Scoring reperfusion by contrast-enhanced magnetic resonance imaging

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Abstract

After acute myocardial infarction, the immediate therapeutic goal is to establish patency of the infarct-related artery. However, because a patient's prognosis after acute myocardial infarction relates directly to the extent of myocardial injury produced during coronary occlusion, attention has shifted away from achieving epicardial artery patency towards the achievement of adequate tissue reperfusion. On the basis of myocardial and microvascular injury assessed by contrast-enhanced magnetic resonance imaging after primary percutaneous coronary intervention, four patterns of tissue reperfusion score might be identified: I, aborted myocardial infarction; II, transmural necrosis limited to less than two left ventricular segments without severe microvascular damage; III, transmural necrosis in more than two left ventricular segments without severe microvascular damage; IV, transmural necrosis in more than two left ventricular segments plus severe microvascular damage.
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Keywords: Acute myocardial infarction, magnetic resonance imaging, primary angioplasty

Introduction

After acute myocardial infarction, the immediate therapeutic goal is to establish patency of the infarct-related artery. Nevertheless, the successful restoration of epicardial coronary artery patency by thrombolysis, primary angioplasty or bypass does not necessarily translate into improved myocardial reperfusion [1–3]. Patients' prognosis after acute myocardial infarction relates directly to the extent of myocardial injury produced during coronary occlusion [4–9]. Postinfarction electrocardiography, echocardiography, and contrast ventriculography are often used as an indirect means of assessing the degree of myocardial damage [10,11], whereas radionuclide studies with ^{99m}Tc sestamibi- and gadolinium-contrast-enhanced magnetic resonance imaging (ceMRI) can measure infarct size directly [12–14]. In addition to the extent of infarcted myocardium, the magnitude of structural obstruction or disruption of the microvasculature, called the ''no reflow'' or ''low reflow'' phenomenon, that is sustained before or during primary percutaneous coronary intervention (PCI) has been related to a worse clinical outcome [14,15], despite successful epicardial revascularization. Therefore, attention has shifted away from merely achieving epicardial artery patency towards the achievement of an adequate myocardial and microvascular reperfusion.

Studies performed in experimental animal models have shown that, after ligation of a coronary artery and subsequent re-opening of the epicardial vessel, the territory injured by the prolonged ischemia is composed primarily of non viable myocardial tissue in which myocytes perish first, followed eventually by

necrosis of the endothelial cells that line intramyocardial capillaries [16,17]. An exact quantification of the final extent of both myocardial and microvascular damage might be possible. In contrast, unlike most animal models of mechanical coronary occlusion, the clinical setting of acute myocardial infarction is more complex: the duration of true ischemia might not be clearly determinable, micro- and macroembolic events might be involved, the collateral circulation may be variable, and preconditioning and myocardial oxygen consumption may have major roles in determining the final amount of myocardial and microvascular injury. ceMRI has emerged as a useful tool with which to undertake a form of ''in-vivo histology'' to examine the infarct characteristics accurately, and has proven useful in both research and clinical areas of cardiology. This article summarizes the pathophysiologic and clinical evidence supporting the importance of scoring tissue reperfusion by ceMRI after successful recanalization of the infarct-related artery by primary PCI.

Magnetic resonance imaging assessment of myocardial and microvascular injury

After acute myocardial infarction, four different zones of myocardium can readily be defined by ceMRI [3,18]: (1) non necrotic, salvaged (stunned) myocardium, (2) necrotic myocardium without microvascular damage, (3) necrotic myocardium with microvascular damage, and (4) normal myocardium. These zones are defined by examining contractility using cine MRI and tissue characteristics using contrast-enhanced techniques, most commonly after administering a gadolinium-based contrast agent. In the case of myocardial necrosis, areas of hyperenhancement (bright) reflect necrotic tissue with intact microvasculature, whereas areas of hypoenhancement (dark) within areas of hyperenhancement reflect necrotic tissue with damaged microvasculature (so-called no-reflow zones). Myocardial necrosis is usually labeled as transmural if hyperenhancement extends to at least 75% of the thickness of the left ventricular segment.

A standard approach to imaging microvascular obstruction has yet to be defined. Two of the most commonly used methods for assessing no reflow involve first-pass perfusion [14,19], and delayed-enhancement imaging [3,19,20]. A comparison between these two techniques undertaken by Lund and colleagues [19] found some differences in sensitivity between first-pass perfusion ceMRI and delayed-enhanced ceMRI, but overall there was a high level of concordance between these two approaches. The investigators suggested that the difference could be explained by extensive microvascular damage resulting in persistent hypoenhancement, even with late imaging.

We favor delayed-enhancement ceMRI for the evaluation of no reflow zones, because we have found this technique to be more specific for severe forms of microvascular damage with persistent contrast filling defects, which have been shown to be related to worse remodeling and outcome [7,9]. When first-pass ceMRI is used, patients with chronic, healed infarcts could be wrongly interpreted as having no reflow zones secondary to the reduced capillary density of scar tissue relative to healthy myocardium. Finally, we and others [21] feel that it is more clinically meaningful to evaluate microvascular injury concomitantly with the evaluation of the extent and the amount of necrosis (hyperenhancement), as they provide additional information regarding the extent and the type of myocardial necrosis and recovery of function [9].

Scoring of tissue reperfusion after primary percutaneous coronary intervention: the tissue reperfusion score

In experimental animal studies, both transmurality and microvascular dysfunction are strongly dependent on the duration of ischemia before reperfusion, and the extent of no reflow is driven by the extent of infarct size for any given delay in time to treatment [22]. We have provided support for the ability of ceMRI to assess myocardial and microvascular damage in patients [3]. In a study of 77 patients with first-time acute myocardial infarction who underwent primary PCI, we found a continuous relationship between duration of ischemia and probability of transmural necrosis and severe microvascular damage assessed by ceMRI. Interestingly, for each 30 min delay in the treatment of patients undergoing successful primary PCI, the risk of transmural necrosis or severe microvascular damage increased by 37% and 21%, respectively (*Figure 1*). Although there was also a close correlation between the presence of severe microvascular damage and evidence of transmural necrosis, it is noteworthy that, for any time of reperfusion the probability of transmural necrosis was greater than that of severe microvascular damage (*Figure 1*). In other words, severe microvascular damage occurs later than transmural necrosis, suggesting that, from a pathophysiological point of view, severe microvascular damage lags behind transmural necrosis, being present exclusively in left ventricle in which at least two segments have transmural necrosis. In a series of patients with acute myocardial infarction, other authors similarly found that the extent of transmural necrosis was the strongest predictor of severe microvascular obstruction on delayed-enhancement ceMRI [23]. So, in summary, this suggests that ''time is muscle and microvasculature damage follows on behind'', and not vice versa.

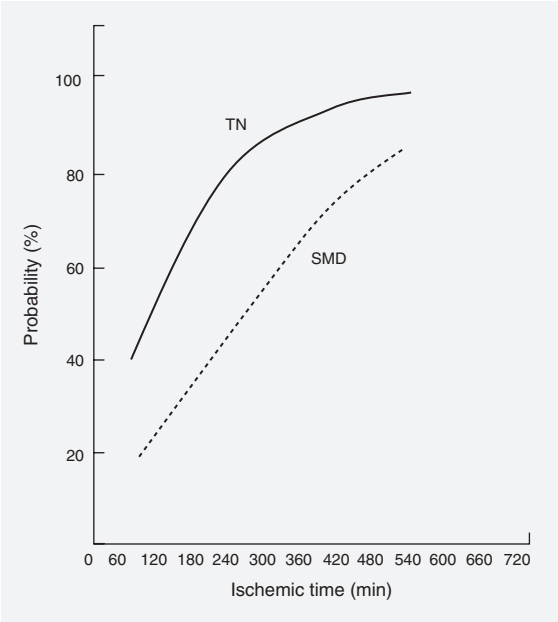

Figure 1. Relationship between duration of ischemia and patients' (in-hospital) probability of transmural necrosis (TN) or severe microvascular damage (SMD). (Modified from Tarantini et al [3], with permission. © Elsevier).

According to the myocardial and microvascular injury assessed by ceMRI after primary PCI, a tissue reperfusion score (TSR) showing four patterns might be identified (*Figure 2*) [3,9,24]:

I Aborted myocardial infarction.
II Transmural necrosis limited to fewer than two left ventricular segments without severe microvascular damage.
III Transmural necrosis in more than two left ventricular segments without severe microvascular damage.
IV Transmural necrosis in more than two left ventricular segments plus severe microvascular damage.

In a clinicopathologic study in two patients in the TSR IV category, who died of cardiogenic shock after reperfused acute myocardial infarction, we demonstrated for the first time that the peculiar signal features of late gadolinium hypoenhancement within the myocardial infarction core can be related to hemorrhage as a result of irreversible vascular injury within transmural acute myocardial infarctions that underwent late reperfusion (at least 5 h) [25]. This finding is consistent with those from experimental models of coronary occlusion and reperfusion, in which hemorrhage always occurs within the area of necrosis and is significantly related to the infarct size and to the coronary occlusion time [1,2,4]. At present, the clinical implications of hemorrhagic as compared with white infarcts remain undetermined.

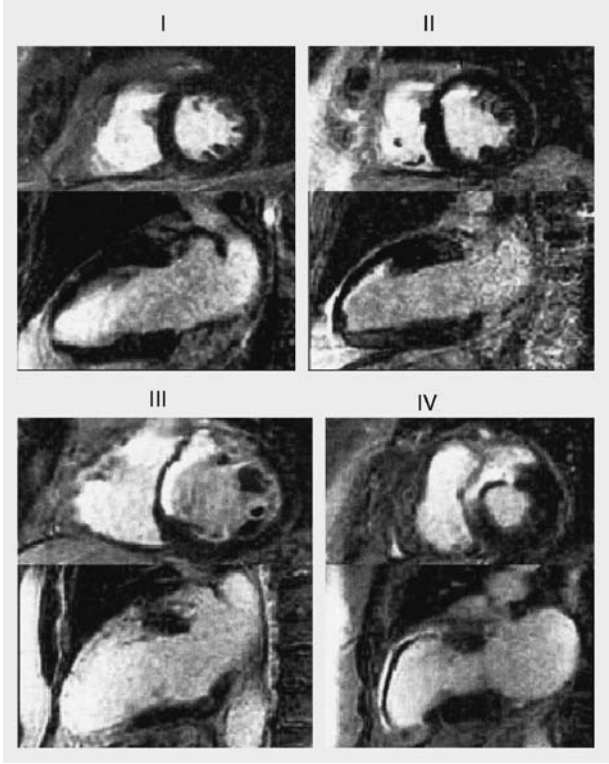

Figure 2. Typical examples of the different tissue reperfusion scores detected by contrast-enhanced magnetic resonance imaging (ceMRI) in patients undergoing primary percutaneous coronary intervention at increasing time delays from the onset of chest pain (see text for details). Upper and lower panels respectively show results of ceMRI obtained at the short-axis level and in the long-axis two-chamber plane. I: Anterior ST-segment elevation myocardial infarct (STEMI); pain to balloon time 70 min; troponin I peak 11.7 ng/mL. At 6 days from the acute event, no signs of necrosis are evident on ceMRI ("aborted" infarct). II: Anterior STEMI; pain to balloon time 170 min; troponin I peak 38.6 ng/mL. At 6 days from the acute event, ceMRI shows a non transmural necrosis in the middle and apical segments of the anterior wall. III: Anterior STEMI; pain to balloon time 240 min; troponin I peak 199 ng/mL. At 8 days from the acute event, ceMRI shows a transmural necrosis of more than two ventricular segments, without evidence of severe microvascular damage. IV: Anterior STEMI; pain to balloon time 310 min; troponin I peak 258 ng/mL. At 7 days from the acute event, ceMRI shows transmural necrosis of more than two ventricular segments, with evidence of a subendocardial dark zone referred to as severe microvascular obstruction. (Modified from Tarantini G et al [3], with permission. © Elsevier).

Summary

Cardiac magnetic resonance after acute myocardial infarction could help: (1) in the evaluation of the effectiveness of reperfusion after primary PCI by the characterization of myocardial and microvascular damage, (2) the early stratification of patients with acute myocardial infarction, to improve the clinical identification of patients at risk of adverse remodeling and outcome, (3) in studies of the effects of hemorrhage after acute myocardial infarction, and (4) to

clarify the consequences of new therapeutic strategies, such as platelet glycoprotein IIb/IIIa inhibitors [26]. ■

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