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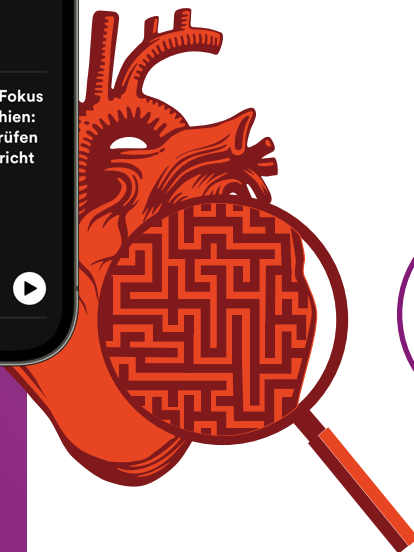


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Cardiology 2002

September 26–28, Vienna, Austria: Abstracts

Poster Presentation I: Neuro-Hormones

Prognostic Value of Brain Natriuretic Peptide in Patients With Complex Congenital Heart Disease

H. M. Gabriel, N. Jordanova, R. Rosenhek, M. Zehetgruber, J. Bergler, K. Huber, G. Maurer, H. Baumgartner

Department of Cardiology, University of Vienna, Austria

Background Serum brain natriuretic peptide (BNP) has been reported to indicate ventricular dysfunction and to be an independent predictor of outcome in patients with cardiomyopathy and primary pulmonary hypertension. However, its prognostic value in patients with congenital heart disease (CHD) has not been studied yet.

Methods To evaluate its prognostic value, BNP was measured in 72 pts. (36 female, mean age 34 ± 12 years) with complex CHD, who were followed for 17 ± 8 months. The relation of BNP levels to NYHA functional class and ventricular function (VF) at entry as well as to the occurrence of events during follow-up (FU) in terms of death, transplantation or congestive heart failure requiring hospital admission (CHF) was analysed.

Results In 36 pts. with pulmonary hypertension (PHT), consisting of Eisenmenger pts. and other pts. with complex CHD and significant pulmonary vascular disease, 12 events occurred during FU (deaths 7, transplantation 2, CHF 3). BNP was significantly higher in pts. with events as compared to those without events (338 ± 254 vs 61 ± 133 pg/ml; $p < 0.0001$). Pts. with events were on average also in a higher NYHA class (3.0 ± 0.5 vs 1.9 ± 0.6 ; $p < 0.0001$) and presented more frequently with abnormal ventricular function ($p < 0.005$). BNP was significantly higher in pts. with abnormal as compared to those with normal VF in this group (335 ± 270 vs 51 ± 92 pg/ml; $p < 0.0001$). Of 12 pts. with BNP > 150 pg/ml (group A; BNP 325 ± 162 pg/ml) 10 had an event during FU (83 %) whereas only 2 of 24 pts. with BNP ≤ 150 (group B, BNP 31 ± 34 pg/ml) had an event (17 %). All pts. except 1 (sudden death) with events in group A developed CHF and 6 eventually died, one underwent lung transplantation. Events in group B were sudden death (1) and heart lung transplantation (1). Only one pt. in group A remained stable whereas 22 of 24 pts. in group B remained stable during FU. In 36 pts. with complex CHD but without significant PHT, no event occurred during FU. Nevertheless, 9 of them had BNP levels > 150 pg/ml (325 ± 162 pg/ml). In contrast to the pts. with PHT, in this group of pts. without PHT, BNP levels did not significantly differ between pts. with normal and those with abnormal VF (96 ± 138 vs. 128 ± 193 ; NS).

Conclusion Serum BNP level appears to be an important predictor of outcome in pts. with complex congenital heart disease who have pulmonary hypertension. In this group, pts. with BNP > 150 pg/ml require close follow-up and intensive treatment. They may require transplantation within a short time period.

Elevated Neurohormones in Patients With Symptomatic Aortic Stenosis

J. Bergler-Klein, U. Klaar, T. Binder, B. Richter, R. Rosenhek, G. Maurer, H. Baumgartner, R. Pacher

Department of Cardiology, University of Vienna, Austria

Background Chronic heart failure is associated with high levels of neurohormones known to imply poor prognosis. Severe aortic

stenosis leads to increased myocardial strain, hypertrophy and dysfunction. The B-type natriuretic peptide (BNP) is known to be stimulated by ventricular strain, but little is known about the neurohormone pattern including the atrial and ventricular prohormones and big-endothelin(-ET) in aortic valve stenosis. In severe aortic stenosis, surgery is usually performed when patients develop clinical symptoms. However, symptoms may be difficult to assess objectively and persistent myocardial damage may result if surgery is delayed too long. Therefore, additional non-invasive parameters for early detection of deteriorating myocardial function are desirable in monitoring these patients.

Methods 33 consecutive pts (age 69 ± 11 yrs) with symptomatic aortic stenosis documented by echocardiography and admitted for preoperative coronary angiography were included in this neurohormonal pilot study. Serum BNP, Nt pro-BNP, Nt pro-ANP and big-ET were determined according to standardised methods. Pts with renal insufficiency were excluded from the study.

Results Left ventricular function in echocardiography was normal in 28 pts, borderline in 3 pts, reduced in 2 pts (ejection fraction 37 % and 25 %, respectively). The aortic mean gradient was 62 ± 20 mmHg, peak gradient 102 ± 33 mmHg, and aortic valve area 0.64 ± 0.17 cm². A significant correlation between pro-ANP (mean 5548 ± 3602 , range 1789–11,066 fmol/ml) and mean aortic gradient was observed ($r = 0.47$; $p < 0.01$) (Fig. 1). BNP (mean 255 ± 346 , range 9–1300 pg/ml) showed trends to correlate with aortic valve area ($r = -0.34$, $p = 0.06$), mean aortic gradient ($r = 0.26$, $p = \text{n.s.}$), and left ventricular hypertrophy (mean 15 ± 2 mm; $r = 0.29$), but did not reach statistical significance, as well as pro-BNP (mean 357 ± 213 , range 77–810 fmol/ml; mean gradient, $r = 0.25$). Big-ET (mean 1.8 ± 1.2 , range 0.1–4.6 fmol/ml) showed no correlation to the gradients.

Conclusion Serum neurohormones (natriuretic peptides) but not big-ET are markedly elevated in a high percentage of pts with symptomatic aortic stenosis. Neurohormones may have importance for timing of surgery and preoperative risk stratification in aortic stenosis.

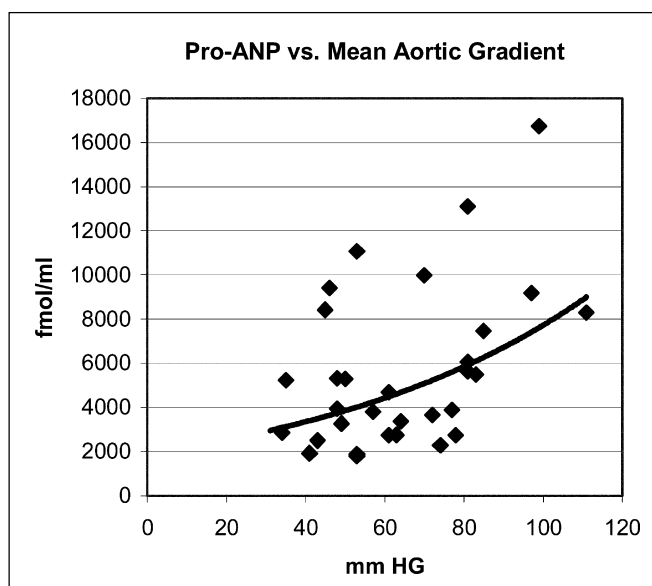


Figure 1: J. Bergler-Klein et al.

ANP But Not BNP Reflects Early Left Diastolic Dysfunction in Type 1 Diabetics With Myocardial Dysinnervation

M. Bayerle-Eder¹, M. Zangeneh², G. Kreiner², H. Vierhapper¹, W. Waldhaeusl¹, H. Pleiner³, S. Gasic¹

¹Department of Internal Medicine III, Division of Endocrinology and Metabolism, ²Department of Cardiology, ³Department of Clinical Pharmacology, University of Vienna, Austria

Abstract We investigated if plasma concentrations of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) reflect impaired diastolic relaxation or its improvement after ACE inhibition in diabetes mellitus type 1 (DM T1).

Methods 7 long-term DM T1 with echocardiographically assessed normal systolic but impaired diastolic function and with sympathetic myocardial dysinnervation and 10 gender- and age-matched controls (C) were included. Exercise tolerance and maximal O₂ uptake were evaluated by bicycle exercise prior to the study. ANP, BNP and norepinephrine/epinephrine (NE/E) were determined at baseline, at 80 % VO₂max workload and after recovery, before and following 12 weeks of treatment with Fosinopril (F, 10 mg/d).

Results Isovolumetric relaxation time (IVRT) and A/E wave ratio were increased by 26.7 ± 11.5 % and 54.4 ± 26.1 % in diabetic patients as compared to C, respectively (p < 0.02). After 12 weeks of F treatment no differences in IVRT or A/E wave ratio were detectable between groups. ANP was enhanced in DM T1 as compared to C (baseline: 9.2 ± 3.06 vs. 4.5 ± 1.1; exercise: 22.4 ± 7.7 vs. 7.9 ± 1.2; recovery: 20.3 ± 4.6 vs. 9.5 ± 2.0 fmol/ml, p < 0.02). F treatment abolished any differences between groups. BNP plasma levels did not differ between groups and no exercise dependent changes were observed. NE- and E-increase was greater at 80 % VO₂max workload in DM T1 than in C (p < 0.05). Again, F abolished differences between groups. Blood pressure response to exercise was not different between groups before or after treatment respectively.

Conclusion In DM T1 impaired diastolic function is associated with elevated ANP and catecholamine plasma levels which are normalised after ACE inhibition. Thus, ANP but not BNP appears to be a sensitive biochemical marker for early diastolic dysfunction in DM T1.

Chronic Suppression of B-Type Natriuretic Peptide Plasma Concentrations by Darusentan

B. Stanek, J. Bergler-Klein, R. Berger, A. Bojic, R. Pacher
Department of Cardiology, University of Vienna, Austria

Background The normal heart senses its pressure and volume load and modifies it via the release of natriuretic hormones into the circulation. In heart failure B-type natriuretic peptide (BNP) plasma levels are sensitive markers of ventricular impairment and have prognostic value [1, 2]. As BNP plasma levels reflect also drug-induced changes in cardiac filling pressures, it can be used to monitor treatment effects.

Methods and Results We determined the effect of darusentan, a specific endothelin receptor A (ETA) antagonist, on repetitive BNP (by RIA), N-terminal atrial natriuretic peptide (N-ANP, by ELISA) and big endothelin (by RIA) plasma levels in 26 patients with NYHA class III heart failure and left ventricular ejection fraction ≤ 35 % as part of the multicenter study ET 004. Patients received 30 mg/d, 100 mg/d, or 300 mg/d darusentan or placebo as randomised in the original trial. After 3 weeks, darusentan (average dose 144 mg/d) resulted in a 30 % increase in cardiac index (p < 0.0001) and a 30 % decrease in BNP plasma levels (from average 90 fmol/ml to 63 fmol/ml p < 0.01) in 19 patients. Placebo had no effect in 7 patients. Plasma N-ANP levels only tended to decrease after darusentan confirming the superiority of BNP as a marker of left ventricular

dysfunction. Like after ETA/B blockade with bosentan, the levels of big endothelin remained unchanged.

Conclusion The chronic suppression of BNP production in the failing heart most likely results from sustained favorable reduction in ventricular pressure and volume load secondary to (extracardiac) ETA receptor blockade. As endothelin stimulates BNP gene expression *in vitro*, cardiac ETA receptor blockade might add to darusentan's effects.

1. Stanek B, Frey B, Hülsmann M, et al. Prognostic evaluation of neurohumoral plasma levels before and during β-blocker therapy in advanced left ventricular dysfunction. *J Am Coll Cardiol* 2001; 38: 436–42.
2. Berger R, Hülsmann M, Strecker K, Bojic A, Stanek B, Pacher R. B-type natriuretic peptide predicts sudden death in patients with chronic heart failure. *Circulation* 2002; 105: 2392–7.

Prediction of 2 Year Survival and Composite Endpoints Using the TIMI-7 Risk Score Extended by N-terminal Pro-Brain Natriuretic Peptide Levels

Rudolf Jarai¹, Robert Jarai¹, Ferenc Jarai¹, N. Iordanova¹, W. Speidl¹, W. Woloszczuk², G. Geyer², J. Wojta¹, K. Huber¹

¹Department of Cardiology, University of Vienna, ²Ludwig-Boltzmann Institute for Experimental Endocrinology, Vienna, Austria

Background The TIMI-7 Risk Score is a useful risk stratification tool for identifying patients with unstable angina at high risk of death, myocardial infarction or future revascularization procedures. The Brain Natriuretic Peptide (BNP) and the N-terminal fragment of it's prohormone (N-terminal Brain Natriuretic Peptide, NBNP) are strong, independent predictors of death in patients with congestive heart failure, after acute myocardial infarction and even after unstable coronary disease. However, there exists at present no scoring system for the assessment of patient's risk that combines clinical risk scores with one of these natriuretic peptides. Therefore, we investigated the importance of the determination of the NBNP levels in patients with unstable angina in combination with the TIMI-7 Risk Score.

Patients and Methods Plasma levels of the NBNP were determined in 145 consecutive patients (unstable angina and non-ST-elevation myocardial infarction; UA/NSTEMI) admitted to our clinic (Nt-proBNP ELISA, Biomedica, Austria), and were divided into three risk groups according to their TIMI-7 score: high risk (6–7), medium risk (4–5) and low risk (1–3). With assistance of the data mining technique, decision tree (AnswerTree, SPSS Inc., USA), we extended these TIMI Risk groups with the patients NBNP levels. The so developed combined scoring system consists of 4 groups: very high (NBNP > 0.6 nmol/l), high (TIMI high risk group or TIMI medium risk group and NBNP > 0.33 nmol/l), medium (TIMI medium or TIMI low risk group and NBNP > 0.33 nmol/l) and low (TIMI low risk group).

Results The relative risk of death in the TIMI high, medium and low risk groups was 30 %, 10 % and 2 %, respectively (p < 0.001, for trend). If the NBNP level was higher than 0.33 nmol/l (75 percentile) the relative risk of the TIMI groups increased to 44 % in the high, to 31 % in the medium and to 10 % in the low risk group. If the NBNP level was below this cut-off level, the relative risk of death was 24 %, 4 % and < 1 % in the respective TIMI groups. The relative risk of death in the combined TIMI-NBNP groups was 47 %, 20 %, 4 %, and 1 %, respectively (p < 0.0005, for trend). The receiver operating characteristic (ROC) curve analysis for survival was performed to test and to compare the predictive accuracy of the respective scoring systems. The area under the ROC-curve was 0.77 for the TIMI score and 0.87 for the TIMI-NBNP score, and for the composite endpoint (death and recurrent myocardial infarction) 0.7 and 0.79, respectively.

Conclusion Although the cohort of patients is relative small, we could demonstrate the importance of additional measurement of NBNP levels for risk stratification in patients with UA/NSTEMI.

Poster Presentation II: Congenital and Valvular Heart Disease

Wall Thickness in Ascending Aortic Aneurysms

C. Baytaroglu, D. Bondermann, Ch. Adlbrecht, M. Lang, J. Jakowitsch, M. Grabenwoeger, B. Pikula, I. M. Lang

Department of Cardiology, University of Vienna, Austria

Background Ascending aortic aneurysms are frequent and life-threatening cardiovascular disorders. However, little is known about the vascular remodelling occurring within aneurysmatic, non-dissected segments of the aortic wall.

Patients and Methods We studied 24 patients with ascending aortic aneurysms undergoing aortic root replacement and 20 control subjects undergoing cardiac surgery for other cause, or autopsy (**Table 1**). Aortic diameter was assessed by preoperative multi-detector computed tomography and/or *in situ* measurements. Aortic wall thickness was measured with a caliper.

Results Mean wall thickness was significantly increased in patients, and was correlated with aortic diameter at the sinu-tubular junction ($p = 0.0041$). Gross histologic analysis showed that thickened wall segments were not affected by intramural haematoma.

Conclusions Our data contradict the current concept that the aortic wall is thinned in aneurysmatic wall segments. On the average, aortic wall is thickened in patients with aneurysmatic dilatation of the ascending aorta. Further experiments will shed light on the mechanisms underlying this type of vascular remodelling.

Table 1: C. Baytaroglu et al. Patient characteristics

	Age (years)	Sex	BMI	Wall thickness* (mm)	Aortic diameter (mm)
Patients	56 ± 17	10 f/14 m	24 ± 3	2.84 ± 0.8	63.5 ± 8.8
Controls	58 ± 16	7 f/13 m	28 ± 5	1.99 ± 0.2	29.1 ± 3.0

* $p < 0.0001$

How Flow Contraction, Pressure Recovery, and Viscous Resistance Affect Doppler Measurements Across Tunnel Obstructions – An *In-Vitro* Study

R. Rosenhek, J. Mascherbauer, L. Huber, H. Schima, G. Maurer, H. Baumgartner
Department of Cardiology, University of Vienna, Austria

Background We have previously shown that Doppler measurements may not only underestimate pressure gradients across tunnel obstructions as reported by others but may also markedly overestimate them. This phenomenon was observed in tunnels as short as 5 mm and in settings where relevant pressure recovery distal to the obstruction was excluded. We suspected that the Doppler-catheter gradient relation in tunnel obstructions is determined by the combination of flow contraction, pressure recovery and viscous losses, which varies with diameter, length, inlet and outlet geometry of the tunnel.

Methods To test this hypothesis, tunnels with a length of 20 mm, a diameter of 5.5 mm and with gradually tapering inlet and/or outlet (20°) or with abrupt narrowing and/or expansion were studied in a pulsatile flow model. Doppler and catheter measurements were simultaneously performed. Catheter gradients were estimated with the distal pressure port either at the tunnel entrance ($\Delta p C1$), at the tunnel exit ($\Delta p C2$) or 10 cm downstream ($\Delta p C3$). Flow was visualised with a Laser system and recorded with a high-speed video camera.

Results Doppler gradients ($\Delta p Do$) showed excellent agreement with $\Delta p C1$ in all settings (mean difference 0.8 ± 2.4 mmHg). In tunnels with abrupt narrowing, $\Delta p Do$ overestimated $\Delta p C2$ by 54 ± 19 %. Flow visualization demonstrated that this dramatic change in lateral pressure within the tunnel was caused by marked flow contraction at the tunnel entrance resulting in a high velocity and low pressure field followed by readaptation of the flow to the full cross-

section with only little turbulence resulting in significant pressure recovery within the tunnel itself.

In contrast, in tunnels with gradually tapering inlet, $\Delta p Do$ underestimated $\Delta p C2$ by 8 ± 2 %. In this setting, flow contraction was totally avoided and the neglect of viscous resistance in the simplified Bernoulli equation caused this Doppler-catheter gradient discrepancy. Due to various extent of distal pressure recovery, $\Delta p C3$ was 30 ± 7 % lower than $\Delta p C2$ in tunnels with gradually tapering outlet but only 9 ± 1 % lower in abruptly expanding tunnels. This added various degrees of overestimation of $\Delta p C3$ by $\Delta p Do$.

Conclusion Thus, the Doppler-catheter gradient relation in tunnel obstructions is determined by the individual extent of (1) flow contraction with pressure recovery within the tunnel, (2) viscous resistance, and (3) pressure recovery distal to the tunnel. The predominance of one of these phenomena depends on inlet and outlet geometry, length and diameter of the obstruction. Overestimation and underestimation by Doppler as well as “pseudoagreement” can occur.

Midterm Follow-Up of the Medtronic Bioprosthesis in Aortic Position

J. Bialy, Ch. Springer, P. Simon, E. Wolner, R. Seitelberger

Department of Cardio-Thoracic Surgery, University of Vienna, Austria

Objective The aim of this study was to collect clinical follow-up data on the Mosaic bioprosthesis implanted in aortic position. The Mosaic bioprosthesis is a porcine aortic valve cross-linked in glutaraldehyde solution under zero-pressure fixation and treated with alpha amino oleic acid to reduce the potential for calcification.

Methods From August 1997 to June 2001, the Mosaic bioprosthesis was implanted in 192 patients for aortic valve replacement (AVR). 101 (52.6 %) of those patients were female. The mean age of the patients was 74.7 years \pm 6.4 (range: 50–91). Coronary artery disease was present in 41 %. Patients have been prospectively evaluated at 6 month intervals with a mean follow-up of 1.5 years and a maximum follow-up of 3.8 years. The follow-up was 95 % complete.

Results There were 14 operative and 12 late deaths. The actual survival at 3.5 years was 78 ± 8 %. At 3.8 years, freedom from thromboembolism and bleeding was 100 %. Up to now, no cases of structural valve deterioration have been detected. Three reoperations were performed due to a paravalvular leak, postoperative development of an aortic aneurysm and valve endocarditis in one case. The latest follow-up revealed mean Doppler gradients of 20.5 ± 8.6 mmHg, 21.5 ± 6.1 mmHg and 15.6 mmHg, for the 21 mm, 23 mm and 25 mm valves. In addition, a substantial functional improvement was observed postoperatively, with 55.6 % of the patients in NYHA Class I, 40 % in Class II and 4.4 % in Class III, as compared to the preoperative evaluation with 2.1 % in Class I, 34 % in Class II, 53 % in Class III and 10 % in Class IV, respectively.

Conclusion The midterm follow-up of the Mosaic bioprosthesis implanted in the aortic position demonstrated its excellent clinical and haemodynamic performance with no incidence of thromboembolism and only one case of endocarditis. However, long-term follow-up is mandatory to draw final conclusions with regard to durability and clinical performance.

Abnormal Blood Pressure Response to Exercise – A Common Finding in Patients with Moderate Aortic Stenosis That Does Not Predict Outcome?

H. M. Gabriel, R. Rosenhek, G. Mundigler, A. Podolsky, J. Mondrzyk, P. Haber, G. Maurer, H. Baumgartner

Department of Cardiology, University of Vienna, Austria

Background Abnormal blood pressure (BP) response to exercise is a well known consequence of haemodynamically severe aortic stenosis (AS) and is used for decision whether to operate on asymptomatic patients. However, little is known about exercise testing and its prognostic value in patients with moderate AS.

Methods and Results Therefore, we performed bicycle exercise tests in 30 asymptomatic patients (mean age 31 ± 11 years, 19 male) with moderate AS (mean pressure gradient between 20 to 50 mmHg, mean \pm SD 37 ± 9 mmHg, normal ventricular function) and followed them for 33 ± 22 months. Abnormal blood pressure response to exercise was observed in 11 pts. (37 %): slow BP increase (< 10 mmHg/25 Watts) in 4, BP plateau in 6 and BP drop (> 10 mmHg) in 1 patient. Patients with normal BP response and those with abnormal response did not differ with respect to age (32 ± 10 vs 29 ± 12 years), mean gradient (38 ± 10 vs 36 ± 9 mmHg), %exercise capacity of expected (89 ± 17 vs 88 ± 29 %), and VO_2 max (29.8 ± 5.6 vs 27.4 ± 6.2 ml/kg bodyweight). During follow-up, 6 of 30 pts. (20 %) had an event: one patient died suddenly and 5 developed severe symptomatic AS requiring surgery. Pts. without event and those with an event did not significantly differ with respect to age (30 ± 11 vs 33 ± 9 years), mean gradient at study entry (37 ± 9 vs 38 ± 10 mmHg), exercise capacity (84 ± 15 vs 107 ± 34 %) and VO_2 max (28 ± 6 vs 33 ± 4). Abnormal BP response was no significant predictor of outcome. 2 events occurred in 11 pts. with abnormal BP response (18 %) and 4 events (including the sudden death) in 19 pts. with normal BP response (21 %).

Conclusion Thus, abnormal blood pressure response to exercise is a relatively common finding in asymptomatic pts. with moderate aortic stenosis but does not appear to be a significant predictor of outcome. Furthermore, these results may question whether pts. with severe aortic stenosis and abnormal blood pressure response to exercise who are otherwise asymptomatic and have good exercise capacity should undergo elective surgery.

How Useful Is Valve Resistance For The Distinction Between True Severe Stenosis and "Pseudostenosis" in Low Flow – Low Gradient Aortic Stenosis

J. Mascherbauer, R. Rosenhek, H. Schima, G. Maurer, H. Baumgartner
Department of Cardiology, University of Vienna, Austria

Background Although we and others have shown that – in contrast to previous suggestions – aortic valve resistance (R) is flow dependent, the question whether R is of value for the distinction between true severe stenosis and "pseudostenosis" (functionally small aortic valve area [AVA]) in patients with aortic stenosis (AS) who present with small AVA but low flow and low gradient remains controversial.

Methods To evaluate the value of R in this particular setting, models of stenotic aortic valves without doming (plates), models of doming valves (nozzles) and biological stenotic valves with various degrees of stenosis severity and extensible orifices were studied in a pulsatile *in-vitro* circuit using Doppler ultrasound and direct pressure and flow measurement. Anatomic AVA ranged from 0.5 to 1.25 cm² and cardiac output was varied from 2.0 to 8.9 l/min. R (dynes \times s \times cm⁻⁵) was calculated as $1333 \times$ mean transvalvular pressure gradient \times ejection time/stroke volume. Effective orifice areas (EOA) were calculated with the continuity equation. Orifices of the biological stenotic valves were recorded with a high-speed video camera for AVA planimetry. Valves with EOA < 0.85 cm² and mean gradients between 10 and 40 mmHg at low cardiac output (≤ 3.5 l/min) were divided into 2 groups. Group A = true severe stenosis: EOA remained < 0.85 cm² at normal flow. Group B = pseudostenosis: increase of EOA beyond 0.85 cm² at normal flow.

Results R was significantly smaller in pseudostenosis as compared to true severe stenosis (129 ± 28 vs 176 ± 33 , 120 dynes \times s \times cm⁻⁵; $p < 0.001$) even when baseline AVA did not significantly differ between groups. However, there was a wide overlap that did not allow the clear distinction between the two entities on the basis of an individual R value in the majority of settings. Nevertheless, R of < 120 dynes \times s \times cm⁻⁵ accurately identified non-severe stenosis. When subgroups of A and B without significant difference in gradient were compared, R was no longer significantly different between group A and B (162 ± 26 vs 141 ± 22 ; $p = 0.08$).

Conclusion Valve resistance is not only flow-dependent, it is also of limited value for the distinction between true severe stenosis and pseudostenosis in the setting of aortic stenosis with small AVA but low flow and low gradient. Only a very low R of < 120 dynes \times s \times cm⁻⁵ accurately identifies pseudostenosis. In most instances, procedures that attempt to normalize flow and repeat AVA calculations such as dobutamine echocardiography will be necessary for correct diagnosis.

Assessment of Aortic Valve Calcification Allows Risk Stratification in Mild and Moderate Aortic Stenosis

R. Rosenhek, T. Binder, J. Pixner, U. Klaat, M. Heger, C. Scholten, G. Maurer, H. Baumgartner
Department of Cardiology, University of Vienna, Austria

Background The degree of aortic valve calcification has been shown to be a significant predictor of outcome in severe aortic stenosis. In addition, aortic sclerosis has recently been reported to be associated with a significant increase in mortality. However, it remains unknown whether the degree of aortic valve calcification is of prognostic value in mild and moderate aortic stenosis (AS).

Methods 176 consecutive patients (73 female, age 58 ± 19 years) who were found to have mild to moderate AS defined by a jet velocity between 2.5 and 4.0 m/s in 1994 were followed for 51 ± 18 months. The degree of aortic valve calcification and other risk factors were assessed. The rate of haemodynamic progression was determined and the clinical outcome was analysed.

Results Kaplan-Meier event-free survival for the entire patient group, with endpoints defined as death ($n = 34$) or aortic valve surgery ($n = 33$) indicated by the development of severe symptomatic AS, was 95 ± 2 % at 1 yr, 75 ± 3 % at 3 yrs, and 60 ± 5 % at 5 yrs. Presence of moderate or severe aortic valve calcification, presence of coronary artery disease and peak aortic jet velocity (AV-Vel) at entry were significant independent predictors of outcome ($p < 0.0001$, $p < 0.001$ and $p < 0.01$, respectively). Event-free survival for patients with moderate or severe valve calcification was 92 ± 4 % at 1 year, 61 ± 7 % at 3 and 42 ± 7 % at 5 years versus 100 %, 90 ± 4 % and 82 ± 5 % for patients with no or mild calcification. Diabetes, hypercholesterolaemia and arterial hypertension were not significant predictors of outcome. The mean rate of haemodynamic progression was significantly faster for patients with an event (0.43 ± 0.04 m/s/yr) than for those without an event (0.14 ± 0.02 m/s/yr, $p < 0.0001$). Of 129 patients with a follow-up echocardiographic exam, 59 (46 %) developed severe AS (AV-Vel > 4 m/s) during follow-up.

15 cardiac and 19 non-cardiac deaths occurred. Mortality was 1.8 times higher than that of an age- and gender-matched control population ($p < 0.005$).

Conclusion Rapid progression to severe aortic stenosis and an increased mortality have to be considered in mild and moderate AS. In particular, patients with significant calcification of their aortic valve but also those with coronary artery disease and patients in whom serial echocardiograms reveal a rapid progression of the aortic jet velocity have a poor outcome. Thus, moderate and even mild aortic stenosis cannot be considered a benign disease. Serial Doppler studies and the assessment of valve calcification are crucial for the management of these patients as they identify high-risk patients who require closer follow-up than currently recommended.

Can Transcatheter Closure of Patent Foramen Ovale be Safely And Effectively Performed Without Transesophageal Echocardiography?

H. Baumgartner, R. Rosenhek, H. Gabriel, Th. Binder, G. Mundigler, M. Zehetgruber, G. Maurer, P. Probst
Department of Cardiology, University of Vienna, Austria

Background The use of transesophageal echocardiography (TEE) during transcatheter closure of patent foramen ovale (PFO) adds sig-

nificantly to patient discomfort. TEE, particularly when performed with general anaesthesia significantly increases procedure time and demands on personal and equipment resources, thus raising costs. Therefore, we studied safety and efficacy of PFO closure without routine use of TEE.

Methods After a learning period during which PFOs were closed under TEE surveillance, procedures were performed with fluoroscopy only. Results were evaluated with right atrial angio and transthoracic echo (TTE) before device release. TEE was restricted to situations where appropriate implantation remained uncertain. Amplatzer PFO occluders were used and the choice between size 25 and 35 mm was based on preinterventional TEE studies (PFO size, location, septal aneurysm). Patients received Aspirin 2 days prior to intervention and the following 6 months. Heparin was administered during the procedure, only. TTE was performed 1 day, 1 week, 3, 6, 12 and 24 months after intervention. Echo contrast studies were repeated until complete closure was documented.

Results 100 patients (56 female, age 47.6 ± 11.5 years) underwent PFO closure. In one pt. the procedure was terminated before implantation because of technical problems at the groin site, in one pt. no implantation was performed because the PFO presented with such a small fixed channel that predilation would have been necessary and in one pt. no PFO was found and repeat TEE showed that the preinterventional study had been false positive. In the remaining 97 pts, device implantation was successfully performed with a mean total procedure time of 32 ± 11 minutes. Unplanned TEE during the procedure was necessary in only 2 pts (2%). Complications were: pseudoaneurysm requiring surgery (1), uncomplicated coronary air embolism (1), atrial fibrillation with spontaneous conversion (1), AVNR-tachycardia (2). Residual shunt as documented by echo contrast was frequent on the first day (23%) but only present in one pt. at 3 months and in no pt. after 6 months. During a mean follow-up of 291 ± 221 days, one stroke and 4 TIAs occurred. A residual shunt at the time of the event was found in only one pt. One pt. developed multiple sclerosis, one pt. epilepsy.

Conclusion These results demonstrate that PFO closure can safely and effectively be performed without routine TEE and, thus, without general anaesthesia. However, they also emphasize the dilemma of patient selection for the procedure and the necessity of ongoing randomised trials comparing PFO closure and medical treatment.

Poster Presentation III: Heart Failure

Prediction of the Tolerability of Beta-Blockers by Neurohumoral Activation

M. Huelsmann¹, R. Berger¹, A. Bojic², P. Moser², C. Scholten¹, D. Moertl¹, R. Pacher¹

¹Department of Cardiology, University of Vienna, ²Ludwig Boltzmann Institute of Cardiovascular Research, Vienna, Austria

Background Betablockade is an established therapy in patients with congestive heart failure. Nevertheless there remains an amount of about 20%, where this therapy is not well tolerated. This is discussed to be related to the severity of the disease. Neurohumoral activation plays a central role in the pathogenesis of CHF and increases with the progression of heart failure. In order to answer the questions whether non-tolerability of beta-blockers can be unmasked by neurohumoral activation we investigated 49 patients with congestive heart failure.

Patients and Methods Inclusion criteria were NYHA class I–III after optimised oral treatment and stable conditions. Mean LVEF was $27 \pm 8\%$, distribution of NYHA class was I = 4, II = 29, III = 16 pts. Mean ACE-inhibitor was $83 \pm 23\%$ of the maximum recommended dosage. At time of first drug intake blood was obtained for

determination of N-ANP and BNP. Non-tolerability was defined as a symptomatic drop in blood pressure, drop in heart rate lower than 60 bpm or worsening heart failure within 4 weeks after initiation of beta-blocker.

Results 23 patients received carvedilol and 26 pts received bisoprolol. 40 patients (group A) tolerated the initiation of a beta-blocker and 9 (group B) did not. There was no difference between the two beta-blockers (80 vs 82% tolerability). Patients did not differ in respect to LVEF (A: 28 ± 8 vs B: $24 \pm 8\%$) or NYHA class between groups. BNP was elevated in both groups and was twofold higher in group B (A: 497 ± 809 vs. B: 922 ± 682 fmol/ml n.s.) but this was not statistical significant. N-ANP was increased threefold in patients of group B compared to group A and this was statistical significant (A: $10,795 \pm 13,654$ vs B: $27,910 \pm 23,203$ fmol/ml, $p < 0.03$). Five pts. experienced worsening heart failure during follow-up, all patients out of group B.

Conclusion The intolerability of beta-blockers is not different between carvedilol and bisoprolol. N-ANP has the power to unmask the intolerability of beta-blocker.

Effects of AT1-Antagonists-Addition to Beta-Blocker and ACE-Inhibitor Pretreated Patients with Severe Chronic Heart Failure

B. Gremmler¹, M. Kunert¹, H. Schleiting¹, C. Funke¹, K. Kisters², L. J. Ulbricht^{1,3}
¹Cardiol. Dept. of Marien Hospital, Bottrop, ²University of Muenster, ³University of Witten/Herdecke, Germany

Background Beta-blockers are well established in the therapy of severe chronic heart failure. Furthermore, the importance of ACE-inhibition concerning chronic heart failure is well known. The combining of these drugs is of great concern. According to a different pharmacological mechanism the sartans act by blocking the locally and not ACE-generated angiotensin II in the vessel wall and myocardium. Therefore, a benefit concerning chronic heart failure was expected in combining these three differently acting drug groups. Nevertheless, this was not observed in a subgroup analysis of Val-HeFT. Because our clinical impression contradicted these findings we performed a follow-up of our patients treated with an AT1-antagonist supplementary to the existing beta-blocker and ACE-inhibitor medication.

Design and Methods We made a follow-up from our patients ($n = 36$; mean age 65.6 ± 10.8 years) long-term pretreated with beta-blockers, ACE-inhibitors and diuretics due to a severe chronic heart failure. After clinical recovery a partly additional treatment with AT1-antagonists was performed.

There were three groups: treated only with beta-blockers, ACE-inhibitors and diuretics (control group, $n = 12$), additionally to the beta-blockers, ACE-inhibitors and diuretics treated with eprosartan (508.3 ± 137.9 mg; $n = 12$) or telmisartan (67.6 ± 17.3 mg; $n = 12$). Haemodynamic measurements concerning cardiac output were made by impedance cardiography at baseline and after 9.8 ± 4.0 days.

Results Additional treatment with sartans to the existing beta-blocker and ACE-inhibitor medication resulted in an improvement of cardiac output. There was an increase in cardiac output from 2.24 ± 0.75 to 2.92 ± 1.03 l/min ($p = 0.047$) in the eprosartan-group and from 2.34 ± 0.63 to 3.02 ± 0.107 l/min ($p = 0.003$) in the telmisartan-group while there was no significant increase of cardiac output in the control group (2.46 ± 0.76 to 2.54 ± 1.07 l/min).

Conclusion The additional treatment of severe heart failure patients who received digitalis, diuretics, beta-blockers and ACE-inhibitors with the AT1-receptor antagonist Eprosartan or telmisartan shows a beneficial effect by significant increasing cardiac output. An explanation for the observed effects may be, that in advanced stage of chronic heart failure a patho-physiological activation of local angiotensin II exists despite ACE-inhibitor and beta-blocker treatment. By blocking this locally acting angiotensin II an additional protection may be possible.

The Relationship between ProBNP Values and Invasively Determined Left Ventricular Ejection-Fraction

B. Gremmler¹, M. Kunert¹, H. Schleiting¹, B. Berg¹, C. Funke¹, K. Kisters², L. J. Ulbricht^{1,3}

¹Cardiol. Dept. of Marien Hospital, Bottrop, ²University of Muenster, ³University of Witten/Herdecke, Germany

Background Pro brain natriuretic peptide (proBNP) is synthesized predominantly in the left ventricle of the heart. In response to transmural pressure it is secreted into circulation and consequently cleaved to yield the active hormone BNP and its N-terminal fragment NT-proBNP. Determination of serum/plasma levels of NT-proBNP is used as an aid in the diagnosis of left ventricular dysfunction within chronic heart failure.

Design and Methods We analysed proBNP-level before a left-heart catheterization in 86 patients (m = 64; f = 22; mean age 61.2 ± 9.6 years). The determination of NT-proBNP in plasma was performed by utilising the electrochemiluminescence technology in the fully automatic Elecsys[®] analyser and the Elecsys[®] proBNP immunoassay. The calculation of the left ventricular ejection fraction in the angiogram was made semi-automatically by the computerised analysis-tool Shimadzu[®]. Finally we compared the observed values (Table 2).

Conclusion Concerning severe angiographic low ejection-fractions, in all cases a typical increase of proBNP-values was seen. These results were already observed in many studies.

However, a strong correlation of the BNP-value to the angiographic EF-calculation was not found in the cases of middle and moderate heart failure. Regarding the high standard-deviation in these groups it may be possible to discriminate an unfavourable course of heart failure in early stage. This possibility should be observed in long-term studies.

Table 2: B. Gremmler et al.

EF %	15–30	31–40	41–50	51–60	61–70	71–80	> 80
Mean proBNP (pg/ml)	2058	2040	281.8	442.3	209	144.7	136.5
±	741	1846.6	119.9	361.5	323.8	120.8	143.5

Sequential Big Endothelin Plasma Levels in Heart Transplant Recipients: Impact of Bridging Therapy and Heart Transplantation

J. Strametz-Juranek, M. Huelsmann, R. Pacher, T. Kos, W. Woloszczuk, M. Grimm, A. Zuckermann, B. Stanek

Department of Cardiology, University of Vienna, Austria

Study Objective The purpose of the present study was to investigate the impact of successful heart transplantation in patients with refractory heart failure receiving bridging therapy on sequential plasma levels of big endothelin, norepinephrine, atrial natriuretic peptide and aldosterone.

Patients and Methods 14 patients (2 female, 12 male) with severe chronic heart failure refractory to optimised oral therapy with angiotensin converting enzyme inhibitors and furosemide in New York Heart Association functional class IV and left ventricular ejection fraction below 15 %, accepted for heart transplantation were studied. Right heart catheterization was performed in all patients (cardiac index 1.9 ± 0.1 l/min/m², pulmonary capillary wedge pressure 30 ± 2 mmHg, systemic vascular resistance index 2827 ± 253 dynes × sec/cm⁵ × m²). As bridging therapy patients received either prostaglandin E1, prostaglandin E1 and dobutamine or dobutamine alone as a continuous infusion. Neurohumoral variables were measured prior to bridging therapy, 3.5 months prior and 7 and 10 months after successful heart transplantation.

Results Big endothelin, norepinephrine and atrial natriuretic peptide plasma levels decreased from 7.4 ± 2.9 fmol/ml, 1112 ± 686 pg/ml and 366 ± 312 pg/ml to 6.0 ± 4.5 fmol/ml, 720 ± 503 pg/ml, 198 ± 160 pg/ml after bridging therapy and further to 2.1 ± 0.9 fmol/ml (p < 0.0001 vs. baseline), 527 ± 31 pg/ml (p < 0.02 vs. baseline) and 115 ± 70 pg/ml (p < 0.03 vs. baseline) after cardiac transplantation. Aldosterone plasma levels decreased from 242 ± 220 pg/ml to 183 ± 142 pg/ml during bridging therapy and increased after heart transplantation to 252 ± 189 pg/ml. Plasma creatinine levels increased from 1.2 ± 0.4 mg/dl at baseline to 1.4 ± 0.2 mg/dl after transplantation (n.s.).

Conclusion The current study suggests that the excessive overproduction of big endothelin, atrial natriuretic peptide and norepinephrine is predominantly related to pump failure and after that cardiac transplantation, a moderate spillover of big endothelin persists. Its specific origin, however, remains to be elucidated. Further, our data suggest a protective effect of prostaglandin E1 on kidney function after heart transplantation.

Chronic Low-Frequency Stimulation of Thigh Muscles is an Effective Training Method in Patients with Advanced Chronic Heart Failure

M. Quittan¹, M. J. Nuhr¹, R. Berger², R. Crevenna¹, M. Huelsmann², D. Pette⁴, Richard Pacher^{2,3}

¹Dept. of Physical Medicine and Rehabilitation, ²Department of Cardiology, University of Vienna, ³Ludwig Boltzmann Institute for Cardiovascular Research, Vienna, Austria, ⁴Department of Biology, University of Konstanz, Germany

Background Patients with chronic heart failure (CHF) exhibit detrimental skeletal muscle changes contributing distinctly to the impaired exercise capacity. Chronic low-frequency electrical stimulation (CLFS) of thigh muscles can counteract changes of muscle properties and physical performance. This study investigates the potential of this novel method in patients with severe CHF.

Methods In a randomised, prospective, double-blind, placebo-controlled trial 40 CHF patients (53 ± 10 years) with LVEF of 22 ± 5 %, NYHA II–IV, and under optimized drug therapy were randomised to receive either CLFS or a sham stimulation (CG). Group difference was stimulation intensity eliciting a strong muscle contraction only in the CLFSG whereas the CG received only current input up to sensory threshold. Functional capacity was assessed by peakVO₂, work capacity, and a standardized 6-min walking test (6-MWT). Skeletal muscle properties were assessed by muscle biopsy of the right vastus lateralis muscle. Muscle tissue was analysed for myosin heavy chain (MHC) isoform proportions, citrate synthase (CS), and glyceraldehydephosphate dehydrogenase (GAPDH) activities.

Results Peak VO₂ (ml × min⁻¹ × kg⁻¹) increased significantly from 9.6 ± 3.5 to 11.6 ± 2.8 (20.8 ± 48 %, p < 0.001) in the CLFSG and decreased from 10.6 ± 2.8 to 9.4 ± 3.2 (–6.4 ± 9.2 %, p < 0.05) in the CG. The increase in the CLFSG was paralleled by a significant increase in maximal workload (p < 0.05) and oxygen uptake at the ventilatory threshold (p < 0.01), whereas the corresponding values of the CG remained unchanged (n. s.). 6-MWT in the CLFSG: 227 ± 138 m vs. 299 ± 137 m (p < 0.001), in the CG 237 ± 132 m vs. 243 ± 145 m (n. s.). MHC isoforms proportions: CLFSG: MHC-I increased (28.3 ± 7.7 % vs. 33.8 ± 5.8 %, p < 0.01), MHC-II decreased (31.2 ± 8.3 % vs. 25.1 ± 6.2 %, p < 0.01) and remained unchanged in the CG (MHC-I: 30.2 ± 7.4 vs. 28.7 ± 7.3; MHC-II: 32.1 ± 10.2 % vs. 33.2 ± 9.8 %, all n.s.). Enzyme activity patterns: CLFSG: CS activity increased (3.3 to 4.3 U × g⁻¹ wwt, p < 0.05), whereas GAPDH activity decreased (277 to 236 U × g⁻¹ wwt, p < 0.01).

Conclusion Our results suggest that CLFS represents a suitable treatment to counteract detrimental changes in skeletal muscle and increase exercise capacity of patients with severe CHF.

Extensor (M. quadriceps) and Flexor Muscle (Hamstring) Strength as a Predictor of Long-Term Outcome in Congestive Heart Failure

M. Huelsmann¹, M. Quittan², R. Berger¹, R. Pacher¹

¹Department of Cardiology, ²Department of Physical Medicine and Rehabilitation, University of Vienna, Austria

Background Exercise tolerance, expressed as peakVO₂, 6-minute walk test or workload, is impaired in patients with congestive heart failure. A myriad of investigations demonstrated the independent predictive power of those parameters. In contrast, isolated muscle strength itself was never evaluated also a relationship to the severity of the disease is known in extensor muscles.

Methods In order to investigate the predictive power of the strength of the M. quadriceps and the hamstring muscle we studied 122 consecutive patients (LVEF 21 ± 7 %, 108 male, isch. CMP in 70 cases, NYHA I 11 pts, NYHA II 42 pts, NYHA III 46 pts, NYHA IV 23 pts) of our outpatient unit. Follow-up time was up to 60 months. Muscle strength of the extensor muscle and the flexor muscle were investigated by a Cybex 6000 dynamometer under standardised conditions based on a protocol previously adapted for heart failure patients. Peak torque was additionally adapted to weight (peak torque index) to exclude the influence of wasting. Patients were grouped according to their outcome. Group A (n = 59) comprised patients who survived the study period and group B (n = 34) comprised those who died. Patients who were transplanted (n = 29) were excluded from survival analysis. LVEF did not differ between groups (A: 20 ± 7 vs. B: 21 ± 7 %, n. s.) and NYHA functional state was comparable between groups (n. s.).

Results The peak torque of the extensor was similar in both groups (A: 111 ± 45 vs. B: 98 ± 37 Nm) as well as its index (A: 132 ± 47 vs. B: 112 ± 35 Nm × 100/kg). Groups differed significantly in peak torque of the knee flexor muscles (A: 64 ± 29 vs. B: 51 ± 24 Nm, p < 0.03) and more pronounced in the index of the flexor muscle peak torque (A: 79 ± 30 vs. B: 62 ± 25 Nm × 100/kg, p < 0.01). Kaplan-Meier life time analysis revealed a significant difference at a cutpoint of 68 Nm × 100/kg (p < 0.01) of the flexor muscle peak torque index.

Conclusion Muscle strength is a useful predictor of long-term outcome of patients with congestive heart failure. Flexor muscles appear to be superior to extensor muscles to unmask morphologic alterations, which are known in congestive heart failure.

Dependence of Prescription Rate on Hospital and Age: A Data Based Substudy of the European Heart Failure Survey

D. Moertl¹, M. Huelsmann¹, R. Berger¹, A. Bojic², R. Pacher¹

¹Department of Cardiology, University of Vienna, ²Ludwig Boltzmann Institute of Cardiovascular Research, Vienna, Austria

Aims We evaluated the prescription rate of neurohumoral drugs in congestive heart failure patients. Especially we focused on differences in hospitals with cardiac care and without/and differences in age.

Methods and Results Three hospitals with 341 consecutive patients took part at this data based substudy of the European Heart Failure Survey 2000. Prescription rate of renin-angiotensin (RAAS) antagonists and β-blocker at time of discharge were evaluated. All over prescription rate and dosage was lower than recommended. Hospitals with cardiac care had a significant higher prescription rate than those without (p < 0.001). Patients elder than 75 years received significantly less therapy compared to younger patients (p < 0.001) and a lower dosage of RAAS antagonists (p < 0.01). Younger patients were treated more intensive in hospitals with cardiac care (p < 0.05). Patients aged > 75 years were under-treated independent of the hospital (n. s.). Kaplan Meier analysis revealed that patients aged > 75 years with optimised treatment have a significant survival benefit (p < 0.02) compared to those with less treatment.

Conclusion Patients with congestive heart failure are still under-treated in clinical practice. Younger patients profit from hospital

with cardiac care concerning therapy. Elder patients are distinctly less treated than the younger. Optimised treatment (combined RAAS antagonist and beta-blocker) results in a survival benefit in patients elder than 75 years.

Poster Presentation IV: Rhythmology

Optimised Pharmacological Treatment Decreases The Incidence of Device Therapies in Patients With Implantable Cardioverter Defibrillators

T. Winter, J. Reisinger, M. Gattermeier, E. Zeindlhofer, K. Hoellinger, P. Kuehn, P. Siostrzonek

Department of Cardiology, Krankenhaus der Barmherzigen Schwestern, Linz, Austria

Aim of the Study To evaluate the effects of optimised pharmacological treatment on the incidence of device therapies in patients (pts) with implantable cardioverter defibrillator (ICD).

Methods We analysed all pts in our institution who underwent ICD implantation according to class-I indication following AHA/ACC guidelines and compared demographic variables, concomitant medication and the incidence of ICD-related therapies at 12 months after implantation to data reported in the AVID (Antiarrhythmics Versus Cardioverter Defibrillators) study population.

Results Mean patient age was 59 ± 18 years and mean ejection fraction was 35 ± 12 % in our patients versus 65 ± 11 years and 32 ± 1.3 % in the AVID population, respectively. The use of beta-blockers, lipid lowering agents and amiodarone was significantly higher in our population than in AVID (p < 0.0001, p = 0.003, p = 0.01 respectively). Device therapies occurred in 4 of our pts within the first 12 months, reflecting an annual incidence of 19 % compared to a reported annual rate of 60 % in the AVID study (p < 0.0001).

Conclusion This suggests that intensified medical treatment including beta-blockers, lipid lowering agents and amiodarone may lower the rate of device-related therapies in pts with ICD.

Variation of Intracardiac R- And T-Wave Amplitudes: A Specific Cause for Inappropriate Shocks in a Patient With Brugada Syndrome and Implantable Cardioverter Defibrillator

T. Winter, J. Reisinger, M. Mori, E. Zeindlhofer, K. Hoellinger, P. Kuehn, P. Siostrzonek

Department of Cardiology, Krankenhaus der Barmherzigen Schwestern, Linz, Austria

Aim of the study To determine the specific mechanism of inappropriate therapies in a patient with Brugada syndrome and implantable cardioverter defibrillator (ICD).

Materials and Methods We analysed five episodes of inappropriate shocks in a patient with Brugada syndrome and ICD (Medtronic Gem 7227) and evaluated the effects of beta-blockade. Exercise testing with the device programmed on "passive" was performed before and after administration of pindolol (5 mg od) to document exercise-dependent episodes of inappropriate sensing.

Results All five episodes of inappropriate shocks were caused by T-wave oversensing due to cycle-length dependent increased intracardiac T- and decreased R-wave amplitudes. In the lead between Can and Coil, which resembles a left ventricular surface lead, no changes in R- and T-waves were documented indicating that the electrophysiological substrate for inappropriate sensing was predominantly in the right ventricle. Exercise testing with the device programmed on "passive" showed 38 episodes of inappropriate sensing with a maximum heart rate of 170 bpm. After administration of pindolol no further episodes of inappropriate sensing were noted at rest or during exercise testing.

Conclusion Our results suggest that T-wave oversensing due to variation of intracardiac right ventricular R- and T-wave amplitudes

may be a specific cause for inappropriate shocks in patients with Brugada syndrome and ICD. Exercise testing with the device programmed on “passive” may be of value in identifying patients at risk for inappropriate therapies. Administration of beta-blockers seems to be effective in reducing inadequate therapies in these patients.

The Microwave Ablation MAZE is an Effective Treatment for Chronic Atrial Fibrillation

W. Wisser¹, C. Khazen¹, G. Stix², H. Schmidinger², R. Seitelberger¹, E. Wolner¹
¹Department Of Cardiothoracic Surgery, ²University Clinic for Internal Medicine II, University of Vienna, Austria

Objective The MAZE procedure is an effective surgery in patients with atrial fibrillation (AF), but constitutes an extensive and complex procedure. We tested the efficacy and safety of a new microwave ablation device, designed to create linear lesions.

Methods Between 2/2001 and 1/2002, 21 patients with chronic AF > 6 months (64.5 ± 2.2 years, 9 male) underwent concomitant valve surgery (aortic in 8, mitral in 18, tricuspid in 6) and the MAZE procedure. The mean duration of AF was 63 ± 29 months (range 7–384 months). Surgery was carried out creating linear lesions in both atria with the microwave ablation device and following the concept of the Cox III procedure.

Results The MAZE procedure added 22 ± 2 minutes aortic cross clamp time (total time: 88 ± 3 min). Postoperative complications with prolonged ICU stay occurred in only one patient due to severe SIRS. For the remaining patients, the length of intubation was 19.7 ± 7.1 hours, and ICU stay was 1.9 ± 0.7 days. No procedure related complications were recorded. During the hospital stay, 54 % were treated with sedacurone and 64 % needed cardioversion to maintain sinus rhythm. 25 % of the patients required pacemaker implantation for intermittent A-V block or sick sinus syndrome. At the mean follow-up of 8.0 ± 0.9 months (2.2–13 months) 81 % of the patients were in sinus rhythm, 4.7 % presented with a junctional rhythm and 14.3 % with atrial fibrillation or flutter.

Conclusion Microwave ablation according to the Cox III-MAZE concept combines low surgical risk with a high success rate in patients with chronic AF and combined valve pathology.

Risk Management of Patients with Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

Th. Pezawas, G. Stix, M. Wolzt, J. Kastner, Ch. Mayer, H. Schmidinger
 Department of Cardiology, University of Vienna, Austria

Aim To evaluate electrophysiologically guided risk management and treatment of patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C), since guidelines have not been established.

Methods and Results In 26 ARVD/C patients (18 with documented sustained monomorphic ventricular tachycardia (smVT), 2 with ventricular fibrillation (VF), 5 with non-smVT and 1 with syncope) programmed ventricular stimulation (PVS) was performed for risk-stratification. Epsilon-waves and late potentials were found in 9 and 12 patients, respectively (left/right ventricular ejection fraction = 58 ± 7 %/23 ± 14 %). On PVS 13/18 patients with smVT (72 %) were inducible in smVT. Fast smVT (249 ± 25 msec) was induced in 8/13 patients. In these 8 patients and in another 3 (2 documented VF/1 non-smVT [194 msec]) cardioverter defibrillators (ICD) were implanted (ICD group, n = 11). The remaining patients had documented slow VT (316 ± 33 msec) and were left on radiofrequency-ablation or antiarrhythmic drug therapy (non-ICD group, n = 14). Nine out of 11 ICD patients received appropriate therapies during a follow-up period of 6.7 ± 3.3 years: fast mVT in 4 patients (258 ± 13 msec) and VF in 5 patients (230 ± 7 msec); one non-ICD patient (7 %) experienced smVT (290 msec). One ICD patient died of non-device related sepsis, another committed suicide. The positive and negative predictive values of PVS for fast VT or sudden cardiac death were 89 % and 88 %, respectively (sensitivity 80 %, specificity 94 %).

Conclusion In patients with ARVD/C clinical and induced tachycardias do correlate well. Patients are at risk for life-threatening tachyarrhythmias if they have either fast documented VT (< 280 msec) or are inducible in fast smVT on PVS. Non-inducible patients are at high risk if they have very fast documented non-smVT (< 200 msec) or are survivors of sudden death. In these patients ICD implantation is the treatment of choice. Spontaneous and induced slow VT (> 280 msec) on PVS indicate a benign prognosis justifying drug treatment or VT ablation.

Efficacy and Safety of Ibutilide in Patients With Atrial Tachyarrhythmias and Pretreatment With Class I and/or Class III Antiarrhythmic Agents

U. Eidher, F. Freihoff, W. Kaltenbrunner, K. Steinbach
 Ludwig Boltzmann Institute for Arrhythmia Research, Wilhelminenhospital, Vienna, Austria

Background Conversion (CONV) rates of Ibutilide (IBU) in atrial fibrillation (AF) and atrial flutter (AFLU) have been reported in the range of 35–50 % and 60–80 %, respectively. The incidence of proarrhythmic complications (COMPL) is reported to be 2–8 %.

Aim of the Study To investigate CONV and COMPL rates in our patient (PAT) cohort with atrial tachyarrhythmias and pretreatment with class I (CI) and/or class III (CIII) antiarrhythmic (AA) agents scheduled for IBU application.

Methods PAT with recurrent AF, AFLU or monomorphic atrial tachycardia (AT) under CI and/or CIII AA agents were treated with IBU for acute CONV. PAT with a left ventricular ejection fraction (LVEF) less than 40 % were excluded. PAT received 0.87 mg of IBU over ten minutes; in case of persistence of the arrhythmia another dose of 0.87 mg IBU was applied after another ten minutes. PAT were monitored during and for 4 hours after IBU application.

Results 53 PAT (34 m, 19 f; mean age 66 ± 10 years) were included, 25 PAT with AF, 14 PAT with AFLU and 14 PAT with AT. Structural heart disease was present in 42/53 PAT (79 %): hypertensive heart disease in 27/42 PAT, CHD in 7/42 PAT. AA pretreatment consisted of amiodarone (AMIO) in 36 PAT, flecainide (FLECA) in 9, sotalol (SOTA) in 4 and propafenone in 1 PAT. In the remaining PAT, pretreatment was combination therapy with AMIO/FLECA and SOTA/FLECA. 38/53 PAT had a normal LVEF; mean left atrial size was 45 ± 6 mm.

For the whole cohort CONV rate was 38 % (20/53); in PAT with AF 36 % (9/25), in PAT with AFLU 64 % (9/14) and in PAT with AT 14 % (2/14). No COMPL during or after IBU application did occur.

Conclusion The efficacy of IBU in acute CONV of AF and AFLU in PAT with recurrence of their arrhythmia under CI and/or CIII AA pretreatment is comparable to that in PAT cohorts without AA pretreatment. IBU treatment in with AA pretreated PAT with AT is not warranted. In our selected cohort, pretreatment with CI and/or CIII AA did not increase the proarrhythmic potential of IBU.

A Lower Incidence of Permanent Atrial Fibrillation in Single-Lead VDD versus Two-Lead DDD Pacing in the Treatment of AV Block

M. Nuernberg¹, S. Hansen², J. Bodnár³, D. Wojciechowski⁴, M. Novák⁵, W. Kargu⁶, G. Swiatecka⁷, M. Lewandowski⁸, K. Steinbach¹ for the VDD versus DDD study group

¹L. Boltzmann Institute for Arrhythmia Research, Vienna, Austria, ²Biotronik, Berlin, Germany, ³Hospital L. Pasteur, Kosice, Slovakia, ⁴Wolski Hospital, Warsaw, Poland, ⁵St. Ann's Faculty Hospital, Brno, Czech Republic, ⁶Hospital of the Silesian Medical Academy, Katowice, Poland, ⁷Institute of Cardiology of the Medical Academy, Gdansk, Poland, ⁸Institute of Cardiology, Warsaw, Poland

Introduction Single-lead VDD pacing has become a therapeutic alternative to two-lead DDD pacing in patients with AV block and chronotropic competence. Single-lead systems are reliable and safe, and they have the advantage of shortening both implantation time

and X-ray exposure. By comparison, mechanical and electrical irritation of the atrial myocardium has been discussed as an important factor for the incidence of atrial fibrillation (AF) during long-term DDD pacing.

Hypothesis Because single-lead systems usually eliminate atrial stress, we expected a lower incidence of permanent AF, which requires the pacemaker to be reprogrammed to VVI mode during long-term, single-lead VDD pacing compared to two-lead DDD pacing.

Methods In this prospective clinical trial, patients with AV block and normal sinus node function were randomised into two groups: those implanted with a two-lead DDD pacemaker system (90 patients, 68 ± 15 years, 49 % women), and those implanted with a VDD pacemaker with a single lead (90 patients, 69 ± 15 years, 48 % women). Both groups participated in scheduled follow-ups for up to four years. A Kaplan-Meier survival analysis with Log-Rank test was conducted to examine differences in incidences of permanent AF between the two groups for one, two, three, and four years (+ one month, respectively) after implantation.

Results Implantation time was significantly ($p < 0.001$) shorter in the VDD group (54 ± 34 min) than in the DDD group (75 ± 35 min). X-ray exposure was also significantly ($p < 0.01$) shorter in the VDD group (6 ± 5 min) compared to the DDD group (10 ± 7 min). The mean percentage of AV synchronous pacing was similar in both groups: 99 % in the VDD group and 93 % in the DDD group (means calculated from 8 semiannual follow-ups).

The incidence of permanent AF in percentages was as follows: after one year, 0 % in the VDD group vs. 4 % in the DDD group ($p < 0.09$); after two years, 1 % in the VDD group vs. 8 % in the DDD group ($p < 0.05$); after three years, 3 % in the VDD group vs. 12 % in the DDD group ($p < 0.05$); and after four years, 5 % in the VDD group vs. 14 % in the DDD group ($p < 0.05$).

Conclusion The incidence of permanent AF requiring reprogramming to VVI mode was significantly lower in VDD pacing than in DDD pacing over the long-term course of four years, which was probably due to less irritation of the atrial myocardium being caused by single-lead VDD pacing. Due to these advantages, single-lead VDD pacing should be the preferred treatment for AV block.

Special Considerations on Arrhythmias in Women

F. Freihoff, W. Kaltenbrunner, U. Eidher, A. Podczeczek, M. Nuernberg, F. Jug, K. Steinbach

Ludwig Boltzmann Institute for Arrhythmia Research, Wilhelminenhospital, Vienna, Austria

In recent years interest has been continuously growing in gender specific differences in many fields of medicine, especially in cardiology.

Literature data dealing with gender differences in arrhythmias are sparse.

It has long been recognised that women have a higher intrinsic heart rate and a shorter sinus nodal recovery time. Women also have a longer corrected QT interval. There are no other known electrocardiographic or electrophysiologic gender differences. Numerous studies have shown a gender specific difference in the occurrence of different types of supraventricular tachycardias with AV nodal reentrant tachycardia twice as often in women as opposed to WPW syndrome, which shows a 2:1 predominance in men.

The absolute number of men and women with atrial fibrillation appears to be equal though it is more prevalent in men of all age groups.

Sudden cardiac death occurs much more often in men, which is largely attributable to the higher incidence of coronary artery disease.

As women exhibit a longer QT interval at baseline they are more prone to develop torsades de pointes when receiving QT prolonging drugs. Therefore, special caution is mandatory when prescribing such drugs in women.

During pregnancy, the incidence of SVT seems to be higher and there also seems to be a cyclical dependency with more frequent attacks during the luteal phase of the menstrual cycle.

Most therapeutic options for the treatment of arrhythmias (pharmacologic or non-pharmacologic) are just as effective in women as in men. Nevertheless, a better understanding about the mechanisms underlying the gender differences in arrhythmias will likely help to increase the benefit and minimize the risks of these therapies in women.

Poster Presentation V: Experimental Cardiology and Cardiovascular Biology

Impaired Activation of the Fibrinolytic System in Patients With Coronary Artery Disease and Signs of Chronic Inflammation

W. S. Speidl¹, G. Zorn¹, M. Nikfardjam¹, W. Schreiber², N. Jordanova¹, A. Niessner¹, T. W. Weiss¹, S. Pfaffenberger¹, J. Wojta¹, K. Huber¹

¹Department of Cardiology, ²Department of Emergency Medicine, University of Vienna, Austria

Background Inflammation plays an important role in the initiation and progression of atherosclerosis and in the pathogenesis of acute cardiovascular events. The fibrinolytic system of the vessel wall may lead to initiation of endogenous fibrinolysis and prevention of local thrombus formation. Venous occlusion (VO) is a stimulator of the fibrinolytic system. The aim of this study was to assess if chronic inflammation of the vascular wall as measured by the systemic marker C-reactive protein (CRP), an indicator of ongoing atherosclerosis, may be associated with an impaired activation of the fibrinolytic system.

Methods and Results We included 50 patients six months after their first myocardial infarction. We measured plasma levels of CRP, the prothrombotic markers prothrombin fragment 1 + 2 (F1.2) and thrombin-antithrombin (TAT) at baseline and plasma levels of tissue-type plasminogen activator (t-PA), plasminogen activator inhibitor-type-1 (PAI-1), and t-PA-PAI-1-complexes at basal conditions and after a standardized VO of the forearm. CRP plasma levels showed an inverse correlation to VO induced increase of tPA activity ($r = -0.28$, $p < 0.05$). Accordingly, patients without ongoing inflammation (CRP < 0.14 mg/dl; $n = 25$) showed a significantly higher increase of t-PA activity during VO ($p < 0.05$) compared to patients with signs of chronic inflammation (CRP ≥ 0.14 mg/dl; $n = 25$) as well as a significant higher decrease of PAI-1 activity ($p < 0.05$). A multivariate analysis that included cardiovascular risk factors and medical treatment showed that CRP is an independent predictor of tPA response to VO.

Conclusion Ongoing chronic inflammation as determined by increased CRP levels is associated with a decreased fibrinolytic response to VO in patients with a history of myocardial infarction. This impaired endothelial fibrinolytic potential might be an important contributor to the poor prognosis associated with chronic vascular inflammation reflected by an elevation of CRP.

Ultrasound Promotes the Penetration of Tissue-Type Plasminogen Activator Into Blood Clots and Enforces Thrombolysis In Vitro: An Immuno-Histochemical Analysis

S. Pfaffenberger¹, B. Devcic-Kuhar², L. Gheradini², C. Mayer³, E. Tschachler³, M. Groeschl², E. Benes², G. Maurer¹, K. Huber¹, J. Wojta¹, M. Gottsauner-Wolf¹

¹Department of Cardiology, University of Vienna, ²Institute of General Physics, Vienna University of Technology, ³Department of Dermatology, University of Vienna, Austria

Background Ultrasound enhances rt-PA mediated thrombolysis. The possible mechanism is the enforced penetration of the thrombo-

lytic agent into the blood clot. The aim of the study was to evaluate the quantitative effect of sonothrombolysis and to visualize the distribution of plasminogen and rt-PA in the clot after ultrasound treatment.

Methods Clots were sonicated in the presence of rt-PA for 1 hour in a blood vessel mimicking tubing using a frequency of 2 MHz and an intensity of 1.2 W/cm². Immunofluorescence double staining of the sonicated clots and control clots, which were treated with rt-PA in the absence of ultrasound, were performed using antibodies against plasminogen and rt-PA. Thrombolysis evaluation was performed by measuring clot weight loss and by analysing D-dimer concentration in supernatants.

Results Ultrasound enforced fibrinolysis resulted in up to 75 % clot weight reduction. These data correlated to D-dimer levels measured by ELISA. Immunofluorescence staining revealed a 5-fold increase in penetration depth of rt-PA in sonicated clots as compared to control clots. In addition the concentration of plasminogen was elevated in this area as compared to control clots. If ultrasound was used without rt-PA the concentration of plasminogen on the clot surface was similar to the concentration in clots treated with ultrasound and rt-PA.

Conclusion External ultrasound increases rt-PA mediated thrombolysis *in vitro*. We visualized that ultrasound enhances the penetration of the fibrinolytic agent into the clot. This mechanism might contribute to the profibrinolytic effects of ultrasound also seen under *in vivo* conditions.

Endothelin in Acute Coronary Thrombi

Ch. Adlbrecht, D. Bondermann, J. Jakowitsch, G. Beran, M. Derntl, P. Siostrzonek, D. Glogar, R. Pacher, I. M. Lang
Department of Cardiology, University of Vienna, Austria

Background Acute coronary syndrome (ACS) represents the acute phase of coronary artery disease. ACS is thought to be caused by rupture of atherosclerotic plaque, which gives rise to thrombosis and subsequent small vessel dysfunction. Endothelin (ET) is a potent vasoconstrictor peptide that activates polymorphonuclear leukocytes, changes their deformability and adhesion molecule expression and probably promotes microvascular plugging. Therefore, we investigated ET in ACS.

Materials and Methods Coronary thrombus material was collected during acute coronary interventions utilizing the X-Sizer (EndiCOR Medical Inc.) thrombus removal device. One part of the material was fixed in formalin and used for immunohistochemistry (IHC), the remaining thrombus was weighed, suspended in HBS-buffer, homogenised in a glass potter, sonicated, cleaned over C-18 SepPak[®] cartridges and used for ELISAs (ET 1-21 ELISA-kit, Biomedica). Patient plasmas were treated in the same fashion.

Results The predominant cellular components of acute coronary thrombi were polymorphonuclear granulocytes (mean count 3×10^6 granulocytes per mm³ thrombus, i. e., a 100-fold concentration compared with normal whole blood), within a fibrin and platelet-containing meshwork. Serial analysis of thrombus sections (n = 12) revealed that 46 ± 18 % of cells with segmented nuclei displayed cytoplasmic staining for immunoreactive ET-1 (irET-1). The average ET concentration was 266.2 ± 420.1 fmol/100 mg of thrombus (n = 19). For comparison, ET plasma concentrations in patients with ACS were 0.385 ± 1.034 fmol/ml.

Conclusion The data show that coronary thrombi contain high concentrations of ET associated with polymorphonuclear granulocytes. Thrombus-derived ET could play an important role in ACS.

Predictive Value of Prothrombotic and Antifibrinolytic Factors in Chronic Coronary Artery Disease in a Long-Term Follow-Up

A. Niessner, S. Graf, M. Nikfardjam, W. S. Speidl, A. Geppert, R. Huber-Beckmann, G. Zorn, J. Wojta, K. Huber
Department of Cardiology, University of Vienna, Austria

Background and Aim Prothrombotic and antifibrinolytic factors are supposed to be responsible for the formation of thrombi after initial plaque rupture. It was our aim to investigate for the first time the predictive role of circulating prothrombotic/antifibrinolytic factors in patients with chronic angiographically proven coronary artery disease (CAD) for further coronary events in a long-term follow-up.

Methods One hundred forty-one patients with stable coronary artery disease were investigated for their plasma levels of plasminogen activator inhibitor-1 (PAI-1) activity, tissue plasminogen activator (t-PA) antigen, von Willebrand factor (vWF), lipoprotein a (Lp(a)) and IgM and IgG anticardiolipin (aCL) antibodies before balloon angioplasty at the time of inclusion. The incidence of a combined primary endpoint (cardiovascular death, myocardial infarction, revascularization procedures) was determined for a median follow-up period of 13.2 years (range: 1.6–17.6), resulting in a total amount of 1770 follow-up years.

Results 103 patients (73 %) developed at least one of the given endpoints. t-PA in the upper quintile predicted a significantly about 7-fold higher risk to suffer from further coronary events compared to the lowest quintile (χ^2 -test, p = 0.014). PAI-1 activity, vWF, Lp(a) and aCL antibodies failed to predict the occurrence of further events. Higher age (t-test, p = 0.035) and hypertriglyceridaemia (χ^2 -test, p = 0.045) were significant established risk factors for coronary events in our study population.

Discussion and Conclusion In a long-term follow-up for the first time the crucial role of t-PA in CAD in prediction of future coronary events could be emphasized. Elevation of t-PA antigen thereby can be explained by elevation of t-PA/PAI-1 complexes thus indicating the presence of a reduced fibrinolytic potential. In conclusion, measures being aimed to improve the endogenous fibrinolytic system, e. g. by blockade of the renin-angiotensin system and/or a consequent antithrombotic therapy may help to reduce the rate of ischaemic coronary events.

Glycoprotein 130 (gp 130) Mediated Induction of Vascular Endothelial Growth Factor (VEGF-A) in Human Adult Cardiac Myocytes (HACM)

T. Weiss¹, K. Macfelda², W. S. Speidl¹, C. Kaun¹, G. Zorn¹, U. M. Losert², G. Maurer¹, K. Huber¹, J. Wojta¹

¹Department of Cardiology, ²Department of Biomedical Research, University of Vienna, Austria

Background VEGF-A is an endothelium-specific growth factor. It induces proliferation, migration and NO-synthesis in endothelial cells and is able to stimulate neoangiogenesis in ischaemic organs. A significant increase of VEGF-A serum levels was shown after myocardial infarction. These data suggest the importance of the VEGF system during reparation and neovascularization. Recent data showed that glycoprotein 130 (gp 130) is involved in the regulation of VEGF-A. Therefore we investigated whether oncostatin-m (OSM) or Leukemia Inhibitory Factor (LIF) are possible regulators of VEGF-A in HACM *in vitro* and thus might contribute to the neoangiogenesis during cardiac repair processes.

Methods HACM were isolated from recipients' hearts after heart transplantation and characterised by positive staining for actin, troponin-I and cardiotin. The cells were negative for two fibroblast-specific antibodies as well as for desmin and vWF indicating the absence of fibroblasts, smooth muscle cells and endothelial cells. Such characterised HACM were treated with OSM or LIF for 24 hours and VEGF-A was determined by a specific ELISA in the conditioned media of these cells. We performed a RT-PCR in order to

detect gp 130, interleukin-6-receptor (IL-6R), LIF-receptor (LIFR) or OSM-receptor (OSMR).

Results We showed that OSM, but not LIF increased VEGF-A expression in HACM dose-dependently. These results could be confirmed on the level of specific mRNA expression as determined by RT-PCR. We detected the expression of gp130 and OSMR and to a lesser extent LIFR and IL-6-R on HACM by RT-PCR.

Conclusion Our data suggest, that selective expression of the IL-6 superfamily-receptors on cardiac myocytes might be involved in the induction of VEGF-A mediated neoangiogenesis in the heart.

Nucleus Factor κ B Mediated Induction of Proinflammatory Cytokines by Polymorphic Membrane Proteins of *Chlamydia pneumoniae* in Human Umbilical Vein Endothelial Cells *In Vitro*

A. Niessner¹, C. Kaun¹, G. Zorn¹, G. Christiansen², A. S. Pedersen², S. Simon³, A. Georgopoulos³, W. Graninger³, G. Maurer¹, K. Huber¹, J. Wojta¹

¹Department of Cardiology, University of Vienna, ²Department Medical Microbiology, University of Aarhus, ³Department of Internal Medicine I, University of Vienna

Background The chemokines interleukin (IL-8) and monocyte chemotactic protein 1 (MCP-1) and the proinflammatory cytokine interleukin 6 (IL-6) are present in atherosclerotic lesions of the vessel wall. Based on clinical studies a role for *C. pneumoniae* in the development of atherosclerosis is currently discussed. Recent *in vitro* studies have shown that *C. pneumoniae* can activate cultured human umbilical vein endothelial cells (HUVECs) via the nucleus factor κ B (NF κ B)-pathway thereby inducing among other effects also IL-6, IL-8 and MCP-1 expression in these cells.

Aim It was the aim of the present study to investigate whether purified isolated components on the surface of *C. pneumoniae*, namely polymorphic membrane proteins (PMPs) could affect production of IL-6, IL-8 and MCP-1 mediated by the NF κ B-pathway in human endothelial cells *in vitro*.

Methods HUVECs were incubated with purified PMPs. In order to exclude possible LPS-mediated effects aliquots of the respective PMPs were boiled for 5 minutes prior to addition to HUVECs. IL-8, MCP-1 and IL-6 were quantitated by specific ELISAs. HUVECs were transfected with I κ B virus by incubation in order to inhibit NF κ B-mediated effects by overexpression of I κ B.

Results Out of 15 PMPs tested PMP 20 and PMP 21 were the strongest inducers of IL-8, MCP-1 and IL-6 production in HUVECs. The effects were dose and time dependent. The effect of PMP 20 and PMP 21 on IL-6, IL-8 and MCP-1 was abolished by heat-treatment. The stimulatory effect of PMPs was inhibited in HUVECs transfected with I κ B Virus.

Conclusions We conclude from our data that specific PMPs of *C. pneumoniae* induce the NF κ B mediated expression of proinflammatory cytokines in HUVECs *in vitro*. If such a mechanism is also operative *in vivo*, *C. pneumoniae* could by specific interactions of its PMPs with the endothelium contribute to the process of vascular injury during the development of an atherosclerotic lesion.

Comparison of Preliminary Intravascular Ultrasound (IVUS) – Results After Implantation of Colchicin-Coated and Bare Genius Stents in Porcine Coronary Arteries

W. Sperker, M. Gyöngyösi, C. Strehblow, M. Shirazi, D. Glogar
Department of Cardiology, University of Vienna, Austria

Background Various antiproliferative drugs are currently tested on coated stents in order to improve the outcome after intracoronary stent placement. The aim of this study was to investigate the effect of colchicin on neointimal volume after intracoronary stent implantation in pigs.

Methods Normal house pigs (20–30 kg, no special diet) were used for this experiment. After general anaesthesia and administration of

200 IU/kg heparin, either colchicin-coated Genius stents (n = 7, group 1) or bare Genius stents (n = 8, group 2; all stents from EuroCor, Bonn, Germany) were implanted into either the left anterior descending or left circumflex coronary artery. During a 4 week follow-up (FUP), the animals were fed no special diet; 250 mg of acetylic-salicylic acid were administered daily *per os*. After the FUP-period, repeat angiography and IVUS were performed for assessment of neointimal formation. The stents were explanted for histological analysis, the IVUS recordings were analysed using a 3D-analysis system (EchoPlaque, Indec Systems, US).

Results All pigs of group 1 survived until the FUP-angiography, one pig of group 2 died of unknown causes 2 weeks after the intervention. IVUS analysis showed a minimal lumen diameter of 2.4 ± 0.5 mm vs. 2.3 ± 0.4 mm (group 1 vs. group 2, non significant [n.s.]), maximal area stenosis 51.2 ± 15.0 % vs. 50.4 ± 6.4 (n.s.), neointimal volume 37.9 ± 12.5 vs. 35.9 ± 20.5 mm³ and total vessel volume (of the stented segment) 164.7 ± 28.4 vs. 161.6 ± 67.0 mm³.

Conclusion IVUS showed comparable results after the implantation of colchicin-coated and bare Genius stents. Thus, the colchicin-coating did not show any beneficial effects on the development of in-stent-restenosis after 4-week-FUP in porcine coronary arteries.

Usefulness of Intravascular Ultrasound Guided Histological Measurements After Stenting of Porcine Coronary Artery

M. Shirazi, M. Gyöngyösi, C. Strehblow, W. Sperker, U. Windberger, D. Glogar
Department of Cardiology, University of Vienna, Austria

Background We evaluated the usefulness of IVUS in the non-unique distribution of in-stent neointimal hyperplasia, comparing the results of the macroscopic measurements with the standard histomorphometric analysis.

Methods Coronary artery stenting was performed in 33 left coronary arteries of 28 domestic pigs (34.5 ± 9.5 kg, 51 % male) using 14 Tenax (Biotronik GmbH & Co, Berlin, Germany), 8 bare Genius, 6 polymer-coated Genius (Eurocor, Bonn, Germany) and 5 Biodivysio Matrix LO (Biodivysio Ltd., Farnham, Surrey, UK) stents. After 4 weeks, coronary angiography and IVUS were performed. IVUS images were analysed by using 3D quantitative analysis. The stented arterial segments were fixed in formalin, embedded in Technovit 9100, and cut to 4–8 μ m thick slides. The most diseased in-stent segment was 4.49 ± 4.54 mm away from the distal stent edge assessed by IVUS. Sections of these segments were stained for quantitative histomorphometric analysis.

Results A significant correlation was found between IVUS-guided histomorphometric analysis and 3D-IVUS measurements of maximal intimal thickness ($r = 0.6985$, $p < 0.005$) and maximal intimal area ($r = 0.7736$, $p < 0.001$). Macroscopic measurements resulted in a trend to larger maximal intimal thickness (0.91 ± 0.39 vs. 0.81 ± 0.46 mm by IVUS and computerised planimetry) and maximal intimal area (4.53 ± 1.82 vs. 3.45 ± 1.55 mm² by IVUS and computerized planimetry) as compared to histomorphometry. Although the implanted stent length and diameter, nominal stent-balloon inflation pressure and time and injury score (1.52 ± 0.44 for Tenax, 1.47 ± 0.37 for bare Genius, 1.53 ± 0.41 for polymer-coated Genius and 1.56 ± 0.52 for Biodivysio stents) did not differ between the different stents, implantation of bare Genius stents resulted in a significant smaller neointimal hyperplasia expressed as neointimal volume after 4 weeks compared to Tenax, polymer coated Genius and Biodivysio stents: 19.3 ± 5.6 mm³ vs 67.4 ± 34.3 , 70.6 ± 14.3 and 84.2 ± 42.6 mm³, respectively ($p < 0.05$).

Conclusion The significant correlation between IVUS-guided histomorphometric analysis and IVUS measurements confirm the usefulness of IVUS in the evaluation of experimental in-stent restenosis. Implantation of bare Genius stents resulted in a significant lower neointimal hyperplasia as compared to polymer-coated Genius and phosphorylcholine coated Biodivysio stents or Tenax stents.

Poster Presentation VI: Miscellaneous I

Mean Platelet Volume (MPV) is an Independent Risk Factor for Myocardial Infarction but not for Coronary Artery Disease

N. Jordanova¹, G. Endler², A. Klimesch², H. Sunder-Plassmann², M. Schillinger³, M. Exner², Ch. Mannhalter², G. Christl¹, R. Thalhammer², R. Sunder-Plassmann², K. Huber¹

¹Department of Cardiology, ²Department of Laboratory Medicine, ³Department of Internal Medicine II, Division of Angiology and AKH Wien, University Vienna, Austria

Background After rupture of an arteriosclerotic plaque in a coronary artery, platelets play a crucial role in the subsequent thrombus formation leading to myocardial infarction. An increased mean platelet volume (MPV) as indicator for larger, more reactive platelets may represent a risk factor for myocardial infarction. However, this hypothesis is still controversial and most studies addressing the role of MPV were performed comparing patients with myocardial infarction with healthy controls. We intended to identify patients at high risk for suffering myocardial infarction in a group of patients with known coronary artery disease.

Methods and Results 185 consecutive patients with stable coronary artery disease were compared with 188 individuals who had suffered myocardial infarction. Patients within the highest quintile of mean platelet volume (= 11.6 fl) had a significantly higher risk to experience a myocardial infarction compared to patients within the lowest quintile (OR = 2.6, 95 % CI 1.3 to 5.1) in a multivariate analysis that included sex, age, BMI, hyperlipidaemia, hypertension, smoking and diabetes mellitus.

Conclusion Our results indicate that patients with pre-existing coronary artery disease and an increased mean platelet volume (≥ 11.6 fl) are at higher risk for myocardial infarction. These patients can be easily identified during routine haematological analysis and could possibly benefit from preventive treatment.

Assessment of Dynamic Changes in Perfusion Lung Scintigrams of Patients with CTEPH

N. Skoro-Sajer^{1,4}, A. Bechere², W. Klepetko³, M. P. Kneuss⁴, I. M. Lang¹

¹Department of Cardiology, ²Department of Nuclear Medicine, ³Department of Cardiothoracic Surgery and ⁴Department of Internal Medicine IV, Vienna General Hospital and University of Vienna, Austria

Background Chronic thromboembolic pulmonary hypertension (CTEPH) is the result of single or recurrent pulmonary thromboemboli. Over time thrombi become organised obstructions that are thought to expand by recurrent embolisation and *in situ* thrombosis. We performed a quantitative evaluation of ventilation-perfusion scans (V/Q) in patients with inoperable CTEPH in order to assess the natural history of thrombus expansion.

Methods We prospectively studied 11 CTEPH patients (52 \pm 11 years, 7 females, 4 males) over a period of 32 months. The baseline V/Q scan was obtained at the time of diagnosis. Ventilation imaging used [^{99m}Tc] DTPA aerosol. Planar imaging with intravenous [^{99m}Tc]-labelled human albumin macroaggregates of perfusion scans were reconstructed in eight standard projections. The right lung (RL) and the left lung (LL) were subdivided into an upper (RU; LU), middle (RM; LM) and lower (RL; LL) region of interest (ROI). The ratio of the mean count per pixel in the ROI to the count over the heart was calculated as the Lung/Heart index (L/H). The RL and LL variation coefficient (Vc), i. e. the ratio of the count standard deviation and the average count of the ROI were also evaluated.

Results See Table 3.

Conclusion Lung perfusion scintigrams in patients with inoperable CTEPH show a decrease of segmental flow abnormalities. We speculate that, over time, secondary vascular changes or *in situ* thrombosis occur in the late course of

CTEPH and lead into the scintigraphic pattern of non-thromboembolic pulmonary hypertension.

Preoperative Positive Nitric Oxide (NO) Responder Status is a Predictor of Favorable Haemodynamic Outcome After Pulmonary Thromboendarterectomy in Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

D. Bondermann¹, M. B. Lang¹, S. Rezaie-Majd¹, N. Skoro-Sajer¹, M. Kneuss², W. Klepetko³, L. J. Rubin, I. M. Lang¹

¹Department of Cardiology, ²Department of Internal Medicine IV, ³Department of Cardiothoracic Surgery, University of Vienna, Austria

Background Pulmonary thromboendarterectomy (PTE) is a surgical procedure that provides immediate and permanent relief of the pulmonary hypertension (PH) associated with the sequelae of unresolved pulmonary thromboembolic disease. Roughly 10 % of all procedures fail to relieve PH, despite a sizable amount of thrombus removed during PTE. We tested the hypothesis that preexisting secondary vascular changes determine the postoperative outcome, regardless of the thrombus load.

Methods and Results Right heart haemodynamic evaluation including vasodilator testing was performed in 35 patients prior to (pre) and one year after (post) successful PTE. Haemodynamic response with reduction of pulmonary vascular resistance (PVR) and mean pulmonary arterial pressure (MPAP) ≥ 30 % was observed in 7 patients (20 %). Mean reduction of MPAP under 20 ppm NO was 7.7 \pm 11.4 % (range 32.3 to 17 %), mean reduction of PVR was 10.5 \pm 18.2 (range 48.8 to 22). Preoperative NO-PVR responsiveness correlated with the decrease of PVR expressed as the ratio: PVR_{pre}-PVR_{post}/PVR_{pre} (r = 0.663, p < 0.01). Haemodynamic responsiveness was not related to CTEPH disease type, i.e. proximal versus distal location of thromboemboli. However, in a larger cohort of patients including those in whom surgery had been deferred, distal disease was associated with a significantly higher rate of adverse outcome (death, requirement of prostacyclin therapy or lung transplantation) than proximal disease (87 % versus 20 %, p < 0.01, n = 87).

Conclusion NO-responsiveness is observed in 20 % of CTEPH patients, regardless of the type of disease. NO-responsiveness is a predictor of favourable haemodynamic postoperative outcome.

Infection is a Mechanism Underlying Thrombus Persistence in Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

D. Bondermann¹, E. Ghahrebaghi-Schnell¹, J. Jakowitsch¹, M. Exner², R. Zechner³, S. Rezaie-Majd¹, M. B. Lang¹, Ch. Adlbrecht¹, S. Jamieson⁴, W. Klepetko⁵, I. M. Lang¹

¹Department of Cardiology, University of Vienna, ²Department of Laboratory Medicine, University of Vienna, ³Institute of Molecular Biology, Biochemistry, and Microbiology, University of Graz, ⁴Department of Cardiothoracic Surgery, University of California San Diego, USA, ⁵Department of Cardiothoracic Surgery, University of Vienna, Austria

Background CTEPH is the result of single or recurrent pulmonary thromboemboli, leading to pulmonary hypertension and right heart failure. For reasons still unknown, the vascular obstructions fail to resolve but organize into fibrous structures, thus leading to loss of a functional pulmonary vascular bed.

Tabelle 3: N. Skoro-Sajer et al. Results

	MPAP (mmHg)	CO (l/min)	PVR (Wood)	L/H RU ROI	L/H RM ROI	Vc RL
Baseline	48.4 \pm 14.6	4.0 \pm 0.6	9.8 \pm 4.6	4.2 \pm 1.5	6.9 \pm 2.1	58.5 \pm 7.4
Follow-up	51.3 \pm 8.0	3.8 \pm 0.7	10.2 \pm 3.3	6.5 \pm 2.4	9.4 \pm 2.5	45.5 \pm 0.2
P-value	N.S.	N.S.	N.S.	0.0083	0.0024	0.0017

Methods and Results We hypothesized that an analysis of differential gene expression patterns in CTEPH thrombi compared with parent pulmonary artery might provide a clue to the mechanism of pathologic thrombus organization. A classical differential display approach was chosen to analyse twenty-one CTEPH thrombi obtained sterily during pulmonary thromboendarterectomy, in comparison with pulmonary trunk tissue of patients with segmental disease.

Among the few differentially regulated genes, lipoprotein lipase (LPL) loss from CTEPH thrombi was a consistent finding with several primer combinations.

Accordingly, there was significantly less LPL activity associated with CTEPH thrombus extracts than with pulmonary artery extracts (11.4 [0–27.8] versus 58.6 [8.5–137.2] pmol FFA/mg.minLPL, $p = 0.001$). It has been shown that downregulation of LPL may be caused by infection. In a series of consecutive experiments, serum amyloid A was found elevated in CTEPH patients (10.7 ± 10.8 mg/l), in the absence of clinical and serologic markers of inflammation. In a next step, a thorough analysis of medical conditions associated with CTEPH was undertaken ($n = 111$), disclosing a 5 % prevalence of ventriculo-atrial-shunt, a 7 % prevalence of prior splenectomy, a 4 % prevalence of inflammatory bowel disease, and a 7 % prevalence of previous complicated lower extremity injury. Because all those conditions share a strong predisposition for infection, a conserved 16S-ribosomal DNA primery strategy was used for bacterial profiling of CTEPH thrombi. Eight out of 21 CTEPH clots demonstrated various bacterial species (spp), including *Peptostreptococcus*, *Staphylococcus* and *Corynebacterium* spp.

Conclusion The data suggest that infection may play a role in the pathogenesis of CTEPH.

Splenectomy and the Risk of Chronic Thromboembolic Pulmonary Hypertension

D. Bondermann¹, S. Rasoul-Rockenschaub², M. B Lang¹, C. Adlbrecht¹, C. Baytaroglu¹, W. Klepetko², M. P. Kneuss³, M. Schemper⁴, I. M. Lang¹

¹Department of Cardiology, ²Department of Surgery, ³Department of Internal Medicine IV, ⁴Department of Medical Computer Sciences, University of Vienna, Austria

Background Chronic thromboembolic pulmonary hypertension (CTEPH) is the result of single or recurrent pulmonary thromboemboli. For reasons still unknown the pulmonary arterial obstructions fail to resolve and result in severe pulmonary hypertension that develops over decades.

Methods Because of case observations reporting an association between splenectomy and pulmonary hypertension, we performed a case-control-study examining the frequency of prior splenectomy in 110 consecutive CTEPH patients and 300 controls. A careful diagnostic dissection between CTEPH and non-thromboembolic pulmonary hypertension was undertaken by ventilation/perfusion scintigrams, multi-detector computed tomography and pulmonary angiography. Control subjects were individuals admitted to the cardiology department for diagnosis/treatment of coronary artery disease with normal resting pulmonary haemodynamics documented by echocardiography. Controls who were on oral anticoagulation were excluded.

Results 10 of 110 CTEPH patients (9 %) had undergone splenectomy 36–600 months (mean 221 months) prior to diagnosis, while only one splenectomized control (0.3 %) was identified. Reasons for splenectomy were malignancy ($n = 3$), haemolytic anaemia ($n = 3$), trauma ($n = 2$), or complicated abdominal surgery ($n = 2$). In a multiple logistic regression analysis, none of these conditions was by itself a risk factor for CTEPH. In contrast, splenectomy was an independent risk factor (relative risk 24.31; 95 percent confidence interval, 5.31 to 219.33; $p < 0.0001$) after adjustment for sex and age.

Discussion Patients after splenectomy have an increased risk of CTEPH. The underlying mechanisms and the need for early anticoagulation remain to be clarified.

Poster Presentation VII: Miscellaneous II

White-Coat Hypertension and Target Organ Damage – A Systematic Review and Meta-Analysis: Preliminary Results

E. Riedmueller, U. Derhaschnig, A. N. Laggner, M. M. Hirschl, M. Muellner
Department of Emergency Medicine, University of Vienna, Austria

Background There is a continuing debate whether white-coat hypertension is an innocent phenomenon or whether it carries an increased burden of cardiovascular risk and requires treatment. We performed a systematic review of the literature to assess the association between isolated office hypertension and target organ damage, morbidity and mortality.

Methods We searched MEDLINE, EMBASE, PASCAL, and the Cochrane Controlled trial register. The search terms were [(white and coat or white-coat) and hypertension] and (isolated near office and hypertension) and (target organ damage). Hypertension related endpoints were defined as acute myocardial infarction, stroke, congestive heart failure, any death of cardiovascular cause, or hypertensive target organ damage (left ventricular hypertrophy, microalbuminuria, retinopathy).

Results The electronic search revealed 1004 hits and we retrieved 15 studies, including 1832 patients with WC hypertension and 1720 normotensive controls. The quality of these studies was generally low: all studies used different definitions of which 3 fulfilled the Task Force IV criteria for WC hypertension; in 8 studies blinding of outcome assessment was unclear; in 10 studies recruitment of participants was unclear. The mean systolic WC effect was 23 mmHg (95 % CI 18 to 29); the mean diastolic effect was 16 mmHg (13 to 20). Only 2 studies reported a clinical endpoint (mortality), which was comparable between WC patients and controls (odds ratio 0.92, 95 % CI 0.64 to 1.27). Echocardiographic data (10 studies): left ventricular mass index was not different between the groups (mean difference 4 g/m² (–52 to 61)); the diastolic interventricular septum diameter was 0.45 mm thicker (0.29 to 0.62) in the WC group; posterior wall thickness was also higher (mean difference 0.47 mm, 0.3 to 0.6). Severity of microalbuminuria was not different between groups (2 studies). Only one small study reported retinopathy (no difference).

Conclusion Study recruitment is ongoing. WC hypertension is associated with a moderate increase in ventricular wall thickness. There is not enough information available whether white coat hypertension translates into adverse clinical outcomes.

Donor and Recipient Risk Factors of Coronary Artery Disease in Heart Transplant (HTx) Recipients

B. Stanek, C. Springer, J. Bialy, P. Wexberg, R. Pacher, A. Zuckermann, M. Grimm, E. Wolner, S. Rödler
Department of Cardiology and Cardiothoracic Surgery, University of Vienna, Austria

Background Transplant coronary artery disease (TxCAD) is a serious, progressive complication after heart transplantation resulting in myocardial infarction, graft failure and death. Therefore, identification of factors foretelling TxCAD is an important area, with the potential to assist in the prevention of TxCAD-related events and to prolong posttransplantation survival.

Methods and Results To evaluate potential donor and recipient related predictive factors of TxCAD we retrospectively reviewed serial coronary angiograms at 6 (A1), 7 to 18 (A2), 19 to 36 (A3), 37 to 54 (A4), and 55 to 108 months (A5) of 702 patients (590 m, 112 f, 49 ± 12 y, 58 % ischaemic, 30 % idiopathic, 12 % other dilated cardiomyopathy). TxCAD was defined as any reduction in the caliber of a primary epicardial coronary artery imaged by angiography. In selected patients without angiographic lesions intracoronary ultrasound was additionally performed. Cut-off value of intimal thickening was 0.3 mm (Table 4).

Table 4: B. Stanek et al.

	Patients (n)	TxCAD (n)	≥ 0.3 mm (n)
A1	252	26	12
A2	451	65	30
A3	378	70	49
A4	355	79	73
A5	534	154	170

In multivariate regression analysis presence of angiographic TxCAD was independently related to donor factors (age > 40 yrs, $p < 0.0001$; male gender, $p < 0.01$; fibrinogen plasma level, $p < 0.01$) and recipient factors (posttransplantation years, $p < 0.01$; pretransplant hypertension, $p < 0.01$; male gender, $p < 0.05$).

Conclusion To investigate the speed of TxCAD acceleration and to identify patients at highest mortality risk further studies are necessary.

Acute Hyperhomocysteinaemia Induces Reversible Endothelial Dysfunction in Resistance Vessels and Decreases Myocardial Perfusion in CAD-Patients

O. Stanger¹, P. Rehak², R. Konetschny¹, B. Rigler¹, R. Rienmueller³

¹Department of Cardiac Surgery, ²Department of Biomedical Engineering, Computing and Statistics, ³Department of Radiology, Cardiac Imaging; Clinical Research Group Homocysteine and Endothelium, Graz, Austria

Background Homocysteine (tHcy) is an established risk factor for atherosclerosis and endothelial injury. We demonstrated impaired endothelial function of resistance vessels in the forearm of CAD-patients and significant improvement through tHcy-lowering therapy. Organ perfusion is regulated at the level of resistance vessels. The effect of hyperhomocysteinaemia (HHcy) on myocardial perfusion is unclear and has not been investigated before.

Methods 50 male revascularised CAD-patients (mean age 54.9 ± 8.5) were randomly assigned to undergo an oral methionine loading test (oMLT, $n = 30$) or intake of placebo ($n = 20$) in a double-blinded design. Myocardial perfusion was measured non-invasively at baseline and after 4 hours through electron-beam-computed-tomography (EBCT) using intravenous contrast agent. Blood pressure (BP) and a heart rate (HR) variance of max. $\pm 5\%$ was tolerated for analyses.

Results Cardiac variables and major risk factors did not differ between groups and BP was unchanged in all subjects between investigations. In the group undergoing oMLT, tHcy increased 3.2-fold and myocardial perfusion decreased significantly (-6.6% , mean 61 to 57 ml/min/100 g [left ventricular mass, LVM]). tHcy remained unchanged in the placebo group with increase of myocardial perfusion ($+5.2\%$). Myocardial perfusion was only influenced by changes in tHcy and HR between measurements. The effect of HHcy on myocardial perfusion remained significant between groups after correcting for HR ($p = 0.03$).

Conclusion Our data provide strong evidence for a beneficial effect of homocysteine-lowering on endothelial dysfunction and myocardial malperfusion in CAD-patients.

Parallel Existence of Constrictive and Expansive Remodelling in Patients With Peripheral Occlusive Arterial Atherosclerosis Assessed by Intravascular Ultrasound

C. Strehblow, M. Gyöngyösi, W. Sperker, P. Wexberg, M. Haumer, E. Minar, D. Glogar
Division of Cardiology, University of Vienna, Austria

Background Intravascular ultrasonography (IVUS) revealed different types of remodelling in human coronary arteries. Pathological examinations and IVUS in peripheral arteries suggested the existence of constrictive and expansive remodelling in the same artery.

The aim was to investigate the different remodelling types with IVUS and correlate them with the patient's demographics and morphological features of peripheral atherosclerosis.

Methods After diagnostic femoral arteriography in 45 patients (26 male, 70 ± 10 y) with peripheral artery disease, IVUS was performed and analysed computer-assisted (EchoPlaque 2, INDEC Systems, USA). After 3D-reconstruction of the vessel, lumen, plaque and vessel volume, the minimal lumen area (LA), maximal vessel area (VA) and maximal percentage area stenosis (% AS) were calculated automatically.

Results Plaque area correlated positively with VA ($r = 0.777$, $p < 0.001$). Bidirectional changes in VA were observed in response to plaque growing; the dominant feature of arterial remodelling of the vessel was the compensatory enlargement up to 50 % AS (VA 27.1 ± 6.7 mm²) and a gradual constriction between 51 % and 80 % AS (VA 19.0 ± 4.3 mm²), with no further change above 81 % AS (VA 19.4 ± 4.5 mm²). Individual regression plots of plaque and vessel areas revealed the parallel existence of expansive and constrictive remodelling in all patients. Graphical reconstruction demonstrated domination of expansive remodelling in 11 patients (24.5 %), of constrictive in 10 patients (22.2 %), and both types in 24 (53.3 %) patients. Patients with dominant expansive remodelling had higher C-reactive protein levels (1.81 ± 2.4 vs 0.23 ± 0.32 and 0.28 ± 0.43 , $p = 0.037$) than those with dominant constrictive or mixed remodelling.

Conclusion The co-existence of expansive and constrictive remodelling was found in all patients with peripheral occlusive arterial disease, but in some patients, the dominant type of arterial remodelling was expansive or constrictive. The changes in vessel size proved to be at least partly independent of the growing plaque, as the same plaque amount was associated with different vessel sizes.

Echocardiographic Data Predicts Renal Complications in Infective Endocarditis

R. Arzanauskienė, P. Zabiela

Kaunas University Hospital, Department of Cardiology, Lithuania

Aim of the Study To evaluate echocardiographic variables on prognosis of renal complications in infective endocarditis (IE).

Methods and Patients During 1999–2001 131 patients with IE (106 definite and 25 possible according to the Duke criteria) were observed. TTE was performed in all and TEE in 60.3 % cases. Mobility, density and extent of vegetations were graded on a scale of 1 to 4. Valvular insufficiency was graded on a scale of 0 to 4. Glomerulonephritis was diagnosed in 55 (42 %), renal insufficiency without signs of glomerulonephritis in 12 (9.2 %) cases.

Results IE induced glomerulonephritis was most frequent in aortic valvulitis ($p = 0.002$), it was associated with vegetations of IV° mobility ($p = 0.003$) and higher length ($p = 0.03$), with *S. aureus* septicaemia ($p = 0.04$), with other immunologically mediated lesions: hepatitis ($p = 0.0001$), myocarditis ($p = 0.01$), pericarditis ($p = 0.0005$), peripheral cutaneous phenomena ($p = 0.02$) and with increased mortality ($p = 0.04$).

Renal insufficiency without signs of glomerulonephritis was associated with vegetation extent of grade III–IV ($p = 0.04$), with perforation of aortic valve ($p = 0.04$), grade of aortic insufficiency ($p = 0.001$), NYHA f. cl. ($p = 0.04$) and renal infarction ($p = 0.03$).

Increased risk of glomerulonephritis was associated with IV° vegetation mobility (OR = 6.00, $p = 0.0023$) and with IV° density (OR = 4.55, $p = 0.013$).

Higher incidence of glomerulonephritis was associated with vegetation length > 11 mm ($p = 0.042$).

Conclusions 1. Increased risk of IE induced glomerulonephritis is related to vegetation length above 11 mm, IV° mobility and IV° density. 2. Renal insufficiency without signs of glomerulonephritis is associated with III–IV° of vegetation extent and with haemodynamically significant lesions: aortic valve perforation and grade of aortic insufficiency.

Interleukin 1 Receptor Antagonist Genotype is Associated With Coronary Atherosclerosis in Patients With Type 2 Diabetes

R. Marculescu¹, G. Endler¹, M. Schillinger², N. Iordanova³, M. Exner¹, E. Hayden⁴, K. Huber³, O. Wagner¹, Ch. Mannhalter¹

¹Department of Laboratory Medicine, ²Department of Internal Medicine II, Division of Angiology, ³Department of Cardiology, ⁴Department of Business Administration, School of Business, Economics and Computer Science, University of Vienna, Austria

Recently, inflammation received considerable attention in the pathogenesis of both type 2 diabetes and atherosclerosis. Interleukin 1 receptor antagonist (IL-1ra) is a major modulator of the interleukin-1 proinflammatory pathway. We studied the relationship between a variable number tandem repeat (VNTR) polymorphism in intron 2 of the IL-1ra gene (IL1RN) and CAD in patients with and without type 2 diabetes. 787 consecutive patients admitted for suspected CAD were included in the study. According to the current criteria of the American Diabetes Association (ADA) 250 patients had type 2 diabetes mellitus. In this group of patients allele 2 carriers (n = 108) had an increased prevalence of CAD (85.2 %) compared to non-carriers (73.2 %), which remained significant in a multivariate logistic regression model (odds ratio [OR] 2.2, 95 % CI 1.1–4.3, p = 0.02). No association of CAD with allele 2 carrier status was present among non-diabetic patients (n = 527). ELISA assays showed decreased baseline plasma levels of IL-1ra in patients with type 2 diabetes, which may in part explain the role of the IL1RN VNTR in these patients.

Poster Presentation VIII: Invasive Cardiology

Dose Attenuation of Vascular Brachytherapy Sources by Atherosclerotic Vessels: An *Ex Vivo* Dosimetry Study

P. Wexberg¹, C. Kirisits², D. Berger², I. Sulzbacher³, G. Maurer¹, D. Georg², R. Potter², D. Glogar¹

¹Department of Cardiology, ²Department of Radiotherapy and Radiobiology, ³Department of Pathology, University of Vienna, Austria

Background Dose prescription and reporting in vascular brachytherapy is based on the assumption that the vessel wall is water equivalent, which does not consider a possible dose perturbation by atherosclerotic plaque. The actual attenuation has never been measured to our knowledge.

Methods Sr/Y-90 and Ir-192 sources for vascular brachytherapy were fixed to an irradiation phantom embedded in water-equivalent gel in order to deliver a reference dose at 2.5 mm distance. The delivered doses from the source with and without human peripheral arteries surrounding the delivery catheter were read from the radiochromic films. Plaque and vessel wall thickness were measured from HE-stained vessel sections using light microscopy. We assessed 19 sections irradiated with Sr/Y-90 and 7 sections irradiated with Ir-192. The attenuated dose was expressed as ratio of the reference dose, and this ratio was correlated with plaque thickness at the corresponding vessel section based on an exponential function. The attenuation coefficient of atherosclerotic plaque (μP) and of vessel wall (μW) was calculated by regression analysis.

Results The dose attenuation of beta-radiation correlated strongly with maximal plaque thickness ($r = 0.877$, $p < 0.001$), whereas we detected no correlation for gamma-radiation. The attenuation did not correlate with the thickness of the non-diseased vessel wall. μP for radiation delivered from Sr/Y-90 was 0.61, μW was 0.03, whereas the attenuation of Ir-192 was below the measurement uncertainties. In our calculation model a non-diseased arterial wall of 1 mm thickness results in a dose decrease of only 3 %, whereas plaque of the same thickness increases the attenuation to 50 %.

Conclusions Plaque thickness should be considered for future evaluation of dose prescription calculations in vascular brachytherapy with beta-radiation.

Autologous Stem Cells Injection in a Patient After Acute Myocardial Infarction

G. Beran¹, H. Sochor¹, A. Kocher², M. Gyöngyösi¹, M. Dettke³, G. Maurer¹, D. Glogar¹, I. M. Lang¹

¹Department of Cardiology, ²Department of Cardiac Surgery, ³Department of Transfusion Medicine, University of Vienna, Austria

Introduction Experimental data suggest that injection of adult bone marrow (BM) stem cells into the border zones of infarcted heart muscle may reduce myocardial infarction (MI)-size by affecting myocardial remodeling.

Methods and Results A 57-year old male with acute anterolateral MI was initially treated with thrombolysis. Coronary angiography demonstrated severe 1-vessel LAD disease with diffuse lesions not suitable for PCI. 6 weeks post infarction BM stem cells were harvested by aspiration from the iliac crest hipbone and injected intramyocardially. Injections were guided and performed with NOGA-mapping and -injection needle (Biosense Webster). A total of 2×10^9 BM stem cells (5.2 ml) were implanted at 12 different sites into the transition zone between scar and viable myocardium into the anterolateral and -septal region.

Procedural time was 4 hours; no intra- or postinterventional complications occurred. Haemoglobin dropped from 14.1 to 9.8 on day two, but rose to 13.1 g/dl at discharge one week later. Myocardial perfusion imaging (MPI) was performed before, 3 and 6 months after stem cell implantation. Compared to initial MPI, polar map analysis showed decrease in rest extent (34 % to 25 %) of perfusion-defect 6 months after stem cell transplantation. In addition left ventricular ejection fraction (EF) obtained by gated SPECT improved from 33 % to 41 %. NOGA unipolar map showed an increase of 2.6, 1.7 mV and 1.5, 0.3 mV in the mid and basal portion of the septal and lateral segments, respectively. CCS Score decreased from CCS III at baseline to CCS I at follow-up.

Conclusion Intramyocardial injection of BM stem cells was safe and feasible in a patient with recent acute MI. The decrease in MPI rest extent after 6 months and improvement of EF may indicate beneficial remodelling.

Geographical Miss During Intracoronary Irradiation: Impact on Restenosis and Determination of Required Safety Margin Length

B. Syeda¹, P. Siostrzonek¹, R. Schmid¹, P. Wexberg¹, Ch. Kirisits², St. Denk¹, G. Beran¹, A. Khorsand¹, I. M. Lang¹, B. Pokrajac¹, R. Potter², D. Glogar¹

¹Department of Cardiology, ²Department of Radiotherapy and Radiosurgery, University of Vienna, Austria

Objective We aimed to evaluate the incidence and effects of underdosage of injured segments during intracoronary irradiation, and define the minimal length of safety margin required to avoid mismatched source placement.

Background Underdosage of injured segments due to misplacement of the active source has been suggested as underlying mechanism for the occurrence of edge restenosis.

Methods Baseline angiograms of 112 vessels in 109 patients with instant restenosis undergoing coronary reintervention followed by intracoronary irradiation (¹⁹²Ir: Checkmate™, Cordis; ³²P: Galileo™, Guidant; ⁹⁰Sr/Y: Beta-Cath™, Novoste) were analysed. The distances between outermost injury and outermost end of reference isodose length (RIL) were measured. RIL was defined as segment with ≥ 90 % of reference dose at 1 mm vessel wall depth, edges of irradiation as segment with 10 %–90 % of reference dose at 1 mm vessel wall depth (dose fall-off zone), negligible irradiation as segment with < 10 % of reference dose at 1 mm vessel wall depth, safety margin as the distance between outermost injury and outermost end of RIL, geographical miss (GM) as complete injured segment not covered by RIL and no-GM as complete injured segment covered by RIL. Restenosis was defined as percent diameter stenosis > 50 %.

Results Baseline angiographic analysis was performed for 224 edges in 112 vessels. GM was found in 46 (20.6 %) edges. The incidence of target lesion restenosis within the 78 vessels with available angiographic follow-up was 43.3 % for patients with GM vs. 14.9 % for patients with no-GM ($p = 0.005$). The incidence of restenosis at the dose fall-off zone was higher in patients with GM (16.7 %) than in patients with no-GM (4.3 %) ($p = 0.01$). Analysis of various injured segments exposed highest restenosis rates in injured segments with negligible irradiation (27.8 %) in comparison to injured segments with dose fall-off (16.7 %) or injured segments with full dose irradiation (7.7 %) ($p = 0.006$). According to the Receiver Operating Curve Analysis a safety margin length of 10 mm is required per vessel (i.e. 5 mm safety margin for each edge) to achieve 95 % true negative rate of GM.

Conclusion GM is associated with a higher incidence of restenosis at the corresponding edges. Restenosis was more pronounced in injured segments with negligible irradiation than in injured segments at the dose fall-off zones. A safety margin of at least 10 mm per vessel is recommended in order to minimize GM and thus achieve optimal long-term outcome.

Venous Pressure Dynamics During Pressure Controlled Intermittent Coronary Sinus Occlusion (PICSO) Reflect Myocardial Perfusion

I. Kajgana¹, G. Christ², D. Glogar², G. Maurer², W. Mohl¹

¹Department of Cardiothoracic Surgery, ²Department of Cardiology, University of Vienna, Austria

Background About 75 % of the myocardial perfusion drains via the coronary sinus into the right atrium. Pressure controlled intermittent occlusion (PICSO) of the coronary venous outflow produce an elevation of the venous pressure. Previous observations suggested that both myocardial perfusion as well as myocardial force can be related to the coronary venous pressure dynamics during PICSO.

Methods 4 cycles of coronary artery occlusions with subsequent reperfusion (5 minutes proximal LAD occlusion; 5 minutes reperfusion) were performed in 3 adult anaesthetised sheep. PICSO was performed using a coronary sinus balloon occlusion. Coronary venous pressure readings were continuously monitored, digitised and analysed.

Results A significant difference could be observed in the time to reach the plateau and in the pressure reached during these occlusions (Tab. 5).

Conclusion This analysis confirms earlier observations that coronary venous pressure dynamics reflect myocardial perfusion. Since myocardial perfusion cannot be accessed easily, continuous monitoring of coronary venous pressure dynamics during PICSO opens a new horizon in monitoring myocardial performance during ischaemia. Pending clinical studies will elucidate the potential of coronary venous monitoring as a valuable parameter to control changes in myocardial perfusion as they occur in revascularisation procedure.

Arterial Closure Devices After Cardiac Catheterization – Preliminary Results of a Systematic Review and Meta-Analysis

E. Riedmueller, M. Koreny, M. Nikfardjam, P. Siostrzonek, A. N. Laggner, M. Muellner
Department of Emergency Medicine, and Department of Cardiology, University of Vienna, Austria

Background Arterial closure devices (ACD) have been developed to avoid manual compression (MC) and bed rest after percutaneous cardiac catheterization. In this study we perform a systematic review of randomised controlled trials comparing frequently used ACD and MC in diagnostic and interventional procedures.

Methods We searched MEDLINE, EMBASE, PASCAL, BIOSIS, CINHALL, and the Cochrane Controlled Trial Register. The search terms were: vascular or arterial closure device, sealing device, suture

Tabelle 5: I. Kajgana et al.

	LAD occluded	LAD open	
CSOP syst [mmHg]	45.28 ± 23.96	103.80 ± 21.26	$p < 0.005$
CSOP diast [mmHg]	21.72 ± 4.17	44.75 ± 3.84	$p < 0.001$
Time 100 % syst [s]	7.17 ± 0.36	2.30 ± 0.14	$p < 0.000$
Time 100 % diast [s]	5.33 ± 0.84	1.88 ± 0.43	$p < 0.014$

device, haemostatic puncture closure device, vascular haemostatic device, Vasoseal, Angioseal, Duett, Perclose, Prostar Plus, and Techstar. We included randomised controlled trials only. Endpoints were time to haemostasis, time to ambulation, haematoma, bleeding and need for surgical repair.

Results The electronic search revealed 944 hits and finally 24 studies, with a total of 6186 patients, were included. Quality was generally poor. 9 trials compared time to haemostasis (intervention group $n_i = 1015$, control group $n_c = 1001$): the mean difference was 12 min (95 % CI 7–17). Time to ambulation (4 studies, $n_i = 515$, $n_c = 522$) was 8.6 hrs less in the intervention group (95 % CI 6.5–10.8). 15 studies assessed the occurrence of a local haematoma ($n_i = 1079$, $n_c = 955$). The risk of haematoma was lower when an ACD was used (risk ratio 0.7, 95 % CI 0.5–0.99). When excluding one study, which did not use intention-to-treat analysis this difference was not significant anymore. Local bleeding (7 studies, $n_i = 852$; $n_c = 750$) was not different between the groups (0.9, 0.5–1.9). The risk of a local surgical intervention (8 studies, $n_i = 980$, $n_c = 876$) was non-significantly increased in the intervention group (1.7, 0.7–4.0) but increased even further when excluding the one study not using intention-to-treat analysis (2.3, 0.9–5.8).

Conclusion ACD reduces time to haemostasis as well as time to ambulation. Its effect on the risk of haematoma and the need for surgical repair is unclear. Bleeding appears to be comparable in both interventions.

Improved Stent Design Contributes to a Less Incidence of Major Adverse Cardiac Events. Comparison of Different Stents

M. Gyöngyösi, W. Sperker, C. Strehblow, A. Khorsand, P. Wexberg, D. Glogar
Department of Cardiology, University of Vienna, Austria

Aim of the Study The aim of the present study was to examine the effect of stent design on clinical outcome after different intra-coronary stent implantation in patients with significant coronary artery disease.

Methods Clinical, qualitative and quantitative angiographic data on 140 patients with Palmaz-Schatz, 280 patients with AVE Micro and GFX, 340 patients with Multilink Duett and 194 patients with Sequence/Sequest stent implantations were compared. The occurrence of major adverse events (MACE, acute myocardial infarction, death of any origin, coronary revascularization) during the 8 ± 3 months follow-up (FUP) was recorded for all patients. Receiver operator characteristics (ROC) analysis was used to determine the cut-off points of angiographic parameters in prediction of MACE.

Results The baseline clinical and angiographic parameters did not differ between the four groups. The acute stent thrombosis (2.1 %, 1.1 %, 0.6 % and 0 % by using Palmaz-Schatz, AVE, Multilink Duett and Sequence/Sequest stents), subacute stent thrombosis (2.9 %, 2.1 %, 0.9 % and 0.5 %; in the four groups, respectively) decreased significantly. Significantly less incidence of composite MACE occurred by using the two newer generations of stents (29.3 %, 30.7 %, 10 % and 7.7 % by implantation of Palmaz-Schatz, AVE, Multilink Duett and Sequence/Sequest stents, respectively). ROC analysis revealed significantly ($p < 0.05$) smaller pre-stent reference diameter (RD) and post-stent minimal lumen diameter (MLD) cut-off values predicting MACE; for pre-stent RD: 3.16 mm (predictive accuracy/p. a. 0.678) for Palmaz-Schatz; 2.9 mm (p. a. 0.615) for AVE; 2.72 mm (p. a. 0.68) for Multilink Duett and 2.77 mm (p. a. 0.63) for Sequence/Sequest stent implantations; for post-stent MLD:

2.75 mm (predictive accuracy/p. a. 0.66) for Palmaz-Schatz; 2.62 mm (p. a. 0.67) for AVE; 2.53 mm (p. a. 0.636) for Multilink Duett and 2.45 mm (p.a. 0.657) for Sequence/Sequest stent implantations.

Conclusions Improvement of stent design led to a marked decrease in incidence of adverse events, even in small vessel interventions.

Results of the "GENIUS REGISTRY". Final Report of the "GENIUS REGISTRY" of the Angiographic Core Lab of the University of Vienna

M. Gatterer, M. Gyöngyösi, W. Sperker, C. Strehblow, I. M. Lang, P. Siostrzonek, H. Sochor, D. Glogar

Department of Cardiology, University of Vienna, Austria

Aim of the study The study objective was to establish the angiographic results immediately after Genius stent implantation and at the 1 and 6-month follow-up.

Methods Genius stent (Eurocor, Bonn, Germany) was implanted as usual in 40 patients (61.2 ± 11.6 y, 35 % men) in the Cath Lab of University of Vienna. All patients were clinically controlled 30 days and 6.2 ± 1.6 months after the stent implantation. Control coronary angiography after the follow-up was performed in 25 (63 %) patients. The primary endpoint of the study was the 1) occurrence of acute and subacute stent thrombosis; 2) prevalence of target lesion restenosis and target lesion revascularization; 3) occurrence of major adverse cardiac events (MACE) during the follow-up period.

Results The Genius stent was implanted in *de novo* lesion in 36 pts (90 %), 5 pts (12.5 %) had 3-vessel disease. Primary stenting occurred in 22 pts (55 %), the stent/lesion ratio was 1.05. The mean size of implanted stents was 3.0 ± 0.4 mm in diameter and 14 ± 5 mm in length. No stent delivery failure occurred. During the first 30 days, one (2.5 %) patient had developed angina pectoris, and an early coronary angiography revealed target lesion restenosis. During the follow-up, no acute myocardial infarction or death occurred in 40 patients. Coronary angiography on 25 pts revealed target lesion restenosis in 4 patients and target vessel restenosis in another 1 patient. The acute lumen gain (difference between post- and pre-stent minimal lumen diameter) was 1.39 ± 0.38 mm, the late lumen loss (difference between post-stent and follow-up minimal lumen diameter) was 0.34 ± 0.31 mm. The follow-up minimum lumen diameter was 1.96 ± 0.56 mm, the %diameter stenosis 27.8 ± 13.5 %.

Coronary reintervention due to in-stent restenosis was performed in 3 patients (7.5 %). Thus, the occurrence of the follow-up composite major adverse cardiac events was 7.5 %.

Conclusions: Genius stent implantation leads to low angiographic restenosis rate of 12.5 % with a 7.5 % overall rate of major adverse cardiac events after 6-month follow-up.

Pressure Controlled Intermittent Coronary Sinus Occlusion (PICSO) as Salvage of the Ischaemic Myocardium: Meta-Analysis

B. Syeda¹, Ch. Schukro¹, G. Heinze¹, G. Christ¹, D. Glogar¹, G. Maurer¹, W. Mohr²
¹Department of Cardiology, ²Department of Cardiothoracic Surgery, University of Vienna, Austria

Background Pressure Controlled Intermittent Coronary Sinus Occlusion (PICSO) has been described to be effective in salvaging ischaemic myocardium in different experimental models of coronary artery occlusions and during reperfusion. This meta-analysis aims to review the safety and efficacy of PICSO as myocardial salvage in terms of reduced infarct size in experimental models.

Methods Medline research was performed to review published literature on PICSO. Study inclusion criteria were randomised, placebo controlled trials with area of infarction (expressed as a percentage of the area at risk) as primary endpoint. Meta-analysis was performed with Review Manager Version 4.1. All standard error of mean (SEM) were converted to standard deviation (SD) by $SD = SEM \times \sqrt{n}$.

Results 10 experimental trials comprising 171 test animals were found to meet the inclusion criteria (time interval: 1984–2000). Meta-analysis exhibited a weighted mean difference of –40.0 % with confidence interval between –48.2 % and –31.7 % (test for overall effect: p-value p < 0.0001, chi-square test for heterogeneity: p-value < 0.00001). Funnel-block analysis revealed no significant publication bias within the analyzed trials.

Conclusion This current meta-analysis confirms earlier small-scaled trials that demonstrated a potent anti-ischaemic effect of intermittent coronary sinus occlusion. The use of PICSO significantly decreases ischaemic damage during coronary occlusion in experimental models. In-depth research needs to be performed in this field in order to impart this benefit to the ischaemic human myocardium in the clinical routine.

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