Contrast-enhanced magnetic resonance imaging in the assessment of myocardial infarction and viability

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Contrast-enhanced magnetic resonance imaging (MRI) can be used to visualize the transmural extent of myocardial infarction with high spatial resolution. The aim of this review is to provide an overview of the use of contrast-enhanced MRI for characterization of ischemic myocardial injury in comparison to other imaging methods and its relevance in clinical syndromes related to coronary artery disease. Infarcted myocardium appears hyperenhanced compared with normal myocardium when imaged by a delayed-enhancement MRI technique with the use of an inversion-prepared T_1-weighted sequence after injection of gadolinium chelates, such as gadolinium–diethylenetriamine pentaacetic acid. Experimental and clinical studies indicate that the extent of delayed enhancement is reproducible and closely correlates with the size of myocardial necrosis or infarct scar as determined by established in vitro and in vivo methods. Furthermore, MRI appears to be more sensitive than other imaging methods in detecting small subendocardial infarctions. The transmural extent of delayed enhancement potentially predicts functional outcome after revascularization in acute myocardial infarction and chronic ischemic heart disease, indicating that it can accurately discriminate between infarction and dysfunctional but viable myocardium. Further experience from clinical trials is needed to understand the association of delayed enhancement with clinical outcomes. (J Nucl Cardiol 2008;15:105-17.)

INTRODUCTION

Ischemic myocardium that is dysfunctional but viable has the potential for recovery of contractile function after revascularization. The term *myocardial stunning* describes prolonged postischemic contractile depression despite restoration of adequate perfusion after a brief ischemic insult.[1,2] The term *myocardial hibernation* is used to describe a more persistent form of reversible contractile dysfunction due to coronary artery disease (CAD).[3] The mechanisms of myocardial hibernation are incompletely understood.[4] The classic definition of hibernation postulated that myocardial function is reduced to match chronic and severe reduction of resting myocardial blood flow.[3] More recent evidence has shown that resting perfusion is not always significantly reduced in areas of hibernating myocardium.[4] Instead, repetitive stunning caused by repeated ischemic episodes may result in chronic dysfunction.[4] Thus reversible myocardial dysfunction in a patient with chronic ischemic heart disease is likely to present an admixture of stunned and hibernating tissue jeopardized by various degrees of ischemia.

Noninvasive detection of viable myocardium in patients with chronic left ventricular (LV) dysfunction associated with CAD has important clinical implications for treatment.[5] Failure to identify hibernating myocardium may lead to a loss of viable myocytes and reduce changes of functional recovery over time.[6,7] Though limited by the lack of large randomized clinical trials, a meta-analysis of retrospective data indicates that such patients are also at substantial risk of death, which can be effectively reduced by successful revascularization.[8] Furthermore, preoperative assessment of viability may identify patients who are at low risk for serious perioperative complications.[9] Thus discrimination between viable dysfunctional myocardium and scar permits selection of patients who are most likely to benefit significantly from revascularization, allowing others to avoid the risks associated with revascularization when they are unlikely to benefit.

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Noninvasive assessment of myocardial infarct size is also an important clinical goal after an acute myocardial infarction (AMI), allowing risk stratification and evaluation of myocardial salvage. The extent and degree of irreversible myocardial tissue injury after AMI are strong predictors of clinical outcomes, and interventions that reduce injury improve prognosis.[10-14] Thus measurement of infarct size is an attractive surrogate endpoint instead of death for the efficacy of therapeutic strategies in clinical trials.[14]

Conventional nuclear imaging methods, such as single photon emission computed tomography (SPECT) with technetium 99m sestamibi, Tc-99m tetrofosmin, or thallium 201 used as tracers, are currently accepted and validated tools for demonstration of chronically ischemic but viable myocardium and quantification of infarct size.[4,10-14] Technical limitations of SPECT imaging, such as low spatial resolution and the assessment of only relative tracer inhomogeneities resulting from soft-tissue attenuation or scatter, may compromise the delineation of small infarcts and the diagnostic accuracy of SPECT. The assessment of inotropic reserve, in terms of the response to low-dose dobutamine as determined by echocardiography, is another widely used and extensively validated method by which to detect viability.[15] Provided that it is performed by experienced investigators, its diagnostic accuracy has been reported to be comparable to that of nuclear imaging methods. Evaluation of myocardial glucose utilization with fluorine 18 fluorodeoxyglucose (FDG) and positron emission tomography (PET) is considered to be the most reliable tool by which to assess myocardial viability.[4,16] Its quantitative nature allows assessment of the amount of viable tissue as a continuum, from fully viable to partially viable in areas of partial infarction to nonviable scar.

Contrast-enhanced magnetic resonance imaging (MRI) appears to be a promising alternative to established nuclear imaging methods capable of visualizing the transmural distribution of viable and infarcted myocardium with excellent spatial resolution. Contrast-enhanced MRI of myocardial infarction (MI) is based on a delayed-enhancement technique using inversion-recovery–prepared T_1-weighted gradient echo pulse sequences after intravenous administration of a bolus (0.10-0.20 mmol/kg) of gadolinium chelates, such as gadolinium–diethylenetriamine pentaacetic acid (Gd-DTPA). Infarcted myocardium appears enhanced relative to normal myocardium when imaged after a delay (typically 5-20 minutes) after intravenous contrast injection. The first reports on visualization of infarction with contrast-enhanced MRI appeared in the mid 1980s.[17-19] Recent advances in pulse sequence development have made it possible to visualize infarcted tissue with high spatial resolution (in-plane resolution of 1-2 mm and slice thickness of 4 mm) and a high contrast ratio between normal and injured tissue (approximately 300%-500%). Furthermore, fast acquisitions during single or repeated breath-holds have resulted in images that are only rarely affected by motion artifacts.[20-22] Given that delayed-enhancement MRI can be performed in conjunction with segmental wall motion analysis on cine MRI images and assessment of myocardial perfusion during the first pass of the contrast agent, detailed characterization of dysfunctional, ischemically injured myocardium with respect to potential functional outcome is possible. The aim of this review is to provide an overview of the use of contrast-enhanced MRI for characterization of ischemic myocardial injury and its relevance in clinical syndromes related to CAD.

MECHANISMS OF DELAYED ENHANCEMENT AND EXPERIMENTAL VALIDATION

Although the exact mechanism of delayed enhancement of infarcted myocardium is not completely understood, there is evidence showing that it involves an increased volume of distribution and altered delivery and washout kinetics of Gd-DTPA, resulting in its accumulation and prolonged presence in the infarcted area.[23-27] Gd-DTPA is biologically inert and passively diffuses in the myocardium throughout the extracellular space, with a half-life in blood of approximately 20 minutes.[28] Experimental studies have provided direct evidence of an increased concentration of Gd-DTPA in both acutely infarcted myocardium and infarct scar relative to normal myocardium.[25,29] Similarly, kinetic modeling demonstrates that the partition coefficient reflecting the distribution volume of Gd-DTPA is increased in acute and chronic human MI.[26,27,30] The presence of infarct scar increases the extracellular space per unit of myocardium.[25] In AMI the potential distribution volume of the contrast agent is increased by loss of cell membrane integrity as a result of myocyte death, allowing Gd-DTPA to distribute into the dead myocytes. Indeed, experimental data show that regions of delayed enhancement are mainly composed of myocytes with ruptured plasma membranes as examined by electron microscopy.[24] Distribution into the previously intracellular space of the dead myocytes could influence myocardial Gd-DTPA kinetics because of the additional time required for contrast molecules to diffuse in and out of the plasma membrane. This has been shown in experimental and human studies demonstrating profound differences in wash-in and washout kinetics of Gd-DTPA within the border-zone and core regions of the infarcted tissue when compared with normal myocardium.[24,26,27]

Several experimental studies have shown that delayed enhancement accurately measures the size of

reperfused or nonreperfused MI regardless of associated wall motion abnormalities and the age of infarction.[20,24,25,31-33] Studies in canine models of reperfused and nonreperfused MIs have shown that the extent of delayed enhancement by ex vivo MRI closely correlated ($r > 0.95$) with the area of myocardial necrosis as demonstrated in the same myocardial tissue samples by triphenyltetrazolium chloride staining from 4 hours until 8 weeks after temporary or permanent coronary occlusion.[20,31] In contrast, myocardial signal intensities after reversible ischemia were the same as those of remote, normal myocardium.[20,31] A good correlation between delayed enhancement and uptake of the porphyrin-based necrosis-specific contrast agent gadophrin has also been shown.[32] Experimental studies indicated that the transmural extent of delayed enhancement in the acute phase of MI is associated with the absence of inotropic reserve,[34] lack of long-term functional improvement,[35] and adverse LV remodeling.[34,36]

Controversy exists about the physiologic significance of delayed enhancement because overestimation of the size of an acute myocardial necrosis has been found in some experimental studies.[23,29,37,38] In line with this finding, some clinical studies have reported that regions of delayed enhancement demonstrated contractile reserve and functional recovery.[39,40] Saeed et al[38] found in a rat model that the delayed enhancement after Gd-DTPA administration encompasses both viable and nonviable portions of the ischemic myocardium and, thus, overestimates infarct size by approximately 10% in the acute phase of reperfused infarction when compared with triphenyltetrazolium chloride staining of tissue samples and imaging with a necrosis-specific porphyrin agent. Potential explanations for delayed enhancement in reversibly injured myocardium may include the presence of increased extracellular volume as a result of tissue edema and inflammation with increased capillary permeability. However, technical factors, such as species differences in the uptake of Gd-DTPA, partial volume effects resulting from insufficient spatial resolution, and low signal-to-noise ratio provided by pulse sequences used in older studies, have also been suggested to play a role.[20] It remains to be seen whether emerging MRI techniques, such as molecular imaging of cardiomyocyte apoptosis with specific nanoparticles, will aid in characterization of the border-zone areas of evolving AMI in more detail.[41]

MICROVASCULAR INJURY

In addition to homogeneous regions with delayed enhancement, those with a non-enhancing "dark" core can be found within the acutely infarcted myocardium by contrast-enhanced MRI (Figure 1).[23,24,42] Persistent impairment of myocardial blood flow despite successful reopening of the infarct-related artery is known as the *no-reflow phenomenon*.[43] Delivery of Gd-DTPA into the infarcted myocardium depends on both the patency of the infarct-related artery and microvascular perfusion. The latter is impaired in areas of no reflow due to extensive damage to myocardial microcirculation. Experimental studies show that hypoenhanced areas correspond to areas of no reflow as defined by histopathologic evidence of microvascular damage and low myocardial perfusion.[23,37] Contrast-enhanced MRI was used to show that the area of no reflow expands over the first 48 hours after reperfused AMI[37] and that it is associated with dysfunction of both the infarcted and adjacent noninfarcted myocardium.[34] The presence of no reflow as demonstrated by hypoenhanced areas is strongly associated with impaired functional recovery after AMI.[44,45] However, because the hypoenhanced regions with concomitant microvascular obstruction represent only a fraction of the infarcted tissue, it underestimates the amount of infarcted myocardium, and thus its sensitivity for predicting functional recovery may remain low.[44,46] Given the association of no reflow with advanced myocardial damage and impaired functional recovery, its assessment with MRI may still help in the clinical stratification of patients after AMI.[43-46]

ACQUISITION OF DELAYED-ENHANCEMENT IMAGES AND QUANTIFICATION OF INFARCT SIZE

Pulse sequences and image acquisition have been reviewed in detail elsewhere.[21,47] Importantly, delayed enhancement appears to remain stable over an extended period of time in chronic ischemic heart failure regardless of revascularization, and the reproducibility of repeated measurements is high, indicating its robustness and feasibility for clinical use.[48-51] However, for accurate detection of infarction by delayed-enhancement MRI, standardization of some parts of the imaging protocol needs to be considered.

First, the performance of inversion-recovery delayed-enhancement sequences that are mostly used for delayed enhancement are highly sensitive to the inversion time (TI) selected. TI is the time interval between an inversion pulse that prepares water protons and the start of actual image acquisition. To optimize the contrast between infarcted and normal myocardium, TI is chosen to "null" normal myocardium. As discussed previously, washout of Gd-DTPA is faster in normal myocardium than in infarcted myocardium.[26,27] The relationship between Gd-DTPA concentration and measured MRI signal is complex, but within the myocardium, a linear relationship between signal intensity and the longitudinal relaxation time (T1) can be assumed because of the

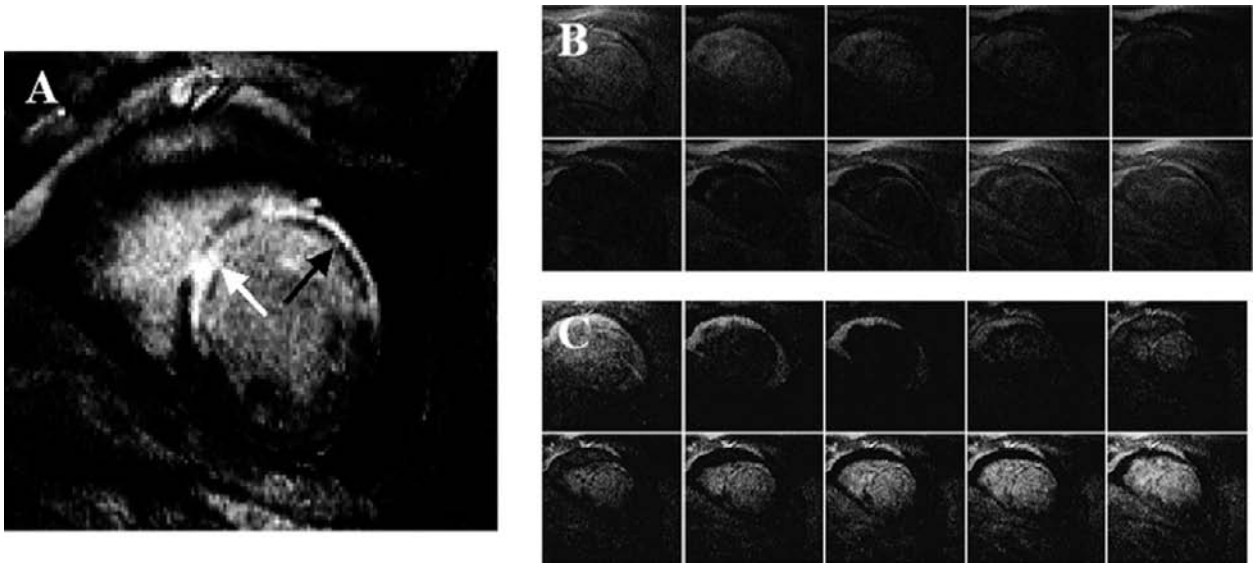

Figure 1. A, Delayed enhancement in acutely infarcted anteroseptal walls (*white arrow*) compared with normal myocardium. It should be noted that there is a subendocardial dark area of hypoperfusion despite successful recanalization of the infarct-related artery (*black arrow*). The optimal TI was chosen by use of the Look-Locker technique that is demonstrated in **B** and **C**. Corresponding medial short-axis views acquired before injection of Gd-DTPA (**B**) and 20 minutes after injection of Gd-DTPA (**C**) with the use of a different TI in each image are shown. Whereas signal intensity in the heart is homogeneous before contrast injection, there is faster relaxation of magnetization in the blood pool and infarcted myocardium after contrast injection. (Reproduced with permission from Klein et al.[27])

relatively small concentrations of the contrast agent. Given that direct measurement of regional T1 is very time-consuming, technically less complex inversion-recovery sequences are used.[52] When the TI is selected so that it matches the current T1 of normal myocardium, no signal is detected. In contrast, infarcted regions show an intense signal. This form of background suppression is widely used in MRI and has contributed substantially to its clinical success. However, washout of Gd-DTPA is a dynamic process. As the blood concentration and hence myocardial concentration of Gd-DTPA decrease over time, the TI will need to be adjusted upward to still null normal myocardium and avoid underestimation of infarct size at later time points. In patients with AMI, a fixed TI at 300 milliseconds resulted in underestimation of infarct size by about 7% of the LV myocardium compared with the size of perfusion defect on SPECT when delayed enhancement was acquired 28 minutes after the injection of Gd-DTPA.[53] To select the proper TI, a series of images is acquired just after the inversion prepulse in a central short-axis slice. Then visual or region-of-interest analysis is used to assess the delay resulting in the lowest signal from normal myocardium. These scout images can be obtained with gradient echo imaging by use of Look-Locker–style,[54] as shown in Figure 1, or with a steady-state free precession sequence.[55] To overcome the need to predefine TI and to allow complete acquisition during 1 cardiac cycle, sequences using steady-state free precession or phase-sensitive detection techniques have also been tested.[21,56-59]

Second, the time delay between injection of Gd-DTPA and image acquisition may also affect the extent of delayed enhancement. Oshinski et al[60] found that delayed enhancement overestimated the size of histologically measured infarct size by 20% to 40% during the first minutes after Gd-DTPA injection in a rat model of AMI. The time required for delayed enhancement to correspond to the infarct size varied from 16 minutes after 2 hours of ischemia to 26 minutes after 30 minutes of ischemia.[60] However, the effects of the time delay on late enhancement appear to be partly related to the TI.[49,61] When the TI is optimized to null normal myocardium, the extent of delayed enhancement is stable over time, from 7 to 42 minutes, after contrast injection and matches well with the defect size on SPECT in patients with reperfused AMI.[53] In practice, however, sufficient time is required to allow the blood pool signal in the LV cavity to decline and provide separation between the LV cavity and delayed enhancement in the subendocardial myocardium.[27,47]

Third, image analysis of cardiac MRI is currently

significantly less automated for wall motion analysis and infarct detection as compared with cardiac SPECT and PET. A major reason for this is the fact that because of time constraints caused by the need to acquire images during breath-holds, they are typically obtained as a stack of short-axis slices with different in-plane resolution and slice thickness (1-2 mm and 4-8 mm). Thus no volumetric analysis, as in nuclear imaging, can be performed. In practice, quantitative measurement of the amount of infarcted myocardium is done by tracing the area of delayed enhancement in each slice and multiplying it by the slice thickness and the myocardial density of 1.05 g/mL to obtain the infarct mass. Another widely used method determines the extent of delayed enhancement within each myocardial segment via a 5-point scale (where 0 indicates no enhancement, 1 indicates 1%-25% delayed enhancement of the segment, 2 indicates 26%-50% delayed enhancement, 3 indicates 51%-75% delayed enhancement, and 4 indicates 76%-100% delayed enhancement) and sums the scores over all segments and divides this sum by the total number of segments. The latter method has practical implications in determining the transmural extent of hyperenhancement and, thus, the ability of delayed enhancement to predict of functional recovery.[33,47]

Nuclear imaging, where the area with highest tracer uptake in the left ventricle is defined as normal and set to 100%, is fundamentally different than MRI, where the situation is inverted, and normal tissue shows essentially the lowest signal. Technically, this raises the problem of reliable thresholding, and to date, no accepted algorithm applicable to images obtained by use of different sequences and equipment from different vendors is available. Systematic analysis using different thresholds for myocardial delayed enhancement has shown considerable variations in the resulting estimate of MI size. Amado et al[61] suggested that the use of the full width at half maximum criterion most accurately determined MI size when compared with histologic analysis. In patients with acute MI a threshold of greater than 200% enhancement of the remote myocardium showed the best agreement of enhancement extent and measurements of perfusion defect by SPECT.[53]

DETECTION OF MI IN HUMAN BEINGS

The current definition of MI strongly relies on the presence of myocardial necrosis as detected by a typical sequence of biochemical markers combined with chest pain, electrocardiographic changes, and demonstration of coronary stenosis.[62] Increased risk in patients with elevated levels of sensitive biochemical markers of necrosis justifies the diagnosis of MI even if the amount of necrosis is very small.

Several studies have demonstrated the accuracy of delayed-enhancement MRI in the detection and quantification of acute infarction[42,53,63-67] and chronic infarction[33,50,68-72] as compared with the clinical criteria and established nuclear imaging methods. An example of delayed-enhancement MRI in comparison with SPECT in human AMI is shown in Figure 2. In 60 patients with 6-day-old AMI and successful revascularization, Lund et al[66] found good agreement between the extent of delayed enhancement and infarct size by Tl-201 SPECT (defined as <2.5 SDs of signal intensity of normal myocardium at rest; mean difference, 1.3% of LV area; $r = 0.73$). Ibrahim et al[53] found that delayed enhancement showed good agreement with infarct size by Tc-99m sestamibi SPECT (mean difference, 3%; $r = 0.86$) in 33 patients with 7-day-old successfully revascularized AMI. In chronic ischemic heart disease, delayed-enhancement MRI showed good accuracy in assessing the amount of nonviable tissue irrespective of the severity of contractile dysfunction as compared with combined PET imaging of resting myocardial perfusion with nitrogen 13 ammonia and FDG uptake as a reference for viability.[50,70,71]

Some features of delayed-enhancement MRI in comparison to SPECT for imaging MI are summarized in Table 1. A major advantage of MRI in the detection of MI compared with nuclear imaging methods is its higher spatial resolution, which makes delayed enhancement suitable to detect small areas of subendocardial infarcts.[33,69] In an experimental study 92% of histopathologically confirmed acute subendocardial infarctions were detected by delayed enhancement whereas only 28% were visualized by SPECT.[33] In a study comparing MRI with SPECT in 78 patients with AMI by use of troponin elevation as the reference standard for MI, delayed enhancement was significantly more sensitive than SPECT for the detection of small infarcts (troponin T <3.0 ng/mL, 92% vs 69%; $P = .03$) and infarctions in a non-anterior location (98% vs 84%, $P = .03$).[53] Similarly, Lund et al[66] found that Tl-201 SPECT failed to detect 20% of small infarctions (mean size, 6.4% $\pm$ 5.7% of LV volume by MRI) in the inferior wall that were detectable with MRI. Delayed enhancement also demonstrates high sensitivity in detecting scars of previous small infarctions. Wagner et al[33] demonstrated in patients with chronic stable CAD that although both SPECT and MRI demonstrated large transmural infarct scars, 47% of subendocardial scars detected by MRI were not detected by SPECT. Given that contractile dysfunction in patients with chronic MI can be systematically observed only when the transmural extent of delayed enhancement approaches 50%, these findings indicate that many of the infarctions detected by delayed-enhancement MRI would be missed by analysis of contractile function alone.[73]

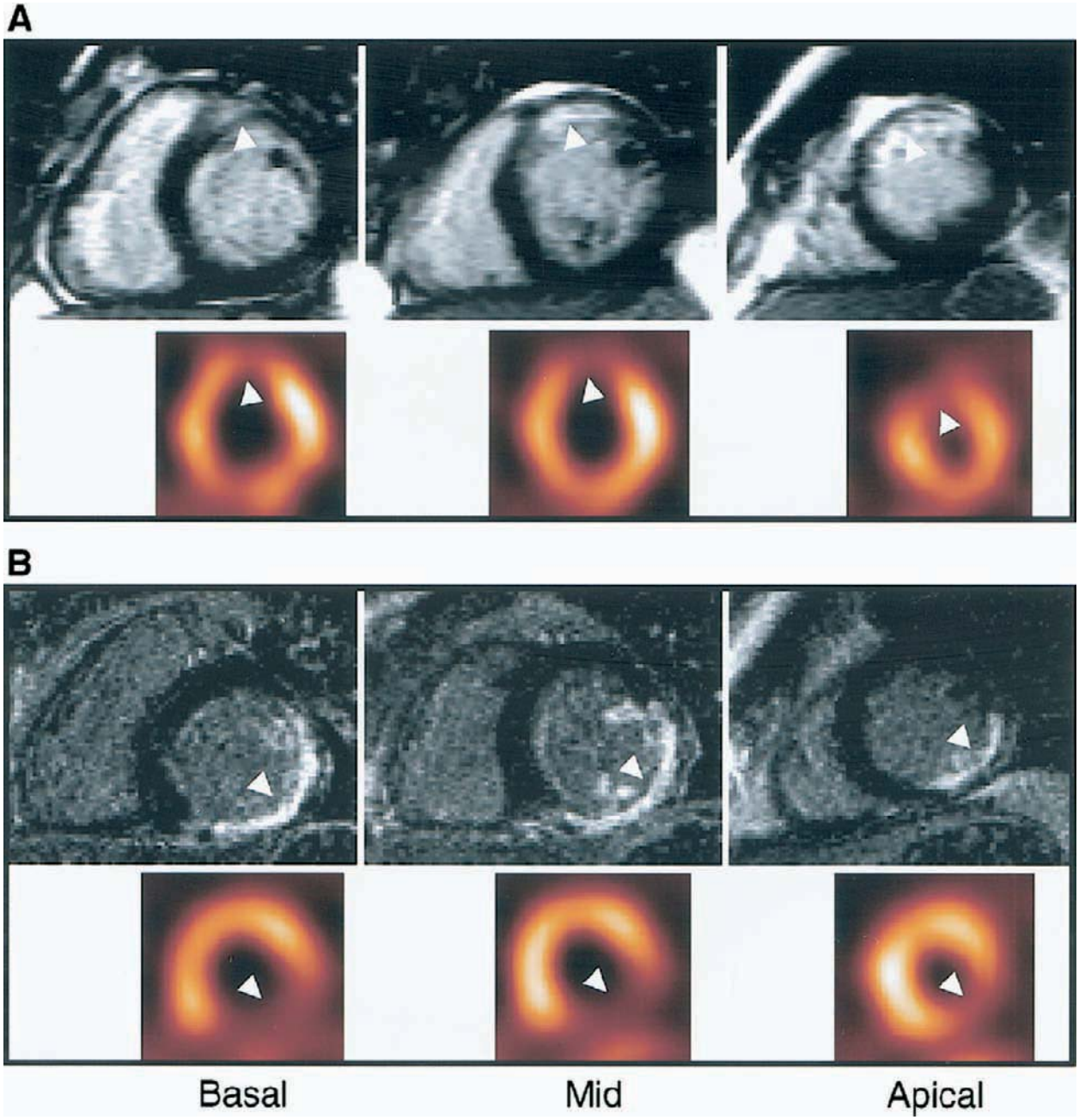

Figure 2. Images demonstrate delayed-enhancement MRI of AMI in comparison to SPECT. **A**, Subendocardial delayed enhancement in anterior and anteroseptal walls (transmural extent, 25%-75%) by use of MRI (*upper row*, *arrowheads*) and corresponding perfusion defect by SPECT (*lower row*, *arrowheads*). **B**, Transmural delayed enhancement in inferior wall (transmural extent, 75%-100%) and subendocardial enhancement extending to lateral wall (transmural extent, 25%-75%) by use of MRI (*upper row*, *arrowheads*) with corresponding perfusion defects on SPECT (*lower row*, *arrowheads*). Both patients were imaged 1 week after AMI. (Reproduced with permission from Ibrahim et al.[53])

High sensitivity, good spatial resolution and the lack of tissue attenuation in MRI have been used in some recent studies to detect, quantify, and map the localization of very small amounts of infarction or scar in suspected acute coronary syndrome, MI caused by distal coronary occlusion, and distal embolization during coronary stenting.[74-76] When combined with assessment of wall motion defects, delayed-enhancement MRI accu-

Table 1. Comparison of some features of SPECT and delayed-enhancement MRI for imaging of MI

Feature	SPECT	MRI
Spatial resolution	Approximately 10 mm	In-plane resolution, 1-2 mm; slice thickness, 4-8 mm
Detection of infarction in human beings	Extensively validated, detects transmural infarcts	Also detects small infarcts and transmural extent of infarction
Reproducibility	High	High
Quantification of infarct size	Automated, comparable between centers	Manual, no comparisons between centers
Prediction of wall motion recovery after revascularization (sensitivity/specificity)	81%/66%*	>90%/26%-68%‡
	87%/55%†	Good negative predictive value
Association with clinical events	Prospective mortality data in AMI, nonrandomized studies on hibernation	Small trials with combined endpoints
Experience in clinical trials	Similar infarct size and outcomes in randomized trials	Small trials

*Tc-99m–labeled tracers.
†Tl-201 imaging, data from Wijns et al.[4]
‡See text for details.

rately detected a high fraction of patients with an acute coronary syndrome.[74] However, the fact that the technique does not allow differentiation of new myocardial injury from old infarction and that, in some patients presenting with unstable angina pectoris, no myocardial damage is expected need to be considered in this setting.[74] Delayed-enhancement MRI served as a standard for revised terminology for the location of MIs that present Q waves on the electrocardiogram.[75,77] Porto et al[76] demonstrated distal embolization of plaque material during percutaneous coronary intervention and stenting. The mean mass of hyperenhancement of the resulting infarctions that might have been missed by other modalities was only 7.6 ± 6.2 g. Concerning the excellent prognosis of patients with no infarction by nuclear imaging methods, future studies will be required to determine whether those with small infarcts, detectable by MRI and not SPECT, have an adverse prognosis.

PREDICTION OF RECOVERY OF WALL MOTION

An improved contractile performance is commonly considered to be the gold standard for assessing myocardial viability, although benefits of revascularization do not appear to be limited to improved function.[78] In the initial study by Kim et al,[48] it was shown that in 41 patients with chronic ischemic heart disease, dysfunctional segments with less than 25% of delayed enhancement were likely to recover (positive and negative predictive values, 71% and 79%, respectively) after complete revascularization. In contrast, segments with more than 50% of delayed enhancement had a very low probability (<10%) of functional improvement.[48] Subsequently, studies together involving more than 200 patients have confirmed the finding that the transmural extent of delayed enhancement is a critical determinant of contractile recovery and that the extent of dysfunctional but viable myocardium measured by contrast-enhanced MRI can predict improvement of global LV function after revascularization in chronic ischemic cardiomyopathy.[79-86] Sensitivity for predicting functional recovery after revascularization has consistently been reported to be more than 90% when the transmural extent of delayed enhancement is less than 50%, which has been suggested to be a clinically useful cutoff value by which to guide therapeutic decisions in chronic ischemic heart disease.[81] Compared with sensitivity, reported specificity values of the technique are lower (26%-68% in different studies), which reflects the uncertainty regarding improvement of function in segments with subendocardial necrosis. Recently, comparable positive predictive values (73%) for functional recovery 6 months after revascularization were found for the lack of delayed enhancement (cutoff value of <50% scar transmurality) and combination of resting myocardial perfusion and uptake of FDG (cutoff value of >50% of normal myocardium) with the use of PET

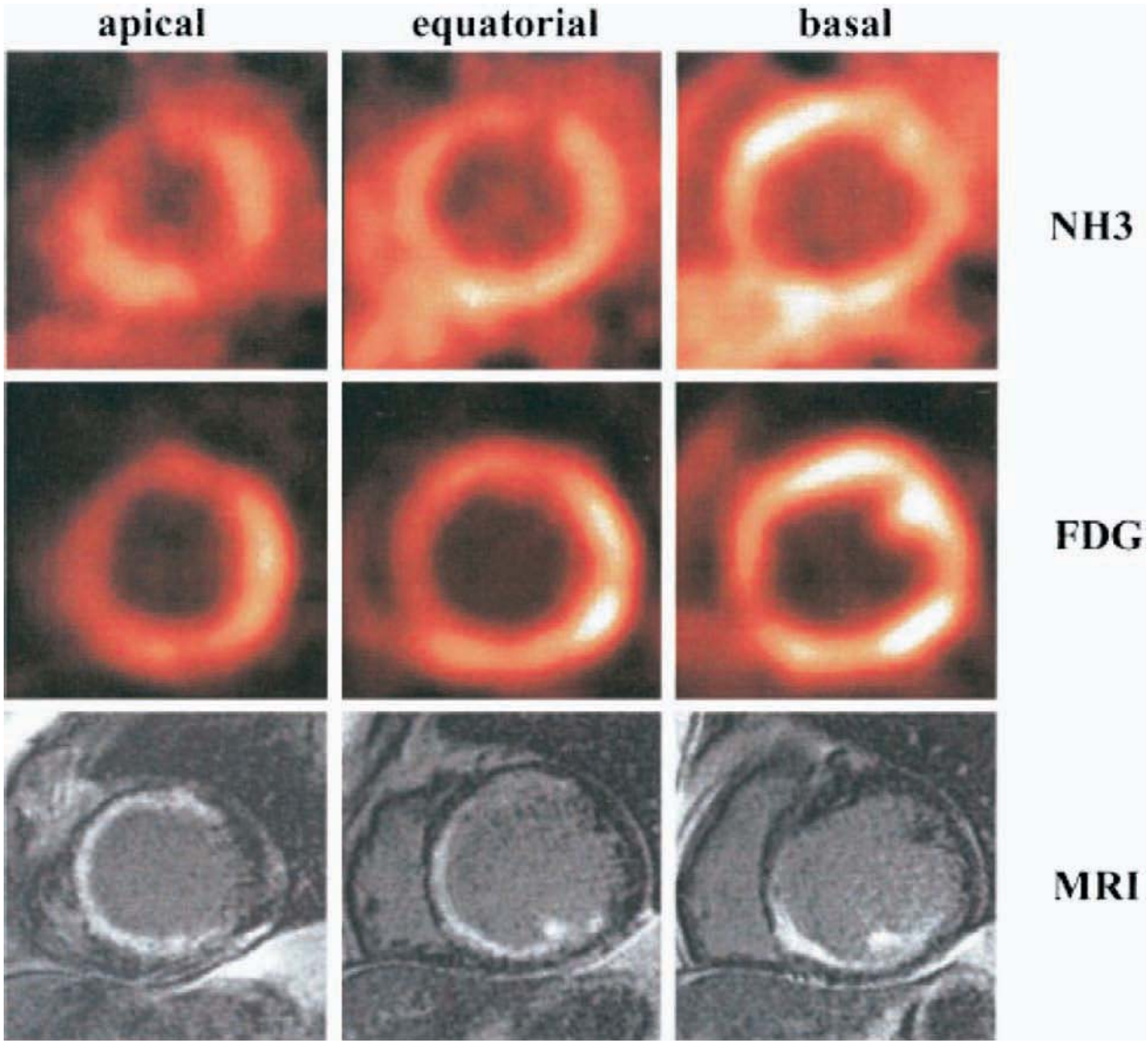

Figure 3. Example of delayed-enhancement MRI and PET viability study including assessment of resting perfusion with ammonia (*NH3*) and glucose metabolism with FDG in a patient with ischemic heart failure. The delayed enhancement in the areas showing reduced perfusion and FDG uptake should be noted. The high spatial resolution of MRI allows distinction between subendocardial, transmural, and papillary defects. (Reproduced with permission from Klein et al.[70])

as a reference method by which to detect viable versus nonviable myocardium.[86] Importantly, delayed-enhancement MRI resulted in fewer false-negative results and a higher negative predictive value than lack of FDG uptake by PET (93% vs 77%).[86] Thus the presence of delayed enhancement may be more accurate than nuclear imaging methods for the identification of segments that are unlikely to recover function after revascularization.[86] An example of delayed-enhancement MRI in comparison to a PET viability study in patients with chronic ischemic LV dysfunction is shown in Figure 3.

The findings from chronic ischemic heart disease appear to apply to AMI in that the extent of delayed enhancement by MRI predicts recovery of wall motion after reperfusion therapy.[44,46,87-90] Consecutive studies together involving 74 patients who were studied approximately 1 week after AMI and coronary intervention indicated that the absence of delayed enhancement or its transmural extent being less than 25% is associated with a good probability of long-term functional improvement 2 to 7 months later (positive and negative predictive values of 73%-75% and 59%-75%, respectively).[44,87,88] The extent of dysfunctional but

viable myocardium and the size of infarction as determined by delayed-enhancement MRI were also associated with changes in global ejection fraction and indexes of LV remodeling after human AMI.[87,91]

Besides wall motion and the absence of delayed enhancement, MRI offers other parameters of viability, such as diastolic wall thickness (>5.5 mm), contractile reserve via dobutamine stress imaging, and the presence or absence of no reflow. Because the delayed-enhancement technique is limited by diminished power for predicting functional recovery when the transmural extent of myocardial necrosis is intermediate, adjunctive information from other markers of viability may help refine the classification of these segments as clinically viable or nonviable.[82,92] The value of inotropic reserve as seen with response to low-dose dobutamine is an extensively validated index of viability.[15] It has been suggested to be more accurate than delayed enhancement in predicting wall motion recovery when the transmural extent of infarction is less than 50% to 75%.[82,90,92] In such cases it was demonstrated that the response to low-dose dobutamine increased the likelihood of functional recovery from 77% to 95% and was associated with greater improvement in wall thickening when compared with delayed enhancement only.[92,93] However, the sensitivity of dobutamine response in identifying viable myocardium decreases when the transmural extent of infarction exceeds 38%.[94]

PREDICTION OF CLINICAL EVENTS

Currently, there are few data on the prognostic value of delayed-enhancement MRI with respect to clinical outcomes in ischemic heart disease. A small study of 44 patients with AMI found that the extent of delayed enhancement was associated with an increased risk of adverse cardiovascular events during follow-up of 16 months.[95] The rate of cardiac death, heart failure, recurrent MI, unstable angina pectoris, or stroke was 71% versus 30% when delayed enhancement indicated large infarct (>30% of left ventricle) instead of small infarct (<18% of left ventricle).[95] A recent study analyzed 19 deaths during 1.7 years of follow-up in 231 patients with CAD and scar from previous MI detected by contrast-enhanced MRI.[96] The probability of death was 6.2 times higher in patients with large scar (involving >6 segments) than in those with small scar (<6 segments). The extent of delayed enhancement predicted death better than LV size or ejection fraction. In another study the size of the infarct measured by use of delayed-enhancement MRI appeared to be associated with inducible ventricular tachycardia on electrophysiologic testing.[97]

Favorable comparisons between MRI and established methods to differentiate MI and viable myocardium may indicate that some of the data on the prognostic value of viability as assessed by nuclear imaging or echocardiography might also apply to delayed-enhancement MRI. However, it is important to emphasize that delayed-enhancement MRI is specific for either AMI or scar from an old infarction, but not for hibernating myocardium. Infarct size has a well-established prognostic value that is also expected to apply to MRI. In contrast, the prognostic value of PET relies on the relative comparison of flow and glucose uptake (mismatch), which has been shown experimentally and clinically to reflect viable but jeopardized myocardium. Several studies have indicated that there is an association between PET "mismatch" and adverse clinical outcome.[98-103] Prospective clinical trials comparing measures of infarction and either hibernation or stunning obtained with the use of MRI and other techniques, in particular the gold standard PET, to obtain prognostic data are needed to better understand its clinical implications.

MRI IN CLINICAL TRIALS

Experience with the use of myocardial infarct size measured by contrast-enhanced MRI as an endpoint in randomized clinical trials, such as those using cell-based therapy for AMI,[104-107] intracoronary devices to protect patients from distal embolization during coronary intervention,[108] on-pump and off-pump coronary surgery,[109] and different reperfusion therapies for AMI,[110,111] is increasing. In a study of 35 patients with chronic heart failure by Bello et al,[112] the amount of dysfunctional but viable myocardium by contrast MRI predicted a favorable response in LV function and remodeling for treatment with β-blockers. In patients with ischemic or nonischemic cardiomyopathy, the spatial extent of delayed enhancement (scar burden) was associated with a poor response to cardiac resynchronization therapy in 2 studies.[113,114] None of the current clinical studies reported a comparison of clinical outcomes with respect to infarct size or the amount of dysfunctional but viable myocardium. For application of contrast-enhanced MRI in larger studies, the reproducibility and comparability of images acquired in multiple centers, as well as the optimal timing of imaging after an AMI, need to be confirmed.

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