lower blood pressure and serum Na and were more likely to have had a recent HF hospitalization (all P < 0.001). Results. Shown below are 1-year Kaplan-Meier rates and Cox model hazard ratios (CRV:PBO):

	Spironolactone			No Spironolactone		
	PBO (n=225)	CRV (n=220)	Hazard ratio	PBO(n=908)	CRV (n=936)	Hazard ratio
All-cause mortality	19.1%	11.4%	0.65	18.4%	11.3%	0.65
Death or hospitalization for worsening HF	39.3%	26.3%	0.63	37.5%	25.4%	0.70
Death or cardiovascular hospitalization	41.6%	29.1%	0.61	41.6%	30.4%	0.75
Death or any hospitalization	47.2%	38.4%	0.76	53.3%	42.1%	0.76

CRV reduced the risk of a major clinical event in patients on spironolactone to an extent similar to that seen in patients not on spironolactone.
Conclusion. These data indicate that the morbidity and mortality of patients with severe HF receiving drugs that interfere with more than one neurohormonal target can be reduced substantially with further neurohormonal antagonism (with CRV).

1157-160 Beta-Blocker Utilization in Heart Failure Patients: Experience From a Heart Failure Clinic

Ritesh Gupta, W.H. Wilson Tang, James B. Young, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Beta blockers (BB) reduce mortality in heart failure (HF) patients. Though, well tolerated in clinical trials, utilization rates in clinical settings have not been studied.
Methods: Retrospective analysis of 500 consecutive HF patients presenting to a HF clinic between 3/01 to 5/01 (mean age 61, 69% males, 53% ischemic, mean LVEF 27%). Chi-square test was utilized for subgroup analysis.
Results: 75% of patients had been given a BB trial and 69% were currently on BB. The use of BB was more in moderate (LVEF 20 - 40, n=236) compared to mild (LVEF >40, n = 92) and severe (LVEF <20, n =141) HF (73% vs. 60% and 65%, p=0.04). BB use also decreased with worsening NYHA class of HF symptoms (I 78%, II 72%, III & IV 60%, p=0.01). No difference in BB use by gender was seen (68% in males vs. 71%, p=0.5). Discontinuation rate was 6.8% and was not influenced by NYHA class (p=0.3). Down titration was required in 5.2%. Side effects leading to stopping or down titration, included dizziness (3.2%), fatigue (2.8%), hypotension (2.6%), bradycardia (2.0%), and others (1.4%). A contraindication could be identified in 44% of patients never tried on BB with respiratory disease being the most common in 33%, uncompensated state in 7%, A-V block in 1% and hypotension in 1.6%. Subgroup of diabetics had lower BB use than non diabetics(60% vs 73%, p=0.02) with more contraindications (36% vs. 18%, p < 0.01) and worse NYHA class (p= 0.03) though LVEF was similar (p=0.5). Trend towards lower BB use was seen in elderly patients (age >74) than younger patients (61% vs. 71%, p=0.06) but there was no difference in rate of contraindication to BB(29% vs. 23%, p= 0.1).
Conclusion: High utilization rates for BB (69% current usage) can be achieved with an aggressive approach to initiating BB therapy. Respiratory diseases are the most common reason of not initiating BB therapy. Diabetics and elderly patients are less likely to be on BB. Diabetics tend to have more contraindications to BB and worse NYHA class than non diabetics, which may explain lower use of BB in them. Elderly patients do not show this trend and lower use in this group needs further investigation.

POSTER SESSION

1158

Chagas, Diabetes, Scleroderma, and Cardiomyopathy

Tuesday, March 19, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1158-146 Phosphoramidan Ameliorates the Functional Sequelae of Experimental Chronic Chagasic Cardiomyopathy

Madhulika Chandra, Herbert B. Tanowitz, Vitaliy Shtutin, Jamshid Shirani, *Albert Einstein College of Medicine, Bronx, New York.*

Background. *Trypanosoma cruzi*, the etiologic agent of Chagas' disease, is an important cause of chronic cardiomyopathy. Coronary microvascular spasm, in part mediated by endothelin-1, appears to play a significant role in the pathogensis of experimental chronic chagasic cardiomyopathy. **Aim.** We sought to assess if the administration of an endothelin inhibitor, phosphoramidan, could influence the severity of cardiomyopathy in mice infected with *T. cruzi*. **Methods.** Therefore we infected cd1 mice (n=21) with 10^4 trypomastigotes of the Brazil strain of *T. cruzi*. Of these, 8 were treated with phosphoramidan. An additional 8 uninfected littermates served as controls (C), 3 of which received phosphoramidan. All mice (n=29) survived and were evaluated at 150 days post infection by transthoracic echocardiography. Left ventricular (LV) end diastolic diameter (EDD), relative wall thickness (RWT), and fractional shortening (FS) were measured. Right ventricular (RV) size was assessed semi-quantitatively on a scale of 0-3. **Results.** There was no effect of phosphoramidan on LV EDD, RWT, FS or RV in uninfected (C) mice. Infected, untreated mice (INF) had increased LV EDD (3.2±0.1 v 2.8±0.1mm, p<0.05), along with reduced FS (39±2 v 57±1%, p<0.05) and RWT (0.4±0.0 v 0.5±0.0, p<0.05), compared with C. Treatment with phosphoramidan reduced the magnitude of these changes, such that the infected, phosphoramidan treated mice (INF+P) had no significant differences in LV EDD (2.9±0.1 v 2.8±0.1mm), RWT (0.5±0.1 v 0.5±0.1), and FS (57±2 v 50±4%) compared with C mice. Similarly, RV was larger in INF compared with both C and INF+P mice (2.1±0.3 v 1.5±0.4, INF v INF+P respectively, p<0.01). **Conclusion.** These data indicate that phosphoramidan ameliorates the functional sequlae of experimental chronic chagasic cardiomyopathy.

1158-147 Molecular Epidemiology of Cardiac Actin Gene Mutations in Dilated Cardiomyopathy

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Background: Dilated cardiomyopathies (DCM) are characterized by a large ventricular dilatation and impaired systolic function. There is a strong genetic component in DCM, estimated to be present in approximately 20-30percent of cases. Mutations in exons 5 (Arg312His) and 6 (Glu361Gly) of cardiac actin gene (ACTC) have been reported in two families with DCM. Methods: In order to evaluate prevalence and characteristics of ACTC gene mutations in DCM, 62 patients from different ethnic backgrounds were studied: 17 with sporadic DCM, 45 with familial DCM (belonging to 31 unrelated families). Two patients with ischemic heart disease were used as controls. Genomic DNA was extracted from blood or explanted heart tissue using standard procedures. PCR products were generated from all 6 exons of the ACTC gene, allowing the inclusion of the exon/intron boundaries. Mutation analysis of all 6 exons was performed using denaturing high performance liquid chromatography (DHPLC) and sequence analysis. Results: No mutation was found in any of the six ACTC exons. A single nucleotide polymorphism was detected by DHPLC, and confirmed by sequence analysis in intron 5 (C-62T). Conclusions: ACTC mutations do not seem to be associated with DCM in our large population of familial and sporadic DCM. ACTC mutations appear to be infrequently associated with DCM.

1158-148 Noninvasive Assessment of Coronary Flow Reserve Impairment in Patients With Systemic Sclerosis

Roberta Montisci, Paolo Colonna, Massimo Ruscazio, LiJun Chen, Carlo Caiati, Pietro Garau, Giuseppe Passiu, Alessandra Vacca, Alessandro Mathieu, Sabino Iliceto, *Department of Cardiovascular and Neurol. Sciences, Cagliari, Italy, Institute of Rheumathology, Cagliari, Italy.*

Background. Systemic sclerosis (SSc) is a chronic connective tissue disorder of unknown etiology, characterized by cutaneous and visceral tissue fibrosis with arteriolar and capillary ischemic dysfunction . The pathogenesis of the cardiac lesion in SSc is controversial, but the primary disorder of microvasculature with diffuse arteriolar and capillary lesions could precede any fibrosis, thus causing ischemic disorder to the heart. CFR is used to evaluate coronary microcirculation, and has been already employed to investigate myocardial microcirculation impairment in SSc. Previous invasive studies have demonstrated that coronary flow reserve (CFR) is impaired in patients (pts) with advanced SS and cardiac involvement. We tested the hypothesis that CFR can be early impaired in patients with systemic sclerosis without cardiac involvement and whether CFR impairment is correlated to the cutaneous subset.
Methods. We studied 26 patients with SSc without clinical evidence of heart disease, (14 with diffuse form and 12 with localized form of SSc) and 22 control group patients, matched in age and gender. We evaluated CFR in the left anterior descending coronary artery (LAD) with a new non-invasive method : contrast (Levovist) enhanced transthoracic Doppler (CEE-TTE) during adenosine infusion. The pulsed wave Doppler of blood flow velocity was recorded in the LAD at rest and after maximum vasodilation by adenosine infusion (140 mcg/Kg/min in 5 minutes).
Results: In patients with SSc, without clinical evidence of heart disease, CFR was impaired (2.65±0.63 vs 3.29±0.52 in controls, p < 0.0005). A significantly , greater percentage of SSc patients had reduction of (≤ 2.5) CFR compared to controls (48% vs 4.5%, p=0.003). Left ventricular mass and ejection fraction were not statistically different in the two groups. A non-significant trend between mean CFR and the severity and duration of the disease was also observed.
Conclusion. In this cross-sectional study we demonstrated that CFR is early reduced in patients with SSc and seems to be correlated to the extension of the cutaneous subset of the disease. A reduction of CFR could be an early sign of cardiac involvement in systemic sclerosis.

1158-149 Clinical Course of Dilated Cardiomyopathy in Asymptomatic Patients Long-Term Treated With Beta-Blocking Agents: The Heart Muscle Disease Registry of Trieste

Andrea Di Lenarda, Gastone Sabbadini, Gerardina Lardieri, Mauro Driussi, Elisa Carniel, Laura Vitali Serdoz, Stefano Pangher, Gianfranco Sinagra, *Department of Cardiology, Trieste, Italy, Department of Medicine and Geriatrics, Trieste, Italy.*

No conclusive data are available on long-term effects of adding a beta-blocker (BB) to ACE-inhibitor (ACE-I) therapy in asymptomatic patients with dilated cardiomyopathy (DC).
Among 447 DC patients consecutively enlisted in the Heart Muscle Disease Registry of Trieste between 1986 and 2000, 307 (68.7%) had HF symptoms (NYHA II-IV, Group 1) while 140 (31.3%) were asymptomatic (NYHA I, Group 2) at enrolment. In Group 2, a previous history of HF was present in 71 patients (50.7%)(Group 2a) and absent in 69 (49.3%)(Group 2b).

As compared to patients of Group 1, those of Group 2 were younger (47±14 vs 41±15 years, p<0.001), and showed less advanced LV dysfunction (EF 28±9 vs 35±9%, p<0.001) and remodelling (end-diastolic diameter index 38±7 vs 35±7 mm/m2, p<0.001) at the time of diagnosis. Most patients of Group 1 and 2 were treated with ACE-I (93% and 88%, p=NS) and BB (83% and 74%, p<0.05).
Five and 10-year transplant-free survival was respectively 73 and 57% in Group1 vs 93 and 86% in Group 2, while hospitalisation-free survival was 47 and 32% in Group1 vs 70 and 57% in Group 2 (both p<0.001). No outcome difference was observed between Group 2a and 2b, whereas 5 and 10-year transplant-free survival was significantly better in patients of Group 2 who were treated with BB than in those not receiving BB (p=0.007 after stratification for the severity of the disease).
At 6 to 8 years of follow-up, 38% of patients of Group 2 developed HF symptoms, and/or a decrease of LVEF>10%, and/or the need of hospitalisation for cardiovascular reasons. The long-term progression of HF symptoms and LV dysfunction was similar in asymptomatic patients of Group 2a and 2b and not significantly different to that of patients of Group 1.
Even though asymptomatic DC patients receiving an optimal medical treatment are characterized by low rates of death or heart transplant, nevertheless during a long-term follow-up they frequently exhibit a worsening of clinical status and LV function. Our data suggest that in these patients an early and aggressive BB strategy should be carefully considered in order to counteract as much as possible the long-term progression of the disease.

1158-150 Functional Significance of Myocyte Endothelin-1 in Experimental Chronic Chagasic Cardiomyopathy

Madhulika Chandra, Herbert B. Tanowitz, Yaz Y. Kisanuki, Masashi Yanagisawa, Jamshid Shirani, *Albert Einstein College of Medicine, Bronx, New York.*

Background. *Trypanosoma cruzi*, the etiologic agent of Chagas' disease, is an important cause of chronic cardiomyopathy. Endothelin-1 (ET-1) has been implicated in the pathogenesis of chronic chagasic heart disease, possibly due to its effect on the coronary microvasculature. **Aim and Methods**. In order to assess the role of ET-1 in the pathogenesis of chronic chagasic cardiomyopathy, we infected ET-1 (flox/flox); α-MHC-Cre (+) (ETKO) mice, in which the ET-1 gene has been deleted from cardiac myocytes, with 10^4 trypomastigotes of *T. cruzi* (Brazil strain). We also infected ET-1 (flox/flox); Cre (-) (FLOX) mice. Uninfected littermates of both groups served as controls. All mice (n=28) survived and were evaluated at 160-170 days post infection by transthoracic echocardiography. Left ventricular (LV) end diastolic diameter (EDD), relative wall thickness (RWT), and fractional shortening (FS) were measured. Right ventricular (RV) size was assessed semi-quantitatively on a scale of 0-3. **Results**. Compared with their respective, uninfected controls, both infected ETKO and FLOX mice had increased LV EDD[(3.8±0.3 v 2.7±0.1mm, FLOX), and (3.0±0.1 v 2.6±0.1mm, ETKO), both p<0.05], along with reduced LV FS[(40±3 v 53±1%, FLOX) and (47±2 v 56±2%, ETKO), both p<0.05] and RWT[(0.4±0.0 v 0.5±0.0, FLOX) and (0.5±0.0 v 0.6±0.0 ETKO), both p<0.05]. However the magnitude of these changes was attenuated in the infected ETKO group as compared with the infected FLOX group (p<0.05 for LV EDD, RWT, and FS). Similarly, RV was larger in infected FLOX compared with ETKO (2.5±0.3 v 0.6±0.3, respectively, p<0.01). **Conclusions**. These data provide support for the role of ET-1 in pathogenesis and progression of chronic chagasic heart disease and indicate that the cardiac myocyte is an important source of ET-1 in this disease.

1158-151 Mitochondrial Respiratory Abnormalities in Ventricular Myocardium of Patients With End-stage Congenital Heart Disease

Seema Mital, Alessandro Barbone, Ralph J. Mosca, Jan M. Quaegebeur, Linda J. Addonizio, Thomas H. Hintze, *Columbia University, New York, New York.*

Background: Nitric oxide (NO) binds to mitochondrial cytochrome oxidase to decrease myocardial oxygen consumption (MVO2). This regulation is disrupted in end-stage heart failure in part due to reduced NO availability. We compared NO mediated regulation of MVO2 in patients with end-stage congenital heart disease (CHD) vs cardiomyopathy (CMP) undergoing cardiac transplantation.
Methods: MVO2 was measured in vitro using a Clark type oxygen electrode in LV muscle segments obtained from explanted failing human hearts at heart transplantation. This included 7 pts with complex CHD (mean age 11±10 years) and 14 pts with dilated CMP (mean age 25±26 years). We measured the effect of increasing doses (10-7-10-4M) of the following NO agonists on MVO2 - amlodipine, ramiprilat, bradykinin - all of which cause kinin-dependent NO production, and exogenous NO donors, S-nitroso N-acetyl penicillamine (SNAP) and nitroglycerin (NTG). MVO2 was measured with and without addition of nitro-L-arginine methyl ester (L-NAME, 10-4 M), NO synthase inhibitor.
Results: All drugs caused a significant dose-dependent decrease in MVO2 in both groups. However, myocardium from CHD pts showed a smaller decrease in MVO2 in response to NO agonists compared to CMP pts. Changes in MVO2 at highest dose in CHD vs CMP respectively are shown - amlodipine, -5±7% vs -29±6%, p<0.001; ramiprilat, -17±8% vs -26±2%, p=0.05; and bradykinin, -22±7% vs -30±5%. NO donors, SNAP and NTG also caused smaller decreases in MVO2 in CHD vs CMP (SNAP, -37±4% vs -49±3% and NTG, -16±6% vs -37±4% respectively)(p<0.01). Therefore, NO donors were unable to completely reverse altered regulation of MVO2 in CHD suggesting abnormal mitochondrial function. L-NAME, NO inhibitor, attenuated the effect of amlodipine, ramiprilat and bradykinin but not of SNAP and NTG.
Conclusion: Abnormal regulation of MVO2 in end-stage heart failure may be secondary to reduced NO availability and can be reversed by use of NO agonists. In end-stage CHD, however, this abnormality may be related at least in part to abnormal mitochondrial function.

1158-152 Improved Glycemic Control Induces Regression of Left Ventricular Mass in Patients With Type 1 Diabetes Mellitus

Franz C. Aepfelbacher, Susan B. Yeon, Larry A. Weinrauch, John D'Elia, Andrew J. Burger, *Beth Israel Deaconess Medical Center, Boston, Massachusetts, Joslin Diabetes Center, Boston, Massachusetts.*

Background: Diabetes mellitus has been associated with abnormalities of cardiac function and left ventricular hypertrophy. However, the effect of improved glycemic control on these parameters is controversial and may be confounded by the type of glycemic therapy or alterations in blood pressure levels.
Methods: We studied 19 patients (mean age 40 ± 9 years) with longstanding type I diabetes mellitus (28 ± 4 years), who participated in a program of stringent glycemic control using insulin injections. Glycemic control was monitored with hemoglobin A1c (Hb A1c) levels; improvement was defined as > 1 % (absolute) decrease of Hb A1c. Two-dimensional and Doppler echocardiograms and 24-hour ambulatory blood pressures (24h ABP) were obtained at baseline and after 1 year. Left ventricular (LV) mass was determined using the area-length method.
Results: Hb A1c and echocardiographic data (mean ± SD) are shown below. Septal thickness decreased for all patients; septal thickness and LV mass regressed for the subgroup with improved glycemic control. Left ventricular function and 24h ABP parameters remained unchanged after 1 year in both groups.
Conclusions: Improved glycemic control induces regression of septal thickness and LV mass without significant effect on systolic or diastolic function. Importantly, these changes occurred in the absence of significant alterations in 24h ABP levels.

	All Patients (n=19)		Patients with improved glycemic control (n=12)	
	Baseline	1 Year	Baseline	1 Year
Hemoglobin A1c (%)	9.5 ± 1.6	8.2 ± 1.5*	9.8 ± 1.5	7.8 ± 1.2*
LV mass (gm)	203 ± 53	185 ± 59	205 ± 35	182 ± 46†
LV septum (mm)	10.3 ± 1.3	9.7 ± 1.6†	10.3 ± 1.4	9.4 ± 1.7†
LV posterior wall (mm)	9.9 ± 1.4	9.6 ± 1.1	9.9 ± 1.3	9.6 ± 0.9
LV diastolic diameter (mm)	46 ± 5.8	46.9 ± 5.7	45.3 ± 4.1	46.3 ± 4.1
LV systolic diameter (mm)	28.2 ± 4.2	28.3 ± 5.8	27.4 ± 3.6	27.7 ± 4.9
Fractional shortening (%)	38.7 ± 5.3	40.2 ± 6.9	39.5 ± 5.7	40.5 ± 6.9
E/A ratio of mitral inflow	1.23 ± 0.4	1.29 ± 0.5	1.25 ± 0.4	1.33 ± 0.5
E-wave deceleration time (ms)	191 ± 40	188 ± 37	176 ± 33	190 ± 40

*p<0.001 vs baseline, †p<0.05 vs baseline

POSTER SESSION

1159 Stress Testing in Coronary Artery Disease: New Information

Tuesday, March 19, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1159-137 Impact of Percutaneous Coronary Intervention on Functional Status: Results from the ADORE Trial

Sabrina Cugno, Mark J. Eisenberg, James Blankenship, Thao Huynh, Michael Azrin, Steven Sedlis, Louise Pilote, *Jewish General Hospital, Montreal, Quebec, Canada.*

Background:
While it is well known that percutaneous coronary intervention (PCI) is effective at reducing angina and other markers of coronary artery disease (CAD), little is known about the magnitude of functional status and angina class improvement as well as the magnitude of anti-anginal drug use after PCI in the general post-PCI patient population.
Method:
To determine the magnitude to which PCI effects functional status, angina class and anti-anginal drug use, 9-month post-PCI results were compared with results obtained 3-months prior to PCI in 109 patients. Patients were enrolled in the Aggressive Diagnosis Of Restenosis (ADORE) Trial, a randomized clinical trial which examined functional testing in patients who underwent complete coronary revascularization by a percutaneous technique.
Results:
A significant improvement in functional status, measured by an increase in METS, was observed 9-months after PCI when compared to 3-months prior (9.7 vs 7.4, p<0.0001). In addition, a significant difference was found between 9-month post-PCI functional test results and those obtained 3-months prior: reversible ischemia detected by ECG (19.4 vs 63.0, p< 0.0001), clinically determined reversible ischemia (10.2 vs 58.6, p<0.0001), and electrically or clinically positive functional test result (23.4 vs 83.7, p<0.0001). A significant improvement in CCS angina class was also found post-PCI (CCS class 1 or 2: 24.5 vs 43.5, p=0.001, and CCS class 3 or 4: 1.0 vs 46.3, p<0.0001). A marked decrease in anti-anginal drug use was further noted after PCI (16.0 vs 30.6, p=0.0001).
Conclusions:
Complete revascularization with PCI leads to substantial improvements in functional status and CCS angina class, and is associated with decreased use of anti-anginal drugs.Thus, this procedure is beneficial in patients with CAD.