JACC: CARDIOVASCULAR IMAGING
VOL. 2, NO. 7, 2009

ISSN 1936-878X/09/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2009.04.007

EDITORIAL COMMENT

Myocardial Edema Imaging of the Area at Risk in Acute Myocardial Infarction

Seeing Through Water*

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"Water is the driving force of all nature"
Leonardo da Vinci (1)

Sudden occlusion of a coronary artery marks the rapid onset of an array of functional, metabolic, and structural injuries within a certain time window in the myocardial area supplied by this coronary artery (2). If not timely reperfused, this area is at definite risk of ischemic death. Currently, quantification of this area at risk (AAR) per se is more interesting from a research rather than a clinical perspective. It is, however, the relation between the AAR and the dynamically evolving wavefront of necrosis within its territory that gives the AAR its clinical importance. In the setting of revascularization, this relation enables quantifying the volume of myocardium that reperfusion successfully salvaged from ischemic death. For quantitative assessment of the AAR, radionuclide imaging with its known limitations has been traditionally used. Several surrogate injuries like defective perfusion or loss of function are characteristics of the AAR and might be detectable noninvasively with echocardiography, radionuclide imaging, or cardiac magnetic resonance (CMR). The clinical value of these surrogates, however, is limited: although these approaches are sensitive in detecting an overwhelming ischemic event like that after coronary occlusion, they have a low specificity to identify the acuity of such an event, simply because a loss of perfusion and function are also features of chronic coronary artery disease or remote infarctions.

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Water accumulation within tissues subjected to acute injury such as ischemia and reperfusion occurs in almost every organ in the body. In the brain, acute tissue edema can be detected through diffusion imaging, allowing for the quantification of the "penumbra," the term used for the cerebral AAR. Unlike the brain, the heart does not have a barrier between blood and tissue and also differs in other structural aspects. Because of these differences, there is an early relative and absolute increase of free water protons and accordingly T2 imaging—a far less technically challenging approach than diffusion imaging—can be used to detect the myocardial AAR. Edematous myocardium "shines" through its free water within the dark myocardium with its bound water.

Edema imaging is an interesting candidate to image the AAR for several reasons. First, it is a low-threshold ischemic injury occurring in reversibly injured myocardium (3,4) like that of the AAR. Second, it is both sensitive (5) and specific (6) to the acuity of an event. Third, edema is a tissue footprint of the AAR lasting for up to 2 weeks after the event, enabling an extended window to assess myocardial salvage (e.g., before patients' discharge).

A landmark study by Aletras et al. (3) established the concept that the area of high T2 signal (edematous myocardium) in CMR reflects the AAR in reperfused acute myocardial infarction (AMI). This confirmed findings from preliminary basic science (7) as well as clinical reports (8) and

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

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paved the way for the large patients' study by Friedrich et al. (5), which systematically assessed the AAR in 92 AMI patients with T2 edema imaging. In combination with late gadolinium enhancement, CMR, which accurately quantifies irreversible injury (9), myocardial salvage can thus be visualized and quantified with a simple CMR protocol.

In this issue of *iJACC*, Wright et al. (10) present data from 108 patients with reperfused AMI in whom the AAR was quantified with 3 different approaches: T2 edema imaging, endocardial surface length (ESL) of late gadolinium enhancement, and finally coronary angiography (BARI [Bypass Angioplasty Revascularization Investigation] score). The authors note a good correlation between T2 and ESL and a moderate correlation between T2 and BARI. The volume of T2 abnormality was consistently larger than that of late enhancement, confirming multiple previous reports (5,8,11). The T2 edema imaging of AMI has recently gained considerable interest, but concerns have been raised regarding its robustness, reproducibility, and vendor- or sequence-dependent differences of its performance. To this end, the current study is a welcome contribution, solidifying knowledge from previous reports in a large number of patients. The correlations presented are definitely interesting from a pathophysiological point of view, but unfortunately their clinical impact is reduced by the study design. Instead of comparing a novel approach (T2 in this case) with a clinically established approach with known limitations (invasiveness, cost, availability, and so forth) with the ultimate goal of replacing the "old" method (e.g., radionuclide imaging in this setting) with a novel one, the reported comparisons do not meet such criteria. The correlation of AAR with the angiographically determined BARI score is not a strong clinical argument, because BARI is rarely—if at all—clinically used to assess salvage in clinical settings and T2 will not replace angiography, which is an integral part of percutaneous coronary interventions. The other correlation deviates even further from such a "replacement" approach by comparing one CMR sequence (T2) with another (late enhancement). These design limitations might have been mandated by the retrospective nature of the analysis (ESL has been only recently proposed [12], whereas patients' recruitment for this study began several years earlier [10]). Despite that, the study should be viewed as a welcome contribution to our knowledge in a widening context of edema imaging in AMI with emerging data confirming its clinical feasibility and utility.

Future research should be directed toward addressing the technical challenges involved and standardizing image acquisition and analysis tools. Furthermore, there is a need to show that myocardial salvage as defined by a CMR-derived index correlates with other well-established methods of salvage assessment, such as radionuclide imaging, and that it does indeed offer a clear advantage over mere necrosis assessment (late enhancement) for assessing novel reperfusion strategies.

There is much to see through water.

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Key Words: myocardial infarction ■ area at risk ■ myocardial edema ■ cardiac magnetic resonance ■ T2-weighted myocardial salvage.