

fluenced diameter of left ventricle but slightly improved LV contractility. Antibiotic treatment was most effective in pts with of significant ventricular arrhythmias and atrio-ventricular conduction disturbances.

P1246 Prevalence and prognostic significance of adrenergic escape under chronic beta-blocker therapy in patients with chronic heart failure

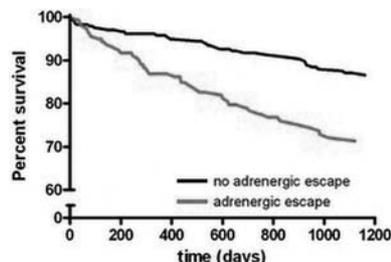


L. Frankenstein, C. Zugck, D. Schellberg, H. Froehlich, M. Nelles, H. Katus, A. Remppis. *University of Heidelberg, Cardiology Dept., Heidelberg, Germany*

Purpose: Systemic neurohumoral activation has been described as the pathophysiological basis of chronic heart failure (CHF). Therefore, similar to aldosterone escape to ACE-inhibitors, an adrenergic escape (AE) to chronic stable betablocker therapy would appear conceivable in CHF. As this has not been directly investigated before, we sought to examine the prevalence and prognostic value of AE in CHF on chronic stable betablocker therapy with respect to different betablocker agents and doses.

Methods: 415 patients with systolic CHF were included in a prospective, observational study and followed up for 71 (57 – 94) months. AE was defined by noradrenaline levels above the upper limit of normal. All-cause mortality was the predefined endpoint.

Results: Irrespective of the individual betablocker agent and the dose equivalent taken, the prevalence of AE was 38%. Noradrenaline levels neither correlated with heart rate ($r=0.02$; 95%CI: $-0.08 - 0.11$; $p=0.74$) nor were they related to underlying rhythm ($p=0.09$) or individual betablocker agents ($p=0.87$). The presence of AE was a strong and independent indicator of mortality (adjusted HR: 1.915; 95%CI: 1.387-2.645; Chi-square: 15.60).



Mortality according to adrenergic escape.

Conclusion: We verified the presence of AE in CHF patients with chronic stable betablocker therapy irrespective of the individual beta-blocker agent and the dose equivalent. As AE might indicate therapeutic failure, the determination of AE could help identifying those patients with CHF that might benefit from more aggressive treatment modalities. Heart rate, however, is not a surrogate for adrenergic escape.

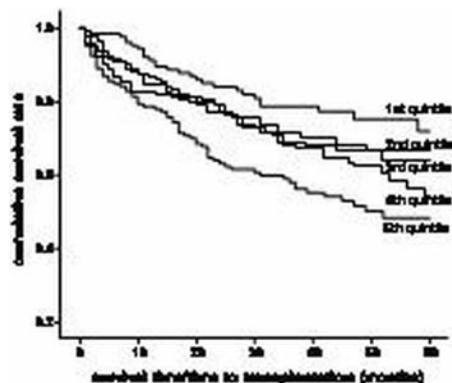
P1247 Prevalence and prognostic significance of gamma-glutamyltransferase (GGT) in chronic heart failure



C. Eberl, H. Achrainger, J. Doerler, H. Ulmer, O. Pachinger, M. Frick, G. Poelzl. *Medical University Innsbruck, Cardiology, Innsbruck, Austria*

Purpose: Recent evidence suggests that serum gamma-glutamyltransferase (GGT) level is associated with incident coronary heart disease, stroke and a risk factor for cardiovascular disease mortality. The aim of our study was to investigate the relevance of this novel cardiovascular risk factor in heart failure.

Methods: From 2000 to 2007 clinical and laboratory parameters of 1023 outdoor



5-years cumulative event rate.

heart failure patients were evaluated. Long-term follow-up (mean 34.4 months) was available in 657 patients. The primary endpoint was defined as death or heart transplantation. Sex stratified Cox proportional hazards models, adjusted for age and established risk factors were performed to calculate hazard ratios (HR) and 95% confidence intervals per quintiles of GGT.

Results: Prevalence of elevated GGT was 43.3% in men (GGT >65 U/l) and 51.6% in women (GGT >38 U/L), which was significantly higher as compared to healthy subjects (21.9% in men, 15.6% in women). GGT was correlated with severity of heart failure as assessed by NYHA class ($r=0.22$; $p<0.001$) but not with LV-ejection fraction. Death of any cause or transplantation was recorded in 253 patients. Compared to the lowest GGT quintile, adjusted HR for patients in the highest quintile were 1.58 (1.00 – 2.50), 1.37 (0.85 – 2.21) in the fourth quintile, 1.20 (0.74 – 1.96) in the third quintile and 1.30 (0.79 – 2.15) in the second quintile ($p<0.05$). Corresponding five years cumulative survival/time to transplantation rates were 48%, 53%, 66%, 63%, and 72%.

Conclusions: These results provide evidence of a high prevalence of elevated GGT levels in chronic heart failure patients and of a positive association between high GGT and death or heart transplantation in these patients. Our findings further highlight the clinical importance of GGT in cardiovascular disease.

P1248 Clinical and prognostic value of serum prolactin levels in patients with chronic heart failure



D. Farmakis, J.T. Parissis, M. Nikolaou, A. Rigas, V. Bistola, K. Venetsanou, G. Filippatos, D. Kremastinos. *Attikon University Hospital, Athens, Greece*

Aim: Hypothalamic axis dysregulation is associated with the clinical severity of chronic heart failure (CHF) and the presence of depression. In a small clinical study, serum prolactin as a marker of this dysregulation, has been correlated with the immune activation in idiopathic dilated cardiomyopathy. We sought to investigate the relationship of serum prolactin levels with neurohormonal/immune activation and depressive symptoms of CHF patients, as well as their long-term prognostic significance in these patients.

Methods: Serum prolactin was measured in 180 CHF patients (aged 65 ± 12 , mean left ventricular ejection fraction $27 \pm 7\%$). Plasma B-type natriuretic peptide (BNP), 6-minute walked distance, Zung self-rating depression scale (SDS), cytokines (IL-6, IL-10, TNF- α), endothelial adhesion molecules (ICAM, VCAM) and apoptotic mediator (Fas, Fas-ligand) were also assessed. Patients were followed for 8 months for major cardiovascular events (MACE), including death or hospitalization for cardiovascular causes.

Results: Prolactin levels were significantly correlated with New York Heart Association (NYHA) class ($r=0.394$, $p<0.001$), 6-minute walked distance ($r=-0.353$, $p<0.001$), left ventricular ejection fraction ($r=-0.314$, $p<0.001$), BNP ($r=0.374$, $p<0.001$), Zung SDS ($r=0.544$, $p<0.001$), IL-6 ($r=0.451$, $p<0.001$), IL-10 ($r=0.426$, $p<0.001$), TNF- α ($r=0.310$, $p=0.001$), Fas ($r=0.333$, $p<0.001$), Fas-ligand ($r=0.517$, $p<0.001$), ICAM ($r=0.409$, $p<0.001$) and VCAM ($r=0.480$, $p<0.001$). Prolactin was significantly higher in patients with a positive Zung SDS (≥ 40) than in those with a negative (<40) score (10.7 ± 5.4 ng/mL versus 6.1 ± 4.5 ng/mL, $p<0.001$). During follow-up, 119 patients (66%) experienced a MACE after a median time of 72 days. Prolactin was an independent predictor of MACE (OR=1.098, 95% CI=1.024-1.176, $p=0.008$), along with NYHA class ($p=0.010$), 6-min walked distance ($p=0.015$) and BNP ($p=0.001$). Prolactin predicted the occurrence of MACE with an area under the curve of 0.653 [SE=0.061, 95% CI=0.534-0.773, $p=0.015$]. A cut-off value of 4.5 ng/mL predicted MACE with 88% sensitivity and 39% specificity. Patients with a baseline prolactin value of 4.5 ng/mL or higher had a significantly lower event-free survival compared to those with a prolactin value lower than 4.5 ng/mL (116 ± 7 versus 181 ± 11 days, $p=0.0001$).

Conclusions: Serum prolactin is closely associated with functional status, exercise capacity, depressive symptomatology as well as with neurohormonal, inflammatory and apoptotic markers, while it is also an independent predictor of long-term outcome in CHF patients.

P1249 Comparison of Copeptin, b-type natriuretic peptide, and amino-terminal pro-B-type natriuretic peptide in patients with chronic heart failure: prediction of death at different stages of the disease



S. Neuhold¹, M. Huelsmann¹, G. Strunk², B. Stoiser¹, J. Struck³, N. Morgenthaler³, A. Bergmann³, G. Gouya¹, M. Elhenicky¹, R. Pacher¹.

¹General Hospital/Medical University, Cardiology, Vienna, Austria; ²University of Economics, Research Institute for Health Care Management, Vienna, Austria;

³BRAHMS AG, Hennigsdorf, Germany

Purpose: Vasopressin has demonstrated to be increasing with the severity of chronic heart failure. Copeptin is a fragment of pre-pro-vasopressin, which is being synthesized and secreted in equimolar amounts to vasopressin. Both hormones have a short life time in vivo - similar to b-type natriuretic peptides - but in contrast to Vasopressin, Copeptin is very stable in vitro. The predictive value of Copeptin has been shown in advanced heart failure, where it was superior to BNP to predict 24-month mortality. Our aim was to evaluate the predictive value of Copeptin over the entire spectrum of heart failure (HF), and compare it to the current benchmark markers, BNP and NT-proBNP.