besteht vor allem bei der Therapie der Herzinsuffizienz, da der erwiesene Vorteil einer Kombinationstherapie offenbar zu wenig genutzt wird.

Identification of Best-Practice Relevant to Long-Term Survival in Patients Hospitalized for Decompensated Heart Failure XIV – 3

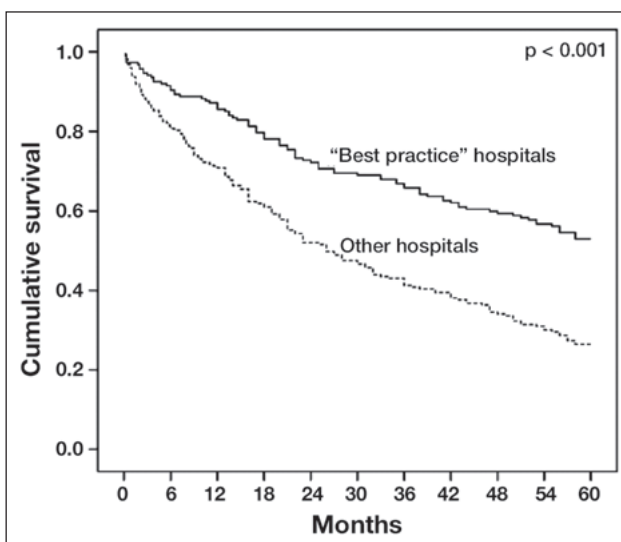
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Background Patients with heart failure (HF) hospitalized for acute decompensation are prone to death following discharge from hospital. The aim of the present study was to identify parameters of best-practice hospitals associated with long-term outcome.

Methods In an explorative approach to detect a best-practice model of treating HF patients hospitalized for acute decompensation, we identified differences between the most successful centers compared to others. In a second step we sought to relate the differences with regard to long-term outcome. Identification of best-practice was based on a step-by-step by pairs comparison of Kaplan Meier curves for 8 participating centers including a total of 406 patients. Two significantly differing groups were assembled based on the log rank test. In the first step the 2 centers with the best clinical outcome were fused, as there was no significant difference between

Table 12: C. Adlbrecht et al.

	Best-practice hospitals (n = 186)	Other hospitals (n = 220)	p-value
Age (years)	70.3	73.5	0.009
Male (%)	70	59	0.031
History of co-morbidities			
Coronary artery disease (%)	68	58	0.041
Previous myocardial infarction (%)	50	40	0.022
Hypertension (%)	70	68	0.748
Diabetes (%)	37	43	0.225
Atrial fibrillation (%)	27	33	0.233
Stroke (%)	12	15	0.467
Chronic obstructive lung disease (%)	20	18	0.707
NYHA functional class			
NYHA II (%)	3	1	0.119
NYHA III (%)	62	55	
NYHA IV (%)	36	44	
Left ventricular ejection fraction (%)	30	29	0.650
Baseline NT-proBNP (pg/mL)	3433 ± 4655	4354 ± 5534	0.088
Systolic blood pressure (mmHg)	121 ± 18	123 ± 20	0.239
Diastolic blood pressure (mmHg)	71 ± 11	72 ± 13	0.335
Heart rate (bpm)	76 ± 16	79 ± 17	0.069
Serum creatinine > 2mg/dL (%)	13	16	0.480
In hospital management			
Heart failure specific medication at discharge			< 0.001
ACE-I/ARB + BB = None (%)	27	47	
ACE-I/ARB + BB = <50% (%)	59	42	
ACE-I/ARB + BB = ≥ 50% (%)	13	9	
ACE-I/ARB + BB = 100% (%)	1	3	
Echocardiogram performed (%)	91	76	< 0.001
Index days in hospital (days)	15 ± 9	17 ± 15	0.022

**Figure 18:** C. Adlbrecht et al.

these 2 groups. Subsequently the remaining centers were fused accordingly, as there was no difference between them concerning outcome respectively. This procedure resulted in 2 significantly different groups, each group consisting of several centers without significant differences in outcome. Bivariate comparison of patient characteristics and in hospital management between the 2 groups was followed by a multivariate Cox regression model. The endpoint for the latter was time to death.

Results During the follow-up period of up to 60 months 253 (61.7%) patients had died. The mean follow-up period was 36.6 ±

23.1 months. The 2 best-practice hospitals included 186 patients and 220 patients were included by the other hospitals. Several parameters differed between best-practice and other hospitals (**Table 12, Figure 18**). In a multiple Cox regression model, patient age (HR 1.04, 95%-CI: 1.03–1.06; $p < 0.001$), male sex (HR 1.41, 95%-CI: 1.08–1.84; $p = 0.012$), length of index hospitalization (HR 1.01, 95%-CI: 1.01–1.02; $p = 0.002$) and the quality of prescribed HF specific medication at discharge from index hospitalization (HR 0.78, 95%-CI: 0.64–0.94; $p = 0.009$) were independently associated with time to all-cause death.

Conclusion Quality of HF specific medical therapy at discharge was identified as an important modifiable parameter associated with long-term survival after hospitalization for decompensated HF.

Therapeutische Interventionen im Rahmen der akuten Herzinsuffizienz: Daten des EuroHeart Failure Survey – Pilot Phase

XIV – 2

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Einleitung Die akute Herzinsuffizienz ist ein komplexes, lebensbedrohliches Syndrom, welches mit einer stark eingeschränkten Lebensqualität, hoher Mortalität und enorm hohen Kosten für das Gesundheitssystem einhergeht. Die schlechte Prognose und der Anstieg der Inzidenz in den vergangenen Jahrzehnten gaben Anlass, die aktuelle Situation der HI im Rahmen einer europaweiten Studie darzustellen. Hierzu wurde von Oktober 2009 bis Mai 2010 das EuroHeart Failure Survey III – Pilot Phase an 136 Krankenhäusern in Europa durchgeführt, darunter 6 aus Österreich. Für die gegenständliche Analyse wurden nur die lokalen Daten des größten Zentrums dieses Surveys herangezogen.

Patienten und Methodik Im Beobachtungszeitraum wurden an einem frei wählbaren (aber konstanten) Wochentag alle Patienten mit akuter Herzinsuffizienz gebeten, an diesem Survey teilzunehmen. Die Patienten wurden über die zentrale Notaufnahme an der gesamten Klinik für Innere Medizin verteilt, die wenigsten wurden auf der kardiologischen Station betreut. Neben Ätiologie, Risikofaktoren, Begleiterkrankungen, Prognoseprädiktoren, und aktuell bestehenden klinischen Zeichen und Symptomen wurden alle diagnostischen und therapeutischen Maßnahmen während des stationären Krankenhausaufenthaltes dokumentiert. Zudem waren nach 3, 6 und 12 Monaten Follow-ups vorgesehen.

Ergebnisse Insgesamt wurden 37 Patienten (17 männlich, 20 weiblich; mittleres Alter 78 ± 12 Jahre) in diese Auswertung eingeschlossen. Vor der Hospitalisierung nahmen 22 Teilnehmer (60 %) einen ACE-Hemmer (ACE-H) bzw. Angiotensin-Rezeptor-Blocker (ARB) ein (ACE-H: $n = 17$ [46 %]; ARB: $n = 5$ [14 %]). Bei Entlassung wurde insgesamt 24 Patienten (67 %) eine der beiden Medikationen (ACE-H: $n = 19$ [53 %]; ARB: $n = 5$ [14 %]) zur Dauertherapie empfohlen. Weiters hatten 25 Rekrutierte (68 %) bei der Aufnahme eine Therapie mit einem Betablocker (BB), welche nach dem Krankenhausaufenthalt in 23 Fällen (64 %) fortgeführt wurde. Spironolacton wurde initial von 4 Teilnehmern (11 %) und am Tag der Entlassung von 6 Patienten (17 %) zur Therapie der HI eingesetzt. 23 Patienten (62 %) hatten eine Vortherapie mit Diuretika, am Entlassungstag wurde diese Therapie bei 29 Patienten (81 %) dokumentiert. Die mittlere Dosierung von Furosemid lag bei Aufnahme bei 51 ± 37 mg und bei Entlassung bei 41 ± 35 mg. Im Verlauf der Hospitalisation nahm die Zahl der mit Digitalis therapierten Patienten von 10 (27 %) auf 16 (44 %) zu. Am Aufnahmetag wurde NT-pro BNP bei 27 (73 %) Erkrankten bestimmt, der mediane Wert lag bei 5222 ng/l (min 824, max 35.000).

Die mediane Aufenthaltsdauer im Krankenhaus betrug 8 Tage (min 1, max 37). Sechs (16 %) Patienten wurden mit Levosimendan therapiert; 4 (11 %) der insgesamt 37 Patienten benötigten eine intensivmedizinische Betreuung. Ein Patient ist während des Aufenthaltes verstorben.

Schlussfolgerungen Im Rahmen des EHFS III wurde die Situation der akuten HI, insbesondere das Management dieser Erkrankung, in Europa dargestellt. Die lokalen Daten einer großen Klinik

für Innere Medizin zeigen, dass weiterhin großer Aufholbedarf in der Therapie der Herzinsuffizienz besteht, vor allem, wenn die Mehrzahl solcher Patienten nicht an einer kardiologischen Station betreut wird.

Prevalence and Prognostic Significance of Elevated Serum Phosphate Levels in Chronic Heart Failure

VII – 4

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Purpose Elevated serum phosphate (SP) levels are associated with an excess risk of cardiovascular disease in patients with and without chronic kidney disease. Also, a graded independent relationship was found between SP and the risk of death or cardiovascular events in patients with prior myocardial infarction. Recently, higher SP was associated with an increased risk of heart failure in a community-based sample. The aim of our study was to investigate the relevance of this emerging cardiovascular biomarker in patients with chronic heart failure.

Methods From 2000 to 2009 clinical and laboratory parameters of 977 ambulatory patients (NYHA class I: 23%, class II: 48%, class III/IV: 29%; mean LV-EF: 32%) of our heart failure program with SP data available were evaluated. Long-term follow-up (mean 40.4 months) was available in 939 patients. The primary endpoint was defined as death of any cause or heart transplantation. Sex stratified Cox proportional hazards models, adjusted for age, ischemic etiology, NYHA class, LV-EF, pulse pressure, heart rate, glomerular filtration rate, body mass index and diabetes, were performed to calculate hazard ratios (HR) and 95% confidence intervals for SP.

Results Prevalence of elevated SP (> 1.45 mmol/l) was 5.8% in men and 6.0% in women. SP was significantly correlated with severity of heart failure as assessed by NYHA class ($p < 0.001$) and LV-EF ($r = -0.10$; $p = 0.002$). Death of any cause or heart transplantation was recorded in 313 patients. Multivariate sex-stratified Cox regression analysis revealed SP to be independently associated with adverse outcome (HR 2.03 [95%-CI: 1.30–3.15]; $p = 0.002$). Compared with the lowest SP quartile, adjusted HR for patients in the second quartile was 1.08 (95%-CI: 0.68–1.51), 1.17 (95%-CI: 0.84–1.63) in the third quartile and 2.08 (95%-CI: 1.53–2.83) in the highest quartile ($p < 0.001$). Corresponding 5 years cumulative survival/time to transplantation rates were 71%, 72%, 69% and 53%.

Conclusions We found an independent relation between higher levels of SP and the risk of death or heart transplantation in ambulatory patients with chronic heart failure, most of whom had SP levels within the normal range. These findings further highlight the clinical importance of serum phosphate in cardiovascular disease.

The Effect of CCM Therapy on Myocardial Efficiency and Oxidative Metabolism in Patients with Heart Failure

XIV – 1

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Introduction Cardiac contractility modulation (CCM) is a device-based therapy that involves delivery of non-excitatory electrical signals resulting in improved ventricular function and a reversal of maladaptive cardiac fetal gene programs. Our aim was to evaluate whether acute application of CCM leads to an increase in myocardial oxygen consumption in patients with chronic heart failure patients using C-11 acetate positron emission tomography (PET).

Methods and Results We prospectively enrolled 21 patients with severe heart failure. C-11 acetate PET was performed before and after activation of CCM device. In 12 patients an additional stress study was performed. At resting conditions, myocardial blood flow (MBF) did not significantly differ between activated and deactivated CCM device (CCM off: 0.81 ± 0.18 ml min⁻¹ g⁻¹; CCM on: 0.80 ± 0.15 ml min⁻¹ g⁻¹; p -value = 0.818), myocardial oxygen con-

sumption remained unchanged (CCM off: 6.81 ± 1.69 µl O₂ min⁻¹ g⁻¹; CCM on: 7.15 ± 1.62 µl O₂ min⁻¹ g⁻¹; p -value = 0.241) and the work metabolic index (WMI) reflecting myocardial efficiency did not alter significantly (CCM off: 4.94 ± 1.14 mmHg × ml/m²; CCM on: 5.21 ± 1.36 mmHg × ml/m²; p -value = 0.344). Under dobutamine, MBF, MVO₂ and WMI did not differ between deactivated and activated CCM-device, but increased significantly when compared to resting conditions.

Discussion These results indicate that CCM does not induce increased myocardial oxygen consumption, even under stress conditions.

New Biomarkers of Kidney Injury as Predictors in Chronic Heart Failure: a Head-to-Head Assessment

VII – 3

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Background Worsening renal failure is an established strong and independent predictor of impaired outcome in chronic heart failure. To estimate kidney function in clinical practice today serum-creatinine or the glomerular-filtration-rate, which is also based on serum-creatinine are used. Serum-creatinine is highly affected by other biological variables and notoriously unreliable to capture an only mild impairment of kidney function. Therefore, new biomarkers of kidney injury, such as Neutrophil gelatinase-associated lipocalin (NGAL) and Cystatin C are currently evaluated across the cardiovascular continuum for their predictive properties. Cystatin C being a marker of glomerular filtration and NGAL a marker of tubular inflammation signal different pathogenetic pathways. To our best knowledge, a head-to-head assessment of these promising biomarkers has never been reported. We have studied these emerging biomarkers in a cohort of stable chronic heart failure patients without substantial renal disease and compared them to traditional markers of renal impairment and NT-proBNP.

Methods In this long-term observational study, 99 consecutive patients with chronic systolic heart failure and without renal dysfunction based on non-cardiac reasons were included. NT-proBNP and Cystatin C were measured using commercially available assays by Roche Diagnostics, NGAL was measured using the standardized clinical platform ARCHITECT® analyzer, Abbott Diagnostics. The endpoint was a combined endpoint consisting of all-cause mortality and hospitalizations for cardiac reasons. The median observation period was 35 months.

Results 82% of the patients were male, 44% had an ischemic etiology of HF the mean age was 61 ± 11 years, mean LVEF was $33 \pm 10\%$. The median GFR was 79.8 ml/min/1.73m² (Q1–Q3 55.5–104), median NT-proBNP was 803 pg/ml (Q1–Q3 404–1942), median Cystatin C was 1.28 mg/L, (Q1–Q3 1.072–1.688) median NGAL was 5.4 ng/mL (Q1–Q3 2.8–10.2) or median NGAL/urine creatinine ratio 0.06 (Q1–Q3 0.03–0.15). 20 patients died, 39 were hospitalized for cardiac reasons within the observation period. Cystatin C concentrations did not correlate with NGAL concentrations. Cystatin C highly correlated with GFR (-0.621 ; $p < 0.001$) and NT-proBNP (0.454; $p < 0.001$) and modestly with proteinuria (0.226; $p = 0.035$). NGAL did not correlate with GFR, NT-proBNP or proteinuria. Using a univariate model only Cystatin C carried prognostic significance ($p = 0.012$, CI: 1.277–7.110, HR 3.01), unlike NGAL, proteinuria or GFR. In a multivariate model consisting of NGAL, Cystatin C, proteinuria, gender and age again only Cystatin C carried prognostic significance ($p = 0.042$, HR 2.912, CI: 1.040–8.155). GFR was left out of the multivariate model due to strong multicollinearity with Cystatin C.

Conclusion Cystatin C proved to be of higher predictive value than traditional markers of renal impairment and the new marker NGAL in this cohort of chronic heart failure patients with only mild renal dysfunction.

Abnormalities in Renal and Liver Function are of Additive Value in Predicting Prognosis in Chronic Heart Failure

VII – 2

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Purpose The cardio-renal syndrome is common and serum creatinine (Crea) is an established biomarker in chronic heart failure (CHF). Recent findings also indicate a predictive role of liver function abnormalities such as gamma-glutamyltransferase (GGT) in CHF. Both renal and liver dysfunction may be attributed to venous congestion in this setting. We therefore aimed to investigate the prevalence of coexisting organ dysfunction and its effect on disease progression in CHF.

Methods From 2000 to 2009 clinical and laboratory parameters of 1221 consecutive ambulatory patients (NYHA class I: 25%, class II: 48%, class III/IV: 27%; median LV-EF: 29%) of our heart failure program were evaluated. Long-term follow-up (median 39 months) was available in 1160 patients. The endpoint was defined as death of any cause or heart transplantation.

Univariate and sex stratified Cox proportional hazards models, adjusted for age, ischemic etiology, NYHA class, LV-EF, heart rate, body mass index, DM were performed to calculate hazard ratios (HR) and 95% confidence intervals for Crea and GGT.

Results Prevalence of sex-specific serum level elevation was 47% for Crea and 44% for GGT. Both variables were significantly correlated with disease severity as assessed by NYHA class and LV-EF. The combined endpoint was recorded in 391 patients. Crea as well as GGT were associated with adverse outcome in univariate ($p < 0.0001$ for both variables) and multivariate analysis ($p = 0.03$ and $p < 0.0001$, respectively).

When patients were stratified according to dichotomized serum level elevations to Crea-/GGT-, Crea-/GGT+, Crea+/GGT-, and Crea+/GGT+ prevalence was, respectively, 32%, 21%, 24%, and 23%. The estimated 5-year event rate in patients with Crea-/GGT- was 14%, as compared to 30% with Crea-/GGT+ (HR 2.24, 95%-CI: 1.63–3.08; $p < 0.0001$) and 24% with Crea+/GGT- (HR 2.30, 95%-CI: 1.66–3.26; $p < 0.0001$). In patients with Crea elevated, additional elevation of GGT (Crea+/GGT+) significantly raised the estimated 5-year event rate to 37% (HR 3.14, 95%-CI: 2.3–4.46; $p < 0.0001$).

Conclusions Both renal and liver function abnormalities are common in ambulatory patients with chronic heart failure and associated with adverse outcome. The presence of liver dysfunction clearly increases the risk of adverse events in patients with cardio-renal syndrome. Our findings further highlight the clinical importance of second organ dysfunction in heart failure.

Guideline Adherence in the Treatment of Chronic Heart Failure. Data from the EuroHeart Failure Survey – Pilot Phase at the University Heart Failure Clinic Graz

XIV – 4

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Introduction Heart failure is an increasing problem in the Western world. The European Society of Cardiology (ESC) has published guidelines to standardize therapy. Although the best treatment is clear reality often drags behind. Therefore, the EuroHeart Failure Survey – Pilot Phase (EHFS) has been initiated by the ESC to gain information about real-world treatment.

Patients and Methods To evaluate guideline adherence, we investigated 66 patients taking part in the EHFS at the university heart failure clinic Graz. The EHFS includes a baseline investigation and a follow-up after 3-, 6- and 12-months. We compared the “ideal” treatment (as recommended by the ESC) to real-world treatment at a large tertiary care centre.

Results 66 patients (15 female, 51 male; median age: 61 years, IQR = 52–70) have been included in the EHFS between October 2009 and May 2010. Follow-up has been done either personally during a routine appointment or by telephone. At baseline treatment comprised of ACE-inhibitors (ACEI) in 43 patients (67%), Angiotensin-receptor-blockers (ARB) in 11 patients (17%), beta-blockers (BB) in 58 patients (89%) and Aldosterone-antagonists (AldoA) in 37 patients (57%). After 12 months 43 patients (69%) were treated with an ACEI, 16 with an ARB (25%), 60 with a BB (95%) and 41 with an AldoA (65%).

In 13 patients (28%) being in NYHA-functional class 1 and 2 at baseline treatment included the recommended ACEI or ARB plus BB, in class 3 and 4, 6 patients (33%) have been treated with ACEI or ARB plus BB plus AldoA. After 12 months 12 patients (35%) in class 1 and 2 got an ACEI or ARB plus BB while in class 3 and 4, 18 patients (62%) got an ACEI or ARB plus BB plus AldoA. Interestingly, patients living in the city of Graz have been treated with better adherence to guidelines than patients from rural areas.

Conclusion Although the percentage of patients taking adequate treatment improved over time combination-treatment according to NYHA-functional classes has considerable room for improvement. Combination therapy in all NYHA-classes should be done more dedicatedly, in consideration of an average guideline-adherence of only 40%.

Prognosis of Chronic Heart Failure Based on Data from the EuroHeart Failure Survey – Pilot Phase at the University Heart Failure Clinic Graz

XIV – 5

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Introduction Heart failure is a common disease of the elderly and, as people grow older these days, it is important to apply standards in heart failure treatment. The European Society of Cardiology (ESC) has published guidelines to standardize therapy. However, treatment may differ significantly from these guidelines in many cases.

Patients and Methods To evaluate guideline adherence, we investigated 66 patients in the setting of the EuroHeart Failure Survey – Pilot Phase (EHFS), which is an observational research program started by the ESC. It includes a basic registry as well as a 3-, 6- and 12-months-followup. We compared the basic registry parameters to the 12-months-follow-up data focusing on pharmacological treatment. The NYHA-classification, rehospitalization and survival have also been examined.

Results 66 patients (15 female, 51 male; median age: 62 years, IQR: 52–70) have been included in the EHFS between October 2009 and May 2010. Primary cause of heart failure has been ischemic in 25 patients (40%), idiopathic in 34 patients (55%) while other causes have been rare ($n = 3$; 5%).

We were able to follow up all patients after 12 ± 2 months either by telephone or personally at routine checkups at the university heart failure clinic Graz. Functional impairment at baseline has been class 1 in 8 patients, class 2 in 38 patients, class 3 in 13 patients and class 4 in 5 patients. After 12 months there have been 7 patients in class 1, 27 patients in class 2, 33 patients in class 3 and 3 patients in class 4. More patients deteriorated than improved over the 12 months period ($n = 22$; 36% vs $n = 12$; 20%, respectively; $n. s.$). 27 patients remained in the same NYHA class within the 12-months.

4 patients (6%; all male) died within the follow up period. Interestingly, those in class 3 or 4 at baseline had a similar risk to die within 12 months as those in class 1 or 2. Furthermore, those with ischemic heart failure had no greater 12-months risk to die than those with non-ischemic etiology. 16 patients (24%; 4 female, 12 male) had to be rehospitalized (1–3 times within the last six months) with heart failure being the reason for 12 rehospitalizations. Cardiac cause other than heart failure, vascular cause and renal dysfunction were documented once each and other causes have been documented twice. Those with a baseline left ventricular ejection fraction (LV-

EF) below 35% had a higher rate of rehospitalization than those with better LV-EF ($n = 8$; 73% vs. $n = 23$; 46%), although the difference did not reach significance.

Conclusion Patients with chronic heart failure taking part in the EuroHeart Failure Survey-Pilot Phase in Graz have a considerable good 1-year prognosis. However, functional capacity worsens during the 12-months follow-up making heart failure a troublesome disease with a high rate of rehospitalization.

ATS/ERS versus GOLD Criteria for Detection of Irreversible Airway Obstruction in Chronic Heart Failure

VII – 5

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Purpose Prevalence of chronic airway obstruction in chronic heart failure (CHF) is a ongoing topic in clinical research. In the latest American Thoracic Society/European Respiratory Society (ATS/ERS) Task Force statement on imperative strategies on lung function tests obstruction is characterized by a percentage of forced expiratory volume in one second to forced vital capacity ratio (FEV1/FVC) with the fifth percentile regarded as lower limit of normal (LLN). However publications on the prevalence of COPD in CHF exclusively use the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (FEV1/FVC < 70%) for diagnosis of chronic obstructive lung disease. We aim at determination of diagnostic reliability of GOLD criteria for the detection of airway obstruction in CHF patients.

Methods We prospectively screened stable CHF patients for irreversible airway obstruction. CHF patients were recruited in an outpatient heart failure clinic and underwent standardized spirometry including postbronchodilator testing. To evaluate diagnostic utility of GOLD criteria, sensitivity, specificity, positive- (PPV) and negative predictive values (NPV) were calculated with the ATS/ERS criteria (FEV1/FVC < LLN) serving as the “gold standard” for diagnosis of airway obstruction.

Results 111 patients were included. Median age was 67 years, 76,6% were male, 41,4% were former smokers and 14,4% current smokers. (Current and former smokers reported a median of 25 pack years). Mean ejection fraction was 34,9%. Median Nt-pro-BNP was 1296 pg/ml. For 95,3% of the participants the LLN for FEV1/FVC was below 70%. ATS criteria for acceptability and reproducibility were met by 77,5% that were included for further analysis. More participants fulfilled GOLD (FEV1/FVC < 70%) than ATS/ERS criteria (FEV1/FVC < LLN) for obstruction (46,5% vs 26,7%; Chi-Square $p < 0,001$). Sensitivity of GOLD criteria was 100%, specificity 73%, PPV 57,5% and NPV 100%. Of all individuals with a FEV1/FVC above the LLN (“normals”) 27% were misidentified by using the GOLD criteria (false positive). We did not observe misidentification in subjects with FEV1/FVC below the LLN using the GOLD criteria (no false negatives). The majority of false positives qualified for airway obstruction GOLD stage I which was observed less frequently in true positives (88,2% vs 30,4%; $p < 0,001$).

Conclusion For interpretation of spirometric tests in CHF patients application of the GOLD criteria may lead to overdiagnosis of irreversible airway obstruction. Therefore we recommend to use the ATS/ERS criteria for clinical purposes as well as for epidemiologic studies.

Fontan-like Circulation as a Criterion for Heart Transplantation in Right Ventricular Cardiomyopathies – A Single Center Experience

VII – 6

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Introduction Right ventricular cardiomyopathies (RVC) are most often associated with worse prognosis. Standard evaluation criteria for heart transplantation (HTx) do not necessarily apply to this con-

dition. Hemodynamic perturbation such as Fontan-like-circulation (FLC) indicates advanced right heart failure. Right heart catheterization may be helpful for the assessment of optimal timing for HTx.

Methods and Results We report on 4 patients (2 males, 41 ± 9 years) with advanced RVC who underwent invasive hemodynamic testing for the evaluation for HTx. The extent of common clinical signs of right heart failure such as leg edema, jugular and/or hepatic vein distension, ascites, and elevation of liver function tests were strikingly heterogeneous. Also, NYHA classification (2.25 ± 0.5) and NT-proBNP (2870 ± 1851.9) did not add unequivocally to decision-making. Right heart hemodynamics revealed markedly reduced CI (2.14 ± 0.64) and FLC with equilibrated pressure tracings between the right atrium (RAm 16 ± 4 mmHg) and the pulmonary artery (PAPm 16 ± 5 mmHg). In this condition blood is propelled passively through the right heart using the left atrium as driving force. Based on these findings all patients were listed for HTx with three of them being already successfully transplanted and one still on the waiting list.

Conclusion In patients with right ventricular cardiomyopathies evidence of Fontan-like-circulation may substantially contribute to evaluation for HTx particularly in patients not clearly fulfilling standard criteria.

ELICARD: Telemonitoring of Severe Chronic Heart Failure Patients in a Real World Setting

XIV – 6

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Background Rates of readmission after hospitalization for heart failure remain high despite considerable advances in medical and device therapy. Telemonitoring patient management may help to detect early signs of decompensation, allowing optimization of treatment in chronic heart failure and improvement of adherence to medical therapy. Recent trials provided conflicting results in terms of the impact of home-based telemonitoring. The purpose of this study was to retrospectively review the 1-year hospitalization due to decompensation.

Methods We observed 21 patients with chronic heart failure after an episode of acute decompensation either assigned to telemonitoring (tele group) or usual care (control group). Telemonitoring was accomplished using a mobile telemonitoring system based on mobile phones and radio frequency identification (RFID) technology. Patients were able to collect daily information about weight, blood pressure, heart rate and self-assessed health status by means of touching smart objects (measurement devices and icons) with the mobile phone. Transmitted values were reviewed every weekday by a clinician responsible for managing heart failure. Patients assigned to control group were followed by their treating clinicians according with the current standards and guidelines for treatment of patients with heart failure. We assessed the effect of telemonitoring in terms of readmission due to worsening heart failure.

Results 11 patients were assigned to tele group and 10 patients to usual care group with a median age of 73.0 yrs and 71.5 yrs, LVEF 25% in both groups and NT pro BNP 2970 pg/ml and 2062 pg/ml respectively. During a mean follow up of 12 months 5 patients (45%) of the tele group were hospitalized due to worsening of heart failure versus 9 (90%) patients of the control group (relative risk reduction 50%).

Conclusion Home monitoring reduced hospitalization due to worsening heart failure in patients with advanced chronic heart failure compared with usual care. In contrary to recent studies our results are based on the involvement of heart failure physicians and their immediate therapeutic response dependent on the telemonitoring data.

■ Interventionelle Kardiologie/Interventional Cardiology

Inoperable Aortenstenose: Anzahl potenzieller Kandidaten für TAVI („transcatheter aortic valve implantation“) in einem Wiener Schwerpunktkrankenhaus

VIII – 1

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Einleitung Die katheterunterstützte Aortenklappenimplantation (TAVI, „transcatheter aortic valve implantation“) stellt eine Alternative zum herkömmlichen chirurgischen Klappenersatz für „inoperable“ Patienten mit schwerer Aortenstenose (AS) dar. Die tatsächliche Zahl potenziell geeigneter Patienten (Pat.) und der daraus resultierende Bedarf an TAVI ist nicht bekannt. Ziel dieser Untersuchung war es, Patienten mit schwerer Aortenstenose in einem Wiener Schwerpunktkrankenhaus retrospektiv hinsichtlich potenzieller Eignung für TAVI zu analysieren.

Material und Methode Die Krankenakten aller Pat. mit der ICD-Entlassungsdiagnose AS in den Jahren 2009 und 2010 wurden retrospektiv analysiert.

Ergebnisse Es fanden sich 164 Patienten mit der Entlassungsdiagnose AS. Von diesen hatten 49 Patienten (Durchschnittsalter 76 ± 9 Jahre) eine symptomatische hochgradige Stenose (definiert als Klappenöffnungsfläche $< 1 \text{ cm}^2$, mittlerer Gradient $\geq 50 \text{ mmHg}$, maximale Flussgeschwindigkeit $> 4 \text{ m/s}$).

Vier Pat. (8 %) mit hochgradiger Aortenstenose verstarben während des stationären Aufenthalts, 5 Pat. (10 %) lehnten jegliche Therapie ab, 21 Pat. (43 %) wurden einem chirurgischen Aortenklappenersatz zugeführt. Die übrigen 19 Patienten (39 %, Durchschnittsalter 84 ± 9 Jahre) wurden aufgrund eines log. Euroscore > 15 % bzw. STS-Score > 10 % und/oder anderer Kontraindikationen (reduzierter Allgemeinzustand/Pflegebedürftigkeit $n = 16$, fortgeschrittenes malignom $n = 2$) keinem chirurgischen Aortenklappenersatz zugeführt. Von diesen wurde eine Patientin für TAVI angemeldet.

Diskussion Innerhalb von 2 Jahren kamen nach aktuellen Kriterien 19 von 49 Patienten (39 %) mit hochgradiger AS für TAVI prinzipiell in Frage. Aufgrund ihres schlechten Allgemeinzustandes und/oder Begleiterkrankungen wurden jedoch alle bis auf eine Patientin konservativ behandelt. Die Patientenselektion für TAVI und die Feststellung des tatsächlichen Bedarfs an dieser Intervention ist von zentraler Bedeutung für die Zukunft dieser Methode.

Langzeitprognose nach perkutaner koronarer Intervention in hochbetagten Patienten – eine Single-Center-Erfahrung

BAIL

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Einleitung Eine perkutane koronare Intervention (PCI) wird immer häufiger in hochbetagten Patienten durchgeführt. Allerdings gibt es kaum Daten zur langfristigen Prognose in diesem Kollektiv.

Methode Es wurden alle ($n = 6820$) Patienten eines Zentrums mit PCI von 1/1998 bis inklusive 12/2008 eingeschlossen. Es wurden alle Patienten und alle Ereignisse (= Tod) erfasst, weil das individuelle, jeweilige Sterbedatum der Statistik Austria bekannt ist. Das Patientenkollektiv wurde nach Alter, Geschlecht und Kalenderjahr der PCI zur Normalbevölkerung mittels Sterbetabelle der Statistik Austria „gematched“. Die relative Hazard Rate (beobachtete Hazard Rate dividiert durch die Populationshazard) wurde auf Basis eines Ramlau-Hansen-Schätzer berechnet. Werte > 1 bedeuten ein höheres Risiko im Patientenkollektiv als in der Normalbevölkerung.

Ergebnisse Die Daten werden in 4 Quartilen zu je 1705 Patienten präsentiert. Das relative Risiko ist im 1. Jahr nach PCI hoch. Jene Patienten, die das 1. Jahr post PCI überleben, haben die nächsten 9

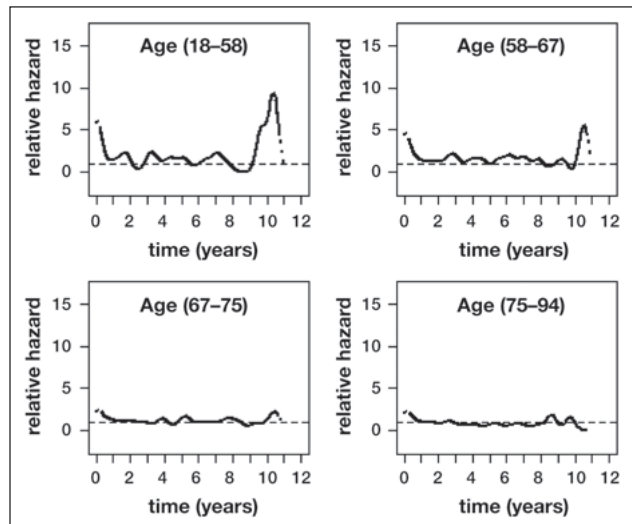


Abbildung 19: B. Frey et al.

Jahre kein erhöhtes Risiko im Vergleich zur Normalbevölkerung. Dies gilt besonders für hochbetagte Patienten (75–94 Jahre), die im Vergleich zur den Jüngsten (18–58 Jahre) eine 51 % längere relative Lebenserwartung hatten (Abbildung 19).

Diskussion Hochbetagte Patienten haben 12 Monate post PCI eine idente Überlebenswahrscheinlichkeit relativ zur hochbetagten Normalbevölkerung. Für Patienten < 58 Jahre gilt das nicht. Daher sollte das Alter alleine kein Kriterium sein, Patienten mit einer Lebenserwartung > 12 Monate nicht für eine PCI zu akzeptieren.

Multiple Electrode Aggregometry and Vasodilator Stimulated Phosphoprotein-Phosphorylation Assay in Clinical Routine for Prediction of Postprocedural Major Adverse Cardiovascular Events

VIII – 2

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Background Reduced antiplatelet effect of clopidogrel assessed with multiple electrode aggregometry (MEA) and vasodilator stimulated phosphoprotein-phosphorylation (VASP-P) assay has been proven to predict major adverse cardiovascular events (MACE) after coronary stenting. So far no consecutive registry has evaluated the usefulness of different adenosine diphosphate-based platelet function tests to predict outcome in unselected patients. Hence, our objective was to determine the feasibility of MEA and VASP-P for clinical routine and whether low-response to clopidogrel as determined by MEA and/or the VASP-P assays predicts MACE in a “real-life” population undergoing coronary stenting.

Methods Three-hundred consecutive patients were included in this prospective registry. Blood was sampled 6–24 hours after stenting to measure MEA and VASP-P assays.

Results The use of glycoprotein-IIb/IIIa-blockers in this unselected cohort limited MEA to 196 measurements. Concerning the VASP-P assay, 300 measurements were achieved. ROC-curves of sensitivity and specificity estimates for MACE were plotted for VASP-P assay. The area under the ROC-curve was 0.683 ($p = 0.014$) for the platelet reactivity index (PRI) calculated from median fluorescence intensities (FI) with an optimal cut-off at 60.2% PRI. Patients above 60.2% had a significantly increased risk for MACE at 6 months follow-up ($p = 0.007$). Estimating the cut-offs for the PRI from mean FI (52%) or from geometric mean FI (56.6%) led to clinically relevant differences in the cut-offs.

Conclusions VASP-P assay is feasible for clinical routine to measure clopidogrel effects and to predict postprocedural MACE in unselected patients. With regard to differing cut-offs, exact stan-

dardization of the VASP-P assay is mandatory. The use of GPIIb/IIIa-blockers prevents MEA testing and limits therefore its usability in unselected patients.

ExoSeal® versus AngioSeal® – Comparison of 2 Arterial Closure Devices in Terms of Bleeding Complications

VIII – 3

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Background The ExoSeal®-system represents a new, purely extravascular closure system, which seals the artery from the outside via an absorbable Polyglycolic acid plug. Up to now one trial (ECLIPSE) reported similar results regarding major access-site-related adverse events when comparing this device with manual compression. As many other institutions we treat almost all femoral puncture sites using a closure device instead of manual compression. The AngioSeal®-device is the most frequently used system, which consists of an intravascular anchor and an extravascular absorbable collagen sponge. The aim of this study was to compare these 2 devices in terms of bleeding complications in every day clinical life.

Material and Methods This study was performed in patients who underwent a coronary angiography at the Medical University of Vienna between July and December 2010. We prospectively analyzed 45 patients who were treated with ExoSeal® and 90 control patients (ratio 1:2) who were treated with AngioSeal® and were matched according to age, sex, and procedure (diagnostic or interventional). The occurrence of bleeding complications was evaluated based on a standard complication feedback form completed by physicians of the cardiology wards.

Results The 2 study groups are homogeneously distributed in terms of gender, age, intra-interventional administration of Heparin, duration of intervention and severity of CHD (Table 13).

Both groups show an equally low rate of bleeding complications (ExoSeal®: n = 1; AngioSeal®: n = 2). One bleeding complication occurred after a diagnostic angiography, the other 2 events occurred after an interventional procedure. All three events were defined as less-severe complication (hematoma), which were treated using conventional compression after assessment by echo or computer tomography.

Conclusion Our results suggest that ExoSeal® is as safe as AngioSeal® for closure of the puncture side of the femoral artery after coronary angiography. These data should be confirmed in a larger patient population.

Table 13: C. Gangl et al.

	AngioSeal® (n = 90)	ExoSeal® (n = 45)	Significance
Gender (m/f)	62 (69 %)/28 (31 %)	31 (69 %)/14 (31 %)	n. s.
Diagnostical/ Interventional	48 (53 %)/42 (47 %)	24 (53 %)/21 (47 %)	n. s.
Age	69 (IQR 61–75)	69 (IQR 62–77)	n. s.
Heparin (IE)	4189	4156	n. s.
Duration of intervention	97 Min	111 Min	n. s.
CHD-severity			
0–VD	12 (13 %)	9 (20 %)	n. s.
1–VD	19 (21 %)	10 (22 %)	n. s.
2–VD	25 (28 %)	15 (33 %)	n. s.
3–VD	34 (38 %)	11 (25 %)	n. s.

5 Years Clinical Follow-up of Patients Treated with Combined Delivery of Intracoronary and Intramyocardial Bone-marrow Mononuclear Cells

XV – 7

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Background The MYSTAR prospective randomized study revealed a moderate but significant increase in global left ventricular ejection fraction (EF) in patients receiving combined delivery of bone-marrow mononuclear cells (BM-MNC) either 3–6 weeks (mean 32 ± 12 days, Early group) or 3–4 months (mean 93 ± 15 days, Late group) post acute myocardial infarction (AMI), with no difference between the groups 3 months post-BM-MNC therapy. We have evaluated the effect of the cardiac stem cell therapy on long-term (5 years) clinical outcome.

Methods Between 2002 and 2006, patients with recent AMI and primary percutaneous coronary intervention, and EF between 30–45% were included in the MYSTAR study. The 5-year clinical follow-up (FUP) included the records of major adverse cardiac events (MACCE, defined as all-cause mortality, re-AMI, reintervention of the infarct-related artery (IRA) and stroke), implantation of automatic cardioverter-defibrillators (ICD) and hospitalization due to angina pectoris or acute or chronic heart failure. Kaplan-Meier survival analyses were performed to compare the clinical outcomes of the Early and Late groups. Predictors for worse long-term outcome were assessed by using Cox proportional hazard analysis.

Results MACCE occurred in 16.7% of patients (10% in Early and 23.3% in Late groups, log-rank $p = 0.197$) during the 5 years FUP. All-cause death occurred only in Late group (10% vs 0%, log-rank $p = 0.024$) (cardiac death 6.7% vs 0%). ICD was implanted in 6.7% and 10% of patients, repeated hospitalization was necessary in 16.7% of patients in both groups (non-significant), respectively. Patients with MACCE had a significantly lower baseline unipolar voltage value of the intramyocardially injected area (6.2 ± 2.7 vs 8.3 ± 2.7 mV; $p = 0.025$). Mortality was associated with significantly lower baseline 99m-Tc-Sestamibi tracer uptake ($44.2 \pm 15.4\%$ vs $58.4 \pm 15.6\%$; $p = 0.042$), unipolar voltage (4.8 ± 1.2 vs 8.3 ± 2.7 mV; $p = 0.002$) and local linear shortening values (index of segmental wall motion disturbance) ($7.4 \pm 3.2\%$ vs $11.1 \pm 3.7\%$; $p = 0.021$) of the injected area, with no other differences regarding the baseline data. Low unipolar voltage value proved to be significant predictor for poor outcome at 5-year FUP by Cox regression analysis when adjusted for the classical predictors of MACCE.

Conclusions Combined delivery of BM-MNC leads to a favorable event-free survival rate in patients with a low (30–45%) EF post-AMI. Late (at least 3 months post-AMI) cardiac stem cell therapy resulted in a higher incidence of death during the 5-year FUP, as compared with the cardiac stem cell therapy between 3–6 weeks post-AMI. NOGA-derived baseline parameter might help to identify patients with significantly better long-term clinical outcome after cardiac stem cell therapy.

AngioSeal® after Femoral Artery Puncture – Does Additional Compression Bandage Increase the Safety?

VIII – 4

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Background To investigate the efficacy of compression bandage in patients after percutaneous transfemoral coronary angiography in addition to the general appliance of AngioSeal®.

Materials and Methods We conducted a randomized controlled study which was approved by the local ethics committee. Included patients were randomly assigned to an additional compression bandage at the arterial puncture site accompanied by bedrest of four hours or just four hours lasting bedrest after direct closure by utilizing AngioSeal®.

Patients' vascular puncture sites were clinically and sonographically investigated the day after the procedure. The occurrence rate of complications at the vascular access site was recorded.

Results We prospectively included 105 patients (60% male). The median age was 67 years (IQR 59–75). We observed six pseudoaneurysms at the vascular access site (3 patients each, $p = 0.94$). Patients in the compression group exhibited more hematomas at the puncture site (9 vs 4 patients; $p = 0.17$). None of the patients underwent transfusion or surgical pseudoaneurysm repair. All pseudoaneurysms were solved conservatively.

Conclusion The appliance of an additional compression bandage after primary closure of the vascular access site by utilizing AngioSeal® was not associated with reduced local puncture-related complication rate. In contrast, bedrest for 4 hours after arterial puncture for coronary interventions without any compression bandage appeared safe.

Perkutane renale Denervation bei Patienten mit therapieresistenter arterieller Hypertonie – Ein Single-Center-Erfahrungsbericht VIII – 5

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Einleitung Trotz der Entwicklung immer neuer Antihypertensiva und des Einsatzes von Mehrfachkombinationen gelingt bei ca. 10 % der Patienten keine leitliniengerechte Blutdruckeinstellung. Für diese Patienten steht mit der perkutanen renalen Denervation (PRD) ein neuer vielversprechender Therapieansatz zur Verfügung.

Methodik Zwischen Juni und September 2010 erfolgte bei 30 Patienten mit therapieresistenter Hypertonie eine PRD mit dem Simplicity-Katheter-System (Fa. Medtronic/Ardian, Mountain View, CA, USA). Dabei wurde über einen transfemorale Zugang der Ablationskatheter in beiden Nierenarterien platziert und abhängig von der Nierenarterienanatomie eine entsprechende Anzahl von Energieabgaben durchgeführt.

Als therapieresistente Hypertoniker wurden Patienten mit einem systolischen Blutdruck > 160 mmHg (Mittelwert aus 3 Messungen in unserer Hypertonieambulanz) bei gleichzeitiger Einnahme von mindestens 3 Antihypertensiva (davon ein Diuretikum) in adäquater Dosis definiert. Nachkontrollen erfolgten nach 1, nach 3 und nach 6 Monaten.

Ergebnisse Bei allen Patienten konnten die Katheter in beiden Nierenarterien stabil platziert werden, sodass durchschnittlich 4,9 Ablationen (3–8) in der linken und 5,1 Ablationen (2–8) in der rechten Nierenarterie durchgeführt werden konnten. Bei einem Patienten trat postinterventionell ein Aneurysma spurium auf.

Die Patienten waren durchschnittlich 64,7 (39–89) Jahre alt, 13 Patienten waren weiblich. Der Ausgangs-Blutdruck betrug im Mittel 179,9/96,4 mmHg ($n = 30$), obwohl die Patienten durchschnittlich 4,2 Antihypertensiva einnahmen. Nach einem Monat lagen die Werte im Mittel bei 164,5/89,2 mmHg ($n = 30$) und nach 3 Monaten bei 157,2/86,2 mmHg ($n = 25$). Sechs Monate nach der Intervention betrug der mittlere Blutdruck 143,5/74,8 mmHg ($n = 10$). Somit ergibt sich eine mittlere Blutdruckreduktion von 15,4/7,2 mmHg nach 1 Monat, 22,7/10,2 mmHg nach 3 Monaten und 36,4/21,6 mmHg nach 6 Monaten. Die Nierenfunktionsparameter (GFR, Kreatinin, Cystatin C) zeigten sich während der Nachsorge stabil.

Diskussion Mit der PRD kann bei Patienten mit therapieresistenter Hypertonie eine substantielle Blutdrucksenkung erreicht werden, wobei sich das Eingriffsrisiko auf die bekannten Komplikationen eines transfemorale Zugangs beschränkt.

Postinterventional Cardiac Marker Release has Limited Prognostic Relevance Compared with Standard Risk Factors and Markers in Patients with Stable Coronary Artery Disease Undergoing Elective Percutaneous Coronary Interventions XV – 8

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Introduction The aim of the study was to investigate the prognostic significance of postinterventional cardiac troponin T (cTnT) and creatine kinase (CK) release in patients with stable coronary artery disease (CAD) undergoing elective percutaneous coronary interventions (PCI).

Materials and Methods Evaluation of mortality and a combined clinical endpoint (mortality, need for coronary revascularization, myocardial infarction, hospitalization for cardiac causes, or stroke) during a 40.5 ± 8.6 month follow-up in 136 consecutive patients (73% males, age: 66.6 ± 9.9 years) receiving 1–5 stents (1 in 77.9%) for 1–3 vessel disease (1 vessel disease in 54.4%). 55.1% of patients had a reduced left ventricular ejection fraction (LVEF). Pre PCI laboratory assessment included CK, cTnT, N-terminal pro B-type natriuretic peptide (NT-proBNP) and high sensitivity C-reactive protein (hs-CRP). Post-PCI CK and cTnT were measured after 4 hours and on the next day if indicated.

Results 13 patients died (6 cardiac death) and 68 patients reached the combined endpoint (37 cardiac events). Post PCI CK increased above the upper reference limit in 11 and cTnT ($> 0.03 \mu\text{g/L}$) in 16 patients. Univariate Kaplan-Meier survival rate analysis showed that hs-CRP and diabetes were the only significant predictors of all-cause mortality, and diabetes and a reduced LVEF of cardiac mortality. hs-CRP, diabetes, and a reduced LVEF were the only significant predictors of combined cardiac events. In an age- and gender-adjusted multivariate Cox regression analysis, hs-CRP and detectable cTnT ($> 0.01 \mu\text{g/L}$) before PCI were the only significant predictors of all-cause mortality, diabetes for cardiac mortality, and a reduced LVEF for combined cardiac events.

Discussion In comparison with traditional risk factors and markers post-PCI cardiac marker release is of low prognostic importance for predicting cardiac mortality and future cardiac events in patients with stable CAD undergoing elective PCI.

Compression of Iatrogenic Femoral Pseudoaneurysm by Instillation of Physiological Saline Solution VIII – 6

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Background Arterial puncture for angiographic procedures carries a considerable risk of access site complications. The incidence of pseudoaneurysms has been reported in up to 8%. Recently, there are data available describing a para-aneurysmal saline injection as novel therapeutic alternative to percutaneous thrombininjection. The aim of the present study was to report the success rate of para-aneurysmal saline injection in patients with post-catheterization pseudoaneurysm at the vascular access site.

Materials and Methods The study was designed as a prospective cohort study. We enrolled consecutive patients with pseudoaneurysms after percutaneous procedures who underwent percutaneous paraaneurysmal saline injection to compress the arterial feeder of respective femoral pseudoaneurysms.

Results We included 51 patients (55% male) in our final analysis. In 22 patients (43%) the paraaneurysmal saline injection appeared successful the day after injection. Demographic variables were well balanced in our study population. We observed no differences in coagulation findings. Interestingly, the larger the angle (median 140° vs median 110° ; $p < 0.001$) between the feeding femoral artery and the fistula and the longer the fistula (median 12.5 mm vs median 10.3 mm; $p = 0.009$) the higher was the investigated treatment suc-

cess. Moreover, the peak systolic velocity in the fistula seems also inversely but not significantly linked to the respective treatment success (median 2.5 m/sec vs median 2.9 m/sec; $p = 0.07$).

Discussion We observed that simple anatomical features of the pseudoaneurysmatic fistula significantly predict the success rate of paraaneurysmal saline injection.

Single-Center Experience with Transcatheter Aortic Valve Implantation: Cumulative Survival and 3-Year Follow-up

BAII

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Background Transcatheter aortic valve implantation (TAVI) is an emerging new treatment option for elderly patients with symptomatic severe aortic stenosis (AS) and high risk for surgical aortic valve replacement. Since TAVI was introduced into clinical cardiology only a few years ago, data on long-term clinical outcome is scarce. Therefore we analyzed our patient series in this regard with a follow-up period of more than 3 years.

Patients and Methods Between May 2007 and March 2011, in our center a total of 165 patients (age: mean $\pm$ SD 81 $\pm$ 6 years, median 82 years, range 62–91 years; male = 37%) underwent TAVI with a 26 or 29 mm self-expanding CoreValve bioprosthesis (Medtronic Inc., Minneapolis, MN). Mean logistic EuroSCORE was 26 $\pm$ 15% (median 20%, range 6–73%). A transfemoral access was used in 162 patients, a left subclavian approach in 3 patients. Follow-up visits, including clinical assessment and echocardiographic evaluation, were scheduled at 30 days, 3 months, 6 months, and 12 months after the procedure, and on a yearly basis thereafter. Cumulative survival rates were calculated using Kaplan-Meier life-table analysis.

Results Acute procedural success rate was 99.4%. In 1 single patient the procedure had to be aborted due to inadequate annulus measurement. Device implantation resulted in a clear-cut clinical improvement accompanied by a significant and sustained reduction of peak and mean transaortic pressure gradients as well as a significant and sustained increase of calculated aortic valve area. Cumulative 30-day, 1-year, 2-year, and 3-year survival rates were calculated as 93.2% (patients at risk = 162), 84.1% (patients at risk = 109), 74.3% (patients at risk = 59), and 70.4% (patients at risk = 36), respectively.

Discussion TAVI emerges as a promising new treatment option for elderly patients with symptomatic severe AS and high risk for surgical aortic valve replacement. Feasibility of the procedure itself has already been proven in numerous cases, and durability of hemodynamic results seems to be encouraging. Cumulative survival after TAVI shows a clear benefit for patients with symptomatic severe AS, who would have been left untreated due to their expected high surgical risk.

Transradial Approach for Percutaneous Coronary Interventions with Thromboaspiration in Patients with STEMI

VIII – 7

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Objective We sought to evaluate the effects of manual thromboaspiration on myocardial reperfusion performed during percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).

Background Complete reperfusion after primary PCI is compromised by the presence of intraluminal thrombus. Thus effective and safe extraction of thrombus in a timely fashion is important for successful reperfusion.

Methods In the period from 01.01.2010–31.12.2010 in 650 patients with STEMI PCI was performed. In 616 patients (94.8%) PCI was performed through transradial approach and in 34 (5.2%) we used

transfemoral access. The mortality rate in examined group was 4.5%. Thirty patients (age 51 $\pm$ 12 years, males 78%) with STEMI and angiographic evidence of intraluminal thrombus underwent thromboaspiration during a 12-month period. Thromboaspiration was performed after the presence of thrombus was confirmed angiographically by the operator. Thrombectomy was performed using 6F-Aspiration Catheter. Myocardial reperfusion using thrombolysis in Myocardial Infarction (TIMI) flow was assessed.

Results The infarct-related artery was left anterior descending (19%), right coronary artery (59%), left circumflex artery (22%). The coronary lesion was Type B in 62% and Type C in 38% patients, with an average length of 18.2 $\pm$ 4.6 mm and reference vessel diameter of 3.2 $\pm$ 0.4 mm. The preprocedural TIMI-flow was 0 in 62%, 1 in 13%, 2 in 22% and 3 in 3% of patients. The postprocedural TIMI flow was 0 in 3%, 1 in 6%, 2 in 25% and 3 in 66% of patients. The in-hospital mortality was 0 and the 30 day mortality was 2%.

Conclusion Manual thrombectomy is safe and effective in establishing myocardial reperfusion after STEMI.

Mesh Covered Stents and Myocardial Blush in ACS Patients: First Results of an Ongoing Trial

XV – 1

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Purpose Our ongoing single centre retrospective trial sets out to examine the outcome of PCI in ACS patients using a mesh covered stent device designed to provide embolic protection compared to a control group in which conventional stent devices were employed. Endpoints were myocardial blush and TIMI immediately after PCI and 6 months mortality.

Method Our trial included 71 ACS-patients (MI or unstable AP) with single vessel disease. In 34 patients the mesh covered stent was employed (median age: 65.5, 70.6% men; 67.7% STEMI, 12.9% NSTEMI, 19.4% unstable AP). The control group with conventional stent devices (DES or BMS) included 34 patients (median age: 63.0, 73.0% men; 72.7% STEMI, 9.1% NSTEMI, 18.2% unstable AP). Myocardial reperfusion after PCI was assessed by Myocardial Blush Grade (MBG) and by using the Quantitative Blush Evaluator (QuBE) a computer program created by Vogelezang et al. (2009) which provides a quantitative measure for myocardial blush. The QuBE value reflects both the filling and emptying phase of the vessels, by summing the maximum increase in greyvalue and the maximum decrease after that. The score is an observer independent mea-

Table 14: N. Preis et al.

		Mesh covered stent	Conventional stent device DES/BMS
TIMI pre PCI	0	50%	46%
	1	5.9%	-
	2	26.5%	16.2%
	3	17.7%	37.8%
TIMI post PCI	0	-	-
	1	-	2.7%
	2	8.8%	16.2%
	3	91.2%	81.1%
MBG post PCI	0	-	-
	1	2.9%	10.8%
	2	5.9%	13.5%
	3	91.2%	75.7%
Modified QuBE value*	Median	4	3
	Q1	3	2
	Q3	5	4
	Min	1	1
	Max	8	8

* Significant differences in quantitative assessment of myocardial blush between patients treated with mesh covered stents and the control group ($p < 0.05$, Mann-Whitney-U-Test).

sure, significantly correlated with MBG and predicts complete ST-elevation resolution, low enzyme levels, and 1 year survival. To apply the Quantitative Blush Evaluator to our angiographic data we modified the method calculating the increase in greyvalue in the filling phase of the vessel and omitting the emptying phase. The modified QuBE value is significantly correlated with MBG ($p < 0.001$). TIMI score was assessed before and after PCI. Information about 6 Months mortality was provided by the Austrian health insurance system.

Results We found a non-significant trend of better TIMI flow grade and MBG after PCI in patients treated with mesh covered stents (TIMI pre PCI: 0: 50%, 1: 5.9%, 2: 26.5%, 3: 17.7%; TIMI post PCI: 2: 8.8%, 3: 91.2%; MBG 1: 2.9%, 2: 5.9%, 3: 91.2%) compared to the control group (TIMI pre PCI: 0: 46%, 1: 0%, 2: 16.2%, 3: 37.8%; TIMI post PCI: 1: 2.7%, 2: 16.2%, 3: 81.1%; MBG: 10.8%; 1: 13.5%; 3: 75.7%) (Table 14). With respect to the quantitative evaluation of myocardial blush patients with mesh covered stents show significantly better results compared to the control group (median: 4, q1/q3: 3/5 vs median: 3, q1/q3: 2/4; $p < 0.05$). With respect to 6 months mortality we found no significant difference between the 2 groups.

Conclusion At the current stage our trial suggests, that employment of MD-Inspire-Stents could lead to better myocardial reperfusion in ACS-patients compared to conventional stent devices. TIMI flow grade, MBG and quantitative assessment of myocardial perfusion.

Combined Treatment of Thrombotic Coronary Occlusions by Thrombectomy and by Intracoronary Administration of Abciximab via an Intracoronary Perfusion Catheter – Which Treatment First? XV – 2

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Aim Thrombectomy as well as intracoronary administration of abciximab via an intracoronary perfusion catheter have been demonstrated to reduce thrombus burden. We analyzed 2 different treatment strategies – (1) first thrombus-aspiration to reduce thrombus size, then lysis of the rest-thrombus by locally administered abciximab via the ClearWay (CW) RX perfusion catheter versus (2) first pharmacological thrombus-reduction by locally administered abciximab, then, if necessary, thrombus-aspiration of the rest-thrombus.

Methods This retrospective study included 43 patients who presented with an acute coronary syndrome due to an intracoronary thrombus between May 2009 and December 2010. Thrombus-aspiration first strategy was performed in 33 patients, abciximab first strategy in 10 patients. The primary endpoint was defined as final improvement in Thrombolysis In Myocardial Infarction (TIMI) flow.

Results Before treatment TIMI flow was similar between the 2 treatment groups (TIMI flow 0 in 24 and 7 patients (73/70%), 1 in 6 and 1 patients (18/10%), 2 in 2 and 1 patients (6/10%), 3 in 1 and 1 patients (3/10%) – n. s.). In the thrombus-aspiration first group local abciximab administration improved TIMI flow by one stage in 34% of patients, by 2 stages in 3% of patients, and by three stages in 3% of patients, and did not improve TIMI stage in 59% of patients. In the abciximab first group local abciximab administration improved TIMI flow by one stage in 44% of patients, by 2 stages in 22% of patients, and by three stages in 22% of patients, and did not improve TIMI stage in 11% of patients (compared to thrombus-aspiration group $p < 0.05$). In the abciximab first group additional thrombus aspiration was performed in 5 patients (50%), whereas in the thrombus-aspiration first group all patients were additionally treated with local abciximab administration. Final TIMI flow was in trend better in the abciximab first group (TIMI flow 3 in all patients) than in the thrombus-aspiration first group (TIMI flow 1 in 6 patients, 2 in 4 patients, 3 in 23 patients – $p = 0.1$).

Conclusion Improvement of TIMI flow by local abciximab administration is more effective when using the abciximab first strategy compared to using thrombus-aspiration first strategy. The abciximab first strategy seems to be more effective to achieve optimal final TIMI flow than the thrombus-aspiration first strategy.

Intracoronary Administration of Abciximab via an Intracoronary Perfusion Catheter in Patients with a Thrombotic Coronary Occlusion – a Single Center Experience XV – 3

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Aim At concentrations superior to those achieved with the standard intravenous dose for coronary procedures, abciximab has an active dethrombotic effect by displacing platelet-bound fibrinogen. This analysis investigates whether administration of abciximab by local intracoronary infusion through the ClearWay Catheter improves coronary blood flow (TIMI flow) by reducing thrombus burden.

Methods and Results This retrospective study included 43 patients who presented with an acute coronary syndrome due to an intracoronary thrombus between May 2009 and December 2010. The primary endpoint was defined as improvement in Thrombolysis In Myocardial Infarction (TIMI) flow after intracoronary application of abciximab via the ClearWay (CW) RX perfusion catheter.

The population (mean age 58 ± 11 years) consisted of 36 patients (84%) with an ST-elevation myocardial infarction and 7 patients (16%) with a non-ST-elevation myocardial infarction. Nine patients (21%) presented with cardiogenic shock. The balloon-diameter of the perfusion catheter was 1 mm in 16 (37%), 1.5 mm in 7 (16%), 2.0 mm in 14 (33%), and 3.0 mm in 6 patients (14%), respectively. Successful positioning of the balloon within the thrombus was not possible in 3 patients (8%). After infusion of abciximab using the perfusion catheter TIMI flow improved by one grade in 14 patients (37%), by 2 grades in 3 patients (8%), and by 3 grades in 3 patients (8%), TIMI flow remained unchanged in 13 patients (34%), and even worsened by one grade in 5 patients (13%) (chi-square-test – $p < 0.0001$). The procedure was complicated by an air embolization in 5 patients (12%). Air embolization occurred using a 2 mm balloon (3 patients) or a 3 mm balloon (2 patients), but not using a 1 mm or 1.5 mm balloon (qui-square-test – $p < 0.07$). After the use of the perfusion catheter in these patients TIMI flow improved by one degree in 2 of these patients, and was unchanged in 2 of these patients (no documentation in one patient). After additional treatment with thrombectomy (38 patients – 88%), initial balloon dilatation (33 patients – 77%), direct stenting (10 patients – 23%), and stent implantation (39 patients – 90%), the final TIMI flow was TIMI 3 in 33 patients (77%), TIMI 2 in 4 patients (9%), and TIMI 1 in 6 patients (14%).

Conclusion The intracoronary infusion of abciximab using the ClearWay (CX) RX perfusion catheter helps to improve myocardial perfusion in patients with acute coronary syndrome due to an intracoronary thrombus. The use of perfusion catheters with a balloon ≥ 2 mm can be associated with air embolism.

The Course of NT-proBNP in Patients who underwent Percutaneous Transcatheter Aortic Valve Implantation XV – 4

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Background Natriuretic peptides have been shown to predict outcome in patients with severe aortic stenosis after aortic valve replacement. The aim of this study was to evaluate the course of N-terminal pro B-type natriuretic peptide (NT-proBNP) in patients

who underwent percutaneous transcatheter aortic valve implantation (TAVI).

Methods Between May 2007 and February 2011, 53 symptomatic pts with severe aortic stenosis successfully underwent TAVI (30 pts received an Edwards Sapien valve, 23 pts a CoreValve). NT-proBNP (Roche Elecsys) were assessed before and 30 days, 3, 6, and 12 months after TAVI.

Results Patients had an age of 83 ± 5.9 years, the logistic EuroScore was $26.3 \pm 11.6\%$, the baseline aortic valve area $0.6 \pm 0.1 \text{ cm}^2$, and the mean gradient $59.6 \pm 19 \text{ mmHg}$. Baseline NT-proBNP was significantly correlated to the logistic EuroScore ($r = 0.43$; $p = 0.002$), and to LVF ($r = 0.5$; $p = 0.0001$), but not to age. After TAVI NT-proBNP decreased in trend from 2364 pg/ml ($n = 50$, IQR 1254–7253) to 1815 pg/ml ($n = 32$; IQR 838–3392; paired t-test $p = 0.045$) after 30 days, to 1536 pg/ml ($n = 29$; IQR 702–3393; $p = 0.238$) after 3 months, to 1382 pg/ml ($n = 29$, IQR 447–3375; $p = 0.095$) after 6 months, to 1290 pg/ml ($n = 17$, IQR 733–3101; $p = 0.145$) after 12 months, and to 737 pg/ml ($n = 10$, IQR 286–1851; $p = 0.032$) after 2 years. Baseline NT-proBNP in 22 pts who died after TAVI during FUP (mean 193 days) was in trend higher (2945 pg/ml, IQR 1641–8618) compared to 31 survivors (1777 pg/ml, IQR 785–3674; $p = 0.105$).

Conclusion After TAVI, NT-proBNP levels tended to decrease. If baseline NT-proBNP seems to be a predictor for outcome after TAVI should be confirmed in larger patient populations.

Phenotyping versus Genotyping for Prediction of Adverse Events in Clopidogrel Non-Responders

XV – 5

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Background and Aim Although prognostic values of different tests for assessment of clopidogrel responsiveness have been shown in independent studies, no direct comparison between the assays has been made so far. Therefore, we investigated which laboratory approach has the best predictive value for adverse events in patients taking clopidogrel.

Methods In this prospective cohort study polymorphisms of CYP2C19*2 and CYP2C19*17 genes, vasodilator-stimulated phosphoprotein phosphorylation (VASP) assay, Multiple Electrode Aggregometry (MEA; adenosine diphosphate + prostaglandine E1: ADP+PGE1), Cone and Platelet Analyzer (CPA: ADP) and Platelet Function Analyzer (PFA100: collagen+ADP) were performed in 416 patients with coronary artery disease undergoing percutaneous coronary intervention. The rates of events (definite and probable stent thromboses and major bleedings) were recorded during a 12-month follow-up.

Results Receiver operator characteristic analysis showed that platelet aggregation by MEA predicted stent thrombosis better (c-index = 0.90; $p < 0.001$; sensitivity = 90%; specificity = 83%) than the VASP assay (c-index = 0.62; $p > 0.05$; sensitivity = 70%; specificity = 38%), CPA (c-index = 0.62; $p > 0.05$; sensitivity = 90%; specificity = 36%), PFA100 (c-index = 0.66; $p > 0.05$; sensitivity = 70%; specificity = 61%) or the CYP2C19*2 polymorphism (sensitivity = 30%; specificity = 71%). Survival analysis yielded that patients classified as non-responders by MEA had a substantially higher risk to develop stent thrombosis than clopidogrel responders (12.5% vs 0.3%; $p < 0.001$), whereas poor metabolisers (CYP2C19*1/*2 or *2/*2 carriers) were not at increased risk (2.7% vs 2.5%; $p > 0.05$). Multiple logistic regression analysis identified response status assessed by MEA as an independent predictor of stent thrombosis. Although the incidence of major bleedings was higher in patients with an enhanced vs. low response to clopidogrel (4% vs 0%) or in ultra-metabolisers vs. regular-metabolisers (CYP2C19*17/*17 vs. CYP2C19*1/*1; 9.5% vs 2%), neither test was predictive for bleeding events during clinical follow-up. The classification and regression tree analysis demonstrated that acute coronary syndrome at

hospitalisation followed by diabetes mellitus were the best discriminators for clopidogrel responder status.

Conclusions Phenotyping of platelet response to clopidogrel by MEA might be a better risk predictor of stent thrombosis than genotyping of the CYP2C19 allele.

Gender Differences in a Large Cohort of Consecutive Patients Undergoing Elective Coronary Angiography For the Evaluation of Suspected Coronary Artery Disease

XV – 6

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Background Gender specific information from consecutive patients undergoing elective coronary angiography (CA) in daily clinical practice is sparse. We investigated gender differences in a large cohort of consecutive patients referred for elective CA for the evaluation of coronary artery disease (CAD).

Methods Data from 7819 consecutive elective patients referred for CA were collected. Furthermore, follow-up data from 345 randomly selected CAD patients without recent or prior myocardial infarction were obtained.

Results On the background of a different risk factor profile, men more frequently had a significant CAD (41.1 vs 65.6%; $p < 0.001$) and consequently underwent more often a percutaneous coronary intervention (PCI) (20.2 vs 32.1%; $p < 0.001$). In patients with sig-

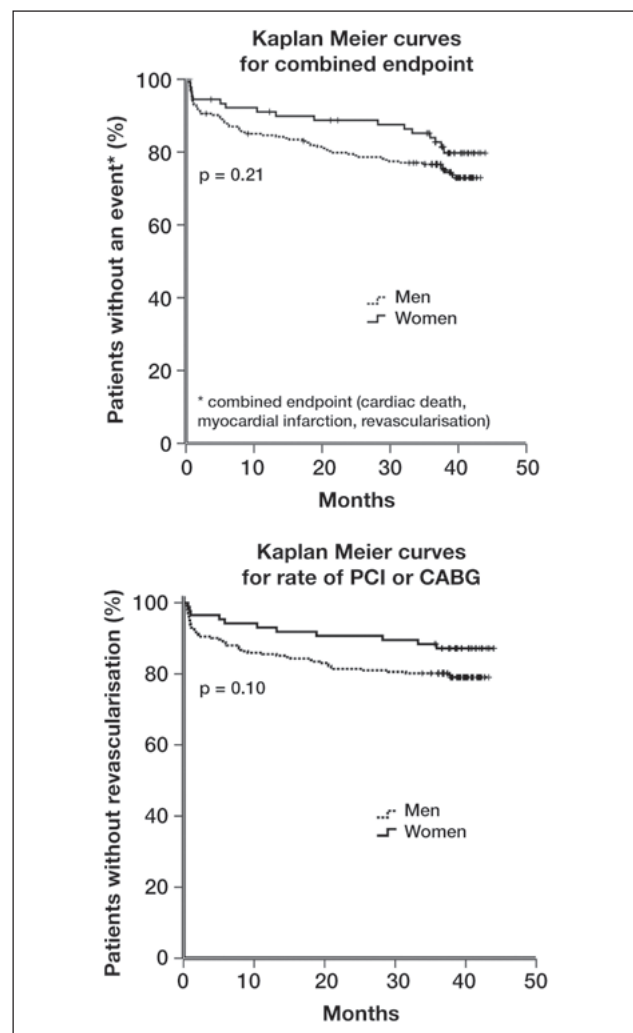


Figure 20: A. Süssenbacher et al.

nificant CAD, PCI rate was not different between gender (49.2 vs 48.6%, women vs men resp.; $p = 0.72$), CABG was more often performed in men (10.4 vs 13.4%; $p = 0.01$). After a mean follow-up of 39 ± 2 months, no difference in the combined endpoint (cardiac death, myocardial infarction, revascularisation) between women and men was found (18.7 vs 25.6 %; $p = 0.18$). Kaplan-Meier analysis also revealed no gender difference using log-rank test (**Figure 20**).

Conclusion In the contemporary management of patients with suspected CAD, women present with a different risk factor profile and have less frequently a significant CAD. However, no gender difference in the rate of PCI exists in patients with significant CAD. The risk of death, myocardial infarction and further revascularisation during the next 3 years seems to be similar for both gender.

Predictors of Periprocedural Myocardial Injury During Percutaneous Coronary Intervention VIII – 8

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Purpose Periprocedural myocardial injury during percutaneous coronary intervention (PCI) has been associated with worse clinical short- and long-term outcome. Aim of this study was to identify patient and lesion related characteristics, which might predict occurrence of myocardial injury during PCI in patients with stable coronary artery disease (CAD) as measured by high-sensitive Troponin T (hs-cTnT).

Methods Two-hundred-fifty-seven consecutive patients who underwent PCI for stable CAD were included in a prospective registry. Blood samples for hs-cTnT were withdrawn before and immediately after a successful PCI with stent implantation.

Results Ninety-seven patients (37.7%) had an increase of hs-cTnT after PCI. Periprocedural hs-cTnT increase showed a correlation with arterial hypertension ($p = 0.009$), and diabetes mellitus ($p = 0.017$), while age ($p = 0.07$), gender ($p = 0.77$), total dilatation time ($p = 0.39$), stent length ($p = 0.13$), stent diameter ($p = 0.61$), renal dysfunction ($p = 0.65$), previous myocardial infarction ($p = 0.35$), heart failure ($p = 0.54$), drug-eluting stent implantation ($p = 0.21$), chronic total occlusion ($p = 0.42$), or multivessel disease ($p = 0.26$) had no impact on periprocedural myocardial injury.

Conclusion In our series only the patient characteristics arterial hypertension and diabetes mellitus were significant predictors for periprocedural myocardial injury during PCI for stable CAD.

Distinctive Benefit of Drug-Eluting Stents in Large Coronary Arteries of Diabetic Patients – a BASKET-PROVE Substudy BAIL

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Background Drug-eluting stents (DES) reduce restenosis rates especially in patients with diabetes mellitus (DM) and small coronary arteries. Less is known about the effect and safety of DES in DM with large coronary arteries (≥ 3.0 mm).

Methods BASKET-PROVE, a prospective multicenter trial, randomized 2314 patients consecutively undergoing large coronary artery stenting (≥ 3.0 mm) in a 2:1 fashion to DES or bare-metal stents (BMS). An *a priori* planned secondary analysis evaluated major adverse cardiac events (MACE: cardiac death, myocardial infarction [MI], target-vessel revascularization [TVR]) in patients with versus without DM (non-DM) up to 2 years. A Cox proportional-hazard model was used to evaluate the relative risk for DM and non-DM receiving either DES or BMS.

Results DM ($n = 363$, 16%) compared to non-DM patients had a higher cardiovascular risk profile and more severe coronary artery disease. Overall, MACE rates were increased in patients treated with

BMS vs DES (11.2% vs 5.8%; $p < 0.0001$; HR 1.8 [1.4–2.4]), but not in DM versus non-DM (8.8% vs 7.4%; $p = 0.33$; HR 1.1 [0.8–1.6]). DM with DES had similar MACE rates compared to non-DM with DES (HR 0.77 [0.43–1.40]), whereas MACE rates for non-DM with BMS (1.75 [1.26–2.44]) and for DM with BMS (2.82 [1.00–7.95]) were higher. Results were driven by differences in TVR rates ($p < 0.01$ for interaction between DM and non-DM) with no difference in cardiac death and MI between DES and BMS.

Conclusions This BASKET-PROVE substudy documents the beneficial long-term effect in safety and efficacy of DES in DM patients also in need of large coronary artery stenting.

Long-term Benefit of Drug-Eluting compared to Bare-metal Stents in Patients With versus Without Chronic Renal Insufficiency – a BASKET-PROVE Substudy BAIL

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Background Chronic renal insufficiency (CRI) is a well established predictor of worse outcomes in patients with coronary artery disease. It is less known, whether CRI influences the benefit-risk balance of drug-eluting stents (DES) vs bare-metal stents (BMS), too.

Methods In the prospective multicenter BASKET-PROVE trial, 2314 patients in need of large coronary artery stenting (≥ 3.0 mm) were randomized 2:1 to DES or BMS and followed for 2 years. In an *a priori* planned secondary analysis, outcomes were evaluated according to estimated glomerular filtration rates (GFR). The primary endpoint was first major adverse cardiac event (MACE: cardiac death, myocardial infarction, target-vessel revascularization) up to 2 years. A Cox proportional-hazard model was used to evaluate the relative risk for patients with normal ($\text{GFR} \geq 60$ ml/kg/min) or reduced ($\text{GFR} < 60$ ml/kg/min) renal function according to the stent type implanted (DES vs BMS).

Results Baseline renal function was known in 1681 patients enrolled. Patients with reduced GFR ($n = 189$, 11.2%) had a 2-year MACE rate of 8.5% and those with normal GFR ($n = 1492$) of 7.4% ($p = \text{n. s.}$). The MACE rate of patients with reduced GFR was lower in those receiving a DES ($n = 123$) than in those receiving a BMS ($n = 66$, 4.9 vs 15.2%; $p = 0.026$) as was the MACE rate after DES compared to BMS implantation in patients with normal GFR (5.6 vs 11.1%; $p < 0.0001$). In the Cox proportional-hazard model including coronary artery disease severity and classic cardiovascular risk factors, the corresponding hazard rates (CIs) for the comparison of DES with BMS within the groups of patients with reduced and normal GFR were 5.06 (1.65–15.53) and 2.07 (1.42–3.01), respectively.

Conclusions This analysis of non-selected patients in need of large coronary artery stenting documents the long-term benefit of DES compared to BMS irrespective of renal function, with a hazard ratio which was twice as high for patients with reduced than with normal renal function.

The EXOSEAL Cohort: Outcomes of a Novel, Painfree, Vascular Closure Device VIII – 9

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Objectives The objective of the study was to assess the efficacy and safety of a novel and painfree vascular closure device, the EXOSEAL, in patients undergoing routine cardiac catheterization (CATH) and intervention (PCI) via a retrograde femoral artery access. Background: Successful use of current-generation vascular closure devices is highly dependent on operator methodology. To reduce dependence on operator technique, the EXOSEAL was designed to automate the closure process, specifically the deployment

of the plug by an automated indicator window and release mechanism. Also, to date, all closure devices are painful to the patient and we examined the pain scores on a standardized pain scale immediately and at given intervals of 7 and 28 days.

Methods This was a prospective single center cohort including 54 patients undergoing 59 procedures with in-laboratory closure using the EXOSEAL after CATH and PCI. The primary outcome measure was the rate of major vascular complications, and secondary outcomes were deployment success, pain scores and in-hospital rates of minor vascular complications through 30 days.

Results There were 26 CATH (48%) and 28 PCI (52%) closures. Overall deployment success was 98% (100% for CATH and 96% for PCI). Consecutive vascular ultrasound was performed in 52 patients. Major vascular complications occurred in 1.9% including 0 in CATH and 1.9% in PCI. Minor vascular complications occurred in 0%, with 0% for CATH and 1.9% for PCI. Average pain score was 0 in 78.8% and was 1.87 on average on a scale of 10 in 21.1%.

Conclusions Automation of the single plug closure of femoral artery access sites with the EXOSEAL resulted in excellent efficacy and safety after routine cardiac catheterization and intervention, as well as in a significant reduction in pain related to the procedure.

■ Koronare Herzkrankheit (KHK)/Coronary Heart Disease (CHD)

Impact of Platelet-Turnover on the Vasodilator Activated Phosphoprotein-Phosphorylation Assay in Patients with Coronary Artery Disease XVI – 1

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Background Variable response to clopidogrel is a well described phenomenon. We sought to investigate the impact of platelet-turnover on the antiplatelet effect of clopidogrel as well as factors influencing platelet-turnover.

Methods Three-hundred consecutive patients with coronary artery disease (CAD), including 192 acute coronary syndrome (ACS) and 108 stable patients, were studied. Blood was sampled 6–24 hours after coronary stenting to measure vasodilator activated phosphoprotein-phosphorylation (VASP-P) and immature platelets via flow cytometry.

Results The immature platelet levels were 3.7% (2.7–4.8%) and were comparable in patients with ACS and stable angina patients ($p = 0.877$). There was no (or very weak) linear correlation of immature platelet levels with VASP-P ($R_s = 0.167$; $p = 0.004$). However, patients with low-response to clopidogrel (VASP-P cut-off 52%) exhibited higher immature platelet levels (3.8% [2.9–4.8%] vs 3.5% [2.4–4.7%]; $p = 0.045$). Multivariable logistic regression confirmed that platelet-turnover was associated with VASP-P, independently of sex, age, CAD-entity, body mass index and proton pump inhibitor use (OR: 1.162 [1.021–1.322]; $p = 0.022$). In a multivariable regression model we tested for variables that were associated with platelet-turnover: Aspartate-transaminase ($p = 0.037$), troponin-I ($p = 0.032$), white blood count ($p = 0.024$), blood urea nitrogen ($p = 0.009$) and platelet count ($p < 0.001$) could be identified.

Conclusion Patients that are classified as low-responders to clopidogrel therapy have an increased amount of circulating immature platelets. Accordingly, once-daily dosing of clopidogrel and/or the commonly used maintenance dose of 75 mg/day might not be sufficient to inhibit enough P2Y₁₂-receptors in patients with an increased platelet turnover.

Stability of the High On-Treatment Platelet Reactivity-Phenotype in Patients on Clopidogrel over Six Months XVI – 2

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Background Variable response to clopidogrel-therapy is an established phenomenon. Previous studies and ongoing trials randomized patients according to the high on-treatment platelet reactivity (HTPR)-phenotype based on single measurements to tailored antiplatelet regimens. The stability of the HTPR-phenotype over time is not known. We therefore investigated the stability of the clopidogrel HTPR-phenotype over 6 months.

Methods One-hundred seventeen clopidogrel treated patients undergoing coronary stenting were consecutively enrolled. Multiple electrode aggregometry (MEA) and vasodilator activated phosphoprotein-phosphorylation (VASP-P) assays were performed at baseline, 1, 3 and 6 months. Based on consensus cut-offs (47U for MEA, 50% for VASP-P assay) patients were stratified according to their HTPR-phenotype.

Results MEA HTPR-phenotype within 1 month was unstable (i.e. crossing the cut-off level) in 42.3% of patients undergoing PCI due to stable CAD. MEA HTPR-phenotype in the maintenance phase (1–6 months) was unstable in 48.3% of stable CAD, 37.8% of UA/NSTEMI and 50% of STEMI patients. VASP-P based phenotype within 1 month was unstable in 31% of stable CAD, 33.3% of UA/NSTEMI and 39.3% of STEMI patients. Long-term (1–6 months) VASP-P HTPR-phenotype was unstable in 41.3% of stable CAD, 33.3% of UA/NSTEMI and 25% of STEMI patients. The assays were not significantly different regarding phenotype stability ($p > 0.05$ for all comparisons).

Conclusion HTPR-phenotype on clopidogrel over 6 months is stable in only half of the patients. The phenotype stability in the early treatment phase (baseline-1 month) is between 60–70% whereas in the steady-state phase (1–6 months) stability varies from only 50–75% as assessed in all patient groups with both assays. MEA and VASP-P are not different with regard to phenotype stability.

Evaluation of Appropriateness of Cardiac Computer Tomography Indications: Differences in Gender Aspects XVI – 3

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Background Well it is known in daily routine, that male (mp) and female patients (fp) with coronary artery disease (CAD) show different symptoms. Thus, our aim was to point out how gender differences affect to CT allocation in regard to clinical presentation and pretest probability.

Methods Mp and fp with prior cardiac computer tomography (CCT) findings were referred to us for invasive coronary angiography (CA). Data from 103 mp and 47 fp (mean age 64.0 ± 9.9) were collected retrospectively. We reviewed the individual allocation to CCT and classified indications as appropriate (A), uncertain (U) or inappropriate (I) as published. Ind not listed were rated as undefinable (UD). For each pt risk factors were calculated and CAD pretest probabilities (pp) were determined.

Results Ind for mp/fp were A in 21/34%, U in 8/6%, I in 64/49% and UD in 7%/11%. Regarding to the pp of CAD, low pp was 2/11%; intermediate pp was 25/38% and high pp was 73/51%. The most common A ind (19.3% of all, 76.3% of total A) was for pts with equivocal stress test, mp representing 53% of all (Figure 21). A exams prevail in pts with an intermediate pp (60.5% of A). The most common I ind was found in pts with a positive stress test (30.7% of all, 51.7% of total I) with 39% mp of all. I exams prevail in pts with a high pp (79.8% of I).

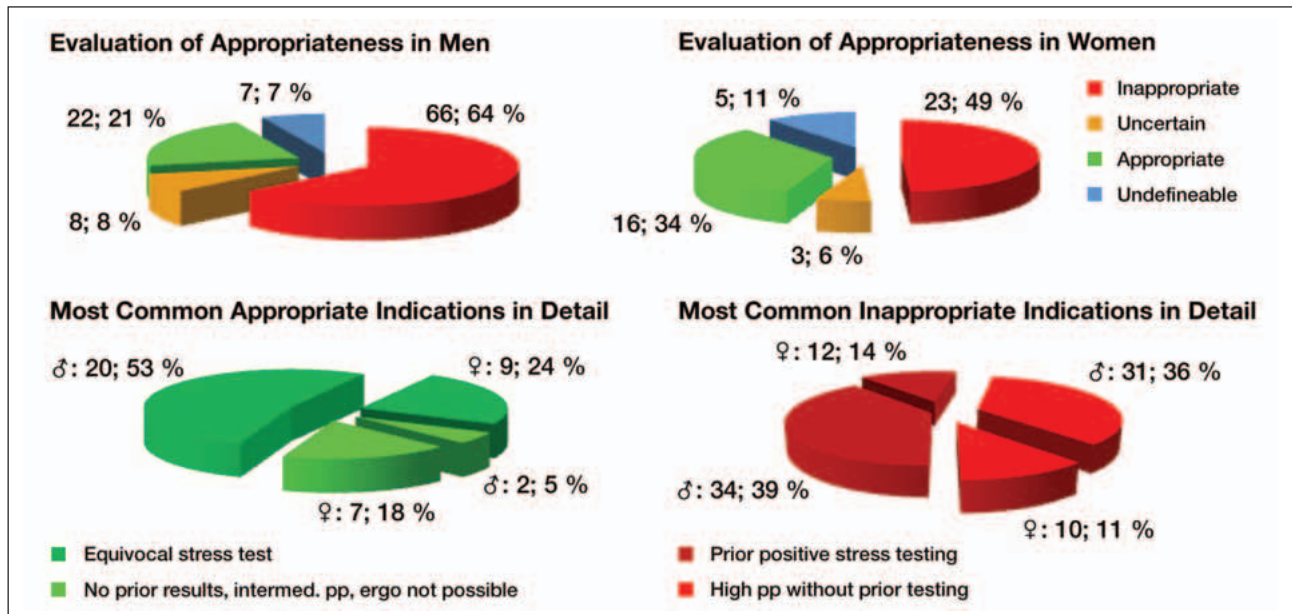


Figure 21: H. Hommel et al.

Conclusions In a preselected pt cohort referred to CA, mp present more often with a high pp for CAD because of presence of multiple risk factors. These pts as well as mp with positive prior test results underwent CCT more often than fp with similar profiles. We conclude that in general, but specially in mp, existing appropriateness criteria need a more refined implementation into clinical practice.

Erfahrungen zur Anwendung der Herzratenvariabilität unter Belastung an 115 Patienten XVI – 5

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Einleitung Die Varianz der RR-Abstände reflektiert die Anpassungsfähigkeit des Herzens an kontinuierliche interne und externe Veränderungen und kann mittels Herzratenvariabilität (HRV) unaufwendig quantifiziert werden. Der Nutzen von 24h-HRV-Messungen zur Risikostratifizierung und als allgemeiner kardiovaskulärer Screeningparameter hat sich gezeigt. Insbesondere mit der Verbreitung der nicht-linearen HRV-Parameter erfahren Kurzzeit- und Provokationsmessungen ein zunehmendes Interesse. Die Analyse der HRV während einer Ergometrie erscheint hier besonders interessant, da die meisten Herzerkrankungen unter Belastung aggravieren bzw. sich demaskieren. Insbesondere bei Herzpatienten bestehen wenige Erfahrungen mit HRV-Belastungs-Messungen, da Nicht-Stationarität, Artefakte, Ektopien und unsystematische Einflüsse, z. B. durch die Bewegung, große methodische Schwierigkeiten darstellen. Diese Studie soll deskriptiv das Verhalten der HRV bei Herzpatienten vor, während und nach Belastung beschreiben, um Nutzen und Problematik der Weiterentwicklung dieser Messmethode abschätzen zu können.

Methodik Bei 115 Herzpatienten, die zur Ergometrie kamen, wurden jeweils 2-minütige HRV-Messungen während jeder Belastungsstufe und in der Erholungsphase mittels Pulsgurtmessung (Polar RS800®) durchgeführt. Die Berechnung der HRV-Parameter (LF, HF, SDNN, RMSSD, SD1, ApEn, $\alpha1$, $\alpha2$, D2) erfolgte nach manueller Artefaktkorrektur mittels Kubios HRV Software®, Version 2.0. Die statistische Analyse wurde mittels SPSS®, Version 16.0 unter Verwendung von parametrischen und nicht-parametrischen Mittelwertsvergleichen durchgeführt.

Ergebnisse Mit Ausnahme von ApEn zeigten alle untersuchten HRV-Parameter unter Belastung zunehmend reduzierte Werte und einen asymptotischen Verlauf auf ein Minimum zu. Das Minimum wurde meist bei ca. 50 % Soll-Last erreicht. Ausnahmen waren $\alpha1$

und SDNN, wo das Minimum erst bei ca. 100 % Soll-Last erreicht wurde (Abbildung 22). Besonders ausgeprägt war diese Dynamik für SDNN, LF, HF, $\alpha1$ und besonders gering ausgeprägt für $\alpha2$ und D2. Die Schwankungsbreite der HRV-Werte nahm unter Belastung kontinuierlich ab. Auch in der Nachbelastungsphase fanden sich mit Ausnahme von $\alpha1$ und $\alpha2$ noch reduzierte HRV-Werte und eine verringerte Schwankungsbreite (Tabelle 15). Bei ca. 5 % der Patienten musste eine manuelle Artefaktkorrektur angewandt werden, während ca. 20 % der HRV-Messungen aufgrund von Artefakten nicht verwertbar waren.

Diskussion Das typische abnehmende Verhalten der HRV unter Belastung in unserem Patientenkollektiv ist mit den publizierten Erfahrungen bei Gesunden und Sportlern vergleichbar. Verwertbare Messungen scheinen bei einem großen Anteil von Patienten ohne Vorhofflimmern möglich zu sein. Günstig für eine HRV-Belastungsdiagnostik ist die systematische Dynamik, während sich die abnehmende Schwankungsbreite ungünstig auf die Diskriminierung eines pathologischen Musters auswirken dürfte. Aufgrund der besonders ausgeprägten Dynamik könnten sich in einem Kollektiv von Herzpatienten SDNN, LF HF und $\alpha1$ als vielversprechende HRV-Parameter erweisen. In der Nachbelastungsphase erscheint die Betrachtung von $\alpha1$ und $\alpha2$ aufgrund der größeren Schwankungsbreite interessant. Hinweise für eine diagnostische Überlegenheit der als robuster geltenden nicht-linearen Parameter (SD1, ApEn, $\alpha1$, $\alpha2$,

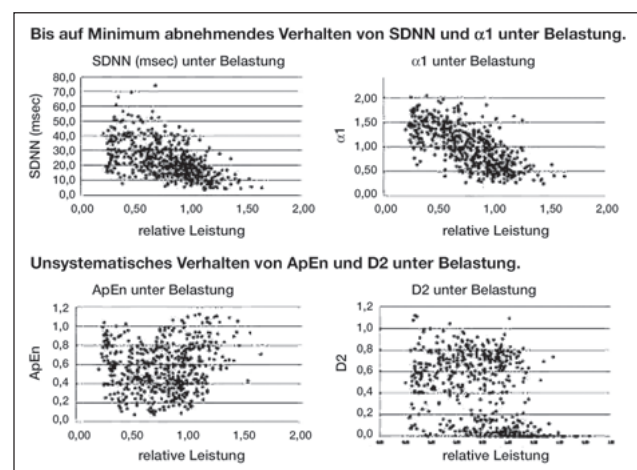


Abbildung 22: S. Kohl et al.

Tabelle 15: S. Kohl et al.**Entwicklung von Mittelwert und Standardabweichung der untersuchten HRV-Parameter unter Belastung und in der Nachbelastung.**

n (115 Patienten)	2 Min Submax2		2 Min Submax1		2 MinMax		2 Min nach Belastung	
HRV-Parameter	Mean (x)	SD(s)	Mean(x)	SD(s)	Mean(x)	SD (s)	Mean (x)	SD (s)
SDNN (msec)	27,495	12,678	20,633	9,388	17,157	8,905	39,798	13,158
RMSSD (ms2)	5,448	3,329	4,159	1,993	3,973	1,631	5,23	3,483
pNN50 (%)	0,065	0,231	0,017	0,088	0,007	0,053	0,516	0,923
LF (ms2)	27,035	41,627	6,278	15,003	2,443	3,616	24,948	35,857
HF (ms2)	10,896	21,164	2,583	5,157	1,287	3,077	6,261	11,729
SD1 (msec)	3,876	2,37	2,957	1,413	2,816	1,162	3,73	2,468
SD2 (msec)	38,402	17,766	28,851	13,2	29,965	12,577	55,889	18,466
ApEn	0,506	0,233	0,55	0,244	0,624	0,253	0,293	0,149
$\alpha 1$	1,178	0,34	0,859	0,309	0,619	0,243	1,173	0,299
$\alpha 2$	1,576	0,266	1,669	0,215	1,653	0,228	1,633	0,152
D2	0,48	0,289	0,399	0,33	0,321	0,345	0,78	0,154

D2) lassen sich aus unseren Ergebnissen nicht gewinnen. Insgesamt ermutigen unsere Daten die Weiterentwicklung einer Diagnostik mit ausgewählten HRV-Parametern während und nach Belastung.

„Ergometrie plus“ – Voruntersuchung an 61 Patienten zur Steigerung der Sensitivität der Ergometrie durch Herzratenvariabilitätsmessung

XVI – 4

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Einleitung Bei der Ergometrie betragen Sensitivität und Spezifität 68 % bzw. 77 %, bei Frauen sogar nur 61 % bzw. 70 %. Trotzdem bleibt die Ergometrie noch immer das Mittel der Wahl zur ersten Abklärung einer KHK, bzw. Klasse-I-Empfehlung bei mittlerer Vortestwahrscheinlichkeit für eine KHK. Die falsch-positiven Befunde führen zu Mehrkosten und teilweise zu erhöhter Invasivität durch sich anschließende bildgebende Verfahren. Das Problem der 32 % falsch-negativen Ergometriebefunde trägt allerdings dazu bei, dass Herzinfarkt und plötzlicher Herztod als fatale Erstmanifestationen der KHK auftreten. Die Herzratenvariabilität (HRV) ist eine unaufwendige und sensitive Messmethode der kardialen Modulationsfähigkeit. Eine eingeschränkte HRV in Ruhe ist ein unabhängiger Risikofaktor für das Vorliegen einer KHK und für erhöhte kardiale Mortalität allgemein. Im Rahmen der Provokation durch körperliche Anstrengung könnten sich ischämiegetriggerte Anpassungsstörungen in einer besonders deutlichen Reduktion der HRV zeigen. Ohne

nennenswerten zusätzlichen Messaufwand ließe sich so möglicherweise die Sensitivität einer Ergometrieuntersuchung erhöhen.

Methodik Bei 61 Patienten ohne Vorhofflimmern, die zur Ergometrie kamen, wurden jeweils 2-minütige HRV-Messungen vor der Belastung, während jeder Belastungsstufe und in der Erholungsphase mittels Pulsgurtmessung (Polar RS800®) durchgeführt. Zudem wurden die Risikofaktoren und, falls bekannt, der Koronarstatus erfasst. Die Berechnung der HRV-Parameter (LF, HF, SDNN, RMSSD, SD1, ApEn, $\alpha 1$, $\alpha 2$, D2) erfolgte nach manueller Artefaktkorrektur mittels Kubios HRV Software®, Version 2.0. Die statistische Analyse wurde mittels SPSS®, Version 16.0 unter Verwendung von parametrischen und nicht-parametrischen Mittelwertvergleichen durchgeführt.

Ergebnisse Während der 2-minütigen Vorbelastungsmessung waren die meisten untersuchten HRV-Parameter (LF, HF, SDNN, RMSSD, SD1, D2) beim Vorliegen einer KHK und bei erhöhtem Procam-Schnelltest-Risikoscore signifikant reduziert (**Abbildung 23**). Mit ansteigender Belastung wurden diese Korrelationen zunehmend schwächer und in der Nachbelastungsphase ließ sich schließlich für keinen HRV-Parameter eine signifikante Reduktion in der Gruppe der KHK mehr nachweisen. Allerdings fanden sich im Gegensatz zur Ruhemessung bei allen Belastungsstufen bei Vorliegen einer KHK signifikant niedrigere Herzfrequenzen und ein signifikant erniedrigter Gesamtanstieg der Herzfrequenz (**Tabelle 16**).

Diskussion Die Ergebnisse geben Grund zur Annahme, dass eine 2-minütige Ruhe-HRV-Messung als zusätzliches Diskriminierungskriterium für eine KHK und als objektiver Messparameter des kardiovaskulären Risikos von Nutzen sein könnte. Die diagnostische

Mittelwertvergleiche der HRV-Parameter (SDNN, RMSSD, SD1, D2) und der Herzfrequenz (HR), während verschiedener Belastungsstufen zwischen Patienten mit und ohne KHK.

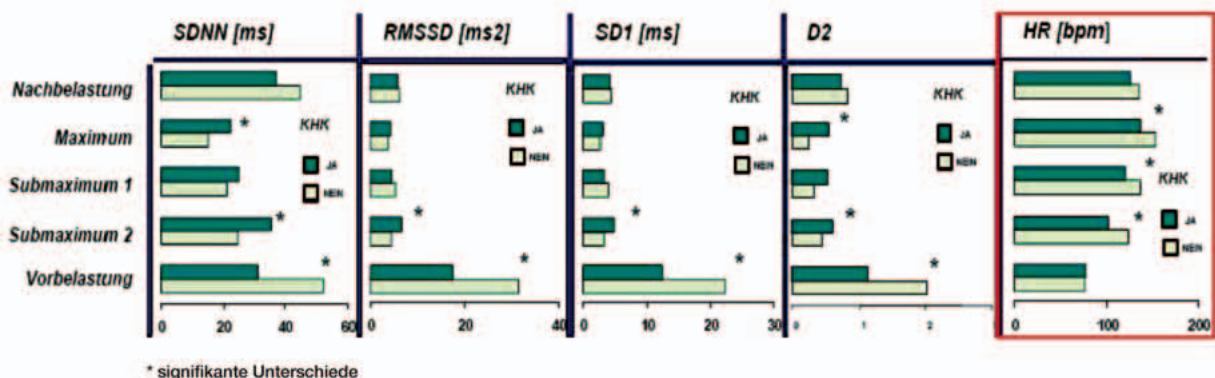
**Abbildung 23:** S. Kohl et al.

Tabelle 16: S. Kohl et al.

	Vorbelastung			Sub Max 2			Sub Max 1			Max			Nachbelastung		
	KHK	keine KHK	p	KHK	keine KHK	p	KHK	keine KHK	p	KHK	keine KHK	p	KHK	keine KHK	p
LF [ms2]	542,35	983,60	0,002	46,24	15,69	0,011	6,82	14,75	0,168	2,67	2,50	0,018	25,50	27,81	0,569
HF [ms2]	96,90	497,75	0,008	12,47	4,46	0,016	2,06	5,25	0,373	1,22	0,81	0,528	4,67	6,56	0,740
SDNN [msec]	31,12	52,15	0,006	35,43	24,62	0,013	24,84	21,11	0,150	22,26	15,27	0,004	36,98	44,78	0,109
RMSSD [ms2]	17,49	31,35	0,047	6,66	4,51	0,016	4,50	5,29	0,505	4,29	3,87	0,580	5,88	6,12	0,512
pNN50 [%]	2,635	10,820	0,011	0,029	0,031	0,885	0,029	0,156	0,931	0,022	0,000	0,346	0,094	0,588	0,483
SD1 [msec]	12,41	22,25	0,047	4,75	3,21	0,018	3,20	3,75	0,482	3,04	2,74	0,557	4,18	4,35	0,468
ApEn	0,82	0,77	0,066	0,47	0,48	0,983	0,49	0,62	0,105	0,53	0,64	0,241	0,36	0,26	0,023
$\alpha 1$	1,35	1,35	0,626	1,42	1,15	0,006	0,98	0,83	0,130	0,68	0,59	0,121	1,14	1,15	0,836
$\alpha 2$	0,98	0,98	0,766	1,58	1,58	0,917	1,66	1,59	0,540	1,72	1,57	0,042	1,59	1,62	0,534
D2	1,12	2,02	0,014	0,61	0,45	0,042	0,53	0,34	0,101	0,54	0,26	0,002	0,74	0,84	0,081
HR [1/min]	78,3	77,9	0,646	101,9	123,9	0,001	119,9	136,5	0,009	136,6	153,8	0,003	126,4	136,0	0,109

Sensitivität der HRV scheint unter Belastung abzunehmen, am ehesten aufgrund von Störfaktoren wie z. B. Atmung, durch Artefakte wie z. B. Ektopien und bedingt durch den dominierenden Reiz der Belastung, der die kardiale Modulationsbreite und damit die HRV insgesamt stark reduziert. Zudem bestätigen unsere Ergebnisse, dass die Beurteilung der chronotropen Kompetenz eine größere Rolle im diagnostischen Vorgehen bei KHK spielen könnte. Diese Studie soll als Voruntersuchung zu einer prospektiven Erhebung der Ruhe-HRV und chronotropen Kompetenz bei unbekanntem Koronarstatus vor anschließender CAG verstanden werden.

Monocyte Subsets Differently Express CD59 and Correlate with Cardiovascular Risk Factors in Stable CAD Patients

XVI – 6

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Purpose Monocytes play a key role in modulating inflammation in coronary artery disease (CAD). Different monocyte subsets can be distinguished via expression of CD14 and CD16. CD59 attenuates atherosclerosis through inhibition of the membrane attack complex. The aim of this study was to analyze the distribution of monocyte subsets and their expression of CD59 in a cohort of patients with stable CAD. Furthermore, the influence of CAD severity and known risk factors for CAD such as inflammation and diabetes should be examined.

Methods 94 patients suffering from angiographically proven stable CAD were enrolled. Monocytes were classified as CD14⁺⁺/CD16^{low} (“classical monocytes”, CM), CD14^{low}/CD16⁺ (“non-classical monocytes”, NCM), CD14⁺⁺/CD16⁺ (“intermediate monocytes”, IM) and CD14^{low}/CD16^{low} (“so far undefined monocytes”, SFUM, a subset that has not been described yet) and expression of CD59 on each subtype was measured. We further measured their correlation with CRP levels, HbA1c and the impact of CAD severity on monocyte distribution.

Results SFUM expressed significantly higher levels of the protective CD59 ($p < 0.0001$) than all other subtypes, NCM showed the lowest levels of CD59 ($p < 0.0001$). Levels of CRP correlated

inversely with levels of SFUM ($\rho = -0.424$, $p < 0.001$), while levels of HbA1c correlated positively with NCM ($\rho = 0.336$, $p < 0.05$). Patients suffering from severe CAD, defined as 3VD, showed higher levels of NCM ($p < 0.05$) and lower levels of CM ($p < 0.05$) than all other subtypes.

Conclusion The fact that “non-classical” monocytes expressed lower levels of CD59 than the other subtypes contributes to the idea that this subset acts “pro-atherogenic”. The very high levels of CD59 on a subset that has not yet been described, the SFUM, together with inverse correlation with levels of CRP, could suggest that this subset acts protective. The positive correlation of HbA1c and NCM contributes to the observation that diabetics are especially prone to atherosclerosis.

Statins Differently Modulate Monocyte Subset Distribution in stable CAD Patients – A New Insight into their Anti-Inflammatory Effects?

XVI – 7

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Purpose Monocytes play a key role in modulating inflammation in coronary artery disease (CAD). Different monocyte subsets can be distinguished via expression of CD14 and CD16. Current therapeutic guidelines suggest the standard use of statins in the therapy of CAD; their effect relies partly on their anti-inflammatory actions. The aim of this study was to analyze the impact of statin therapy on the distribution of monocyte subsets.

Methods 94 patients, suffering from angiographically proven stable CAD, were enrolled. Monocytes were classified as CD14⁺⁺/CD16^{low} (“classical monocytes”, CM), CD14^{low}/CD16⁺ (“non-classical monocytes”, NCM), CD14⁺⁺/CD16⁺ (“intermediate monocytes”, IM) and CD14^{low}/CD16^{low} (“so far undefined monocytes”, SFUM, a subset that has not been described yet). Current statin medication was noted.

Results Patients treated with atorvastatin showed less NCM than patients treated with Simvastatin ($p < 0.05$) and higher levels of CM ($p < 0.05$). Upon closer analysis simvastatin treatment revealed that

patients treated with 40 mg of simvastatin had statistically significant higher levels of CM than patients treated with 20 mg ($p < 0.05$).

Conclusion In our study, the 2 second generation statins simvastatin and atorvastatin showed a different effect on the distribution of monocyte subsets, with atorvastatin leading to a more “anti-inflammatory” distribution. The same effects could be shown for higher dose application of simvastatin. Effects of statin therapy on monocyte distribution might add another piece to the puzzle in understanding the anti-inflammatory effects of statins.

Ectatic Coronary Vasculopathy in Homocysteinosis Alpha-1 Antitrypsin Deficiency: A Case Report

XVI – 8

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Introduction Alpha1-Antitrypsin (AAT) is the most important inhibitor of serine proteases in the blood in humans. Its deficiency causes enhanced activity of neutrophil elastase in blood and lungs and thus an increased risk of panacinar emphysema and chronic obstructive lung disease (COPD) especially among smokers, in addition to hepatic cirrhosis and vascular aneurysms. The deficiency is treated by avoidance of damaging inhalants, by intravenous infusions of the AAT protein and by transplantation of the lungs or liver.

Case Report We report a 45 year old male who was evaluated for lung transplantation because of end-stage COPD with long term oxygen therapy as a result of homocysteinosis AAT-deficiency. The first evaluation for lung transplantation took place in 2008, when the initial coronary angiography was performed, which showed normal findings (**Figure 24**). The patient withdrew his consent to the transplantation at that time. The patient's condition remained stable until spring 2010, when all essential examinations for lung transplantation were repeated because of the patient's worsened condition. Surprisingly, repeated coronary angiography revealed that ectatic coronary vasculopathy had developed within only 2 years, predominantly in the proximal and mid left anterior descending artery. Mild

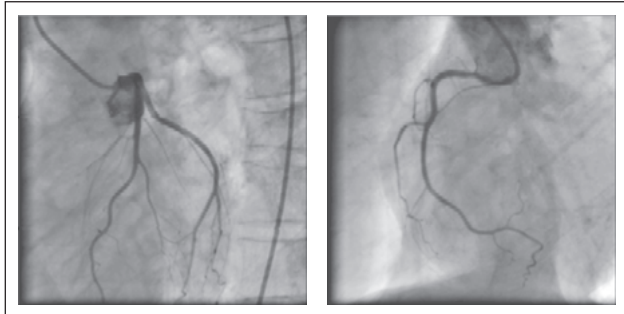


Figure 24: D. Petener et al. Baseline angiogram at the time of first transplant evaluation. Normal left and right coronary artery.

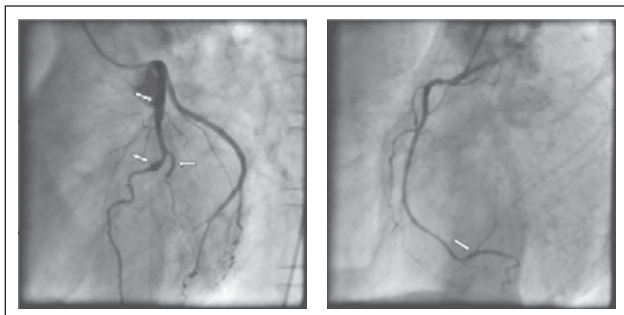


Figure 25: D. Petener et al. Follow-up angiogram 2 years later. Note ectatic segments (arrows) in the proximal and mid-left-anterior descending artery, the 2nd diagonal branch and the distal-right coronary artery.

ectasia was also found in the distal right coronary artery (**Figure 25**). No ectasia or aneurysm was detected in any other investigation such as contrast-agent CT of the aorta or duplex sonography of the carotids.

Discussion Arterial aneurysms and spontaneous dissections are known to occur in arterial territories. To the best of our knowledge, coronary ectatic vasculopathy has not been described in AAT deficiency. The affection of vessels might be explained by the degradation of elastic vascular fibres by enhanced activity of neutrophil elastase which can disrupt the integrity of the vessel wall and cause the formation of ectasia and/or aneurysm. Alternatively, constant hypoxemia due to the patient's lung disease might have caused aneurysm formation: Firstly, coronary dilation is regulated independent from the endothelium by arterial pressure, myocardial metabolism and the autonomic nervous system as well as by arterial oxygen-saturation. Secondly, low blood oxygen saturation stimulates coronary vasodilatation in angiographically normal coronary arterial segments, whereas it does not affect vascular diameters in atherosclerotic segments. In our patient, chronic hypoxemia may have boosted the development of ectatic coronary angiopathy in a setting of increased proteolytic elastase-activity due to AAT deficiency. Our report emphasizes that asymptomatic development of coronary and other aneurysms should be considered during the management of AAT1 deficiency. The clinical management of these patients requires further investigation. On the other hand, the detection of coronary aneurysms might give a hint to underlying connective tissue disease.

Bewusstsein von kardiovaskulären Risikofaktoren, Prävention und Barrieren zur Herzgesundheit bei österreichischen Männern

XVI – 9

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Hintergrund Die koronare Herzkrankheit (KHK) ist die Haupttodesursache in industrialisierten Ländern wie Österreich. Vor dem 45. Lebensjahr haben Männer in Vergleich zu gleichaltrigen Frauen ein deutlich erhöhtes Risiko, eine KHK zu entwickeln und daran zu versterben. Bei Frauen hat sich gezeigt, dass das Wissen über kardiovaskuläre Erkrankungen und deren Risikofaktoren nicht nur ihr Präventionsverhalten verändert, sondern auch langfristig mit einer Reduktion der kardiovaskulären Mortalität assoziiert. Vergleichbare Daten bei Männern sind derzeit nicht verfügbar.

Ziel Ziel der vorliegenden Studie war es daher, das Erkennen typischer Risikofaktoren, die Selbsteinschätzung des individuellen kardiovaskulären Risikos, das männliche Präventionsverhalten aber auch die Barrieren, die eine effektive Prävention verhindern, innerhalb der männlichen, österreichischen Bevölkerung zu untersuchen.

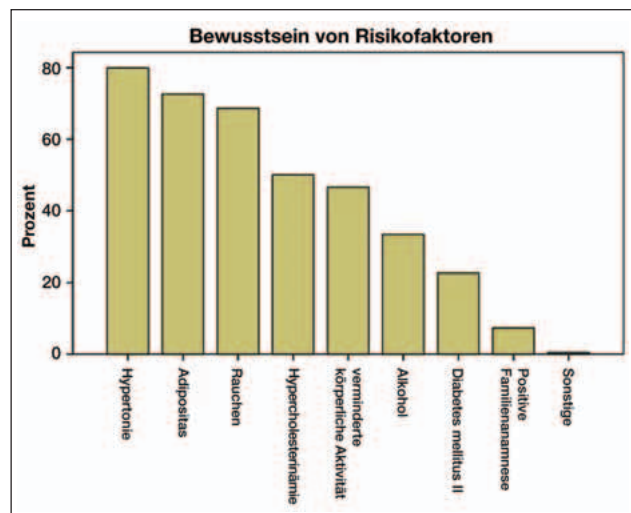


Abbildung 26: M. Zweimüller et al.

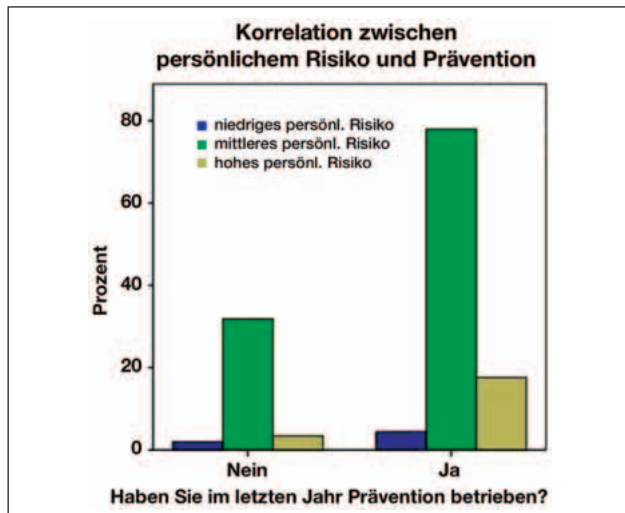


Abbildung 27: M. Zweimüller et al.

Methoden Die Daten wurden mittels anonymisierten Fragebögen bestehend aus 41 Fragen erhoben, welcher an 204 Männer ab 18 Jahren in der urologischen Ambulanz des Krankenhauses der Elisabethinen in Linz, an Patienten einer hausärztlichen Praxis in Langenstein und 3 große Firmen in Wien ausgeteilt wurde. Zur Analyse dieser Daten wurde SPSS Version 17.0 verwendet.

Resultate 70 % der Männer nannten die KHK als häufigste Todesursache in Österreich. Hypertonie und Übergewicht wurden als die wichtigsten Risikofaktoren identifiziert (Abbildung 26). DM II wurde von den Männern allerdings nur zu 21 % mit der KHK in Verbindung gebracht. Gemäß der verwendeten Risikoklassifikation gehörte die Mehrheit der Teilnehmer, mit 77,9 %, der Gruppe mit mittlerem Risiko eine KHK zu entwickeln, an. Männer mit erhöhtem kardiovaskulärem Risiko konnten ihr Herz-Kreislauf-Risiko nicht nur besser einschätzen, sondern waren auch motivierter, Prävention zu betreiben (Abbildung 27). Hauptmotivation für präventive Maßnahmen waren eine Verbesserung des Gesundheitszustandes und sich besser zu fühlen. Dafür betrieben die meisten Männer mehr Sport bzw. ernährten sich gesünder. Männern war mehrheitlich nicht bewusst, dass ihr Präventionsverhalten Vorbildwirkung für ihre Familie, insbesondere ihre Kinder hat. Nur 7,4 % der Männer gaben an, für ihre Familie präventive Maßnahmen ergriffen zu haben.

Schlussfolgerung Das Bewusstsein über KHK, deren Risikofaktoren und die Bedeutung präventiver Maßnahmen muss innerhalb der männlichen österreichischen Bevölkerung eindeutig verbessert werden. Kardiovaskuläre Präventionsprogramme sollten daher zukünftig nicht nur speziell auf weibliche, sondern auch männliche individuelle Bedürfnissen und Anforderungen angepasst werden.

■ Pulmonale Hypertonie/Pulmonary Hypertension

Long-term Treatment, Tolerability and Survival with Subcutaneous Treprostinil for Severe Pulmonary Hypertension

XVII – 1

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Objectives To evaluate long-term treatment, tolerability, dosing regimens and survival with first-line subcutaneous treprostinil, a prostacyclin analogue, we report on a prospective registry of all patients with severe pulmonary hypertension.

Background Recent data suggest that contemporary treatments within randomized controlled trials (RCTs) improve outcomes in

pulmonary arterial hypertension, however RCTs are biased by stringent inclusion criteria, and are critically limited by pre-specified patient subsets and study durations.

Methods Data were collected from patients with advanced pre-capillary pulmonary hypertension (DANA Point group I and IV, mean right arterial pressure ≥ 10 mmHg and/or cardiac index ≤ 2.2 L/min $\times$ m²), with pre-specified hemodynamic evaluations and assessment of events and survival. Dose adjustments were performed according to drug side effects and clinical symptoms.

Results Between 1999 and 2010 111 patients were included in the registry and were followed for a median observational time of 2.9 years (0.8–10.6). Of those, 21 patients (18.9%) discontinued treatment within the first 6 months due to side effects, 10 patients (9%) underwent double lung transplantation, and 41 patients (36.9%) died of all-causes. Twenty-five patients (22.5%) survived non-PH related adverse events. At 1, 5 and 9 years, survival rates were 86%, 60% and 51%.

In a subgroup analysis of 85 patients (76.5%) treated longer than 6 months, significant improvements occurred in six-minute walking distance, Borg Dyspnea Score, mean pulmonary arterial pressure, cardiac output, pulmonary vascular resistance and World Health Organization functional class at a median 38.4 months (range: 16.8–75.6).

Conclusion First-line treatment of severe pre-capillary pulmonary hypertension with subcutaneous treprostinil is safe and efficacious over years, improves survival and enables survival of non-PH related events.

Plasma Levels of Soluble P-Selectin Predict Survival in Chronic Thromboembolic Pulmonary Hypertension

XVII – 2

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Background Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is caused by obstruction of pulmonary arteries with organized thrombus. The role of soluble P-selectin (sP-selectin), a platelet activation marker, in the pathogenesis and outcomes of CTEPH is unknown.

Patients and Methods Soluble P-selectin was determined in 147 patients (pts) at the time of diagnosis. Enzyme-linked immunoassay was used to determine sP-selectin plasma levels. Analysis of overall survival was performed using Kaplan-Meier curves that were stratified by sP-selectin levels above and below median at baseline.

Results Of 147 patients, 72 (49%) were classified as operable and 75 (51%) as inoperable. SP-selectin plasma levels were elevated (median [range]; 109 [52–223]). No significance was found between operable and inoperable CTEPH patients ($p = n.s.$). Patients with sP-selectin values below 109 ng/ml survived longer than those with values above ($p < 0.027$).

Conclusion Soluble P-Selectin is increased in plasma, and predicts survival in CTEPH patients. The data suggest that platelet activation is involved in venous thrombosis.

The Impact of Pulmonary Arterial Compliance, Stroke Volume and Pulmonary Vascular Resistance on Survival in Patients with Chronic Thromboembolic Pulmonary Hypertension

XVII – 3

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Rationale Right ventricular (RV) afterload leads to RV failure and death in patients with pulmonary hypertension (PH). RV afterload is commonly defined by pulmonary vascular resistance (PVR), which reflects the arterial load to a steady flow. However, a complete description of RV afterload should also include pulsatility. The purpose of this study was to quantify RV afterload in patients with

chronic thromboembolic pulmonary hypertension (CTEPH) undergoing pulmonary endarterectomy (PEA). We sought to define the impact of pulmonary arterial compliance (PAC), stroke volume (SV), and PVR on persistent/recurrent PH and long-term survival in CTEPH.

Methods We monitored PAC, SV and PVR in 110 patients who underwent PEA. The data were determined at baseline, postoperative (immediate: within 3 days after PEA) and 1 year after PEA.

PAC was calculated by SV/pulmonary artery pulse pressure. The impact of these parameters on survival/freedom of lung transplantation and persistent pulmonary hypertension were analyzed by Cox proportional hazard models, and T-tests.

Furthermore we analyzed survival using logistic regression models. P values were adjusted from multiple testing by Bonferroni correction.

Results PAC and PVR changed significantly from baseline to immediate postoperative ($+1.4 \pm 1.6$ mL/mmHg, -396.2 ± 334.4 dynes $\times$ cm $^{-1} \times$ s $^{-5}$; $p < 0.001$ i.e.), showing no changes between immediate and 1-year follow-up. SV increased statistically significant from baseline to 1 year ($+10.1 \pm 1.6$ mL; $p < 0.001$), while it did not change immediately postoperative from baseline.

Neither PAC, nor SV, nor PVR at baseline showed any influence on persistent/recurrent PH or long-term survival.

PVR, SV and PAC assessed immediately postoperatively had a significant influence on persistent/recurrent PH ($p < 0.0001$; $p = 0.02$; $p < 0.01$). Immediate postoperative PVR had a significant influence on long-term survival ($p < 0.001$).

Logistic regression model revealed immediate postoperative PVR as predictive of 1 year- ($p = 0.001$), 3 year- ($p = 0.01$) and 5-year persistent/recurrent PH and survival ($p = 0.002$).

Conclusions Pulmonary arterial compliance, stroke volume and PVR assessed immediately after PEA are predictive of persistent/recurrent PH, however PVR was the only predictor of long-term survival in CTEPH patients undergoing PEA.

First Experience with Intravenous Treprostinil Delivered by an Implantable Pump (Lenus Pro®) With Filling Intervals of 28 Days in a Patient with Pulmonary Arterial Hypertension (PAH) – a Case Report

XVII – 4

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Introduction Continuous subcutaneous (s.c.) Treprostinil (Remodulin®) is an established treatment for PAH. Infusion site pain is a frequent complication leading to discontinuation of treatment in about 15%. Intravenous (i.v.) administration of prostanoids using external pumps is problematic with regard to infections. Lenus Pro® implantable pump was specifically developed for i.v. administration of Treprostinil. We report the first implantation of a 40 ml Lenus Pro® pump with a constant flow rate of 1.3 ml/day.

Methods and Results A 70-year old female presented in functional class IV and a history of recurrent syncope during exercise in March 2009. Right heart catheterization confirmed the diagnosis of PAH with a mean pulmonary arterial pressure (mPAP) of 62 mm Hg. Cardiac index at baseline was 1.38 l/min/m 2 , NT-proBNP 1561 ng/l, a 6-minute-walk test (6MWD) could not be performed. Bosentan treatment was started (Figure 28). In June 2009 the mPAP was 51 mm Hg, NT-proBNP increased to 2083 ng/l, recurrent syncope remained and 6MWD still could not be performed. However, additional s.c. Treprostinil therapy (sequential combination therapy according to ESC guidelines 2009) led to a substantial improvement. In January 2010 NT-proBNP had fallen to 797 ng/l and 6MWD was 175 m, and syncope had disappeared. Despite the favorable efficacy of treprostinil the patient experienced site pain, in addition and an infection of the infusion site required hospitalization and systemic antibiotic treatment in November 2009. In 2009 the first Lenus Pro® pump (40 ml) with a flow rate of 2 ml/day was implanted in

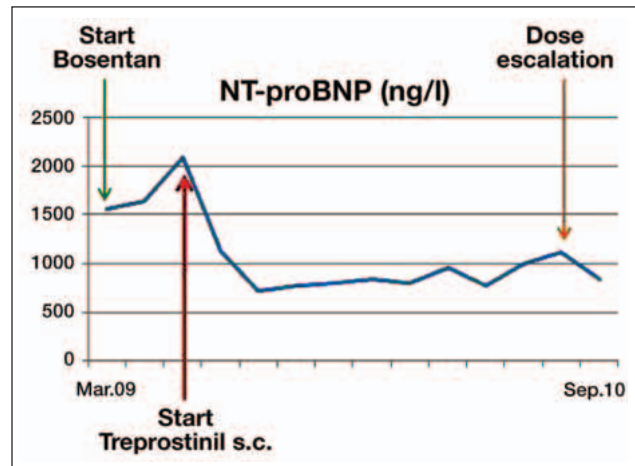


Figure 28: R. Steringer-Mascherbauer et al.

Germany. As a 20-day-filling-interval seemed suboptimal for our purposes we asked the company for a revised version allowing a 28-day-filling-interval. Meanwhile we increased the Remodulin® dose up to 21 ng/kg/min. In August 2010 mPAP was 29 mm Hg, cardiac index 2.41 l/min/m 2 . MR testing showed an improvement of right ventricular function (RVEF increasing from 42% up to 59%). The revised pump was implanted in September 2010 in general anesthesia and filled intraoperatively; subcutaneous Treprostinil was stopped.

Discussion Subcutaneous Treprostinil is a cornerstone of PAH treatment; however site pain leads to discontinuation in about 15%. Our patient improved substantially by s.c. Treprostinil, but suffered from site pain and an infection. Administration of i.v. Treprostinil with the implantable Lenus Pro® pump offers an exciting option for such patients, minimizing the risk of infections. Treprostinil therapy with a filling interval of 28 days in an outpatient setting ensures optimal patient management, compliance and an increase in quality of life.

High Dose Subcutaneous (s. c.) Treprostinil Allows Long-Term Management of a Patient With Severe PAH Refusing Transplantation – a Case Report

XVII – 5

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Interne 2 Kardiologie/Angiologie/Intensivmedizin, Krankenhaus der Elisabethinen Linz

Introduction Continuous long-term s. c. Treprostinil (Remodulin®) in doses up to 40 ng/kg/min has been shown to improve exercise tolerance and symptoms in patients with PAH and may provide a significant survival benefit. The safety and efficacy of high-dose intravenous Treprostinil has been reported in the literature. We describe the successful re-stabilisation of a patient with severe PAH by a high dose of s. c. Treprostinil.

Methods and Results A 50-year old male was diagnosed with PAH in another hospital in February 2007. Treatment with Bosentan was initiated. In October 2007 he presented in NYHA functional class IV at our department. Right heart catheterization confirmed the diagnosis of PAH with a mean pulmonary arterial pressure (mPAP) of 65 mm Hg. Six-minute-walk test (6MWD) was 161 m. Additional s.c. Treprostinil therapy was started, the dose was titrated up to 13.75 ng/kg/min until March 2008 (Figure 29). At that time the patient was in class III with a 6MWD of 214 m. In May 2008 the patient reported dyspnea at rest and refused the 6MWD because of general weakness. Increase in Treprostinil dosage restored stabilization until October 2008. However, due to clinical deterioration to class IV we added Sildenafil, in addition the patient refused lung transplantation. Triple therapy with dose increase of Treprostinil up to 29 ng/kg/min stabilized the patient in class III for another year. However in November 2009 he deteriorated again and refused to be listed for trans-

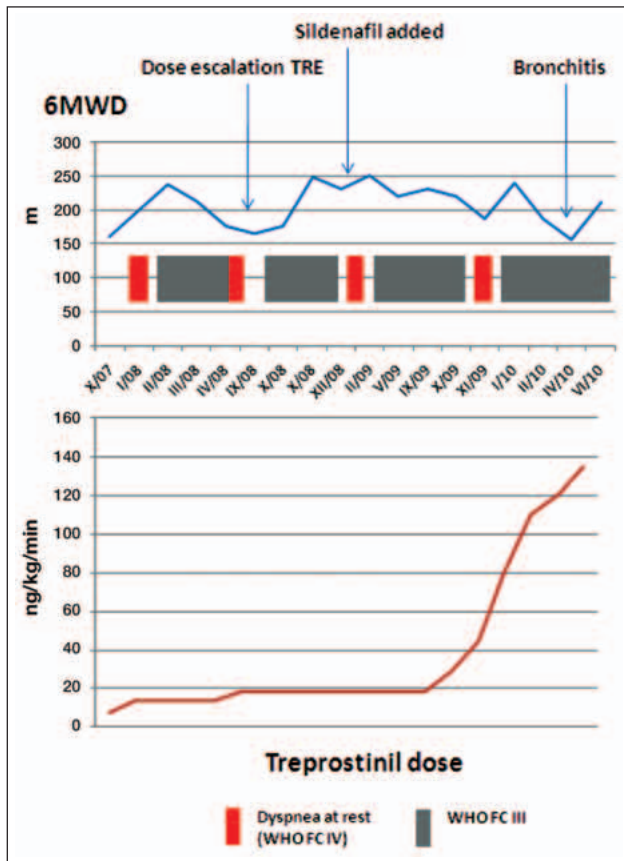


Figure 29: R. Steringer-Mascherbauer et al.

plantation. We increased Treprostinil to 80 ng/kg/min within three months and to a maximum dose of 135 ng/kg/min until September 2010. No dose limiting toxicities were observed. During the whole period the patient was monitored closely, including monthly visits. Currently the patient is stable in class III (last 6MWD 210 m).

Conclusion Subcutaneous Treprostinil is a cornerstone of PAH treatment. In long term treatment doses up to 40 ng/kg/min are effective in most patients. In rare cases, however, increase in dosage is necessary. Our case demonstrates that a triple therapy regime including high-dose s. c. Treprostinil allows clinical re-stabilisation even in a patient with reduced compliance.

Magnetic Resonance Imaging (MRI) Proves Long-Term Efficacy of Treprostinil in a Patient with Pulmonary Arterial Hypertension (PAH) – a Case Report

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Introduction Parenteral Treprostinil (Remodulin®) is an established PAH-treatment. We report a case of substantial long-term clinical improvement documented by MRI.

Methods and Results A 70-year old female presented in NYHA functional class IV accompanied by recurrent syncope during exercise in March 2009. Right heart catheterization confirmed the diagnosis of PAH with a mean pulmonary arterial pressure (mPAP) of 62 mmHg. The cardiac index at baseline was 1.38 l/min/m², NT-proBNP 1561 ng/l, a 6-minute-walk test (6MWD) could not be performed. MRI of the heart documented a stroke volume of 80 ml, a right ventricular ejection fraction (RVEF) of 42% and right ventricular end-diastolic volume of 190 ml. Bosentan treatment was started. In June 2009 the mPAP was 51 mm Hg, NT-proBNP increased to 2083 ng/l, recurrent syncope remained and 6MWD still could not be performed. However, add-on s. c. Treprostinil therapy

led to a substantial clinical improvement. In January 2010 NT-proBNP had fallen to 797 ng/l and 6MWD was 175 m, and syncope had disappeared. Until August 2010 Remodulin® dose was increased up to 21 ng/kg/min. In August 2010 mPAP was 29 mmHg, cardiac index 2.41/l/min/m². MRI evaluation in September 2010 showed a significant improvement of right ventricular function with a stroke volume of 96 ml, a RVEF of 59% and right ventricular end-diastolic volume of 163 ml.

Conclusion This case underscores the importance of continuous follow-up of patients with PAH as proposed by the ESC guidelines. In particular, our patient showed no sufficient response to first-line Bosentan with even increasing NT-proBNP levels. Addition of Treprostinil three months later led to a substantial clinical improvement. Meanwhile the patient has been clinically stable for 15 months. The improvement of right ventricular function was documented by MRI testing. Thus, the MRI is a valuable tool for monitoring of long-term efficacy for PAH treatment.

Rhythmologie/Rhythmology

Potential-Guided Catheter Ablation of Idiopathic Fascicular Left Ventricular Tachycardia

IX – 1

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Introduction Idiopathic fascicular left ventricular tachycardia (ILVT) belongs to the group of normal heart VTs and is a rare arrhythmia in clinical practice. Since the first description in 1979 the characteristics and mechanisms of this peculiar arrhythmia have been investigated in detail. The aim of this retrospective study is to evaluate the electrophysiological properties of ILVT and outcome after RF ablation at a single center.

Methods The case series comprises 4 male patients (mean age 41 ± 12 yrs) who presented with symptomatic ILVT in the last 6 years. Structural heart disease was excluded using echocardiography, coronary angiography and MRI. Two patients demonstrated T wave abnormalities in the inferolateral leads. Twelve-lead ECG during palpitations showed a relatively narrow ventricular tachycardia (VT) with right bundle-branch block morphology and left superior (n = 3) or right inferior (n = 1) axis deviation (233 ± 33 bpm). Acute termination of VT was achieved with amiodarone (n = 3) and electrical cardioversion (n = 1), none of the patients received verapamil.

Results EPS was performed after informed consent and the clinical VT was inducible in 3 of the 4 patients (75%) with programmed ventricular stimulation (n = 2) or atrial burst pacing (n = 1) under atropine and orciprenaline (CL 277 ± 35ms). Paroxysmal atrial fibrillation was found as concomitant arrhythmia in 2 patients and AVNRT in 1 patient. Three-dimensional electroanatomical mapping of the left ventricle was used in one case. Cooled RF-ablation (12 ± 7 applications, 636 ± 348 sec) was delivered either during VT (n = 3) and/or during SR (n = 4) while recording 2 separate serial potentials. Low amplitude diastolic potentials (DP) preceded sharp high frequency Purkinje potentials (PP) during ongoing VT. In SR low-amplitude potentials following the PP and ventricular activation were identified (retro-PP) in the infero-medial (n = 3) or anterior septum (n = 1). No complications occurred in any of the patients. After ablation ECG in SR showed an increase of QRS duration from 98 ± 3 to 112 ± 3 ms. A change of QRS axis was noted in 2 patients (left posterior or left anterior fascicular block), but not in cases with preexisting right or left axis deviations (n = 2). No recurrence of clinical VT occurred on a median follow up of 12 months (range 3–28 months).

Conclusions Catheter ablation is the preferred choice of therapy in patients with ILVT. Targeting specific sites with simultaneous recording of presystolic and diastolic potentials in the septal LV will result in modification of the left posterior or anterior fascicle. Three-

dimensional electroanatomical mapping and potential-guided ablation in SR may be helpful to achieve successful ablation.

Klinische Ergebnisse mit Dronedaron (Multaq®) bei nicht-permanentem Vorhofflimmern IX – 2

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Einleitung Dronedaron (Multaq®) ist ein Mehrkanalblocker, der in Österreich bei nicht-permanentem Vorhofflimmern (VHF) seit Anfang Februar 2010 als zusätzliches Antiarrhythmikum zur Verfügung steht. Wir berichten über unsere Erfahrungen am eigenen Patientengut.

Methodik 40 Patienten (29 männliche/11 weibliche), die bei Einschluss im Schnitt 67 ± 10 Jahre alt waren, wurden untersucht. Von diesen war als Einschlussgrund bei 30 paroxysmales, bei 10 persistierendes VHF festzuhalten, wobei zur Basisvisite bei 9 Patienten VHF und bei 31 Patienten Sinusrhythmus (SR) aufgezeichnet wurde. Echokardiographisch konnte bei 28 Patienten eine normale, bei 12 Patienten eine reduzierte LVEF zwischen 35 % und 50 % erfasst, und eine durchschnittliche Vorhofsgröße von 41 ± 6 mm gemessen werden. Der durchschnittliche CHADS₂-Score wurde mit 1,05 beziffert.

Neben EKG- und Laborkontrollen wurden zu den Visiten die NYHA-Stadien erfasst und die Patienten gebeten, ihre aktuelle Lebensqualität (QoL) hinsichtlich des VHF einzuschätzen (0 = sehr schlecht; 10 = exzellent). Fünf der Patienten hatten einen permanenten Schrittmacher/ICD und 2 Patienten einen Loop-Rekorder implantiert. Die detaillierte Auswertung dieser Geräte soll zur Jahrestagung präsentiert werden.

Resultate Von 40 eingeschlossenen Patienten konnten bei 29 vollständige 6-Monats-Daten erhoben werden. Grund für das Ausscheiden war 9× unzureichende Wirksamkeit von Multaq® (erneut VHF/ Palpitationen), 1× persistierende Diarrhoe und 1× ein chefärztliches Verordnungsproblem. Rehospitalisierung aus kardiovaskulärer Ursache, proarrhythmische Effekte oder Todesfälle waren keine zu verzeichnen.

Im Hinblick auf den Erhalt von SR konnten bei alleiniger Rhythmuskontrolle mittels Ruhe-EKG nach 6 Monaten keine Veränderungen zum Ausgangswert erhoben werden (**Abbildung 30**). Laborchemisch blieben die Leber- und Nierenwerte stabil (**Abbildung 31**, **Abbildung 32**), elektrokardiographisch kam es über 6 Monate zu keiner signifikanten Verlängerung der QTc-Zeit (**Abbildung 33**). Bereits nach 3 Monaten Einnahme von Multaq® gaben die 29 verbliebenen Patienten eine signifikant bessere Belastbarkeit gegenüber der Basisvisite an (NYHA $1,6 \pm 0,6$ vs. $1,1 \pm 0,3$, $n = 29$), die dann

Tabelle 17: M. Derndorfer et al.

Parameter	Mean	N	Std. Deviation	Std. Error Mean	Sig. (2-tailed)
Pair 1 NYHA_1	1,62	29	0,622	0,115	0,0001
NYHA_3	1,1	29	0,31	0,058	
Pair 2 QuoL_1	6,38	29	1,916	0,356	0,134
QuoL_3	6,9	29	1,611	0,299	
Pair 3 bpm_1	73	23	17,3	3,607	0,295
bpm_3	68,96	23	13,573	2,83	
Pair 4 QTc_1	444,52	23	30,707	6,403	0,724
QTc_3	446,65	23	25,831	5,386	
Pair 5 PR_1	171,89	18	38,037	8,965	0,825
PR_3	173,44	18	31,619	7,453	
Pair 6 mmHgSys_1	124,41	29	19,214	3,568	0,09
mmHgSys_3	132,59	29	17,093	3,174	
Pair 7 mmHgDia_1	76,68	28	9,787	1,85	0,668
mmHgDia_3	75	28	14,657	2,77	
Pair 8 Krea_1	1,08	29	0,197	0,037	0,07
Krea_3	1,13	29	0,205	0,038	
Pair 9 gGT_1	58,07	29	72,52	13,467	0,348
gGT_3	45,66	29	41,403	7,688	
Pair 10 GOT_1	28,28	29	11,832	2,197	0,768
GOT_3	28,9	29	7,518	1,396	
Pair 11 GPT_1	31,72	29	18,26	3,391	0,618
GPT_3	30,17	29	8,706	1,617	

NYHA_1 = NYHA-Stadium zu Beginn der Therapie (= Visite 1)

NYHA_3 = NYHA-Stadium nach 6 Monaten Therapie (= Visite 3), ...

bis zur 6-Monats Kontrolle unverändert gut blieb ($p = 0,0001$) (**Abbildung 34**). Dementsprechend wurde auch die subjektive Lebensqualität bereits nach 3 Monaten mit einer Steigerung von $6,38 \pm 1,92$ auf $6,9 \pm 1,61$ Punkte besser beurteilt und diese Entscheidung bis zum letzten Follow-up beibehalten ($p = 0,134$; n. s.) (**Abbildung 35**).

Schlussfolgerung Unter Beobachtung von Klinik, EKG sowie Labor (Serumkreatinin, Leberwerte) zeigt sich Dronedaron nebenwirkungsarm und sicher in der Anwendung. Zudem kam es unter Multaq® zu einer signifikanten Verbesserung der Belastbarkeit (NYHA-Stadium) und einer gering (statistisch nicht signifikant) gebesserten QoL der Patienten (**Tabelle 17**). Die antiarrhythmische Wirksamkeit hinsichtlich des Erhalts von SR kann im Rahmen des angewandten Untersuchungsprotokolls mit der ausschließlichen Erfassung von Ruhe-EKGs nicht exakt beurteilt werden. Die Daten der implantierten Geräte befinden sich aktuell noch in Auswertung.

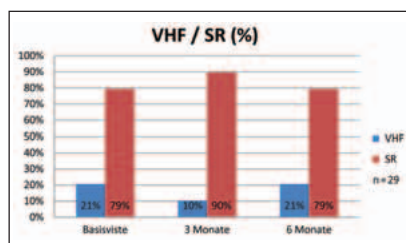


Abbildung 30: M. Derndorfer et al.

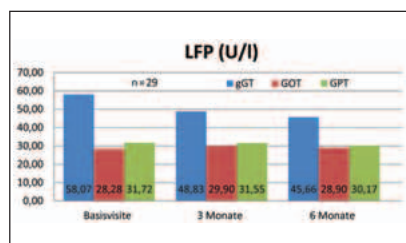


Abbildung 32: M. Derndorfer et al.

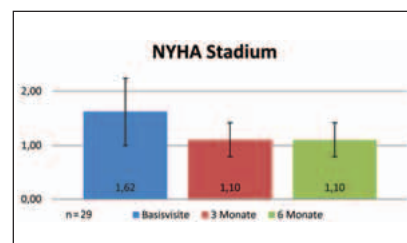


Abbildung 34: M. Derndorfer et al.

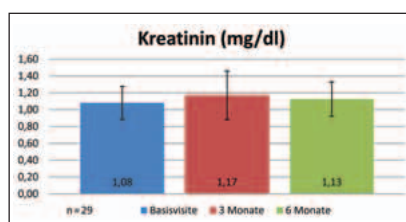


Abbildung 31: M. Derndorfer et al.

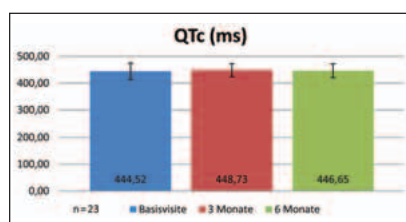


Abbildung 33: M. Derndorfer et al.

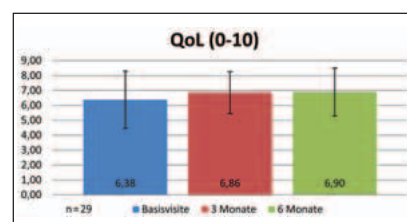


Abbildung 35: M. Derndorfer et al.

Prävalenz von Vorhofflimmern bei kardiologischen Patienten mit Risikofaktoren für Thromboembolie

IX – 4

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Die kürzlich neu herausgegebenen „ESC Guidelines for the management of atrial fibrillation“ führen den CHADS-VASc-Score ein, um das Risiko für thromboembolische Ereignisse bei Patienten mit Vorhofflimmern (VHF) bemessen zu können. Der CHADS-VASc-Score erweitert den bisherigen CHADS-Score (Herzinsuffizienz, Hypertonie, Alter > 75 Jahre, Diabetes, Schlaganfall) um die vormaligen „schwachen“ Risikofaktoren Gefäßerkrankung, weibliches Geschlecht und Alter (65–74 Jahre). Patienten, welche einen CHADS-VASc-Score ≥ 2 aufweisen, sollten eine orale Antikoagulation erhalten. Durch die Einführung der neuen ESC-Leitlinien bedarf es nun einer Reevaluierung des thromboembolischen Risikos. In einer retrospektiven Annäherung quantifizieren und stratifizieren wir die Prävalenz von VHF, sowie die Veränderungen der thromboembolischen Risikobemessung zusammen mit klinischen Parametern der Patienten unserer Kardiomyopathie-Ambulanz und der allgemeinen Kardiologie-Ambulanz. In der laufenden Studie wurden 500 Patienten mit kompletten Datensätzen aufgenommen. Alter $63,1 \pm 14,3$ (Mittelwert $\pm$ Std. Abw.), 72,4 % Männer, 60,4 % mit chronischer Herzinsuffizienz. 32,4 % ($n = 162$) aller Patienten hatten Vorhofflimmern in der Vorgeschichte (CHADS_VASc 0: 14 %, 1: 23 %, 2: 27 %, 3: 28 %, 4: 31 %, 5: 41 %, 6: 59 %, 7: 53 %, 8: 50 %). VHF trat häufiger bei Patienten mit chronischer Niereninsuffizienz auf (47,6 % vs. 26,1 %; $p < 0.001$, chi-square). 78 % der VHF-Patienten nahmen RAS-Hemmer, 88 % Betablocker. 83,3 % ($n = 135$) aller VHF-Patienten hatten im Vergleich zum CHADS-Score nun einen höheren CHADS-VASc-Score. In 66,7 % dieser Patienten führte die Koronare Herzkrankheit (KHK) zu einer Steigerung der Risikobemessung, in 77 % das Alter und in 28,8 % das weibliche Geschlecht. 69,7 % der Patienten mit VHF und CHADS = 1 hatten einen CHADS-VASc-Score ≥ 2 . In der Subgruppe der Patienten mit VHF, deren Risikoscore von 1 (CHADS) auf 2 (CHADS_VASc) stieg, hatten 26,7 % keine orale Antikoagulation (OAK).

Zusammenfassend ergibt sich aus der Neubemessung des thromboembolischen Risikos laut CHADS_VASc ein erhöhter Risikoscore für die Mehrheit der Patienten in unserer kardiologischen Ambulanz. Chronisches Nierenversagen war mit einer erhöhten VHF-Prävalenz assoziiert.

Nurse Led Telemonitoring Using iCARDEA – An Intelligent Platform for Personalized Remote Monitoring of CIED Patients

IX – 5

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Introduction The amounts of CIED devices that have been implanted since 2008 have grown exponentially, resulting in increasing numbers of patient visits in already overcrowded clinics. We also have a shortage of qualified electro physiologists. Accessing patient medical records to obtain up to date information in a timely manner to provide safe and efficient treatment can be a slow process as medical records are often located in many separate areas with access restrictions in the system. New methods need to be created that are safe and efficient to help alleviate the burden on health care services. Introducing telemonitoring with adaptable, computer-interpretable and evidence-based clinical guideline models can be a viable option for a busy clinic, utilizing the nursing staff to assess and evaluate the alerts and reports being sent from the CIED devices.

Methods Using standard interfaces exposed data from the patients CIED provided by the remote monitoring service, electronic health care record (EHR) and patient health care record (PHR) are collected and then correlated. The data are converted to HL7 Clinical Document Architecture (CDA) format to interface with the iCARDEA system. Using state of the art data analysis techniques patient specific warnings and suggestions will be automatically generated enhancing the data presented. An adaptive care planner applying clinical

guidelines and risk assessment will generate alarms. The care planner will be activated whenever an event is detected. An integrated patient health care record (PHR) will enable the patient to obtain knowledge, to make informed responsible decisions for their health care, allow a communication portal between nurse and patient, and provide the care givers an up to date status of the patient. The nurse is responsible for evaluating the information received from all sources including recommendations from the iCARDEA CarePlanner. A cardiologist will be contacted when medical intervention is needed. The nurse is also responsible for the telemonitoring logistics and management.

Results At present care plans have been developed for atrial fibrillation and ventricular tachycardia, as well as for potential technical problems. The nurse activates the care planner whenever an event is detected. The steps for care plan execution are then provided, and a link is given for a graphic monitoring tool providing a work flow that allows the results of each step in the decision process to be visible including the data retrieved from the EHRs (medications lab results etc.). For every step in the decision process the PHR and EHR will be accessed which reduces the time staff needs to accumulate various medical information. After a recommendation is presented different options are provided, such as guidance on prescription of medications, doses, and possible side effects.

Conclusion iCARDEA provides quick access to important medical records supports treatment decisions; assisting the nurse in making sure that the CIED patient is being cared for according to the current clinical guidelines. It will also help facilitate the early detection of events allowing for a timely treatment of the patient. The decrease in clinic visits will decrease the burden on the patient and health care system. A pilot study is planned after all the systems components are completed.

Significant Reduction of Bleeding Complications after Pulmonary Vein Isolation Using Different Types of Anticoagulant Strategies

IX – 6

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Purpose The aim of our study was to examine the occurrence of groin hematoma in patients (P) after pulmonary vein isolation (PVI) using 2 different anticoagulant therapeutic strategies.

Methods A total of 324 P (82 females) were examined in a retrospective manner for clinical relevant hematoma after treatment of PVI for paroxysmal or short persistent atrial fibrillation. Clinical relevant hematoma were defined by requirement of blood transfusion. The first 199 P were treated with intravenous heparin during the ablation with a target-act (activated clotting time) of more than 300 seconds. After the PVI the therapeutic scheme was changed to low molecular weight heparin (LMWH) starting with a single application 3 hours after PVI (weight adjusted – 1 mg/kg 2 times daily). Oral anticoagulation (phenprocoumon) was started on the day of the ablation. The second group was treated with intravenous heparin during ablation with the same target of act, but afterwards heparin was administered in a continuous way with a target-aptt (activated partial thromboplastin time) of 45–55 seconds (which was routinely checked all 4 hours). On the day after ablation, heparin-infusion was stopped and 1 hour later LMWH was administered with a dose of 0.5 mg/kg 2 daily. Oral anticoagulation was initiated on the day of the ablation. Both groups did not vary in terms of clinical and demographic data.

Results In the first group 17 cases of clinical relevant groin-hematoma occurred, whereas 2 clinical relevant hematomas could be observed in the second group. This difference was highly significant with a p-value of 0.005.

In the first group, females developed groin-hematoma significantly more often than men (10 out of 25 females versus 7 out of 174 males, $p < 0.001$). In the second group, 1 female and 1 male developed a groin hematoma, respectively ($p = n. s.$).

Surgical treatment was necessary in 3 patients (2 females, 1 male). No permanent sequelae remained in any patient. No ischemic cere-

brovascular events occurred in either group until therapeutic levels of oral anticoagulation (INR > 2.5) were reached.

Conclusions Continuous intravenous heparin-infusion until the day after ablation followed by LMWH at 1 mg/kg 2 times daily was associated with a significant reduction in groin-hematoma compared to intravenous heparin during ablation and change to LMWH at 0.5 mg/kg twice daily 3 hours after the ablation.

Twelve-lead ECG Patterns Fail to Identify an Epicardial Origin for Left Ventricular Tachycardia in Post-Infarction Patients

BAIL

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Background Several ECG features have been reported to identify epicardial origins for left ventricular tachycardias (LV-VTs) in the absence of myocardial infarction. Only limited data exist in post-infarction patients.

Objective We tested proposed algorithms for non-ischemic tachycardias for their ability to identify epicardial LV-VT origins.

Methods The QRS features of 17 successful epicardial and 29 endocardial RBBB LV-VTs were retrospectively reviewed by four independent electrophysiologists and analyzed for various 12-lead ECG features.

Results All 12-lead ECG features proposed for non-ischemic LV-VTs were unable to consistently predict an epicardial LV-VT origin in infarct-related tachycardias (**Figure 36**). QRS duration was 199 ± 31 ms in epicardial vs 178 ± 40 ms in endocardial LV-VTs ($p = 0.063$) showing significant overlap and therefore lacking a rea-

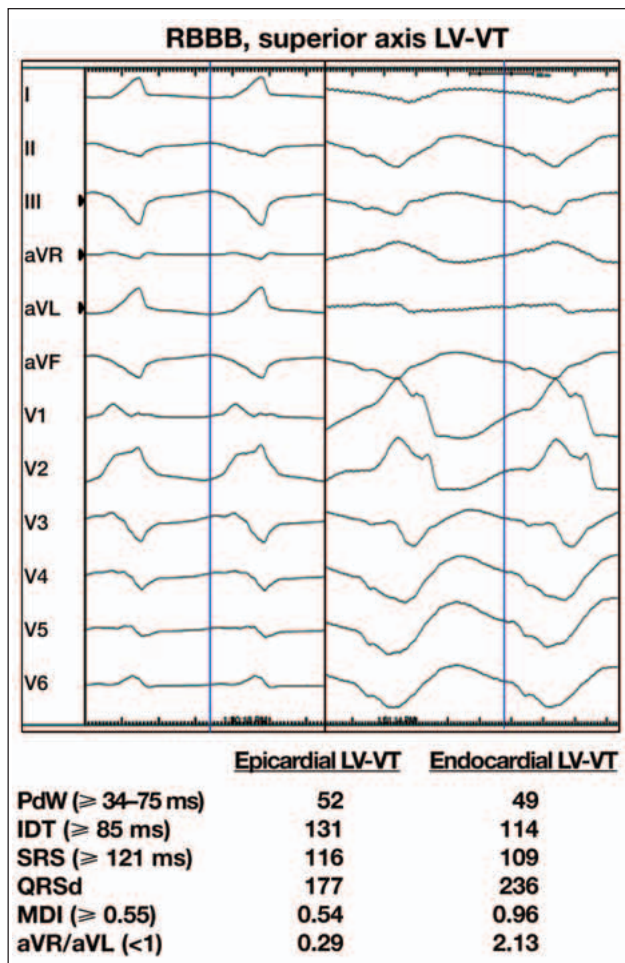


Figure 36: M. Martinek et al.

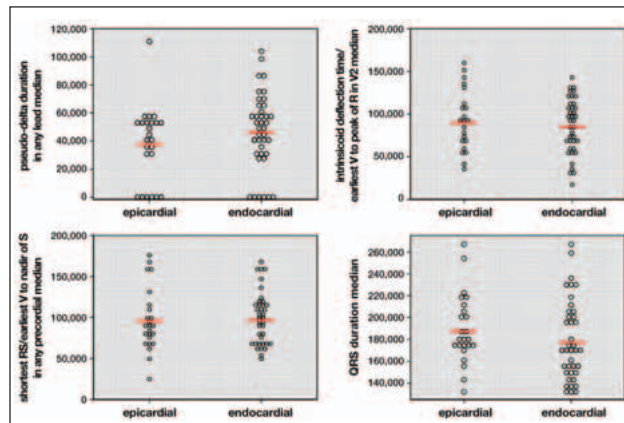


Figure 37: M. Martinek et al.

sonable cutoff-value between epicardial and endocardial LV-VTs. Pseudo-delta duration was 47 ± 9 vs 54 ± 21 ms ($p = n. s.$), intrinsicoid deflection time was 103 ± 32 vs 92 ± 24 ms ($p = n. s.$), shortest RS was 110 ± 36 vs 101 ± 34 ms ($p = n. s.$) and median deflection index was 0.75 ± 0.27 vs 0.85 ± 0.25 ms ($p = n. s.$) (**Figure 37**).

The finding of a Q wave in lead I and absence of a Q wave in the inferior leads failed to predict an epicardial origin in superior LV-VT sites. Q waves in any inferior lead as well as an aVR/aVL ratio < 1 were not specific for an epicardial origin in inferior sites (all $p = n. s.$). Furthermore, most inferior LV-VTs showed a Q wave in the inferior leads which correlated with pre-existing Q-waves in sinus rhythm ECGs ($p = 0.045$) rendering this ECG feature not useful.

Conclusion Proposed 12-lead ECG algorithms for the differentiation of epicardial vs endocardial sites for non-ischemic LV-VTs are not valid in post-infarction patients.

Klinischer Erfolg nach Radiofrequenzisolation der Pulmonalvenen bei paroxysmalem Vorhofflimmern

XVIII – 1

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Einleitung Als potenziell kuratives Verfahren ist bei Patienten mit symptomatischem, medikamentös therapierefraktärem paroxysmalem Vorhofflimmern ohne relevante Komorbiditäten eine Radiofrequenzisolation der Pulmonalvenen (PVI) indiziert (ESC-Guidelines 2010).

Durch die Reduktion bzw. Elimination rhythmusbezogener symptomatischer Vorhofflimmerepisoden kann eine Verbesserung des subjektiven Gesundheitszustandes erreicht werden. Zudem kann bei Therapieerfolg auf eine antiarrhythmische Dauermedikation verzichtet werden.

Ziel dieser Untersuchung ist die Erhebung von Vorhofflimmerepisoden und des subjektiven Gesundheitszustandes 1,5 Jahre (19 ± 3 Monate) nach PVI.

Methodik und Ergebnisse 120 konsekutive Patienten (20 % weiblich, 58 ± 10 Jahre) mit symptomatischem, medikamentös therapierefraktärem paroxysmalem Vorhofflimmern wurden im Jahr 2009 einer Katheterablation unterzogen (85 Erstablationen, 29 Zweitablationen, 5 Drittablationen). Bei 112 Patienten konnte 19 ± 3 Monate postinterventionell eine Erhebung der subjektiven Vorhofflimmerepisoden und des subjektiven Gesundheitszustandes erfolgen, um den Ablationserfolg zu untersuchen. Zusätzlich wurden zu diesem Zeitpunkt Langzeit-EKGs über zumindest 24h durchgeführt.

Voller Erfolg, der als Fehlen von Vorhofflimmerepisoden (mit oder ohne antiarrhythmischer Therapie) bei deutlich besserem Gesundheitszustand nach der Letztablation ($1,3 \pm 0,6$ Ablationen pro Patient) definiert wurde, konnte bei 69 Patienten (61,6 %) verzeichnet werden, wobei 3 Patienten (4,3 %) Antiarrhythmika einnahmen.

Teilerfolg, der durch Reduktion der Vorhofflimmerepisoden und deutlich besserem Gesundheitszustand festgelegt wurde, konnte bei 28 Patienten (25 %) erzielt werden. Von diesen Patienten benötigten 12 Patienten (42,8 %) zusätzlich eine medikamentöse antiarrhythmische Therapie.

Nicht erfolgreich (unveränderte oder gesteigerter Anzahl von Vorhofflimmerepisoden), waren insgesamt 9 Patienten (8,0 %), davon standen 3 Patienten (2,7 %) unter antiarrhythmischer Therapie. Es trat eine (0,8 %; $n = 120$) prozedurabhängige Komplikation auf (Perikardtamponade). 4 Patienten (3,3 %; $n = 120$) wurden 16 ± 8 Monate nach Ablation mittels „Pace and Ablate-Konzept“ weiterbehandelt. 2 Reablationen (1,7 %; $n = 120$) erfolgten wegen anderer atrialen Arrhythmien (rechtsatriale fokale Tachykardie, Vorhofflattern).

Eine orale Antikoagulation konnte bei 77 Patienten (68,6 %) aufgrund des CHADS₂/CHA₂DS₂-VASc-Scores 3 Monate nach PVI abgesetzt werden, 46 Patienten (41,1 %) nahmen nach 19 ± 3 Monaten weder einen Thrombozytenaggregationshemmer noch eine orale Antikoagulation ein (Abbildung 38, Abbildung 39).

Schlussfolgerung Durch Radiofrequenzablation bei paroxysmalem Vorhofflimmern kann bei 86,6 % aller Patienten eine deutliche Besserung des Gesundheitszustandes und Reduktion der Vorhofflimmerepisoden erzielt werden. Völlige Symptombefreiheit ist bei 61,6 % der Patienten nach mehr als 1½ Jahren nach Ablation zu erreichen.

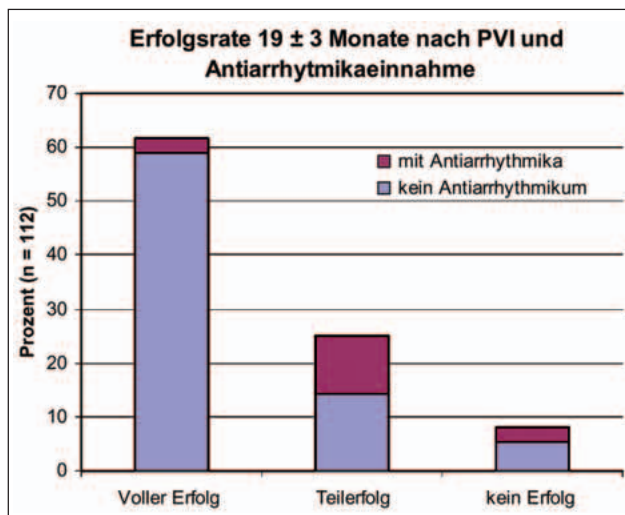


Figure 38: J. Moser et al.

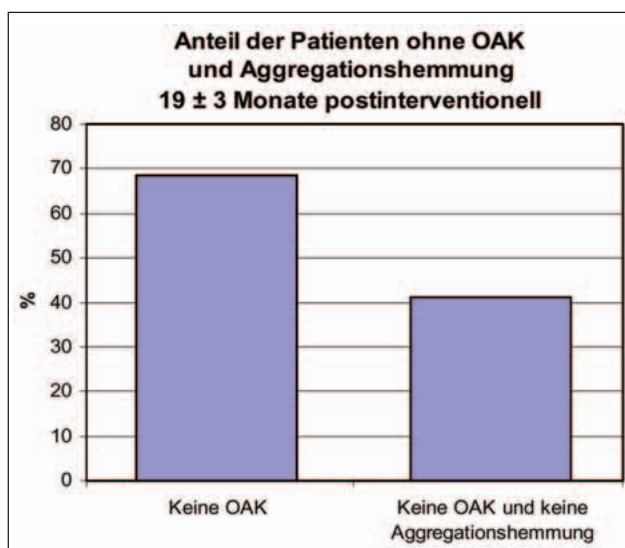


Figure 39: J. Moser et al.

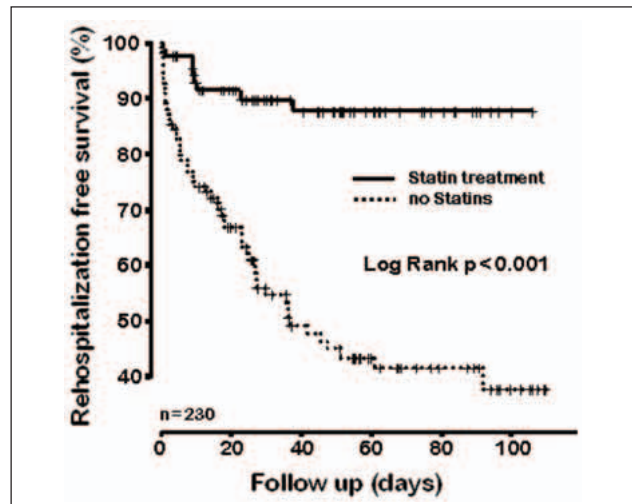


Figure 40: S. Öbel et al.

Rehospitalization of Patients with Persistent Atrial Fibrillation after DC Cardioversion – Impact of Statin Treatment

BAIL

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Background Inflammation and oxidative stress cause structural changes in the atrial myocardium. We aimed to investigate the impact of statin treatment on the maintenance of sinus rhythm in patients with persistent atrial fibrillation after DC cardioversion.

Materials and Methods We identified patients with paroxysmal AF by ICD-Code based chart-search regarding the diagnosis of admittance from January 2003 to December 2010. Patients who spontaneously or drug-induced converted to sinus rhythm had been excluded. Re-admission rates and adverse events were recorded by chart-review.

Results We included 230 patients into our final analysis. The patients were mainly male (71%) and median 66 years (IQR 59–72 years) old. In univariate comparison statins (7% vs. 26%, $p < 0.001$) as well as the use of ACE-inhibitors (33% vs 48%; $p = 0.04$) exhibited significantly reduced hospital re-admission rate due to palpitations and episodes or recurrent atrial fibrillation. This effect remained significant after adjusting for possible confounders in multivariate analysis (OR 0.47; $p = 0.007$).

Conclusion Inhibition of the HMG-coenzyme A reductase by statins may as potent anti-inflammatory and anti-oxidant agents protect the atrial myocytes of inflammation and oxidative stress. Therefore, statins could effectively reduce the hospital re-admission rate most likely based on maintenance of sinus rhythm after DC cardioversion in patients with persistent atrial fibrillation. Our results warrant further investigation in a prospective and randomized fashion (Figure 40).

Markers of Oxidative Stress and Inflammation Predict Early Recurrence of Atrial Fibrillation After Ablation

IX – 7

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Purpose The role of oxidative stress and inflammation after radiofrequency ablation of atrial fibrillation (AF) has not yet been well explored. We sought to assess the time course of biomarkers of oxidative stress and inflammation after AF ablation.

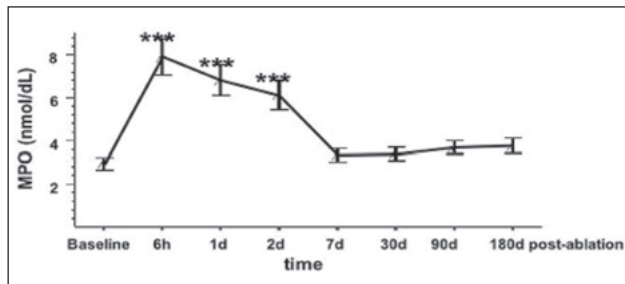


Figure 41: B. Richter et al. Time course of myeloperoxidase (MPO) after ablation and atrial fibrillation.

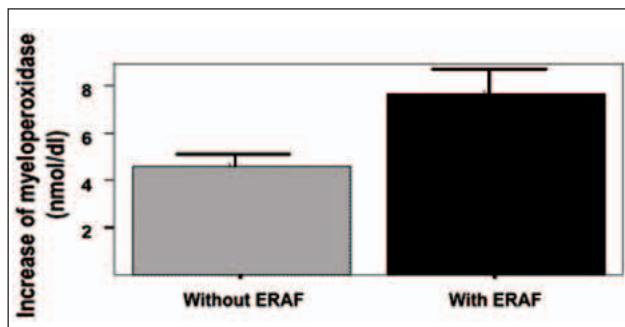


Figure 42: B. Richter et al. Ablation-induced increase of MPO in patients with and without early recurrence of AF (ERAF) within the first month after ablation.

Methods 30 consecutive patients with paroxysmal AF underwent circumferential pulmonary vein (PV) ablation, Lasso-guided PV isolation and ablation of complex fractionated atrial electrograms. Biomarkers were measured in peripheral blood samples before ablation and 6 hours, 1, 2, 7, 30, 90 and 180 days post-ablation.

Results The pro-oxidant enzyme myeloperoxidase increased 2.9 ± 0.2 -fold and was significantly up-regulated until day 2 post-ablation. Oxidized low density lipoprotein reflecting oxidant damage of lipoproteins showed a slight, but significant 1.2 ± 0.1 -fold increase at day 1 and 2. The anti-oxidant enzyme copper/zinc superoxide dismutase did not change significantly. High-sensitivity C-reactive protein (hs-CRP) increased significantly until day 7 (41 ± 8 -fold). The increase of myeloperoxidase and hs-CRP was associated with the amount of radiofrequency energy ($p < 0.05$). The up-regulation of hs-CRP correlated with troponin T levels ($p = 0.008$), while myeloperoxidase and troponin T were borderline associated ($p = 0.054$). Myeloperoxidase and hs-CRP predicted early recurrence of AF within the first post-ablation week (both $p < 0.05$). However, neither the oxidative stress response nor the inflammatory response predicted the 1-year ablation outcome ($p > 0.05$).

Conclusions Markers of oxidative stress and inflammation showed a significant ablation-induced up-regulation detectable for up to 7 days. This up-regulation was related to the radiofrequency energy delivered during ablation and predicted early recurrence of AF, but not long-term ablation outcome (Figure 41, Figure 42).

Pulmonalvenen-Isolation mit dem Cryoballon-Katheter bei Patienten mit paroxysmalem Vorhofflimmern: Ein Single-Center-Bericht XVIII – 2

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Hintergrund Die elektrische Isolation der Pulmonalvenen (PV) ist der methodische Eckpfeiler der interventionellen Therapie von paroxysmalem Vorhofflimmern. Als Alternative zum Radiofrequenz-Strom (RF) hat sich in den vergangenen Jahren Kälte als sichere und effektive Energieform bei der Durchführung von Ablationen etabliert. Der Cryoballon-Katheter (CBK, Arctic Front™, Medtronic, Minneapolis, USA) ermöglicht die Durchführung von

PV-Isolationen durch zirkumferentielles Anfrieren des Ballons an das jeweilige PV-Ostium. Die dafür notwendigen tiefen Temperaturen werden durch Wärmeentzug aus dem Gewebe, vermittelt durch das Verdampfen von Stickstoff im Ballon, erzeugt. Ziel unserer prospektiven Studie war es, die prozedurale Sicherheit und Effektivität der PV-Isolation mit dem CBK sowie die klinischen Ergebnisse nach mindestens 6 Monaten zu untersuchen.

Methodik Es wurden nur Patienten (P) mit symptomatischem PAF eingeschlossen. Der CBK wurde mittels einer steuerbaren Schleuse (Flexcath™, Medtronic) im linken Vorhof manövriert. Je nach Größe der PV wurde pro P nur ein Ballon mit einem Durchmesser von 23 mm oder 28 mm gewählt. Vor der Kälteapplikation wurde die korrekte Okklusion des PV-Ostiums unter Fluoroskopie mittels Kontrastmittelinjektion in die PV über den CBK ermittelt. Um eine Gefährdung des rechten Nervus phrenicus rechtzeitig registrieren zu können, wurde während der Ablation der rechten PVs eine kontinuierliche Stimulation des Nervs vom rechten Vorhof aus durchgeführt. Pro PV wurden 3 Energieabgaben mit einer Dauer von je 5 Minuten durchgeführt. Nach Ablation aller PVs wurde der Ablationserfolg mittels eines Spiralkatheters verifiziert. Bei unvollständiger Isolation erfolgten maximal 2 weitere Kryo-Applikationen pro PV. Bei weiterhin ausbleibendem Erfolg wurde eine 2. transseptale Punktion und eine Touch-up-Ablation mit einem 8 mm Single-tip-Cryoablationskatheter (Freezor Max™, Medtronic) durchgeführt. Als klinischer Erfolg wurde das Fehlen von AF-Rezidiven (ohne oder unter zuvor wirkungslosen Antiarrhythmika) gewertet.

Ergebnisse Wir ablatierten 60 P (42 männlich, mittleres Alter: 58 ± 10 Jahre). Bei 57 P (95 %) konnten sämtliche 4 PV mit dem CBK isoliert werden. Bei 3 P (5 %) mussten jeweils 2 PV (2 linke obere PV, 2 linke untere, 2 rechte untere PV) mittels Touch-up-Ablation isoliert werden. Die mittlere Prozedurdauer betrug 185 ± 45 min mit einer mittleren Durchleuchtungszeit von 44 ± 14 min. Es traten 4 Phrenikusparesen (7 %) auf (alle mit 23-mm-Ballons), die sämtlich innerhalb von maximal 9 Monaten reversibel waren. Thromboembolische Komplikationen oder Perikardtamponaden traten nicht auf. Der mediane Follow-up betrug für 59 P (1 P konnte nicht nachgesorgt werden) 16 Monate (6–24 Monate). Ein klinischer Erfolg wurde bei 44 P (75 %) mit einer Prozedur erzielt, wobei 36 P (61 %) ohne und 8 P (14 %) unter Antiarrhythmika rezidivfrei waren. Die restlichen 15 P (25 %) wurden re-ablatiert.

Schlussfolgerung Bei Patienten mit PAF kann mit dem CBK eine PV-Isolation aller PVs in einem hohen Prozentsatz (95 %) erzielt werden. Die klinische Erfolgsrate beträgt hierbei nach einer Prozedur 75 %. Bei Verwendung des 23-mm-Ballons ist das Auftreten einer (reversiblen) Phrenikusparese rechts jedoch nicht sicher zu verhindern.

Catheterinterventional Redo Procedures After Previous Intraoperative Ablation of Atrial Fibrillation During Cardiac Surgery XVIII – 3

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Background Intraoperative left atrial ablation during cardiac surgery is a well established approach for treating atrial fibrillation (AF).

Objective The purpose of this study was to evaluate recurrent arrhythmias and catheterinterventional redo procedures after surgical AF ablation.

Methods From 01/2008 to 06/2010 42 patients with recurrent symptomatic supraventricular tachycardias (28 patients with macroreentrant atrial tachycardias [MRT] [67%], 14 patients with AF [33%]) after previous intraoperative left atrial ablation for treatment of AF presented for catheter ablation. Using a nonfluoroscopic system (CARTO or NavX) the left atrium (LA) was reconstructed and imageintegrated. Then the documented arrhythmia was mapped by entrainmentmapping and/or pulmonary vein isolation (PVI) checked. According to the findings ablation was performed.

Results In 32 (76%) patients gaps of the PVI required reisolation. Beside that 32 MRTs were documented and ablated: 12 perimitral,

6 LA roof dependent, 5 around pulmonary veins (PVs), 4 around the left atrial auriculum (LAA), 3 septal, 1 within coronary sinus (CS) and 1 cavotricuspid isthmus (CTI) ablation. Tachycardia termination, PVI and noninducibility of any macroreentrant tachycardia was the procedural endpoint. In the follow up of 17 months (3–44) 32 patients (76%) were free of AF or MRT, 7 patients (17%) required a second ablation procedure.

Conclusion Most AF recurrences are due to reconnection of the PVs. In these cases reisolation on an antral level is required. Atrial MRTs represent the majority of surgical redo cases. 3D-entrainment mapping helps to identify those circuits for fast and effective ablation. In these cases however, PVI should be checked and PVs in case reisolated additionally.

Vernakalant: Medikamentöse Kardioversion bei Vorhofflimmern – Erste Erfahrungen am eigenen Patientengut XVIII – 5

E. Sigmund, M. Martinek, H. J. Nesser, H. Pürerfellner

Interne 2 Kardiologie/Angiologie/Intensivmedizin, Krankenhaus der Elisabethinen Linz

Einleitung Bei Vernakalant handelt es sich um einen Wirkstoff, der selektiv atriale Ionenkanäle blockiert (dominante Wirkung auf den IK_{ur}-Kanal). Zugelassen ist das Medikament zur raschen Wiederherstellung des Sinusrhythmus bei Erwachsenen mit Vorhofflimmern von kurzer Dauer (< 7 Tage). Vernakalant ist nur zur intravenösen Infusion bestimmt, die Effizienz und Sicherheit konnte bereits in mehreren Studien nachgewiesen werden. In Österreich ist das Präparat seit Anfang Jänner 2011 in der Dosierung 500 mg/25 ml erhältlich (Brinavess®, Fa. MSD). Wir berichten über unsere ersten Erfahrungen am KH der Elisabethinen Linz.

Methodik 10 Patienten (5 männlich/5 weiblich) im Alter von 65,7 ± 13,2 Jahren wurden bislang behandelt. 8 Patienten berichteten über ein erst kürzlich aufgetretenes Vorhofflimmern (mehrere Stunden bis max. 26 Stunden), 2 Patienten erhielten Vernakalant im Rahmen einer Pulmonalvenenisolation sowie einer elektrophysiologischen Untersuchung einer linksatrialen Tachykardie.

Resultate Die Konversionsrate lag bei 6 Patienten (60 %), davon konvertierten 4 Patienten (40 %) bereits nach der Initialdosis in den Sinusrhythmus, bei 2 Patienten (20%) war die Gabe einer 2. Dosis (15 min. nach Erstdosis) erforderlich. Die Zeit bis zur Kardioversion betrug 10, 13, 20, 25 sowie zweimal 35 Minuten (im Median 25 Minuten). 4 Patienten wurden nach frustrierender Applikation von Vernakalant erfolgreich elektrisch kardiovertiert. Bei 3 Patienten traten am Ende der Infusion unerwünschte Wirkungen auf (Hustenansturm, heftiges Niesen, Flush-Symptomatik, Dysgeusie in Form von metallischem Geschmack sowie nicht-anhaltende VES in Salvenform), diese dauerten zwischen 3–5 Minuten und gestalteten sich selbst-limitierend.

Diskussion Vernakalant erweist sich in unserer bisherigen Erfahrung als ein effektives und sicheres Mittel zur Akutkonversion von Vorhofflimmern mit kurzer Dauer. Der Wirkungseintritt erfolgt rasch und die beobachteten Nebenwirkungen sind von kurzer Dauer. Maligne ventrikuläre Arrhythmien (z. B. anhaltende ventrikuläre Tachykardien oder Torsades-Tachykardien) traten nicht auf und wurden auch in der Literatur bislang nicht berichtet.

Katheterablation von persistierendem Vorhofflimmern – Langzeiterfolgsrate am KH der Elisabethinen Linz XVIII – 4

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Einleitung Die kurative Katheterablation bei medikamentös-therapierefraktärem chronischen Vorhofflimmern (VHF) gewinnt zunehmend an klinischer Bedeutung und ist bereits in den aktuell gültigen Guidelines verankert. Bei Patienten mit lang anhaltendem persistierendem VHF stellen die Pulmonalvenen sehr selten das alleinige

Substrat zur Initiierung und Aufrechterhaltung des VHF dar, sodass die Radiofrequenzablation (RFA) mit einer stufenweisen Erweiterung durch zusätzliche linksatriale Linien sowie Ablation komplexer fraktionierter atrialer Potentiale (CFAE) bis zur Regularisierung oder Termination des VHF weitergeführt wird.

Methodik 42 Patienten (Pat., 79 % männlich, 58 ± 8,1 Jahre) mit medikamentös terapierefraktärem und hochsymptomatischem, persistierendem VHF wurden im Jahr 2009 am KH der Elisabethinen Linz einer linksatrialen Radiofrequenzablation unterzogen. Im Durchschnitt 18,5 ± 3,6 Monate nach Ablationsbehandlung wurde bei allen Patienten ein Holter-Monitoring über mindestens 24 Stunden durchgeführt. Zugleich wurden die Patienten um die Einschätzung ihres aktuellen Gesundheitszustandes gebeten. Bei 6 Patienten (5 SM-Träger, 1 Loop-Rekorder-Träger) erfolgten die Nachkontrollen durch Abfrage des implantierten Systems, sodass hier ein 100%iges Monitoring vorhanden war. Der Gruppe „voller Erfolg“ wurden Patienten zugeordnet, bei denen weder subjektiv wahrgenommene noch objektiv detektierte VHF-Episoden (> 15 sec/24 h) ohne antiarrhythmische Medikation beobachtet wurden. Als „Teilerfolg“ wurde bewertet, wenn bei deutlicher Besserung der klinischen Symptomatik sowie der Lebensqualität mit oder ohne antiarrhythmischen Therapie zumindest eine Konversion von persistierendem in ein paroxysmales VHF detektiert werden konnte.

Resultate Die Ergebnisse des Ablationserfolges aller Prozeduren bei persistierendem VHF im Jahr 2009 (42 Patienten) sind in **Tabelle 18** zusammengefasst.

Diese inkludieren 25 Erstprozeduren (59,5 %), 15 Zweitprozeduren (35,7 %) sowie 1 Drittprozedur (2,4 %; 1 unbekannt, 2,4 %), davon 13 (30,9 %) Reablationen wegen VHF-Rezidiv und 2 Reablationen wegen anderer atrialer Arrhythmien. Bei 5 Pat. (11,9 %) war ein „Misserfolg“ zu erheben, von denen 4 einer neuerlichen Ablationsbehandlung unterzogen wurden, welche bei 75% erfolgreich verlief. Bei 2 Pat. folgte eine palliative ablate and pace-Therapie. Die sub-

Tabelle 18: E. Sigmund et al.

Ablationserfolg (Outcome) bei persistierendem VHF aus dem Jahr 2009 in einem Beobachtungszeitraum von durchschnittlich 18,5 ± 3,6 Monaten nach Vorhofflimmerablation

Patientengruppen	Anzahl der Patienten	Erfolg (%)
Voller Erfolg	18	42,9 %
Teilerfolg		
– ohne Antiarrhythmikum	14	33,3 %
– mit Antiarrhythmikum	4	9,5 %
Klinische Erfolgsrate gesamt	36	85,7 %
Misserfolg	5	11,9 %
Unbekannt	1	2,4 %

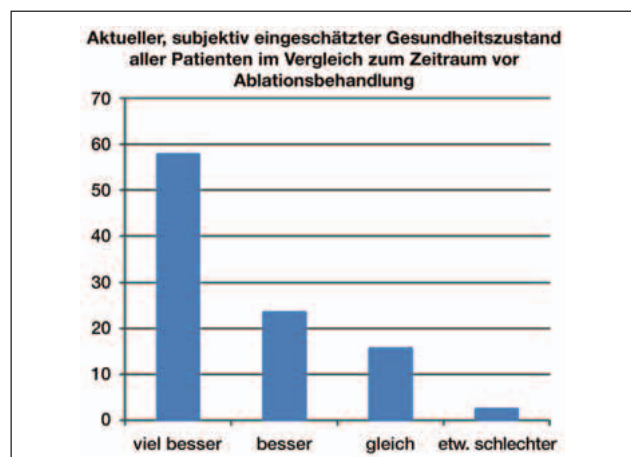


Abbildung 43: E. Sigmund et al.

jektive Einschätzung des Gesundheitszustandes aller Patienten ist in **Abbildung 43** veranschaulicht.

Nach Ablation wurden alle Patienten für mindestens 3 Monate nach RFA mit einem INR-Zielwert von 2,0–3,0 oral antikoaguliert, die weitere Antikoagulation (OAK) war vom CHADS₂-Score des Patienten abhängig. Somit war bei den betreffenden Pat. bei 26,2 % weder eine OAK noch eine thrombozytenaggregationshemmende Therapie notwendig, bei 26,2 % konnte auf Acetylsalicylsäure gewechselt werden, 45,2 % sind weiterhin auf einer OAK (2,4 % unbekannt). Postprozedural ist mit oben genanntem Antikoagulationschema in der Beobachtungszeit kein thromboembolisches Ereignis aufgetreten.

Diskussion Die Isolation der Pulmonalvenen in Kombination mit zusätzlichen atrialen Läsionen ist eine effektive therapeutische Alternative zur antiarrhythmischen Medikation für Patienten mit persistierendem VHF. Auch wenn nach RFA nur ein Teil der Pat. gänzlich frei von VHF ist, steigt die Lebensqualität durch eine deutliche Reduktion von Anzahl und Dauer der Episoden sowie der damit verbundene Symptomatik signifikant an.

Robotic Navigation for Catheter Ablation of Paroxysmal and Persistent Atrial Fibrillation: A Single-Center Experience after 110 Cases

XVIII – 6

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Introduction Remote navigation systems represent a novel method for catheter ablation of atrial fibrillation (AF). The Sensei™ robotic navigation system (Hansen Medical, Mountain View, USA) enables remote catheter navigation via a robotic steerable sheath (Artisan™, Hansen Medical). The aim of this study is to report the first Austrian experience with the Sensei™ system for the treatment of patients (P) with paroxysmal and persistent AF.

Materials and Methods Between November 2009 and November 2010, 110 P (59 ± 9 years, 89 males) underwent robotic circumferential pulmonary vein isolation (PVI) for paroxysmal AF (56 P, 51%) or robotic circumferential PVI plus robotic creation of a left atrial roof line for persistent AF (54 P, 49%). The EnSite NavX™ system (St. Jude Medical, Minneapolis, USA) was used for 3-dimensional mapping. For ablation, a 3.5 mm open-irrigated cooled-tip ablation catheter (Therapy Cool Path ns™, St. Jude Medical) was used. PVI was confirmed by a multipolar spiral catheter (Optima™, St. Jude Medical) as second left atrial catheter. Completeness of block along the roof line was confirmed by appropriate left atrial pacing manoeuvres. All procedures were performed during deep sedo-analgesia after left atrial thrombi had been excluded by transesophageal echocardiography.

Follow-up consisted of 48-hour ECG monitoring at 3, 6, and 12 months after ablation plus additional ECGs recorded during episodes of suspicious symptoms. Freedom from atrial arrhythmias ≥ 30 seconds was counted as clinical success.

Results PVI of all pulmonary veins was achieved in 103 P (94%). In 7 P (6%), one pulmonary vein could not be isolated, respectively.

Block along the roof line could be achieved in all cases. The mean procedure time was 237 ± 51 minutes (232 ± 50 minutes in paroxysmal AF versus 242 ± 48 minutes in persistent AF; p = n. s.). The mean fluoroscopic time was 27 ± 8 minutes (27 ± 9 minutes in paroxysmal AF vs 26 ± 8 minutes in persistent AF; p = n. s.). The mean operator's fluoroscopy exposure was 13 ± 6 minutes. As complications, 2 groin hematoma requiring transfusion and one pericardial tamponade (after the end of the procedure) requiring pericardiocentesis occurred, respectively.

After a median follow-up of 9 months (range 3–14 months), the success rate after a single procedure was 65% for P with paroxysmal AF and 52% for P with persistent AF, respectively.

Success rates increased to 79% in paroxysmal AF and 74% in persistent AF, respectively, after a second procedure (in 27% of P with paroxysmal and in 40% of P with persistent AF).

CHA₂DS₂-VASC und HASBLED-Score bei Patienten mit Vorhofflimmern

IX – 3

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Einleitung In den aktuellen Guidelines der europäischen kardiologischen Gesellschaft wird zur Bestimmung des embolischen und Blutungs-Risikos bei Vorhofflimmern (AF) die Anwendung von CHA₂DS₂-Vasc- und HASBLED-Score empfohlen, während früher zur Ermittlung des Embolierisikos der CHADS₂-Score verwendet wurde. Ziel der Studie war es, bei AF-Patienten CHADS₂- und CHA₂DS₂-Vasc-Score zu vergleichen, den HASBLED-Score zu errechnen und embolische Ereignisse, Blutungen und Rehospitalisierungen im Follow-up zu ermitteln.

Material und Methode Eingeschlossen wurden 100 konsekutive AF-Patienten, die zwischen Dezember 2009 und Jänner 2010 stationär aufgenommen worden waren. Aus den Entlassungsbriefen wurden die für die Ermittlung der Scores benötigten Informationen entnommen. Im Februar 2011 wurde mithilfe des Online-Informationssystems des Wiener Krankenanstaltverbundes nach Rehospitalisierungen, embolischen Ereignissen und Blutungen gesucht.

Ergebnisse Von den 100 Patienten waren 47 weiblich. Das Durchschnittsalter betrug 74 ± 12 Jahre. Der durchschnittliche CHADS₂-Score betrug 2,4 ± 1,4. Der durchschnittliche CHA₂DS₂-Vasc-Score betrug 4,2 ± 2. Einen CHADS₂-Score von 1 oder 2 wiesen 47 % der Patienten auf, damit wurden sie als „moderate risk“ mit fraglicher Indikation zur oralen Antikoagulation eingestuft. Einen CHA₂DS₂-Vasc-Score ≥ 2 wiesen 91 % der Patienten auf (**Tabelle 19**) – entsprechend den Guidelines wäre bei ihnen eine orale Antikoagulation indiziert. Tatsächlich wurde eine orale Antikoagulation 54 % der Patienten empfohlen. Bei den antikoagulierten Patienten betrug der CHADS₂-Score 2,7 ± 1,3, der CHA₂DS₂-Vasc-Score 4,6 ± 1,9, bei den nicht-antikoagulierten betrug der CHADS₂-Score 2,0 ± 1,4, der CHA₂DS₂-Vasc-Score 3,8 ± 2. Der durchschnittliche HASBLED-Score betrug 3,5 ± 1,5, bei den antikoagulierten Patienten 3,3 ± 1,5 und bei den nicht-antikoagulierten 3,7 ± 1. In einem Nachbeobachtungszeitraum von 13–14 Monaten ist es bei 46 Patienten zu einer oder mehreren Rehospitalisierungen gekommen, davon 2 infolge

Tabelle 19: C. Stöllberger et al.

CHA₂DS₂-Score und CHA₂DS₂-Vasc-Score von 100 Patienten mit Vorhofflimmern

	CHA ₂ DS ₂ -Vasc 0	CHA ₂ DS ₂ -Vasc 1	CHA ₂ DS ₂ -Vasc 2	CHA ₂ DS ₂ -Vasc 3	CHA ₂ DS ₂ -Vasc 4	CHA ₂ DS ₂ -Vasc 5	CHA ₂ DS ₂ -Vasc 6	CHA ₂ DS ₂ -Vasc 7	CHA ₂ DS ₂ -Vasc 8	CHA ₂ DS ₂ -Vasc 9
CHADS ₂ 0	3 (37,5 %)	2 (25 %)	2 (25 %)	1 (12,5 %)						
CHADS ₂ 1		4 (20 %)	5 (25 %)	9 (45 %)	2 (10 %)					
CHADS ₂ 2			1 (3,7 %)	13 (48,2 %)	10 (37 %)	3 (11,1 %)				
CHADS ₂ 3					3 (12,5 %)	9 (37,5 %)	12 (50 %)			
CHADS ₂ 4					1 (7,1 %)	2 (14,3 %)	8 (57,2 %)	3 (21,4 %)		
CHADS ₂ 5								2 (40 %)	3 (60 %)	
CHADS ₂ 6										2 (100 %)

von Schlaganfällen, und zu 11 Todesfällen. Blutungen sind bei keinem Patienten aufgetreten. Bei den 43 überlebenden, nicht-rehospitalisierten Patienten war der CHA₂DS₂-Vasc-Score $4,0 \pm 2,1$, der HASBLED-Score $3,1 \pm 1,5$, bei den verstorbenen $4,8 \pm 1,3$ und $4,7 \pm 0,9$, bei den rehospitalisierten $4,2 \pm 2$ und $3,5 \pm 1,5$.

Diskussion Durch Anwendung des CHA₂DS₂-Vasc-Scores nimmt die Zahl der AF-Patienten zu, bei denen eine orale Antikoagulation indiziert ist. In der Praxis werden nicht alle Patienten antikoaguliert, bei denen dies indiziert wäre. Die Nützlichkeit des HASBLED-Scores zur Ermittlung des Blutungsrisikos kann aus unseren Daten infolge der geringen Patientenzahl, der kurzen Nachbeobachtungszeit und des Fehlens von Blutungen nicht beurteilt werden.

Langzeitwirkung des hämodynamischen Nutzens einer AV-Zeit-Optimierung bei Patienten mit VDD-Schrittmacher

BAI

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Einleitung AV-Zeit-Optimierung mit Verkürzung der nominalen AV-Zeit bewirkt eine hämodynamische Verbesserung bei Patienten mit konventioneller Schrittmacher- (SM-) Indikation wegen AV-Block. Wir überprüften die Stabilität dieses hämodynamischen Nutzens im Langzeitverlauf, mit besonderer Beachtung der Änderung des Schlagvolumens (SV) und des Cardiac Output (CO), am Beginn und bei der Nachkontrolle, sowie der Reproduzierbarkeit des hämodynamischen Nutzens durch die AV-Zeit-Optimierung.

Methode In einer prospektiven Studie wurden 80 Patienten (33 Frauen, 47 Männer; Altersdurchschnitt 76 ± 11 Jahre) mit einem implantierten VDD-SM und einer AV-Leitungsstörung eingeschlossen. 64 Patienten stimmten einer Kontrolluntersuchung nach 3 Monaten zu. Mit dem Task Force® Monitor (TFM) wurde das SV von Schlag zu Schlag mittels Impedanz-Kardiographie, der CO, die Herzfrequenz (HR) und der Blutdruck (BP), sowohl zu Beginn, als auch bei einer Nachkontrolle gemessen. Wir haben in beiden Untersuchungen die nominale mit der optimierten AV-Zeit verglichen. Die optimale AV-Zeit wurde dabei durch die Koglek-Formel (Programmierung einer Verzögerung von 100 ms, gemessen vom Ende der wahrgenommenen P-Welle zur Spitze/Tiefpunkt des stimulierten Kammerkomplexes) errechnet. Bei der 3-Monats-Kontrolle wurde ein kurzer Fragebogen bezüglich der Lebensqualität ausgefüllt.

Ergebnis

1. Hochsignifikanter Anstieg des SV ($55,3$ ml vs. $69,9$ ml; $p < 0,001$) und des CO ($3,91$ vs. $5,01$; $p < 0,001$) durch Optimierung der AV-Zeit (83 ± 20 [median 75] ms vs. 179 ± 35 [median 180] ms; $p < 0,001$) in der Erstuntersuchung.
2. Bei der 3-Monats-Kontrolle blieb der optimierte CO stabil ($5,01$ vs. $4,81$; $p = 0,09$), während das optimierte SV eine geringfügige, aber signifikante Abnahme ($71,3$ ml vs. $65,4$ ml; $p = 0,001$) zeigte.
3. Der signifikante Anstieg des SV und des CO durch die AV-Optimierung kann in der Nachuntersuchung (SV: $53,7$ ml vs. $65,2$ ml; $p < 0,001$; CO: $3,91$ vs. $4,81$; $p < 0,001$ im Vergleich zur ursprünglichen Nominalwerteinstellung) reproduziert werden.
4. Von den 64 Patienten bevorzugten 46 (72 %) die optimierte AV-Zeit-Einstellung nach der 3-Monats-Kontrolle. Nur 3 Pat. (5 %) bevorzugten die nominale Einstellung.

Diskussion Eine AV-Zeit-Optimierung bei Patienten mit implantiertem VDD-Schrittmacher führt zu einem signifikanten Anstieg des SV und des CO. Langfristig bleiben die Effekte der AV-Zeit-Optimierung stabil, sind reproduzierbar und bewirken eine bessere Lebensqualität. Eine AV-Optimierung sollte im klinischen Alltag bei allen SM-Patienten mit notwendiger ventrikulärer Stimulation durchgeführt werden.

AV-Zeit-Optimierung bei Patienten mit VDD-Schrittmacher wegen AV-Block

BAI

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Einleitung Seit der Behandlung der Herzinsuffizienz (HI) mit biventrikulären Schrittmacher- (SM-) Systemen wissen wir, dass die nominale AV-Zeit verkürzt werden muss. Das Ziel der Studie war bei konventioneller anti-bradykarder SM-Indikation ohne Zeichen einer HI den hämodynamischen Vorteil einer AV-Zeit-Optimierung mittels der EKG-Formel von Koglek und dem nicht-invasiven Task Force® Monitor (TFM) nachzuweisen.

Methode Es wurden in einer prospektiven Studie 80 Patienten (33 Frauen, 47 Männer; Altersdurchschnitt 76 ± 11 Jahre) mit einem implantierten VDD-SM bei AV-Leitungsstörung eingeschlossen. Gemessen wurden das Schlagvolumen (SV) von Schlag zu Schlag mittels Impedanz-Kardiographie, der Cardiac Output (CO), die Herzfrequenz (HR) und der Blutdruck (BP), sowohl bei der nominalen als auch bei optimierter AV-Zeit. Die optimale AV-Zeit wurde dabei durch die Koglek-Formel (Verzögerung von 100 ms, gemessen vom Ende der wahrgenommenen P-Welle zur Spitze/Tiefpunkt des stimulierten Kammerkomplexes) berechnet.

Ergebnis

1. Das optimierte wahrgenommene AV-Zeit-Intervall betrug 83 ± 20 (median 75) ms gegenüber dem nominalen Wert von 179 ± 35 (median 75) ms; $p < 0,001$.
2. Das SV nimmt durch die AV-Zeit-Optimierung signifikant zu ($55,3$ ml vs. $69,9$ ml; $p < 0,001$).
3. Es kommt dementsprechend zu einem signifikanten Anstieg des CO ($3,91$ vs. $5,01$; $p < 0,001$).
4. Es kann kein Unterschied bei Blutdruck ($97,6$ vs. $97,5$ mmHg; $p = 0,9$) und Herzfrequenz ($72,6$ vs. $71,8$; $p = 0,09$) während der Messung von SV und CO beobachtet werden.
5. Es besteht ein hämodynamischer Vorteil bei jedem Patienten, unabhängig von der zugrundeliegenden Herzerkrankung.
6. Der Vorteil der AV-Optimierung ist von der Tragezeit des Schrittmachers unabhängig (AV-Optimierung durchschnittlich 43 Monate nach der Implantation).

Diskussion Die AV-Zeit-Optimierung erfordert eine deutliche Verkürzung des nominalen AV-Intervalles und bewirkt eine signifikante Verbesserung der hämodynamischen Parameter (SV und CO), unabhängig von der Ursache der Herzerkrankung oder der Dauer der Schrittmachertragezeit. Eine optimierte AV-Zeit sollte bei jedem SM-Patienten mit notwendiger ventrikulärer Stimulation zur Erhaltung der Pumpfunktion programmiert werden.

Ultra-Mobile Patient-Operated Long-Term Full-Disclosure Single-Channel ECG Monitoring

XVIII – 7

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Background Continuous ECG monitoring may improve detection of symptomatic and asymptomatic arrhythmias and subsequent patient treatment. However, due to technical obstacles and patient comfort issues, ambulatory continuous full-disclosure ECG monitoring has not been commercially available. The aim of this study was to determine the feasibility of a patient-managed long-term full-disclosure ECG monitoring system using a miniaturized single-channel waveform recorder and a customized mobile computing system.

Methods Thirty-three subjects underwent 72-hour conventional Holter monitoring followed by a 7-day period of continuous 1-channel ECG monitoring with a customized patient-operated monitoring system. Information related to patient symptoms and activity was collected utilizing an electronic patient log. A questionnaire was used to assess factors determining patient satisfaction and attitudes towards long-term use of the system.

Results Patient-managed long-term ECG monitoring was feasible in all subjects (54% male, age range 22–78 years). Overall, 5400 hours of continuous ECG tracings were recorded. Mean duration of monitoring was 19.7 ± 2.2 hours per day. Overall satisfaction with the monitoring procedure was high (82% of patients). Electrode skin irritation was the strongest factor for patient discomfort, resulting in discontinuation of ECG recording in one subject. The quality of ECG waveforms allowed determination of cardiac rhythm in 98% of time. Extending monitoring duration from 72 hours to 10 days resulted in an increased diagnostic yield of 23% ($p < 0.04$).

Conclusion Ambulatory patient-managed full-disclosure ECG recording is feasible and increases diagnostic yield compared with conventional holter monitoring. A relatively simple setup provides high-quality single-channel ECG recordings, which allows reliable diagnosis of cardiac arrhythmias while reducing interference with everyday activities. Further research is warranted to enhance long-term tolerability of continuous ECG monitoring.

■ Risikofaktoren – Stoffwechsel – Lipide I/ Risk Factors – Metabolism – Lipids I

New and Old Criteria for the Diagnosis of Diabetes Mellitus in Patients with Peripheral Arterial Disease

XIX – 1

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Recently, an International Expert Committee concluded that haemoglobin A1c (HbA1c) may be a better means of diagnosing diabetes than glucose levels. A diagnosis of diabetes was recommended with $\text{HbA1c} \geq 6.5\%$. Data on the concordance of new and old criteria for the diagnosis of diabetes are very scarce; no data at all are available for patients with peripheral arterial disease (PAD).

We enrolled 278 consecutive patients without previously known diabetes (195 men and 83 women) in whom PAD was verified sonographically. HbA1c was measured and standard 75 g oral glucose tolerance tests were performed.

From the patients with newly diagnosed diabetes according to the new diagnostic criterion of an $\text{HbA1c} \geq 6.5\%$ ($n = 26$), 62% fulfilled the WHO glucose criteria for diabetes, 15% had impaired glucose tolerance (IGT), and 23% normal glucose tolerance (NGT). Conversely, the $\text{HbA1c} \geq 6.5\%$ criterion was fulfilled in 52% of the 31 patients with diabetes newly diagnosed according to WHO criteria, in 8% of the 51 patients with IGT and in 3% of the patients with NGT. Compared to the standard of WHO criteria, the proposed $\text{HbA1c} \geq 6.5\%$ for the diagnosis of diabetes had a sensitivity of 52% and a positive predictive value of 62% for detecting previously undiagnosed diabetes, whereas specificity and negative predictive value were 96% and 94%, respectively.

The recently recommended HbA1c criterion for the diagnosis of diabetes among PAD patients is highly specific but not sensitive. This might strongly limit its use as a screening tool for identifying individuals with diabetes.

Auch die Bestimmung des Direct-LDL-Cholesterin unter Statinen unterschätzt vermutlich das kardiovaskuläre Risiko

X – 7

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Hintergrund Bei Patienten mit einem Gesamtcholesterin < 150 mg/dl gilt die Bestimmung des (mittels Friedewald-Formel) errechneten LDL-Cholesterins als ungenau, da sie das LDL-Cholesterin unterschätzt, in unserem Haus wird daher in diesem Fall kein errechnetes LDL-Cholesterin bestimmt; als Alternativen bieten sich die Bestimmung

des Apo B sowie des Direct-LDL-Cholesterin an. Apo B gilt wegen der im Vergleich mit errechnetem LDL-Cholesterin besseren Korrelation mit der LDL-Partikelzahl v. a. unter Statintherapie sowie der Erfassung anderer atherogener Lipide als zuverlässigerer Risikomarker, für den auch Zielwerte vorliegen. Die Methoden der Bestimmung des Direct-LDL-Cholesterin sind heterogen, und es liegen keine Zielwerte vor. Bei Patienten mit Triglyzeriden < 200 mg/dl besteht im Allgemeinen eine enge Korrelation zwischen Apo B und LDL-Cholesterin, eigene Erhebungen haben jedoch ergeben, dass die Ratio Direct-LDL-Cholesterin/Apo B trotzdem recht stark streut (Werte zwischen 0,66 und 1,63). Das Ziel der vorliegenden Arbeit ist, zu untersuchen, ob – wie bereits von der Ratio errechnetes LDL-Cholesterin/Apo B bekannt – auch die Ratio Direct-LDL-Cholesterin/Apo B durch die Einnahme von Statinen beeinflusst wird.

Patienten und Methoden In einem Zeitraum von 6 Monaten wurde bei 36 konsekutiven Patienten mit hohem kardiovaskulärem Risiko (LDL-Zielwert < 70 mg/dl) und Triglyzeriden < 200 mg/dl, deren Gesamtcholesterin < 150 mg/dl lag oder die bereits Statine eingenommen haben, nüchtern neben den Triglyzeriden, dem Gesamtcholesterin und dem Non-HDL-Cholesterin auch das Apo B sowie das Direct-LDL-Cholesterin bestimmt (Apo ver.2 bzw. LDL-C plus 2. Generation, jeweils von Roche).

Ergebnis Zwischen Direct-LDL-Cholesterin und Apo B bestand eine enge Korrelation ($r = 0,88$). Patienten, die in den letzten 6 Wochen ein Statin eingenommen hatten, zeigten eine tendenziell geringere Ratio Direct-LDL-Cholesterin/Apo B als Patienten, die in den letzten 6 Wochen kein Statin eingenommen hatten ($1,08 \pm 0,12$ vs. $1,17 \pm 0,25$ [$p = 0,07$]).

Schlussfolgerung Wie bereits von der Ratio errechnetes LDL-Cholesterin/Apo B bekannt, nimmt auch die Ratio Direct-LDL-Cholesterin/Apo B unter der Einnahme von Statinen tendenziell ab, d. h. auch durch die Bestimmung des Direct-LDL-Cholesterins wird in dieser Situation die Atherogenität der LDL-Partikel bzw. das kardiovaskuläre Risiko tendenziell unterschätzt. Für den klinischen Alltag ist daraus abzuleiten, dass v. a. unter Statinen die Bestimmung des Direct-LDL-Cholesterins gegenüber der Bestimmung des errechneten LDL-Cholesterins keinen wesentlichen Vorteil bietet.

Awareness of Cardiovascular Risk Factors, Preventive Action taken and Barriers to Cardiovascular Health: A comparison between Turkish migrants living in Austria and Indigenous Austrians

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Background Cardiovascular disease (CVD) is the leading cause of death for men and women in industrialized countries. The aim of this study was to investigate differences in the awareness of cardiovascular risk factors, preventive action taken and barriers to cardiovascular health between the Turkish minority living in Austria and the indigenous people. All results were analyzed gender-specifically.

Method An anonymous questionnaire was handed out to 349 women and 276 men with no immigration background and compared with 257 female and 250 male Turkish migrants in Turkish language living in Austria. The data gained was analyzed using SPSS.

Results Turkish men were younger ($30 \pm 10,3$ years) than the male cohort ($54,7 \pm 15,3$ years) without an immigration background. Also the Turkish women were on average 6 years younger compared to the Austrian females. The majority of Turkish women (66,4%) were unemployed compared to 35% with a full time job in the Austrian cohort. By contrast, more Turkish men had a full time job compared to the Austrian men asked (85% vs 51%). The Austrian cohort was more likely to be aware of CVD as the leading cause of death (71%) than the Turkish minority (48,5%). Both had a lack of knowledge about CVD risk factors, especially the Diabetes mellitus II (DM II) was only identified by 25% of the Austrians and 22% of the Turkish minority. Two third of the Austrian cohort did do prevention in the last year compared to 25% of Turkish men and 50% of Turkish

women. More than 50% of the Turkish migrants believe that god or a higher power plays a role in the origin of the disease.

Austrian women can identify more risk factors, their main barrier to CVD health is the inability to assess their personal risk correctly, while Turkish women show a lack of knowledge of how to do prevention.

Conclusion There is lack of information about CVD and its risk factors, concerning the Turkish minority to a greater extent. The main barrier for preventive action for the Turkish minority is a low educational and acculturation level, while Austrian women have difficulties in assessing their personal risk correctly. In order to minimize CVD, future preventive programs have to be conceived gender-specific and have to focus on minorities too, as the reasons that anticipate prevention show differences between indigenous Austrians and the Turkish minority.

Clinical and Angiographic Features of Coronary Heart Disease in Menopausal Women

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Aim The aim of this retrospective study was to assess clinical characteristics of coronary artery disease (CAD) in peri- and postmenopausal women in Romania.

Material and Methods We studied women with chest pain and abnormal rest ECGs admitted between January 1, 2007 and December 31, 2010. Patients were divided in 2 groups: perimenopausal women with 49.8 ± 3.5 years of age and postmenopausal women at 59.6 ± 3.2 years of age. Clinical and angiographic data were assessed. A database was constructed, and statistical analysis was performed. Continuous variables were reported as mean $\pm$ SD. Dichotomous variables were reported as percentage with 95 percent confidence interval, comparisons were formed with a Pearson chi-square test. For comparison of continuous data, a 2-tailed Student test was performed when appropriate. A value of $p < 0.05$ was considered significant.

Results In perimenopausal women stable angina was most common in 40%, while in postmenopausal women acute coronary syndromes accounted for up to 50% of first clinical presentations. Cardiac syndrome X was found in 16% of pre- and 12% of postmenopausal women. Coronary angiograms revealed normal coronary arteries in 16% of pre- and 12% of postmenopausal women. Muscle bridges double and triple vessel disease were observed in 12 of pre- and 10% of postmenopausal women. The LAD (left anterior descending artery) was the most commonly affected vessel, both in single and 2-vessel disease (where it was mostly associated with RCA disease). There were statistically significant differences regarding obesity 61% vs. 79% ($p = 0.04$), diabetes mellitus 12% vs 27% ($p = 0.03$). Cholesterol levels, including HDL levels were higher in postmenopausal patients (92% vs 86%, and 97% vs 82%; $p = 0.04$), and a statistically significant difference was found for elevated triglyceride levels (77% in premenopausal and 52% in postmenopausal women; $p = 0.001$).

Conclusions In premenopausal women, stable angina was the most common first clinical manifestation of CAD, while after menopause unstable angina and acute myocardial infarction, with 2- and 3-vessel disease were common primary CAD manifestations. Women after menopause have a significantly increased incidence of cardiovascular risk factors such as: obesity, diabetes mellitus and elevated lipid levels. Primary preventive measures are warranted in Romania.

Alpine Skiing and Endothelial Progenitor Cells: Results of a 12-week Skiing Intervention in Healthy Elderly Skiers

X – 1

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Introduction Numerous studies have shown that modulation of cardiovascular risk factors is associated with significant changes in endothelial biology. Endothelial dysfunction predisposes for cardiovascular events and can be counteracted by exercise training. This is the first randomized study to assess the effects of alpine skiing on endothelial markers and endothelial progenitor cells (EPC) in elderly recreational skiers.

Material and Methods We randomized 25 apparently healthy elderly subjects into a group of 12 weeks of guided alpine skiing (intervention group, IG, $n = 14$; 6 males/8 females; age: 66.6 ± 2.1 years) or a control group (CG, $n = 11$; 3 males/8 females; age: 67.5 ± 5.0 years). EPC as defined as CD3⁺/CD34⁺/CD45⁺/KDR⁺ mononuclear cells were assessed before and after alpine skiing intervention using flow cytometry. Furthermore we measured cardiovascular biomarkers (E-Selectin, ICAM, VCAM, Endothelin-1).

Results Study participants completed 28.4 ± 2.5 skiing days (skiing time: 65.9 ± 7.9 minutes lift and resting time: 121.1 ± 15.9 minutes, break time: 24.0 ± 20.9 minutes per day) at an average heart rate of $72.7 \pm 8.5\%$ of maximum heart rate and maintained an average of 5137 ± 828 meters of altitude per skiing day. Logarithmically transformed EPC counts increased in IG (1.36 ± 0.56 to 1.74 ± 0.36 ; $p = 0.020$) but remained unchanged in CG (2.03 ± 0.54 to 1.89 ± 0.52 ; $p = 0.563$; IG vs CG: 0.023). Subjects that skied longer had higher EPC levels ($r = 0.605$; $p = 0.022$). However, no correlation could be found between altitude exposure and changes in EPC levels ($r = -0.49$; $p = 0.130$). Biomarkers (E-Selectin, ICAM, VCAM, Endothelin-1) for endothelial function and low-grade inflammation were not elevated and similar in IG and CG, and did not change throughout the study.

Conclusion Alpine skiing in the elderly increased endothelial progenitor cells indicating a change in endothelial biology. The beneficial changes were more pronounced in skiers that skied more often.

Effects of a 12-week Skiing Intervention on Glucose Homeostasis and Cardiovascular Biomarkers in Elderly Alpine Skiers

X – 5

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Objective Alpine skiing involves elements of static and dynamic exercise training, and may therefore improve insulin sensitivity and cardiovascular biomarkers.

Material and Methods Healthy elderly men and women who were beginners/intermediate level alpine skiers, were studied before (PRE) and immediately after (POST) 12 weeks of alpine ski training. After additional 8 weeks a third test (retention study, RET) was performed. The subjects were randomized into an intervention (IG, $n = 22$, age = 66.6 ± 0.4 yrs) or a control group (CG, $n = 20$, age = 67.0 ± 1.0 yrs). Plasma glucose decreased ($p < 0.05$) in CG, but increased ($p < 0.05$) again at RET, while a continued decrease was seen in IG (RET vs POST; $p < 0.05$). Plasma insulin decreased ($p < 0.05$) with training in IG, while no effect was seen in CG. HOMA index for insulin resistance decreased ($p < 0.05$) from 0.80 ± 0.08 to 0.71 ± 0.09 in IG. The value at RET (0.57 ± 0.08) tended ($p = 0.067$) to be different from POST. In CG the corresponding values were 0.84 ± 0.09 , 0.81 ± 0.12 and 0.70 ± 0.09 , respectively. Biomarkers for endothelial function and low-grade inflammation were not elevated and similar in IG and CG, and did not change throughout the study.

Conclusions Alpine skiing improves glucose homeostasis and insulin sensitivity in healthy, elderly individuals.

Resistance Training in Patients with Type 2 Diabetes: Effects on Glycemic Control, Endothelial Function, Muscle mass and Strength

X – 2

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Objective To compare the effects of 2 different resistance training protocols in combination with aerobic endurance training (AET) in type 2 diabetes mellitus (T2DM) on body composition, glycemic control, endothelial function, muscle mass and strength.

Research Design and Methods We performed an 8-week randomized controlled training intervention in 32 T2DM patients (age 64.8 ± 7.8 years). Patients were randomly assigned to either AET (cycle ergometer, 70% of heart rate reserve) combined with hypertrophy resistance training (HRT, $n = 16$, 2 sets, 10–12 repetitions, 70% of the one-repetition maximum) or with endurance resistance training (ERT, $n = 16$, 2 sets, 25–30 repetitions, 40% of the one-repetition maximum). Body composition, blood analyses, physical work capacity, endothelial function, as well as muscle mass and strength were measured pre- and post-intervention.

Results At baseline, no statistically significant differences were found between groups with the exception of intra-abdominal mass in ERT ($p < 0.006$) and greater upper arm strength during back pull in HRT ($p < 0.002$). After 8 weeks of intervention, fasting plasma glucose ($p = 0.04$) and fructosamine ($p = 0.002$) improved significantly in the HRT group and there was a trend toward an improvement in ERT ($p = 0.06$ and $p = 0.08$ respectively). Muscle mass showed a significant increase in both groups without significant differences between groups (HRT: $p = 0.003$; ERT: $p = 0.005$, Δ HRT vs Δ ERT: $p = 0.86$). Upper body strength improved in both groups (chest-press: HRT: $p < 0.001$; ERT: $p < 0.001$; back-pull: HRT: $p < 0.001$; ERT: $p < 0.001$), whereas a greater increase was achieved by HRT during chest press (Δ HRT vs Δ ERT: $p = 0.01$). Improvement in physical work capacity, waist circumference, and subcutaneous fatty tissue was comparable in both groups (all $p < 0.05$).

Conclusion Glycemic control and muscle mass improved in both groups by a similar magnitude, whereas gain in upper body strength was superior in HRT. Overall, both resistance training protocols can be judged equally potent and be included into the exercise regime of patients according to their personal preference. This will further individualize exercise programs and may result in a greater sustainability of training effects.

SASES – Salzburg Skiing for Elderly Study: Skiing and Cardiovascular Risk Factors in the Elderly

X – 4

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Introduction Numerous studies have shown that modulation of cardiovascular (CV) risk factors is associated with a reduced risk of myocardial infarction. Despite the fact that exercise training is a potent treatment choice for CV risk factors this is the first randomized study to assess the effects of alpine skiing on CV risk factors in elderly skiers.

Method We randomized 42 subjects into a group of 12 weeks of guided skiing (intervention group, IG, $n = 22$; 12 males/10 females; age: 66.6 ± 2.1 years) or a control group (CG, $n = 20$; 10 males/10 females; age: 67.3 ± 4.4 years). CV risk factors were assessed before and after the intervention period.

Results Subjects averaged 28.5 ± 2.6 days of skiing and 3.5 hours of skiing for each ski day. No CV event occurred within a total of 2168 hours of skiing. A significant increase in exercise capacity in IG (Δ VO₂max: $+2.0$ ml/kg/min; $p = 0.005$) but not in CG (-0.1 ml/kg/min; $p = 0.858$; IG vs CG: $p = 0.008$) as well as a decrease in body fat mass (Δ IG: -2.3% [$p < 0.0001$]; Δ CG: 0.0% [$p = 0.866$]; IG vs CG: $p < 0.0001$) was achieved. Blood pressure, blood lipids, heart rate and everyday physical activity remained essentially unchanged.

Conclusion Alpine skiing in the elderly led to beneficial changes in predictors of cardiovascular risk, since it was associated with an increase in exercise capacity and muscle mass as well as a decrease in fat mass. A thorough sports medical assessment prior to skiing proved effective in identifying patients at risk. For elderly skiers who pass such a comprehensive exam skiing can be seen as safe and can thus be recommended as an ideal form of exercise training.

The Innsbruck and Salzburg Physician Lifestyle Assessment (TISPLA): Physical Fitness Protects Physicians from Workplace Stress

X – 3

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Purpose Workplace stress is a known cardiovascular risk factor, which can be counteracted by a healthy lifestyle and a good physical fitness. Despite the fact that physicians counsel their patients in how to cope with workplace stress, they themselves are increasingly exposed to it.

Table 20: D. Niederseer et al.

	Very good	Good	Average	Not good	Bad	p-value
Gender: male; female (n [%])	17 (65); 9 (35)	56 (53); 50 (47)	92 (51); 89 (49)	45 (63); 26 (37)	9 (75); 3 (25)	0.003
Age (years)	39.1 ± 10.7	37.8 ± 8.3	36.3 ± 7.8	37.2 ± 6.6	43.3 ± 8.0	0.029
Leading position (n [%])	11 (42.3)	37 (34.9)	50 (27.6)	18 (25.3)	10 (83.3)	< 0.001
Health Check up (n in last 5 years)	1.4 ± 1.9	0.9 ± 1.4	0.7 ± 1.1	0.3 ± 0.7	0.9 ± 1.7	0.003
Total papers published (n)	20.4 ± 30.8	14.9 ± 26.7	8.4 ± 18.4	9.1 ± 13.1	19.4 ± 22.4	0.023
Monthly income (€)	2846	2691	2545	2413	3091	0.023
Have you ever had a suicidal idea? True (n [%])	1 (3.9)	7 (6.6)	13 (7.2)	13 (18.3)	4 (33.3)	< 0.001
Sleep disturbances per week	1.0 ± 1.7	1.2 ± 1.5	1.5 ± 1.9	1.8 ± 2.1	2.9 ± 2.3	0.015
Sexual satisfaction (5 very good; 1 bad)	3.5 ± 1.5	3.5 ± 1.3	3.5 ± 1.2	3.1 ± 1.4	2.1 ± 0.9	0.001
Number of days away sick in last year (n)	1.4 ± 1.7	3.2 ± 7.3	3.5 ± 5.2	3.3 ± 4.4	14.7 ± 28.3	< 0.001
I often or always suffer from stress! True (n [%])	7 (26.9)	38 (35.9)	74 (40.9)	37 (52.1)	8 (66.7)	0.004
My job overburdens me! True (n [%])	1 (3.9)	2 (1.9)	12 (6.3)	3 (4.2)	2 (16.7)	0.010
My job impairs my private life! True (n [%])	6 (23.1)	35 (33.0)	62 (34.3)	33 (46.5)	8 (66.7)	0.015

Methods From July to December 2005 we conducted a cross-sectional online survey with 170 items among all physicians working in 2 university clinics in Austria (Innsbruck and Salzburg).

Results Of 1877 physicians contacted, 590 (31.4%) filled out an online questionnaire and 396 (21.1%) were included into final analysis. The sample (37.3 ± 8.1 years, 219 [55.3%] males, 177 [44.7%] females) was stratified into 5 groups according to their perceived fitness status: very good ($n = 26$), good ($n = 106$), average ($n = 181$), not good ($n = 71$) and bad ($n = 12$). Strong correlations could be found for health parameters, stress coping, sexual satisfaction, research activities, work performance and job position of the participating physicians (**Table 20**).

Conclusions In hospitals in Austria good physical fitness of physicians was significantly associated with the ability to cope with workplace stress. Unfortunately, only a minority of physicians in Austria is physically fit enough to withstand the threat of workplace stress.

Randomized Evaluation of the Effects of a Structured Education Program on Blood Pressure (BP) in Essential Hypertensive Patients (Pts) (herz.leben)

X – 6

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Objective Despite improved awareness and excellent therapeutic options hypertension remains one of the most powerful cardio- and cerebrovascular risk factors. A major impact of pts related aspects like life-style and adherence to medical recommendations is acknowledged broadly. In this respect a structured educational program for diabetics has got remarkable merits (DAFNE-trial). For hypertensives this strategy might provide significant benefits as well. A previously evaluated structured curriculum imparted in cooperation by doctors and hypertension nurses was used. Groups of 6–10 pts were instructed on issues of BP self measurement, healthy salt reduced diet, active life style and pharmacologic antihypertensive therapy. In order to determine the isolated effect of participation in the educational program neglecting the possible impact of more intense care this prospective multicenter randomized controlled study was designed (NCT00453037).

Design and Methods Between 2007 and 2010 256 pts in 13 center (9 offices of GPs and 4 outpatient departments) were enrolled into the study. After initial evaluation (T0) and written informed consent all pts were invited to 2 follow-up visits after 6 (T6) and 12 (T12) months. Pts at each center were randomly assigned to 2 groups (G). G-I ($n = 137$) underwent the educational program at T0, G-II ($n = 119$) was designated for participation after T6. Primary endpoint was a suspected difference in office and home BP at T6. At this point of time similar conditions of care for all pts could be assumed, but only G-I had undergone the educational program.

Results Pts characteristics and BP at baseline were comparable (office BP G-I vs G-II $158 \pm 18/88 \pm 11$ and $161 \pm 18/88 \pm 14$ mmHg, ns/ns). At T6 systolic office and home BP was significantly to lower in G-I compared to G-II (office BP $142 \pm 17/81 \pm 11$ vs $150 \pm 24/84 \pm 12$; $p < 0.01$ /ns; home BP $134 \pm 8/80 \pm 8$ vs $142 \pm 16/82 \pm 9$; $p < 0.01$ /n.s.). At T12 all pts had undergone the educational program; at this point of time differences in BP observed at T6 disappeared completely. Patient flow was as follows: At T6/T12 120/88 pts of G-I and 97/88 pts of G-II adhered to the scheduled visits.

Conclusion The results of this multicenter RCT provide significant evidence for benefit by participation in a structured educational program. Positive effects seem to be mediated by achieving higher levels of information and patient empowerment. Therefore, educational strategies should be considered strongly as standard of care for hypertensive pts.

High Prevalence of Impaired Glucose Metabolism in Overweight Patients With Peripheral Arterial Disease

XIX – 3

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Epidemiologic studies show a high prevalence of type 2 diabetes mellitus (T2DM), impaired glucose tolerance (IGT), and of impaired fasting glucose (IFG) in patients with coronary artery disease. However, the prevalence of abnormal glucose metabolism in patients with sonographically proven peripheral arterial disease (PAD) is unclear and is addressed in the present study.

We enrolled 294 overweight and obese patients (223 men, 71 women) who underwent routine duplex sonography for the evaluation of suspected or established PAD and in whom PAD was verified sonographically. Oral glucose tolerance tests were performed in non-diabetic subjects.

From our patients, 119 (40.5%) had a normal glucose tolerance, 31 (10.5%) IGT, and 144 (49.0%) T2DM (previously known in 121 and newly diagnosed in 23 patients). Impaired fasting glucose was diagnosed in 39 patients with normal glucose tolerance and in 12 patients with IGT. Thus, glucose metabolism was normal in only 80 (27.2%) of our PAD patients.

In conclusion, the prevalence of abnormal glucose metabolism is extremely high in overweight PAD patients. Routine screening for abnormal glucose metabolism (including oral glucose tolerance tests) in PAD patients therefore is warranted.

Prevalence of Diabetes and of Impaired Glucose Tolerance in Patients with Atherosclerosis: The Importance of the Involved Arterial Beds

XIX – 2

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We aimed at comparing the prevalence of impaired glucose metabolism between patients with peripheral arterial disease (PAD), patients with coronary artery disease (CAD), and controls.

We enrolled 937 consecutive Caucasian patients undergoing coronary angiography for the evaluation of stable CAD and who did not have a history of PAD. Patients with significant coronary stenoses $\geq 50\%$ were defined as having significant CAD ($n = 500$), and those without such lesions served as controls ($n = 424$). Additionally, we enrolled 447 patients undergoing duplex sonography for the evaluation of suspected or established PAD and in whom PAD was verified sonographically. Oral glucose tolerance tests were performed in non-diabetic subjects.

The prevalence of diabetes was significantly higher in patients with significant CAD than in controls (27.2 vs 17.7%; $p = 0.001$) and was highest (41.8%) in PAD patients, in whom it was significantly higher than both in controls ($p < 0.001$) and in subjects with significant CAD ($p < 0.001$). Similarly, the prevalence rates of impaired glucose tolerance significantly increased from the control group over the group of patients with CAD to the group of patients with PAD (31.4, 41.4 and 54.1%, respectively; $p < 0.001$); it was significantly higher in CAD patients than in controls ($p = 0.002$) and significantly higher in PAD patients than in both controls and CAD subjects ($p < 0.001$ for both analyses).

In conclusion, diabetes and impaired glucose tolerance are highly prevalent in patients with CAD and even more so in patients with PAD. Routine screening for abnormal glucose metabolism including oral glucose tolerance tests is therefore warranted for these patients.

Type 2 Diabetes and the Progression of Visualized Atherosclerosis to Clinical Cardiovascular Events

XIX – 4

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We aimed at prospectively evaluating to what extent pre-existing coronary artery disease (CAD) accounts for the increased long-term vascular event risk of patients with type 2 diabetes (T2DM). We hypothesized that baseline CAD among patients with T2DM may account substantially for their increased cardiovascular risk.

Over 8 years we recorded vascular events in 750 consecutive patients whose baseline CAD state was verified angiographically.

The prevalence rates of CAD (87.8% vs 80.4%; $p = 0.029$) and of significant coronary stenoses $\geq 50\%$ (69.5% vs 58.4%; $p = 0.010$) as well as the extent of CAD, defined as the number of significant coronary stenoses (1.7 ± 1.6 vs 1.4 ± 1.5 ; $p = 0.014$) were higher in patients with T2DM ($n = 164$) than in non-diabetic subjects. During follow-up, T2DM strongly predicted vascular events ($n = 257$) independently from the presence and extent of baseline CAD (hazard ratio [HR] 1.36 [1.03–1.81]; $p = 0.032$); conversely, the presence and extent of baseline CAD predicted vascular events independently from T2DM (HRs 3.29 [1.93–5.64]; $p < 0.001$ and 1.37 [1.23–1.53]; $p < 0.001$, respectively). The overall risk increase conferred by T2DM was driven by the extremely high 53.3% event rate of patients with both T2DM and significant CAD at baseline; individuals with T2DM who did not have significant CAD at baseline showed a significantly lower event rate (22.0%; $p < 0.001$).

We conclude that T2DM and angiographically visualized coronary atherosclerosis are mutually independent predictors of vascular events. The overall risk increase conferred by T2DM is driven by accelerated progression of pre-existing atherosclerosis to clinical cardiovascular events.

Impact of Diabetes Mellitus on Exercise Related Antiangiogenic Endostatin/Collagen XVIII Release: Does Gender Matter?

XIX – 5

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Background Type 2 diabetes mellitus (T2DM) is one of the most important risk factors for cardiovascular diseases in men and women resulting in endothelial dysfunction and subsequent atherosclerosis. However, the cardiovascular risk is higher in diabetic women compared to diabetic men. Endostatin (Endo), a fragment of collagen XVIII, induces inhibition of proliferation and migration of endothelial cells and stimulation of endothelial nitric oxide synthase (e-NOS), and has been shown to contribute to the beneficial vasoprotective effects of physical exercise in young, healthy men. Therefore the aim of the present study was to investigate the impact of gender and diabetes on exercise related Endo/collagen XVIII release.

Study Population and Methods A total of 64 patients, divided into diabetics (11 female; 14 male; mean age 58.5 ± 10.1) and young healthy non-smokers (20 female; 19 male; mean age 23.1 ± 3.9), were investigated during a graded physical stress test. Venous blood samples for deterioration of Endo was measured (ng/ml, by ELISA) at baseline (Sample 1) and at peak work-load (Sample 2) (Figure 44). Furthermore heart rate, BMI and blood pressure were measured.

Results Endo serum levels were similar in the young healthy group in both genders at baseline (female: 89.3 ± 15.32 vs male: 93.4 ± 15.0 ng/ml) and increased to 112.1 ± 26.1 in females and to 114.8 ± 20.7 ng/ml in males at maximum workload. Male diabetics showed markedly elevated baseline Endo levels compared to healthy male controls (108.5 ± 17.4 vs 93.4 ± 15.0 ng/ml) but a blunted Endo increase at peak workload (119.9 ± 15.8 vs 114.8 ± 20.7 ng/ml). However, diabetic females showed statistically significant higher base-

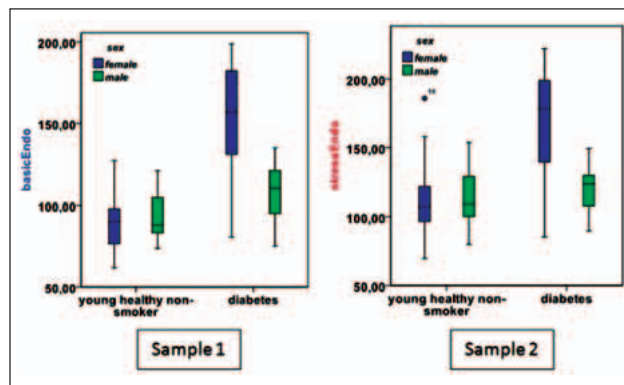


Figure 44: M. Sponder et al.

line Endo levels compared to young females (150.8 ± 41.0 vs 89.3 ± 15.3 ng/ml) as well as to the male diabetics (108.5 ± 17.4 ng/ml) but a blunted increase at peak work load compared to the young female control group (150.8 ± 41.0 to 165.6 ± 48.3 vs 89.3 ± 15.3 to 112.1 ± 26.1 ng/ml).

Conclusion/Discussion We could show for the first time that

- (1) in young healthy controls graded exercise is associated with a significant increase in Endoserum levels comparable in both genders
- (2) male diabetics have statistically higher baseline Endo levels compared to young healthy males however exercise-related Endo increase is blunted compared to the control group
- (3) female diabetics show markedly increased baseline Endo serum levels compared to young healthy females as well as diabetic males, but an albeit blunted exercise related Endo increase, reflecting a markedly decreased platelet-derived Endo production

Thus, altered Endo release may be the missing link to impaired endothelial function, inflammation and advanced progression of atherosclerosis in diabetics. However, in diabetic females platelet-derived Endo release seems to be physiologically markedly up-regulated reflecting a physiological adaptive effect sustaining normal endothelial function in the female vasculature.

Influence of Age, Smoking and Diabetes on Exercise Related Antiangiogenic Endostatin/Collagen XVIII Release in Men

XIX – 6

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Background Smoking and diabetes mellitus II (T2DM) are important cardiovascular risk factors inducing endothelial dysfunction and atherosclerosis. However, men are more affected by cardiovascular diseases before the age of 50 compared to females. Endostatin (Endo), a fragment of collagen XVIII, induces inhibition of proliferation and migration of endothelial cells and stimulation of endothelial nitric oxide synthase (e-NOS), and has been shown to contribute to the beneficial vasoprotective effects of physical exercise in young, healthy men. Therefore the aim of the present study was to investigate the impact of age, smoking and diabetes on exercise related Endo/collagen XVIII release in men.

Study Population and Methods A total of 101 patients, divided into elderly male smokers (> 45 years), elderly non-smokers (> 45 years), young healthy non-smokers (< 45 years) and diabetics (> 45 years) were investigated during a graded physical stress test. Venous blood samples for deterioration of Endo (ng/ml) (by ELISA) were measured at baseline (Sample 1) and at peak work load (Sample 2) (Figure 45). Furthermore heart rate, BMI and blood pressure were measured.

Results Young, healthy male non-smokers showed the lowest Endo baseline levels (90.8 ± 17.0 ng/ml) with a significant exercise-

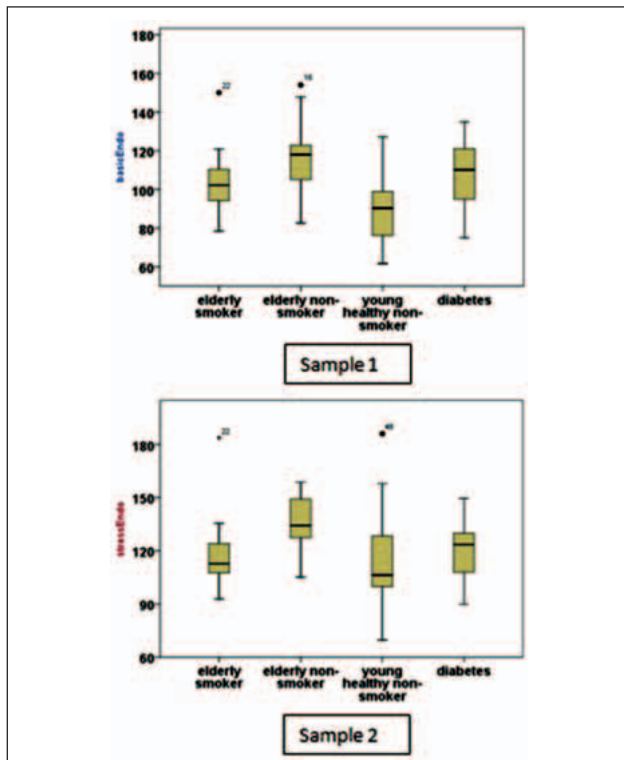


Figure 45: M. Sponder et al.

related Endo increase to 116.4 ± 27.1 ng/ml ($p < 0.001$). Male aging was not only associated with a profound increase in Endo baseline levels (116.6 ± 16.7 ng/ml) but also with significantly higher Endo serum levels at peak work load (136.6 ± 14.8 ng/ml) compared to young, healthy males. However, smoking was associated with lower baseline (103.3 ± 16.4 vs 116.6 ± 16.7 ng/ml; $p = 0.021$) as well as statistically significant lower peak load levels (118.5 ± 20.8 vs 136.6 ± 14.8 ng/ml; $p < 0.001$) compared to elderly non-smokers. Diabetic men however, showed comparable baseline levels to the smoking group (108.5 ± 17.4 ng/ml) and a blunted exercise-related increase compared to elderly non-smokers (119 ± 15.8 vs 116.6 ± 16.7 ng/ml).

Conclusion/Discussion We could show for the first time that:

- (1) male aging is not only associated with a profound increase in baseline but also with higher peak load Endo levels reflecting a physiological adaptive effect sustaining normal endothelial function
 - (2) smoking and T2DM in men are not only associated with lower baseline levels but also with a markedly blunted exercise-related Endo release, reflecting decreased platelet-derived Endo production
- Thus, impaired Endo release may be the missing link to impaired endothelial function, inflammation and advanced progression of atherosclerosis in smoking and diabetes. Hence, further studies are needed to investigate the impact of Endo on the development of atherosclerosis are needed.

Insulin Resistance is Associated with the Metabolic Syndrome But Not With Peripheral Arterial Disease

XIX – 8

A. Vonbank, C. H. Saely, P. Rein, C. Boehnel, V. Jankovic, J. Breuss, S. Greber, H. Drexel
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Insulin resistance (IR) is the key feature of the metabolic syndrome (MetS); its association with peripheral arterial disease (PAD) is unclear. We hypothesised that insulin resistance is associated with both the MetS and sonographically proven PAD.

IR was determined using the HOMA index in 197 patients with sonographically proven PAD as well as in 214 controls who did not have a history of PAD and in whom coronary artery disease was ruled out angiographically; the MetS was defined according to NCEP-ATPIII criteria.

HOMA-IR scores were higher in MetS patients than in subjects without the MetS (5.9 ± 6.2 vs 2.9 ± 3.9 ; $p < 0.001$). However, HOMA IR did not differ significantly between patients with PAD and controls (4.2 ± 5.4 vs 3.3 ± 4.3 ; $p = 0.124$). When both, the presence of the MetS and of PAD was considered, HOMA-IR was significantly higher in patients with the MetS both among those with PAD (6.1 ± 5.7 vs 3.6 ± 5.2 ; $p < 0.001$) and among controls (5.8 ± 6.8 vs 2.3 ± 1.8 ; $p < 0.001$), whereas it did not differ significantly between patients with PAD and controls among patients with the MetS (5.8 ± 6.8 vs 6.1 ± 5.7 ; $p = 0.587$) nor among those without the MetS (2.3 ± 1.8 vs 3.6 ± 5.2 ; $p = 0.165$). Similar results were obtained with the IDF or harmonized consensus definitions of the MetS.

We conclude that IR is significantly associated with the MetS but not with sonographically proven PAD.

Lipid Parameters in Acute Coronary Syndromes Versus Stable Coronary Artery Disease

XIX – 7

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Differences in lipid parameters between patients with acute coronary syndromes (ACS) and patients with stable coronary artery disease (CAD) are unclear and are addressed in the present study.

We enrolled 582 patients with angiographically proven stable CAD, of whom 26.9% had diabetes mellitus type 2 (T2DM) and 182 patients with ACS, of whom 35.8% had T2DM.

When compared to patients with stable CAD, HDL cholesterol (45.8 ± 15.5 mg/dl vs 50.2 ± 16.1 mg/dl; $p < 0.001$) and apolipoprotein A1 (139.0 ± 30.4 mg/dl vs 154.6 ± 31.0 mg/dl; $p < 0.001$) were significantly lower in patients with ACS in the total population as well as among subjects with T2DM. Analysis of covariance confirmed an independent impact of the ACS state on these lipid parameters after multivariate adjustment both in the total population and among subjects with T2DM. In contrast, total cholesterol, LDL cholesterol and apolipoprotein B neither in the total population ($p = 0.583$, $p = 0.884$ and $p = 0.834$ respectively) nor among subjects with T2DM ($p = 0.133$, $p = 0.234$, and $p = 0.371$, respectively) differed significantly between ACS and stable CAD patients. Triglycerides were significantly higher in patients with ACS than in patients with stable CAD in total study population (155.8 ± 121.1 mg/dl vs 140.8 ± 90.6 mg/dl; $p = 0.037$) but not in patients with T2DM ($p = 0.972$).

We conclude that HDL cholesterol and apolipoprotein A1 are lower in the ACS state than with stable CAD; this particularly holds true among patients with T2DM.

Evaluation of a "Vascular Age" Score for the Prediction of Coronary Artery Disease Prevalence and Severity – Analysis of 2265 Elective Patients

X – 8

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Background Although many risk stratification models exist for the incidence of cardiovascular events, little data are available evaluating the association of risk scores with coronary artery disease (CAD) prevalence and/or severity.

Methods 2265 statin-naïve patients without a history of prior myocardial infarction or revascularisation procedures undergoing elective coronary angiography for the invasive evaluation of suspected CAD were analyzed. Coronary risk factors were assessed by questionnaire and by routine laboratory. Coronary angiograms were graded by visual estimation of lumen diameter stenosis ($\geq 70\%$ stenosis) as 1-, 2- or 3- vessel disease (VD), as non-significant CAD

(stenosis < 70%) or as non-CAD (no lumen irregularities). A modification of a “vascular age” score (VAS) developed in the Framingham cohort was analyzed in regard to CAD prevalence and severity.

Results 878 patients had non-CAD and 1387 had any form of CAD (n = 505 non-significant CAD, n = 438 1-VD, n = 232 2-VD, n = 212 3-VD). The latter had a significant higher VAS on univariate analysis (13.5 ± 5.0 vs 10.9 ± 9.2 ; $p < 0.001$). On multivariate analyses, the VAS remained a strong independent predictor of CAD prevalence (per point: OR 1.21 [1.16–1.25], $p < 0.0001$). Additionally, VAS was also independently associated with CAD severity in general. ROC analyses for CAD prevalence revealed an AUC of 0.705 [0.683–0.726] ($p < 0.0001$). The sensitivity and positive predictive value for CAD prevalence of a VAS of > 10 were 83.1% and 70.0% (specificity and negative predictive value: 43.7% and 62.1%).

Conclusion A modification of this vascular age score – initially developed to predict the incidence of cardiovascular events – is also independently associated with CAD prevalence and severity. Therefore it may be a useful and easily applicable tool in the decision making process for or against further testing of patients with suspected CAD.

■ Vitien/Cardiac Defects

Assessment of Disease Severity by Speckle Tracking Echocardiography in Patients with Low Flow-Low Gradient Aortic Stenosis: Results from the Multi-center TOPAS Study XX – 2

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Purpose Patients with severely reduced left ventricular function and aortic stenosis of unknown significance remain a diagnostic and therapeutic challenge. NT-proBNP has been shown to be a strong prognostic marker in these patients. We investigated whether peak systolic global longitudinal 2d-strain (GLS) obtained by speckle tracking could serve as a new echocardiographic modality for evaluation of disease severity in patients with low flow, low gradient aortic stenosis (LFAS).

Methods We consecutively enrolled 46 patients with LFAS, which was defined by aortic valve area (AVA) ≤ 1.2 cm² and indexed AVA ≤ 0.6 cm²/m², LVEF $\leq 40\%$ and mean pressure gradient ≤ 40 mmHg. As a measure of stenosis severity, projected valve area (AVAprj.) from dobutamine stress echocardiography was calculated as described previously. LVEF was assessed using biplane Simpson method. Offline GLS analysis was derived from the apical 4, 2, and long axis views by a blinded observer using commercial software. NT-proBNP was measured at the time of echocardiographic examination in a subset of 36 patients.

Results 39 (85%) male and 7 (15%) female patients, age 73 ± 11 years were examined. LVEF was $28 \pm 6\%$, indexed AVA 0.4 ± 0.1 cm²/m², AVAprj. 0.92 ± 0.15 cm², GLS $-7 \pm 2\%$, and NT-proBNP 7578 ± 8722 pg/ml. Correlation between GLS and NT-proBNP was $r = 0.536$; $p = 0.001$, and between EF and NT-proBNP $r = -0.491$; $p = 0.003$. AVAprj. was inversely related to GLS ($r = -0.386$; $p = 0.008$).

Conclusions GLS is impaired in patients with LFAS and associated to stenosis severity. Moreover, GLS is related to NT-proBNP and therefore may provide a new echocardiographic technique for evaluation of disease severity and risk stratification in patients with LFAS.

First Austrian Experiences with the MitraClip System in Elderly Patients with Significant Mitral Regurgitation, Distinct Impairment of LV-Function and Co-Morbidities BAI

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Introduction Significant valvular heart disease is an increasing challenge for public health with a prevalence up to 13% of the population aged 75 years and older. Mitral regurgitation (MR) is the second most common valvular disease and symptomatic patients should undergo valve surgery. Previous studies showed, that only half of these patients were sent to cardiac surgery because of impaired LV-function, older age or multiple co-morbidities. Recently edge-to-edge repair using the MitraClip system was introduced as an alternative treatment option.

Methods and Results So far, we treated 19 patients, as the first department in Austria, starting in August 2009. Indication for percutaneous catheter-based mitral valve repair with the MitraClip system was significant MR $\geq$ grade 3.

18 patients were refused by cardiac surgeons, 1 had failed surgical mitral repair. 10 patients (53%) presented with functional MR, 4 patients (21%) with degenerative disease and 5 patients (26%) had a mixed pathology. Patients mean age was 70.6 ± 9.8 years and 47.4% were male. A single clip was successfully implanted in 16 patients (84%), whereas 2 patients (11%) received 2 clips. In one patient the clip could not be positioned successfully. Seven patients (37%) had a LVEF $\leq 35\%$ and 7 further patients (37%) of even $\leq 25\%$.

Complications One patient developed cardiac tamponade treated successfully by conservative means. In-hospital and 30 days mortality was 0. ICU mean duration was 2 days and total hospitalisation was median 11 ± 8 days (9.3–33 days). The logistic Euroscore of the overall group was $22.1 \pm 13.7\%$ and increased in the patient group with LVEF $\leq 35\%$ up to $25.6 \pm 13.7\%$. In the very high surgical risk group (LVEF $\leq 35\%$) including multiple co-morbidities the 12 month mortality was 28.7%. The mean device implantation time was 114.7 ± 63 minutes. Mitral regurgitation intensity could be reduced from grade 3.5 ± 0.3 to grade 1.75 ± 1.5 .

In the high risk surgical group (LVEF $\leq 35\%$) one year mortality correlated significantly with high pre- ($p = 0.034$) and postinterventional NTproBNP levels ($p = 0.034$).

Conclusion Mitral valve repair using the MitraClip system was shown to be feasible with high success rate in patients with significant mitral regurgitation. Particularly patients with distinct impaired LV-function in combination with co-morbidities may improve but have to be selected very carefully.

Single Center Experience in TAVI with the CoreValve System in Symptomatic Patients with Advanced Age and Significant Aortic Valve Stenosis XX – 3

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Introduction Aortic valve stenosis (AS) is the most common degenerative valve disease in the elderly and an increasing problem for public health. Symptomatic patients should be treated by valve replacement but Transcatheter Aortic Valve Intervention (TAVI) is an alternative option for patients with symptomatic aortic valve stenosis deemed high risk or unsuitable for surgical valve replacement.

Methods and Results From October 2007 to March 2011, a total of 75 patients (mean 83 ± 5 yrs, 41.3% male) with a logistic Euroscore of $25.3 \pm 14.3\%$ with severe, symptomatic aortic stenosis (mean valve area 0.59 ± 0.14 cm²) underwent TAVI with the third generation 18-Fr. Medtronic CoreValve prosthesis. Preinterventional the mean instantaneous gradient was 97.4 ± 24.8 mmHg and decreased

postprocedural significantly to 22.9 ± 6.9 mmHg ($p = 0.008$). Mean LVEF was $45.8 \pm 7.4\%$ in the overall population. Procedural technical success was achieved in 98.6%. Paravalvular regurgitation was mild in the majority of cases (90.5%). Initially 9.5% of patients had a postprocedural regurgitation > grade 2 which decreased to 5.1% after 1 year. Permanent pacemaker implantation after TAVI procedure was necessary in 24% due to relevant conduction disturbances. Complications included pericardial tamponade in 10.6%, stroke in 6.6% and myocardial infarction in 1.3%.

30 days mortality in the overall study population was 10.7% and was mainly driven by complications related to the first patient's group when we started already in 2007, despite assistance of an experienced proctor.

After changing devices and proceeding (ballon and wires), in cooperation with the company, remarkable improvement in patient outcome could be achieved. This resulted in less 30 day- (8.5%) and 12 month mortality rate (15.6%).

Conclusion TAVI procedure with the CoreValve device in very advanced age and high risk for a surgical approach, was associated with high technical success rate and acceptable complication rates in appropriately selected patients. In none of our patients switch to open heart surgery was necessary, however, careful patient selection is mandatory to maintain good results.

Prädiktion der intraoperativen Implantationsebene mittels 128-Zeilen-Dual-Source-„FLASH“-CT-Angiographie: Sinnvoll zur Planung von Transkatheter Aortic Valve Implantationen (TAVI)?

XX – 4

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Einleitung und Fragestellung Transkatheter Aortenklappenimplantationen (TAVI) erfordern eine präoperative nicht-invasive Evaluierung des Gefäßsystems. Die 128-Dual Source High-Pitch-CT-Angiographie erlaubt neben aorto-iliakaler CTA eine bewegungsartefaktfreie Darstellung der Aortenwurzel (1) und Koronarostien (2), bei geringer Strahlenexposition. Evaluierung der Genauigkeit der präoperativen Bestimmung der intraoperativen Implantationsebene aus 128-DSCT-High-Pitch-CT-Angiographie, sowie Messung der Koronarostienhöhe und effektive Strahlenexposition.

Methoden 25 Patienten (15 männlich, 10 weiblich, mittleres Alter: 78.5 ± 9.8 Jahre) wurden zwischen Jänner 2010 und Jänner 2011 mittels 128-Zeilen-Dual-Source-Aaorto-iliakaler „FLASH“ CT-Angiographie in prospektiver EKG-Synchronisation (high-pitch, 3.4) für eine mögliche TAVI gescannt. Folgende Messwerte wurden erhoben: 1) Die optimale LAO/RAO und CC (kranio-kaudale) Ebene zur Projektion der 3-CSA Ebene (3-coronary sinus alignment plane) aus 128-DSCT 3D-VRT-Rekonstruktionen. Die endgültig intraoperativ verwendete angiographische Ebene (C-Bogeneinstellung) diente als Referenz. Als Toleranzgrenze wurden $\pm 5^\circ$ Abweichung angenommen. 2) LCA- und RCA-Koronarostienhöhe: kraniale Distanz von der Annulusebene: < 8 mm wurde als „kritisch-niedrig“ definiert (= „Risiko“-Overstenting), 8–11 mm als „niedrig- ausreichend“, und > 11 mm als „hoch“. 3) Effektive Strahlendosis der aorto-iliakalen 128-Zeilen-CTA.

Ergebnisse In 14 (56 %) von 25 Patienten wurde eine TAVI tatsächlich durchgeführt. Implantiert wurden 1 Medtronic Core Valve und 13 Edwards-Sapien Valves (Durchmesser 23 mm; $n = 6$ und 26 mm; $n = 8$). Die übrigen 11 (44 %) Patienten wurden entweder konventionell operiert oder konservativ behandelt.

1. In 13 von 14 (93 %) Patienten konnte die mittels CTA gemessene 3-CSA-Ebene intraoperativ als angiographische Implantationsebene verwendet werden. Sowohl LAO-Werte (mittlere Abweichung: 2.64°) als auch CC-Angaben (mittlere Abweichung: 1.34°) stimmten mit der intraoperativ verwendeten Implantationsebene überein.

2. Kein Patient musste aufgrund von einer „kritisch-niedrigen“ Koronarostiumhöhe < 8 mm ausgeschlossen werden. In allen 14 Patienten

mit „niedriger“ und „hoher“ Ostiumhöhe konnte die Prothese erfolgreich implantiert werden. Es wurde kein „Overstenting“ der Koronarostien als Komplikation beobachtet.

3. Die mittlere Strahlenexposition der 128-Zeilen-CTA betrug 4,57 mSv (mittlere CDTIvol: 4,93 mGy, mittlere DLP: 236,5)

Schlussfolgerung Die Definierung der 3-CSA-Alignment-Implantationsebene mittels 128-Slice-Dual Source-CT im Rahmen des TAVI-Screenings aus konventionellen High-Pitch 128-DSCT-Datensätzen ist eine verlässliche Methode zur Prädiktion der intraoperativen angiographischen Implantationsebene (C-Bogen) und könnte die intraoperativ verwendete Kontrastmittelmengende reduzieren.

Structural Valve Degeneration in Bioprosthetic Aortic Valves is Frequent and Strongly Related to Prosthesis-Patient Mismatch

XX – 5

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Background Recent data suggest that structural valve degeneration (SVD) after aortic valve replacement is related to the presence of prosthesis-patient mismatch (PPM).

Methods 260 consecutive patients (mean age 73.6 ± 7.5 years) who underwent bioprosthetic valve replacement for isolated aortic stenosis were prospectively followed by our clinic for valvular heart disease, including yearly echocardiograms. SVD was diagnosed when calcification was present combined with a peak aortic valve velocity of > 3,6 m/s (stenosis-type) or when moderate/severe regurgitation (incompetence-type) was shown. PPM was diagnosed when the indexed prosthetic orifice area was less than ≤ 0.8 cm²/m².

Results Patients were followed for 5.9 ± 2.8 years. SVD was present in 35 (13.5 %) patients and was diagnosed 32.5 ± 33.8 months after surgery. 26 patients (74.3%) had stenosis-type SVD, whereas 9 (25.7%) suffered from incompetence type SVD. The frequency of SVD was similar among patients with PPM (25 patients, 11.9%) compared to patients without mismatch (10 patients, 14.3%, $p = 0.60$). However, 80% of stenosis-type SVD occurred in patients with PPM ($n = 20$, $p = 0.04$). In 9 patients (3.5%) SVD occurred early within 6 months after surgery (6 stenosis-type, 3 incompetence-type). All early stenosis-type SVD patients had PPM, as well as 2 of the 3 patients with incompetence-type SVD.

Conclusions SVD within 6 years after bioprosthetic aortic valve replacement is more common than previously shown. In our series 13.5% of patients were affected. Stenosis-type SVD is more frequent than incompetence-type SVD and strongly related to PPM, particularly in patients who present with early stenosis-type SVD. Therefore, SVD might be preventable to some extent by the use of as large bioprostheses as possible.

Veränderung des N-terminalen pro-B-Typ-natriuretischen Peptids nach kathetergestütztem Aortenklappenersatz (TAVI) in Relation zu klinischen und echokardiographischen Veränderungen

XX – 1

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Hintergrund Für viele Patienten mit symptomatischer hochgradiger Aortenstenose ist das operative Risiko für einen konventionellen chirurgischen Herzklappenersatz zu hoch. Für dieses Kollektiv bietet der kathetergestützte Aortenklappenersatz (TAVI) eine neue therapeutische Option. Wir untersuchten Veränderung des N-terminalen pro-B-Typ-natriuretischen Peptids (NT-proBNP) nach kathetergestütztem Aortenklappenersatz in Relation zu klinischen und echokardiographischen Veränderungen.

Methoden 18 Patienten (6 männlich, 12 weiblich) mit symptomatischer hochgradiger Aortenstenose wurden über einen Zeitraum von 6 Monaten nach TAVI verlaufs kontrolliert. Das mittlere Alter der Patienten betrug $81 \pm 6,8$ Jahre. Der Eingriff erfolgte bei 9 Pati-

enten von transfemoral, und in der anderen Hälfte von transapikal. Beurteilt wurden echokardiographische Parameter, wie maximaler und mittlerer Druckgradient über der Aortenklappe sowie die links-ventrikuläre Ejektionsfraktion (LVEF), und Basislaborwerte unter besonderer Berücksichtigung des NT-proBNP. Zusätzlich wurde der klinische Verlauf dokumentiert. Die Messzeitpunkte lagen vor und ca. 6 Monate nach TAVI.

Resultate Der maximale Druckgradient über der Aortenklappe nahm von $75,3 \text{ mmHg} \pm 18,2$ auf $12,3 \text{ mmHg} \pm 10,5$ ($p = 0,008$), und der mittlere Gradient von $50,2 \text{ mmHg} \pm 13,3$ auf $7,45 \text{ mmHg} \pm 6,6$ ($p = 0,005$) ab. Die LVEF veränderte sich von $49,6\% \pm 13,6$ auf $54,3\% \pm 9,5$ nach 6 Monaten nicht signifikant ($p = 0,363$). Beim NT-proBNP war ein nicht signifikanter Rückgang ($p = 0,20$) von initial Median 2406 ng/L ($987\text{--}30124 \text{ ng/L}$) auf 1621 ng/L ($452\text{--}8064 \text{ ng/L}$) zu verzeichnen. Eine Besserung des klinischen Allgemeinzustandes (AZ) konnte bei 12 Patienten erreicht werden, ein unveränderter AZ bestand bei 4, bei 2 Patienten verschlechterte sich der AZ. Es bestand keine signifikante Korrelation zwischen der Abnahme des Druckgradienten und der Abnahme des NT-proBNP.

Schlussfolgerung Die Mehrheit der Patienten zeigte nach TAVI eine Besserung des AZ. Durch TAVI konnte erwartungsgemäß der Druckgradient über der Aortenklappe signifikant gesenkt werden, die LVEF wurde hingegen nur nicht-signifikant verbessert. Leber- und Nierenfunktionsparameter zeigten keine signifikante Änderung, beim NT-proBNP bestand ein statistisch nicht-signifikanter Trend der Abnahme nach TAVI.

Impact of Tricuspid Regurgitation on Survival in Patients with Chronic Heart Failure. A Long-Term Observational Study XX – 6

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Purpose Tricuspid regurgitation (TR) is common in patients with chronic heart failure (CHF). However, data about the prognostic value of significant TR in CHF patients are sparse.

Methods 575 consecutive patients with CHF were prospectively included. Patients represent an unscreened contemporary cohort of CHF patients treated according to current guidelines in a tertiary heart failure clinic. At study entry detailed clinical and echocardiographic data were collected. The prognostic impact of significant TR was assessed and compared with established risk factors.

Results Patients were followed for 69.18 ± 50.24 months. TR was common in the study population. 10.6% of patients had severe, 24.0% moderate, and 65.4% of patients had no or mild TR. Kaplan Meier analysis showed a considerably increased mortality rate of patients with moderate and severe TR ($p < 0.0001$). However, by multivariable analysis NTpro-BNP ($p = 0.0054$), systolic blood pressure ($p = 0.0012$), heart rate ($p = 0.0152$), age ($p < 0.0001$), serum creatinine, ($p < 0.0001$), serum sodium ($p = 0.0449$) and left ventricular function ($p = 0.0130$), but not TR independently predicted mortality. These independent predictors of mortality were used to define disease severity to analyze the predictive value of TR at different stages of CHF. In patients with mild and moderate CHF, characterized by NT-proBNP concentrations $< 500 \text{ mg/pg}$, serum-creatinine levels $< 1.5 \text{ mg/dl}$, sustained systolic blood-pressure $> 100 \text{ mmHg}$, heart rate $< 90/\text{min}$, severe TR was highly predictive of mortality ($p < 0.0001$ for all, except NTproBNP $p = 0.00175$). In patients with advanced disease, however, significant TR did not add additional information.

Conclusion The prognostic impact of TR strongly depends on the severity of heart failure. Whereas TR excellently predicts excess mortality in mild to moderate CHF, it has no additive value in advanced CHF when compared with established risk factors. Since it is only in mild to moderate CHF that severe TR is associated with adverse outcome it is this group of patients that might benefit from tailored pharmacological or surgical interventions.

Outcome and Risk-Stratification in Asymptomatic Combined Stenotic and Regurgitant Aortic Valve Disease XX – 7

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Background Outcome and criteria for surgery have been defined for isolated aortic stenosis and for isolated aortic regurgitation. We sought to describe the outcome of patients with combined stenotic and regurgitant aortic valve disease.

Methods 71 consecutive asymptomatic patients (21 female, age 52 ± 17 yrs) with at least moderate aortic stenosis in combination with at least moderate aortic regurgitation were included and followed at regular intervals. Patients with other significant valvular lesions were excluded. 35 patients had bicuspid aortic valves, of the remaining 36 patients, all but 5 had moderately to severely calcified valves. There was no rheumatic etiology. Outcome was assessed and event-free survival with events defined as indication for aortic valve replacement based on current practice guidelines or cardiac death was determined.

Results During a median potential follow-up of 33 ± 5 months, 50 patients developed criteria warranting aortic valve replacement. No cardiac deaths were observed before indications for surgery were reached. Event-rate was high with an event-free survival for the entire patient-population of $76 \pm 4\%$, $56 \pm 5\%$, $43 \pm 5\%$ and $28 \pm 5\%$ at 1, 2, 3 and 4 years, respectively. Indications for surgery were symptoms, 33; positive exercise test, 3; rapid hemodynamic progression, 5; aortic aneurysm, 3; aortic dissection, 1; before major noncardiac surgery, 2; endocarditis, 2; and left ventricular dysfunction, 1. There was no perioperative mortality. In patients with combined stenotic and regurgitant aortic valvular disease, event-free survival was significantly worse for patients with severe aortic stenosis as compared to moderate aortic stenosis ($p < 0.001$) but was not different between the groups with severe or moderate aortic regurgitation ($p = 0.805$). Peak aortic-jet velocity (AV-Vel), which accounts for both stenosis and regurgitant severity, was a significant quantitative predictor of outcome with event-free survival rates of $61 \pm 8\%$, $34 \pm 9\%$ and $13 \pm 7\%$ for patients with an AV-Vel $\geq 5 \text{ m/s}$ compared to $86 \pm 5\%$, $70 \pm 7\%$ and $42 \pm 7\%$ for patients with an AV-Vel between 4 and 5 m/s and $94 \pm 4\%$, $86 \pm 6\%$ and $65 \pm 8\%$ for patients with an AV-Vel between 3 and 4 m/s, after 1, 2, and 4 years, respectively ($p < 0.001$).

Conclusion Patients with combined stenotic and regurgitant aortic valve disease have a high event-rate and require close follow-up. Peak aortic jet velocity, is a prognostic marker representing the hemodynamic load of combined aortic valve disease, permitting risk-stratification in these patients.

Delayed Symptom-Reporting in Aortic Stenosis: Importance of Risk Stratification and Impact of a Valve Clinic Program on Timing of Surgery BAI

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Background We sought to assess the impact of a valve clinic based regular follow-up program on timing of surgery for patients with severe aortic stenosis (AS).

Methods The severity of symptom onset and the delay in symptom reporting was assessed in 388 consecutive patients (198 female, age 71 ± 10 yrs) having an indication for aortic valve replacement due to AS based on current practice guidelines. Of these, 100 patients had been regularly followed in our valve clinic (including serial clinical and echocardiographic exams): these patients were instructed to promptly report the onset of symptoms and had developed indications for surgery during follow-up. 288 pts presented with an indication for surgery at first presentation in our valve clinic.

Results AS severity (peak aortic-jet velocity $5.1 \pm 0.6 \text{ m/s}$, aortic valve area $0.6 \pm 0.2 \text{ cm}^2$) and prevalence of cardiovascular risk fac-

tors (hypertension, hypercholesterinemia, diabetes or coronary artery disease) were not significantly different between the 2 groups. The delay of symptom reporting was significantly longer in the group of patients being symptomatic at the first visit (351 ± 471 days) than for patients being regularly followed (88 ± 141 days, $p < 0.001$). Despite being instructed to promptly report symptoms after their onset, only 21 of the 100 patients being regularly followed reported a symptom-onset before their next scheduled exam (delay of symptom onset reporting: 21 ± 26 days), whereas 79 of these 100 patients reported symptoms at the scheduled follow-up visit only (delay of symptom onset reporting: 106 ± 154 days, $p < 0.001$). Severe symptom onset (NYHA or CCS class ≥ 2.5) was observed in 61% of pa-

tients being symptomatic at their first visit and in 33% of patients followed in the valve clinic ($p < 0.001$). A very severe symptom onset (NYHA or CCS ≥ 3) was found in 25% of patients who presented with an indication for surgery and in 9% of patients enrolled in the follow-up program ($p < 0.001$).

Conclusion Delayed symptom reporting is common in patients with aortic stenosis. In patients being regularly followed in a valve clinic program, symptoms are detected at an earlier and less severe stage resulting in an optimized timing of aortic valve surgery. These findings also emphasise on the importance of risk stratification to identify patients benefiting from early elective surgery.

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