

Results: In Cox-proportional hazard analyses, low peak VO_2 ($p = 0.0014$), low LVEF ($p = 0.0004$), and high UA ($p < 0.0001$, RR 1.007 [95% CI 1.005-1.010]), but not age ($p = 0.09$) predicted poor prognosis. Patients with event-free survival had a mean UA of 451 ± 110 mol/l (patients with event 591 ± 166 mol/l, $p < 0.0001$). UA levels above median (>468 mol/l, RR 4.23 [95%CI 2.0-9.2]), in the highest tertile (≥ 560 mol/l, RR 6.75 [3.3-14.0]), and in the highest quartile (≥ 590 mol/l, RR 7.29 [3.6-14.7]), all $p < 0.0001$ were strong prognostic predictors, independently of age, peak VO_2 , LVEF and diuretic dose. LVEF $< 25\%$ (RR 3.29 [1.5-7.1]), $p = 0.0014$ and peak $VO_2 < 14$ (RR 2.02 [1.03-4.0]), $p < 0.05$ were less strong prognostic markers. Of the 7 patients that had UA ≥ 590 , LVEF < 25 , and a peak $VO_2 < 14$ (i.e. 3 RF) none survived >482 days (16 months). The 18-month survival of patients with 2 RF (37% [95% CI 33-60%]), 1 RF (79% [77-91%]) and no RF (92% [82-100%]) was better.

Conclusion: High UA levels are a strong marker of impaired prognosis in CHF patients, additive to other established risk factors.

1070-32 Acute Peripheral Edema in Patients With Chronic Heart Failure Is Associated With Endotoxemia and Immune Activation

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Background: It has been recognized that patients with chronic heart failure (CHF) exhibit immune activation. We have recently hypothesized that immune activation may be induced by bacterial translocation from the intestine to the blood stream due to venous congestion and altered gut permeability. Thus, we studied patients at the onset of severe peripheral edema postulating that these patients were most likely to have bowel wall edema.

Methods: Patients with CHF (n = 39) and healthy controls (n = 8) underwent routine physical examination, ECG, blood testing, and chest x-ray, at the beginning of the study. Sixteen patients were diagnosed with severe peripheral edema (CHF-edema). Blood samples for endotoxin measurements (LAL test) were collected in endotoxin free tubes. In a subgroup of patients (n = 14) and controls (n = 4) CD3, CD4, CD8, CD25 were measured by FACS analysis.

Results: Endotoxin levels were lower in controls (0.391 ± 0.096 EU/ml) than in patients without edema (0.436 ± 0.057 EU/ml; $p = n.s.$) and CHF-edema (0.799 ± 0.119 EU/ml; control and CHF vs CHF-edema, both $p < 0.01$). While no significant differences were detected for CD3, CD4, and CD8, results for CD3/25 and CD8/25 mirrored those of endotoxin levels, with highest levels in CHF-edema (CD3/25: controls, 10.25 ± 0.629 vs CHF-edema, $32.67 \pm 12.68\%$, $p < 0.02$; CD8/25: controls, 4.5 ± 0.29 vs CHF-edema, $18.67 \pm 6.48\%$, $p < 0.02$), which is suggestive of acute immune activation.

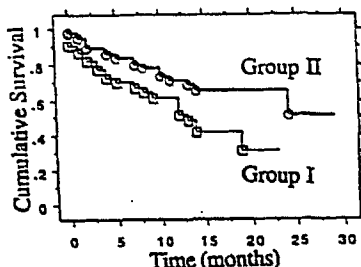
Conclusion: These findings suggest a possible role for endotoxin-induced immune activation in CHF patients with recent onset of peripheral edema.

1070-33 The Association of High Dose Diuretics With Prognosis in Heart Failure

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Background: Diuretic agents are commonly employed in the management of patients (pts) with heart failure (HF). We sought to assess the relation between the use of high doses of diuretics and long-term outcome in HF.

Methods: 111 pts (63% men; age 69 yrs) with moderate to severe LV dysfunction (EF $\leq 30\%$) were followed for 9.8 ± 7.6 months following a hospitalization for HF. We classified pts into those who were consistently treated with high doses of diuretics (furosemide ≥ 80 mg/d or equivalent amount of other diuretic) for outpatient maintenance therapy (Gr I; n = 47) and those who were not (Gr II, n = 64). We compared the occurrence of poor



outcome, defined as death (n = 44) or urgent heart transplantation (n = 3), over the follow-up period between the two groups.

Results: The groups were similar in age, gender, race, and incidence of hypertension, CAD, diabetes, and atrial fibrillation. Gr I pts had a higher incidence of RV dysfunction (65 vs 40%) and were more likely to have NYHA class III or IV (53% vs 33%; $p < 0.05$ for all). Poor outcome was seen more frequently in Gr I (51 vs 28%; $p = 0.01$); survival analysis (graph) showed earlier occurrence of poor outcome in Gr I ($p = 0.01$). In multivariate analysis, high dose diuretic use was independently associated with poor outcome (odds ratio 3.9; 95% CI 1.6-9.6).

Conclusions: In pts with HF, the need for outpatient therapy with high dose diuretics is a strong marker of poor long-term outcome.

1070-34 Reproducibility of the Natriuretic Peptides for the Detection of Ventricular Dysfunction - Comparison to the Clinical Evaluation in Different Populations

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The use of Brain (BNP), C-terminal Atrial (C-ANP), and N-terminal Atrial (N-ANP) natriuretic peptides to detect LV dysfunction (LVD) has been proposed. To determine if these peptides perform consistently in out-patients (pts) at risk for LV dysfunction as compared to clinical predictors of LVD, we analyzed clinical parameters, BNP, C-ANP and N-ANP in 304 out-pts (Grp A) referred for echo to check EF because of symptoms of or risk factors for LVD. A clinical score (+ or -) using the history, CXR and ECG predictive of LVD was developed. The clinical score and peptides were then tested prospectively in 162 pts (Grp B). Receiver operating characteristic (ROC) analysis was performed. For detection of an EF $< 35\%$, the areas under the ROC curve (AUC) for Grp A were: BNP = 0.88, N-ANP = 0.67, C-ANP = 0.82 and for Grp B were: BNP = 0.99, N-ANP = 0.79, C-ANP = 0.96 ($p < 0.02$ vs. BNP). An abnormal BNP ($>$ or = 37 pg/ml) was 87% sensitive and 61% specific in Grp A and 100% sensitive and 62% specific in Grp B. A + clinical score was 100% sensitive and 62% specific for detection of an EF $< 35\%$ in Grp A and 83% sensitive and 54% specific in Grp B. In conclusion, the predictive value of BNP or C-ANP is reproducible and was equivalent to that derived from a complete clinical evaluation including physician visit, CXR and ECG. These data support the use of BNP or C-ANP to screen for LVD.

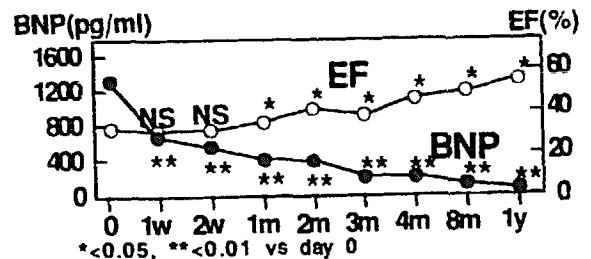
1070-35 Plasma BNP Concentration Is the Most Sensitive Marker for Management of Chronic Congestive Heart Failure

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Background: Echocardiography is the golden standard for evaluating the effect of treatments in patients with chronic congestive heart failure (CHF), but sometimes the changes are too small to make objective evaluation. Brain natriuretic peptide (BNP) is an only humoral factor released from ventricular cardiomyocytes and its plasma level is augmented in accordance with severity of CHF. In this study we evaluated whether BNP could be a sensitive marker for the management of CHF.

Methods: 10 patients with acute decompensation of CHF were treated with diuretics, ACE inhibitors and b-blockers.

Results: The plasma BNP level was significantly decreased after 1 week treatment, although ejections fraction (EF) was not changed at this time (fig) EF had subsequently improved 1 month later. Left ventricular diastolic dimension had no significant change during 1-year follow up. ANP had tendency to decrease after the 1-week treatment.



Conclusion: The change in the plasma BNP concentration in patients with CHF precedes the improvement of EF, and so the plasma BNP concentration is one of the most sensitive markers of cardiac function in patients with CHF.