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

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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 [10%] 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 (extrasystole [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

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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.
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

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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 the 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.

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

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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 territory. 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 STElevation Myocardial Infarction

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

**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/pdominant 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**

**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, BNP ≤ 0.71 mg/dl) and high (n = 418, 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 (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, re-infarction 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**

**Introduction** Coronary artery vasospasm, or smooth muscle contraction 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 amiodipin. 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, 3-times daily and nitrates p.o. were added (Isosorit-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

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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 acetetylsalicylic 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 diaphragmatic leads. Angiography showed diffuse arteriosclerotic plaques and severe spasms in both coronary arteries. After intra-coronary Nitroglycerin administration spasms resolved and symptoms improved. He received antiplatelet (GPIb/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 years and the patient was on inhalative steroid therapy. Furthermore he suffered from chronic sinusitis and nasal polypos.

Chest pain and dyspnea 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 trypptide 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 Cycloooxygenase 1 are able to cross react with ASS, and inhibit vasodilatatory 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 live 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

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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 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 %438 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 limit is used also the early sensitivities on admission of both assays 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 looses AMI specificity at 0.01 µg/L. However, with the endpoint sensitivity for the early diagnosis of acute myocardial infarctions the 4th cTnT assay generation 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

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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 non-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 75 U in the ADPtest®. Patients with > 47 U in the ASPItest® were classified as clopidogrel low- or non-responders.

Results The platelet reactivity in the ASPItest® ranged from 0–79 U (mean 16 ± 19 U) with 9 low-responders (48 U, 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

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Material und Methode Retrospektive Analyse des MCI-Registern der UK für Notfallmedizin (1991–2008), Patienten nach kardio-pulmonaler 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. Die Mortalität im Vergleich zur niedrigsten Quartile (< 120 mmHg) auf 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 diastolisches 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 Pulsmplitude 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).

D. Roth et al.

Akute Koronarsyndrome bei Migranten: Risikoprofil und angiographische Befunde

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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.


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 2.5 %, eine Dreifach- oder Mehrfachläsion 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 Zentral- 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 Gesamtbevölkerung (Migrantinnen 24 % vs. Österreichinnen 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 Mehrgefäßerkranzung hatten mehr Migranten als Österreichier (43 vs. 30 %), allerdings waren die Unterschiede erster oder überhalb 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).

Konsensus. 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 NSTE-ACS in der Steiermark – Eine Subgruppenanalyse des steirischen ACS-Registers

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13er Internäre Abteilung, Klinikum Wels-Grieskirchen; 2Klinische Abteilung für Kardiologie, Medizinische Universitätsspitzen Graz


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 intervention 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-Beobachtungstudie**

**XI – 5**

R. van Tulder, C. Havel, H. Herkner, W. Schreiber
Universitätsklinik für Notfallmedizin, Medizinische Universität Wien


**Tabelle 4:** R. van Tulder et al.

<table>
<thead>
<tr>
<th>Vorher</th>
<th>Nachher</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>105</td>
</tr>
<tr>
<td>Alter</td>
<td>60 ± 13</td>
</tr>
<tr>
<td>Weiblich</td>
<td>26 (24,8 %)</td>
</tr>
<tr>
<td>Diabetiker</td>
<td>18 (17,1 %)</td>
</tr>
<tr>
<td>Hypertonie</td>
<td>51 (46,4 %)</td>
</tr>
<tr>
<td>Raucher</td>
<td>41 (39,0 %)</td>
</tr>
<tr>
<td>Hyperlipidämie</td>
<td>28 (26,6 %)</td>
</tr>
<tr>
<td>Familienerkrankungen</td>
<td>23 (21,9 %)</td>
</tr>
<tr>
<td>Frühere PCI</td>
<td>8 (7,6 %)</td>
</tr>
<tr>
<td>VVI</td>
<td>42 (40,0 %)</td>
</tr>
<tr>
<td>HWI</td>
<td>28 (26,6 %)</td>
</tr>
<tr>
<td>NAI</td>
<td>11 (10,5 %)</td>
</tr>
<tr>
<td>NAW</td>
<td>61 (58,1 %)</td>
</tr>
<tr>
<td>RTW</td>
<td>10 (9,5 %)</td>
</tr>
<tr>
<td>Ambulant</td>
<td>17 (16,2 %)</td>
</tr>
<tr>
<td>STEMI</td>
<td>70 (66,6 %)</td>
</tr>
</tbody>
</table>

**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-Range (IQR) 25–75 % berechnet. Wir analysierten das Patientendelay mit einem Mann-Whitney-U-Test (Abbildung 2).

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

**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 (NSTE-ACS) on Long-Term Mortality**

**XI – 7**

B. Vogel, S. Farhan, S. Mahne, I. Koanii, R. Jarai, K. Huber
2nd Department of Internal Medicine, Cardiology and Emergency Medicine, Wiener Krankenanstalten, Vienna

**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 NSTE-ACS.
Methods  This data is derived from a registry with 813 consecutive patients admitted to the cardiology department with the diagnosis of non NSTE-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 ± 9.2) than patients without, p = 0.001. The glucose level at admission was higher in patients with STEMI (17.3 vs 8.2; p = 0.034, HR 2.15 95%-CI: 1.0-4.4 and 46.3% vs 23.7%, 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.

<table>
<thead>
<tr>
<th>Table 5: B. Vogel et al.</th>
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<tbody>
<tr>
<td>Sig.</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Female gender</td>
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<td>Pos Trop I</td>
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<tr>
<td>ST-deviation</td>
</tr>
<tr>
<td>Crl &lt; 60</td>
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<tr>
<td>Admission glucose</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
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<tr>
<td>Adipositas</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Invasive treatment</td>
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■ Basic Science

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

Christian Doppler Laboratory for the Diagnosis and Regeneration of Cardiac and Thoracic Diseases, Medical University Vienna

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-1β), 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, atherosclerosis 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, citrata and EDTA plasma). Blood tubes were either centrifuged initially within 20 minutes after venipuncture and kept frozen at -80°C until further testing or were stored at 4°C, at room temperature (RT) or at 37°C for up to 24 hours. Samples were evaluated for IL-1β, IL-6, TNF-α and for selected chemokines such as Interleukin-8, Epithelial neutrophil-activating protein 78 (ENA-78) and Granulocyte chemo tactic peptide-2 (GCP-2) using commercially available Enzyme-linked immunosorbent assay (ELISA) kits.
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$\beta$ and TNF-$\alpha$ were not detectable at baseline but rose up to 1157 pg/ml (IL-1$\beta$; $p < 0.03$) and 488 pg/ml (TNF-$\alpha$; $p < 0.03$).

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 initiation 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

A. Bühner, E. Holzwart, D. von Lewinski, H. Mächler, R. Gasser
Department of Internal Medicine, Medical University Graz

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-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. Ar-
Der Multikinaseinhibitor Sunitinib hat akute Auswirkungen auf die kardiale Kontraktilität

Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin, Medizinische Universität Graz


Methoden Humane endokardiale Trabekel (n = 26) aus dem rechten Vorhof (n = 6) wurden in modifizierter Tyrode im Organbad bei 37 °C, pH 7,4 und 2 mM Ca2+ mit 1 Hz stimuliert. Die entwickelte Kraft (in % der Kraft bei optimaler Vordehnung, Lmax = 100 %), die diastolische Spannung und die Kontraktionskinetik blieben von Sunitinib unbeeinflusst.

Results In our microarray experiments, we find that, in particular, pyruvate dehydrogenase kinase isoform 4 is significantly less expressed under nebulol both during O2 perfusion and simulated ischemia, an effect practically negligible under atenolol. Here, nebulol 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 a trend towards a decrease in pyruvate dehydrogenase kinase-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 nebulol (1,97 ± 0,06; p < 0,05): pyruvate dehydrogenase kinase-expression is decreased during normoxia (trend) and ischemia (significant) in the presence of nebulol.

Conclusion Here, confirmed by real time PCR, the finding that pyruvate dehydrogenase kinase gene expression is down-regulated by nebulol 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 nebulol compared to standard beta-blockers like atenolol. Especially patients with angina may profit from this particular property of nebulol over atenolol.

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

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LBC for Cardiovascular Research, Vienna

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 (IR) 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 express the microinfarct size (IS) and area at risk (AAR). IS and AAR were expressed as percentage of the left ventricle. The remaining hearts were used for analysis of microinfarct size (IS) and area at risk (AAR). We find that, without the influence of micro-RNAs, the developed myocardial infarct size (IS) and area at risk (AAR) is significantly larger in group 2 (group 1: 17.5%; group 2: 32.0%; 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 = 67.9%, n. s.). However, viable myocardium in the ischemic area (AAR-IS) was significantly larger in group 2 (group 1: 102 ± 16%, n. s.; group 2: 85 ± 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 = 67.9%, n. s.). However, viable myocardium in the ischemic area (AAR-IS) was significantly larger in group 2 (group 1: 102 ± 16%; group 2: 85 ± 16%; p < 0.05).

Discussion We were able to establish a standardized, reproducible in vivo IR-model in the rat. In this model, protective effects of different cardioprotective 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 IR injury. Thus, improvement of endothelial protection might be an interesting therapeutic target to gain better outcome in these high-risk patients.

ÖKG-Annual Conference 2011 – Abstracts

J KARDIOL 2011; 18 (5–6) 151
Experimental Acute Type B Aortic Dissection – Different Sites of Primary Entry Tears Cause Different Ways of Propagation

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1Universitätsklinik für Chirurgie, Klinische Abteilung für Herz-Thorax-Chirurgie, Medizinische Universität Wien; 2Universitätsklinik für Herzchirurgie, Innsbruck; 3Herz-Gefäßchirurgie, Inselspital Bern, Schweiz

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 anagrade propagation length of the dissecting membrane was 65 mm. The median retrograde propagation length in primary entry tears at the concavity was 20 mm and was stopped by the left subclavian artery. In aortas with the primary entry tear at the convexity, 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

R. Gasser, A. Bühner, D. von Lewinski
Department of Internal Medicine, Medical University Graz

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 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 are key elements in this context. Leukocyte-derived markers such as myeloperoxidase (MPO) correlates with outcome in ischemic heart disease.

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 is 1.3× up-regulated in nebivolol under hypoxia and 4× under normoxia. MPO is 350× up-regulated in atenolol under hypoxia and 1.5× 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

R. Gasser, E. Holzwart, H. Mächler, A. Bühner, D. von Lewinski
Department of Internal Medicine, Medical University Graz

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 modulators of 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; ± 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 (Oko = well oxygenated, no ischemia, no drug; Nko = experimental ischemia, no drug; Oat = well oxygenated, ischemia, atenolol present; Ntat = experimental ischemia, atenolol present; Oneb = well oxygenated, nebivolol present; Nneb = experimental ischemia, nebivolol present).
Regulation of Gene Expression associated with NOS Inhibition during Experimental Ischemia

S. Gasser, A. Bühner, D. von Lewinski, E. Holzwart, H. Mächler, R. Gasser
Experimental Cardiology, Department of Cardiology, Medical University Graz

Introduction
Methylation of arginine residues in proteins and subsequent proteolysis results in the liberation of free methylarginines, including asymmetric dimethylarginine (ADMA; R-Me2), an inhibitor of nitric oxide synthetase (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 NOS pathways. However, it has been shown by chemical biology and gene deletion techniques that 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 nebivolol 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 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
In the microarray preliminary analyzes we found that DDAH gene expression is significantly down-regulated by nebivolol compared to atenolol in both normoxia and hypoxia, where atenolol is recognized as a beta-blocker. 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.

Conclusion
In the present study we find that the myocadial expression of DDAH is reduced in the presence of nebivolol in both normoxia as well as hypoxia. The decreased measure of DDAH seen under nebivolol but not with atenolol both during normoxia and hypoxia could be a measure for the increased availability of NO brought about by nebivolol 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 nebivolol.

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

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1Division of Cardiology, Department of Medicine II, Medical University Vienna; 2Ludwig Boltzmann Institute for Clinical and Experimental Traumatology/AUVA Research Center Austrian Cluster for Tissue Regeneration; 3Department of Biomolecular Medicine and Pharmacology, Institute of Vascular Biology and Thrombosis Research, Medical University Vienna; 43rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna

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 intra-coronarily 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 micro-vascularization 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 × mm²; p = 0.029), and at the border zone (338 ± 81 vs 185 ± 38 intensity × 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 immunochemistry 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 ± 0.4 vs 5.3 ± 5.2%; p = 0.046). This 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
Results

The number of apoptotic cells in relation to the total number of intimal labeling (TUNEL) was carried out to calculate the percentage of the intimal area (score 0–3), fibrin deposition (0–3), haemorrhagia (0–3) and the in

Comparing the data of the 4 groups, higher apoptosis index was associated with higher neointimal area (r = 0.501; p = 0.022) and neointimal hyperplasia (r = 0.501; p = 0.022) and neointimal hyperplasia, suggesting a direct role of apoptosis-induced releases of different mediators (such as IL-1β) which promote neointimal development after coronary interventions.

Discussion

The next animal was treated with balloon dilation (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 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 right circumflex coronary arteries (LCX) before implantation of bare metal stent (BMS) (group BMS-Inhibitor) or balloon dilation 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.

Inhibition of IL-1β-converterase and caspase-1 inhibitor acetetyl-tyrosinyl-valylalanyl-aspartylchloromer-

The results of a heart of intracoronary delivery group. The next animal was treated with balloon dilation (PTCA).

The next animal was treated with balloon dilation (PTCA).

Inhibition of IL-1β-converterase and caspase-1 Reduces Intimal Apoptosis Paralleled with Inhibition of Inflammation and Neointimal Hyperplasia After Balloon Injury and Stenting of the Porcine Coronary Arteries


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ÖKG-Annual Conference 2011 – Abstracts
Direct Epicardial Shock Wave Therapy for Myocardial Regeneration in Ischemic Heart Disease

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Introduction
Recently shock waves are well known to induce tissue regenerative effects. Transsthoracic 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.

Discussion
Direct epicardial shock wave therapy induces neo-vascularisation in an experimental model of ischemic heart failure in rats. High numbers of circulating endothelial progenitor cells could be detected in the treatment group. 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

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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 ischemic 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 myocardial 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 ischemic 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

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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 remodeling 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 showed higher numbers of circulating endothelial progenitor cells (EPC) in the ischaemic myocardium 72 hours after AMI as compared to controls. Moreover, these rats revealed an improved functional recovery 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).

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. Intravascular 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

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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 remodelling 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 model using the NOGA three-dimensional technology. In a further experiment, myocardial infarction in an experimental AMI rat model and in a porcine model using the NOGA three-dimensional technology. In a further experiment, APOSEC led to higher values of ejection fraction (57.0% vs 40.5%; p < 0.01) and a reduced extent of infarction size (12.6% vs 6.9%; p < 0.02) as determined by MRI. Administration of APOSEC was performed with proteome membrane arrays and at the site of ischaemic injury. In our present experiment we have investigated the effect of soluble factors present in APOSEC was performed with proteome membrane arrays and at the site of ischaemic injury. In our present experiment we have investigated the effect of soluble factors present in APOSEC on ventricular remodelling after AMI.

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 lymphoidized medullary 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).

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

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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 ≥ 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

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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 × 10⁶ 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
Selective Mobilization of Different Endothelial Progenitors in Experimental Closed-Chest Reperfused Myocardial Infarction

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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 CD34+CD90+CD45+ endothelial mature progenitor cells from bone marrow (BM) after ischemic preconditioning. However, no data exist on mobilization of different early endothelial progenitor cells (CD34+ and progenitor cell subtypes (EPS, such as CD34+CD31+) in experimental closed-chest reperfused AMI (most similar to human STEMI with primary percutaneous coronary intervention).

Methods
Under general anesthesia, closed chest reperfused STEMI was induced in 22 domestic pigs by 90-min occlusion of the 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+, CD31+ and CD34+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

Methoden
Isolierte humane atriale Herzmuskel trabekel; 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 μM, 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 Ankoppelsversuche mit stetig abnehmendem Stimulationssignal 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 ± 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 μM und 1 μM 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
Mild Hypothermia Does Not Further Excite Sympathetic Activation after Cardiac Arrest in Pigs

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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-frequent-fraction (HF, 0.07–0.5 Hz) of HRV represented parasympathetic tone, the ratio between low-frequent-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

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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.
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 intracoronary balloon catheter and an intravascular cooling device. 45 μm 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 ± 6% vs. 86 ± 4), but decreased during MH (65 ± 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 ± 1% vs. 16 ± 1, NT: 14 ± 1 vs. 17 ± 1) (Figure 11). Also, LV dp/dtmax was less decreased vs. control in MH (–31 ± 4 %) than in NT (–45 ± 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 ± 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

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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 (PAl)s.

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 ST2 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

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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 ischemic 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-1 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 (TV and IM) injected rats was composed by 5.5% ± 1.1 and 8.9% ± 2.2 of elastic fibres compared to 0.2% ± 0.1 in controls.

Figure 12: G. Werba et al.
and 2.9% ± 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.

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**Bildgebung/Imaging**

**Vitalitätsdiagnostik in hochgradig wandverdünnten Myokardabschnitten mittels kardialer Magnetresonanztomographie**

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**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 Infarktanamnese (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 Auswurffraktion (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 ± 36,7 ml; 223–316 ml), die LVM im Verhältnis dazu nur gering erhöht (194,6 ± 30,6 g; 160–235 g). Die EF betrug im Mittel 25,7 ± 11,0 %; 12–40 %). Bei 4 Patienten fand sich im wandverdünnten akinetischen Bereich eine transmurale Narbe/Fibrose sowohl im GE-IR 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.

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**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**

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**Purpose** In patients with low flow-low gradient aortic stenosis (LFAS) dobutamine stress echocardiography allows discrimination 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) ≤ 1.2cm² (indexed AVA ≤ 0.6cm²/m²), LVEF ≤ 40% and mean pressure gradient ≤ 40 mmHg. All patients underwent N-13 ammonia (perfusion scan...
and 18FDG-PET (metabolism scan) and were thus classified as follows: Normal (N-13 ammonia 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 ± 12years (mean ± SD) were examined. LVEF was 29 ± 11%, AVA-index 0,4 ± 0,1cm²/m². 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 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 viability 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.
Simultane 64-Zeiler-Spiral-CT-Koronarangiographie bei kardialer CT-Untersuchung vor geplanter Katheterablation von Vorhofflimmern – Ergebnisse eines prospektiven Registers

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Einleitung

Fallbericht
Ein 61-jähriger Mann wurde mit einem akuten Koro-narsyndrom stationär aufgenommen. Troponin T war mit 0,26 ng/ml erhöht, die CK lag im Normbereich, das EKG war unauffällig. 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 überaus geringe bis fehlende Vitalität. Oft wird aus diesem Grund von Revaskularisierungsmaßnahmen Abstand genommen. Die klinische Beobachtung pektanginöser Beschwerden trotz der beschriebenen Morphologie gibt Anlass zu der Vermutung, dass auch bei wandverdünnten Myokardvitales Gewebe vorliegen kann.

Diskussion

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

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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 \((20.0 \pm 11.7\% \text{ of left ventricular mass})\) was significantly \((p < 0.001)\) smaller than the AAR assessed by T2-weighted imaging \((35.6 \pm 10.9\% \text{ of left ventricular mass})\) or the APPROACH-score \((27.9 \pm 10.5\% \text{ of left ventricular mass})\) 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?**

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

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

**Ergebnisse** Insgesamt wurden in der 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 (79,0 %). 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 lief 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“).

Um kumulative Strahlendosis zu sparen, wurde bei 17/31 ein strahlenpersparing Algorithmen verwendet („tep and shoot“).

**Diskussion** Wenn die kMSCT technisch gelingt, kann die Charakteristik des Koronarverschlusses mit ausreichender Qualität dargestellt werden. Dies ermöglicht eine bessere Planung der Therapiestrategie 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**

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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 × 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) \((n = 42, \text{ mean age 46.6 ± 20.3 years, 11 female})\). 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 \((4.93 ± 0.59 \text{ vs } 9.16 ± 3.57 \text{ [m/s]}; p < 0.001)\) and DC ascending \((23.07 ± 8.47 \text{ vs } 6.80 ± 4.34 \text{ [10 – 3 × mmHg]; p < 0.001})\). Local ascending aortic PWVQA, however, failed to detect differences between healthy volunteers and CAD patients \((3.48 ± 1.79 \text{ vs } 2.46 ± 3.49 \text{ [m/s]; p = 0.267})\). 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**

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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).

**BAI**
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 (LVM, g) and total infarct size (% of LVM) 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 LVM 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 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 ± 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-
**Refinement of Echocardiographic Criteria for Left Ventricular Non-Compaction**

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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 trabecular 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 prominent 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.

**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 kam 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.


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

**Projekt „CQI Echo“ – Systematisches Qualitätsmanagement im Echolabor**

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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 dieser Basis der 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...
Chirurgie/Surgery

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

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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 BIH 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 Intratrastral Communications

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

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Methods and Results
We analyzed 523 consecutive patients undergoing TEVAR irrespective of the underlying indication, atherosclerotic aneurysms, acute type B dissections, penetrating ulcers/intramural hematoma as a contraindication for surgery in these patients.

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

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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

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Objective
Minimally invasive intracardiac surgery through a lateral mini-thoracotomy 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 dilation >40 mm. Left atrial ablation (RF-Maze) was performed using unipolar radiofrequency for chronic AF.
Hybrid Treatment of Aortic Stenosis and Coronary Artery Disease by Transcatheter Aortic Valve Replacement and Percutaneous Coronary Intervention

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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 peri-operative mortality (30-days). Three patients died during follow up (between 43–84 days post-operative). No coronary or valvular reintervention 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.
Minimally Invasive Double Valve Surgery Can Safely Be Combined with Additional Procedures

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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

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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 rethoracotomy 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

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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 venous 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). Intratrautal 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. Medium sternotomy is only performed in smaller children any longer at our institution.

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

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Resultate 74 Patienten (42 Frauen, 32 Männer, mittleres Alter 74,6 ± 7,6 Jahre) erhielten eine Freedom-SOLO-Prothese in Aortenposition, jeweils 50 % isolierter bzw. kombinierter AKE. Der durchschnittliche „logistic EuroScore“ betrug 11,0 ± 7,6. Die durchschnittliche EKZ bzw. AKZ lag bei 117,4 ± 29,6 bzw. 78,3 ± 22,3 Minuten. Das FU erfolgte durchschnittlich nach 14,3 ± 8,2 Monaten. Der maximale bzw. mittlere Druckgradient betrug früh-postoperativ 19,0 ± 8,8 bzw. 10,9 ± 5,4 mmHg PO und 19,9 ± 12,2 bzw. 11,22 ± 7,8 im FU. Kein Patient verstarb während des Eingriffes. 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 re-operiert werden.
Kardiomyopathie/Cardiomyopathy (CMP)

Seizure-Associated Tako-Tsubo-Cardiomyopathy

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), hypotremia (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

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 = 313) 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.
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.

**Background** Left ventricular non-compaction syndrome is often associated with arrhythmias and neuromuscular disorders (NMD). Cardiac implantable electronic devices (CIED) like anti-bradycardic pacemakers (PM), implantable cardioverter-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%; p < 0.001), 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.

**Diverse/Sundry**

**NT-ProBNP for Detection of Sunitinib-Induced Cardiac Toxicity in Renal Cell Carcinoma**

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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-
Patients and Methods All patients with mRCC assigned for first-line treatment with sunitinib were included for history or evidence of cardiac diseases. Monitoring included assessment of clinical symptoms, electrocardiograms, echocardiograms and biochemically 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

VNT-Institute, Feldkirch

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 ~50 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 dl–1 × h; p = 0.001). Furthermore, eccentric exercise significantly improved triglyceride tolerance (1841 ± 893 vs 1460 ± 650 mg dl–1 × h; p = 0.002) and postprandial leukocyte count (69.4 ± 11.7 vs 67.0 ± 13.0 G L–1 × 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

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


Es zeigte sich eine Abnahme der INR-Werte außerhalb des therapeutischen Bereiches, umso länger die Patienten in Kontrolle waren. Als häufigste Komplikationen sind Hämatome 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. Auffällend war hier, dass die Patienten von Therapeubeinn an nicht zufriedenstellend einzustellen. 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
Frage, ob eine Therapieumstellung auf ein Ersatzpräparat einen Vor teil bringen würde. Hier muss aber auch erwähnt werden, dass zumeist als Ursache eine Incompatibility of Therapiebeginn an vor lag und somit ein Therapieerfolg unter anderen Medikamenten eben so nicht zu erwarten wäre.

Neue Biomarker zur Früherkennung und Risikostratif ika tion kardiovaskulärer Ereignisse – die „Graz Heart Study“ (Comet-Projekt „BioPersMed“) C. Colantonio, G. Steiner, E. Krahiger-Kraainer, S. Pätzold, A. Schmidt, B. Pieske


Erste Ergebnisse In einer Pilotstudie zu Zeitaufwand, Unter suchungsdauer und Compliance wurden seit Ende 2010 19 Proban den eingeschlossen. Die Teilnehmer wiesen mindestens einen klas sischen kardiovaskulären Risikofaktor auf: Arterielle Hypertonie (100 %), Dyslipoproteinämie (93 %), Adipositas (BMI > 25kg/m²: 79 %). 26 % der Patienten hatten ein manifestes Diabetes, 32 % einen HbA1c ≥ 6 %. 58 % der asymptomatischen, subjektiv gesun den 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 groß populationsbasierten Ansatz an subjektiv gesunden Patienten mit erhöhtem kardiovaskulärem Risiko die Bedeutung neuer biophysikaler und biochemischer Biomarker für Risikostratif ika tion und Fradiktion 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 Standard untersuchungsprogramm. Es zeigte sich, dass asymptomatische, bisher als gesund klassifizier te Probanden mit kardiovaskulärem Risiko bereits in erheblichem Umfang erhöhte NTproBNP-Werte und ein pathologisches E/E’ als möglichen Indikator für subklinisches kardiovaskuläres Remodelling aufwiesen. Dieser erste Befund belegt die klinische Relevanz dieses Forschungsprojektes.

Schlussfolgerung

Der Neuigkeitswert der Arbeit besteht darin, besonders diejenigen Werkzeuge und Methoden aufzuziehen 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

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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 zu analysieren, und dabei die maximale Leistungsfähigkeit, die maximale erbrachte Leistung (Pmax) und die maximale Sauerstoffaufnahme auf das Körpergewicht bezogen (VO2max/kg) herangezogen werden. 

Ergebnisse


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

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Zusammenfassung

Considerable improvements in HRQoL were associated with a pronounced increase in HAD anxiety and depression score: Clinically significant decrease of 0.5 or more were found in 45 %–54 %, clinically significant decrease of 1.0 or more in 10%–20% of the patients. The baseline before discharge probable caseness of anxiety disorder (HADS anxiety ≥ 1) 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...
Effect of Drug-eluting Stent and Drug-Eluting Balloon On Endothelium-Dependent and -Independent Vasomotion of the Coronary Arteries

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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 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 vasomotion reaction. Isometric circular wall tension (contractile response) and maximal vasodilatation 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

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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 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.

No surgery was indicated but dabigatran was resumed, dalteparin 5000 IE/bid and 40 µg alprostadil-infusion were started. After 8 months 359 mg/dl, antithrombin 87%, INR 2.5 and D-dimer 20 µg/ml. 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 are strengthened by the case of a male with atrial fibrillation (AF) for 30 years.

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

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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 patients.
Results During the follow-up period of up to 60 months 253 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.

### Table 12: C. Adlbrecht et al.

<table>
<thead>
<tr>
<th>Best-practice hospitals (n = 186)</th>
<th>Other hospitals (n = 220)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.3 (73.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Male (%)</td>
<td>70 (59)</td>
<td>0.031</td>
</tr>
<tr>
<td>History of co-morbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>68 (58)</td>
<td>0.041</td>
</tr>
<tr>
<td>Previous myocardial infarction (%)</td>
<td>50 (40)</td>
<td>0.022</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>70 (68)</td>
<td>0.768</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>37 (43)</td>
<td>0.225</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>27 (33)</td>
<td>0.233</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>12 (15)</td>
<td>0.467</td>
</tr>
<tr>
<td>Chronic obstructive lung disease (%)</td>
<td>20 (18)</td>
<td>0.707</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA II (%)</td>
<td>3 (1)</td>
<td>0.119</td>
</tr>
<tr>
<td>NYHA III (%)</td>
<td>62 (55)</td>
<td></td>
</tr>
<tr>
<td>NYHA IV (%)</td>
<td>36 (44)</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>30 (29)</td>
<td>0.650</td>
</tr>
<tr>
<td>Baseline NT-proBNP (pg/mL)</td>
<td>3433 ± 4655</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>121 ± 18</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>71 ± 11</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>76 ± 16</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine &gt; 2mg/dL (%)</td>
<td>13 (16)</td>
<td>0.480</td>
</tr>
<tr>
<td>In hospital management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure specific medication at discharge</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>ACE-ARB + BB = None (%)</td>
<td>27 (47)</td>
<td></td>
</tr>
<tr>
<td>ACE-ARB + BB = 50% (%)</td>
<td>59 (42)</td>
<td></td>
</tr>
<tr>
<td>ACE-ARB + BB = ≥ 50% (%)</td>
<td>13 (9)</td>
<td></td>
</tr>
<tr>
<td>ACE-ARB + BB = 100% (%)</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Echocardiogram performed (%)</td>
<td>91 (76)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Index days in hospital (days)</td>
<td>15 ± 9</td>
<td>0.022</td>
</tr>
</tbody>
</table>

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

VII – 4

M. Ess, K. Heitmair-Witzorrek, H. Umler, M. Frick, G. Poelzl
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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

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

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 deactivated and activated 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 consumption 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: 4.93 ± 1.14 mmHg x ml/m²; CCM on: 5.21 ± 1.36 mmHg x 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 ± 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 1.02–1.688) 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 (r = 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 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

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Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin III, Medizinische Universität Innsbruck

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 Prevvalence 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/(-GT), Crea/(-GT+), Crea+/-GT-, and Crea+/-GT+ prevalence was, respectively, 32%, 21%, 24%, and 23%. The estimated 5-year event rate in patients with Crea/-GT- was 14%, as compared to 30% with Crea/-GT+ (HR 2.24, 95%-CI: 1.63–3.08; p < 0.0001) and 24% with Crea+/-GT- (HR 2.30, 95%-CI: 1.66–3.26; p < 0.0001). In patients with Crea elevated, additional elevation of GGT (Crea+/GT+) significantly raised the estimated 5-year event rate to 37% (HR 3.14, 95%-CI: 2.3–2.46; 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

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Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin; Universitätsklinik für Frauenheilkunde und Geburtshilfe, Medizinische Universität Graz

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 I 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 LVEF (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**

R. Steinacher, B. Strohmer, J. Eichinger, J. Kraus, M. Pichler, J. Altenberger
Universitätsklinik für Innere Medizin II, Landeskrankenhaus Salzburg

**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 < LLN) for obstruction (46,5% vs 26,7%; Chi-squared 0,01). We measured 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 were identified 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**

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1Universitätsklinik für Innere Medizin II, Landeskrankenhaus Salzburg; 2Universitätsklinik für Innere Medizin III, Kardiologie, Medizinische Universität Innsbruck

**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 condition. 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**

T. Sturnberger, V. Eder, C. Ebner
Kardiologie, Krankenhaus der Elisabethinen Linz

**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 to 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 years 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

2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien


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 Klappenöffnungsfäche < 1 cm², mittlerer Gradient ≥ 50 mmHg, maximale Flussgeschwindigkeit > 4 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 Pat. (39 %) wurden aufgrund eines log. Euroscore > 15 % bzw. STS-Score > 10 % und/oder anderer Kontraindikationen (reduzierter Allgemeinzustand/Pflegebedürftigkeit n = 16, fortgeschrittenes Malignom n = 2) einem chirurgischen Aortenklappenersatz zugeführt. Von diesen wurde eine Patientin für TAVI angemeldet.


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

B. Frey, A. Lassnigg, S. Frantal, H. Mayr
3. Medizinische Abteilung, Landeskrankenhaus St. Pölten

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


Ergebnisse Die Daten werden in 4 Quartilen zu je 1705 Patienten präsentiert. Die relative Risikostufe ist getrennt für Patienten älter als 75 Jahre in den Zeitpunkten 1, 2, 3 und 5 Jahre. Jene Patienten, die das 1 Jahr nach PCI überlebt, haben die nächsten 9
Our results suggest that ExoSeal® is as safe as conventional compression after assessment by echo or computer tomo-graphy.

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 tomo-graphy.

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.

<table>
<thead>
<tr>
<th>Variable</th>
<th>AngioSeal® (n = 90)</th>
<th>ExoSeal® (n = 45)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (m/f)</td>
<td>62 (69 %)/28 (31 %)</td>
<td>31 (69 %)/14 (31 %)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Diagnostical/Interventional</td>
<td>48 (63 %)/42 (47 %)</td>
<td>24 (63 %)/21 (47 %)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Age</td>
<td>69 (IQR 61–75)</td>
<td>69 (IQR 62–77)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Heparin (IE)</td>
<td>4189</td>
<td>4196</td>
<td>n.s.</td>
</tr>
<tr>
<td>Duration of intervention</td>
<td>97 Min</td>
<td>111 Min</td>
<td>n.s.</td>
</tr>
<tr>
<td>CHD-severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-VD</td>
<td>12 (13 %)</td>
<td>9 (20 %)</td>
<td>n.s.</td>
</tr>
<tr>
<td>1-VD</td>
<td>19 (21 %)</td>
<td>10 (22 %)</td>
<td>n.s.</td>
</tr>
<tr>
<td>2-VD</td>
<td>25 (28 %)</td>
<td>15 (33 %)</td>
<td>n.s.</td>
</tr>
<tr>
<td>3-VD</td>
<td>34 (38 %)</td>
<td>11 (25 %)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

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

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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 ± 15.4% vs 58.4 ± 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 ± 3.2% vs 11.1 ± 3.7%; p = 0.021) of the injected area, with no other differences regarding the baseline data. Low unipolar voltage value proved to be a 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?

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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®.
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

**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 µg/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 µg/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**

**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 pseudoaneurysm 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 para-aneurysmal 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-
surgical risk. AS, who would have been left untreated due to their expected high surgical aortic valve replacement. Feasibility of the procedure itself for elderly patients with symptomatic severe AS and high risk for Discussion

(30-day, 1-year, 2-year, and 3-year survival rates were calculated as cumulative survival. Device implantation resulted in a clear-cut clinical improvement accompanied by a significant and sustained reduction of transmural atherosclerosis. Cumulative 30-day, 1-year, 2-year, and 3-year 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 = 110), 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

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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 use transfemoral access. The mortality rate in examined group was 4.5%. Thirty patients (age 51 ± 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 ± 4.6 mm and reference vessel diameter of 3.2 ± 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

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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 were employed (DES or BMS) included 34 patients (median age: 63.0, 73.0% men; 72.7 % STEMI, 9.1% NSTEMI, 18.2% unstable AP). The control group in which conventional stent devices were employed. 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 were employed (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 Vogelzang 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 measurement.

Table 14: N. Preis et al.

<table>
<thead>
<tr>
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<td>2</td>
<td>8.8%</td>
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<td>3</td>
<td>91.2</td>
<td>81.1%</td>
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<tr>
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</table>

* 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)
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

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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 5 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 5 patients (8%). TIMI flow remained unchanged in 13 patients (34%), and even worsened by one grade in 5 patient (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 2 patients, and was unchanged in 2 of these 2 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 (CW) 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

Department of Medicine II, Division of Cardiology, Department of Cardio-Thoracic Surgery, Medical University of Vienna

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 ± 11.6%, the baseline aortic valve area 0.6 ± 0.1 cm², and the mean gradient 59.6 ± 19 mmHg. Baseline NT-proBNP was significantly correlated to the logistic EuroScore (r = 0.43; p = 0.002), and to LVF (r = 0.3; 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**

**JV – 5**


Universitätsklinik für Klinische Pharmakologie; Universitätsklinik für Innere Medizin III, Medizinische Universität Innsbruck

**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 disphosphate + 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 (Cytochrome 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*1/*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**

**JV – 6**


Universitätsklinik für Innere Medizin III, Medizinische Universität Innsbruck

**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.](image-url)
significant CAD, PCI rate was not different between gender (49.2 vs 48.6%; women vs men resp.; p = 0.72), CABB was more often performed in men (10.4 vs 13.4%; p = 0.01). After a mean follow-up of 39 ± 24 months, no difference in the combined endpoint (cardiac death, myocardial infarction, revascularization) 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 revascularization during the next 3 years seems to be similar for both gender.

Predictors of Periprocedural Myocardial Injury During Percutaneous Coronary Intervention

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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

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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 patients with normal (GFR ≥ 60 ml/kg/min) or reduced (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 = 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

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1. Medizinische Abteilung, SMZ-Ost Donauespital, Wien

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 mecha-
nism. Also, to date, all closure devices are painful to the patient and we
examined the pain scores on a standardized pain scale immedi-
ately 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 out-
comes 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 pa-
tients. 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 scale of 10 in 21.1%.

Conclusions Automation of the single plug closure of femoral ar-
tery 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.

Stability of the High On-Treatment Platelet Reacti-
vity-Phenotype in Patients on Clopidogrel over Six

March 2011 – Acts

M. Freynhofer, V. Bruno, I. Brozovic, R. Jarai, S. Farhan, M. Willheim, J. Wojta,
K. Huber

Background Variable response to clopidogrel-therapy is an estab-
lished phenomenon. Previous studies and ongoing trials randomized
patients according to the high on-treatment platelet reactivity
(HTPR)-phenotype based on single measurements to tailored anti-
platelet 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 un-
dergoing coronary stenting were consecutively enrolled. Multiple
electrode aggregometry (MEA) and vasodilator activated phos-
phrotein–phosphorylation (VASP-P) assays were performed at base-
line, 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 pheno-
type 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

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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 differ-
sent symptoms. Thus, our aim was to point out how gender differ-
ences 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 angiogra-
phy (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 undefin-
able (UD). For each pt risk factors were calculated and CAD pretest
probabilities (pp) were determined.

Results Ind for mpfp 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 ex-
ams 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).
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

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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 α1 und SDNN, wo das Minimum erst bei ca. 100 % Soll-Last erreicht wurde (Abbildung 22). Besonders ausgeprägt war diese Dynamik für SDNN, LF, HF, α1 und besonders gering ausgeprägt für α2 und D2. Die Schwankungsbreite der HRV-Werte nahm unter Belastung kontinuierlich ab. Auch in der Nachbelastungsphase fanden sich mit Ausnahme von α1 und α2 noch reduzierte HRV-Werte und eine ver ringerte 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 α1 als vielversprechende HRV-Parameter erweisen. In der Nachbelastungsphase erscheint die Betrachtung von α1 und α2 aufgrund der größeren Schwankungsbreite interessant. Hinweise für eine diagnostische Überlegenheit der als robuster geltenden nicht-linearen Parameter (SD1, ApEn, α1, α2,
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

VXI – 4
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Einleitung

Methodik

Ergebnisse

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

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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 impact of statin therapy on monocyte distribution in stable CAD patients.

**Methods**
94 patients suffering from angiographically proven stable CAD were enrolled. Monocytes were classified as CD14+/CD16− (“classical monocytes”, CM), CD14low/CD16+ (“non-classical monocytes”, NCM), CD14+/CD16+ (“intermediate monocytes”, IM) and CD14low/CD16low (“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 (p = -0.424, p < 0.001), while levels of HbA1c correlated positively with NCM (p = 0.536, 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

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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+/CD16low (“classical monocytes”, CM), CD14low/CD16low (“non-classical monocytes”, NCM), CD14+/CD16+ (“intermediate monocytes”, IM) and CD14low/CD16low (“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 2nd 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 Homocygous Alpha-1 Antitrypsin Deficiency: A Case Report**

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12. Medizinische Abteilung, Krankenanstalt Rudolfstiftung; 2Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin II, Medizinische Universität Wien

**Introduction** Alpha-1-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 infusion 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 homocygous 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 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 AAT 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**

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**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.

**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.

**Abbildung 28:** M. Zweimüller et al.
Methods Data were collected from patients with advanced pre-capillary pulmonary hypertension (DATA Point group I and IV, mean right arterial pressure ≥ 10 mmHg and/or cardiac index ≤ 2.2 L/min x 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

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

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

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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 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 (DATA Point group I and IV, mean right arterial pressure ≥ 10 mmHg and/or cardiac index ≤ 2.2 L/min x 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

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

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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.
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, postoperatively (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 ± 1.6 mL/mmHg, −396.2 ± 334.4 dynes × cm⁻¹ × s⁻²; 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 ± 6.9 mL; p < 0.001), while it did not change immediately postoperatively 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**

Interne 2 Kardiologie/Angiologie/Intensivmedizin, Krankenhaus der Elisabethinen Linz

**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 prostanooids 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 January 2009. Right heart catheterization confirmed the diagnosis of PAH with a mean pulmonary arterial pressure (mPAP) of 29 mm Hg, cardiac index 2.41 l/min/m². MR testing showed an improvement of right ventricular function (RVEF increasing from 42% up to 59%). Treprostinil 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**

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-
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, 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 syncpe 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/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.

Figure 29: R. Steringer-Mascherbauer et al.

Magnetic Resonance Imaging (MRI) Proves Long-Term Efficacy of Treprostinil in a Patient with Pulmonary Arterial Hypertension (PAH) – a Case Report
Interne 2 Kardiologie/Angiologie/Intensivmedizin, Krankenhaus der Elisabethinen Linz

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/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.

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Potential-Guided Catheter Ablation of Idiopathic Fascicular Left Ventricular Tachycardia

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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 axis (n = 3) or right inferior axis (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 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

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Einleitung: Dronedaron (Multaq™) ist ein Mehrkanalblocker, der in Österreich bei nicht-permanenten 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 Einchluss im Schnitt 67 ± 10 Jahre alt waren, wurden untersucht. Von diesen war als Einschlusskriterium lediglich, dass die Patienten zu Beginn der Multaq™-Therapie an NYHA-Stadium 1,6 ± 0,6 (n = 29) litten. Die letztendlich behandelten Patienten zeigten eine signifikant bessere Belastbarkeit gegenüber den nicht behandelten mit NYHA 1,1 ± 0,3. Bereits nach 3 Monaten Einnahme von Multaq™ gaben die 29 verbliebenen Patienten eine signifikant bessere Belastbarkeit gegenüber den entsprechenden Patienten der Kontrollgruppe.


M. Derndorfer et al.

Abbildung 30: M. Derndorfer et al.
Abbildung 31: M. Derndorfer et al.
Abbildung 32: M. Derndorfer et al.
Abbildung 33: M. Derndorfer et al.
Abbildung 34: M. Derndorfer et al.
Abbildung 35: M. Derndorfer et al.

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 Kardiologische Ambulanz und der allgemeinen Kardiologie-Ambulanz. In der laufenden Studie wurden 500 Patienten mit kompletten Datensätzen aufgenommen. Alter 63,1 ± 14,3 (Mittelwert ± Standardabweichung), 72,4 % Männer, 60,4 % mit chronischer Herzinsuffizienz, 32,4 % (n = 162) hatten Vorhofflimmern vor einer tiefen intraoperativen Antikoagulation (CHADS-VASc 0; 14 %; 1: 23, 2: 27, 3: 28, 4: 31, 5: 41, 6: 59, 7: 53, 8: 50, 9: 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 = 15) aller VHF-Patienten hatten im Vergleich zum CHADS-Score nur 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 höheren 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.

**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 plan 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 workflow 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**

iCARDÉA provides quick access to important medical records supporting 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.

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**Significant Reduction of Bleeding Complications after Pulmonary Vein Isolation Using Different Types of Anticoagulant Strategies**

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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. The second 135 P were treated with molecular weight heparin (LMWH) starting with a single application 3 hours after PVI (weight adjusted – 1 mg/kg 2 times daily).

**Results**

In the first group 17 cases of clinical relevant groin hematoma (LMWH) starting with a single application 3 hours after PVI (weight adjusted – 1 mg/kg 2 times daily).

**Conclusion**

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**

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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 reasonable 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-VTs. 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**


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**Einleitung** Als potenziell kuratives Verfahren ist bei Patienten mit symptomatischem, medikamentös therapierefraktären paroxysmalem Vorhofflimmern ohne relevante Komorbiditäten eine Radiofrequenzisolation der Pulmonalvenen (PVI) indiziert (ESC-Guidelines 2010).

Durch die Reduktion bzw. Elimination rhythmusbezogener symptomatischer Vorhofflimmernepisoden 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 Vorhofflimmernepisoden und des subjektiven Gesundheitszustandes 1,5 Jahre (19 ± 3 Monate) nach PVI.


Voller Erfolg, der als Fehlen von Vorhofflimmernepisoden (mit oder ohne antiarrhythmische Therapie) bei deutlich besseren Gesundheitszustand nach der Letztablation (1,3 ± 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 besseren 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 gesteigerte 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 atrialer Arrhythmien (rechtsatriale folake 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.

Schlussfolgerung: Durch Radiofrequenzablation bei paroxysmalem Vorhofflimmern kann bei 86,6 % aller Patienten eine deutliche Besserung des Gesundheitszustandes und Reduktion der Vorhofflimmerepisoden erzielt werden. Völlige Symptomfreiheit ist bei 61,6 % der Patienten nach mehr als 1½ Jahren nach Ablation zu erreichen.

Rehospitalization of Patients with Persistent Atrial Fibrillation after DC Cardioversion – Impact of Statin Treatment

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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

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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.
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first month after ablation.

patients with and without early recurrence of AF (ERAF) within the

after ablation and atrial fibrillation.

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Medtronic, Minneapolis, USA) ermöglicht die Durchführung von

paroxysmale Vorhofflimmern. Als Alternative zum Radio-

Die elektrische Isolation der Pulmonalvenen (PV)

Hintergrund

Beside that 32 MRTs were documented and ablated: 12 perimitral,

 OBJekte in die Abteilung aufgenommen wurden, wurde die Indikation für die Eingriffe in die Abteilung gestellt. Der Eingriff wurde dann aufgebaut und die Indikation zur operativen Behandlung abgeleitet.

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 oxidative 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 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


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


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 Stimulierung 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 Cryoballonkatheter (Freezor Max™, Medtronic) durchgeführt. Als klinischer Erfolg wurde das Fehlen von AF-Rezidiven (ohne oder unter zuvor wirkungslosen Antiarrhythmika) gewertet.

Ergebnisse

Wir abladierten 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 PV, 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-abladiert.

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 jedoch nicht sicher zu verhindern.

Catheterinterventional Redo Procedures After Previous Intraoperative Ablation of Atrial Fibrillation During Cardiac Surgery

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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. Besides that 32 MRTs were documented and ablated: 12 perimital,
Einleitung


Methodik


Resultate


Diskussion


Katheterablation von persistierendem Vorhofflimmern – Langzeiterfolgsrate am KH der Elisabethinen Linz

E. Sigmund, M. Martinek, H. J. Nesser, H. Pürerfellner

Einleitung

Die kurative Katheterablation bei medikamentös-the rapierefraktären chronischen Vorhofflimmern (VHF) gewinnt zunehmend an klinischer Bedeutung und ist bereits in den aktuellen gultigen Guidelines verankert. Bei Patienten mit lang anhaltendem persistierendem VHF stellen die Pulmonalvenen sehr selten das alleini ge Substrat zur Initiierung und Aufrechterhaltung des VHF dar, so dass die Radiofrequenzablation (RFA) mit einer stufenweisen Er weiterung durch zusätzliche linksschirale Linien sowie Ablation komplexer fraktionierter atrialer Potentiale (CFAE) bis zur Regularisierung oder Termination des VHF weitergeführt wird.

Methodik


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 %). Davon 13 (30,9 %) Reablationen wegen VHF-Residiv und 2 Reablationen wegen anderer atrialer Arrhythmien. Bei 5 Pat. (11,9 %) war ein „Missfolg“ zu erheben, von denen 4 einer neuernen Ablationsbehandlung unterzogen wurden, welche bei 75 % erfolgreich verlief. Bei 2 Pat. folgte eine palliative ablate und pace-Therapie. Die sub
Experience after 110 Cases

In 7 P (6%), one pulmonary vein could not be isolated, respectively.

Results

PVI of all pulmonary veins was achieved in 103 P (94%).

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).

CHA<sub>D</sub>S<sub>VASC</sub> und HASBLED-Score bei Patienten mit Vorhofflimmern

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Einführung

In den aktuellen Guidelines der europäischen kardiologischen Gesellschaft wird zur Bestimmung des embolischen und Blutungs-Risikos bei Vorhofflimmern (AF) die Anwendung von CHADS<sub>2</sub>-Vasc- und HASBLED-Score empfohlen, während früher aufgetreten.

Ergebnisse

Von den 100 Patienten waren 47 weiblich. Das Durchschnittsalter betrug 74 ± 12 Jahre. Der durchschnittliche CHADS<sub>2</sub>-Vasc-Score betrug 4,2 ± 2. Einen CHADS<sub>2</sub>-Score von 1 oder 2 wiesen 47 % der Patienten auf, damit wurden sie als „moderate risk“ mit fraglicher Indikation zur oralen Antikoagulation eingestuft. Einen CHADS<sub>2</sub>-Vasc-Score ≥ 2 wiesen 91 % der Patienten auf (Tabelle 19) – entsprechend den Guidelines wäre bei ihnen eine orale Antikoagulation indiziert.

Tabelle 19: C. Stöllberger et al.

| CHADS<sub>DS</sub> Score und CHA<sub>D</sub>S<sub>VASC</sub>-Score von 100 Patienten mit Vorhofflimmern |
|---|---|---|---|---|---|---|---|---|---|---|
| CHA<sub>D</sub>S<sub>VASC</sub> 0 | CHA<sub>D</sub>S<sub>VASC</sub> 1 | CHA<sub>D</sub>S<sub>VASC</sub> 2 | CHA<sub>D</sub>S<sub>VASC</sub> 3 | CHA<sub>D</sub>S<sub>VASC</sub> 4 | CHA<sub>D</sub>S<sub>VASC</sub> 5 | CHA<sub>D</sub>S<sub>VASC</sub> 6 | CHA<sub>D</sub>S<sub>VASC</sub> 7 | CHA<sub>D</sub>S<sub>VASC</sub> 8 | CHA<sub>D</sub>S<sub>VASC</sub> 9 |
| CHADS<sub>DS</sub> 0 | 3 (37,5 %) | 2 (25 %) | 2 (25 %) | 1 (12,5 %) | | | | | |
| CHADS<sub>DS</sub> 1 | 4 (40 %) | 5 (25 %) | 9 (45 %) | 2 (10 %) | | | | | |
| CHADS<sub>DS</sub> 2 | 2 (3,7 %) | 13 (48,2 %) | 10 (37 %) | 3 (11,1 %) | | | | | |
| CHADS<sub>DS</sub> 3 | | 3 (12,5 %) | 9 (37,5 %) | 12 (50 %) | | | | | |
| CHADS<sub>DS</sub> 4 | 1 (7,1 %) | 2 (14,3 %) | 8 (33,3 %) | 3 (21,4 %) | | | | | |
| CHADS<sub>DS</sub> 5 | | | 2 (40 %) | 3 (60 %) | | | | | |
| CHADS<sub>DS</sub> 6 | | | | | | | | | | 2 (100 %)

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 CHADS<sub>DS</sub>-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 % unbe- kannt). 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 antarrhythmischen 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

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Introduction

Remote navigation systems represent a novel method for catheter ablation of atrial fibrillation (AF). The Senseitherapy (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 Senseitherapy 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 transoephaegal 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.
Einleitung
AV-Zeit-Optimierung mit Verkürzung der nominalen
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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. Der AV-Zeit-Verkürzung kommt daher ein hämodynamischer Vorteil zu.

AV-Zeit-Optimierung bei Patienten mit VDD-Schrittmacher

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Risikofaktoren – Stoffwechsel – Lipide I/

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Patienten und Methoden
In einem Zeitraum von 6 Monaten wurde bei 36 konsekutiven Patienten mit hohem kardiovaskulären Risiko (LDL-Zielwert < 70 mg/dl) und Triglyceriden < 200 mg/dl, deren Gesamtcholesterin < 150 mg/dl lag oder die bereits Statine eingenommen haben, nüchtern neben den Triglyceriden, 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 Wo- chen 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 ± 0,12 vs. 1,17 ± 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 Atherosklerose des LDL-Pools der kardiovaskulären Risiko tendenziell unterschätzt. Für den klinischen Alltag ist daraus abzuleiten, dass v. a. unter Statinen die Bestimmung der Direct-LDL-Cholesterins gegenüber der Bestimmung des errechneten LDL-Cholesterins keinen wesentlichen Vorteil bietet.

New and Old Criteria for the Diagnosis of Diabetes Mellitus in Patients with Peripheral Arterial Disease

ViViT-Institute, Feldkirch

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 hba1c ≥ 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 HbA1c ≥ 6.5% (n = 26), 62% fulfilled the WHO glucose criterion for diabetes, 15% had impaired glucose tolerance (IGT), and 23% normal glucose tolerance (NGT). Conversely, the hba1c ≥ 6.5% criterion was fulfilled in 52% of the 31 patients with diabetes neuropathy 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 hba1c ≥ 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

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Hintergrund

Patienten und Methoden
In einem Zeitraum von 6 Monaten wurde bei 36 konsekutiven Patienten mit hohem kardiovaskulären Risiko (LDL-Zielwert < 70 mg/dl) und Triglyceriden < 200 mg/dl, deren Gesamtcholesterin < 150 mg/dl lag oder die bereits Statine eingenommen haben, nüchtern neben den Triglyceriden, 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).

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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 ± 10,3 years) than the male cohort (54,7 ± 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 not take prevention in the last year compared to 25% of Turkish men and 50% of Turkish men.
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 asssessed. A database was constructed, and statistical analysis was performed. Continuous variables were reported as mean ± 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**

D. Niedersser, M. Mayr, J. Cadamuro, W. Patche, F. Dola, E. Müller, J. Niebauer
Sportmedizin, Universitätsklinikum Salzburg

**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 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 ± 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 where 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**

D. Niedersser, F. Dola, Ch. Finch, J. Cadamuro, W. Patche, E. Müller, J. Niebauer
Sportmedizin, Universitätsklinikum Salzburg

**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 where 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

Sportmedizin, Universitätssklinikum Salzburg

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 < 0.005) but not in CG (p = 0.058; IG vs CG: p = 0.008) as well as a decrease in body fat mass (deltaIG: –2.3%; p < 0.001; deltaCG: 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 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

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Sportmedizin, Universitätssklinikum Salzburg

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 day. No CV event occurred within a total of 2168 hours of skiing. A significant increase in exercise capacity in IG (deltaVO2max: +2.0 ml/kg/min; p = 0.005) but not in CG (–0.1 ml/kg/min; p = 0.058; IG vs CG: p = 0.008) as well as a decrease in body fat mass (deltaIG: –2.3%; p < 0.001; deltaCG: 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

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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 council their patients in how to cope with workplace stress, they themselves are increasingly exposed to it.

Table 20: D. Niederseer et al.

<table>
<thead>
<tr>
<th></th>
<th>Very good</th>
<th>Good</th>
<th>Average</th>
<th>Not good</th>
<th>Bad</th>
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<tbody>
<tr>
<td>Gender: male; female (n [%])</td>
<td>17 (65); 9 (35)</td>
<td>56 (53); 50 (47)</td>
<td>92 (51); 89 (49)</td>
<td>45 (63); 26 (37)</td>
<td>9 (75); 3 (25)</td>
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<tr>
<td>Age (years)</td>
<td>39.1 ± 10.7</td>
<td>37.8 ± 8.3</td>
<td>36.3 ± 7.8</td>
<td>37.2 ± 6.6</td>
<td>43.3 ± 8.0</td>
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<tr>
<td>Leading position (n [%])</td>
<td>11 (42.3)</td>
<td>37 (34.9)</td>
<td>50 (27.6)</td>
<td>18 (25.3)</td>
<td>10 (83.3)</td>
</tr>
<tr>
<td>Health Check up (n in last 5 years)</td>
<td>1.4 ± 1.9</td>
<td>0.9 ± 1.4</td>
<td>0.7 ± 1.1</td>
<td>0.3 ± 0.7</td>
<td>0.9 ± 1.7</td>
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<tr>
<td>Total papers published (n)</td>
<td>20.4 ± 30.8</td>
<td>14.9 ± 26.7</td>
<td>8.4 ± 18.4</td>
<td>9.1 ± 13.1</td>
<td>19.4 ± 22.4</td>
</tr>
<tr>
<td>Monthly income (€)</td>
<td>2848</td>
<td>2691</td>
<td>2545</td>
<td>2413</td>
<td>3091</td>
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<tr>
<td>Have you ever had a suicidal idea? True (n [%])</td>
<td>1 (3.9)</td>
<td>7 (6.6)</td>
<td>13 (18.3)</td>
<td>4 (33.3)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Sleep disturbances per week</td>
<td>1.0 ± 1.7</td>
<td>1.2 ± 1.5</td>
<td>1.5 ± 1.9</td>
<td>1.8 ± 2.1</td>
<td>2.9 ± 2.3</td>
</tr>
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<td>Sexual satisfaction (5 very good; 1 bad)</td>
<td>3.5 ± 1.5</td>
<td>3.5 ± 1.3</td>
<td>3.5 ± 1.2</td>
<td>3.1 ± 1.4</td>
<td>2.1 ± 0.9</td>
</tr>
<tr>
<td>Number of days away sick in last year (n)</td>
<td>1.4 ± 1.7</td>
<td>3.2 ± 7.3</td>
<td>3.5 ± 5.2</td>
<td>3.3 ± 4.4</td>
<td>14.7 ± 28.3</td>
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<tr>
<td>I often or always suffer from stress? True (n [%])</td>
<td>7 (26.9)</td>
<td>38 (35.9)</td>
<td>74 (40.9)</td>
<td>37 (62.1)</td>
<td>8 (66.7)</td>
</tr>
<tr>
<td>My job overburdens me! True (n [%])</td>
<td>1 (3.9)</td>
<td>2 (1.9)</td>
<td>12 (6.3)</td>
<td>3 (4.2)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>My job impairs my private life! True (n [%])</td>
<td>6 (23.1)</td>
<td>35 (33.0)</td>
<td>62 (34.3)</td>
<td>33 (46.5)</td>
<td>8 (66.7)</td>
</tr>
</tbody>
</table>
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 pharmalogic 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 centers (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-I) 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 ± 18/88 ± 11 and 161 ± 18/88 ± 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 ± 7/81 ± 11 vs 150 ± 24/84 ± 12; p < 0.01/1ns; home BP 134 ± 8/80 ± 8 vs 142 ± 16/82 ± 9; p < 0.01/1ns.). 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


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


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 ≥ 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

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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 ≥ 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?

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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 ± 15.3 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-

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

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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-
Insulin Resistance is Associated with the Metabolic Syndrome But Not With Peripheral Arterial Disease

VIVIT-Institute, Feldkirch

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

VIVIT-Institute, Feldkirch

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

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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 (≥ 70% stenosis) as 1-, 2- or 3-vessel disease (VD), as non-significant CAD
First Austrian Experiences with the MitraClip System in Elderly Patients with Significant Mitral Regurgitation, Distinct Impairment of LV-Function and Co-Morbidities


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 ≥ 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 ≤ 35% and 7 further patients (37%) of even ≤ 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 ± 13.7% and increased in the patient group with LVEF ≤ 35% up to 25.6 ± 13.7%. In the very high surgical risk group (LVEF ≤ 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 1.75 ± 1.5.

In the high risk surgical group (LVEF ≤ 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


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 ± 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 ± 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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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 n = 7). Der Patienten betrug 81 ± 6,8 Jahre. Der Eingriff erfolgte bei 9 Pati-
enten von transferosal, und in der anderen Hälfte von transapikal. Beurteilt wurden echokardiographische Parameter, wie maximaler und mittlerer Druckgradient über der Aortenklappe sowie die linksventrikuläre Ejektionsfraktion (LVEF), und Basalabnormalen 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 mmHg ± 18,2 auf 12,3 mmHg ± 10,5 (p = 0,008), und der mittlere Gradient von 50,2 mmHg ± 13,3 auf 7,45 mmHg ± 6,6 (p = 0,005) ab. Die LVEF veränderte sich von 49,6% ± 13,6 auf 54,3% ± 9,5. 5/6 Monaten nach NT-proBNP war ein nicht signifikanter Rückgang (p = 0,20) von initial Median 2406 ng/L (987–3012 ng/L) auf 1621 ng/L (452–806 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**

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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 NT-proBNP (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 mg/pg, serum creatinine levels < 1.5 mg/dl, sustained systolic blood-pressure > 100 mmHg, heart rate < 90/min, severe TR was highly predictive of mortality (p < 0.0001). However, NT-proBNP was not predictive (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 unclear in which setting moderate 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**

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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 ± 4%, 56 ± 5%, 43 ± 5% and 28 ± 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 ± 8%, 34 ± 9% and 13 ± 7% for patients with an AV-Vel ≥ 5 m/s compared to 86 ± 5%, 70 ± 7% and 42 ± 7% for patients with an AV-Vel between 4 and 5 m/s and 94 ± 4%, 86 ± 6% and 65 ± 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**

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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 ± 0.6 m/s, aortic valve area 0.6 ± 0.2 cm²) 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 ≥ 2.5) was observed in 61% of patients 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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