CARDIAC MRI EVALUATION IN A RAT MODEL OF PULMONARY HYPERTENSION

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Introduction

Primary pulmonary hypertension (PPH) is a life threatening disease characterized by increased pulmonary vascular resistance which results in right ventricle (RV) hypertrophy, dilation, and potential RV increased right ventricular afterload. Animal models of pulmonary hypertension have included knockout mice, hypoxia in rats and mice, and monocrotaline (MCT) induced pulmonary hypertension in rats. MCT is a toxic plant alkaloid that causes endothelial cell damage, pulmonary vascular injury, and pulmonary hypertension after a single injection in rats and thus has become a well-established model to study this disease. MRI is being used clinically on patients with PH receiving treatment as a way to monitor hemodynamic effects and stoke volumes. Therefore we sought to use MRI to characterize the RV size and function with the development of MCT induced PH rats and determine its potential use in evaluation of treatment in PH.

Experimental

Rats weighing 200-225g were divided into five groups (4 escalating doses of MCT and a PBS control) and evaluated by MRI at 4 weeks post-injection. MRI of the rat cardiac cycle was performed with a 4.7 T Bruker Avance spectrometer. The animals were anesthetized and monitored using the Small Animal Instrument (SAI) monitoring and gating system for respiration rate and cardiac triggering. Short axis images were prescribed from the base to the apex of the heart and collected with a Fast Low Angle Shot (FLASH) sequence (matrix= 256 x 192, TE = 2.7 msec, FOV = 40 mm x 30 mm, thickness = 1 mm) triggered at the peak of the R-wave. Repetition time was dependant on the heart rate of the animal and R-R interval. Approximately 14-20 frames were used to capture the entire cardiac cycle. RV and LV volumetric measurements were done using OsiriX Medical Imaging software (Figure 1). RV mass was calculated at end diastole by: (RV epicardial vol. – RV endocardial vol.) x 1.05. RV EF was calculated by (RV EDV – RV ESV) / RV EDV x 100. Short axis mid-ventricle images were used with Paravision software to measure RV wall thicknesses. RV mass at necropsy was obtained by separating the RV from the rest of the heart, with the septum being included with the LV.

Results and Discussion

RV wall thickness correlated with RV mass and peak PA systolic pressure. The PA:LV pressure ratio, which increases with the development of PH, correlates with increasing RV:LV end-diastolic volume. MRI RV measured mass also has excellent correlation with RV mass obtained at necropsy. Additionally, MRI can be used to measure RV systolic function and RV ejection fraction is shown to be significantly lower in rats with PH.

Conclusions

Rat models of pulmonary hypertension are essential in studying the development, pathophysiology, and treatment strategies for PH. It is essential to evaluate the RV during experimental treatment protocols. This study demonstrates that MRI is an important and valuable tool to determine RV mass, volumes, and systolic function in this model of PH. MRI measurements correlate with hemodynamic and necropsy measures. Other than the need for anesthesia, cardiac gated MRI is non-invasive and can be used for longitudinal study of the RV in this model.

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References