

## Surgical Model of Right Heart Failure

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**Background:** Development of new treatment strategies for right heart failure in congenital heart disease (CHD) mandates creation of animal models that mimic the physiological stresses faced by the right ventricle (RV) in these diseases. Growth and development inherent to pediatric patients add another layer of complexity in pathogenesis of CHD. Our objective was to establish a large animal model of right heart failure simulating the hemodynamic stresses faced by RV in CHD, which can be used to evaluate new diagnostic and therapeutic strategies.

**Methods:** Piglets were born by cesarean delivery. At 4-weeks of age the piglets underwent baseline testing and were randomized to control (sham) or test groups. The test animals underwent left thoracotomy and tight pulmonary artery banding (PAB) was performed. The banding was titrated for each individual animal to the severity that cardiac output was reduced to near hemodynamic collapse. Physical observations were made daily and formal veterinary exams were conducted weekly. Clinical chemistry and vital signs were obtained at baseline and 4, 6, 8 and 12 weeks after surgery. Echocardiography was performed at baseline, 6, and 12 weeks and cardiac MRI at 4, 8 and 12 weeks after surgery. Animals were euthanized and necropsy was performed at the end of study (12 weeks after surgery).

**Results:** A total of 21 piglets were randomized; 8 controls and 13 test. The average of mean systolic Doppler gradient across the pulmonary artery band was 50 mmHg. The average of peak systolic velocity of tricuspid regurgitation was 5.7 m/s in test animals. The test animals showed progressive RV hypertrophy and tricuspid valve regurgitation, leading to progressive RV dilation, followed by reduction in ejection fraction and development of ascites (38% of test animals). MRI results are summarized in the figure. Sixty nine percent of test animals survived to the end of study, as compared to 87% in control group. Histological assessment showed diffuse myocardial fibrosis in test animals.

**Conclusion:** Application of a tight PAB to young piglets creates an animal model of right heart failure that mimics the hemodynamic stresses of RV in children with CHD, i.e., sustained increased pressure load (PAB) and volume load (tricuspid regurgitation). This model can be used to test novel imaging strategies focused on RV function and to test therapeutic strategies targeting RV myocardial dysfunction.

**Figure:** Comparison of cardiac MRI data obtained at 4, 8 and 12 weeks after surgery. EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; LGE, late Gadolinium enhancement; RV, right ventricular; TV, tricuspid valve; \*, p-value <0.05.

