Results. Ejection fraction was 29±7% (mean±SD), the pulmonary capillary wedge pressure was 18±7 mmHg, left ventricular end-diastolic pressure was 22±8 mmHg and mean pulmonary artery pressure (mPAP) was 26±8 mmHg. Plasma ET-1 levels were similar in pulmonary artery (0.931±0.71 fmol/ml) and aorta (0.906±0.6 fmol/ml, p=0.769) and did not correlate with mPAP (r=-0.139, p=0.521). Single pass pulmonary ET-1 extraction was reduced compared with historical controls (31±15% vs 47±2%, p<0.001), as was plasma clearance of ET-1 (912±610 ml/min vs 1424±77 ml/min, p=0.01). Lung clearance inversely correlated with mPAP (r=-0.490, p=0.014).
Conclusions. Pulmonary ET-1 clearance is reduced in relation with the severity of pulmonary hypertension (PHT) in patients with CHF. While it does not seem to contribute to the increase in plasma ET-1 levels, this evidence for reduction in endothelial ETB receptor activity may contribute to the development of PHT.

1061-82 Evaluation of Platelets in Heart Failure: Is Platelet Activity Related to Etiology, Functional Class, or Clinical Outcomes?

Paul A. Gurbel, Wendy A. Gattis, Sergey F. Fuzaylov, Laura Gaulden, Vic Hasselblad, Victor L. Serebruany, Christopher M. O'Connor, Sinai Center for Thrombosis Research, Baltimore, MD, Duke University Medical Center, Durham, NC

Objectives: We sought to determine whether platelet activity in patients with heart failure (HF) is related to an ischemic versus non-ischemic etiology, clinical disease severity or adverse clinical outcomes. Background: Platelets activity may affect outcome in patients with HF. A prospective evaluation of the relation of baseline platelet function to HF etiology, NYHA class, and clinical outcomes has not been previously reported. **Methods:** Ninety-six consecutive ambulatory heart failure outpatients with an EF< .40 and NYHA Class II-IV symptoms who presented to the Duke Heart Failure Clinic and fourteen healthy controls formed the study groups. Baseline characteristics were determined and blood was analyzed for thromboxane (Tx) B2, 6-keto PGFI, platelet contractile force, ADP/collagen shear-induced closure time, whole blood aggregation (WBA) and CD 41, CD31, CD62p and CD51/CD61 by flow cytometry. Survival status and hospitalizations were determined in the heart failure patient cohort. **Results:** The median age was 65 years (22% female, 64% caucasian). An ischemic etiology was present in 61%. The population has mild-moderate HF: NYHA class I (1%), II (41%), III (46%), and IV (12.5%) and severe ventricular dysfunction (median EF = .20). There were 39 clinical events (7 deaths, 3 cardiac transplants, 29 other first hospitalizations) in 305 median days follow-up. Platelet activity, indicated by WBA with 5μmol ADP (p=.04) and Tx B2 (p=.01), was higher in HF patients. WBA was greater than 90th percentile in 22% of HF patients vs 7% of controls. Markers of platelet function did not differ between the ischemic and non-ischemic groups and was not affected by antecedent aspirin. There was no relation of NYHA class or the occurrence of events to platelet activity. **Conclusion:** Platelet activity is heightened in 22% of outpatients with stable heart failure symptoms and is not affected by antecedent aspirin therapy. The degree of platelet activation is similar in ischemic and non-ischemic HF and is not related to clinical disease severity. Current methods to assess platelet activation do not appear to predict outcome.

1061-83 Uric Acid and Survival in Chronic Heart Failure: Validation and Application in Metabolic, Functional, and Hemodynamic Staging

Stefan D. Anker, Wolfram Doehner, Mathias Rauchhaus, Christoph Knosalla, Roland Hetzer, Andrew J. Coats, NHLI London, London, United Kingdom, Charité Medical School, Berlin, Germany

Background: Serum uric acid (UA) could be a valid prognostic marker and useful for metabolic, hemodynamic, and functional (MFH) staging in chronic heart failure (CHF).
Methods: We performed a series of 3 studies. For the initial derivation study, 112 CHF patients (age 59±12 y, peak oxygen consumption [VO_2] 17±7 mL/kg/min) were recruited. We validated the prognostic value of UA in a second, independent study (n=182). In a third study, we investigated the relationship between MFH score and the decission to list patients for heart transplantation (n=120).
Results: In the derivation study (12-month mortality: 24%) the best mortality predicting UA cut-off (at 12 months) was 565 μmol/L (independently of age, peak VO_2, LVEF, diuretic dose, sodium, creatinine, and urea: p<0.0001). In the validation study (12-month mortality: 15%), UA ≥565 μmol/L predicted mortality (hazard ratio 7.14, p<0.0001).
In 16 patients (from both studies) with UA ≥565 μmol/L, LVEF ≥25%, and peak VO_2 ≥14 mL/kg/min(i.e. with MFH score 3), 12-month survival was lowest (31%), compared to patients with 2 (64%), 1 (77%), or no risk factor (98% , p<0.0001). Considering all 294 CHF patients, we found a graded relationship between serum UA and mortality in CHF (p<0.0001). Patients with UA in the normal range (≤400 μmol/L) had the best survival (at 12-months: 93%), compared to patients with UA between 401 and 600 μmol/L (87%, RR 1.76), patients with UA between 601 and 800 μmol/L (54%, RR 6.27), and patients with UA >800 μmol/L (17%, RR 18.53).
In an independent study, 51% of patients with MFH score 2 and 89% of patients with MFH score 3 were listed for transplantation. The positive predictive value of not being listed for heart transplantation with an MFH score 0/1 was 100%.
Conclusions: High serum UA levels are a strong and independent marker of impaired prognosis in patients with moderate to severe CHF. The relationship between serum UA and survival in CHF is graded. MFH staging of CHF patients is feasible.

POSTER SESSION

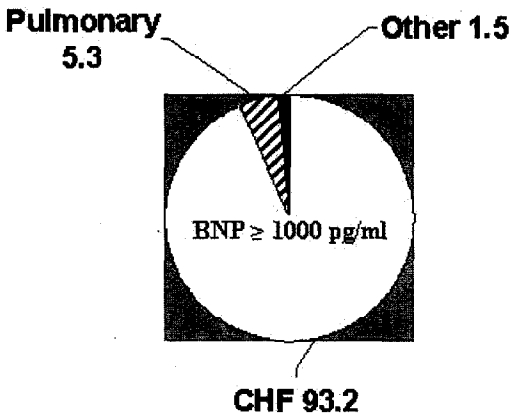
1062 Clinical Heart Failure: Miscellaneous

Sunday, March 30, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 4:00 p.m.-5:00 p.m.

1062-59 What Is in the Differential Diagnosis of a B-Type Natriuretic Peptide Level of 1,000 pg/ml?

Peter A. McCullough, Richard M. Nowak, James McCord, Torbjorn Omland, Catherine W. Knudsen, Philippe Duc, Judd E. Hollander, Philippe Gabriel Steg, Marie-Claude Aumont, Arne Westheim, Alan B. Storrow, William T. Abraham, Sumant Lamba, Alan H. Wu, Alan S. Maisel, BNP Multinational Study Investigators, William Beaumont Hospital, Royal Oak, MI, University of California, San Diego School of Medicine, Veterans Affairs Medical Center, San Diego, CA

Introduction: Recent, approved indications for blood B-type natriuretic peptide (BNP) for the diagnosis of congestive heart failure (CHF) and as a prognostic indicator in patients with acute coronary syndromes raise questions on how to interpret very high BNP values.
Methods: The BNP Multinational Study was a seven-center prospective study of 1586 patients presenting with acute dyspnea who had blinded BNP levels measured. The reference standard for CHF was adjudicated by two independent cardiologists, also blinded to BNP results.
Results: A total of 264 subjects (mean age 70.4 years, 57.2% male) had BNP values on arrival to the ED of ≥ 1000 pg/ml. Subjects had the following characteristics: prior history of CHF 62.1%, history of coronary heart disease 48.5%, hypertension 65.5%, and lung disease in 30.3%; physical exam: rales 69.7%, S3 18.9%, elevated jugular venous pressure 44.3%, hepatic congestion 24.6%, and peripheral edema 66.3%. Abnormal chest x-rays were present in 90.5%. The final diagnoses are shown in the pie chart. Of those with pulmonary disease, all subjects had at least one sign of volume overload on physical exam. Other diseases in the differential included atrial fibrillation, acute cardiac ishemia, and chronic renal failure.
Conclusion: A BNP level ≥ 1000 pg/ml indicates the presence of CHF in 93.2% of cases. In 6.8% of cases without CHF, other serious conditions are present suggesting cardiac pressure and or volume overload.



1062-60 The Prognostic Value of Inflammatory and Neurohumoral Activation in Patients With Chagas' Heart Disease

Victor S. Issa, Amilcar O. Mocelin, Fernando Bacal, Guilherme V. Guimaraes, Edecio Cunha, Giovanni V. Bellotti, Jose F. Ramires, Edimar A. Bocchi, Heart Institute (InCor)-University of Sao Paulo Medical School, Sao Paulo, Brazil

Background. Inflammatory mediators are of paramount importance in heart failure. Despite experimental evidence that cytokines play a central role in Chagas' disease, data in humans is scarce. We studied the pattern of inflammatory and neurohumoral response in patients with Chagas' disease as compared to patients with idiopathic dilated cardiomyopathy (IDC).
Methods. We studied 35 patients with IDC (IDC group) and 28 patients with Chagas' heart disease (CHAGAS group); we measured and compared plasma tumor necrosis factor alfa (TNF-a), soluble TNF-a receptor type 1(sTNF-R1), soluble Fas (sFas), interleukin 6 (IL-6), and brain natriuretic peptide (BNP) concentrations in both groups; the association between the substances measured and clinical events (heart transplantation or death) was ascertained. Patients were stratified according to functional class and peak oxygen consumption (VO2max).

Results. Plasma TNF-a level was higher in IDC (mean 4.82; 95% confidence interval 3.82-6.07 pg/ml) and CHAGAS (6.28 pg/ml; 4.98-7.94pg/ml) as compared to controls (1.30pg/ml; 0.93-1.83 pg/ml)(p<0.001). Plasma TNF-a level was higher in CHAGAS than in IDC after stratification for VO2max (p=0.049). Plasma sTNF-R1 level was higher in IDC only after stratification for functional class (p=0.04). Plasma of IL-6 level were higher in IDC (3.18 pg/ml; 2.35-4.32 pg/ml) and in CHAGAS (6.07pg/ml; 4.42-8.36pg/ml) as compared to controls (0.84pg/ml; 0.63-1.12pg/ml); plasma IL-6 concentration was higher in CHAGAS than in IDC after stratification for functional class (p=0.005). Higher IL-6 levels were associated with worst clinical outcome (p=0.03 for group I; p=0.003 for group II); Plasma BNP concentrations were higher in IDC (350pg/ml) and in CHAGAS (444.6pg/ml) as compared to controls (20.3pg/ml)(p<0.001); higher BNP level was associated to death and heart transplantation. Plasma sFas level was similar among the groups.
Conclusions. Systemic inflammatory and neurohumoral activation is present in patients with Chagas' heart disease, differs from patients with IDC and is associated with heart failure severity and outcome. Thus, it should be considered in the follow-up of patients with Chagas' heart disease.

1062-61 B-Type Natriuretic Peptide Predicts Cardiac Injury and Dysfunction After Subarachnoid Hemorrhage

Poyee P. Tung, Alexander Kopelnik, Nader M. Banki, Michael Lawton, Daryl Gress, Barbara Drew, Elyse Foster, William Young, William Parmley, Jonathan G. Zaroff, UCSF Medical Center, San Francisco, CA

Background: An elevated B-type natriuretic peptide (BNP) level is a poor prognostic marker in heart failure and myocardial infarction. However, its role in neurocardiogenic injury after subarachnoid hemorrhage (SAH) is unknown. In this study, we sought to determine the relationship between BNP and cardiac outcomes after SAH. **Methods**: We conducted a prospective study in 57 patients admitted for SAH. On day 1,3, and 6 after enrollment, we collected clinical data (serum troponin I, two-dimensional echocardiogram and chest radiograph) on our subjects. Serum BNP and C-reactive protein levels were measured as soon as possible.
Results: The mean BNP level was 322 ± 518 pg/ml (range 0.8- 3330 pg/ml). Wilcoxon rank-sum tests showed a significant relationship between elevated BNP levels and cardiac endpoints, defined as a high regional wall motion score, impaired diastolic function (impaired relaxation, pseudonormalization, restrictive physiology), radiographic evidence of pulmonary edema, and an elevated troponin I level (see table). In contrast, CRP level, a marker of inflammation, was not associated with any short-term cardiac outcome after SAH.
Conclusions: Elevated BNP, but not CRP, is associated with cardiac injury and dysfunction after SAH. These findings are consistent with the hypothesis that neurocardiogenic injury after SAH is related to neurohumoral activation rather than systemic inflammation. BNP may be a useful marker in identifying SAH patients at high risk of cardiac complications.

BNP is related to cardiac endpoints after SAH

	Mean ± SD (pg/ml)	p	N (%) with cardiac endpoints
RWMS (1.0 vs ≥ 1.0)	267 ±533 vs 488 ±441	0.032	14 (25)
Diastolic function (normal vs abnormal)	128 ±174 vs 383 ± 570	0.037	44 (77)
Pulmonary edema on chest radiograph (no vs yes)	195 ±246 vs 1096 ± 965	0.001	8 (14)
Troponin I (≤1.0 vs >1.0 ug/L)	240 ±508 vs 662 ± 429	0.004	11 (19)

1062-84 Phenotypic and Genotypic Heterogeneity in Cardiac Amyloidosis

Enrica Perugini, Claudio Rapezzi, Fabrizio Salvi, Michela Santi, Giovanni Bracchetti, Carlo Magelli, Ornella Leone, Angelo Branzi, Institute of Cardiology, Bologna, Italy, Bellaria Hospital, Bologna, Italy

Background. Most of the current knowledge on cardiac amyloidosis comes from the AL type (in which precursor plasma protein is an immunoglobulin light chain) while the characteristics of myocardial involvement and the possible genotype-phenotype correlations in ATTR (caused by mutant transthyretin produced by the liver) remain to be defined.
Methods. We compared echocardiographic and clinical findings of three groups of patients with established amyloidotic myocardial involvement: 60 of AL type, 10 with ATTR Met30 mutation (in which methionine replaces valine at position 30), 16 with non-Met30 ATTR mutations. We also considered ATTR pts as a single group.
Results

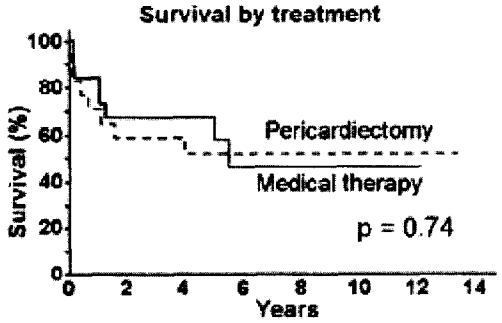
	AL	Non-Val30Met ATTR	Val30Met ATTR	ATTR overall	p AL vs ATTR	p ANOVA
N. of pts	**60**	16	10	**26**		
Age (yrs)	**60 ± 9**	47 ± 12	54 ± 17	**49 ± 14**	< .0001	<.0001
IVS (mm)	**18.3 ± 4.4**	16.2 ±4.6	14.3± 5.1	**15.4 ± 4.8**	= .0003	.02
LPW (mm)	**15.9±6**	14.8 ±2.9	12.1± 4.1	**13.8 ± 3.6**	= .02	NS
LVEDID (mm)	**42 ±7.8**	42 ± 3.7	41 ± 3.2	**42 ± 1.4**	NS	NS
LV mass (gr)	**304 ± 35**	305± 125	215± 30	**287 ± 117**	NS	<.0001
LA (mm)	**43.3 ± 8.5**	40 ± 7	36.5± 6.3	**38.3 ± 6.7**	= 0.0001	.03
LV FS (%)	**22 ± 8**	27.8± 11.5	47 ± 2.8	**36 ± 4**	<.001	<.001
Dec time E wave	**128 ± 30**	130 + 14	162± 12	**148 ± 14**	= .001	.001
NYHA>III (%)	**52%**	25%	0	**15%**	= .003	.007
Sinus rhythm (%)	**65%**	88%	100%	**92%**	<.0005	<.001

IVS = Interventricular Septal thickness; LPW = Left Posterior Wall thickness; LVEDD = Left Ventricular End-Diastolic Internal Dimension; LV = Left Ventricular; LA = Left Atrial end-systolic diameter; FS = Fractional Shortening;
Conclusions. Myocardial involvement is more severe in AL than in ATTR. This explains why AL patients develop more frequently diastolic and systolic dysfunction and clinical signs of heart failure. A genotype - phenotype correlation does exist within ATTR amyloidosis. A wide spectrum of morphologic and functional involvement is detectable in cardiac amyloidosis. This impairment is maximal in AL, intermediate in non-Met30 ATTR and minimal in Met30 ATTR.

1062-85 Does Pericardiectomy Improve Outcome of Patients With Mixed Constriction and Restriction?

Hirotsugu Yamada, Jeanne K. Drinko, Annitta J. Morehead, Leonardo Rodriguez, Mario J. Garcia, James D. Thomas, Allan L. Klein, The Cleveland Clinic Foundation, Cleveland, OH

Background: Pericardiectomy can relive symptom in most patients with constrictive pericarditis. However, a significant subgroup of these patients has also restrictive myocardial involvement. The outcome of patients with this mixed disease has not been well described. **Methods:** Study subjects consisted of 38 patients (57 ± 14 yrs, 8 female, 30 male) who were diagnosed as having mixed physiology based on clinical history, transthoracic and/or transesophageal echocardiography, MRI, cardiac catheterization, endomyocardial biopsy and/or surgical findings. Major etiology of the patients included coronary bypass surgery (CABG) after radiation (11), radiation therapy alone (8), CABG without radiation (9), idiopathic (4), heart transplantation (3). Seventeen patients treated with pericardiectomy (58 ± 15 yrs) and 21 patients treated medically (57 ± 14 yrs) were compared using Kaplan-Meier survival analysis. **Results:** There were no differences in age, left ventricular ejection fraction, prior radiation between both groups. Mean observation time was 4.0 ± 3.8 years and maximum observation period was 13.4 years. Five years mortality was 51% in the pericardiectomy group and 58% in the medical therapy group and the survival was not significantly different between both groups (p = 0.739, figure). **Conclusions:** Patients with mixed physiology of constriction and restriction have a high mortality rate. Pericardiectomy for these patients may not improve their survival time.



1062-86 Cardiac Function in Patients With Fukuyama-Type Congenital Muscular Dystrophy

Toshio Nakanishi, Masako Sakauchi, Hirofumi Tomimatsu, Kayoko Saitou, Makoto Nakazawa, Makiko Oosawa, Tokyo Women's Medical University, Tokyo, Japan

Backgroud: Fukuyama-type congenital muscular dystrophy (FCMD) is an autosomal recessive disorder characterised by generalised skeletal muscle weakness and hypotonia from early infancy and mental retardation. Mutation of fukutin gene on chromosome