Variations in T2 mapping-assessed area at risk after experimental ischemia/reperfusion

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Cardiac magnetic resonance (CMR) allows an accurate myocardial tissue characterization. Contrast-enhanced CMR is well validated as a surrogate for infarct size. CMR also depicts post-myocardial infarction (MI) edematous regions using T2based sequences (T2 weighted (T2w) and T2-mapping).(1,2) The extent of T2w/T2mapping abnormalities after MI has been proposed as a surrogate for area at risk (AAR) under the premise that the entire ischemic region displays an edematous reaction stable for several days. In recent years, our group demonstrated in a large animal model that the post-MI edematous reaction is bimodal,(3) with an initial wave of edema secondary to reperfusion, and a delayed one secondary to tissue healing.(4) The post-MI bimodal edematous phenomenon also takes place in patients suffering a ST-elevation myocardial infarction.(5) In all these reports, the extent of edema was quantified on qualitative Short Tau Inversion Recovery T2w (T2w-STIR) sequences; thus, it remains to be demonstrated that a similar trajectory of post-MI CMR edema extent occurs when using a parametric T2-mapping sequence.

Here we are reporting the temporal evolution of the extent of post-MI T2-mapping abnormalities in a group of animals undergoing different ischemia/reperfusion (I/R) protocols, including different ischemia durations and application of cardioprotective maneuvers.(6)

The study was approved by the Instutional and Regional Animal Research Committees. Four groups of 5 animals each (male Large White pigs) were studied.(6) The first group of animals underwent 40 minutes left anterior descending coronary (LAD) occlusion followed by reperfusion (control). The second and third groups of pigs underwent the same procedure but preceded by the protective stimuli ischemic preconditioning (three 5-minute cycles) or followed by local post-conditioning (four 1-minute cycles). A fourth group of pigs underwent shorter LAD occlusion (20 min) and reperfusion. Serial CMR exams were performed at 120 minutes, 1, 4 and 7 days after MI. All CMR images were acquired on a Philips 3T-TX Achieva scanner (Philips Healthcare, Best, The Netherlands). T2-GraSE mapping was acquired on three 6-mm slices (basal, mid and apical left ventricle (LV)). Automatic quantification of edema extent on T2mapping was defined by thresholding segmentation based on the remote area (mean+2 standard deviations (SD) from remote myocardium). Manual correction was allowed to remove LV cavity areas of slow flow, and to include areas of microvascular obstruction and/or hemorrhage in the core of edematous regions. T2-mapping extension was expressed as %

LV area included in the 3 slices. We used previously acquired and reported data (6) about the extent of edema on T2W-STIR in the same set of animals, and performed a sub-analysis of the same 3 slices used for the present T2 mapping study. The investigator who performed the measurements was blinded to the group and time since the acute myocardial infarction.

Generalized linear mixed models were applied for the study and comparison of the temporal evolution of T2-mapping abnormalities (surrogate for edema extension), within and between different groups.

Results of the extent of edema at each time point in the different groups, as measured by T2-mapping, are presented in Figure 1. In summary, in all groups of animals undergoing 40 min I/R, edema extent was significantly reduced at day 1 reperfusion as compared to 120 min reperfusion. Thereafter, the area of edema significantly enlarged on days 4 and 7 in controls and in the absence of effective cardioprotection (i.e. postconditioning).(5) The extension of edema on day 7 in animals undergoing the protective ischemic pre-conditioning stimuli was smaller than in animals undergoing regular 40 min I/R. In animals undergoing 20 min I/R, edema extension reduction on day 1 was maintained on days 4 and 7. These results closely reproduce the time course of edema extent previously observed by the use of non-parametric CMR imaging.(5)

In conclusion, post-MI edema extent measured by T2-mapping confirms a bimodal edema pattern in the first week after reperfusion. The extension of edema is significantly reduced at 24h. On days 4 and 7 post-MI, edema extension as quantified by T2-mapping is modulated by the application of cardioprotective maneuvers (i.e. reduced edema extension in animals undergoing ischemic pre-conditioning or brief ischemia duration). These data supports the notion that there are actual variations in post-MI edema, which significantly impact the quantification of CMR-based AAR regardless of the sequence used.

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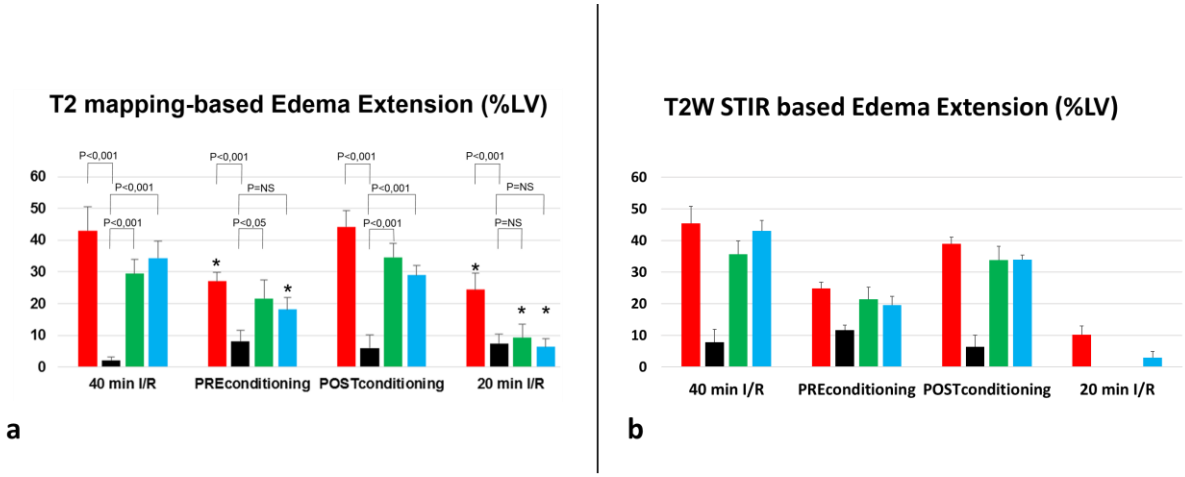
FIGURE 1. Time profile of edema extension as assessed by T2 mapping (a) and T2W STIR sequence (b) in pigs undergoing different I/R protocols.



Time points relate to reperfusion. Data are shown as mean±standard error of the mean. *Statistically significant differences (P<0.05) as compared with the same time point in the 40- min I/R (control) group. P values are adjusted for multiple comparisons among groups for each time point and among time points for each group, following the Holm-Bonferroni method. The extent of edema as measured by T2W-STIR shown in panel b slightly differs from previously reported data (6) because for the present analysis such extension was computed taken into account only three slices co-localized with T2-mapping ones. I/R: ischemia/reperfusion.