MRI Demonstrates a Decrease in Myocardial Infarct Healing and Increase in Compensatory Ventricular Hypertrophy Following Mechanical Microvascular Obstruction

Hisham Z. Bajwa[1], Lois Do[1], Mohammed Suhail[1], Steve W. Hetts[1], Mark W. Wilson[1], and Maythem Saeed[1]
[1]*Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, California, United States*

Target audience: interventionists, cardiologists, cardiac MR physicists, pathologists and medical device manufacturers
Purpose: To provide direct evidence that mechanical obstruction of microvessels inhibits infarct resorption (healing) and enhances LV remodeling using MRI.
Methods: Animals (n=20 pigs) served as controls (group I, n=4) or were subjected to either 90min LAD coronary artery occlusion/reperfusion (group II, n=8) or 90min LAD occlusion/microemboli delivery/reperfusion (group III, n=8). Coronary angiograms were acquired before, during and after occlusion. MRI (cine and delayed contrast enhanced MRI, DE-MRI) was performed at 3 days and 5 weeks after interventions and used for assessing LV function, mass, extent of myocardial damage and microvascular obstruction (MVO) using semi-automated threshold method. At postmortem, LV rings were stained with hematoxylin-eosin and Masson trichrome to microscopically characterize myocardial and microvascular changes. Continuous variables were presented as mean ± SEM. Two-tailed paired and unpaired Student t-tests and regression analyses were performed to assess the significance and correlations within and between the groups, respectively.
Results: Group I control animals showed no evidence of infarct on imaging and no change in ejection fraction, though the LV volumes did increase as a result of growth of the animals over the course of 5 weeks. Persistent (at >10min) MVO in the core of contiguous infarct was larger and more frequent (n=8/8, 3.9±0.3g) in group III than II (n=4/8, 1.6±0.8g, $P<0.02$) on DE-MRI at 3 days (Fig.1). The total infarct size at 3 days was not significantly different between groups II (11.7±0.7g, 15.5% of LV) and III (12.9±0.5g, 16.5% of LV). At 5 weeks however, infarct resorption was significantly less in group III (24±2%, 9.8±0.3g) compared with group II (35±2%, 7.6±0.5g, $P<0.01$). The decline in LV ejection fraction on cine MRI (Fig.2) was greater in group III (31±1% at 3 days, 32±1% at 5 weeks) than group II (36±1% at 3 days, 39±%1 at 5 weeks) and group I controls (52±3% at 3 days, 51±1% at 5 weeks). Group III also exhibited correspondingly greater increases in end diastolic and end systolic volumes over the course of 5 weeks when compared with group II ($P<0.02$ for both volumes). Both groups showed significantly higher end diastolic and end systolic volumes than group I controls ($P<0.02$). At 3 days, there was no significant difference between any of the groups with regard to LV mass. However, at 5 weeks, the increase in mass was significantly greater in group III (66±8%) compared with group II (33±4%, $P<0.002$) and I (24±6 %, $P<0.001$). Microscopically, traces of inflammatory cells were observed in the contiguous infarct at 5 weeks in group III, but not II, confirming delayed infarct healing. In remote myocardium, the myocytes appeared larger in group III than I and II.

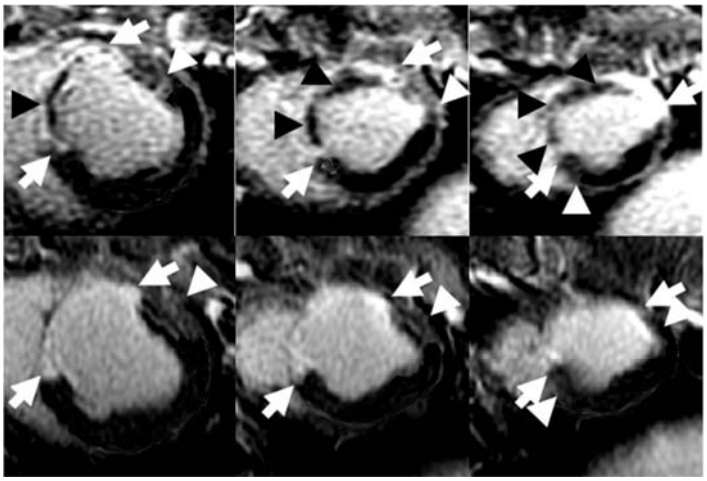

Fig.1. DE-MR images from a representative group III animal show hyperenhanced contiguous AMI (top row, white arrows), hypoenhanced large MVO in the core of the infarct (black arrowheads) and patchy micro microinfarcts at the border zone (white arrowheads) 3 days post-intervention. At 5 weeks (bottom row), infarct scar and compensatory hypertrophy were evident (bottom row, white arrows).

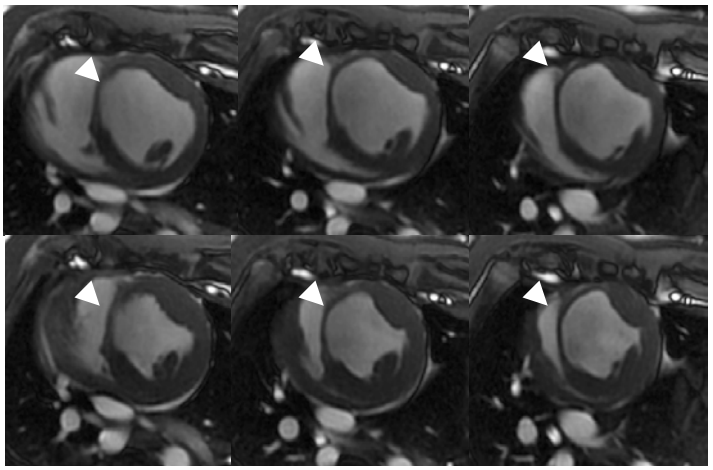

Fig.2. Sample multi-slice diastolic (top row) and systolic (bottom row) cine MR images acquired at 5 weeks in a group III animal. White arrowheads point to the site of infarction and show wall thinning at 5 weeks. The remote myocardium appears thicker and hypertrophied.

Discussion: This MRI study supports the conjecture by Kloner (1) and Wu (2) that MVO in acute myocardial infarction delays/inhibits optimal infarct healing by slowing the delivery of inflammatory cells and nutrients. Furthermore, the extent of MVO correlates with the magnitude of the decline in ejection fraction as well as the degree of functional recovery. Moreover, larger MVO due to microemboli accentuates LV remodeling (increased LV volumes and mass/compensatory hypertrophy of remote myocardium) compared with infrequent MVO caused by reperfusion injury only.
Conclusion: This MRI study supports the notion that MVO delays/inhibits infarct resorption (healing) and accentuates LV hypertrophy and pathological remodeling. It illustrates the need for documenting the presence and/or extent of MVO following acute myocardial infarction and highlights the importance of development of novel methods/devices to trap/dissolve coronary microemboli during/after coronary interventions. Such treatment could limit the extent of microvascular obstruction and enhance infarct healing and functional recovery, potentially improving patient morbidity and mortality.
References:

1) Kloner RA. No-reflow phenomenon: maintaining vascular integrity. J Cardiovasc Pharmacol Therap 2011; 16:244-250.
2) Wu KC. CMR of microvascular obstruction and hemorrhage in myocardial infarction. J Cardiovasc Magn Reson 2012; 14:68-84.