

INTRAMYOCARDIAL CD 133+ BONE MARROW STEM CELL TRANSPLANTATION AT THE TIME OF CORONARY SURGERY IN PATIENTS WITH CHRONICALLY IMPAIRED LV FUNCTION

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Objective: Cell transplantation for treatment of heart failure is a novel field of research that offers the perspective of developing curative approaches by regenerating lost myocardium and inducing growth of new blood vessels. We tested the hypothesis that direct intramyocardial injection of CD133⁺ bone marrow stem cells in conjunction with CABG improves LV function more than CABG alone.

Materials and Methods: In an initial safety trial we treated 15 patients. Subsequently, 40 patients were randomized to undergo CABG and intramyocardial CD133⁺ cell injection or CABG alone (20 patients in each group). Bone marrow was harvested either from the iliac crest one day prior to surgery (early phase) or from the sternum (intraoperative cell processing, late phase). Up to 80x10E6 CD133⁺ progenitor cells were isolated using magnetic bead-conjugated antibody. Cells were directly injected into the infarct border zone. LV function was measured by echocardiography and myocardial perfusion by SPECT. More recently, cardiac MRI was used to confirm the echocardiographic data.

Results: In the phase-1 safety trial LVEF increased from 39±9% to 47±6% at 2 weeks (p=0.004) and 50±8% at 6 months (p=0.0007). LVEDV decreased from 148±38% to 123±32% (p=0.01) and 125±28% (p=0.05, all paired t-test). No procedure-related complications were observed for up to 3 years. In the controlled phase-2 trial LVEF rose from 37.4±8% to 47.1±8% at 6 months in the cell-treated group (p=0.005), and from 37.9±10% to 41.3±9% in CABG-only patients (p=0.47, all paired t-test). Comparing both groups statistically (unpaired t-test), the mean LVEF was not different at 2 weeks postop. (p=0.7) but significantly higher in the cell-treated group at 6 months (p=0.04). The increase in LVEF over 6 months was also significantly higher in cell-treated patients (p=0.009). Similarly, perfusion in the infarcted myocardium improved more in cell-treated patients than in CABG-only patients. Regression analysis indicated that patients with preoperative LVEF <30% benefit more from CABG and cell therapy than those with only moderately impaired LVEF.

Conclusion: In patients with chronically impaired LV function CABG and CD133⁺ bone marrow stem cell injection results in better functional recovery than CABG alone.