

Imaging myocardial edema

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Abstract

Cardiac magnetic resonance (CMR) imaging offers a powerful noninvasive technique for assessing the effects of ischemia–reperfusion injury in the context of acute coronary syndrome (ACS). T2-weighted CMR sequences performed after coronary occlusion accurately identify regions of myocardial edema downstream of the obstructed vessel that enables retrospective determination of the area at risk. Comparing the area at risk with gadolinium-enhanced infarct sizing provides an important tool for clinical decision making and research as it defines the degree of heart muscle salvage following an ischemic injury. The currently available techniques for assessing myocardial edema in ACS are described in this review with an overview of how these inform our understanding of myocardial salvage following primary coronary intervention.

Keywords: Acute myocardial infarction; cardiovascular magnetic resonance; myocardial salvage

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Introduction

Acute coronary syndrome (ACS) may rapidly lead to myocardial hypoxia and ischemia within the territory of the occluded vessel. Cardiac magnetic resonance (CMR) imaging provides a powerful tool for defining the extent of ischemia by using T2-weighted imaging to detect tissue edema. This approach reveals the potential infarct size, which is a key parameter in evaluating therapies that aim to maximize myocardial salvage. Reperfusion injury is a major contributor to final infarct size and T2-weighted imaging plays an emerging role in the characterization of reperfusion hemorrhage following revascularization. T2-weighted imaging also has a clinical application in differentiating acute from chronic infarctions and in investigating inflammatory conditions that mimic ACS.

What does T2-weighted imaging show?

T2 relaxation of the magnetic resonance signal is caused by the dephasing of magnetic spins [1]. T2 decay varies between different tissues, and by increasing the echo time image contrast becomes progressively more T2-weighted. Contrast can be further improved by combining fat suppression techniques such as short TI inversion recovery with dual inversion black blood imaging to null the magnetization of blood in the imaging slice [2]. The signal intensity in T2-weighted imaging is very sensitive to changes in mobile water content, which increases during acute ischemia as a result of intracellular sodium accumulation [3] and cell swelling [4]. CMR using T2-weighted sequences provides the optimal technique for quantifying acute myocardial edema in the aftermath of ACS, and offers an important insight into the effects of therapy on ischemia–reperfusion injury.

Assessing myocardial salvage

Maximizing myocardial viability during ST elevation myocardial infarction (STEMI) is the principal means by which patients benefit from coronary reperfusion [5, 6]. Time to reperfusion is critically important as a wave front of irreversible ischemic injury progressively advances throughout the area at risk in the territory of the infarct-related artery [7, 8]. As tissue perfusion is re-established there is the potential for salvaging viable myocytes leading to recovery of contractile function within transiently ischemic myocardium [9]. Myocardial salvage represents the difference between the potential infarct size and the final infarct size, which is a key concept because its measurement can be used to develop strategies to optimize the management of acute myocardial infarction [10]. Edema within acutely ischemic myocardium is manifested by a zone of hyperintensity on T2-weighted imaging, which develops within the first hour of coronary occlusion (Fig. 1) [11]. This zone on T2-weighted imaging closely corresponds to the ischemic territory determined with fluorescent microspheres [12] and perfusion single-photon emission computed tomography [13]. Preclinical research has shown that this zone includes both reversibly and irreversibly injured myocardium within reperfused sub-endocardial infarctions [14]. The size of the ischemic vascular bed depends on the anatomical boundaries of the occluded coronary artery, but the extent of necrosis within that zone is variable and may be arrested by timely coronary reperfusion [15]. Late gad-

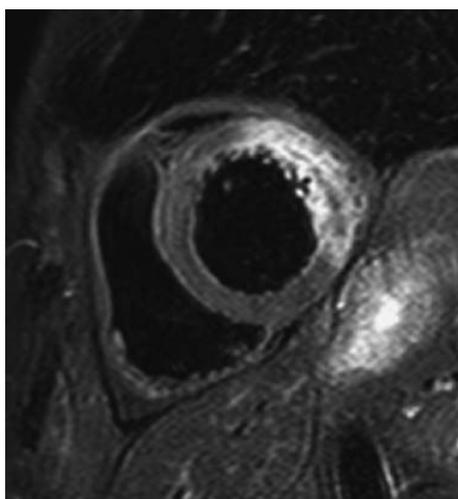


Fig. 1 Black blood T2-weighted image in the left ventricular short axis of a patient 24 hours following coronary intervention for acute myocardial infarction. Extensive high-signal edema is present throughout the lateral wall.

olinium enhancement (LGE) defines the final infarct size as a region of hyperintense necrosis [16]. Combining the two techniques of T2-weighted imaging and LGE enables irreversibly injured myocardium to be distinguished from ischemic but potentially viable myocardium [17]. The resulting myocardial salvage index provides an important parameter for assessing the effectiveness of reperfusion after primary percutaneous coronary intervention (PPCI).

Primary endpoints in the clinical evaluations of reperfusion therapy, such as death or major adverse cardiac events, have a low incidence in short-term follow-up. Using salvage as a surrogate endpoint of clinical trials in STEMI provides immediate biological data on the effect of treatment that also controls for variations in the size of the area at risk [18, 19]. Although the use of CMR endpoints in STEMI has been criticized for a lack of validation studies [20] recent data support the use of myocardial salvage as an endpoint for clinical trials investigating novel reperfusion strategies that outperform the assessment of infarct size alone [21, 22].

A range of signal intensity thresholds has been used to quantify the area at risk on T2-weighted images, and as yet there is no consensus on which of these offers the most accurate or reliable approach [13, 17, 22, 23]. More sophisticated segmentation techniques have shown promise for semi-automated image analysis and direct parametric mapping of signal relaxation, which has recently been used to map the T2 decay constants throughout the left ventricle after STEMI [23–26]. For salvage measurement and assessment of the peri-infarct border zone careful co-registration between T2-weighted imaging and LGE is also necessary [27]. The extent of hyperintensity on T2-weighted images appears stable during the first week after infarction before declining over the subsequent 6 months so there is a window of opportunity to assess the area at risk [28, 29]. However, it has been suggested that the extent of myocardial edema shown on T2-weighted imaging may be influenced by reperfusion injury extending beyond the infarct margins [30]. In contrast, the extent of LGE is dynamically evolving during the first week after reperfusion, so quantification of infarct size is critical in the interval after PPCI [29, 31, 32]. Hemorrhage within the infarct opposes the effect of high-signal edema and this may lead to a substantial underestimate of the area at risk in

more extensive infarcts [23]. Salvage measurement is therefore not straightforward but is achievable with the right expertise and suitable software tools (Fig. 2).

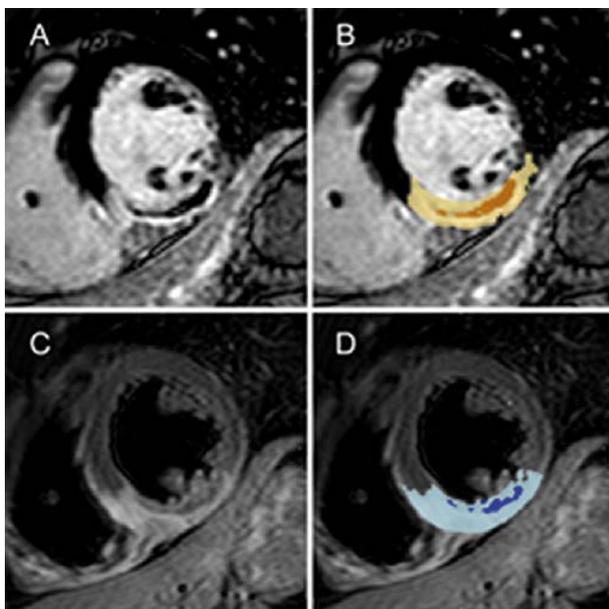


Fig. 2 Salvage quantification in an acute inferior myocardial infarction. In this case there is transmural late gadolinium enhancement with microvascular obstruction (A) throughout the ischemic bed, which is represented by the high signal on T2-weighted imaging (C). The paired images are co-registered and segmented to show the final infarct size (B) and the potential infarct size (D).

Reperfusion hemorrhage

Prompt restoration of myocardial perfusion is the most important goal of PPCI in treating STEMI patients; however, despite re-establishing patency of the infarct-related coronary artery, achieving optimal tissue perfusion and myocyte salvage in all patients has remained elusive [33, 34]. The process of restoring blood flow to ischemic tissue can itself induce myocyte damage and this phenomenon, known as ischemia–reperfusion injury, can paradoxically reduce the beneficial effects of myocardial reperfusion [35]. This process results in the death of cardiac myocytes that were viable immediately before myocardial reperfusion and may be responsible for up to half the final infarct size [36]. Interstitial hemorrhage occurs within severely ischemic myocardium during reperfusion, and provides a potential means for identifying reperfusion injury with imaging [37, 38]. Blood products have paramagnetic properties that cause signal loss within the zone of edema on spin-echo T2-weighted images [23, 39]. T2*-weighted gradient-echo imaging

provides an even more sensitive technique for detecting iron, and allows the extent of reperfusion hemorrhage to be quantified (Fig. 3) [40, 41]. CMR studies have shown that hemorrhage is a frequent complication after apparently successful coronary intervention, and is an independent predictor of adverse ventricular remodeling regardless of the initial infarct size [42].

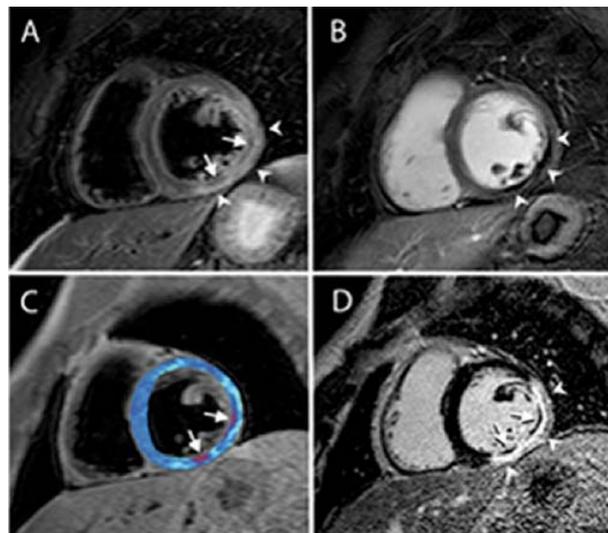


Fig. 3 Comprehensive cardiac magnetic resonance assessment of ischemia–reperfusion injury following revascularization of a circumflex territory infarction. Acute edema is shown on the T2-weighted image (A) in the ischemic area at risk (arrowheads) including focal areas of low-signal hemorrhage (arrows). Early gadolinium enhancement reveals areas of microvascular obstruction (B), which coincide with interstitial hemorrhage on a T2* map (C). Late gadolinium enhancement (D) shows the extent of necrosis (arrowheads) with islands of subendocardial microvascular obstruction (arrows).

Mimics of acute coronary syndrome

T2-weighted imaging enables acute ischemia to be distinguished from chronic infarction, and can be a valuable tool in the investigation of patients with multivessel disease as it is able to define the area at risk even in the absence of infarction, which can then be used to direct interventional strategies to the culprit artery [43].

The diagnosis of acute myocarditis may be difficult because of the nonspecific clinical features, and CMR provides an accurate method for diagnosis [44]. In the context of myocarditis there is edema and usually some fibrosis that is most commonly localized to the basal lateral and inferolateral walls. Although the distribution of edema is often focal and coincides with the zone of LGE (Fig. 4) [45], it is often diffuse and measurement of the signal intensity ratio between myocardium and skeletal muscle is often required [46].

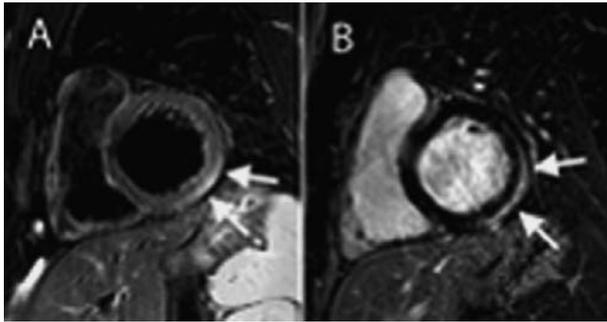


Fig. 4 Cardiac magnetic resonance images of a patient with acute myocarditis. Typical basal subepicardial edema and necrosis is shown on T2-weighted imaging (A) and late gadolinium enhancement (B), respectively.

Stress-induced (*takotsubo*) cardiomyopathy is typically manifested by transitory apical (or mid-ventricular) dyskinesia in the absence of significant coronary artery disease [47]. CMR demonstrates the characteristic wall motion abnormality and the absence of an infarct on LGE. In the majority of *takotsubo* cases myocardial edema is present on T2-weighted images, which may be due to inflammation, increased wall stress or transient ischemia [48]. Signal abnormalities on T2-weighted images may also be observed in hypertrophic cardiomyopathy and cardiac sarcoidosis, which may reflect underlying focal ischemia and inflammation, respectively [49, 50].

Conclusions

T2-weighted imaging enables acute inflammation, including that observed throughout ischemic myocardium, to be diagnosed and quantified. It plays a crucial role in determining the success of reperfusion therapies by showing the potential infarct size as it was before coronary intervention. Hemorrhage on T2-weighted imaging also reveals the effects of reperfusion injury, which may prove to be a useful marker for chronic remodeling. Finally, as part of a comprehensive CMR assessment, T2-weighted imaging provides useful diagnostic information in the evaluation of acute chest pain in the absence of coronary artery disease. •

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