

9:45

**CLINICAL DETECTION OF CARDIAC ALLOGRAFT REJECTION USING <sup>31</sup>P NMR SPECTROSCOPY**

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The reliable noninvasive detection of acute cardiac allograft rejection remains an elusive goal. Since animal studies have demonstrated early changes in phosphocreatine (PCr)/adenosine-triphosphate (ATP) ratio by P-31 NMR spectroscopy, we evaluated 11 patients with 37 serial studies beginning 3-5 weeks after cardiac transplantation. In addition, eight volunteers were studied as controls. Image-guided localized P-31 NMR spectroscopy was performed using a 1.5T Philips Gyroscan with a selected volume of 75-150cc of the left ventricle. Histologic evaluation was used to categorize myocardial biopsies (performed within 24hrs of NMR analysis) into mild, moderate, or severe rejection using the Billingham criteria.

The PCr/ATP's for normal volunteers and non-rejecting transplants (mild histological) were  $1.35 \pm 0.26$  (SD) (n=8) and  $0.95 \pm .25$  (n=28) (p<.0001). A decrease in PCr/ATP was predictive of rejection (moderate or severe by histologic grade) within 2 weeks of the NMR study. The mean PCr/ATP for the rejecting group was  $0.83 \pm 0.10$  (n=16) compared to  $1.00 \pm 0.25$  (n=21) unassociated with rejection within 2 weeks (p<.01). Inferences:

- The bioenergetics in the transplanted heart (reflected by the PCr/ATP) is significantly different from normal volunteers.
- This preliminary clinical study suggests that P-31 NMR spectroscopy may allow the detection of acute cardiac rejection.

Thursday, March 7, 1991

8:30AM-10:00AM, Room 202, East Concourse  
New Imaging Agents and Techniques

8:30

**ASSESSMENT OF VENTRICULAR FUNCTION WITH THE MULTIWIRED GAMMA CAMERA AND TANTALUM-178 DURING PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY**

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The recently developed mobile multiwire gamma camera and the short-lived (T-1/2 = 9.3 minutes), generator-produced isotope tantalum-178 provide rapid, serial assessment of regional and global ventricular function by first-pass radionuclide angiography, at bedside, and thus for the first time enable the use of nuclear techniques to study the changes in LV and RV function during coronary angioplasty. Accordingly, we performed first-pass radionuclide angiography at baseline and during 51 episodes of transient coronary occlusions during coronary angioplasty, using the multiwire camera and doses of up to 100 mCi of tantalum-178. Occlusion of the left anterior descending (LAD) artery (n=23) caused severe decreases in LV ejection fraction ( $55 \pm 13\%$  to  $32 \pm 10\%$ , p=.001), peak diastolic filling rate ( $2.5 \pm 0.7$  to  $1.7 \pm 0.6$  EDV/sec, p=.0001), LV dilation, fall in stroke volume and cardiac output indices, and severe anterior hypokinesis or akinesis (all p<.05). These changes were all more striking during proximal LAD occlusion. Occlusion of non-LAD arteries (n=28) caused regional dysfunction but insignificant changes in global LV function. RV ejection fraction fell during LAD ( $43 \pm 9\%$  to  $39 \pm 9\%$ , p<.05), circumflex ( $44 \pm 9\%$  to  $39 \pm 8\%$ , p=.03), and proximal right coronary artery ( $43 \pm 5\%$  to  $36 \pm 7\%$ , p<.01) occlusions. Only the latter caused RV dilation.

We conclude that the LV function is markedly depressed during transient balloon occlusion of the LAD, but not of non-LAD coronary arteries. RV function decreases during LAD, circumflex or proximal right coronary artery occlusions, but only the latter causes ischemic RV dilation.

8:45

**ANTIMYOSIN SCINTIGRAPHY IN MYOCARDITIS: EVALUATION OF DIAGNOSTIC METHODOLOGY**

Jagat Narula, Tsunehiro Yasuda, James F. Southern, Ban An Khaw, Igor F. Palacios, John B. Newell, G. William Dec, John T. Fallon, H. William Strauss, Edgar Haber, Massachusetts General Hospital, Boston, MA

Fifty patients with no evidence of ischemic, valvular or congenital cardiac abnormality underwent antimyosin scintigraphy (AMS) and right ventricular endomyocardial biopsy (FMB) for the diagnosis of myocarditis (age: 18-77 years; M:F, 27:23). Planar images and tomographic reconstruction of the AMS were obtained and criteria for interpretation as positive and negative scans were established. Blinded random sequence evaluation of the reproducibility of AMS interpretation revealed good to excellent chance-corrected agreement within an observer (kappa A1-A2,  $0.84 \pm 0.14$ ) and between two observers (kappa A1-B,  $0.65 \pm 0.14$ ; A2-B,  $0.72 \pm 0.14$ ). EMB detected myocarditis or borderline myocarditis in 15 patients. AMS results revealed a high sensitivity ( $88 \pm 5\%$ ) and negative predictive value ( $83 \pm 5\%$ ) for the diagnosis of myocarditis, although specificity was low ( $30 \pm 6\%$ ). Mean heart to lung ratio (H/L) for the AM antibody uptake in biopsy- and AMS-positive cases ( $1.67 \pm 0.28$ ) was essentially similar to that in AMS-positive, biopsy-negative cases ( $1.61 \pm 0.21$ ) suggesting the possibility of identical underlying pathology. Mean H/L was significantly lower in biopsy- and AMS-negative patients ( $1.31 \pm 0.18$ ; p<.001). A high sensitivity and negative predictive value with identical H/L in concordant and discordant positive AMS suggests that nonspecific uptake of AM antibody is less likely and that AMS may in fact detect myocarditis that EMB failed to detect. The study highlights a methodological problem of using an established standard of unproven sensitivity for the evaluation of a new diagnostic test, since a comparison test with higher sensitivity than the standard may be deemed to have poor specificity.

9:00

**NONINVASIVE IMAGING OF CARDIAC TRANSPLANTATION REJECTION IN PRIMATES USING TWO NEW ANTIMYOSIN IMAGING AGENTS**

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Indium-111 labeled monoclonal antimyosin Fab (using DTPA chelate)(AMFab) has been used to image myocardial infarction and transplant rejection with localization only in myocardial cells that have suffered irreversible loss of cell membrane integrity. Potential technical limitations are dosimetry, limited by 72 hr half life of In-111, slow blood clearance delaying optimal imaging to 24-48 hrs after injection and hepatic uptake. Therefore 2 new AM imaging agents, polylysine In-111AM ( $0.023$ mgFab modified with a 3.3kd polymer of PLA and labeled with In-111) and Tc-99m AM ( $0.5$ mg Fab' AM labeled using the RP-1 ligand technique, Centocor) were compared in 6 primates, 5 having undergone heterotopic xenographic (2) or orthotopic allographic (3) transplantation. Each animal was injected first with 12-23 mCi Tc-99mAM and after completion of imaging injected with  $0.72-1.88$  mCi In-111PLA and reimaged. Biexponential curves were fit to the blood sample data and rate constants were determined and expressed as T1/2 values. The initial clearance for Tc-99mAM was more rapid than for In-111PLA (T1/2  $2.2 \pm 1.7$  min vs  $7.7 \pm 12.0$  min) but there was no significant difference between late slow components ( $9.9 \pm 2.8$  vs  $7.7 \pm 3.4$  hrs.). Planar imaging was performed at a mean of 18 hr postinjection for the In-111PLA and at a mean of 8.5 hr postinjection for the Tc-99mAM. One normal animal was injected and imaged at corresponding time intervals and showed no blood pool activity. Heart to lung count ratios for In-111PLA and Tc-99mAM ranged from 1.10-2.6 respectively and correlated with pathology scores (modified Billingham score) which ranged from 1.54 to 2.0.

In conclusion both AM compounds show promise as agents for imaging cardiac transplantation rejection within 24 hrs of injection in man.