Is MRI Really the Gold Standard for the Quantification of Salvage From Myocardial Infarction?

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Infarct size is the major determinant of post myocardial infarction remodeling and heart failure and ultimately of patients’ prognosis. Infarct size itself is determined by the area at risk, that is, the perfusion territory of the occluded coronary artery, the duration of ischemia, the magnitude of collateral blood flow, and only to a small extent by the hemodynamic situation, notably heart rate. The only way to salvage ischemic myocardium from impending infarction is by timely reperfusion; however, reperfusion also inflicts injury on the previously ischemic myocardium and contributes to final infarct size. Such reperfusion injury can be attenuated by ischemic conditioning strategies and certain drugs, which recruit part of the signal transduction of ischemic conditioning strategies, both in experimental animal models and in patients with reperfused acute myocardial infarction.

The magnitude of salvage by reperfusion and cardioprotective strategies can only be quantified by comparing the actual infarct size to the hypothetical infarct size if no reperfusion had occurred, that is, the area at risk of infarction. In experimental animals, such quantitative comparison is performed by delineation of the area at risk, that is, by measurement of regional myocardial blood flow with microspheres during coronary occlusion or by infusion of a dye into the aorta during postmortem coronary reocclusion, and of infarct size by postmortem triphenyl tetrAZolium chloride staining.

Clinically, infarct size can be estimated from regional dysfunction in ventriculography or from ECG changes, which permit also a gross infarct localization from biomarker (creaTine kinase-muscle brain, troponin) release without any localization, or from late gadolinium contrast enhancement in MRI during coronary occlusion or by infusion of a dye into the aorta after reperfusion by intravenous infusion of a radioactive tracer and its detection by single photon emission computed tomography or positron emission tomography.

The idea of taking the spatial extension of edema in reperfused myocardial infarction as a surrogate for the original occluded coronary artery perfusion territory, which could even be delineated retrospectively by T2-weighted MRI was, therefore, attractive and highly welcome.

Indeed, studies in pigs with reperfused acute myocardial infarction revealed edema in the area at risk, which could be delineated by T2-weighted MRI and correlated with an area at risk measurement by a fluorescent dye. Similarly, studies in dogs with acute myocardial infarction found excellent correlation between T2-weighted MRI and the microspheres method in area at risk delineation 2 days after reperfusion, as well as in nonreperfused myocardial infarction; similar data were reported for area at risk delineation by T1 mapping in dogs. Subsequently, the 1-stop quantification of both area at risk by T2-weighted MRI and of infarct size by late gadolinium contrast enhancement in the week after reperfusion of acute myocardial infarction was advocated to assess salvage from impending infarction for clinical decision making and research.

However, the use of T2-weighted MRI to delineate area at risk and, in conjunction with late gadolinium enhancement quantification of infarct size, assess myocardial salvage has been seriously criticized and challenged, from biological and technical perspectives. Edema in reperfused acute myocardial infarction is spatially and temporally dynamic, and its retrospective use a few days after reperfusion to make a binary decision on inside/outside of area at risk is questionable. In fact, edema in viable reperfused myocardium is modest at best (≈10% higher water content than in remote myocardium), and it is much more pronounced in infarcted myocardium (+40%) (Figure A). Therefore, the difference between infarcted and viable myocardium within the area at risk would be expected to be far greater than that between viable area at risk and remote myocardium, which is not seen in the above studies advocating T2-weighted MRI for area at risk delineation. Also, the edema extends into the remote myocardium (Figure A) such that the T2-weighted MRI area at risk delineation overestimates that by postmortem dye infusion. Temporally, edema development is biphasic with an acute peak just at reperfusion, dissipation at 24 hours, and reappearance 7 days after reperfusion (Figure B), which is again not compatible with a binary assessment of inside/outside of area at risk at any given time point within the first week after reperfusion. Finally, edema

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is attenuated along with infarct size by cardioprotective ischemic postconditioning, the reduction of both infarct size and area at risk when delineated by MRI would, therefore, induce systematic underestimation of salvage/ cardioprotection (Figure C).

From a technical perspective, issues such as motion artifacts, poorly defined different thresholds, and artificial hyperintensity because of hypokinesis of infarcting myocardium were raised. Kim et al previously suggested that T2-weighted MRI hyperintensity measures not area at risk, consistent also with the transmural extent of the infarct.

In the present study, they provide experimental and clinical evidence for this notion. They subjected anesthetized dogs to coronary occlusion of different duration and then compared gold standard pathology (infarct size by triphenyl tetrazolium chloride staining, area at risk by fluorescent microspheres) to T2 weighted and late gadolinium enhancement MRI after 4±1 days reperfusion. There was a much better correlation to T2 weighted and late gadolinium enhancement MRI after 24 hours and a second peak after 7 days reperfusion, dissipation after 24 hours and a second peak after 7 days reperfusion.

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