POSTER SESSION

1039 Dilated Cardiomyopathy: Basic and Clinical

Sunday, March 30, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: Noon-1:00 p.m.

1039-59 Simvastatin Preserves Myocardial Function by Enhancing Endothelial Nitric Oxide Production in Heart Failure

Seena S. Abraham, Juan C. Osorio, Jie Wang, James K. Liao, Shunichi Homma, Seema Mital, The New York-Presbyterian Hospital, New York, NY, Brigham & Women's Hospital, Boston, MA

Background: Endothelial nitric oxide synthase (ENOS) is reduced in heart failure (HF). Statins upregulate NO production independent of lipid-lowering. We evaluated the ability of simvastatin (Sim) to reverse ventricular remodeling and dysfunction by restoring coronary NO production and NO mediated regulation of apoptosis.
Methods: Five month old cardiomyopathic (CMP) hamsters were divided into 2 groups - Sim (n=5), and Untreated (n=5). Age-matched normal hamsters were used as controls (n=6). Sim group received 20 mg/kg Sim daily by oral gavage for 6 weeks. Serial 2D echocardiograms were obtained at baseline and 2 week intervals. LV function and dimensions indexed to body surface area were compared between groups. Myocardial apoptosis was evaluated by immunostaining and caspase 3 activity assay. Myocardial ENOS expression was measured by Western blot and immunohistochemistry.
Results: At baseline, CMP hamsters had lower LV shortening fraction (SF) compared to controls (17±2% vs.59±2%), higher LV diastolic volume (30±2 vs.6±0.5 ml/m^2) and lower LV mass/volume ratio (0.5±0.02 vs. 0.72±0.02 mg/ml, p<0.001). Untreated CMP hamsters demonstrated a progressive decrease in LVSF (12±1%, p<0.05) and increase in LV volume from baseline (37±2 ml/m^2, p<0.05). The Sim group showed no deterioration in LV function (SF 18±1%) or LV dilatation (LV volume, 26±2 ml/m^2, p<0.05) compared to the untreated group. Immunostaining revealed a higher percentage of apoptotic nuclei in the HF group compared to controls (0.096±0.04% vs.0.032±0.02%, p<0.002). Caspase 3 activity was lower in the Sim compared to the untreated group (p<0.001). Inhibiting endogenous NO increased caspase 3 activity in the Sim (p=0.05) but not in the untreated group. Myocardial ENOS staining revealed increased capillary density per 3 high power fields in the Sim (110±12, p<0.05) compared to controls (47±9) and untreated hamsters (56±11).
Conclusions: Sim administration preserves myocardial function, decreases LV remodeling and retards the progression of HF. This may be related to an increase in coronary microvasculature resulting in increased endothelial NO availability and reduced cardiomyocyte apoptosis.

1039-60 Pregnancy-Associated Cardiomyopathy: Early Versus Late Presentation

Mohammed W. Akhter, Avraham Shotan, Afshan Hameed, Harpreet Singh, Salman Khan, Usman Ahsan, Muhammad T. Khan, Uri Elkayam, University of Southern California, Los Angeles, CA

Background: Initial diagnostic criteria have limited Pregnancy associated cardiomyopathy (PACM) to last month of gestation or 5 months after delivery. These criteria however, were established 4 decades ago and may have been limited by inferior diagnostic capabilities and small number of patients. We have therefore reexamined the timing of symptoms onset as well as diagnosis in 137 patients (pts) recently diagnosed with PACM.
Methods: We reviewed records of 137 pts with PACM with the following criteria: 1. Development of heart failure (HF) during pregnancy or first 6 months postpartum (PP), 2. Absence of identifiable cause of HF, 3. Depressed ejection fraction (EF)≤ 40 %.
Results: Timing of symptoms onset and diagnosis were as follows:

TIME	<27 WEEKS	28-36 WEEKS	37-40 WEEKS	1 MONTH PP	2-6 MONTHS PP
Symptoms onset	8%	21%	6%	58%	7%
Diagnosis	3%	13%	6%	62%	16%

PACM was diagnosed early (<37 weeks) in 20 pts and late (≥ 37 weeks) in 102 pts. There was no difference in age (30 ± 6 vs 31 ± 6 years, p=0.74), gravity (2.5 ± 6.3 vs 2.7 ± 2.3, p=0.65) or EF both at time of diagnosis (32 ± 11% vs 31 ± 12%, p=0.93) and follow up of 26 months (44 ± 16% vs 45 ± 15%, p=0.53) between the 2 groups.
Conclusions: Although PACM mostly presents during the first month PP, almost 30% of cases present during the 2nd and 3rd trimester prior to last gestational month. Increased awareness of early presentation of PACM is important to allow early diagnosis and appropriate care of this potentially life threatening condition.

1039-61 Predictors of In-Patient Mortality Following Emergency Heart Failure Hospitalization

Colin Berry, Michael Brett, Karen Stevenson, John Norrie, John McMurray, University of Glasgow, Glasgow, United Kingdom

Introduction: Much of the information on heart failure (HF) has been derived from clinical trials. We sought to determine the characteristics which may be associated with survival in 'real-life', hospitalized, HF patients.
Methods: We examined the clinical characteristics and predictors of in-hospital case-fatality in 547 consecutive emergency admissions with HF to one acute urban University hospital over 1 year period.
Results: Average age was 72 (SD 13) years, 49% were male and 476 patients (87%) survived to discharge. 414 (75%) had an echocardiogram, of whom 133 (32%) had preserved left ventricular systolic function (LVSF). Mean hemoglobin (Hb) concentration was 12.5±2.1 g/dL in males and 12.0±1.9 g/dL in females. 52% of men and 37% of women were anemic (normal range men Hb 13 - 18 g/dL, women Hb 11.5 - 16.5g/dL). The % of men with Hb < 13, 12, 11, 10 g/dl was 16, 14, 10 and 12% respectively (women, % Hb < 11.4, 10.4, 9.4 and 8.4 g/dl was 21, 8, 6 and 3%). Mean white cell count (WCC) was 9.24 x 109/L (4-11 x 109/L), and 22% of patients had low WCC. Mean lymphocyte count (LC) was1.6 x 109/L and 58% of patients had a low LC. In-patient case fatality rate tended to be higher for patients with impaired LVSF, compared to preserved LVSF (13% vs 8%; P=0.06).The probability of being alive at discharge was increased by treatment with an ACE inhibitor (odds ratio (OR) 1.1, 95% CI 1.0-1.2; P=0.02) or an HMG CoA reductase inhibitor (OR 1.1, CI 1.0-1.2; P=0.004). A higher Hb concentration was also positively associated with survival (OR 1.03 per g/dL, CI 1.0-1.05; P=0.02). Factors associated with an increased risk of death during admission were the presence of renal dysfunction (OR 1.2, CI 1.1-1.3; P=0.01) and ischemic chest pain (OR 1.2, CI 1.1-1.3; P= 0.001). Diabetes (OR 1.1; CI 0.97-1.2; P=0.2) and an elevated C-reactive protein concentration (OR 1.01; CI 1.00-1.02; P=0.08) tended to be associated with an increased risk of death.
Conclusion: Both low WCC/LC (by increasing the risk of infection) and low Hb may contribute to HF decompensation. Statin therapy and Hb concentration may be two new markers of short term prognosis. The potentially protective effects of a higher Hb and statin therapy merit prospective investigation in HF.

1039-62 Impact of Peripheral Endothelial Vasomotor Function on Exercise Capacity and Adhesion Molecules in Idiopathic Dilated Cardiomyopathy

Barbara M. Richartz Friedhelm Kuethe, Hans R. Figulla, Gerald S. Werner, Friedrich-Schiller-University Jena, Jena, Germany

Background: Exercise tolerance- which has been linked to impaired blood perfusion of skeletal muscles - varies significantly between patients with heart failure. Recent studies have shown endothelial dysfunction of peripheral resistance arteries and an impaired flow-dependent-dilation (FDD) of conduit vessels. This study was designed to determine the degree of impaired FDD on exercise capacity and endothelial activation.
Methods: In 38 patients with idiopathic dilated cardiomyopathy (IDC) longitudinal radial artery images were obtained with a high-resolution (10 MHz) vascular transducer. FDD was determined by maximal radial diameter after exactly 60 s of reactive hyperemia compared to baseline vessel diameter. FDD was defined as a change > 5%. Serum concentrations of ICAM-1 and VCAM-1 were analyzed by ELISA. The severity of heart failure was assessed in accordance to NYHA-classification, hemodynamic parameters (pulmonary capillary wedge pressure, left ventricular ejection fraction), and peak oxygen consumption.
Results: Two distinct patterns of peripheral FDD could be distinguished: In 21 patients (group 1, 55%) radial artery dilates in response to reactive hyperemia, whereas in 17 patients (group 2, 45%) impaired FDD was observed implicating endothelial dysfunction (for details cf. table).

FDD (mm)	Group 1	Group 2	p-value
LVEF (%)	+0.55 ± 0.17	+0.04 ± 0.11	<0.05
PCWP (mmHg)	24 ± 8	28 ± 9	NS
VO2 (ml/min/kg)	22 ± 7	17 ± 7	NS
VCAM-1 (ng/ml)	22 ± 5	14 ± 3	<0.05
ICAM-1 (pg/ml)	333 ± 121	478 ± 149	<0.05
NYHA	218 ± 134	342 ± 129	<0.05
	2.2 ± 0.3	2.9 ± 0.3	0.065

Conclusions: The severity of heart failure in IDC and thus exercise intolerance is closely linked to peripheral endothelium vasomotor dysfunction and accompanied by endothelial activation.

1039-63 Clonal T-Cell Composition Detected by Family Specific Polymerase Chain Reaction of the T-Cell Receptor Beta Chain Is Exclusively Present in Dilated Cardiomyopathy

Michel Noutsias Jan H. Blohm, Chalid Assaf, Nadine Bigdeli-Issazadeh, Michael Hummel, Rahat S. Warraich, Magdi H. Yacoub, Harald Stein, Heinz P. Schultheiss, Matthias Pauschinger, UKBF, Free University, Berlin, Germany, NHLI, Harefield Hospital, Middlesex, United Kingdom

Background: Autoimmunity, resulting from molecular mimicry between viral and cryptic cardiac antigens, is postulated for the pathogenesis of dilated cardiomyopathy (DCM). Autoimmunity directed against distinct antigens evokes expansion of specific T-cell clones infiltrating the target tissue. This phenomenon leads to a clonal predominance of T-cells harboring an identical rearranged T-cell receptor gene (TCR), which can be reliably identified by family specific PCR for the Vβ-N-Dβ-N-Jβ-region of the TCR gene in combination with high-resolution GeneScan-analysis.