SMALL VESSEL CORONARY OCCLUSIVE DISEASE AFTER CARDIAC TRANSPLANTATION

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Coronary occlusive disease (COD) is the main cause of graft failure after the first year in cardiac transplant recipients. The functional effects of this disease on the small resistance vessels are as yet unclear. We investigated the changes in coronary flow reserve (CFR) to the non specific smooth muscle vasodilator papaverine. A 2F Doppler probe was inserted into the left anterior descending coronary artery in 40 patients following orthotopic heart transplantation. Studies were performed in 36 males and 4 females with a mean age of 47.6 years (range 23-61). The median time from operation was 4 years (range 3 months to 8 years). Coronary flow reserve (CFR) was defined as the ratio of peak to resting velocities. The 16 patients with evidence of minor epicardial vessel disease (<25% stenosis) or small vessel disease in the LAD artery on angiography had a significantly reduced peak hyperemic response to papaverine compared to the patients without COD (CFR 2.8 +/-1.15 VE 4.2 +/- 1.3, p<.0005).

We found no correlation with age, original diagnosis, active rejection, blood pressure, HDL or LDL cholesterol levels, CMV status, ischemic time or cyclosporin levels. This demonstrates that significant reductions in non-endothelial dependent flow reserve are present when only "minor" COD is seen angiographically.

IDENTIFICATION OF TRANSPLANT ARTERIOPATHY IN ORTHOTOPIC CARDIAC TRANSPLANT RECIPIENTS USING EXERCISE SPECT THALLIUM-201

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A major determinant of morbidity and mortality of cardiac transplant patients (PTx) is the development of transplant arteriopathy, which necessitates periodic cardiac catheterization (Cath). The purpose of this study was to determine the utility of exercise thallium-201 (TI) scintigraphy using single photon emission computed tomography (SPECT) in screening PTx for the presence of coronary artery disease (CAD). We evaluated 32 studies in 29 patients (28 men and 1 woman), who had TI and Cath within 6 months. Patients were studied a mean of 3.6 years post-transplant. They exercised an average of 7.9 +/- 3.5 minutes on the Bruce protocol, and attained maximal heart rates of 135 +/-24 beats per minute. 6 (19%) patients had abnormal electrocardiographic responses. Representative apical, mid and basal short axis thallium sections were selected and quantitated using radial profiles. The limits of normal were defined as 2.5 standard deviations below the mean of a previously defined normal database. A study was defined as abnormal if two 18 sectors were more than 2.5 standard deviations below the mean of the normals. A Cath was considered abnormal if there was at least one vessel with a stenosis > 50%. Of the 11 abnormal caths 9 showed defects on thallium imaging (Sensitivity = 82%). Of the 21 normal caths 17 had normal thallium images (Specificity = 81%). Both false negatives were 1 vessel CAD (1 distal LAD, 1 septal). All 4 false positive thalliums were mild lateral defects and may reflect increased attenuation of the lateral wall due to the increased clockwise rotation of the transplanted heart. We conclude that exercise TI SPECT is effective for screening cardiac transplant recipients for the presence of transplant arteriopathy.

PREVENTION OF HYPERCHOLESTEROLEMIA BY STEROID FREE MAINTENANCE IMMUNOSUPPRESSION (SFMI) AFTER HEART TRANSPLANTATION (HTX)

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Between 5/87 and 7/90 a group of high risk HTX patients (n=35) were selected to receive OKT3 induction therapy (10-14 days) with SFMI after 6 weeks (cyclosporine and azathioprine only). This group was compared with a group of HTX patients (n=47) that received triple drug (TDI) immunosuppression (cyclosporine, azathioprine, and prednisone) during the same time interval. One and 3 year actuarial survival was 97% and 91% (OKT3) and 91% and 85% (TDI). The incidence of freedom from rejection at 3 months and 1 year was 77% and 55% (OKT3) and 61% and 59% (TDI). The incidence of infection was higher during the initial 3 months in the OKT3 group (29% vs 6%) (p=0.007). Six percent (TDI) vs 6% (OKT3) became diabetic post transplant. Total serum cholesterol (mSOD) were measured at intervals and are shown below:

<table>
<thead>
<tr>
<th>Time</th>
<th>OKT3</th>
<th>TDI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretransplant</td>
<td>189±71</td>
<td>197±56</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td>207±54</td>
<td>250±48</td>
<td>0.004</td>
</tr>
<tr>
<td>1 year</td>
<td>205±59</td>
<td>260±56</td>
<td>0.003</td>
</tr>
</tbody>
</table>

In conclusion, OKT3 induction with SFMI after HTX prevents the development of hypercholesterolemia and diabetes in treated patients, with no increase in mortality or incidence of rejection.

CORONARY RESPONSE TO NITROGLYCerin in CARDIAC TRANSPLANT RECIPIENTS: EVALUATION WITH INTRAVASCULAR ULTRASOUND


Intravascular ultrasound offers a new method for real-time evaluation of coronary vasomotion responses to pharmacologic interventions. The coronary artery vasomotion response to nitroglycerin (NTG) was studied using a 5 French 30 mHz intracoronary ultrasound imaging catheter (CVIS, Inc) in 10 cardiac transplant recipients undergoing routine arteriograms 3 weeks to 9 years after transplantation. End diastolic cross sectional luminal area (L-CSA) and derived diameter (L-Dia) were measured at a fixed position in the left anterior descending coronary artery immediately before, and every thirty seconds for five minutes after, 0.4 mg of sublingual NTG. All patients demonstrated a vasodilatory response to NTG. Four patients had biopsy proven mild or moderate rejection at the time of the ultras. Results: L-CSA increased from a baseline of 13.5 mm² ± 5.3 to 17.0 mm² ± 4.7 at five minutes and L-Dia increased from 4.1 mm ± 0.8 to 4.6 mm ± 0.6. The increase reached statistical significance (p<0.01) at 1.5 minutes after administration of NTG and the mean maximum increase occurred at 4.5 minutes (34% for L-CSA and 14% for L-Dia). The NTG response was well preserved in patients up to 9 yrs after transplantation. Neither the coronary intimal thickness as measured with intravascular ultrasound nor the rejection status impacted the vasodilation response.

Conclusion: Intravascular ultrasound provides real time documentation of NTG-induced coronary vasodilation in cardiac transplant recipients. This response is well preserved in long term survivors and is not related to the degree of intimal disease or the presence of rejection. This suggests that medial muscular function is retained in transplant coronary arteries, including those with intimal proliferation.