Impact of Unrecognized Myocardial Scar Detected by Cardiac Magnetic Resonance Imaging on Event-Free Survival in Patients Presenting With Signs or Symptoms of Coronary Artery Disease

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Background—Contrast-enhanced cardiac magnetic resonance imaging (CMR) can determine the extent of myocardial scar from infarction (MI). However, the prognostic significance of unrecognized myocardial scar by CMR in patients without a history of MI is unknown.

Methods and Results—One hundred ninety-five patients without a known prior MI underwent CMR for assessment of left ventricular (LV) function and late gadolinium enhancement (LGE). We assessed the prognostic value of LGE and other CMR variables beyond the strongest clinical predictors and built the best overall models for major adverse cardiac events (MACE) and cardiac mortality. During a median follow-up of 16 months, 31 patients (18%) experienced MACE, including 17 deaths. LGE demonstrated the strongest unadjusted associations with MACE and cardiac mortality (hazard ratios of 8.29 and 10.9, respectively; both \( P < 0.0001 \)). Patients in the lowest tertile of LGE-involved myocardium (mean LV mass, 1.4%) experienced a >7-fold increased risk for MACE. By multivariable analyses, LGE was independently associated with MACE beyond the clinical model \(( P < 0.0001 \)) or the clinical model combined with angiographically significant coronary stenosis \(( P = 0.0007 \)), LV ejection fraction \(( P = 0.001 \)), LV end-systolic volume index \(( P = 0.0006 \)), or segmental WMA \(( P = 0.002 \)). LGE remained the strongest predictor selected in the best overall models for MACE and cardiac mortality.

Conclusions—Among patients with a clinical suspicion of coronary artery disease but without a history of MI, LGE involving a small amount of myocardium carries a high cardiac risk. In addition, LGE provides incremental prognostic value to MACE and cardiac mortality beyond common clinical, angiographic, and functional predictors. (Circulation. 2006;113:2733-2743.)

Key Words: coronary disease ■ electrocardiography ■ magnetic resonance imaging ■ myocardial infarction ■ survival

Population-based studies have revealed that one fourth of myocardial infarctions (MIs) demonstrated by Q waves on the ECG are clinically unrecognized. The true prevalence of unrecognized MI may be even higher, owing to the insensitivity of Q waves. The 10-year mortality from unrecognized MI has been estimated to be 45% to 55%, comparable to or higher than in patients with recognized MI. Late gadolinium enhancement (LGE) imaging by contrast-enhanced cardiac magnetic resonance imaging (CMR) can detect scar due to MI unrecognized by clinical history and without a segmental wall motion abnormality (WMA). We therefore assessed the prognostic utility of LGE in a consecutive series of patients who underwent CMR for clinical purposes. All had a clinical suspicion of coronary artery disease (CAD) but no history of MI. We tested the hypothesis that LGE imaging by CMR provides an incremental prognosis beyond the clinical and left ventricular (LV) function assessments of patients.

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Methods

Patient Population
We studied a consecutive series of patients with symptoms or signs suspicious of CAD who underwent CMR for clinical purposes. Patients had either (1) an unknown status of CAD and were referred...
for assessment of LV function and myocardial scar as part of a noninvasive CAD work-up or (2) known angiographically determined CAD and were referred for prediction of segmental wall motion recovery after revascularization. Patients with any of the following conditions were excluded: (1) MI by history, medical record, or abnormal cardiac enzyme values; (2) suspected or confirmed (by biopsy) myocarditis or infiltrative cardiomyopathy (including cardiac hemochromatosis, amyloidosis, or sarcoidosis); or (3) suspected or known pericardial disease or hypertrophic cardiomyopathy. Patients without coronary stenosis on the coronary angiogram within 2 weeks before CMR were also excluded. Other exclusion criteria included concurrent unstable angina, New York Heart Association class IV heart failure, hemodynamic instability, claustrophobia precluding CMR, and metallic hazards. Patients provided informed consent before CMR, and the institutional ethics committee of Brigham and Women’s Hospital (Partners Healthcare system) approved the study.

Clinical Evaluation
Demographic characteristics (listed in Table 1) were obtained before the CMR. A history of CAD included ≥70% stenosis by angiography or prior coronary revascularization. Hypertension, hypercholesterolemia, diabetes, and family history of premature CAD were defined by published criteria.7–10 Significant smoking was defined by >10 pack-years of tobacco use. Patients were referred for noninvasive assessment for ischemia or coronary angiography at the discretion of the attending physicians. Noninvasive assessment of ischemia included dobutamine cine CMR, exercise single-photon emission computed tomography (SPECT), or dobutamine echocardiography. Dobutamine cine CMR and echocardiography were interpreted according to standard criteria for ischemia, defined by ≥1 grade deterioration of segmental systolic wall motion.11 A sum difference score of ≥3 defined myocardial ischemia by SPECT.12

ECG Criteria for Unrecognized MI
Resting 12-lead ECGs were obtained, on average, 8.2 days (range, 0 to 68 days) from CMR. We excluded any ECG for which a cardiac event or revascularization occurred between the ECG and the CMR. We applied the Minnesota Code criteria for significant Q waves (codes 1-1 through 1-2, except 1-2-8) as ECG evidence of an unrecognized MI.11 This evidence was interpreted by computer analysis followed by visual overreading by a single reader blinded to the CMR results and the clinical outcome. We used the Sokolow-Lyon index to indicate LV hypertrophy on the ECG.14

CMR Imaging
All patients were studied in the supine position in a 1.5-T CMR system (SignA CV/i, GE Healthcare, Milwaukee, Wis) with a 4- or 8-element phased-array surface coil. The CMR study consisted of cine steady-state free-precession imaging (repetition time, 3.4 ms; echo time, 1.2 ms; in-plane spatial resolution, 1.6×2 mm) of LV function and LGE imaging (repetition time, 4.8 ms; echo time, 1.3 ms; inversion time, 200 to 300 ms) for myocardial scar. All images were acquired with ECG gating and breath-holding. Cine and LGE images were obtained in 8 to 14 matching short-axis (8-mm thickness with 0-mm spacing) and 3 radial long-axis planes. A previously described segmented inversion-recovery pulse sequence for LGE was used,15 starting 15 minutes after a cumulative 0.15-mmol/kg dose of gadolinium-DPTA. A single reader categorized the LGE image as either typical (including the subendocardium) or an atypical (subepicardial, patchy midwall, or diffuse, circumferential, subendocardial pattern) MI.

Quantitative Analysis of Segmental Wall Motion and LGE
All images were analyzed with specialized software (CineTool 2.80, GE Healthcare). We graded segmental systolic wall motion as 1 to 4 (1=normokinesia, 2=hyperkinesia, 3=akinesia, and 4=dyskinesia) according to the standard 17-segment model.16 For each patient, we determined a total wall motion score (WMS; maximum, 68) and calculated a WMS percentage (WMS%) by dividing the total WMS by 68 and multiplying by 100. Scoring of the WMS% of any segment required agreement from the short-axis and matching long-axis location and the consensus of 2 experienced readers. When disagreement arose as to whether any WMA existed, we measured systolic wall thickening of the segment and defined a ≥3-mm systolic wall thickening as normal segmental wall motion.17 When disagreement arose about the wall motion grade, a third reader provided an independent interpretation to reach consensus. All LGE images were analyzed in a session separate from that for the interpretation of segmental wall motion. We interpreted LGE as present or absent and quantified the myocardial mass of the LGE by a semiautomatic detection method (Figure 1). We used the 17-segment nomenclature in assigning the coronary distribution of the myocardial segments with abnormal LGE.16 To quantify the myocardial mass of the LGE, the endocardial and epicardial borders of the short-axis LV on LGE images were manually traced. Then the computer-assisted detection algorithm defined an LGE as any region with a signal intensity >2SD above a reference remote myocardial region, as previously reported.18,19 We expressed LGE mass as a percentage of the LV mass. We manually traced epicardial and endocardial borders of the matching short-axis cine locations at end systole and end diastole to determine the LV ejection fraction (LVEF), end-diastolic volume index (LVEDVI), end-systolic volume index (LVESVI), and LV myocardial mass (end diastole only).20,21 LVEF was measured by the standard Simpson’s rule.21

Follow-Up
At least 6 months after the CMR (range, 6 to 42 months), clinical information was obtained from patient telephone interviews, contact with the patients’ physicians, and hospital records. A standard questionnaire was used during the telephone interview. Survival information was obtained from the National Social Security Death Index for patients lost on first contact.22 Major adverse cardiac events (MACE) included any of the following: (1) cardiac death, (2) new acute MI, (3) unstable angina requiring hospitalization, (4) development or progression of heart failure requiring hospitalization, or (5) ventricular arrhythmias requiring appropriate discharge from an internal cardioverter/defibrillator (ICD). We reviewed all available data to determine whether a cardiac etiology was the immediate cause of death and categorized deaths into sudden cardiac death, nonsudden cardiac death, and noncardiac death. Sudden cardiac death was defined by published criteria.23,24 New acute MI was defined by an elevated serum troponin value. Unstable angina was defined by hospitalization for new chest pain of noncardiac origin and either angiographically documented coronary stenosis ≥70% or ischemia on noninvasive imaging. Heart failure was defined by hospitalization for new or worsening symptoms of heart failure. We reviewed all available ICD records for patients who underwent ICD implantation after CMR for ventricular arrhythmias that required ICD discharge. When a patient experienced >1 MACE, the first event was chosen. When ≥2 MACE occurred simultaneously, the worse event was chosen (death>MI>unstable angina>congestive heart failure>ventricular arrhythmias requiring ICD discharge). CMR results were made available to the attending physicians on the day of the CMR.

Statistical Analysis
Baseline differences between patients with and without LGE were compared by Student t test or Fisher exact test. Kaplan-Meier distributions for MACE and cardiac mortality stratified by LGE were compared by log-rank tests. We fitted Cox proportional-hazards models to estimate the unadjusted hazard ratios (HRs) of all variables. To determine the relation of MACE to the entire range of LGE percentages, we assessed the unadjusted HR by LGE% tertiles. We tested the interobserver agreement of LGE by the κ statistic. Two experienced observers also independently quantified the LGE percentages for 36 random CMR cases to assess the interobserver agreement with Bland-Altman analysis.25 We used 2 separate multivariable approaches to analyze the predictive value of CMR variables for MACE and cardiac mortality.
TABLE 1. Demographic Characteristics of the Study Cohort

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>All Patients (n=195)</th>
<th>LGE Present (n=44)</th>
<th>LGE Absent (n=151)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>59±13</td>
<td>62±12</td>
<td>58±13</td>
<td>0.1</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>63 (32)</td>
<td>9 (20)</td>
<td>54 (36)</td>
<td>&lt;0.07</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29±5</td>
<td>29±6</td>
<td>28±5</td>
<td>0.4</td>
</tr>
<tr>
<td>Resting heart rate &gt;100 bpm, n (%)</td>
<td>8 (4)</td>
<td>2 (5)</td>
<td>6 (4)</td>
<td>0.99</td>
</tr>
<tr>
<td>History of hypertension, n (%)</td>
<td>103 (53)</td>
<td>30 (68)</td>
<td>73 (48)</td>
<td>0.03</td>
</tr>
<tr>
<td>History of diabetes, n (%)</td>
<td>49 (25)</td>
<td>16 (36)</td>
<td>33 (22)</td>
<td>0.07</td>
</tr>
<tr>
<td>History of hypercholesterolemia, n (%)</td>
<td>109 (56)</td>
<td>31 (70)</td>
<td>78 (52)</td>
<td>0.03</td>
</tr>
<tr>
<td>Resting heart rate, bpm, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of CAD, n (%)</td>
<td>31 (16)</td>
<td>4 (9)</td>
<td>27 (18)</td>
<td>0.24</td>
</tr>
<tr>
<td>History of PCI, n (%)</td>
<td>26 (13)</td>
<td>7 (16)</td>
<td>19 (13)</td>
<td>0.62</td>
</tr>
<tr>
<td>History of cardiac bypass surgery, n (%)</td>
<td>25 (13)</td>
<td>12 (27)</td>
<td>13 (9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of angiographically significant coronary stenosis before CMR, n (%)</td>
<td>22 (11)</td>
<td>10 (23)</td>
<td>12 (8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any history of CAD before CMR, n (%)</td>
<td>57 (29)</td>
<td>22 (50)</td>
<td>35 (23)</td>
<td>0.01</td>
</tr>
<tr>
<td>Risk factor score</td>
<td>3.5±1.7</td>
<td>4.4±1.7</td>
<td>3.3±1.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blocker, n (%)</td>
<td>95 (49)</td>
<td>30 (68)</td>
<td>65 (43)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Calcium channel blocker, n (%)</td>
<td>30 (15)</td>
<td>7 (16)</td>
<td>23 (15)</td>
<td>0.99</td>
</tr>
<tr>
<td>ACE inhibitor, n (%)</td>
<td>77 (39)</td>
<td>25 (57)</td>
<td>52 (34)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>105 (53)</td>
<td>32 (73)</td>
<td>73 (48)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Resting ECG*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsinus rhythm</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>0.99</td>
</tr>
<tr>
<td>LV hypertrophy on ECG, n</td>
<td>11</td>
<td>7</td>
<td>4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>QRS duration, ms</td>
<td>101±22</td>
<td>110±25</td>
<td>99±21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Left bundle-branch block, n</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>0.001</td>
</tr>
<tr>
<td>Right bundle-branch block, n</td>
<td>13</td>
<td>3</td>
<td>10</td>
<td>0.99</td>
</tr>
<tr>
<td>ST-segment depression ≥1 mm, n</td>
<td>29</td>
<td>11</td>
<td>18</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>T-wave inversion in 2 contiguous leads, n</td>
<td>34</td>
<td>9</td>
<td>25</td>
<td>0.5</td>
</tr>
<tr>
<td>Corrected QT interval, ms†</td>
<td>431±34</td>
<td>442±35</td>
<td>428±33</td>
<td>0.02</td>
</tr>
<tr>
<td>Significant Q waves by Minnesota Code criteria</td>
<td>25</td>
<td>7</td>
<td>18</td>
<td>0.45</td>
</tr>
<tr>
<td>Diagnosis of myocardial ischemia by noninvasive imaging by study end, %‡</td>
<td>21 (11)</td>
<td>9 (20)</td>
<td>12 (8)</td>
<td>0.03</td>
</tr>
<tr>
<td>Diagnosis of angiographically significant coronary stenosis by study end, n (%)‡</td>
<td>59 (30)</td>
<td>26 (59)</td>
<td>33 (22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CMR</td>
<td></td>
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<tr>
<td>Mean LVEF, %</td>
<td>54±14</td>
<td>41±19</td>
<td>60±10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>53±10</td>
<td>56±12</td>
<td>51±8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVEDV, mL*</td>
<td>165±58</td>
<td>203±76</td>
<td>154±46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEDVI, mL/m²†</td>
<td>84±27</td>
<td>103±37</td>
<td>79±21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVESVI, mL/m²†</td>
<td>38±27</td>
<td>61±41</td>
<td>32±15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Presence of any segmental WMA, n (%)</td>
<td>52 (27)</td>
<td>34 (77)</td>
<td>18 (12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WMS%</td>
<td>28±8</td>
<td>35±13</td>
<td>26±5</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

PCI indicates percutaneous coronary intervention; ACE, angiotensin-converting enzyme; LVEDD, LV end-diastolic diameter; LVEDV, LV end-diastolic volume; and LVESVI, LV end-systolic volume index.

*Five patients had ECG data excluded because of the occurrence of a cardiac event between the CMR and ECG performance. One hundred one patients underwent coronary angiography before or during the study follow-up period. One patient had LV volume data missing owing to nonvolumetric coverage of the LV by cine CMR imaging.

†Defined by 70% coronary stenosis on x-ray angiography.
‡Diagnosis made before or after CMR study.
In the first approach, we analyzed the incremental associations of each CMR variable to MACE and cardiac mortality beyond clinical variables. We first built a multivariable Cox proportional-hazards regression clinical model by a stepwise forward strategy to select the strongest clinical predictors associated with MACE and cardiac mortality. All clinical variables in Table 2 were considered with \( P < 0.1 \) as the inclusion level. To assess the incremental prognostic information from noninvasive assessment of myocardial ischemia, angiographically significant coronary stenosis, and CMR variables, we then entered each of the variables in Table 2 into the clinical models (for MACE and cardiac mortality) and used likelihood-ratio (LR) tests to assess any significant incremental prognostic information beyond the clinical models. We tested the confounding effects of a noninvasive diagnosis of myocardial ischemia, angiographically significant coronary stenosis, and each of the CMR variables against the variables in the clinical model, with significant confounding defined by a >20% change in the effect estimate of any variable in the model. In each of the final models, the validity of the proportional-hazards assumption was tested by adding a time-dependent interaction variable for each of the predictors in the models. This assumption was tested valid for all the variables in the final models.

In the second approach, we determined the set of predictors that formed the best overall models for the prediction of MACE and cardiac mortality. We again used a stepwise forward-selection strategy and considered all clinical variables, status of coronary stenosis on angiography during the course of the study, noninvasive assessment of myocardial ischemia during the course of the study, and CMR predictors, with \( P < 0.1 \) again as the significance level for inclusion. The validity of the proportional-hazards assumptions of the final models for MACE and cardiac mortality was again tested valid according to the same technique as previously described. We also calculated a risk factor score (range, 0 to 7) as the sum of age \( > 55, 2^{nd} \) male sex, hypertension, diabetes, hypercholesterolemia, history of bypass surgery, and any medication (\( \beta \)-blocker, angiotensin-converting enzyme inhibitor, or aspirin use, where yes=1 and no=0). All analyses were performed with SAS 9.1 (SAS Institute, Cary, NC).

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

### Results

#### Baseline Characteristics

From a consecutive series of 221 patients, 14 (6%) had an unsuccessful CMR due to large body habitus or technical problem. Two patients (0.8%) with an atypical LGE pattern were excluded. One of these 2 patients experienced sudden cardiac death 6 months after CMR. Five patients were lost to follow-up but were reported to be alive. Another 5 patients died of noncardiac causes (cancer, \( n = 4 \); sepsis, \( n = 1 \)) and were excluded from analysis. The remaining 195 patients (132 male; mean ± SD age, 59 ± 13 years) formed the study cohort and were followed up for a median of 16 months (range, 6 to 42 months). Twenty-two patients (11%) had a known history of angiographically significant coronary stenosis at the time of CMR. Presenting reasons included chest pain (49%), dyspnea (32%), syncope (6%), and abnormal ECG (13%). Patients with LGE had more coronary risk factors and were more likely to have ischemia or angiographically significant coronary stenosis diagnosed during the study period (Table 1). There was high interobserver agreement in detecting LGE (\( \kappa \) statistic, 0.83) and in quantifying the LGE% (Figure 2).

#### Cardiovascular Outcome

At the end of the study, 31 patients (16%) had experienced MACE, including 17 cardiac deaths, 6 unstable angina events, 5 exacerbations of heart failure, and 3 ventricular tachycardias necessitating ICD discharge. No patient experienced a new acute MI during follow-up. Among the 17 cardiac deaths, 7 were nonsudden and 10 were outpatient sudden cardiac deaths. Seventy-nine patients (41%) were reported to have myocardial ischemia. One hundred one patients (52%) were reported for coronary angiography: 32 before and 69 after CMR. Only 22 patients (11%) had angiographically significant coronary stenosis at the time of CMR. By the end of the study, 37 additional patients (59 total) were found to have angiographically significant coronary stenosis. An unadjusted analysis of adverse events is presented in Table 2. Although noninvasive assessment of myocardial ischemia, angiographically significant coronary stenosis, LVEF, LVEDVI, LVESVI, and a segmental WMA all demonstrated significant associations with MACE and cardiac mortality, the presence of LGE demonstrated the strongest unadjusted associations with MACE and cardiac mortality (unadjusted HR, 8.29; \( P < 0.0001 \); and HR, 10.9; \( P < 0.0001 \), respectively). Kaplan-Meier estimates illustrated reduced periods of MACE and cardiac mortality in patients with LGE (Figure 3). Two cases are presented in Figure 4.

Figure 5 illustrates the univariable HRs for MACE in each tertile of LGE% percentage and WMS%. We noticed a “threshold effect” in which even a very small LGE% was strongly associated with MACE. Patients in the lowest LGE% tertile (mean, 1.4 ± 1.1%) experienced a >7-fold hazard increase for MACE (\( P = 0.0002 \)) compared with patients without LGE. Although LGE was correlated with segmental WMA (\( P < 0.0001 \)), the association of LGE% with MACE was stronger than that for WMS% across all LGE% and WMS% tertiles. The number of myocardial segments with LGE also demonstrated strong associations with MACE and cardiac mortality (unadjusted HR, 1.34; \( P < 0.0001 \); and HR, 1.43; \( P < 0.0001 \), respectively). Patients with LGE in the left anterior descending and right coronary artery territories experienced higher rates of MACE (HR, 4.78; 95% confidence interval [CI], 2.26 to 10.1; and HR, 6.06; 95% CI, 2.81 to 13.1, respectively) and cardiac mortality (HR, 4.88; 95% CI, 1.76 to 13.5; and HR, 16.8; 95% CI, 5.97 to 47.3, respectively). The associations of LGE in the
TABLE 2. Unadjusted HRs for MACE and Cardiac Mortality

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>MACE (n=31)</th>
<th>P</th>
<th>Cardiac Mortality (n=17)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>1.03 (1.00-1.07)</td>
<td>&lt;0.05</td>
<td>1.03 (0.99-1.07)</td>
<td>0.20</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.54 (0.22-1.31)</td>
<td>0.17</td>
<td>0.72 (0.23-2.22)</td>
<td>0.56</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (n=153)</td>
<td>2.11 (0.73-6.09)</td>
<td>0.17</td>
<td>2.43 (0.54-10.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>Black (n=18)</td>
<td>1.44 (0.50-4.16)</td>
<td>0.5</td>
<td>1.26 (0.28-5.63)</td>
<td>0.76</td>
</tr>
<tr>
<td>Other (n=24)‡‡‡‡</td>
<td>‡‡‡‡</td>
<td></td>
<td>‡‡‡‡</td>
<td>‡‡‡‡</td>
</tr>
<tr>
<td>Body mass index (in kg/m²)</td>
<td>1.05 (0.98-1.12)</td>
<td>0.21</td>
<td>1.03 (0.94-1.14)</td>
<td>0.53</td>
</tr>
<tr>
<td>Resting heart rate 100 bpm</td>
<td>0.66 (0.09-4.89)</td>
<td>0.66</td>
<td>1.28 (0.17-9.74)</td>
<td>0.81</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1.79 (0.84-3.83)</td>
<td>0.13</td>
<td>1.44 (0.52-3.98)</td>
<td>0.48</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>2.12 (1.02-4.41)</td>
<td>0.04</td>
<td>2.40 (0.89-6.47)</td>
<td>0.08</td>
</tr>
<tr>
<td>History of hypercholesterolemia</td>
<td>1.58 (0.74-3.39)</td>
<td>0.24</td>
<td>0.76 (0.28-2.03)</td>
<td>0.58</td>
</tr>
<tr>
<td>Heavy smoking</td>
<td>1.76 (0.86-3.61)</td>
<td>0.12</td>
<td>2.56 (0.95-6.90)</td>
<td>0.06</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>0.50 (0.15-1.64)</td>
<td>0.25</td>
<td>0.63 (0.14-2.81)</td>
<td>0.55</td>
</tr>
<tr>
<td>History of PCI</td>
<td>1.12 (0.39-3.20)</td>
<td>0.84</td>
<td>1.06 (0.24-4.68)</td>
<td>0.94</td>
</tr>
<tr>
<td>History of cardiac bypass surgery</td>
<td>1.91 (0.78-4.69)</td>
<td>0.16</td>
<td>1.74 (0.50-6.13)</td>
<td>0.39</td>
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<tr>
<td>History of angiographically significant coronary stenosis before CMR</td>
<td>2.84 (1.22-6.64)</td>
<td>0.02</td>
<td>4.41 (1.53-12.7)</td>
<td>0.006</td>
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<td>Any history of CAD before CMR</td>
<td>2.63 (1.28-5.40)</td>
<td>0.009</td>
<td>2.39 (0.89-6.44)</td>
<td>0.09</td>
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<td>Risk factor score</td>
<td>1.42 (1.14-1.79)</td>
<td>0.002</td>
<td>1.26 (0.93-1.70)</td>
<td>0.14</td>
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<tr>
<td>Medications</td>
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<td>β-Blocker use</td>
<td>4.00 (1.71-9.32)</td>
<td>0.001</td>
<td>2.62 (0.91-7.56)</td>
<td>0.07</td>
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<td>Calcium channel blocker use</td>
<td>1.38 (0.56-3.37)</td>
<td>0.48</td>
<td>0.37 (0.05-2.77)</td>
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<td>ACE inhibitor use</td>
<td>1.64 (0.80-3.37)</td>
<td>0.17</td>
<td>2.74 (0.99-7.53)</td>
<td>0.05</td>
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<td>Aspirin use</td>
<td>2.07 (0.95-4.53)</td>
<td>0.07</td>
<td>1.94 (0.67-5.58)</td>
<td>0.22</td>
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<td>ECG*</td>
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<tr>
<td>Nonsinus rhythm</td>
<td>2.49 (0.59-10.6)</td>
<td>0.22</td>
<td>2.33 (0.30-18.0)</td>
<td>0.42</td>
</tr>
<tr>
<td>LV hypertrophy on ECG</td>
<td>3.72 (1.28-10.8)</td>
<td>0.02</td>
<td>1.68 (0.22-12.9)</td>
<td>0.62</td>
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<tr>
<td>QRS duration (in ms)</td>
<td>1.01 (0.99-1.02)</td>
<td>0.42</td>
<td>1.00 (0.98-1.02)</td>
<td>0.93</td>
</tr>
<tr>
<td>Left bundle-branch block</td>
<td>3.41 (1.39-8.40)</td>
<td>0.008</td>
<td>2.07 (0.47-9.18)</td>
<td>0.34</td>
</tr>
<tr>
<td>Right bundle-branch block</td>
<td>‡‡‡‡</td>
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<td>‡‡‡‡</td>
<td>‡‡‡‡</td>
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<tr>
<td>ST-segment depression ≥1 mm</td>
<td>2.70 (1.15-6.35)</td>
<td>0.02</td>
<td>3.31 (1.03-10.6)</td>
<td>0.04</td>
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<td>T-wave inversion in 2 contiguous leads</td>
<td>1.41 (0.57-3.48)</td>
<td>0.45</td>
<td>2.06 (0.65-6.50)</td>
<td>0.22</td>
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<tr>
<td>Corrected QT interval (in ms)</td>
<td>1.01 (0.99-1.02)</td>
<td>0.18</td>
<td>0.99 (0.98-1.01)</td>
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<tr>
<td>Significant Q wave by Minnesota Code criteria</td>
<td>0.73 (0.22-2.39)</td>
<td>0.6</td>
<td>1.51 (0.43-5.30)</td>
<td>0.52</td>
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</table>

Myocardial ischemia by noninvasive stress imaging, angiographically defined coronary stenosis, and CMR variables

| Diagnosis of myocardial ischemia by noninvasive imaging by study end | 3.08 (1.31-7.22) | 0.01 | 3.67 (1.17-11.5) | 0.03 |
| Diagnosis of angiographically significant coronary stenosis by study end | 4.41 (2.12-9.17) | <0.0001 | 4.97 (1.80-13.7) | 0.002 |

CMR

| LVEF (every 10% change)† | 0.65 (0.53-0.78) | <0.0001 | 0.63 (0.48-0.81) | 0.0004 |
| LVEDVI (every 10-mL/m² change)‡ | 1.21 (1.10-1.33) | <0.0001 | 1.22 (1.08-1.39) | 0.002 |
| LVESVI (every 10-mL/m² change)‡ | 1.23 (1.23-1.33) | <0.0001 | 1.25 (1.12-1.39) | <0.0001 |
| Presence of any segmental WMA | 4.79 (2.32-9.92) | <0.0001 | 6.17 (2.23-17.1) | 0.0005 |
| WMS% | 1.04 (1.01-1.07) | 0.004 | 1.05 (1.02-1.09) | 0.0006 |
| Presence of any LGE | 8.29 (3.92-17.5) | <0.0001 | 10.9 (3.75-31.9) | <0.0001 |
| No. of myocardial segments with LGE | 1.29 (1.15-1.45) | <0.0001 | 1.34 (1.17-1.54) | <0.0001 |
| LGE% (every % of LV mass)† | 1.09 (1.05-1.12) | <0.0001 | 1.10 (1.06-1.15) | <0.0001 |

See the text and the footnote to Table 1 for an explanation of abbreviations.

*Five patients had ECG data excluded owing to MACE between the CMR and ECG performance. One hundred one patients underwent coronary angiography before or during the study follow-up period. One patient had LV volume data missing owing to nonvolumetric ventricular coverage by cine CMR imaging.

†Unadjusted HR for every 10% change in LVEF and LGE% and for every 10 mL/m² change in LVEDVI or LVESVI.

‡HR could not be estimated owing to low occurrence.
left circumflex territory with MACE and cardiac mortality were not significant.

Five of the 31 MACE cases (14%) were heart failure hospitalizations. Though limited by the small numbers, heart failure hospitalization did not appear to be related to myocardial ischemia (only 1 of these 5 patients had ischemia) or acute infarction (no patient infarction occurred in the follow-up period) but rather to clinical signs and symptoms of cardiac decompensation. There was a trend association between heart failure hospitalization and LGE ($P=0.08$). However, among patients with LGE, those who experienced heart failure hospitalization did not have a higher LGE% burden (8.9% versus 7.4%, $P=NS$) or a worse LVEF (45% versus 51%, $P=NS$). The strong association of LGE with MACE was maintained regardless of race: HRs for whites and nonwhites were 7.03, $P<0.0001$ and, 5.38, $P=0.003$, respectively. Table 3 summarizes the first multivariable approach in modeling MACE and cardiac mortality. The variables contained in each model are displayed in columns for MACE (top) and cardiac mortality (bottom), respectively. The LR $\chi^2$ for MACE in each model is shown at the bottom. As indicated in the first column from the left in Table 3, forward selection resulted in a significant clinical model for MACE, consisting of LV hypertrophy on the ECG, left bundle-branch block, and a history of CAD ($P=0.001$). The next 5 columns illustrate the incremental prognostic value of adding LGE, angiographically significant coronary stenosis, LVEF, LVESVI, and any segmental WMA. When LGE was entered individually into these 4 models, angiographically significant coronary stenosis, LVEF, LVESVI, and segmental WMA each lost its significance in the respective models.

In Table 3, we applied the same approach in assessing possible associations with cardiac mortality. As indicated in the first column from the left in Table 3, forward selection included only a history of CAD at the time of CMR in a clinical model for cardiac mortality ($P=0.01$). Illustrated by the next 5 columns, LGE, angiographically significant coronary stenosis, LVEF, LVESVI, and any segmental WMA each provided independent significant associations with MACE adjusted to the clinical model. Among these 5 models, the presence of LGE most strongly improved the clinical model (LR $\chi^2$ increased from 5.97 to 23.78, $P<0.0001$, at 2 df). Noninvasive assessment of myocardial ischemia, LVEDVI, or WMS% (not shown in Table 3) each provided a less substantial though significant improvement to the clinical model ($P=0.02$, $P=0.04$, and $P=0.04$, respectively). Inclusion of LGE further improved each of the models containing the clinical model plus angiographically significant coronary stenosis, LVEF, LVESVI, or segmental WMA. When LGE was entered individually into these 4 models, angiographically significant coronary stenosis, LVEF, LVESVI, and segmental WMA each lost its significance in the respective model. Results of the second multivariable approach are illustrated in Table 4. LGE was the strongest multivariable predictor for MACE (Table 4) and for cardiac mortality (Table 4) (adjusted HR for MACE and cardiac mortality were 5.98; 95% CI, 2.68 to 13.3; and 9.43; 95% CI, 3.15 to 28.3, respectively). Although the best overall model for MACE included LGE and angiographically significant coronary stenosis at study completion, the best cardiac mortality model included both LGE and myocardial ischemia by noninvasive stress imaging.

The risk factor score demonstrated a significant unadjusted association with MACE but not with cardiac mortality (Table 2). However, when LGE and LGE% were added separately to the risk factor score, strong independent associations of LGE and LGE% with MACE beyond the risk factor score were demonstrated by increases in the model LR $\chi^2$ from 10.01 to 33.89 ($P<0.0001$) and to 20.19 ($P=0.001$), respectively. The association of risk factor score to MACE was no longer significant when adjusted to either LGE or LGE%.

**Relation of LGE to MI by ECG,Segmental WMA, and Their Associations to MACE and Death**

Significant Q waves on the ECG were not correlated with LGE (Table 1) and did not demonstrate a significant prognostic association with MACE or cardiac mortality (Table 2). Among 170 patients without significant Q waves, LGE was present in 37 (22%) patients, and it demonstrated significant associations with MACE (HR, 7.39; $P<0.0001$) and cardiac mortality (HR, 8.15; $P=0.0003$). Among the 25 patients with significant Q waves on the ECG, 18 (72%) patients did not
have any LGE. None of these 18 patients developed MACE, but 3 of the remaining 7 patients with LGE and ECG Q waves developed MACE during the study follow-up.

Segmental WMA was associated with LGE \((P<0.0001)\). Although segmental WMA demonstrated significant univariable associations with MACE (HR, 4.79; \(P<0.0001\)) and cardiac mortality (HR, 6.17; \(P=0.0005\)), these associations were no longer significant when adjusted to LGE (HR, 0.64 and \(P=0.59\), respectively). Among the 143 patients without segmental WMA, LGE was present in 10 (7%) patients, and the presence of LGE demonstrated strong associations with MACE (HR, 10.12; 95% CI, 3.01 to 34.1; \(P=0.0002\)). Among the 52 patients with segmental WMA, 18 (35%) did not have any LGE, and the absence of LGE was associated with a lower trend to MACE hazards (HR, 0.24; 95% CI, 0.05 to 1.05; \(P=0.06\)). An association of significant Q waves on the ECG and the presence of segmental WMA did not reach statistical significance.

**Discussion**

Although contrast-enhanced CMR has high accuracy in quantifying infarct size\(^5\),\(^27\) and high sensitivity in detecting myonecrosis,\(^6\) little is known about its prognostic significance in patients without known MI. The current study has demonstrated that in patients with a clinical suspicion of CAD but without a known MI, the presence and extent of unrecognized myocardial scar by CMR provide strong prognostic value. The primary findings from the present study include the following: (1) The presence of LGE by CMR was the strongest multivariable predictor of MACE and cardiac mortality compared with common clinical, ECG, and LV functional variables; (2) a primarily “threshold effect” was observed, wherein even a very small myocardial scar by LGE (<2% mean LV mass) was associated with a >7-fold increase in MACE hazards; and (3) LGE provides complementary and incremental associations with MACE and cardiac mortality beyond clinical predictors alone or combined with angiographic or LV function predictors. Because the prognosis of patients with an unrecognized MI is comparable to or worse than that of patients with a recognized MI,\(^3\),\(^28\) we propose that contrast-enhanced CMR can improve the current risk assessment of patients without a prior known MI and who are presenting with possible CAD.
Clinical Implications

Several imaging studies have demonstrated strong correlations between infarct size and adverse outcomes in patients with acute MI. Wu et al reported significant associations of the extent of MI and microvascular obstruction by CMR to subsequent cardiac events. Hombach et al described similar findings and also reported an association with adverse LV remodeling. Patients without a history of MI who present with cardiac symptoms represent a challenging population that can benefit from accurate risk assessment. Although cine CMR demonstrated normal resting global and segmental LV function, LGE was noted in the subendocardial region of the anterior wall of the LV (arrows). This patient presented 13 months later with unstable angina and was found to have diffuse and severe stenoses of the left anterior descending and the right coronary arteries.

Patients in our cohort with unrecognized myocardial scar by LGE exhibited a number of known demographic or clinical confounders to MACE. To assess the strength and robustness of the incremental prognostic association of LGE to MACE beyond these confounders, we used 2 independent multivariable regression approaches in selecting the strongest sets of predictors and also calculated a patient-based risk factor score. We found strong and consistent prognostic associations of LGE with MACE adjusted to known predictors such as parameters of LV function, angiographic status of coronary stenosis, segmental WMA, or patient risk factor score.

Several reasons may explain why LGE provided incremental prognostic value beyond the parameters of LV function. First, silent ischemia is well known to cause subclinical subendocardial scar that acts as a substrate for serious arrhythmic events without LV dysfunction. Bello et al have reported that the myocardial extent of LGE by CMR demonstrates a stronger association with inducible monomorphic ventricular tachycardia than does LVEF. The possible association of life-threatening arrhythmia with unrecognized myocardial scar is supported by the increased incidence of cardiac death in patients with LGE in our study. Second, the presence of any LGE may be a marker of a severe burden of coronary atherosclerosis. In our study, there was a strong correlation between LGE and angiographically significant involving biomarkers of MI and risk of future cardiac events. Large-scale clinical studies of acute coronary syndromes have indicated that although there is a direct relation between serum troponin levels and subsequent risk, even patients with minimal elevations of troponin are at increased risk for adverse events. Importantly, LGE imaging allows the detection of small myocardial scar from subclinical coronary events that will no longer be detected by serum troponin values after the acute phase of myocardial injury. Small, subendocardial myocardial scar detected by contrast-enhanced CMR (in-plane resolution of 2 mm) is also missed by nuclear scintigraphy. ECG, or segmental wall motion.

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TABLE 3. Multivariable Cox Proportional-Hazards Analyses for MACE and Cardiac Mortality

<table>
<thead>
<tr>
<th>Variables</th>
<th>Clinical Model (CM)</th>
<th>CM + LGE*</th>
<th>CM + Angio Stenosis#*</th>
<th>CM + LVEF#</th>
<th>CM + LVESVI#</th>
<th>CM + Seg WMA#</th>
<th>CM + Angio Stenosis + LGE#*</th>
<th>CM + LVEF + LGE#</th>
<th>CM + LVESVI + LGE#</th>
<th>CM + Seg WMA + LGE#</th>
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</thead>
<tbody>
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</tr>
<tr>
<td>LHV on ECG</td>
<td>5.73§ (1.88-17.5)</td>
<td>2.33 (0.72-7.53)</td>
<td>3.90§ (1.24-12.5)</td>
<td>4.68§ (1.60-15.0)</td>
<td>4.32§ (1.35-13.8)</td>
<td>3.81§ (1.21-12.0)</td>
<td>1.82 (0.54-6.12)</td>
<td>2.22 (0.71-7.55)</td>
<td>2.26 (0.70-7.33)</td>
<td>2.33 (0.72-7.55)</td>
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<tr>
<td>LBBB on ECG</td>
<td>3.27§ (1.28-8.33)</td>
<td>1.53 (0.55-4.26)</td>
<td>4.10§ (1.58-10.6)</td>
<td>1.72 (0.62-4.48)</td>
<td>1.86 (0.65-5.34)</td>
<td>2.20 (0.81-5.92)</td>
<td>1.97 (0.69-5.63)</td>
<td>1.28 (0.44-3.73)</td>
<td>1.36 (0.47-3.92)</td>
<td>1.54 (0.55-4.34)</td>
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<td>History of CAD</td>
<td>2.43§ (1.13-5.24)</td>
<td>1.50 (0.65-3.44)</td>
<td>1.15 (0.45-2.90)</td>
<td>1.79 (0.79-4.08)</td>
<td>1.71 (0.72-4.07)</td>
<td>1.65 (0.71-3.80)</td>
<td>1.01 (0.41-2.52)</td>
<td>1.37 (0.58-3.24)</td>
<td>1.32 (0.53-3.30)</td>
<td>1.52 (0.64-3.58)</td>
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<td>Angiostenosis</td>
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<td>LVEF (per 10%)</td>
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<td>LVEF (per 10%)</td>
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<td>Seg WMA</td>
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<tr>
<td>Model LR χ²†</td>
<td>15.96</td>
<td>31.64 (P&lt;0.001)†</td>
<td>24.29 (P&lt;0.01)†</td>
<td>22.25 (P&lt;0.01)†</td>
<td>20.06 (P&lt;0.05)†</td>
<td>22.46 (P&lt;0.01)†</td>
<td>35.64 (P&lt;0.001)†</td>
<td>32.50</td>
<td>31.93</td>
<td>31.66</td>
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<tr>
<td>History of cath CAD‡</td>
<td>4.41§ (1.53-12.7)</td>
<td>2.77 (0.94-8.17)</td>
<td>1.70 (0.49-5.87)</td>
<td>2.36 (0.69-8.02)</td>
<td>2.07 (0.59-7.33)</td>
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<td>1.75 (0.51-5.08)</td>
<td>2.48 (0.67-9.22)</td>
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<td>2.70 (0.88-8.34)</td>
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<td>Angiostenosis</td>
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<tr>
<td>Model LR χ²†</td>
<td>5.97</td>
<td>23.78 (P&lt;0.001)†</td>
<td>10.55 (P&lt;0.03)†</td>
<td>12.60 (P&lt;0.01)†</td>
<td>12.79 (P&lt;0.01)†</td>
<td>15.40 (P&lt;0.01)†</td>
<td>25.23</td>
<td>23.87</td>
<td>23.73</td>
<td>23.80</td>
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</table>

Angiostenosis indicates angiographically significant coronary stenosis (≥70%) diagnosed before or after the CMR study; seg WMA, the presence or absence of a segmental WMA; LHV, LV hypertrophy; LBBB, left bundle-branch block; and cath, catheterization.

*Presence or absence of LGE.
†LR test P value compared with the LR χ² of the clinical model.
‡History of angiographically significant coronary stenosis at the time of CMR.
§P<0.05.
||P<0.01 for columns with the same superscripted letter.
#P<0.001 for columns with the same superscripted letter.
¶P<0.0001 for columns with the same superscripted letter.

Coronary stenosis. Extensive atherosclerosis is well recognized to be the predisposing cause of acute cardiac events from a postmortem series of sudden death victims without known heart disease. A majority of these cases have areas of healed myocardial necrosis that can be identified by contrast-enhanced CMR.

Although both segmental LV function and LGE reflect an underlying CAD burden, LGE% demonstrated a stronger prognostic association with MACE compared with WMS% across all tertiles. Segmental wall motion may be preserved in the presence of nontransmural scar. Conversely, abnormal segmental wall motion may be the result of hibernation, stunning, or cardiomyopathy without scarring. In the current study population, LGE primarily represented areas of myocardial scar from CAD. Thus, assessment of segmental wall motion is inherently less sensitive or specific than is LGE imaging by CMR for detecting myocardial scar from CAD, which probably explains the better prognostic value of LGE compared with segmental LV function.

ECG Identification of Unrecognized MI

Imaging studies have shown that the development of Q waves requires a critical extent of scar, and micromyonecrosis often exists without significant Q waves. The results of the current study emphasize the prognostic limitation of current ECG criteria for MI, which probably reflects both poor sensitivity and poor specificity for detecting MI. Most patients with LGE by CMR in our study did not have significant Q waves, and most patients with significant Q waves did not have LGE.

Limitations

First, because the patients in this single-center study were clinically referred for CMR, referral bias may limit the generalizability of the clinical characteristics of our cohort to the population at risk for unrecognized MI. Second, although angiographically significant coronary stenosis demonstrated a strong, unadjusted association with MACE, by design, coronary angiography was performed at the discretion of the treating physician and was not performed in all patients. It is therefore unclear whether LGE imaging would maintain its incremental prognostic significance beyond coronary angiographic findings if all patients in the cohort had undergone coronary angiography. Third, the results of the CMR studies...
were made available to the physicians providing clinical care on the same day of the CMR study. As a result, important treatment decisions about cardiac catheterization, coronary revascularization, or medication were influenced by the CMR results. However, it is unclear how the LGE results might have altered the decisions for catheterization or revascularization. On one hand, an extensive transmural LGE in a coronary territory suggesting little viability may have led to a decision against catheterization or revascularization. On the other hand, the presence of a small, unrecognized myocardial scar by CMR in patients without known CAD may have triggered the decision for catheterization or revascularization. It is also unclear whether and how invasive procedures have altered patient prognoses. With such limitations in a clinical study design, the current results do not allow determination as to whether physicians’ knowledge of the CMR results might have influenced the prognostic association of LGE to MACE. Further, other limitations include the technical aspects of quantifying LGE%. Delineating the endocardial border from the bright LV blood pool is occasionally difficult and may alter the size of the LGE%. We attempted to improve the manual tracing of the LV endocardial border on the short-axis LGE image by comparing it to the endocardial contour on the short-axis cine image matching in slice location and closest in cardiac phase. Performing LGE imaging 15 minutes after injection of gadolinium-DTPA, when the blood pool signal has become less intense, also improved the contrast between the bright LV blood pool is occasionally difficult and may alter the size of the LGE%. We attempted to improve the manual tracing of the LV endocardial border on the short-axis LGE image by comparing it to the endocardial contour on the short-axis cine image matching in slice location and closest in cardiac phase. Performing LGE imaging 15 minutes after injection of gadolinium-DTPA, when the blood pool signal has become less intense, also improved the contrast between the bright LV blood pool and the LGE image.

Conclusions
In this consecutive series of patients without a known prior MI and presenting with clinical suspicion of CAD, we have demonstrated that the presence and extent of myocardial scar as detected by CMR is a strong predictor of MACE and cardiac death. The presence of LGE provides incremental prognostic value beyond common clinical predictors combined with angiographic coronary data, noninvasive myocardial ischemia assessment, or segmental or global LV functional parameters and is the strongest predictor in the overall best model for either MACE or cardiac mortality. Therefore, CMR can improve risk stratification of patients who present with a clinical suspicion of CAD but without a history of MI. CMR may also represent a better standard for unrecognized MI than ECG for future population-based studies. Whether these findings can result in better patient outcomes by guiding management decisions, such as implantation of ICDs, coronary revascularization, or intensive medical treatment, requires additional study.

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Disclosures
None.

References
Patients with a subclinical myocardial infarction (MI) experience major adverse cardiac events (MACE) at a rate even higher than those with a recognized MI. Late gadolinium enhancement (LGE) by cardiac magnetic resonance imaging (CMR) can detect and quantify the extent of myocardial scar due to MI with high sensitivity and accuracy. In this clinical study conducted in a cohort of 195 patients with a clinical suspicion of coronary artery disease but without a known history of MI, the presence of LGE by CMR was among the strongest multivariable predictors of MACE and cardiac mortality. A primarily threshold effect was observed, wherein even very small myocardial scar detected by LGE (of MI, the presence of LGE by CMR was among the strongest multivariable predictors of MACE and cardiac mortality.}

**Clinical Perspective**

Patients with a subclinical myocardial infarction (MI) experience major adverse cardiac events (MACE) at a rate even higher than those with a recognized MI. Late gadolinium enhancement by cardiac magnetic resonance imaging (CMR) can detect and quantify the extent of myocardial scar due to MI with high sensitivity and accuracy. In this clinical study conducted in a cohort of 195 patients with a clinical suspicion of coronary artery disease but without a known history of MI, the presence of LGE by CMR was among the strongest multivariable predictors of MACE and cardiac mortality. A primarily threshold effect was observed, wherein even very small myocardial scar detected by LGE was among the strongest multivariable predictors of MACE and cardiac mortality. A primarily threshold effect was observed, wherein even very small myocardial scar detected by LGE was among the strongest multivariable predictors of MACE and cardiac mortality. A primarily threshold effect was observed, wherein even very small myocardial scar detected by LGE was among the strongest multivariable predictors of MACE and cardiac mortality.
Impact of Unrecognized Myocardial Scar Detected by Cardiac Magnetic Resonance Imaging on Event-Free Survival in Patients Presenting With Signs or Symptoms of Coronary Artery Disease

Raymond Y. Kwong, Anna K. Chan, Kenneth A. Brown, Carmen W. Chan, H. Glenn Reynolds, Sui Tsang and Roger B. Davis

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In the article by Kwong et al, “Impact of Unrecognized Myocardial Scar Detected by Cardiac Magnetic Resonance Imaging on Event-Free Survival in Patients Presenting With Signs or Symptoms of Coronary Artery Disease,” which published in the June 13, 2006, issue (Circulation. 2006;113:2733–2743), the term “myocardial ischemia” was mistakenly edited and abbreviated as “MI” in the last line of Table 4. The line should read, “Myocardial ischemia by noninvasive imaging.” We regret the error.

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