Measurements of diastolic function in rats using high resolution cine-MRI

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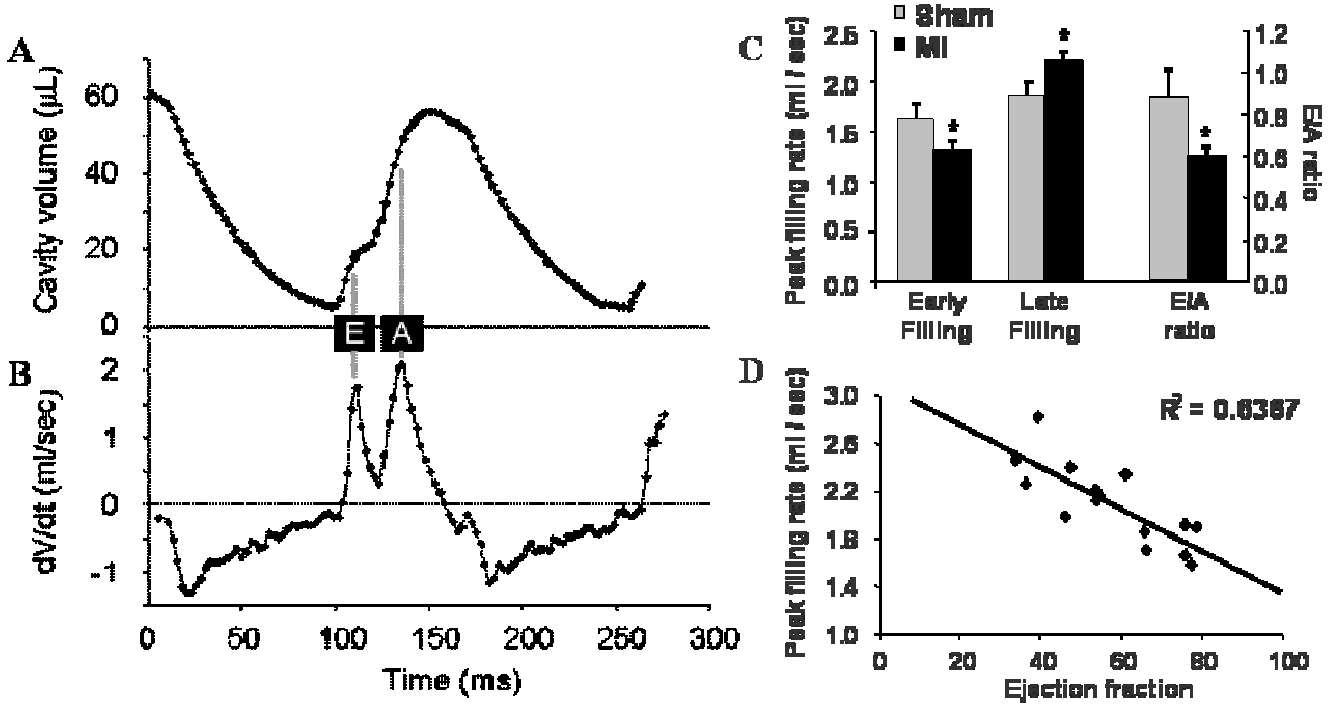
Heart disease can result in alterations to the pattern of left ventricular filling due to myocardial stiffening and reduced active relaxation arising from changes in metabolism. Doppler echocardiography has been used to measure the early (E) and late (atrial (A)) filling phases of the left ventricle during diastole in humans, with the peak filling rate and E/A ratio related to the degree of diastolic dysfunction (1). These measurements have also been made in small animals, although accurate and reproducible manual positioning of the transducer at the correct location across the aortic valve is difficult in rodents and high heart rates can lead to fusion of the filling phases (2). Hence, we aimed to develop a cine-MRI based method to measure left ventricular filling in control and chronically-infarcted rats.

Methods; Myocardial infarction was induced in ten male Wistar rats by occlusion of the left anterior descending coronary artery. After three weeks, heart function was measured in the infarcted rats, and in five sham operated and six control rats, using cine-MRI in an 11.7T MR system with a Bruker console and a 60 mm birdcage coil, as described (3). A stack of contiguous 1.5 mm true short axis ECG and respiratory gated cine images (FOV, 51.2 mm^2; matrix size 256×256; TE/TR, 1.43/4.6 ms; 17.5° pulse) were acquired to cover the entire left ventricle. The temporal resolution was increased by altering the cine-MRI sequence (matrix size 128×128; TE/TR, 0.86/2.4 ms; 60° pulse) and data acquired over two cardiac cycles to allow diastolic function to be measured in a mid-papillary slice.

Results; The alterations to the cine-MRI sequence typically doubled the number of frames per cardiac cycle, from 32 to 62, when the heart rate was 400 bpm. This allowed the early and late phases of diastolic filling to be separated and the E/A ratio to be calculated (*Figure A & B*). Repeated measurements performed on six control rats on separate days gave average E/A ratios of 0.83 ± 0.06 and 0.89 ± 0.07, with a mean error of 11 ± 5% indicating that the measurements were reproducible. In the infarcted rats, as compared with shams, peak atrial filling was higher and peak early filling was lower, leading to a 32% reduction in E/A ratio (*Figure C*). A strong correlation between ejection fraction and peak filling rate was identified (*Figure D*).

Conclusions; High resolution cine-MRI provides reproducible measurements of left ventricular filling parameters in the rat. In agreement with findings in human subjects using Doppler echocardiography, myocardial infarction leads to a reduced E/A ratio. This is consistent with the reduced energy state and increased fibrosis of the infarcted rat heart (4). This technique could be applied to studying changes in diastolic function that occur in animal models of disease and after therapy.



A: Time/volume and **B:** first derivative curves acquired from a mid-papillary slice of a rat heart. *E = peak early filling, A = atrial filling phase*. **C:** Comparison of peak early filling, peak atrial filling and the E/A ratio acquired from infarcted and sham operated rat hearts. **D;** Correlation between left ventricular ejection fraction and peak atrial filling rate. * $p < 0.05$ compared with shams.

References
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