Noninvasive detection of congestive heart failure in postinfarction rats

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Target audience: Preclinical/basal researchers in cardiovascular research

Purpose: Congestive heart failure (CHF) is a serious outcome of myocardial infarction (MI), which remains a major cause of cardiac death. In preclinical research that aims to unveil the mechanisms responsible for the development of CHF in the postinfarction heart, the rat model of MI plays an irreplaceable role. However, not all rats develop CHF after induced MI[1, 2]. It is therefore imperative to establish robust in vivo diagnostic criteria for CHF in postinfarction rats.

Left ventricular end-diastolic pressure (LVEDP) reflects preload and has traditionally been used as a main criterion for CHF in rats, but it requires cannulation of one of the carotid arteries and thus prevents longitudinal studies. However, congestion increases right ventricular (RV) afterload, and it has been shown that ex vivo RV weight is increased rats with CHF concurrently with elevated LVEDP[2].

The purpose of this study was thus to evaluate whether MRI can provide robust noninvasive criteria for detection of CHF in postinfarction rats by including measurement of RV mass.

Methods: Six weeks after induction of MI through ligation of the left coronary artery, 40 male Wistar rats (labelled MI rats) were examined using magnetic resonance imaging (MRI). 13 sham-operated rats served as a control group. MRI experiments were performed on a 9.4T horizontal bore MR system (Agilent Technologies, Inc., USA), utilizing an RF-spoiled motion compensated gradient echo cine MRI sequence prospectively triggered by ECG and gated for respiration. A stack of left ventricular short-axis slices covering the heart from the base to apex was acquired. Key acquisition parameters were: TE = 1.97ms, TR = 2.80ms, field-of-view=45x45mm, matrix 192x192 after 2x zero filling, slice thickness 1.5mm, flip angle 15°, signal averaging=3x. Acquisition time was approximately 20 min.

Using a purpose-written post processing tool (Matlab, The MathWorks, USA), LV and RV mass and infarct size were measured from the cine MRI stacks[3].

After MRI, LVEDP was measured by inserting a 1.4F micromanometer-tipped catheter (Millar Inc., USA) retrogradely via the right common carotid artery into the left ventricular cavity. MI rats with LVEDP ≥ 15 mmHg was defined as failing (labelled MI_{CHF}), while MI rats with LVEDP < 15mmHg was defined as non-failing (labelled MI_{NF})[1]. The rats were subsequently euthanized by neck dislocation, and the lungs and right ventricles were dissected and weighted in a subgroup of rats (N=9 for sham, N=15 for MI_{NF} and N=10 for MI_{CHF}).

Group	Sham (N=13)	MI_{NF} (N=22)	MI_{CHF} (N=18)
Infarct size (%)	-	26.25 (11.15)	41.06 (6.09) †
LV mass (mg)	697.4 (58.8)	787.6 (58.9) *	785.8 (92.8) *
RV mass (mg)	158.7 (53.1)	187.3 (37.7)	486.1 (94.6) *†
LVEDP (mmHg)	2.2 (1.1)	5.4 (3.5) *	26.2 (4.1) *†

Table 1: *Comparison between the three groups, defined from LVEDP (left ventricular end-diastolic pressure). LV=left ventricle, RV=right ventricle. Values are shown as mean (standard deviation). *: p<0.05 versus sham, †: p<0.05 versus MI_{NF}.*

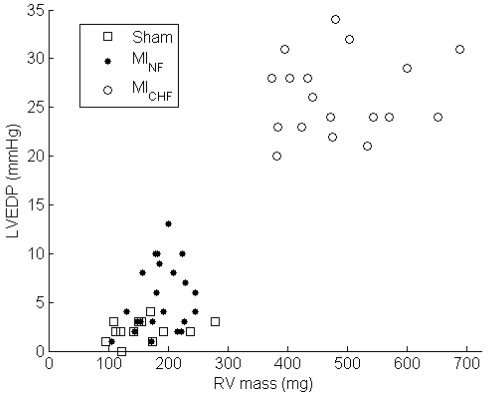

Figure 1: *MRI-derived right ventricular (RV) mass is a strong noninvasive marker for elevated LV end diastolic pressure (LVEDP).*

The parameter means were compared between groups using one-way ANOVA and Tukey-Kramer's post hoc test. Values are shown as mean (standard deviation).

Results: In all MI rats, infarcts were located in the anterolateral wall, and the infarct size was larger in the MI_{CHF} rats than in MI_{NF} (Table 1). LV mass was increased in the infarcted hearts compared to sham, but did not differ between MI_{NF} and MI_{CHF} (Table 1). However, not only was MRI-derived RV mass increased in the MI_{CHF} group, it also successfully discriminated between rats with and without elevated LVEDP without overlap (Figure 1); all MI_{CHF} had RV mass > 300 mg and all MI_{NF} had RV mass < 300 mg. In the subgroup with ex vivo organ weights, MRI-derived RV mass correlated well with post mortem RV weight (r=0.84, p<0.001). Moreover, lung weight was increased in the MI_{CHF} group compared to the other two groups (4.36 (0.83) g in MI_{CHF} vs 1.74 (0.38) g in MI_{NF} and 1.37 (0.28) g in sham, p<0.001).

Discussion: For the first time, we have shown that MRI successfully discriminates between failing and non-failing MI rats. It has previously been shown that echocardiography successfully identifies CHF in postinfarction rats using posterior wall shortening velocity[1], but no study has explored whether MRI is able to provide such discrimination. Another issue is that parameters describing cardiac function (such as myocardial tissue velocities) may be affected by anesthesia depth and experiment duration. In the present study, we therefore sought to investigate whether structural parameters, which are assumed to be more robust than functional parameters in that they are independent of anesthesia, could provide the ability to successfully discriminate between non-failing and failing hearts.

It has recently been shown that RV hypertrophy (causing an increase in ex vivo RV weight) 30 days after induction of MI is associated with elevated LVEDP in postinfraction rats[2]. Our findings support this, and concurrently demonstrate the ability of MRI to accurately classify CHF in postinfarction rats.

Conclusion: We demonstrate that MRI-derived measurement of RV mass accurately distinguishes between rats without and with elevated LVEDP, and thus constitute a noninvasive tool for longitudinal evaluation of degree of congestive heart failure in the postinfarction rat.

References:

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