A Closer Look on the Battlefield
The Salvaged Area at Risk as an Outcome Marker for Myocardial Reperfusion*

Matthias G. Friedrich, MD
Calgary, Alberta, Canada

Acute myocardial infarction requires immediate reperfusion, because an open artery will likely improve the status and the prognosis of the patient. The potential benefit of acute revascularization for cellular and functional recovery, quality of life, and prognosis, however, might be lost within hours after occlusion (1), and the role of reperfusion strategies with respect to time of onset of symptoms is still being discussed (2).

In the study published in this issue of JACC, Carlsson et al. (3) report a cardiac magnetic resonance (CMR) study including T2-weighted imaging and late gadolinium enhancement for visualizing and quantifying myocardial salvage. Sixteen patients with first and acute ST-segment elevation infarction were studied at days 1 and 7 as well as 6 weeks and 6 months after the event. The presence, location, and volumetric extent of the area at risk were compared with 99mTc-tetrofosmin single-photon emission computed tomography studies done before the revascularization. The authors found an excellent agreement between both methods within the first week. As expected, the increased signal intensity seen on T2-weighted CMR images largely disappeared within 6 weeks. The authors conclude that T2-weighted CMR of acute reperfused infarction not only correctly determines the area at risk within 1 week after the event but—in combination with late gadolinium enhancement images acquired during the same CMR session—also quantifies myocardial salvage.

The study provides clinical validation of previous reports on the accuracy and clinical feasibility of T2-weighted CMR imaging in acute myocardial infarction (4) and for visualizing the area at risk in animal models (5). The results validate previous studies (6,7) applying the combination of T2-weighted CMR with late gadolinium enhancement for quantifying myocardial salvage in patients. The finding that the area at risk was accurately visualized after 7 days is particularly important and underscores the utility of this method for post-procedural patient follow-up and as an end point for clinical trials on acute coronary revascularization.

Acute severe ischemia, likely through an increase of “unbound” water protons after decoupling of water from intracellular/mitochondrial proteins,
leads to prolongation of T1 (8) and T2 (9,10) relaxation times. In T2-weighted CMR images, tissues with longer T2 appear with higher signal intensity, despite the fact that the absolute difference of tissue water content between edematous and normal tissue is small (actually, the water content of all body parts is generally very similar yet still sufficient to cause visible signal differences between various tissues in T2-weighted images).

In clinical research, T2-weighted CMR was used for visualizing acute myocardial infarction in humans as early as 1985 (11). Its clinical applicability, however, was limited by its susceptibility to motion artifacts and low signal-to-noise properties. Advances in CMR, however, have led to improved image quality, and several studies have confirmed the utility of T2-weighted CMR to visualize acute myocardial ischemic injury (4,7,12–14). Image quality, however, might vary between scanners and sequence parameter settings. Recent reports indicate that T2-weighted steady-state free precession techniques might provide more consistent image quality and a higher signal-to-noise ratio (15,16), albeit without improving the contrast-to-noise ratio.

The sequence used in this study might be particularly sensitive to water because of its inversion-recovery approach (17). $^{99m}$Tc-tetrofosmin is a validated technique to accurately depict the perfusion bed of an occluded artery and therefore—limited only by its lower spatial resolution—is suitable as an in vivo standard of truth.

There are some limitations to the study, with the small sample size being the most important. The patient cohort has a surprisingly high rate of complete coronary occlusions, and the proportion of 75% myocardial salvage within the area at risk is higher than expected.

A more widespread clinical application will depend on access to scanners and workflows for timely scanning of patients with reperfused acute infarction. Although the CMR study itself is safe, the transport of critically ill and unstable patients to CMR departments might expose patients to increased risk. Pacemakers, implanted defibrillators, and other implanted devices generally preclude patients from CMR studies. Also, in many institutions there is a lack of experienced CMR technologists.

Despite some remaining issues, T2-weighted CMR can be considered an important component of a comprehensive CMR study in patients with acute reperfused infarcts. Knowledge about myocardial salvage might improve clinical decision-making and quality management. Myocardial salvage as a marker for success would enable us to more efficiently investigate interventional strategies, procedures, peri-interventional care, and devices.

The study by Carlsson et al. (3) provides important clinical validation for this concept.

Other clinical settings might also benefit from this approach, such as imaging edema in patients with unstable angina.

CMR is emerging as the most accurate noninvasive tool to quantitatively assess myocardial salvage. In addition to the versatility and safety of CMR, its utility as a comprehensive tool for the assessment of cardiac morphology, function, and tissue characteristics will continue to increase its clinical role.

Reprint requests and correspondence: Dr. Matthias G. Friedrich, Stephenson Cardiovascular MR Centre at the Libin Cardiovascular Institute of Alberta, Department of Cardiac Sciences and Radiology, University of Calgary, 1403 29th Street Northwest, Calgary, Alberta T2N 2T9, Canada. E-mail: matthias.friedrich@ucalgary.ca.

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