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Progenitor Cell Types and Cardiac Repair

Abstract 3464: Differential Effects of Progenitor Cell Populations on Myocardial Neovascularization and Left Ventricular Remodeling after Myocardial Infarction

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Background: Cardiac progenitor cell transfer may improve myocardial repair after acute myocardial infarction (AMI), but responsible cell types and mechanisms remain uncertain.

Methods: In a blinded, randomized, controlled study, we infused allogeneic porcine LentiGFP-infected mesenchymal stem cells (MSC, n=11, $10\pm2x10^6$ CD29 – 44 –90 cells, capable of adipogenic and osteogenic differentiation), autologous late-outgrowth endothelial progenitor cells (EPC, n=10, $34\pm22x10^6$ CD29 –31 cells, capable of tube formation) or vehicle (CON, n=10) in

the CX artery 1 w after AMI induced by 90 min balloon occlusion. Hemodynamic and cine MRI measurements ($dP/dt_{max/min}$ and ejection fraction, EF) were performed at 1w and 7w follow-up. We measured LV remodeling from end-diastolic and end-systolic volumes (EDV, ESV) and quantified infarct size and transmurality on late enhanced images. We evaluated the secretome of cultured EPC and MSC and compared changes in relative upslope (RU) of first-pass perfusion images and vascular density on postmortem sections from infarct core and border zones.

Results: While systolic function ($dP/dt_{max/min}$ and EF) at 7 w was similar between groups, LVEDV increased in MSC and CON pigs, but not in EPC pigs [+23.3 (25–75th percentile 1.7;27.9) and +26 ml/m^2 (17.9;31.9) vs +0.8 ml/m^2 (–10.1;18.8), resp, $P<0.05$]. A similar trend was noted for LVESV [+11.1 (10.4;15.4) and +10.7 ml/m^2 (5.9;14.5) in MSC and CON, resp], vs –1.8 ml/m^2 (–13.5;0.7) in EPC ($P=0.06$). After EPC transfer, infarct size decreased more in segments with >50% infarct transmurality ($P=0.01$ vs MSC and CON). Myocardial perfusion increased more in EPC than in MSC and CON [RU +72% (–2;119) vs –2% (–28;84) and +25% (–33;236), resp], and was associated with greater vascular density in infarct border zones ($P=0.01$) and with higher levels of pro-angiogenic growth factors, PLGF and FGF2 in EPC secretome (1730±1002 and 75±44 pg/10^6 cells resp vs 73±16 and 19±12 in MSC secretome,,n=5). No evidence of cell transdifferentiation was observed at 7w.

Conclusion: Infusion of late-outgrowth EPCs after AMI limits negative LV remodeling but does not mediate cardiomyogenesis. EPC transfer may hold promise for heart failure prevention via paracrine matrix-modulating or pro-angiogenic effects.