ORAL CONTRIBUTIONS
813  Cardiac Allograft Vasculopathy: Basic Mechanisms and Clinical Correlates
Monday, March 08, 2004, 11:00 a.m.-12:15 p.m.
Morial Convention Center, Room 217

813-1 Cytomegalovirus Infection Is Proportional to Cardiac Allograft Vasculopathy in Heart Transplant Recipients

Background: Cytomegalovirus (CMV) infection is a risk factor for cardiac allograft vasculopathy (CAV) in heart transplant (HT) recipients. However, few human studies have addressed the question of infectious burden and its direct role in CAV severity. The aim of this analysis was to determine whether increasing viral burden was predictive of CAV.

Methods: Forty-six consecutive HT recipients enrolled at Bologna (n=40) and Stanford (n=6) HT units (5±1 year; 78% males) were monitored for CMV activation, either by PCR or antigenemia testing of peripheral blood obtained weekly during the initial month, and then at monthly intervals after HT. CMV management consisted of either prophylaxis with ganciclovir for 4 weeks after HT, or pre-emptive treatment with ganciclovir only when parameters exceeded 50 cells/ml of leukocytes. Patients were divided into three groups based on viral burden: 1) CMV negative throughout follow-up (n=14); 2) asymptomatic CMV infection (n=6); and 3) CMV infection (n=16). CAV progression was quantified by coronary intravascular ultrasound (IVUS) performed at 1 and 12 months after HT.

Results: Overall, coronary intimal area (IA) increased by 70% (P<0.01) during the follow-up. IA increased by 30% in Group 1 recipients, by 90% in Group 2 and by 115% in Group 3 (P=0.01 for trend; P<0.05 for Group 1 vs. Group 3 and for Group 2 vs. Group 3, after corrections for prophylactic vs. pre-emptive strategy, recipient's and donor's age, lipid levels and rejection score index. Multivariable analysis suggested a direct correlation between CAV progression and CMV infection, regardless of prophylactic vs. pre-emptive strategy. These results strongly suggest the hypothesis of a direct involvement of CMV in CAV pathophysiology.

11:15 a.m. 11:00 a.m.
813-2 Incremental Value of Redox Pattern in Predicting Cardiac Allograft Vasculopathy After Heart Transplantation
Oberdan Parodi, Benedetta De Chiara, Fabio Turazzz, Jonica Campolo, Andrea Garascia, Riccardo Bigi, Maria Frigerio, Silvio Klumpp, CNR Clinical Pathology Institute, Milan, Italy, Niguarda Ca' Granda Hospital, Milan, Italy

Background: Cardiac allograft vasculopathy (CAV) is the main factor limiting survival after heart transplantation (HTX). This study was aimed to identify predictors of CAV among clinical (age, cause of HTX, donor age, time from HTX, acute rejection and ischemia time), biochemical (fasting plasma glucose, creatinine, total cholesterol, LDL-cholesterol and triglycerides) and redox patterns (plasma total and reduced homocysteine, cysteine, glutathione (GSH), reduced GSH in erythrocytes (GSEh) and vitamin E variables).

Methods: 56 male patients (60±11 years) underwent angiography 53±36 months after HTX. Clinical (model 1), conventional biochemical (model 2) and redox pattern (model 3) data were sequentially entered into a multiple stepwise regression model to predict CAV. The increase in global $r^2$ of the model after the addition of each block of variables identified an incremental diagnostic value.

Results: CAV was found in 18 (32%) patients. After adjusting for the most significant variables, GSH (OR 0.98, 95% CI 0.97-0.99 per pmol/l, P=0.02) was independently associated to CAV. The addition of conventional biochemical variables reduced the overlap...
all power of the model, whilst a significant improvement was obtained after entering redox pattern data (Figure).

Conclusions: The assessment of redox pattern yields incremental diagnostic value over clinical and biochemical data in predicting CAV. In particular, GSH/HG may represent a clinically useful marker of risk.

**Methods:** Fourteen pts (60 ± 10 y, 12 males) with ischemic cardiomyopathy were treated with H.E.L.P. apheresis treatment. H.E.L.P. apheresis reduces the plasma levels of LDL-cholesterol and lipoprotein (a) by 48% (p<.001), fibrinogen by 42% (p=.000), plasma viscosity by 14%, and erythrocyte aggregation by 28%. Osmolality (<1%) and hematocrit (<1%) remained unchanged. The PET scans were positive for focal tracer uptake in the neck and 10 were negative. Actin +/- or apheresis improves heart transplant outcome. Clinical long-term studies demonstrating that cholesterol reduction either with statins and/or apheresis improves heart transplant outcome. Conclusion: A single apheresis treatment significantly increased myocardial blood flow at rest by 17.5% (p<.01) and hyperemic flow by 27% (p<.02). Coronary flow reserve increased by 9% (p=.09). Hyperemic flow following adenosine infusion increased plasma VEGF levels only before H.E.L.P. apheresis, indicating a better ischemic tolerance after apheresis.

**Conclusions:** Myocardial perfusion in transplanted hearts significantly increases following H.E.L.P. apheresis treatment. The present study provides complementary evidence to clinical long-term studies demonstrating that cholesterol reduction either with statins and/or apheresis improves heart transplant outcome.

**Results:** 11:00 a.m.

**813-4**

**Smooth Muscle Cell Proliferation Index Correlates With Indium-111 Z2D3 Antibody Uptake in a Transplant Vasculopathy Swine Model**

Javier Jimenez, Dillip Sawatt, Tammy Donahay, Lorraine Schofield, Ban An Khaw, Lynne L. Johnson, Rhode Island Hospital, Providence, RI

**Background:** Smooth muscle cell (SMC) proliferation is a hallmark of transplant vasculopathy (TV). The goal of this study was to determine the ability of gamma camera imaging of a monoclonal antibody (Z2D3) tagged with Indium-111 to detect TV.

**Methods:** Coronary to right carotid transplantation was performed in 10 Yucatan mini pigs using farm pigs as donors. In 5 of these experiments the RC was also grafted into the LC (homografts) and in one farm pig the LC and RC were switched. After 44±22 days animals were injected with BrdU, underwent planar and SPECT imaging and were sacrificed and vessels removed. Tissue was sectioned and stained. Quantitative morphometry was performed. SMC proliferation index (BrdU-actin cells/actin x 100) was correlated with in vivo and ex vivo uptake.

**Results:** Patency was obtained in only 5/10 allografts and 3/7 homografts. Six of the pigs were positive for focal tracer uptake in the neck and 10 were negative. Actin +/- BrdU + cells were seen in the media of allografts and in the reanlanced lumen of occluded homografts. A SMC proliferative index of 30% was used as a cut-off for scan positivity. By chi square there was significant concordance in 14 experiments and discordance in 2 (p<0.008). When ex vivo vessel counts were correlated with SMC proliferation index there was a significant correlation with r2=0.528 (p<0.01).

**Conclusion:** The use of the monoclonal antibody Z2D3 tagged with Indium-111 allows the detection of proliferating SMC and correlates with the intensity of cell proliferation.

**Risk Factors for CAV**

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<thead>
<tr>
<th>Hazard Ratio</th>
<th>CI</th>
<th>P</th>
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<tbody>
<tr>
<td>Statin Therapy</td>
<td>0.29</td>
<td>0.09 – 0.96</td>
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<tr>
<td>Late Rejection</td>
<td>2.27</td>
<td>1.31 – 3.92</td>
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<td>Earlier Year of Transplant</td>
<td>2.03</td>
<td>1.03 – 4.16</td>
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**ORAL CONTRIBUTIONS**

**814 Heart Failure: Cell Therapy**

Monday, March 08, 2004, 11:00 a.m.-12:15 p.m.

**Morial Convention Center, Room 254**

11:00 a.m.

**815**

**Transendocardial Injection of Autologous Bone Marrow Mononuclear Cells May Enhance Myocardial Viability Around Cell Injection Site**

Emerson C. Pereira, Hans F. Doehmann, Radovan Borejecvic, Joao A. Assad, Guilherme V. Silva, Suzana A. Silva, Andre L. Sousa, William K. Vaughn, Isabel Rossi, Antonio C. Carvalho, Jung Y. Geng, Hans J. Dohmann, James T. Willerson, Texas Heart Institute, Houston, TX, Pro-Cardiaco Hospital, Rio de Janeiro, Brazil

**Background:** Autologous Bone Marrow Mononuclear Cell (ABMMMC) injection in humans has shown improvement in areas reversible perfusion detects possibly through the promotion of localized angiogenesis. Electromechanical voltage maps (EMVM) are capable of assessing myocardial viability through the magnitude of underlying myocardial electrical signals. Improvement in voltage values of previously non-viable tissue surrounding cell injection sites was observed. We sought to systematically determine if ABMMMC injections might expand areas of myocardial viability.

**Methods:** Fourteen pigs (60 ± 10 y, 12 males) with ischemic cardiomyopathy were treated with ABMMMC transendocardial injections in a target area of reversible defect by SPECT and viability by EMVM voltage criteria. Average electrical unipolar voltage was quantified in the injected area and in the area surrounding injections (peri-injection area) immediately before and 4 months after the procedure. To assess the reproducibility of EMVM a