Delayed Enhancement and T2-Weighted Cardiovascular Magnetic Resonance Imaging Differentiate Acute From Chronic Myocardial Infarction

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Background—Delayed enhancement (DE) cardiovascular magnetic resonance (CMR) detects acute and chronic myocardial infarction (MI) by visualizing contrast media accumulation in infarcted segments. T2-weighted CMR depicts infarct-related myocardial edema as a marker of acute but not chronic myocardial injury. We investigated the clinical utility of an approach combining both techniques to differentiate acute from chronic MI.

Methods and Results—Seventy-three MI patients were studied in 2 groups. Group A consisted of 15 acute MI patients who were studied twice, on day 1 and 3 months after MI. In group B, 58 patients with acute or chronic MI underwent 1 CMR scan. T2-weighted and DE images of matched slices were acquired on a 1.5-T system. In group A, quantitative segmental and region of interest–based analyses were performed to observe signal changes between the acute and chronic phases. In group B, T2-weighted and DE images were examined visually by 2 blinded observers for the presence or absence of hyperintense areas in corresponding segments. For infarct localization, coronary angiography and/or ECG changes served as the reference standard. In group A, the contrast-to-noise ratio on T2-weighted images dropped in the infarcted segments from 2.7±1.1 on day 1 to 0.1±1.2 after 3 months (P<0.0001). There was no significant change in contrast-to-noise ratio in DE images (1.9±1.5 versus 1.3±1.0; P=NS). The qualitative assessment of T2-weighted and DE images in group B yielded a specificity of 96% to differentiate acute from chronic lesions.

Conclusions—An imaging approach combining DE and T2-weighted CMR accurately differentiates acute from chronic MI. (Circulation. 2004;109:2411-2416.)

Key Words: edema ■ magnetic resonance imaging ■ myocardial infarction

Differentiating acute from chronic irreversible myocardial injury is a frequent demand for clinical decision-making yet represents a challenge for existing imaging modalities. Both patterns of injury present as a regional wall motion abnormality in echocardiography, and although wall thinning is a feature of chronic infarcts, this finding is not observed in nontransmural infarcts. In the absence of viable myocardial cells, both acute myocardial infarction (MI) and chronic MI fail to uptake radioactive tracers in radionuclide imaging and thus appear as fixed defects. Finally, although delayed enhancement (DE) cardiovascular magnetic resonance (CMR) accurately detects irreversible myocardial injury, both acute MI and chronic MI exhibit DE regardless of their age. One aspect that has not been fully assessed in this setting is the use of myocardial edema to differentiate the 2 types of injuries. The mechanisms underlying the development of myocardial edema in acute MI appear to involve a disruption of the energy-regulated ionic transport mechanisms across the cell membrane after the ischemic insult.

With reperfusion, edema is further intensified and then gradually resolves as the infarct heals. The relatively large extracellular matrix of the developed scar, however, allows gadolinium-based contrast media to accumulate, resulting in DE. A strong body of evidence supports the notion that T2-weighted CMR sensitively detects infarct-associated myocardial edema, justifying its use to differentiate acute from chronic MI. Yet myocardial edema per se does not reflect irreversible myocardial injury in MI, a feature accurately outlined by DE. On the basis of these considerations, we hypothesized that an approach combining DE and T2-weighted CMR should be able to differentiate acute from chronic MI.

Methods

Study Design

We first studied patients with MI in both the acute and chronic phases using DE and T2-weighted CMR (group A). Results of this...
analysis were used to investigate patients with MI regardless of its age (group B) to test the utility of this imaging approach in differentiating acute from chronic MI.

**Subjects**
MI diagnosis was based on infarct-typical ECG changes combined with 2-fold elevation of creatine kinase and/or positive troponin T. The reference for infarct localization was the site of ECG changes in conventional 12-lead ECG and/or the territory of the culprit vessel as defined by coronary angiography in the acute phase.

**Group A**
Fifteen MI patients were studied twice: 1 day after the acute event and 3 months later (1 patient was followed up after 6 months). Inclusion criterion was a first, 1-day old, reperfused MI.

**Group B**
Fifty-eight acute or chronic MI patients were consecutively enrolled regardless of infarct reperfusion or the presence of previous infarcts. MI was considered acute if the clinical event occurred 2 weeks ago and chronic if it occurred >4 weeks ago.

Patients were not enrolled if they were clinically unstable or had severe arrhythmia or known contraindications to CMR. Written informed consent was obtained from all patients, and the local ethics committee approved the study.

**Methods**

**Cardiovascular Magnetic Resonance**
CMR studies were performed with a 1.5-T system (Signa CV/i, GE). Localization was performed by use of breath-hold real-time and steady-state free-precession images of true anatomic axes of the heart. We applied a breath-hold, black-blood, T2-weighted triple inversion recovery sequence (TR, 2×R-to-R interval [RR]; echo time [TE], 65 ms; inversion time [TI], 140 ms) in 3 (basal, midventricular, and apical) short-axis slices (slice thickness, 15 mm; gap, 5 mm; field of view, 34 to 38 cm; matrix, 256×256; 1 = number of excitations [NEX]). Details of this sequence are described elsewhere. In short, a pair of slice-selective and -nonselective 180 inversion pulses are applied to null the blood signal, and a third inversion pulse is applied to null the fat signal. A contrast-enhanced inversion-recovery gradient-echo sequence (TR, 7.1 ms; TE, 3.1 ms; TI, 250 ms; matrix, 256×192) was then applied 10 minutes after intravenous injection of gadolinium-DTPA (Magnevist, Schering) with an automated injector (Medrad). The contrast dose was 0.1 mmol/kg in group A and 0.2 mmol/kg in group B. In group A, the protocol was repeated, and care was taken to obtain the same slice position guided by anatomic landmarks of the heart. In 3 acute patients of group B, the number of slices was 3 (2 in 2 patients, 1 in 1 patient). Additional long-axis slices were obtained to visualize the full extent of small subendocardial infarcts.

**Coronary Angiography**
Coronary angiography was performed on a standard angiography suite (Hicor, Siemens). The interstudy duration between angiography and CMR was 1 day in group A and 3 ± 3 days in group B patients with acute MI. Angiography was performed before CMR in all but 4 patients in group B.

**CMR Image Analysis of Group A**
DE and T2 images were analyzed with validated software (MASS 5.0, Medis). Endocardial and epicardial borders were manually traced in each slice, and the myocardium was divided into 16 equiangular segments (6 basal, 6 midventricular, 4 apical) starting from the anterior insertion of the right ventricle. The mean signal intensity (SI) of each segment and the background noise were measured. Segments with an SI greater than the mean SI plus 2 SD of normal myocardium were considered abnormal. The CNR of each segment was calculated from the following formula: CNR = (mean SI_infarct - mean SI_remote)/mean SI_noise, where SI_infarct is the SI of infarcted segments, SI_remote is the SI of the remote normal myocardial segments, and SI_noise is the mean SI of a region of interest (ROI) positioned in the background air 2 to 3 cm anterior to the patient’s chest wall.

In T2-weighted images, the same segmental analysis was repeated for the epicardial 50% of the myocardial wall. ROIs were then drawn.
within areas of DE and copied to corresponding areas in T2 images. CNR was calculated as above. In selected patients, we used a tool in a recent release of MASS 6.0 software that delineates areas of abnormal SI (more than normal myocardium plus 2 SD) in color (Figure 1).

CMR Image Analysis of Group B
Two observers (J.S.-M., H.A.-A.) qualitatively evaluated DE and T2 images on 2 separate days but on the same workstation. The observers were aware that the patients had MI but were blinded to the rest of the clinical data. They were asked to determine the infarct type (acute or chronic) and its location according to the following criteria (within the same segment) as established by the results of group A: acute MI, DE plus transmural high T2 signal, or chronic MI, DE but absent or nontransmural high T2 signal.

Results of this analysis were correlated with the infarct-related artery (IRA), ECG changes (infarct location), and clinical data (infarct age) for each observer. Myocardial segments were assigned to coronary arterial territories according to the imaging guidelines of the American Society of Nuclear Cardiology except for the apical segment (segment 17), which was not included in our analysis. ROI-based analysis similar to that in group A was then performed.

Image Analysis of Coronary Angiography
One observer blinded to CMR data evaluated the angiographic studies for IRA, defined according to the presence of at least 2 of the following criteria: plaque/irregular stenosis morphology, relation to infarct-characteristic ECG changes, or recovery of ECG changes after PTCA. The observer also evaluated TIMI flow and collateral flow (present or absent).

Statistical Analysis
Values are presented as mean±SD. A value of P<0.05 was considered significant. Statistical analysis was performed with commercially available software (StatView 4.5). All statistical tests were 2 tailed. Continuous data were compared by use of the Student’s t test. Correlation between continuous variables was calculated from the correlation Z test. Interobserver agreement was measured with κ statistics.

Results
Four studies were discarded, all from acute MI patients of group B: 3 had poor image quality (severe motion artifacts), and 1 could not complete the examination.

Group A
Mean time to reperfusion was 10.2±7 hours. After intervention (PTCA and stenting), 12 had TIMI 3 and 3 had TIMI 2. There were no major cardiac events between MR scans except for 1 patient, who presented with acute coronary syndrome (ACS) 10 weeks after the first MR scan because of subtotal in-stent stenosis. Table 1 summarizes the characteristics of group A.

T2-Weighted Imaging
Of 240 segments, 81 exhibited higher signal-to-noise ratio (SNR) than the normal myocardium (10.4±2.7 versus
8.2±2.5; \( P<0.0001 \)). These segments matched the territorial distribution of the IRA in every case. Their CNR dropped significantly in the follow-up study from 2.7±1.1 to 0.1±1.2 (\( P<0.0001 \)). The average percentage of CNR reduction was 101.2±51.1\% and 217.3\% in the patient with interstudy ACS. There was no correlation between the percentage of CNR reduction and reperfusion time, maximum CK, or ejection fraction at presentation. CNR did not significantly differ between infarcts with or without collaterals (2.7±1.3 versus 2.7±0.9; \( P=\text{NS} \)). In the ROI-based analysis, the CNR of MI dropped from 4.6±1.6 (acute) to 0.8±1.3 (chronic) (\( P<0.0001 \)). Visually, the high T2-weighted signal in the acute phase was transmural in all cases, whereas in the chronic phase, it appeared to resolve earlier from the subepicardium.

This finding was supported by the results of selective epicardial (50% myocardial wall) T2 SI measurement of the infarcted segments in the chronic phase, which was significantly lower than that of the normal myocardium plus 2 SD (81.4±20.2 versus 89.6±20.9; \( P<0.003 \)). In 3 patients, however, the SI 50% epicardium was higher than that limit (patient 11, 103.44 versus 96.29; patient 12, 57.94 versus 57.12; and patient 15, 105.99 versus 104.79). In the last 2 patients, we repeated the analysis for 40% epicardium instead of 50%. The SI 40% epicardium of patient 12 was then 55.26 (less than the normal limit of 57.12) and 95.68 in patient 15 (less than the normal limit of 104.79). Transmural high T2 signal in the acute phase was a consistent feature regardless of ST-segment changes (Figure 1), with no significant CNR differences between ST-segment elevation myocardial infarction (STEMI) and non-STEMI (2.23±0.57 versus 2.10±0.88; \( P=\text{NS} \)).

Delayed Enhancement

DE was visible in all cases in the acute and follow-up studies with no significant CNR differences between the 2 studies in either the segment-based (1.9±1.5 versus 1.3±1.0; \( P=\text{NS} \)) or the ROI-based (5.4±3.5 versus 5.8±3.5; \( P=\text{NS} \)) analysis. The segmental distribution corresponded to the IRA territorial distribution in every case.

Group B

Fifty-seven infarcts (33 acute, 24 chronic) in 54 patients were evaluated. One patient had both acute and chronic MI, and 2 patients presented with 2 chronic MIs. Of 33 acute infarcts, 10 (30\%) were nonreperfused (6 STEMI, 4 non-STEMI) because revascularization was not attempted before CMR (\( n=8 \)) or revascularization attempts had failed (\( n=2 \)). Table 2 summarizes group B patient characteristics. Figure 2 and Figure 3 show 4 patients from Group B.

T2-Weighted Imaging

The SNR of acute MI was higher than that of the remote myocardium (11.8±2.9 versus 6.5±2.2; \( P<0.0001 \)). In chronic infarcts, there was no significant difference between the SNR of infarcted and remote myocardium (7.4±1.9 versus 6.9±2.0; \( P=\text{NS} \)). The CNR of acute infarcts was significantly higher than that of chronic MI (5.3±1.6 versus 1.1±2.0; \( P<0.0001 \)). There was no significant difference between the CNR of acute reperfused and nonreperfused infarcts (5.5±1.9 versus 4.9±0.8; \( P=\text{NS} \)).

Delayed Enhancement

CNR did not significantly differ between acute and chronic infarcts (5.5±3.0 versus 6.2±4.1; \( P=\text{NS} \)). Table 3 summarizes the results of qualitative analysis. Acute MI was identified with a sensitivity of 91\% and 94\% and specificity of 92\% and 100\% for observers 1 and 2, respectively. The interobserver agreement to designate MI as acute or chronic was high (\( \kappa=0.90 \)). The matching between the CMR-determined infarct location and that expected from the IRA (in cases with identifiable IRA) was 96\% for observer 1 and 98\% for observer 2. In the 9 cases with unidentifiable IRA, CMR infarct location matched that of infarct-associated ECG changes.

Table 4 summarizes the results of coronary angiography analysis.

Discussion

Our results indicate that an imaging approach using DE and T2-weighted CMR provides a clinically reliable tool to differentiate acute from chronic MI.

### Table 2. Characteristics of Group B Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Acute MI</th>
<th>Chronic MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>33</td>
<td>21</td>
</tr>
<tr>
<td>Age, y</td>
<td>59±10</td>
<td>55±10</td>
</tr>
<tr>
<td>Male gender, n</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Infarct age</td>
<td>4±3 d</td>
<td>17±19 mo</td>
</tr>
<tr>
<td>Maximum CK, IU</td>
<td>1793±1451</td>
<td>2394±1617*</td>
</tr>
<tr>
<td>STEMI, n</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>ECG Q-waves, n</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>47±13</td>
<td>53±14</td>
</tr>
<tr>
<td>Risk factors, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>Smoking</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

*Data are missing for 6 patients.

### Table 3. Diagnostic Performance of DE and T2-Weighted Imaging to Differentiate Acute From Chronic MI

<table>
<thead>
<tr>
<th>Clinical Diagnosis, n</th>
<th>Acute MI</th>
<th>Chronic MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observer 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute MI</td>
<td>30</td>
<td>2</td>
</tr>
<tr>
<td>Chronic MI</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>24</td>
</tr>
<tr>
<td>Observer 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute MI</td>
<td>31</td>
<td>0</td>
</tr>
<tr>
<td>Chronic MI</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>24</td>
</tr>
</tbody>
</table>

\( n=57 \).
TABLE 4. Results of the Angiographic Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A, n</th>
<th>Group B, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern of coronary artery disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Vessel</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>2 Vessel</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>3 Vessel</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>IRA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>RCA</td>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>LCx</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Uncertain</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>TIMI flow grade before intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>8</td>
<td>24</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Collaterals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>Absent</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Uncertain</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

LAD indicates left anterior descending; RCA, right coronary artery; and LCx, left circumflex.

Despite a substantial difference in tissue structure between acute and chronic MI, both injuries exhibited DE in our series. This finding is in agreement with previous studies and appears to be related, at least in part, to the increased volume of distribution of gadolinium chelates secondary to extracellular space expansion in acute MI and chronic myocardial scars. The underlying mechanism of this extracellular space enlargement, however, differs in relation to infarct age. In acute MI, there is loss of membrane integrity of the already edematous cardiomyocytes, allowing communication between the extracellular and intracellular spaces. Moreover, the induction of reperfusion marks the rapid evolution of an inflammatory-like response of which interstitial edema is a substantial feature. In chronic MI, on the other hand, enlargement of the extracellular space is mostly the result of the relatively large collagen matrix in the absence of myocardial edema.

These considerations explain our findings that DE is a feature of MI regardless of its age and that high SI in edema-sensitive T2-weighted imaging is a feature of acute but not chronic MI. Yet, T2-weighted sequences are sensitive not only to edema-related signal changes but also to a variety of pathological phenomena taking place during infarct healing. Of these, myocardial fibrosis casts a specific relevance. Collagen deposition is a dynamic process starting within days after MI and may continue for years thereafter. T2 relaxation times are inversely related to the amount of collagen in muscle tissue, resulting in low SI of mature fibrous tissue. This also could have contributed to the apparent “normalization” of T2 SI that we and others have observed in chronic MI.

The relation between the transmurality of T2 signal abnormality and the reperfusion status of acute MI is complex and has not been fully elucidated. Our results of transmural T2 signal abnormality in reperfused infarcts agree with those of Nilsson et al but disagree with those of Johnston et al, who found no significant change in epicardial T2 relaxation times after 3 hours of coronary occlusion with or without reperfusion. In a later report, however, Johnston and colleagues studied patients with acute reperfused MI and found that a high T2 signal was consistently transmural. The relatively shorter occlusion time in their earlier study compared with ours does not explain the different results. Karolle et al observed a significant increase in epicardial T2 relaxation times after only 2 hours of coronary occlusion, explaining our findings in nonreperfused infarcts. Interestingly, however, they found a discrepancy between the change in epicardial relaxation times and myocardial water content, underscoring that other processes (ie, changes in water physical characteristics or in the biochemical environment of ischemic cells) could also contribute to T2 signal abnormality.

The results of the patient who developed ACS before the second CMR warrant special attention. We expected that the resolution of the high T2 signal in this patient would be hampered by a newly developing myocardial edema secondary to the reischemia/reperfusion injury. That, however, was not the case. This could mean either that myocardial edema has to reach a certain threshold to be detected as a high signal in T2 imaging (which may not be achieved in ACS) or that the newly developing edema was completely resolved by the time the second CMR was performed. Further studies using T2 imaging in ACS are warranted.

Clinical Implications

There are 3 major clinical scenarios in which the combined application of T2-weighted and DE imaging can add important information to conventional imaging approaches and might direct further therapy. The first situation occurs when there is clinical evidence for acute MI with a positive troponin assay but other findings such as the ECG are unable to localize the culprit lesion. Angiography reveals multiple coronary lesions. Positive DE detects areas of old and new infarctions, whereas T2 imaging identifies the area of the acute event. In the second situation, there has been a clinical event compatible with acute MI within the last 2 weeks. Troponin is equivocal. A high T2 signal proves acute MI, whereas DE shows the extent of necrosis. The third scenario occurs when there is no clinical history of infarction but resting regional wall motion abnormalities are detected. Positive DE proves an old unrecognized infarction, whereas “normal” T2 images exclude acute MI. The ability of this approach to exclude unstable angina in this setting remains unknown.

Technical Considerations and Limitations

The triple inversion recovery sequence we used is sensitive to changes in T1 relaxation times and thus should be applied before gadolinium injection to avoid confusion in image interpretation resulting from the T1 shortening effect of gadolinium. Furthermore, to suppress ventricular blood signal, the sequence requires that the blood be expelled out of the slice during systole, which may not be the case.
especially in patients with reduced wall motion in which the nonsuppressed blood signal may hinder accurate identification of the endocardial border. This, however, did not affect image interpretation because all our acute infarcts showed a transmural signal abnormality.

We used a slice thickness of 15 mm, which may reduce the sensitivity to detect small lesions. We used it to compensate for the signal loss caused by the long TE in T2 images and to reduce the number of breath-holds while still covering as much myocardial tissue as possible.

In group A, coronary angiography was performed only in the acute phase; thus, we are not able to confirm the status of coronary arteries or stents at the time of second examination. Nevertheless, 14 of 15 patients did not experience cardiac events during the follow-up period, rendering the possibility of significant coronary pathology rather unlikely.

Conclusions
We have shown that an approach combining DE and T2-weighted CMR is a clinically reliable tool to differentiate acute from chronic MI. Although DE is a powerful marker of nonviability and therefore detects infarction at any disease stage, transmural high T2 signal accurately identifies the area of the acute event.

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References
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