Intralipid Reduces Post-MI Ventricular Remodeling and Heart Failure after Ischemic Injury

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Target audience: MR researchers, cardiologists, and animal imaging specialists

INTRODUCTION

Coronary heart disease is the leading cause of death in US. Timely re-circulation has greatly decreased 30-day in-hospital death, and increased survival rate during the acute phase of myocardium infarction (MI). However, even with successful blood-flow restoration, ischemia reperfusion injury (IRI) can result in greater tissue damage and adverse remodeling. The rate of developing post-MI heart failure increases as the acute mortality decreases. Long-term post-MI ventricular remodeling and the consequent potential heart failure remains a challenge. We have previously reported that Intralipid can preserve cardiac function after IRI. The goal of this study is to investigate the beneficial effects of Intralipid in LV remodeling and post-MI heart failure.

METHODS

Animal model: We employed a rodent ischemic injury model with 45-min transient left anterior descending (LAD) coronary artery occlusion, followed by reperfusion.

Experimental design: After IRI, cardiac function was evaluated with multi-parameter cardiac MRI on day 0, 2, 3,4, 5, or 7 for acute phase evaluation; then at 2, 3, 4, 5, or 6 weeks for long-term changes. Hearts were harvested at 1, 2, 3, 4, 5, or 6 weeks for myocardial fiber quantification and LV remolding evaluation by *ex vivo* MRI

***In-vivo* cardiac function evaluation:** Routine cine imaging is used to access SV, EF, and anatomical changes. Regional wall motion was assessed by tagging MRI followed by strain analysis. Myocardial perfusion and infarction is measured by 1st-pass dynamic with a single bolus Gd and late gadolinium enhancement.

Diffusion-spectrum-imaging (DSI) for myocardial fiber quantification: The ventricular remodeling was quantified by *ex-vivo* diffusion-spectrum-imaging, with 2D-stimulated echo sequence, with a total of 101 diffusion acquisitions and 0.3mm isotropic resolution at Bruker 11.7-Tesla. The b-table was supplied manually using the grid-101 scheme, with maximum b-value=6,000mm/sec; diffusion time=80ms, TR=2.6 sec; TE=10ms; with 26 slices to cover the whole heart volume.

RESULTS

After transient ischemia, Intralipid-treated animals preserved much of the cardiac function after ischemic insults. Intralipid-treated hearts showed to preserve SV and EF, regional wall motion, and myocardial perfusion.Three weeks after ischemic injury, hearts of untreated animals showed compromised SV, EF, and significant wall thinning (Fig. 1 A & C), indicating adverse post-MI LV remodeling. Animals with Intralipid treatment, however, showed reduced *in-situ* inflammation, and preserved most of the cardiac function, such as SV, EF, regional wall motion, and myocardial perfusion. Additional, Intralipid-treated hearts did not exhibit similar myocardial atrophy 3 weeks after ischemic injury (Fig. 1 B &D). Diffusion spectrum imaging (DSI) showed untreated hearts with ischemic injury exhibited dis-integration of myocardial fibers (Fig. 2 B, E), but the Intralipid-treated IRI heart (Fig. 2 C,F) preserved much of myocardial architecture and integrity, which is comparable to the control heart (Fig. 2 A, D). This indicates that the Intralipid-treated hearts experienced less post-MI remodeling after IRI.

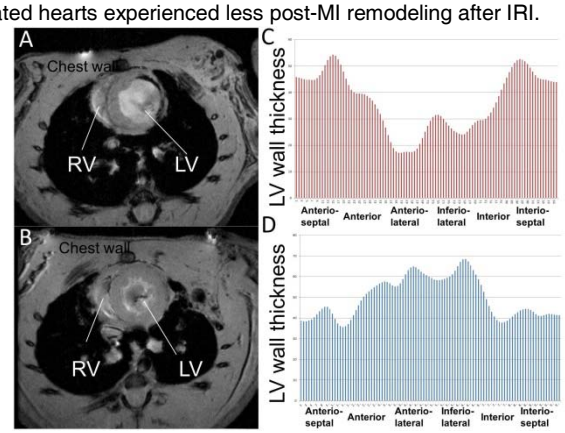

Figure 1 (A.B) Anatomical MRI of an untreated heart at 3 weeks after ischemic injury (A) and an Intralipid-treated heart at 3 weeks after ischemic injury (B). (C,D) Distance between endocardium and epicardium at 100 different locations of the myocardium, starting at the mid-point of the septum, going counterclockwise direction for the untreated heart in A (C), or the Intralipid-treated heart in B (D). Different myocardial regions are indicated as anterio-septal, anterior, anterio-lateral, inferio-lateral, interior, and inferio-septal wall.

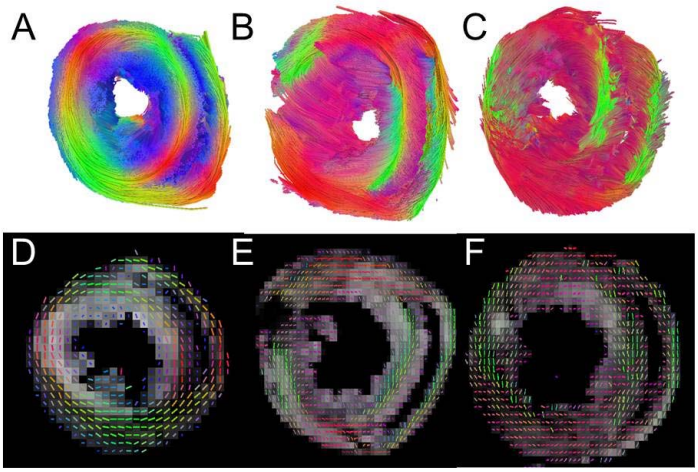

Figure 2 Intralipid treatment reduces myocardial fiber disruption after ischemic-reperfusion injury, quantified by diffusion tensor imaging (DTI). Tractography (upper panels A, B, C) and Fiber orientation Mapping (lower panels, D, E, F) of a normal heart (A, D), an untreated heart with IRI (B, E), and an Intralipid-treated heart with IRI (C, F)

CONCLUSION

Our results indicate that Intralipid treatment can protect hearts against ischemic injury and the subsequent adverse myocardial remodeling, and as a result, may potentially help reducing post-MI heart failure.

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