

Embolization of the first diagonal branch of the left anterior descending coronary artery as a porcine model of chronic trans-mural myocardial infarction.

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Public Summary:

BACKGROUND: Although the incidence of acute death related to coronary artery disease has decreased with the advent of new interventional therapies, myocardial infarction remains one of the leading causes of death in the US. Current animal models developed to replicate this phenomenon have been associated with unacceptably high morbidity and mortality. A new model utilizing the first diagonal branch of the left anterior descending artery (D1-LAD) was developed to provide a clinically relevant lesion, while attempting to minimize the incidence of adverse complications associated with infarct creation. **METHODS:** Eight Yucatan miniature pigs underwent percutaneous embolization of the D1-LAD via injection of 90 µm polystyrene micro-spheres. Cardiac structure and function were monitored at baseline, immediately post-operatively, and at 8-weeks post-infarct using transthoracic echocardiography. Post-mortem histopathology and biochemical analyses were performed to evaluate for changes in myocardial structure and extracellular matrix (ECM) composition respectively. Echocardiographic data were evaluated using a repeated measures analysis of variance followed by Tukey's HSD post hoc test. Biochemical analyses of infarcted to non-infarcted myocardium were compared using analysis of variance. **RESULTS:** All eight pigs successfully underwent echocardiography prior to catheterization. Overall procedural survival rate was 83% (5/6) with one pig excluded due to failure of infarction and another due to deviation from protocol. Ejection fraction significantly decreased from $69.7 \pm 7.8\%$ prior to infarction to $50.6 \pm 14.7\%$ immediately post-infarction, and progressed to $48.7 \pm 8.9\%$ after 8-weeks ($p = 0.011$). Left ventricular diameter in systole significantly increased from 22.6 ± 3.8 mm pre-operatively to 30.9 ± 5.0 mm at 8 weeks ($p = 0.016$). Histopathology showed the presence of disorganized fibrosis on hematoxylin and eosin and Picro Sirius red stains. Collagen I and sulfated glycosaminoglycan content were significantly greater in the infarcted region than in normal myocardium ($p = 0.007$ and $p = 0.018$, respectively); however, pyridinoline crosslink content per collagen I content in the infarcted region was significantly less than normal myocardium ($p = 0.048$). **CONCLUSION:** Systolic dysfunction and changes in ECM composition induced via embolization of the D1-LAD closely mimic those found in individuals with chronic myocardial infarction (MI), and represents a location visible without the need for anesthesia. As a result, this method represents a useful model for studying chronic MI.

Scientific Abstract:

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