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EDITORIAL COMMENT

Myocardium at Risk by Early Gadolinium Enhancement MR Imaging

A Moving Target?*

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Despite major advances in reperfusion therapy during recent decades, resulting in impressive reductions of infarct size and infarct-related deaths, ST-segment elevation myocardial infarction remains the major cause of heart failure and premature death. The major factors to improve outcomes are timely reperfusion and reduction of microvascular obstruction. The reperfusion injury induced by the therapy itself, however, remains an elusive treatment target. In the evaluation of different strategies to reduce reperfusion injury, measurement of the amount of salvaged myocardium as a percentage of myocardium at risk (MaR), that is, the myocardial salvage index (1 − infarct size/MaR), is directly instrumental in providing a quantitative measure of the efficacy of a treatment independently of the size of the MaR and hence vessel anatomy in experimental as well as clinical studies (1).

Historically, MaR has been challenging to measure in clinical studies. Scoring of left ventricular contraction patterns or occluded vessels on coronary angiograms has had limited performance compared with later direct measures of MaR such as myocardial perfusion single-photon emission computed tomographic imaging (2). Myocardial perfusion single-photon emission computed tomographic imaging, however, is limited by the need for radioisotope injection immediately prior to revascularization and provides, at the time of radioisotope injection, a snapshot of the hypoperfused area (i.e., the MaR). Therefore, to represent MaR, if defined as the vascular bed that supplies the myocardium, the coronary artery must be occluded at the time of tracer injection (3). Cardiovascular magnetic resonance (MR) has provided several means of imaging MaR under stable conditions up to at least 1 week after reperfusion. These include methods such as T2-weighted imaging (4,5) and T1 or T2 mapping (6,7) before contrast injection as well as contrast-enhanced steady-state free precession imaging (8) and early gadolinium enhancement (EGE) imaging (9) after contrast injection. These MR methods do not provide a snapshot of perfusion but rather image the cumulative consequences of ischemia. Of these, EGE, suggested by Matsumoto et al. (10) in 2011, must be acquired in a narrow time window immediately after the injection of contrast agent, whereas the other MR methods are stable over time during the acquisition of the MR protocol, regardless of contrast injection.

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In this issue of *iJACC*, Hammer-Hansen et al. (11) provide a rigorous histopathologic validation of EGE in a canine experimental model of reperfused myocardial infarction by using microspheres as the reference standard and comparing the results with T1 and T2 mapping. For EGE to be fully useful, it requires whole-heart coverage imaging to be performed in a very short time. To that end, the investigators developed an MR sequence resulting in a slice acquisition every 2 s. The study showed that the size of EGE agrees well with microsphere measurements of MaR at 3 min after contrast injection both for the entire left ventricle (1.4 ± 17.4%, bias and error) and in a per slice comparison (−3.0 ± 28.1%) as well as with T1 and T2 mapping (2.4 ± 6.9% and 5.2 ± 17.8%). These are convincing data. This experimental study, however, does not provide information on the time dependence of imaging after contrast injection as Matsumoto et al. (10) did in a recent human study.

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The time dependence is likely an important aspect to investigate in future studies, because EGE is a moving target after contrast injection and likely dependent on the species studied because of differences in collateral perfusion and plasma clearance of contrast agent.

Differences, advantages, and drawbacks of different MR methods for assessing MaR have been discussed for years. T2-weighted imaging has been used in several multicenter studies and has been debated (12,13). A recent experimental study demonstrated that edema, as detected by T2-weighted imaging, followed a bimodal pattern during the first week after reperfusion (14). This finding could not be confirmed in multicenter studies of reperfused ST-segment elevation myocardial infarction in humans, where the T2-weighted signal for measurement of MaR was stable over the first week and paralleled the signal from the contrast-enhanced steady-state free precession method (15). T1 and T2 mapping techniques are sparsely validated with independent methods for the measurement of MaR and have not yet been used in multicenter studies for this purpose. EGE will likely join the arsenal of debated methods, because neither EGE nor the other MR methods are fully understood as to their pathophysiological nature.

Possible explanations for different results using different MR sequences might be found in differences in extracellular contrast kinetics among species. The first-pass behavior could differ depending on, for example, collateralization. The later parts could differ because of different rates of kidney clearance; for example, dogs have exceptionally rapid clearance. Other factors could be that different MR sequences image different aspects of the ischemic injury. Image evaluation methods such as validated or unvalidated threshold methods may also contribute to different results. Therefore, it is of great importance to complement MR studies with independent imaging methods as well as other methods both in vivo and ex vivo. The present study is such an example of a necessary validation.

The debate over the different MR methods may indicate shortcomings but will likely prove to be a strength, because the different methods can be used in the same study complementing one another to visualize different aspects of the same injury, which all are related to the edema resulting from ischemic injury but are different in appearance. Nevertheless, MR has provided several methods to measure MaR, and together with infarct size it enables calculation of myocardial salvage index in clinical cardioprotection trials, which reduces the sizes of the studied populations with preserved statistical power (1). Although EGE is a moving target because of the need for careful timing after contrast injection, the present experimental validation study by Hammer-Hansen et al. (11) is another important step in elucidating the pathophysiological mechanisms behind the different patterns produced by different MR sequences in salvaged myocardium.

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