Long-Term Clinical Outcome of Catheter-Based First Human Heart Myoblast Allograft

Background: Recent experimental studies have demonstrated bone marrow cell (BMC) implantation tumor preconditioning and improves heart function and myocardial function. Despite enthusiasm for these pioneering clinical trials, the long-term safety and efficacy of implanting autologous BMCs into the human myocardium remains a major concern. The purpose of this study was to evaluate the long-term clinical outcome of implanting autologous BMCs into patients (pts) with end-staged coronary artery disease (CAD).

Methods: We evaluated the long-term clinical outcome in 12 pts (mean age: 60±10 yrs, 11 males) who underwent catheter-based autologous BMC cells implantation guided by electromechanical mapping. A mean of 1.1±0.2 mL of mononuclear cells (10^6 cells/ml, 2.9±2.6% of CD34+ cells) was injected to 16 ischemic regions. No elevation in cardiac enzyme or pericardial effusion observed after the procedure. 2 pts died of stroke (8 mths) and myocardial infarction (20 mths), respectively. After 23±6 mths follow-up, there were significant improvement in NYHA class (2.1±0.8 vs 1.2±0.3), angina class (2±0.9 vs 3.3±0.5) and quality of life (SF-36: 65±14 vs 51±15).

Conclusions: Our study demonstrate that BMC implantation using a percutaneous catheter-based cellular transplantation procedure for severe CAD.

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**1026-66 Biological Markers of the Restenosis**

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Background: The incidence of coronary restenosis 6 months following angioplasty is 25 to 45% according to selected definitions. The detection of restenosis by non-invasive means remain particularly disappointing. The purpose of this study was to evaluate the evolution of potential biological markers of restenosis after angioplasty and identify whether some are predictive of restenosis.

Methods and Results: A total of 229 consecutive patients with chronic stable angina or stabilised unstable angina, were recruited in five centers. Measurements of fibrinogen, CRP, PAI, Ag, VWF, Apolipoprotein(a) were performed. A prolonged elevation of CRP and fibrinogen was observed over the first four months of follow-up with some decrease at two months and reascension at four months (32% increase of CRP between the second and fourth month; p<0.01; 4% increase of the fibrinogen; p=0.002). A similar evolution was observed for the plasma levels of f.VIIc, f.VIIa, f.VII Ag, f.PAI. All the variables return to baseline levels at six months. These biological profiles are consistent with the restenosis process which occurs mainly between 2 and 4 months. However, after multivariate analysis, no biological variable was significantly and consistently (with regards to the various definitions) associated with restenosis, at any time point.

Conclusion: Our findings suggest that inflammation occurs and can persist for 4 months after angioplasty but no biological variable was found to be independently predictive of clinical and/or angiographic restenosis.

**1026-67 Acute Ischemic Syndromes, Approaches, and Evaluation**

Sunday, March 07, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

**1025-66 Long-Term Clinical Outcome of Catheter-Based Intramyocardial Autologous Bone Marrow Cells Implantation in Patients With End-Stage Coronary Artery Disease**

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Background: We report here the world's first myoblast allografts into two CAD patients. Endomyocardial myoblast injections deposited myofilaments and augmented contractility. Inflammation was not observed.

Methods: BMCs were isolated from healthy donors and identified as positive for cGMP/ISO 9001 to yield 3.64x10^9 myoblasts that were 98.3% pure (desmin immunostaining), 91.5% viable, potent in myotube formation, and negative for endotoxin, mycobacteria, and hepatitis C. Cells were infused into patients with end-stage CAD who underwent the catheter-based autologous BMC implantation-guided by electromechanical mapping.

Results: 2 pts died of stroke (8 mths) and myocardial infarction (20 mths), respectively. After 2.8±0.5 mths follow-up, there were significant improvement in NYHA class (2.1±0.8 vs 1.2±0.3), angina class (2±0.9 vs 3.3±0.5) and quality of life (SF-36: 65±14 vs 51±15). In 12 pts (mean age: 60±10 yrs, 11 males) with end-staged CAD who underwent catheter-based autologous BMC cells implantation guided by electromechanical mapping. A mean of 1.1±0.2 mL of mononuclear cells (10^6 cells/ml, 2.9±2.6% of CD34+ cells) was injected to 16 ischemic regions. No elevation in cardiac enzyme or pericardial effusion observed after the procedure. 2 pts died of stroke (8 mths) and myocardial infarction (20 mths), respectively. After 23±6 mths follow-up, there were significant improvement in NYHA class (2.1±0.8 vs 2.8±0.5), angina class (2±0.9 vs 3.3±0.5) and quality of life (SF-36: 65±14 vs 51±15) compared to baseline (all p<0.05). Stress SPECT-sestamibi studies demonstrated significant improvement in myocardial perfusion in 9/12 (75%) pts at 6 mths. Magnetic resonance imaging showed at baseline, 3 and 6 mths after procedure showed no evidence of intramyocardial tumor formation, myocardial damage or change in left ventricular function (58±9 vs 50±11 vs 58±16%, p>0.05). Furthermore, no patient developed symptomatic ventricular tachyarrhythmias nor detected by 24 hrs Holter at 3 and 6 mths follow-up.

Conclusions: Our study demonstrate that BMC implantation using a percutaneous catheter-based cellular transplantation procedure for severe CAD.