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[815] Cardiac Repair with Mesenchymal Stem Cells following Myocardial Infarction in Pigs

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Background. Whether adult bone-marrow harbors precursor cells capable of engrafting and repairing damaged heart tissue remains highly controversial. To address this, we performed a randomized trial of catheter-delivered *allogeneic* bone-marrow derived mesenchymal stem cells (MSCs) in a swine model of myocardial infarction (MI).

Methods and Results. Farm pigs were chronically instrumented to measure left-ventricular pressure, dimension, and oxygen consumption. Three days after MI, placebo or MSCs ($2X10^8$) were injected into the myocardium via catheter. Anterior MI caused a dramatic deterioration in systolic and diastolic ventricular function and impaired cardiac energy metabolism ($p<0.05$ *vs.* pre-MI values). The degree of left ventricle dysfunction was near identical in both groups (p=NS between groups). In placebo, impaired post-MI cardiac function showed either no sign of recovery or further deterioration over 8-weeks. Conversely, MSCs produced robust long-term cellular engraftment, and led to an early and sustained improvement in mechanoenergetic coupling (SW/MVO_2, from 2.5±0.6 to 10±5.6, $p<0.05$ *vs.* placebo), followed by almost normalization of contractile (100.3±51.2% increase in Ees) and diastolic function (30.4±1.5% enhancement in isovolumic relaxation time; both $p<0.05$ *vs.* placebo). Despite near-identical hemodyamic impairment immediately post-MI, infarct size at autopsy was substantially reduced with MSC therapy (16±7.2% and 3.3±1.2% of the LV, respectively for placebo and MSC group; $p<0.05$). Engrafted MSCs adopted cardiomyocyte-like and vascular smooth muscle phenotypes.

Conclusion. These findings demonstrate substantial benefits of MSC therapy in a highly relevant model of post-MI heart failure and have clear implications for the design and conduct of clinical trials.