Diffusion Tensor MRI Quantifies Dynamic Changes of Myocardial Fiber Structure in Remodeling Rat Hearts after Myocardial Infarction

J. Chen[1], W. Liu[1], H. Zhang[2], L. Lacy[2], X. Yang[2], S-K. Song[3], S. A. Wickline[2], X. Yu[4]

[1]Department of Biomedical Engineering, Washington University, St. Louis, MO, United States, [2]Cardiovascular MR Laboratories, Washington University School of Medicine, St. Louis, MO, United States, [3]Departments of Chemistry and Radiology, Washington University, St. Louis, MO, United States, [4]Department of Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio, United States

Introduction

Changes in myocardial fiber orientation during cardiac contraction are postulated to be a key determinant of the cardiac function. Our previous studies demonstrated that the myofiber and sheet reorientation at end-systole contributed to circumferential shortening and systolic wall thickening [1]. After MI, the ventricle undergoes progressive structural remodeling as a prelude to heart failure. However, post-infarct adaptations in the myofiber architecture and its dynamic responses during cardiac contraction have not been fully investigated. In this study, alterations in diastolic and systolic myofiber structure after myocardial infarction (MI) were evaluated in Langendorff perfused rat hearts using diffusion tensor MRI (DTI). Hearts were first arrested at end-diastole with excessive potassium and then at end-systole after barium induced contracture for DTI.

Methods

Animal Model. Transmural infarction in anteroapical region was created in 2-4 month old Sprague-Dawley rats by permanent occlusion of the left anterior coronary descending artery (n=10). Four weeks after the surgery, the rat heart was excised and cannulated for Langendorff retrograde perfusion with oxygenated Krebs buffer (37°C). A fluid-filled latex balloon was inserted into the left ventricle (LV) through mitral valve. The balloon was connected to a pressure transducer to record left ventricular pressure and heart rate.

DTI of hearts arrested at end-diastole. Cardiac arrest was induced by perfusing the heart with oxygenated cardioplegic (high [KCl]) solution (20°C). DTI of arrested hearts at end-diastole was performed on a Varian 4.7T scanner using a 2 cm solenoid coil. A multi-slice spin-echo sequence with diffusion sensitizing bipolar gradient was used to acquire short-axis diffusion-weighed images. Imaging parameters were: TE, 36 ms; TR, 1.3 s; Δ, 20 ms; δ, 6 ms; b-value, 948 s/mm^2; slice thickness, 1 mm; inter-slice distance, 0.5 mm; number of slices, 7; number of averages, 4; data matrix, 128×128. Image acquisition required about one hour.

DTI of hearts arrested in end-systole. Upon the completion of image acquisition, the arrested heart was perfused with normal Krebs buffer to resume contraction. Once cardiac work was stabilized, the balloon was deflated and taken out of the ventricle. A PE-50 tubing was inserted into LV to drain the remaining fluid. Sustained systolic arrest was achieved by $BaCl_2$ induced contracture. Specifically, heart was perfused with modified Tyrode solution with 0.078 mM Ca^{2+} for 1.5 min, followed by Tyrode solution with 2.5 mM $BaCl_2$ for 5 min. Adenosine was added to both solutions at 1 mg/min to maximally dilate the coronary vessels. At the end, heart was rapidly fixed at end-systole by perfusing with 5% formalin. Immediately after systolic fixation, heart was suspended in 5% formalin and imaged in the same coil. DTI of 11 continuous short-axis images were acquired using the same parameters as those for diastolic image acquisition, except that TR was 1.7 s. Slice thickness was adjusted according to ventricular shortening in longitudinal direction.

DTI data analysis. The three eigenvectors of diffusion tensor were calculated. The primary eigenvector, which corresponds to the myofiber orientation, was transformed from magnet Cartesian coordinates to the wall-bound myocardial coordinates. A prolate spheroid was fit to the epicardial surface to define the local wall-bound myocardial coordinates. Orientation angles of myofiber were specified by helix and transverse angles. Transmural myofiber structure was characterized on the basal, mid-ventricular and apical slices of the heart. DTI determined fiber structure in normal rat hearts (n=11), acquired in a previous study [1], was used as the control.

Statistical analysis. All results were expressed as mean±SD. The transmural course of fiber helix angles was characterized at each 10% transmural depth (TD) from endocardial surface (5% TD) to epicardial surface (95% TD). Unpaired student's t-test was used to compare the transmural courses of fiber angle between the infarct and control hearts. A 2-tailed value of $p<0.05$ was considered as significant.

Results

Transmural courses of myofiber helix angle at the base, midventricle and apex in the control and infarct hearts are shown in Figure 1. By end-diastole, the transmural courses of fiber angle in the infarct and control hearts were similar at the base (p=N.S. at all TD), midventricle (p=N.S. except at 15%, 25% and 85% TD), and apex (p= N.S. except at 5%, 15% and 95% TD).

However, the adaptation of fiber reorientation by end-systole was heterogeneous in the infarct hearts. At the base, the transmural course of helix angle by end-systole was similar to that of the control hearts (p= N.S. except at 15% and 25% TD). At the midventricle, it was significantly lower than that of the control hearts ($p<0.05$ except at 95% TD). At the apex, it was significantly lower at sub-endocardium (5% to 35% TD) and showed a trend to decrease from midwall to sub-epicardium (45%-95% TD). Specifically, the transmural course of fiber angle by end-systole changed from 77°±6° to –46°±7°, 63°±7° to –56°±5°, and to 43°±21° to –55°±13° at the base, midventricle and apex, respectively.

Conclusion

The current study presents the first observations that directly elucidate the dynamic structural alterations of myofiber from diastole to systole in the post-infarct remodeling heart. The DTI determined end-diastolic fiber structure was similar between the infarct and control hearts, which was in agreement with our previous observation of well-preserved fiber orientations despite replacement of myocytes with fibrous scar tissue [2]. However, the extent of myofiber reorientation by end-systole decreased from the base to the apex in the infarct hearts, corresponding to the decreased circumferential strain after MI [3]. Thus, the heterogeneous dynamic responses of fiber reorientation are closely correlated to the adaptation of regional ventricular function in the cardiac remodeling program after myocardial infarction.

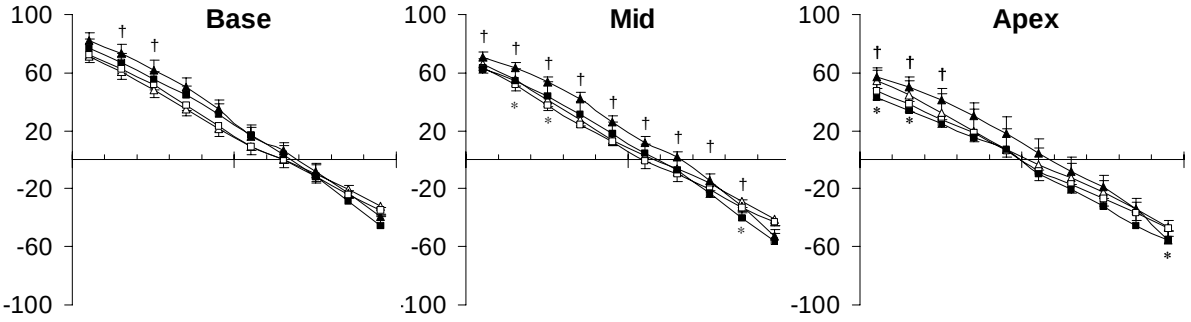

Figure 1. Transmural courses of myofiber helix angle at end-diastole and end-systole in the infarct and control hearts. Data were quantified on basal, midventricular (Mid) and apical slices. △ -- End-diastole, Control; □ -- End-diastole, Infarct; ▲ -- End-systole, Control; ■ -- End-systole, Infarct.

∗, $p<0.05$ for infarct versus control at end-diastole.†, $p<0.05$ for infarct versus control at end-systole.

References

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