MYOCARDIAL ISCHEMIA AND INFARCTION

CLINICAL RELEVANCE OF ISCHEMIC LARGE ANIMAL MODELS IN STEM CELL THERAPY; AN OVERVIEW AND META-ANALYSIS.

ACC Poster Contributions
Ernest N. Morial Convention Center, Hall F
Monday, April 04, 2011, 9:30 a.m.-10:45 a.m.

Session Title: Myocardial Ischemia/Infarction -- Basic
Abstract Category: 1. Myocardial Ischemia/Infarction--Basic
Session-Poster Board Number: 1070-333

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Background: Stem cell therapy is a new strategy for ischemic heart disease in patients. Randomized controlled trials (RCT) showed 4% improvement in left ventricle ejection fraction (LVEF). Meta-analysis of all available ischemic preclinical data could provide important clues to design future clinical trials.

Methods: Random-effects meta-analysis was performed on pig, dog or sheep studies investigating the effect of cell therapy after ischemic cardiomyopathy. Endpoints were LVEF and death.

Results: Eighteen cohorts and 34 RCT (N=888 animals) were included; ischemia/reperfusion infarction was performed in 22 studies and chronic occlusion in 30 studies. Pooled analysis showed a LVEF difference of 7.5% at follow-up after cell therapy vs. control (95% confidence interval (CI), 6.2% to 8.9%; P<0.001). By exploratory multivariable meta-regression significant predictors of LVEF improvement were: cell type (bone marrow mononuclear cells showed less effect than other cell types, e.g. mesenchymal stem cells; P=0.040) and type of infarction (left anterior descending artery 8.0% vs. left circumflex artery 5.8%; P=0.045). Cell therapy was not associated with a higher mortality (P=0.68). Sensitivity analysis showed trends towards more improvement due to cell therapy regarding: high cell number (≥107), chronic occlusion models and late injections (>1week). After follow-up of 8 weeks the effect of cell therapy decreased to 6%.

Conclusions: This meta-analysis showed that large animal models are valid to predict outcome of clinical trials. Our results showed that cell therapy is safe, led to a preserved LVEF and revealed important clues for designing (pre-) clinical trials that should be performed according to a new guideline.