Transplantation of Autologous Bone Marrow
Mononuclear Cells Does Not Alter Arrhythmia
Threshold in Adult Swine With Chronic Myocardial
Ischemia

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Background: Bone marrow-derived mononuclear cells (BM-MNCs) can give rise to endot-
heelial progenitor cells and localized transplantation of BM-MNCs in ischemic myocardium may augment neovascularization. However, not much is known of the arrhythmogenic potential of BM-MNCs after intramyocardial transplantation. Objective: Evaluate the threshold for ventricular arrhythmia induction with conventional electrophysiology study (EPS) with programmed stimulation in swine with chronic ischemic cardiac treated with autologous BM-MNCs. Methods: Adult Yucatan swine underwent left circumflex (LCX) ameroid implantation. At 4 weeks, animals were randomized to receive either BM-
MNCs (n=8) or DMEM culture medium as control (n=8). Bone marrow (30-50ml) was aspirated from sternum and if necessary, iliac crest. Mononuclear cells were isolated using density gradient centrifugation. Catheter-based (Boston Scientific Stiletto™) intramyocardial injections were performed with combined fluorescent and intracardiac echocardiography (ICE) guidance. The treatment group received total of 1 x 10^7 BM-
MNCs at 10 sites, 5 in ischemic (LCX), and 5 in non-ischemic (LAD) region. Four weeks after cell treatment, global wall motion score index (GWSMI) was evaluated by do-
butamine stress echocardiography. Subsequently, electrophysiologic study was performed with right ventricle stimulation at apex and outflow tract, using a basis cycle length of 500 and 400 millisecond and 1-3 extrastimuli. Results: No difference was found in total number of cases with inducible arrhythmias in BM-MNC and control groups: 3 out of 8 animals (38%) in BM-MNC group (2 polyomorph VC and 1 VF) and 3 out of 8 animals (38%) in control group (1 monomorphic VT and 2 VF). There was also no difference in global wall motion (GWSMI=1.03 in BM-MNCs; 1.17 in sham, p=0.38) and there was no correlation between GWSMI and ventricular arrhythmia induction (1.29 for induced pigs; 1.10 for non-induced, p=0.41). Conclusion: Transplantation of autologous BM-MNCs into ischemic myocardium did not alter the threshold for ventricular arrhythmia. Left ventricu-
lar dysfunction was not related to arrhythmia inducibility.

Monocyte Chemotactant Protein-1 Induced Monocyte
Infiltration and Angiogenesis Does Not Result in
Arteriogenesis or Improved Cardiac Function in
Chronically Infarcted Myocardium

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Monocyte chemotactant protein 1 (MCP-1) stimulates invasion of monocytes into ischemic tissue with concomitant adhesion to endothelial cells. This process has been shown to be involved in the induction of arteriogenesis, i.e., the development of functional blood vessels and endothelial cells, respectively. In a subset of animals, hearts were excised 24 hours after MCP-1 injection (n=4) or saline injection (n=4) administration for assessment of monocyte infiltration by staining of the CD31 antibody. EF decreased from 60% to 25% at 4 weeks after injection (p=0.005), and from 58% to 26% at 4 weeks after injection (p=0.005) after coronary occlusion, with further changes four weeks after treatment (EF 28% in group 1, EF 25% in group 2). At the injection site, 39±10 endothelial cells were found in group 1 versus 28±14 in group 2 (p=0.005). Monocyte infiltration was shown in MCP-1 treated animals but not in saline treated animals. There were 19±2 arteriolar structures in group 1 versus 16±1 in group 2, p=0.05. A single intramyocardial injection of MCP-1 into the infarct border zone induced neo-angiogenesis and monocyte infiltration. MCP-1 injection did not result in arteriogenesis or functional improvement of chronically infarcted myocardium in this experimental rat model.

Preoperative QRS Widening and Ventricular
Dysrhythmia Predict Adverse Outcomes Following Left
Ventricular Reconstruction for Ischemic
Cardiomyopathy

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Objective: Interventions that target the cardiac conduction system such as AICD place-
ment and biventricular pacing improve symptoms and survival in patients with congestive heart failure. However, the role of the conduction system in outcome after surgical ventricu-
lar reconstruction, the exclusion of dyskinetic and akinetic segments of myocardium, remains undefined. We reviewed our experience with left ventricular reconstruction (LVR) in patients with ischemic cardiomyopathy to determine the effect of preoperative conduc-
tion abnormalities on outcome after surgery.

Methods: LVR was performed in 223 pts (80% male, mean age 62±10 yrs, 66% NYHA Class III/IV) between 1997 and 8/02. Mean pre-operative EF was 26±9%. QRS duration was 122±30ms and an AICD was present in 15%. Time related outcomes considered were 1) survival, 2) freedom from composite event (transplant, return of NYHA class IV, and LVAD), and 3) readmission for heart failure. Mean follow-up is 1.5±1.1 yrs.

Results: Survival at 30 days, 1yr, and 3 yrs was 98%, 92%, and 86% respectively. Patients who had an AICD preoperatively had a higher early mortality (p=0.002). Freedom from readmission for heart failure was 98%, 95%, and 61% at 30 days, 1 yr, and 3 yrs. Patients with a prolonged preoperative QRS had more frequent rehospitalizations (p=0.006).

Conclusion: Surgical left ventricular reconstruction in heart failure patients with ischemic cardiomyopathy yields an encouraging medium term survival and freedom from hospitalization for heart failure. Preoperative predisposition to lethal ventricular arrhythmia requir-
ing an AICD was a strong predictor of mortality. This deserves closer examination. Left ventricular dysynchrony (prolonged QRS) was a strong predictor of residual or recurrent heart failure and further underscores the importance of ongoing investigations of cardiac resynchronization therapy as an adjunctive treatment to surgery for heart failure in this group of at risk patients.