intended to study metabolic changes in skeletal muscle biopsy specimens in patients with mild to moderate heart failure after myocardial infarction to evaluate the influence of ramipril treatment on these changes.

Methods: Biopsies were obtained from the Vastus muscle at baseline and after 6 months of treatment with ramipril or placebo. Biopsies were analysed for ATP, creatine, creatine phosphate, glycogen and lactate. Ejection fraction was evaluated by two dimensional echocardiography. Twenty-three male and 10 female patients, mean age 67 years (range 43–81 years), with symptoms of heart failure after myocardial infarction participated in this study. Eighteen men and 6 women mean age 65 years (range 54–75 years), with no history or clinical signs of heart disease admitted for minor surgery, were used as controls.

Results: Patients had mild to moderate left ventricular dysfunction, mean ejection fraction of 48%. We found a reduction in ATP 20% $p < 0.0001$, total creatine 13% $p < 0.0005$ and glycogen 15% $p < 0.05$ in patients compared to healthy controls. Six months treatment with ramipril didn't alter these changes.

Conclusions: Depletion of energy rich substrates ATP, creatinine and glycogen is seen in patients with mild to moderate heart failure early after myocardial infarction. Treatment with ramipril seems not to revert this depletion when developed.

1227 Cardiac Transplantation: Studies of Coronary Flow

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 4:00 p.m.–5:00 p.m.

1227-56 Microvascular Endothelial Dysfunction Is Associated With Expression and Activation of Nitric Oxide Synthases and Endothelin Early After Cardiac Transplantation in Humans

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Background: Expression and Production of vasoactive mediators may contribute to endothelial dysfunction and graft atherosclerosis after heart transplantation (HTx). We investigated the relationship of inducible, constitutive nitric oxide synthases (iNOS, cNOS), endothelin (ET) and cytokines and microvascular endothelial dysfunction (ED) in 42 humans 37 ± 5 days after HTx.

Methods: Gene expression of iNOS, cNOS and ET was performed by RT-PCR. Coronary sinus (CS) and aortic plasma ET (fmol/ml) and nitrite (μM) were measured. Endothelium dependent vasomotion was assessed with Acetylcholine (ACh, 30 μg/min) by Doppler flowire. Exclusion criteria were acute infection or rejection episodes and presence of CAD.

Results: In 26.1% (n = 11) an impaired flow increase (1.65 ± ± 0.23) suggesting ED. In all patients (pts) iNOS, cNOS and ET expression was present. Transcardiac cytokine production was noted in nearly 60% of pts for IL-6, TNF-Rp2 and TNF-alpha. An increase in nitrite release was found (Aorta: 43.9 ± 3.7 vs CS: 52.8 ± 5.6, $p < 0.05$) suggesting transcardiac nitric oxide production. CS nitrite correlated with CS TNF-alpha levels ($r = 0.44$, $p < 0.05$). A transcardiac ET net extraction was found in patients with ED: (Aorta: 12.9 ± 0.57 vs CS: 9.8 ± 0.4, $p < 0.05$).

Conclusions: These findings provide evidence the microvascular endothelial function is impaired in 26% of pts in an early phase after HTx. Correlation between vasoactive mediators and pro-inflammatory cytokines suggest a chronic (smolder) immunologic process in the development of microvascular ED which may be an important therapeutic target in pts after HTx.

1227-57 The Effects of Acute Cellular Rejection on Intimal Thickening and Coronary Flow

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Transplant coronary arteriopathy (TCA) is postulated to develop secondary to chronic vascular immune responses. The effects of repeated episodes of acute cellular rejection on the subsequent development of TCA and on coronary flow reserve (CFR) have not been well studied. In 44 patients ≥1 year post-transplant the CFR was measured (Doppler guide wire and adenosine) in the LAD, CFX, and RCA. Intracoronary ultrasound (ICUS) was performed in the LAD or CFX of each patient and analyzed to assess average vessel mean intimal index and mean intimal thickness. An average biopsy score for the first 6 months post transplant was calculated using a numerical grading scale (0 = 0, 1A = 1, 1B = 1.5, 2 = 2, 3A = 3, 3B = 3.5) divided by the number of biopsies. The mean CFR and ICUS parameters were correlated with the average biopsy score using the non-parametric Spearman's rank correlation.

Results: Higher average biopsy grades in the first 6 months post transplant correlated with lower coronary flow reserves ($r = -0.34$, $p = 0.038$). There was no correlation between rejection history and any ICUS parameter.

Conclusion: The cumulative affect of early chronic acute cellular rejection results in late microvascular dysfunction as measured by a diminishment in CFR but has no correlation with the subsequent development of epicardial TCA.

1227-58 Intraindividual Variability of Coronary Flow Reserve in Heart Transplant Recipients With Angiographically Normal Coronary Arteries. A Study With Intracoronary Doppler and Ultrasound

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Background: Coronary flow reserve (CFR) is an important parameter of graft function after heart transplantation (Htx). In most reports on patients after Htx, CFR measurements performed in one of the epicardial vessels were considered representative for global graft function. The purpose of this study was to assess potential differences in CRF values between different coronary artenes.

Methods: We studied 57 patients (P, mean age 48 ± 13 years) with normal coronary angiography 38 ± 41 months after HTx using intracoronary Doppler (0.014 in. Doppler guide wire) and ultrasound (ICUS). CFR was determined after i.c. administration of 16 μg adenosine both in the left anterior descending artery (LAD) and in the circumflex artery (LCx). The extend of graft vasculopathy (TxCAD) was quantitated by ICUS (motorized pullback) using the mean intimal index of each vessel.

Results: CFR ranged from 1.1 to 5.7. CRF values showed no differences between LAD and LCx (3.1 ± 0.9 vs. 2.9 ± 0.6, NS). The correlation of flow parameters between both coronary artenes was good ($r = 0.74$, $p < 0.001$). However, the relative difference in CRF values between LAD and LCx ranged from 1% to 42% (mean, 17 ± 11%). In 17% of the P with normal CFR (> 2.5) in the LAD, reduced values (< 2.5) were in observed in the LCx. Mean intimal index in both vessels was comparable (16 ± 14% vs. 15 ± 15%).

Conclusion: In individual patients, coronary flow reserve measurements may show marked differences between LAD and LCx. These findings should be taken into account when data of CFR measurement obtained in one epicardial vessel are considered representative for global graft function.

1228 Atrial Tachycardia and Fibrillation

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 4:00 p.m.–5:00 p.m.

1228-161 Electrophysiologic Remodeling of the Atrium in Patients With Atrial Fibrillation

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Previous studies have shown that sustained atrial fibrillation [AF] causes atrial electrophysiologic remodeling. Whether remodeling affects the atrium uniformly and consistently in patients [pts] with paroxysmal AF [PAF] and chronic AF [CAF] is unclear. We measured: 1) atrial conduction time [CT] at multiple sites in right atrium [RA] (mid & low) and left atrium [LA] (proximal, mid & distal coronary sinus [DCS]) during sinus rhythm; 2) effective refractory periods [ERPs] at high RA [HRA], low RA [LRA] and DCS at 400 & 600 ms drive cycle length (4 × threshold) in 11 pts (mean age:61 ± 15 yrs) with CAF (mean AF duration: 19 ± 6 mths) after successful transvenous defibrillation; 8 pts (mean age: 47 ± 14 yrs) with PAF and 10 controls (C) (mean age: 50 ± 12 yrs).