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Performance of CMR Methods for Differentiating Acute From Chronic MI

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ABSTRACT

OBJECTIVES The purpose of this study was to assess the performance of cardiac magnetic resonance (CMR) methods for discriminating acute from chronic myocardial infarction (MI).

BACKGROUND Although T2-weighted CMR is thought to be accurate in differentiating acute from chronic MI, few studies have reported on diagnostic accuracy, and these generally compared extremes in infarct age (e.g., <1 week old vs. more than 6 months old) and did not evaluate other CMR methods that could be informative.

METHODS A total of 221 CMR studies were performed at various time points after ST-segment elevation myocardial infarction in 117 consecutive patients without a history of MI or revascularization enrolled prospectively at 2 centers. Imaging markers of acute MI (<1 month) were T2 hyperintensity on double inversion recovery turbo spin echo (DIR-TSE) images, microvascular obstruction (MO) on delayed-enhancement CMR, and focally increased end-diastolic wall thickness (EDWT) on cine-CMR.

RESULTS The prevalence of T2-DIR-TSE hyperintensity decreased with infarct age but remained substantial up to 6 months post-MI. In contrast, the prevalence of both MO and increased EDWT dropped sharply after 1 month. T2-DIR-TSE sensitivity, specificity, and accuracy for identifying acute MI were 88%, 66%, and 77% compared with 73%, 97%, and 85%, respectively, for the combination of MO *or* increased EDWT. On multivariable analysis, persistence of T2-hyperintensity in intermediate-age infarcts (1 to 6 months old) was predicted by larger infarct size, diabetes, and better T2-DIR-TSE image quality score. For infarct size ≥10% of the left ventricle, a simple algorithm incorporating all CMR components allowed classification of infarct age into 3 categories (<1 month old, 1 to 6 months old, and ≥6 months old) with 80% (95% confidence interval: 73% to 87%) accuracy.

CONCLUSIONS T2-DIR-TSE hyperintensity is specific for infarcts <6 months old, whereas MO and increased EDWT are specific for infarcts <1 month old. Incorporating multiple CMR markers of acute MI and their varied longevity leads to a more precise assessment of infarct age. (J Am Coll Cardiol Img 2015;8:669–79) © 2015 by the American College of Cardiology Foundation.

It is vital to determine whether a myocardial infarction (MI) is recent or chronic because there are implications for patient management and prognosis. The determination, however, can be challenging because acute MI is often clinically unrecognized, and if testing is delayed 1 to 2 weeks, diagnostic electrocardiographic changes and elevated biomarkers have usually resolved (1).

T2-weighted cardiac magnetic resonance (CMR) can detect necrosis-associated myocardial edema, and recent expert reviews and consensus guidelines have touted this technique as an excellent method to

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CMR = cardiac magnetic resonance

CNR = contrast-to-noise ratio

DE-CMR = delayed-enhancement cardiac magnetic resonance

DIR-TSE = double inversion recovery turbo spin echo

EDWT = end-diastolic wall thickness

IRA = infarct-related artery

LV = left ventricular

MI = myocardial infarction

MO = microvascular obstruction

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

distinguish acute from chronic MI (2–4). However, the time frame for detecting "acute" T2-weighted CMR changes is unclear, and, to date, only 3 studies have reported on diagnostic performance in 54, 50, and 46 patients, respectively (5–7). Moreover, these studies have the potential limitation of spectrum bias in that enrolled patients generally had extremes in infarct age (e.g., <1 week vs. more than 6 months). Hence, the diagnostic utility of T2-weighted CMR requires additional validation, especially in patients with intermediate-age infarcts.

Additionally, other CMR markers may be useful in discriminating acute from chronic MI, including the presence of microvascular obstruction (MO) on delayed-enhancement CMR and focally increased end-diastolic wall thickness (EDWT) on cine CMR. The utility of these methods in comparison with T2-weighted techniques has not been previously reported.

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The purpose of the present 2-center study was to examine the diagnostic performance of CMR methods in differentiating acute from chronic MI. Unlike previous reports, we: 1) included patients with intermediate-age infarcts (1 to 6 months old); 2) compared multiple CMR methods that could be informative; and 3) incorporated an assessment of image quality to help distinguish potentially artifactual from true findings.

METHODS

POPULATION. We prospectively recruited 122 patients with a first-time ST-segment elevation myocardial infarction (STEMI) at 2 centers (Maastricht University Medical Center, Maastricht, the Netherlands; Duke Cardiovascular Magnetic Resonance Center, Durham, North Carolina). The diagnosis of STEMI required appropriate cardiac biomarkers with 12-lead electrocardiography showing ST-segment elevation (≥0.2 mV in 2 or more contiguous precordial leads or ≥0.1 mV in ≥2 contiguous limb leads) (1). Consecutive patients admitted for primary PCI who agreed to undergo CMR were enrolled. Patients with previous MI, revascularization, or CMR contraindications were excluded. CMR was performed for research, and results were not used for clinical decision making. Four patients did not complete CMR (hemodynamic instability or claustrophobia); 1 had recurrent MI before CMR and was excluded. No patient was excluded because of image quality. The final population consisted of 117 patients. Because of scheduling, 5 did not undergo scanning for 1 month. Hence, 112 underwent CMR <1 month after acute MI. Eighty-six and 23 patients underwent scans 1 to 6 months and ≥6 months post-AMI, respectively (total of 221 scans). In patients with multiple scans, there were no cardiac events between scans. The ethics board at both sites approved the study; all patients gave written informed consent.

Admission data including medications were recorded. Coronary angiograms were reviewed to assess infarct-related-artery (IRA) reperfusion. Thrombolysis In Myocardial Infarction (TIMI) flow grade (8) was scored as follows: 0 = absence of flow; 1 = faint flow with incomplete filling; 2 = delayed flow with complete filling; 3 = normal flow.

CARDIAC MAGNETIC RESONANCE. Scanners (1.5-T, Philips Intera, Best, the Netherlands or Siemens Avanto, Erlangen, Germany) with standard protocols were used. Cine images were acquired in multiple short-axis and 3 long-axis views using steady-state free precession (slice thickness, 6 mm; gap, 4 mm; in-plane resolution, ~1.7 × 1.4 mm). A short-axis stack of T2-weighted images encompassing the left ventricle and matched in location with cine images was obtained using a double inversion recovery turbo spin echo (DIR-TSE) sequence (repetition time, 2 R-R intervals; echo time, 100 ms [Philips], 80 ms [Siemens]; slice thickness, 8 mm; gap, 2 mm; in-plane resolution, ~1.9 × 1.4) with spectrally selective fat suppression and vendor-supplied coil-intensity correction. A conventional black-blood sequence was used so that findings could be placed in context with previous studies reporting diagnostic performance (5–7). Additionally, black-blood sequences are the most commonly used in clinical practice because they are commercially available from all magnetic resonance imaging scanner vendors. Delayed enhancement imaging was performed using a segmented inversion recovery sequence, 10 to 20 min after 0.15 to 0.20 mmol/kg gadolinium contrast (gadolinium-diethylenetriaminepentaacetic acid or gadoversetamide).

IMAGE ANALYSIS. Scans were interpreted in random order by consensus of 3 observers blinded to patient identity, clinical data, and CMR date. Three separate interpretations were performed, weeks apart: first, with only T2-DIR-TSE images available; second, with only cine-CMR and delayed-enhancement CMR DE-CMR images available; and third, with all components available. Standard quantitative assessments were performed to measure infarct size and left ventricular (LV) ejection fraction based on manual

planimetry of DE-CMR and cine-CMR images, respectively.

Pre-specified imaging markers. The presence and location of CMR abnormalities were determined visually using the 17-segment model. Window and level were preset according to society guidelines so that noise was still detectable and infarcted regions were not overly saturated (9). The following were used as markers of acute MI: 1) hyperintense myocardium on T2-DIR-TSE; 2) the presence of MO on DE-CMR (central hypoenhancement within hyperenhancement) (10); and 3) increased EDWT on cine-CMR (>150% of remote, measured in the segment with most severe dysfunction). Regional wall thinning (EDWT <50% of remote) was also noted. In patients with T2-DIR-TSE hyperintensity both <1 month and 1 to 6 months post-AMI, quantitative analysis of signal intensity ratio and contrast-to-noise ratio (CNR) were performed: signal intensity (SI) ratio = (mean $SI_{hyperintense\ area}$/mean $SI_{remote\ area}$) and CNR = (mean $SI_{hyperintense\ area}$ − mean $SI_{remote\ area}$)/(1.5 × SD of background signal outside body) (11).

Match with IRA. Angiograms were analyzed blinded to the identity and CMR to localize the IRA perfusion territory on the 17-segment model (12). The location of the CMR abnormality was considered correct if the number of segments with CMR abnormality within the IRA was greater than that outside the IRA.

Image quality was graded as follows: 0 = equivocal: major artifacts, diagnosis uncertain; 1 = satisfactory: minor artifacts, images interpretable; 2 = excellent: high diagnostic confidence. The presence and location of slow-flow (nonsuppressed blood signal adjacent to endocardium) and signal dropout (myocardial signal similar to noise) artifacts were scored using the 17-segment model.

STATISTICAL ANALYSIS. Continuous data are reported as mean ± SD. Comparisons of continuous data were made using 2-sample or paired Student *t* tests. Comparisons of discrete data were made using chi-square tests. The prevalence of CMR abnormalities according to infarct age was assessed using the chi-square test for trend. McNemar's test was used to compare diagnostic performance. To identify characteristics associated with T2-DIR-TSE hyperintensity, univariable logistic regression analysis was performed. Characteristics with a p value <0.1 were considered candidates for subsequent multivariable analysis. Final model variables were determined by stepwise selection. Statistical tests were 2 tailed; $p < 0.05$ was considered significant (SAS version 9.3, SAS Institute, Cary, North Carolina).

RESULTS

POPULATION. The baseline clinical characteristics are shown in Table 1 (60% and 40% enrolled at Maastricht University and Duke University, respectively). Overall, patients had moderate infarct size (15.7 ± 10.8%) and preserved LV ejection fraction (48.6 ± 10.3%).

PREVALENCE OF CMR ABNORMALITIES. T2-DIR-TSE hyperintensity. The prevalence of T2-hyperintensity was high (88%) during the first month post-MI (Figure 1A). Of the 13 (12%) that did not have T2-hyperintensity during the first month, 12 had small infarcts (<10% LV) or poor image quality. The prevalence of T2-hyperintensity then steadily decreased with infarct age, but was still 33% for MIs 3 to 6 months old and 17% for MIs ≥6 months old. After

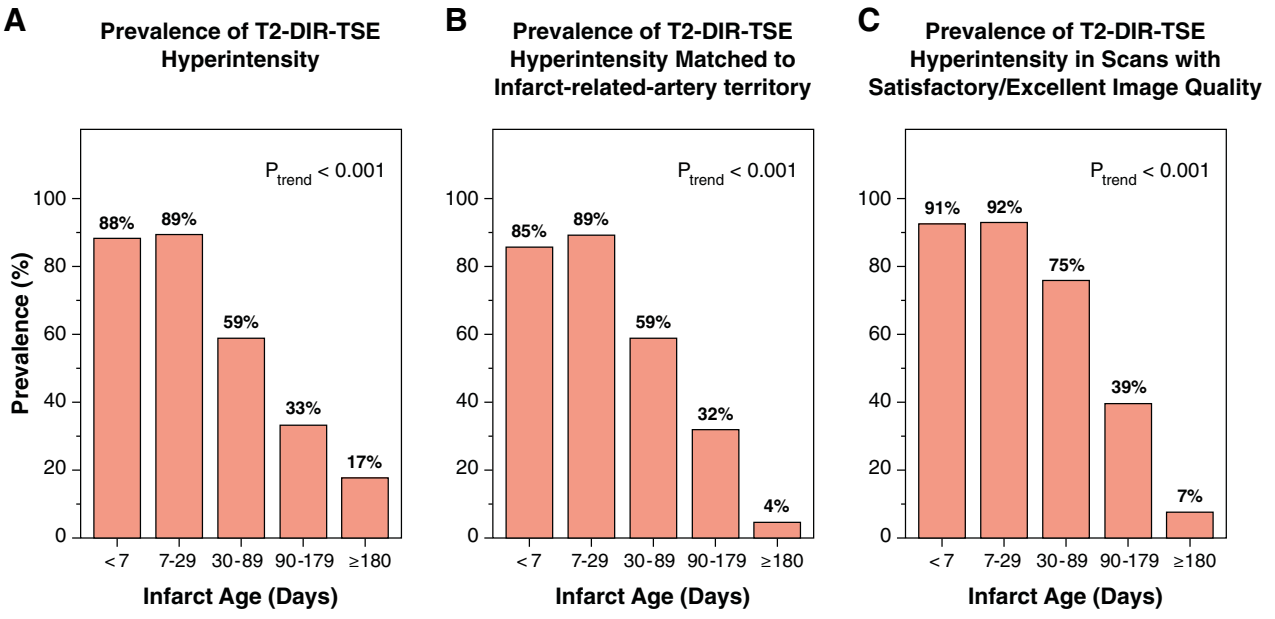
TABLE 1 Baseline Patient Characteristics (N = 117)

Age, yrs	57.8 ± 11.1
Male	98 (83.8)
Clinical history	
Coronary artery disease risk factors	
Hypertension	49 (41.9)
Diabetes	12 (10.3)
Hypercholesterolemia	47 (40.2)
Positive family history	55 (47.0)
Smoking	91 (77.8)
No. of risk factors	2.2 ± 1.0
Medications during AMI hospitalization	
Aspirin	115 (98.3)
Beta-blocker	114 (97.4)
ACE inhibitor	99 (84.6)
Statin	116 (99.1)
Thienopyridine	108 (92.3)
Glycoprotein IIb/IIIa inhibitor	27 (23.1)
Cardiac enzymes*	
Peak troponin T, μg/l	5.3 ± 4.4
Peak CK-MB, U/l	177.3 ± 129.5
Cardiac catheterization	
No. of diseased vessels†	
1	61 (52.1)
2	29 (24.8)
3	27 (23.1)
Infarct-related artery	
RCA	55 (47.0)
LAD	42 (35.9)
LCx	20 (17.1)
Pre-procedure TIMI flow grade 3	21 (17.9)
Final TIMI flow grade 3	104 (88.9)

Values are mean ± SD or n (%). *Five patients had troponin I measurements. †Significant coronary artery disease defined as >70% stenosis.

ACE = angiotensin-converting-enzyme; AMI = acute myocardial infarction; CK-MB = creatine kinase-myocardial band; LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction.

FIGURE 1 Prevalence of T2-DIR-TSE Hyperintensity at Different Time Points Post-Myocardial Infarction



(A) All scans. **(B)** Only scans with T2-hyperintense regions that match the infarct-related artery determined by angiography included. **(C)** Only scans with satisfactory or excellent image quality included. T2-DIR-TSE = T2-weighted double inversion recovery turbo spin echo.

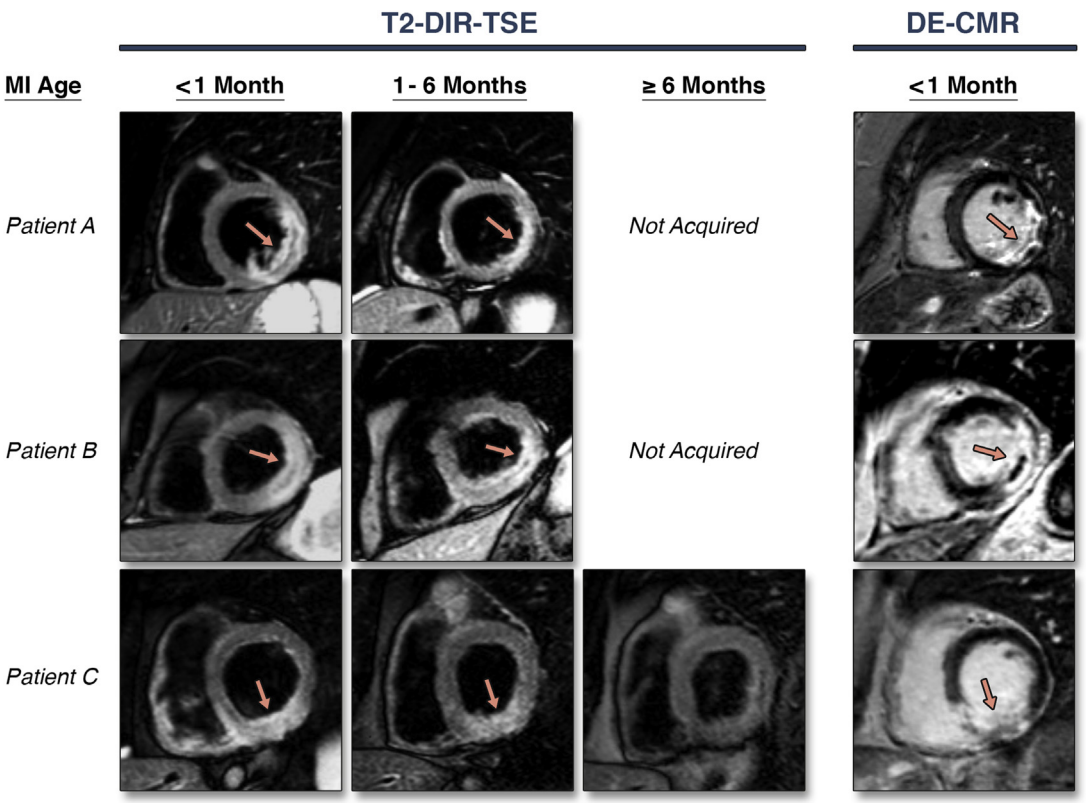
discounting hyperintense regions that were remote from the IRA territory and thus likely artifactual, the prevalence decreased to 4% for MIs ≥6 months old, but remained relatively high at 32% for MIs 3 to 6 months old (Figure 1B). Patient examples with persistent T2-hyperintensity in intermediate-age infarcts are shown in Figure 2.

DE-CMR and Cine-CMR. Examples of MO and regionally increased EDWT are shown in Figure 3A. Even early post-MI, the prevalence of MO and increased EDWT were moderate, and both decreased sharply with infarct age (Figure 3B). In all cases, MO and increased EDWT were located in the correct IRA territory. The combination of MO *or* increased EDWT allowed a higher detection rate of MIs <1 month old (73% vs. 55% for MO alone and 42% for increased EDWT alone) without significantly increasing the detection rate of MIs ≥1 month old. The prevalence of regional wall thinning steadily increased with infarct age; however, given that 6% of infarcts <1 week old had wall thinning, it was not an absolute marker of chronic MI, nor was it sensitive for chronic MI in that only 35% of infarcts ≥6 months old had thinning.

Effect of image quality. Of T2-DIR-TSE images, 66% were graded satisfactory or excellent compared with 92% and 93% for DE-CMR and cine-CMR, respectively (Figure 4A). T2-DIR-TSE slow-flow artifact was usually apical, whereas signal dropout was often inferolateral; however, any location could be affected (Figure 4B). When only scans with satisfactory or excellent image quality were included, the prevalence of T2 hyperintensity increased for intermediate-age MI (Figure 1C), whereas it remained low (7%) for MIs ≥6 months old. There was no effect of DE-CMR and cine-CME image quality score on the prevalence of MO and increased EDWT, respectively.

DIAGNOSTIC PERFORMANCE. Table 2 shows the diagnostic performance of CMR for individual components and combinations. When T2-DIR-TSE was interpreted alone, there was relatively high sensitivity (88%; 95% confidence interval [CI]: 81% to 94%) but moderate specificity (66%; 95% CI: 56% to 75%) for the diagnosis of acute MI (<1 month old). In contrast, when only delayed-enhancement and cine-CMR images were available, the finding of MO and increased EDWT, individually, had poor sensitivity (55% and 42%, respectively) but both were very specific (98% and 99%, respectively). The combination of MO *or* increased EDWT provided a substantial increase in sensitivity (73%; 95% CI: 64% to 81%), while maintaining a high specificity (97%; 95% CI: 92% to 99%), which was greater than the specificity seen for

FIGURE 2 Patient Examples



Examples demonstrating that T2-DIR-TSE hyperintensity **(arrows)** seen acutely (<1 month) can persist when reimaged 1 to 6 months post-MI. In all 3, T2-hyperintense regions match the location of DE-CMR hyperenhancement **(arrows)**. DE-CMR = delayed-enhancement cardiac magnetic resonance; MI = myocardial infarction; T2-DIR-TSE = T2-weighted double inversion recovery turbo spin echo.

T2-DIR-TSE ($p < 0.001$). When all CMR components were made available during the interpretation, sensitivity, specificity, and accuracy were slightly higher than for T2-DIR-TSE alone ($p = 0.16$, $p = 0.05$, $p = 0.02$, respectively).

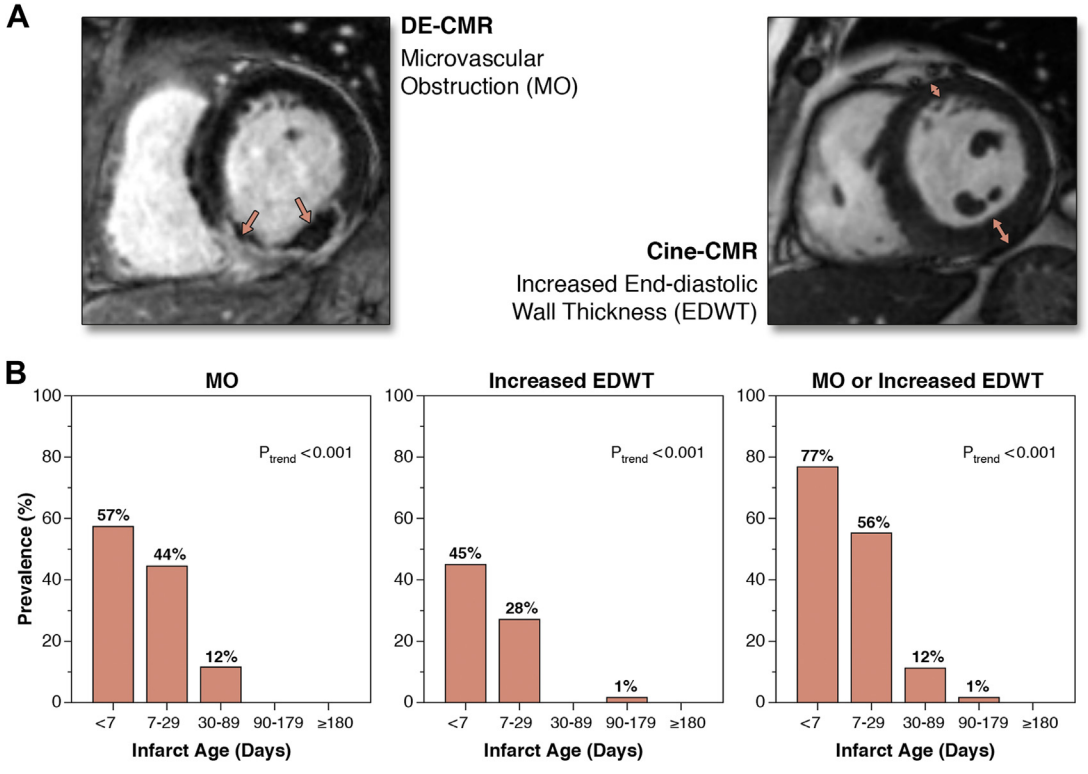
For MIs <6 months old, the specificity of T2-DIR-TSE alone was 83% (95% CI: 66% to 99%). The specificity rose to 93% (95% CI: 79% to 100%) when considering only those scans with satisfactory or excellent image quality. Likewise, the specificity of T2-DIR-TSE increased to 96% (95% CI: 87% to 100%) when the complete examination was made available because T2-hyperintense regions remote from the infarcted territory (by DE-CMR) were considered artifactual.

PRESENCE OF T2-DIR-TSE HYPERINTENSITY IN ACUTE MI. Of 112 scans performed <1 month post-MI, 96 had T2-hyperintensity identified in the correct IRA territory. Multivariable logistic regression analysis demonstrated that the presence of increased EDWT and higher T2-DIR-TSE image quality score were associated with successful identification of T2-hyperintensity (Table 3). The presence of MO was not associated with the identification of T2-hyperintensity in acute MI.

PERSISTENCE OF T2-DIR-TSE HYPERINTENSITY IN INTERMEDIATE-AGE MI. Eighty-three patients had scans performed both <1 month and 1 to 6 months post-MI. The mean extent of T2-hyperintensity was less on the later scan (4.5 ± 2.7 vs. 1.1 ± 1.8 segments, $p < 0.001$). The degree of hyperintensity as measured by SIR (1.77 ± 0.51 vs. 1.35 ± 0.18, $p < 0.001$) and CNR (35.8 ± 23.4 vs. 17.4 ± 11.2, $p < 0.001$) was also lower. Multivariable analysis demonstrated that the presence of diabetes, larger infarct size, and better T2-DIR-TSE image quality on the 1- to 6-month scans were independently associated with persistence of T2-hyperintensity in intermediate-age infarcts (Table 4).

CLASSIFICATION INTO INFARCT AGE CATEGORIES. Because T2-DIR-TSE hyperintensity appeared to be

FIGURE 3 Prevalence of MO and Increased EDWT



(A) Example of MO and increased EDWT in patients with 3-day-old inferior myocardial infarction. **(B)** Prevalence of MO, increased EDWT, and the combined marker MO *or* increased EDWT over time. DE-CMR = delayed-enhancement cardiac magnetic resonance; EDWT = end-diastolic wall thickness; MO = microvascular obstruction.

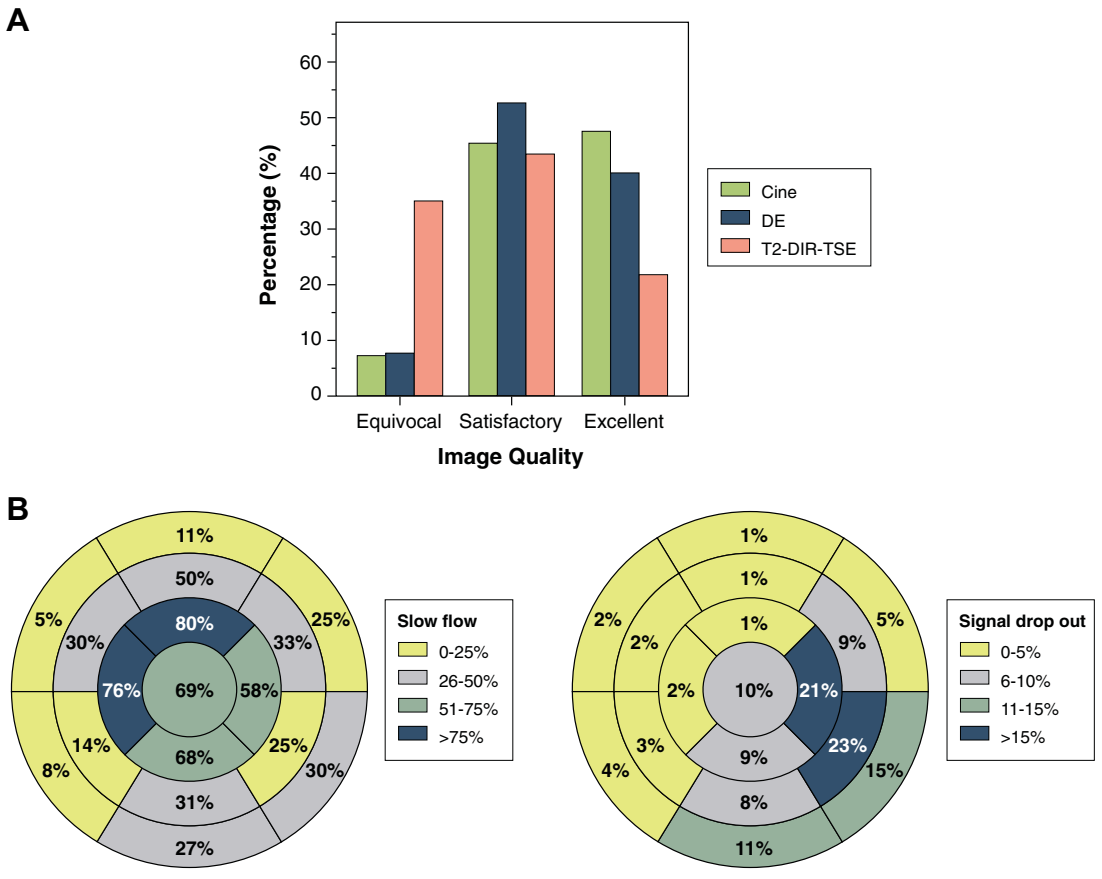
specific for infarcts <6 months old and MO and increased EDWT were specific for infarcts <1 month old, a simple algorithm incorporating all components was devised. The presence of MO *or* increased EDWT was used to signify MIs <1 month old; the presence of T2-hyperintensity in the absence of MO *or* increased EDWT to indicate MIs 1 to 6 months old; and the absence of MO *or* increased EDWT *and* T2-hyperintensity to indicate MIs more than 6 months old. Infarct sizes ≥5% or ≥10% of LV mass occurred in 62% or 84% of the population, respectively, and the algorithm was 70% (95% CI: 63% to 77%) or 80% (95% CI: 73% to 87%) accurate in categorizing infarct age, respectively.

DISCUSSION

Differentiating an MI that is 1 to 2 weeks old from an MI that is months old is crucial for patient management and risk stratification. For example, the risk of sudden death is highest within 30 days after MI among patients with LV dysfunction; thus, early implementation of strategies to reduce the risk of sudden death may be warranted in selected patients (13). However, primary prevention implantable cardioverter-defibrillator implantation should not be performed for at least 40 days post-MI, even in those with the requisite level of LV dysfunction, in part because of the dynamic nature of LV functional improvement in the first several weeks after MI (14). Hence, knowledge of infarct age is essential to follow contemporary practice guidelines, yet the majority of acute MI events are clinically unrecognized, precluding this determination (15).

In this 2-center study of patients with STEMI who underwent CMR at known time points after a documented MI, we found that T2-DIR-TSE hyperintensity in infarcted regions was specific for infarcts <6 months old, whereas microvascular obstruction and increased EDWT was specific for infarcts <1 month old. Multivariable analysis demonstrated that persistence of T2-hyperintensity in intermediate-age

FIGURE 4 Image Quality



(A) Frequency of image quality scores. **(B)** Frequency of T2-DIR-TSE artifacts according to location. DE = delayed enhancement; T2-DIR-TSE = T2-weighted double inversion recovery turbo spin echo.

infarcts (1 to 6 months old) was predicted by larger infarct size, the presence of diabetes, and better T2-DIR-TSE image quality. A simple algorithm was developed incorporating multiple CMR markers of acute MI and accounting for their different longevity. This allowed classification of infarct age into 3 specific categories (<1 month old, 1 to 6 months old, and more than 6 months old) rather than just "acute" or "chronic" categories, and for infarct size ≥10% of the left ventricle, the algorithm was found to be accurate in 80% of cases.

Our finding that T2-DIR-TSE is 66% specific for differentiating MIs <1 month old appears to be at odds with previous studies. For instance, Abdel-Aty et al. (5) reported 96% specificity for discriminating acute from chronic MI (chronic defined as more than 4 weeks old). Likewise, Stork et al. (6) and O h-Ici et al. (7) reported 98% and 99% specificity, respectively. However, it is important to note that these earlier studies were not designed to evaluate a broad spectrum of infarct age. Instead, the focus was on extremes, comparing MI within days of admission with infarcts sometimes years older. Specifically, Abdel-Aty et al. (5) compared patients with infarcts 4 ± 3 days old versus 17 ± 19 months old, Stork et al. (6) compared MIs 5 ± 3 days versus 8 ± 3 months old, and O h-Ici et al. (7) compared MIs 4 ± 1 days old versus 196 ± 39 days old. Hence, given the potential for selection bias, it is possible the reported specificity values are overly optimistic.

The primary basis for the low specificity that we report using the threshold of <1 month for acute MI is the observation that T2-DIR-TSE hyperintensity often persists for several months post-MI (**Figures 1 and 2**). From the literature, the duration of T2-hyperintensity after acute MI is unclear. The few published studies

TABLE 2 Diagnostic Performance of CMR for Detecting Acute (<1 Month Old) Myocardial Infarction

CMR Abnormality	Sensitivity (%)	Specificity (%)	Accuracy (%)
Individual components			
T2-DIR-TSE hyperintensity	88 (81–94)	66 (56–75)	77 (71–83)
MO	55 (46–65)	98 (94–100)	76 (70–82)
Increased EDWT	42 (33–52)	99 (95–100)	70 (64–76)
Combinations			
MO *or* increased EDWT	73 (64–81)	97 (92–99)	85 (80–89)
T2 *or* increased EDWT	87 (79–92)	70 (60–78)	78 (72–83)
T2 *or* MO	92 (85–96)	70 (60–78)	81 (75–86)
All CMR components available			
MO *or* increased EDWT *or* T2	92 (85–96)	70 (60–78)	81 (75–86)

Values are % (95% confidence interval).

CMR = cardiac magnetic resonance; EDWT = end-diastolic wall thickness; MO = microvascular obstruction; T2-DIR-TSE = T2-weighted double inversion recovery turbo spin echo.

TABLE 3 Characteristics Associated With the Presence of T2-DIR-TSE Hyperintensity in MIs <1 Month Old

	Univariable		Multivariable	
	OR (95% CI)	p Value	OR (95% CI)	p Value
General				
Age	1.01 (0.96–1.06)	0.78		
Male	0.72 (0.15–3.45)	0.68		
Clinical history				
Hypertension	0.92 (0.32–2.67)	0.88		
Diabetes	*			
Hypercholesterolemia	1.38 (0.44–4.29)	0.58		
Positive family history of coronary artery disease	0.85 (0.29–2.44)	0.76		
Smoking	1.84 (0.57–5.94)	0.31		
No. of risk factors	1.28 (0.75–2.19)	0.37		
Cardiac enzymes				
Peak troponin T	1.09 (0.94–1.26)	0.25		
Peak CK-MB	1.002 (0.998–1.007)	0.33		
Cardiac catheterization				
Infarct-related artery: RCA	0.37 (0.12–1.14)	0.08		
Pre-procedure TIMI flow grade 3	0.94 (0.60–1.47)	0.78		
Final TIMI flow grade 3	†			
No. of diseased vessels	0.62 (0.33–1.16)	0.14		
CMR				
LVEF	1.000 (0.948–1.054)	1.00		
Infarct size	1.02 (0.97–1.08)	0.40		
MO	1.73 (0.59–5.02)	0.32		
Increased EDWT	13.80 (1.75–108.7)	0.013	12.81 (1.57–104.76)	0.017
MO *or* increased EDWT	4.60 (1.53–13.80)	0.007		
T2-DIR-TSE image quality score	4.01 (1.62–9.88)	0.003	4.09 (1.52–11.02)	0.005

*Cannot be calculated because in the patient group without T2-hyperintensity, none had diabetes. †Cannot be calculated because in the patient group without T2-hyperintensity, all had TIMI flow grade 3.

CI = confidence interval; LVEF = left ventricular ejection fraction; OR = odds ratio; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Tables 1 and 2.

are inconsistent. In 8 canines, Aletras et al. (16) reported that none of the T2-hyperintense regions seen at 2 days post-MI were observed at 2 months. However, Ghugre et al. (17), in a porcine model, demonstrated persistent T2 elevation in the infarcted region at 6 weeks post-MI, albeit only 4 animals were studied at this time-point. Schulz-Menger et al. (18) showed in 8 patients with hypertrophic cardiomyopathy and iatrogenic MI from septal artery embolization that infarct-related T2-hyperintensity visible at 28 days had entirely resolved by 90 days in all 8 patients. In contrast, Mather et al. (19) reported that 73% of patients with a first STEMI who underwent primary percutaneous coronary intervention had visible T2-hyperintensity at 90 days; Nilsson et al. (20) suggested that T2-hyperintensity was detectable even at 1 year, although this occurred only in 3 patients. Thus, there is discordance in the literature, and a complicating factor is that the studies are unclear as to whether T2-DIR-TSE images were interpreted separately or in conjunction with the rest of the CMR data, nor is it clear whether interpretations were performed blinded to the CMR study date. In the present study, the sample size was larger, T2-DIR-TSE images were interpreted separately from other CMR data blinded to the study date, image quality was assessed, and the IRA territory was determined by coronary angiography to help distinguish true from artifactual findings.

We used a conventional black-blood sequence to obtain T2-weighted images because it is the most commonly used in clinical practice and has the most extensive literature (2). Although image quality occasionally can be suboptimal with this sequence, we believe that T2-hyperintensity by other sequences may also be specific for MIs <6 months old for the following reasons. First, when only scans with better image quality were considered, the specificity of T2-DIR-TSE hyperintensity for MIs <6 months old increased to 93% (from 83%). Second, for scans with better image quality, T2-DIR-TSE hyperintense regions were invariably within the correct IRA perfusion territory by coronary angiography and matched the infarct location determined by DE-CMR. Third, when T2-DIR-TSE images were read in conjunction with cine and delayed-enhancement images (complete examination available), so that apparent T2-hyperintense regions remote from the infarcted territory could be considered artifactual, the specificity of T2-hyperintensity for MIs <6 months old increased to 96%. These findings suggest that any technical limitations with the T2-DIR-TSE sequence should not affect the general interpretation that T2-hyperintensity is specific for

MIs <6 months old because a different sequence with better image quality would likely result in an even higher specificity of T2-hyperintensity for MIs <6 months old.

The underlying cause of T2-DIR-TSE hyperintensity after MI is thought to be edema (2,5). However, the data in the present study are perhaps not entirely consistent with this conjecture. In animal models, myocardial tissue water content increases markedly within minutes to hours after acute reperfused MI (21). In patients, the rapid, near-doubling in LV EDWT in the setting of acute MI is assuredly the consequence of increased tissue water (22,23). Hence, an acute increase in EDWT should provide a quantitative measure of edema. With this in mind, it is interesting that the time course of increased EDWT was clearly different from that of T2-DIR-TSE hyperintensity in the present study because it was exceedingly rare for increased EDWT to be present in infarcts more than 1 month old. This finding is consistent with that reported by Ghugre et al. (17), who demonstrated complete resolution of acutely thickened myocardium by 4 weeks and, moreover, found this was matched in time with the resolution of edema, as verified by histopathology. Similarly, in a human postmortem study, Fishbein et al. (24) reported that infarction-related edema and inflammation, which was ubiquitous in the early days after acute MI, had entirely resolved by 35 days. These findings strongly suggest that infarction-related edema should resolve by 1 month, and T2-DIR-TSE hyperintensity that persists far beyond this time is due to a different mechanism. We propose that T2-DIR-TSE hyperintensity seen 1 to 6 months post-MI, long after resolution of increased EDWT, reflects a fundamental alteration in underlying tissue, involving vascular, fibroblastic, and collagenous proliferation in replacement of necrotic myocytes (24) rather than simply excess water content.

Although the sensitivity of T2-DIR-TSE for acute MI (<1 month old) was relatively high at 88%, this is lower than that reported by the initial studies. More recently, Viallon et al. (25) compared a variety of black-blood and bright-blood T2-weighted sequences in the setting of a first STEMI and also reported a lower sensitivity in detecting acute MI, with a high of 80% among all sequences. The authors attributed the lower sensitivity (and the apparent discrepancy with older reports) to the fact that T2 images were read in isolation, blinded to all other CMR data, which was not the case in previous investigations.

It is well established that MO can complicate acute MI, and this signals a poor prognosis (10). However, because many acute infarcts do not have MO, it has not been thought to be particularly useful for differentiating acute from chronic MI. The results of the present study corroborate those of earlier reports regarding the prevalence and time course of MO. These studies consistently report a prevalence of ~50% in the first week after MI (6,26), with a rapid decrease to near zero within 1 month (17,19). The present study, however, is the first to suggest that MO and increased EDWT may be synergistic for the detection of acute MI. The combination provided higher test sensitivity without reducing specificity for the identification of MIs <1 month old (**Table 2**). From a pathophysiological viewpoint, this suggests that although both phenomena are associated with larger infarct sizes, the 2 may represent different pathways of post-infarction injury. Indeed, MO, by virtue of restricting myocardial tissue level reperfusion, may limit acute edema (and therefore limit increased EDWT), albeit with the consequence of reducing cellular infiltration that could speed infarct healing.

TABLE 4 Characteristics Associated With Persistence of T2-DIR-TSE Hyperintensity in Intermediate-Aged MI

	Univariable		Multivariable	
	OR (95% CI)	p Value	OR (95% CI)	p Value
General				
Age	1.02 (0.98–1.06)	0.45		
Male	0.50 (0.16–1.60)	0.24		
Clinical History				
Hypertension	1.19 (0.48–3.00)	0.71		
Diabetes	4.17 (0.96–18.10)	0.06	5.53 (1.13–27.10)	0.035
Hypercholesterolemia	0.91 (0.34–2.40)	0.84		
Positive family history of coronary artery disease	0.69 (0.28–1.72)	0.43		
Smoking	1.16 (0.36–3.79)	0.80		
Number of risk factors	1.12 (0.69–1.81)	0.65		
Cardiac Enzymes				
Peak Troponin T	1.09 (0.98–1.21)	0.13		
Peak CK-MB	1.003 (1.000–1.007)	0.048		
Cardiac catheterization				
Infarct Related Artery—RCA	0.32 (0.12–0.80)	0.015		
Pre-Procedure TIMI flow grade 3	0.59 (0.32–1.09)	0.09		
Final TIMI flow grade 3	*			
Number of diseased vessels	0.62 (0.33–1.16)	0.14		
CMR (on baseline scan)				
LVEF	0.94 (0.89–0.99)	0.031		
Infarct size	1.08 (1.03–1.13)	0.003	1.08 (1.03–1.14)	0.002
MO	3.56 (1.37–9.24)	0.009		
Increased EDWT	0.84 (0.34–2.07)	0.71		
MO *or* Increased EDWT	2.57 (0.84–7.85)	0.10		
CMR (1–6 months scan)				
T2-DIR-TSE Image Quality Score	2.02 (1.08–3.79)	0.029	2.18 (1.10–4.33)	0.026

*Cannot be calculated because in the patient group without T2-hyperintensity, all had TIMI flow grade 3.
Abbreviations as in Tables 1, 2, and 3.

STUDY LIMITATIONS. By leveraging the multiple CMR markers of acute MI and their different longevity, we developed a simple algorithm to classify infarct age as <1 month old, 1 to 6 months old, and more than 6 months old. We emphasize that this algorithm should be considered only a guide. In patients with acute MI but small infarct size (e.g., <10% of the left ventricle), MO and increased EDWT are frequently absent. Thus, the presence of T2-DIR-TSE hyperintensity may reflect MIs either <1 month old or 1 to 6 months old, and, accordingly in this situation, infarct age should be interpreted simply as <6 months old. An additional limitation is that many infarcts 1 to 6 months old did not have T2-DIR-TSE hyperintense regions. This was associated with infarct size; therefore, at present, it appears prudent to consider small infarcts without T2-DIR-TSE hyperintense regions (and without MO and increased EDWT) simply as more than 1 month old. Despite this limitation, the lack of persistent T2-DIR-TSE hyperintensity was also associated with suboptimal image quality, and it is likely the significance of this limitation will decrease with technical advances in CMR.

CONCLUSIONS

In this prospective 2-center study, we found that T2-DIR-TSE is sensitive but not specific for detecting MIs <1 month old because T2-hyperintensity often persists for months. In contrast, the presence of MO or focally increased EDWT was observed to be specific for MIs <1 month old, and, when used in conjunction with T2-hyperintensity, the combination frequently provided a more precise assessment of infarct age.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Determining whether a MI is recent or chronic is sometimes difficult, but there are important implications for patient management and prognosis. A multicomponent CMR examination involving cine, T2-weighted imaging, and delayed-enhancement imaging can help to distinguish between acute, subacute, and chronic MI.

TRANSLATIONAL OUTLOOK: T2-weighted CMR is promulgated as an excellent method to noninvasively identify myocardial edema associated with injury from a variety of disorders. However, the mechanism of T2-weighted hyperintensity requires further investigation, given that T2-weighted hyperintensity may persist for several months after acute MI—long after the time when edema has resolved.

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