MR Relaxation Measurement of Microvascular Obstruction in Reperfused Acute Myocardial Infarction

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Introduction: Microvascular obstruction (MO) or no-reflow phenomenon occurs in 30%-40% of patients post acute myocardial infarction (AMI) and is a strong unfavorable determinant for short and/or long-term clinical prognosis in these patients (1). Many non-invasive imaging techniques such as myocardial contrast echocardiography, MR myocardial perfusion and delayed contrast-enhanced MRI are capable of identifying its presence and further quantifying its volume; however, the underlying physiology of MO is still poorly understood. This study investigates the measurement of MR relaxation characteristics in MO and underlying mechanisms for the observed signal behaviour in a porcine model of reperfused AMI using a T1 and T2 preparation sequence.

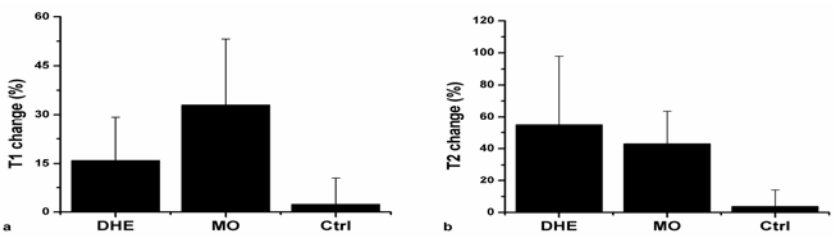
Materials and Methods: All experimental protocols were approved from our institutional animal care and use committee. In fourteen Yorkshire pigs, a reperfused AMI was produced using a 90-minute percutaneous balloon occlusion of the left anterior descending artery distal to the second diagonal branch under x-ray guidance. Amiodarone and lidocaine were used to reduce the risk of severe arrhythmia throughout the experiment. All MRI studies were performed on a GE 1.5T Signa Excite system (GE Healthcare, Milwaukee). A 5-inch surface or GP flex coil was used. Peripheral gating was realized through a plethysmography trace placed on the pig's tail. All pigs underwent a baseline MRI study that included a steady-state free precession (SSFP) functional study, T1, and T2 measurement. T1 measurement uses a modified Look-Locker pulse sequence producing 8 difference images from a set of spiral acquisitions in a train of 15-deg excitations at intervals of 120 ms, obtained with and without a preceding inversion at the same cardiac phase (2). A flow-insensitive T2-weighted magnetization preparation that consisted of a train of non-selective composite refocusing pulses bounded by non-selective composite 90° and -90° pulses was used for myocardial T2 measurement (3). The in-plane spatial resolution for T1 and T2 measurements was 1.07 mm and 1.38 mm. Following reperfusion, SSFP, T1, and T2 preparation pulse sequences were repeated in the same location as in the baseline MRI scans. First pass myocardial perfusion (FPMP) data were also obtained immediately after a Gd-DTPA bolus injection (0.2 mmol/kg Magnevist, Schering) followed by a continuous intravenous drip of Gd-DTPA at a rate of 0.004 mmol/kg/min. DE-MRI (IR-prepared FGRE) was performed 30 minutes post Gd-DTPA injection and T1 measurement was performed again 45 minutes post-contrast at steady state.

For quantitative T1 and T2 relaxation analysis, regions of interests (ROIs) corresponding to three distinct components of reperfused AMI, namely MO (the core of AMI), hyperenhanced regions in DE-MRI (DHE, peripheral regions of AMI) and control regions (remote normal region), were identified and drawn manually based on FPMP, DE-MRI and T1 preparation difference images post-contrast where the various components can be visualized clearly. These contours were saved and propagated onto T1 and T2 preparation images pre-contrast. Fine contour adjustments were made manually to allow for movement during the cardiac cycle. T1 and T2 values were calculated via Xcinema (Stanford) or Functool 2 (GE Healthcare) software. For T1 calculation, T1* values were first acquired through the non-linear least squares fit of signal magnitudes and sampling times; the true T1 values took account of the effect of RF sampling on longitudinal magnetization relaxation recovery and were obtained by the following equation (4): $1/T1 = 1/T1^* + \ln(\cos(\alpha))/\Delta TI$, where α is the flip angle of each tip-down pulse and ΔTI is the inter-pulse delay. T2 values were determined by fitting of signal magnitudes and sampling times to a monoexponential decay. All data are expressed as the mean value ± SD. Statistical significance in parameter changes was evaluated using the Student's paired t-test.

Results: In all fourteen pigs TTC staining and/or histology verified the presence of reperfused AMI. MO was identified in eleven pigs as the persistent hypoenhancement in the infarcted myocardium in FPMP and DE-MRI. Thus, the incidence of MO in this experimental porcine AMI study was high (78.6%). MRI relaxation measurements using T1 and T2 preparation pulse sequence before Gd-DTPA injection are summarized in Fig.a-b. T1 and T2 values at reperfusion from MO and DHE regions were greater than those at baseline (ΔT1: MO regions -- 33±20%, n=11, P=0.0002; DHE areas -- 16±13%, n=11, P=0.0012; ΔT2: MO regions -- 43±20%, n=11, P<0.0001; DHE areas -- 55±43%, n=11, P=0.001). For comparison, T1 and T2 values for control regions are similar between baseline and reperfusion and within statistical errors (ΔT1: 2±8%, n=11, P=0.41; ΔT2: 4±10%, n=11, P=0.31). Also at reperfusion T1 and T2 values from MO were greater than those in control regions (ΔT1: 28±17%, n=11, P=0.0003; ΔT2: 44±20%, n=11, P<0.0001).

Discussion and Conclusion: Longitudinal and transverse relaxation measurements (T1 and T2) have been performed in experimental animals and patients with reperfused AMI before. Those previous studies all demonstrated that both T1 and T2 relaxation times were elevated in the infarction region, in concordance with our findings. The elevation has been attributed primarily to the increased water content in intracellular or extracellular interstitial space (5). However, more detailed analysis of MRI relaxation measurements was lacking for regions within MO and the surrounding infarcted myocardium in reperfused AMI. In this study, we used the ROIs defined from DE-MRI and T1 preparation difference images in which the distinctive differentiation between MO and the surrounding infarcted tissue was clear. We noticed that T1 relaxation times in regions of MO after reperfusion were mildly elevated (~12%) compared to those in the surrounding infarcted tissue. Meanwhile, the difference between T2 relaxation times at reperfusion for MO vs the surrounding infarcted myocardium had not reached statistical significance. The pre-contrast T1 relaxation times at reperfusion from MO were also greater than those in control regions; this difference will facilitate the differentiation between MO in the infarct core from non-ischemic myocardium.

The mechanisms which underly very early differences between the T1 and T2 of MO and other regions of reperfused infarcted myocardium have not been clarified. It is generally accepted that MO regions are subjected to more severe ischemia prior to reperfusion, and that a combination of neutrophil plugging, micro-thrombosis, endothelial cell swelling, and edematous microvascular compression may contribute to abnormally low perfusion, termed 'no-reflow', despite macrovascular blood flow restoration (6). From a mechanistic perspective, the high volume fraction of swollen blood cells may elevate T1 and/or T2 above that of the infarct displaying DHE. That the obstructing cells may be swollen and intact is consistent with the observations of concordant hypointensity in delayed enhancement and reduced Gd-DTPA partition coefficient. That T2 in MO may be reduced from that of the edematous infarction (not demonstrated yet to significance), while T1 is high, is consistent with the known susceptibility of the porcine infarct model to intramyocardial hemorrhage (7), which is mid-myocardial in nature and localized to regions of particularly severe ischemia. At these early injury time points, the hemorrhagic iron should be predominantly compartmentalized as deoxyhemoglobin within intact red blood cells. In conclusion, differences may exist between the endogenous T1 and T2 of early microvascular obstruction and reperfused infarct presenting with DHE, which may help to define more comprehensively the underlying pathophysiology of reperfused infarction.



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