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MYOCARDIAL ISCHEMIA AND INFARCTION

INDUCED PLURIPOTENT STEM CELL THERAPY SYNCHRONIZES GLOBAL AND REGIONAL MYOCARDIAL FUNCTION POST-INFARCTION

ACC Poster Contributions
Ernest N. Morial Convention Center, Hall F
Sunday, April 03, 2011, 3:30 p.m.-4:45 p.m.

Session Title: Acute Myocardial Infarction -- Pharmacological, Stem Cell and other Adjunctive Therapies
Abstract Category: 3. Acute Myocardial Infarction—Therapy
Session-Poster Board Number: 1037-310

Authors: *Satsuki Yamada, Timothy J. Nelson, Almudena J. Martinez-Fernandez, Garvan C. Kane, Andre Terzic, Mayo Clinic, Rochester, MN*

Background: Induced pluripotent stem cells (iPS) are considered the next generation therapy in heart disease. However, the impact of iPS therapy on electromechanical synchrony in diseased heart has not been tested.

Methods: iPS were engineered from fibroblasts transduced with stemness factors OCT3/4, SOX2, KLF4, and c-MYC. Infarcted C57BL/6 mice (n=16) were randomized into fibroblast- and iPS-treated groups (200,000 cells/heart by epicardial injection), and followed by M-mode/2-D/speckle-tracking echocardiography (30-MHz probe, heart rate 478±14 bpm, frame rate 219±11 fps), electrophysiology, and pathology, up to 3 months post-infarction.

Results: The fibroblast-treated cohort (F) developed left ventricular (LV) dilatation, reduced contractility, and QRS/QT prolongation. iPS-treated hearts improved LV ejection fraction (F 37±2%, iPS 69±5%; P<0.01), and were free from overt pathological remodeling and dysrhythmia (LV end-diastolic dimension; F 4.7±0.2 mm, iPS 3.8±0.1 mm; P<0.01). Speckle-based strain analysis demonstrated abnormal LV systolic strain and intra-ventricular delay originating from infarcted areas of fibroblast-treated ventricles. In contrast, iPS delivery normalized regional and global LV strain, maintaining synchronous LV wall motion (radial strain; infarcted areas, F 16±2%, iPS 41±4%; P<0.01: LV global average, F 17±2%, iPS 30±4%; P<0.01: standard deviation of time to peak systolic strain; F 16±3 ms, iPS 9±1 ms; P=0.02: stretch to shortening ratio; F 15±4%, iPS 2±1%; P=0.02). There was no adverse effect of iPS-treated hearts on follow-up.

Conclusions: iPS intervention secured a safe and beneficial outcome on LV systolic and diastolic function, structure and synchrony in the setting of myocardial infarction. This study provides first evidence for iPS-based cardiac resynchronization.