Simultaneously Quantitative Analysis for Right Ventricular and Left Ventricular Functions with MRI in a Rat Pulmonary Hypertension Model

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Introduction

Chronic pulmonary hypertension (PH) results in right ventricular (RV) hypertrophy, leading to RV dysfunction and heart failure. However, accurate quantitative analysis for RV function is challenging with conventional imaging modalities, such as echocardiography, because of its complex shape. In addition, hemodynamic functions of RV have only been studied by invasive catheterization. Therefore, MRI, which can directly visualize the size and shape of RV without geometric assumption, might potentially be a suitable imaging modality to evaluate RV function as well as morphology. In this study, we have firstly achieved to non-invasively evaluate RV and left ventricular (LV) hemodynamics simultaneously in a rat PH model and we also explored the role of angiotensin converting enzyme inhibitor (ACE-I) as a potential therapeutic agent.

Material and Methods

1. Animal model: Male Sprague-Dawley rats treated with monocrotaline (MCT) showed similar manifestations observed in the RV failing patients with severe PH. Three groups of rats were subjected to MRI evaluation: (i) MCT (40 mg/kg) (n=6) (ii) MCT with ACE-I enalapril maleate (4.4 mg/kg/day) (n=4) (iii) Age and body-weight matched controls without treatment (n=8).

2. MRI protocols: Multi-planar (8-12 slices) EKG and respiratory gated density-weighted spin-echo images were used to cover the whole volume of the heart and the whole 3D volume data were acquired at 8 to 12 time points in a cardiac cycle. RV and LV were evaluated by contouring the outline of ventricular cavity from each slice. RV wall (RVW), LV free wall (LVFW), and interventricular septal (IVS) wall (IVSW) mass were derived from end-diastolic (ED) wall volume and the specific gravity of myocardium (1.055 g/cm3). Cardiac tagging was achieved by modified DANTE sequence. All MRI scans were performed on Bruker AVANCE DRX 4.7-T system.

Results

1. Morphology and mass: Six weeks after single MCT injection, severe RV hypertrophy (RVH) was developed (Figs.1B & 3A). Associated with RVH, both RV and LV changed their morphology. However, this deformed morphology was reversed by ACE-I treatment daily for 4 weeks, starting 2 weeks after MCT injection (Figs.1C & 3A). RV/LV+IVS wall mass ratios are 0.208, 0.729 and 0.235, for control, MCT only, and MCT+ACE-I treated rats respectively.

2. Hemodynamic functions:

(1) Timing of contraction: In control rats (Fig.2A), both LV and RV exhibit similar ejection fraction (EF) about 70% and both reached end-systole (ES) at the similar timing, at 40-45% of cardiac cycle. Simultaneously, LVFW volume increased significantly during contraction, while RVW and IVSW volume did not change as much. In contrast, both LV (Fig.2B) and RV (Fig.2C) showed delayed timing for ES in MCT-retreated rats. The systolic phase of MCT rats prolonged about 25%. Interestingly, ACE-I which inhibited RVH could reverse the prolonged systolic phase for LV, but not in RV.

(2) Contractility: During contraction, the volume of LVFW of control hearts increased about 30-50%, whereas minimal increase was observed in RV and IVS walls (Fig.3B). However, in MCT-treated rats, the volume of LVFW did not increase compared with control hearts, but RVW showed significant increase. This indicated that the hypertrophied RV may acquire better ability to contract but also hindered contractility of the LV. ACE-I treated rats exhibited similar contractility as controls. The hindrance of LV contractility by hypertrophied RV can be clearly seen with myocardiac tagging (Fig. 4). At ES, both IVSW and LVFW contracted well in control and ACEI-treated rats. However, MCT rats demonstrated that IVSW almost did not contract at all, due to geometric constrain from hypertrophied RV, although LVFW still preserved its contractility.

Conclusion

We have shown for the first time that cardiac MRI could non-invasively quantitate RV hemodynamics simultaneously with LV function. In addition to morphology, cardiac MRI is useful in analyzing RV dynamics. Our data showed that MCT-induced RV hypertrophy hindered LV contractility associated with prolonged systolic phase, even though its ejection fraction remained unchanged.

Acknowledgement

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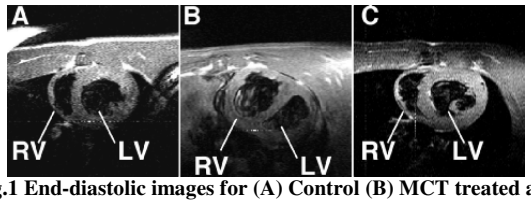

Fig.1 End-diastolic images for (A) Control (B) MCT treated and (C) MCT-ACEI treated rats.

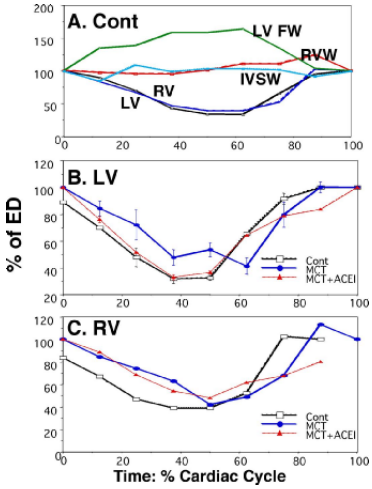

Fig.2. (A) Changes in time for normalized ventricular volume and wall mass for a control rat. (B) LV and (C) RV volume changes in time for all rat groups. All values are normalized with ED.

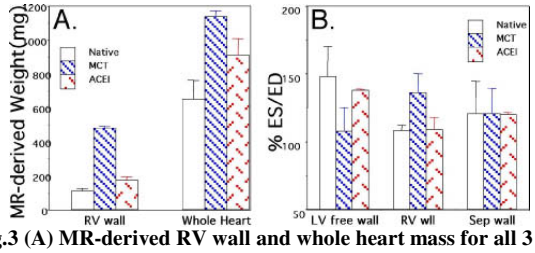

Fig.3 (A) MR-derived RV wall and whole heart mass for all 3 rat groups. (B) Relative wall volumes between ES and ED.

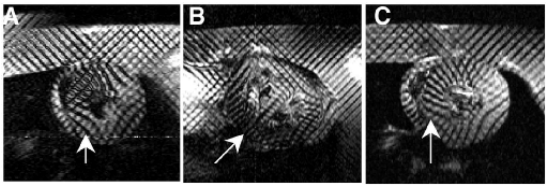

Fig. 4 Contractility revealed by cardiac tagging. All images were acquired at the ES for (A) Control (B) MCT and (C) MCT-ACEI treated rats. IVSW is indicated by white arrowheads.