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EDITORIAL COMMENT

Imaging Acute MI in the 21st Century*

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Myocardial perfusion imaging (MPI) in acute myocardial infarction (MI) has had its ups and downs over the past 4 decades (1). "Cold-spot" imaging with thallium-201, technetium-99m tetrofosmin and sestamibi, wall motion assessment with gated radionuclide angiography, and "hot-spot" imaging with radionuclide-bound pyrophosphate, glucarate, antimyosin, annexin V (2), and more recently, duramycin (to target phosphatidylethanolamine) (3) have focused on diagnosis and are now seldom used because of the availability of sensitive biomarkers. In the current era, MPI risk-stratifies patients presenting to emergency departments with chest pain and intermediate probability for acute coronary syndrome (4), and assesses infarct size after acute MI and myocardial salvage after coronary revascularization (1).

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For patients presenting to emergency departments with chest pain, studies have suggested benefit from imaging with various modalities including MPI, 2-dimensional echocardiography, magnetic resonance imaging (MRI), and computed tomography (5). Myocardial salvage has mostly been done with MPI and more recently MRI. The study by Hadamitzky et al. (6) provides the largest comparison to date between the 2 methods. The authors measured the area at risk (AAR) and scar in patients with ST-segment elevation myocardial infarction (STEMI) (n = 121) and non–ST-segment elevation myocardial infarction (NSTEMI) (n = 59) with MPI and MRI. The initial MPI was done before percutaneous coronary intervention (PCI) (to measure AAR). The second MPI scan (to measure scar) and MRI were scheduled to occur at 5 to 7 days after PCI but were performed earlier (interquartile range [IQR]: 3.6 to 4.9 days for MRI; time between MRI and MPI 1.4 to 25.1 h). The AAR and scar by MPI were measured using automated analysis of polar maps (50% threshold of regional tracer activity to define abnormal perfusion). With MRI, AAR was assessed using a T2-weighted turbo spin echo sequence acquired before contrast injection whereas scar was assessed 15 min after injection of contrast agent on T1-weighted inversion-recovery turbo fast low-angle shot sequence.

Hadamitzky et al. (6) concluded that assessment of AAR by MRI correlates well with MPI ($r = 0.80$, $p < 0.0001$). A reasonable correlation was found for salvage area (AAR − scar) ($r = 0.66$). Overall, the salvage area by MRI was significantly smaller than by MPI. In 38% of patients, results of both methods diverged by >10% of left ventricular volume (salvage area smaller in 25% and larger in 13% by MRI than MPI), a difference that may be clinically significant. The scar size was slightly larger by MRI, which could be explained by higher spatial resolution of MRI resulting in detection of small subendocardial scars missed by MPI.

The authors point out that MRI is not associated with potentially harmful radiation exposure and needs 1 exam at ~5 days after the acute event. By

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contrast, MPI requires pre- and post-PCI scans. Nevertheless, MRI has drawbacks of its own. It is relatively contraindicated in patients with pacemakers and defibrillators, and hard to perform in those who suffer from claustrophobia. Thus, in this study of 441 patients who had MPI for assessment of myocardial salvage, 8% were ineligible for MRI due to renal function or presence of pacemaker/defibrillator, and 45% did not have an MRI for various reasons, including lack of consent by patient due to claustrophobia and logistical problems in scheduling MRI before discharge. Also, because the T2-weighted turbo spin echo sequence has a low contrast-to-noise ratio, it requires a low threshold of 2 SD for edema detection, which makes it vulnerable to artifacts. The microvascular obstruction area was delineated manually, again introducing the possibility of measurement error with clinical application. Further, in patients with tachycardia, arrhythmia, pleural effusion, and heart failure, all common, particularly after large infarctions, image quality is suboptimal, and valid image analysis may not be possible. In the current study, the exclusion rate of 13% because of insufficient image quality reflects these limitations in an experienced, controlled setting. What these rates will translate to in community practice is unknown. Thus, although MRI may offer an alternative to MPI for myocardial salvage assessment, contraindications of this modality and limitations in the currently established imaging sequences may cause a considerable rate of data loss, which prevents widespread clinical applicability.

It is interesting that in this study, 50% of patients with STEMI and 59% with NSTEMI had Thrombolysis In Myocardial Infarction flow grade >0 before PCI, and yet they had detectable AAR (often large). Despite coronary revascularization with PCI, most patients had scar ($14.7 \pm 16.9\%$ of left ventricle), and there was no correlation between time from symptom onset to coronary revascularization and myocardial salvage. The median time between symptom onset and PCI was 4.9 h in STEMI (IQR: 3.4 to 8 h) and 12.6 h in NSTEMI (IQR: 8.4 to 23.6 h); the door-to-balloon time was not stated. These studies therefore do not negate the possibility that earlier reperfusion might have resulted in a more complete salvage. Alternatively, imaging 2 to 4 weeks rather than 5 days after the index MI/PCI may have yielded different results because the processes of metabolic stunning, microvascular reperfusion, and myocardial remodeling may be active beyond the first few days of an MI (7).

The time delay between symptom onset and reperfusion suggests that measured AAR may have included myocardium that had already infarcted and was beyond salvage. It is possible that the AAR may have been exaggerated in some patients who had an initial perfusion abnormality (which later resolved) despite the presence of antegrade flow before PCI. This is not unlike the well-documented situation seen in patients with rest MPI perfusion defects after subsidence of chest pain resolution of ST changes (8). This phenomenon is probably related to complex kinetics of sestamibi, which is more than a "pure flow tracer." It is important to remember that the uptake mechanism of sestamibi is dependent on the mitochondrial electromagnetic gradient, which is susceptible to metabolic derangements that are initiated by ischemia (9). The ischemia cascade with emphasis on state of the myocardium rather than conduit arteries is yet another explanation for dissociation of vessel patency and perfusion/cell edema patterns.

The correlations between MPI and MRI measurements with functional data such as left ventricular volumes and ejection fraction, although significant, are modest. This is not unexpected because these variables are load dependent, and contractility in remote myocardium is variable, depending on myocardial blood flow, load condition, associated diseases, medications, and remodeling (10). It is the less-than-perfect correlation between perfusion and function that explains the additive prognostic value of these variables (11). Regrettably, prognostic data were not provided in this study. Also not provided are repeatability data for MPI and MRI. These data are important for sample size calculations for future studies. Despite the significant correlations between the 2 modalities, the Bland-Altman plots show wide limits of agreement for measurement of AAR, scar, and salvage area, and therefore, these modalities should not be used interchangeably on serial testing.

The authors should be congratulated for providing correlative data on a large sample size, especially since assessment of AAR is not routinely done for clinical care. Promising developments in MRI technology could allow for assessment of increasing proportion of patients and improve image quality to decrease the number of inadequate studies. Newer MPI imaging tracers that examine myocardial me-

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tabolism and allow for measurement of myocardial blood flow in target and remote zones may further improve our understanding of AAR, hibernation, stunning, and scar in vulnerable patients with acute coronary syndrome.

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