1109-134 **Clinical Features of Mixed Physiology of Constriction and Restriction**

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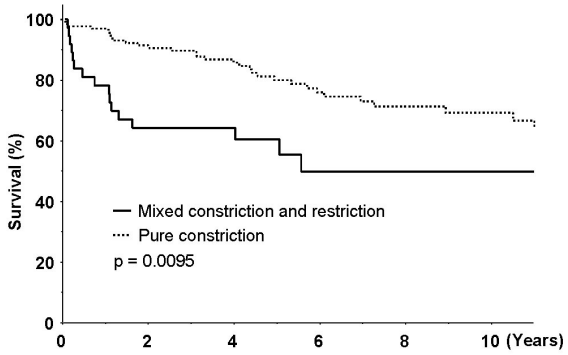
Background: Patients with mixed physiology of constriction and restriction have been reported, but their long-term survival has not been well documented.
***Methods*:** Study subjects consisted of 38 patients (57 ± 14 yrs, 8 female, 30 male) who were diagnosed as having mixed physiology based on echocardiography, MRI (or CT), cardiac catheterization, endomyocardial biopsy and/or surgical findings. We evaluated their echocardiographic, clinical features and calculated Kaplan-Meier survival curve to compare with that in patients with pure constriction.
Results: Prior radiation therapy was the most frequent (50%) cause of mixed physiology followed by coronary artery bypass graft without prior radiation and heart transplantation. The respiratory variation of peak early diastolic transmitral flow velocity was 10.7% in patients with sinus rhythm, 18.1% in patients with atrial arrhythmia. Pericardial thickening was localized in 29 patients. All-cause 5-year mortality was 40 % and unrelated to age, etiology, left ventricular systolic function and therapeutic course. There was a significant difference between the survival rates in patients with mixed physiology and in 133 patients with pure constriction (Figure).
***Conclusions*:** Because of the high mortality in mixed disease, discrimination of this entity from pure constriction is important. Echocardiography is helpful noninvasive technique in diagnosis and understanding the physiology of the patients with mixed constriction and restriction.



ORAL CONTRIBUTIONS

834 Dilated Cardiomyopathy: Basic and Clinical II

Tuesday, March 09, 2004, 8:30 a.m.-10:00 a.m.
Morial Convention Center, Room 217

8:30 a.m.

834-1 **Vascular and Autonomic Dysfunction in the Asymptomatic Stage of Chagas's Disease**

Juan C. Guzman, Hernando Leon, Ronald G. Garcia, Juan P. Casas, Federico A. Silva, Patricio Lopez-Jaramillo, Carlos A. Morillo, Fundacion Cardiovascular de Colombia, Floridablanca, Colombia

Background: Chagas' Disease (ChD) is associated with impaired cardiac automic function (CAF) and altered peripheral endothelial vascular reactivity. The relationship between these two alterations has not been explored in the early asymptomatic stage of ChD.
Methods: 22 asymptomatic seropositive subjects to ChD were compared with 19 asymptomatic seronegative subjects (CON). All patients had a noninvasive assessment of CAF: deep breathing test (DBT), arterial baroreflex (BRS) and lower body negative pressure @ -10mmHg (LBNP) and endothelial function measured by forearm blood flow (FBF), peripheral vascular resistance (PVR) and venous occlusion plethysmography with vasoactive substances: nitroglycerine (NTG) and acetylcholine (Ach)
Results No significant differences were found between the two groups at baseline. A significant reduction was found ($p<0.01$) in the BRS 17.6±8.3 vs 28.3±14.1 and DBT 11.0 ±5.7 vs 17.2 ±7.2 in ChD patients vs CON. Significant differences were found between ChD vs CON in FBF at rest;1.4±0.4vs.2.3±0.7 ($p<0.001$) and during LBNP;1.0±0.3vs.1.5±0.6. Moreover significant differences were found in PVR at rest 65.3±20.2 vs 41.1±15.4 ($p<0.05$), LBNP 103.7±26.6 vs 71.8±43.01. ChD group had lower response than CON in terms of percentage of change of FBF in response to the infusion of incremental dosages of NTG: 8 nmoll/min 49.7±34.5 vs. 82.7±58.0; 16 nmol/min 62.2±43.5 vs 159.6±83.6; 34 nmol/min 77.9±54.8 vs 197.13±10.8.5 and with Ach 25 nmol/min 88.4±57 vs 172.8±104; 50 nmol/min 103.1±46 vs 172.7±128; 100 nmol/min 125.3±93 vs 210.5±123.
Conclusion: Asymptomatic ChD patients have early impairment of vascular endothelial function mediated by an increase in efferent sympathetic activity that leads to elevated PVR. These findings may be related to alterations in the endothelial production of nitric oxide and lower vascular smooth muscle response to NO. These alterations may play a role in precipitating and maintaining the progressive damage of myocardial microvasculature and contribute to the development and progression of the Chagasic cardiomyopathy. (Colciencias Grant: 6566-04-10268)

8:45 a.m.

834-2 **Clonal T-Cell-Receptor Composition Is Not Associated With Enteroviral or Adenoviral Infection in Dilated Cardiomyopathy: Implications for the Pathogenesis of Dilated Cardiomyopathy**

Michel Noutsias, Michael Hummel, Chalid Assaf, Harald Stein, Uwe Kuhl, Heinz Peter Schultheiss, Matthias Pauschinger, Charité - Campus Benjamin Franklin, Berlin, Germany

Background: Autoimmunity, resulting from molecular mimicry between viral and cryptic cardiac antigens, is postulated for the pathogenesis of dilated cardiomyopathy (DCM). Autoimmunity targeting distinct antigens evokes expansion of specifically reactive T-cell clones infiltrating the target tissue, which can also result from chronic presentation of foreign (e.g. viral) antigens.
Methods: DNA extracted from explanted DCM hearts (n=17, 1 female; 49±13 years; LVEF: 18±5%) were investigated by a family specific PCR for the Vß-N-Dß-N-Jß-region of the TCR gene and GeneScan-analysis for clonal TCR rearrangement. Non-DCM-hearts (ischaemic cardiomyopathy: n=2, valvular heart disease: n=3, donor hearts: n=3) served as controls. The TCR-PCR-products analyzed by high-resolution fragment analysis (GeneScan), displayed a Gaussian-like distribution profiles in polyclonal and single dominant peaks in monoclonal T-cell populations. Clonal TCR-ß PCR-products were directly sequenced. Enteroviral and adenoviral genome was amplified by PCR.
Results: The GeneScan analysis of the TCR-ß PCR-products demonstrated a clonal T-cell population in n=9/17 (53%) of the DCM hearts. In contrast, exclusively polyclonal composition of the TCR-Vß PCR-products were obtained from the non-DCM hearts. Sequence analysis of the clonal TCR-Vß PCR-products from the n=9 DCM hearts determined Vß19.01 in n=6 cases (67%), and Vß6-1.01, Vß6-3.01 and Vß10-3.04 in each of the remaining cases. Clonal TCR-composition was not significantly ($p>0.05$) associated with PCR amplification of viral genome.
Conclusions: Clonal TCR rearrangement is exclusively present in DCM but not in further cardiomyopathies. The clear predominance of Vß19.01 family T-cell clones in DCM indicates that these TCR clones target specific antigens. Our results are consistent with the autoimmune hypothesis of DCM, since entero- or adenoviral persistence are not significantly associated with a specific clonal TCR rearrangement. Eventually, a TCR-based immunotherapy in DCM (e.g. with anti-TCR antibodies or DNA vaccines) might be a feasible therapeutic option in DCM with clonal TCR-composition.

9:00 a.m.

834-3 **Impaired Hyperaemic Myocardial Blood Flow Is Related to Systolic Function in Idiopathic Dilated Cardiomyopathy**

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Aim. Hyperaemic myocardial blood flow is impaired in patients with idiopathic dilated cardiomyopathy (DCM). The degree of impairment is related to diastolic dysfunction and prognosis. This study was conducted to evaluate the relation between hyperaemic myocardial blood flow and systolic function in patients with DCM.
Materials & Methods. Patients with advanced stage of idiopathic dilated cardiomyopathy (NYHA III or IV; EF<35%) and healthy control subjects were studied. Myocardial blood flow (MBF) was determined by positron emission tomography (PET) using ^{15}O-labelled water under baseline conditions and during pharmacologically induced stress. MR tissue tagging was performed for quantification of regional myocardial function. End systolic circumferential shortening (ESCS) was calculated using the Harmonic Phase (HARP) method.
Results. Ten patients with DCM (mean age 54±10 yrs, 5 male) and 7 control subjects (mean age 28±3 yrs, 6 male) were studied. Mean rest MBF was similar for DCM and controls (0.91±0.33 vs. 0.97±0.21 ml/min/g, respectively, p=NS). Hyperaemic MBF and ESCS were reduced in DCM (2.23±1.01 ml/min/g and 6.1±2.4%, respectively) compared to controls (4.09±0.80 ml/min/g and 15.2±1.3%, respectively, $p<0.01$). There was a significant correlation between stress MBF and ESCS in DCM ($r=0.89$, $p<0.01$). No correlation was present between rest MBF and systolic function in DCM.
Conclusions. The combination of PET and MRI offers a unique opportunity to quantitatively assess global and regional perfusion and function. In patients with advanced stage of DCM, the degree of impaired hyperaemic blood flow is related to systolic dysfunction.

9:15 a.m.

834-4 **Coronary Vasodilator Responses Are Impaired Independent of Nitric Oxide and Endothelial Function in Conscious Dogs With Dilated Cardiomyopathy**

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Background: Dilated cardiomyopathy (DCM) has been associated with nitric oxide (NO) deficiency and endothelial dysfunction, resulting in depressed systemic and coronary vasodilator responses to endothelium-dependent challenge. However, it remains controversial as to whether endothelium-independent vasomotor function is preserved in DCM,