Background—Left ventricular ejection fraction is a powerful independent predictor of survival in cardiac patients, especially those with coronary artery disease. Delayed-enhancement magnetic resonance imaging (DE-MRI) can accurately identify irreversible myocardial injury with high spatial and contrast resolution. To date, relatively limited data are available on the prognostic value of DE-MRI, so we sought to determine whether DE-MRI findings independently predict survival.

Methods and Results—The medical records of 857 consecutive patients who had complete cine and DE-MRI evaluation at a tertiary care center were reviewed regardless of whether the patients had coronary artery disease. The presence and extent of myocardial scar were evaluated qualitatively by a single experienced observer. The primary, composite end point was all-cause mortality or cardiac transplantation. Survival data were obtained from the Social Security Death Index. The median follow-up was 4.4 years; 252 patients (29%) reached one of the end points. Independent predictors of mortality or transplantation included congestive heart failure, ejection fraction, and age ($P<0.0001$ for each), as well as scar index (hazard ratio, 1.26; 95% confidence interval, 1.02 to 1.55; $P=0.033$). Similarly, in subsets of patients with or without coronary artery disease, scar index also independently predicted mortality or transplantation (hazard ratio, 1.33; 95% confidence interval, 1.05 to 1.68; $P=0.018$; and hazard ratio, 5.65; 95% confidence interval, 1.74 to 18.3; $P=0.004$, respectively). Cox regression analysis showed worse outcome in patients with any DE in addition to depressed left ventricular ejection fraction (<50%).

Conclusion—The degree of DE detected by DE-MRI appears to strongly predict all-cause mortality or cardiac transplantation after adjustment for traditional, well-known prognosticators. (Circulation. 2009;120:2069-2076.)

Key Words: magnetic resonance imaging ▪ myocardium ▪ prognosis ▪ survival

Although mortality associated with coronary artery disease (CAD) has declined in recent decades, CAD remains the leading cause of death in adults in developed countries.1 Multiple studies have shown that besides age, left ventricular (LV) ejection fraction (LVEF) is among the most important predictors of survival in CAD patients.2-4

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Cardiovascular magnetic resonance imaging (CVMRI) is the preferred method of measuring LV function. Exquisite contrast, spatial, and temporal resolutions and a lack of geometric assumptions make CVMRI measurement of LV volumes both accurate and reproducible.5,6 In addition, CVMRI is noninvasive, lacks constraints such as acoustic windows, and does not use ionizing radiation.

Delayed-enhancement MRI (DE-MRI) is a CVMRI technique that accurately delineates irreversible myocardial injury with extraordinary spatial resolution,7-9 which enables CVMRI to discriminate easily between subendocardial and transmural scar.7,8,10,11 This feature of DE-MRI may be valuable because recently published studies12,13 have shown that the transmural extent of irreversible injury or scar predicts LV functional recovery in patients.

Small studies suggest that DE-MRI provides independent prognostic information about survival in both ischemic and nonischemic patients.14-16 We therefore examined the prognostic value of DE-MRI results in 857 consecutive patients referred for CVMRI in a tertiary cardiac care center. We also attempted to determine whether the presence of DE, when combined with LVEF, could provide additional discriminatory information about patient prognosis and survival.

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Methods

Patients
The study cohort comprised patients referred to our institution for DE-MRI between 2001 and 2004. All patients who had complete DE-MRI evaluation with LV functional analysis were included in the study, except those diagnosed with hypertrophic cardiomyopathy, myocarditis, sarcoidosis, or other infiltrative cardiomyopathy. The Institutional Review Board at St. Luke’s Episcopal Hospital approved the study and waived the requirement for informed consent.

Image Acquisition and Postprocessing
All imaging was performed on 1.5-T commercial scanners (Philips NT-Intera or Philips Achieva, Philips Medical Systems, Cleveland, Ohio). A 5-element cardiac coil was used with vector-cardiac gating in all patients.

For each patient, we obtained standard bright-blood cine images, including vertical long-axis view, 4-chamber view, and LV outflow tract view, as well as a set of short-axis series covering the entire LV. The cine imaging sequence was a steady-state free-precession sequence with the following parameters: repetition time/echo time, 3.4/1.7 ms; flip angle, 55°; temporal resolution, 36 to 40 ms; in-plane resolution, 1.5 to 1.75 mm² (depending on the patient’s size); and breath-hold duration, 10 to 12 heartbeats per slice.

Fifteen minutes after an MRI contrast agent (gadolinium chelate, 0.2 mmol/kg) was administered, an inversion-recovery–prepared, T₁-weighted, gradient-echo sequence was used to collect DE-MRI images. After the inversion pulse, 16 to 24 gradient echoes (repetition time/echo time/flip angle, 7.0 ms/2.0 ms/15°) were collected per heart beat during diastole, with an inversion delay that was iteratively adjusted to optimally null the signal from normal myocardium. The total acquisition time was 16 heartbeats per slice. Selected 8-mm-thick long-axis slices were acquired, along with a series of continuous short-axis slices (8-mm slices with 2-mm gaps), to cover the entire LV with the same orientations as the cine images.

Data Collection and Computation
From electronic medical records and the Texas Heart Institute CVMRI database, we obtained demographic and significant medical history data, including history of CAD (indicated by previous myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention [PCI], positive stress test [ie, any nuclear, echocardiographic, or MRI test result showing reversible perfusion defects or wall-motion abnormalities that developed during stress], or coronary angiogram showing >50% stenosis in at least 1 coronary artery), diabetes mellitus, peripheral vascular disease, stroke, hypertension, serum creatinine, and hyperlipidemia; all diagnoses were confirmed by International Classification of Disease, revision 9, coding. Patients were classified as not having CAD if they had a negative x-ray angiogram or stress test.

Furthermore, 2 postscan variables—receiving an automatic implantable cardioverter-defibrillator or biventricular pacemaker (AICD/BiVPM) and undergoing any PCI or cardiovascular surgical procedure within 1 month after CVMRI—were included in the statistical analysis as dichotomous variables. For statistical analysis purposes, LVEF was divided into 3 categories: <30%, 30% to 50%, and >50%.

The primary end point was combined all-cause mortality and cardiac transplantation. Cardiac transplantation was included in the end point because every patient who underwent this procedure was in end-stage cardiomyopathy and probably would not have survived without a transplant. The mortality data were confirmed through the Social Security Death Index, and the data for transplantation were obtained through a medical records review.

Imaging data were analyzed on a commercially available postprocessing workstation (EasyVision or ViewForum, Philips Medical Systems). Endocardial and epicardial contours were prescribed manually on the series of short-axis cine slices of the LV at end diastole and end systole to obtain end-diastolic volume, end-systolic volume, LVEF, and LV mass.

Figure 1. DE-MRIs of the LV in 2 different patients. A, Two-chamber orientation showing dense subendocardial scar (25% to 50% myocardial thickness) in the distal two thirds of the anterior wall and transmural scar (75% to 100% myocardial thickness) in the apex. B, Short-axis view at the midpapillary level with transmural scar involving the midinferoseptum and the inferior and lateral walls.

The LV was analyzed in the standard 17-segment model. All examinations in this study were clinically indicated for assessment of myocardial viability. After the imaging data were acquired, the images were analyzed by a single cardiovascular imager (S.D.F.) with >13 years of experience in CVMRI. The extent of DE (representing the percentage of the myocardial thickness involved) within the myocardium was quantified visually according to the procedure described by Kim et al. For the purpose of statistical analysis, a modified scoring system was used on the DE data: no hyperenhancement (score=1), 1% to 25% myocardial hyperenhancement (thin subendocardial scar, score=2), 26% to 50% myocardial hyperenhancement (dense subendocardial scar, score=3; Figure 1A), 51% to 75% myocardial hyperenhancement (near-transmural scar, score=4), and >76% to 100% myocardial hyperenhancement (transmural scar, score=5; Figure 1B). A scar index was computed for each patient as the sum of the scar scores of all 17 segments divided by 17. A patient with no evidence of DE would therefore have a scar index of 1.

Because midmyocardial DE has been described in patients with nonischemic dilated cardiomyopathy, patients who had midmyocardial DE (n=19) were included in the analysis. These patients all had a small amount of midmyocardial DE that was thin and linear, equivalent to <25% myocardial enhancement (ie, a scar score of 2) in the involved segment on qualitative assessment. The scar index was computed as described above.

Statistical Analysis
The study cohort was analyzed both as a whole and according to the presence or absence of CAD. Continuous variables with normal distributions were reported as mean±SD; otherwise, variables were expressed as median with lower and upper quartiles. The Student t test was used to test for differences in normally distributed continuous variables, and the Wilcoxon rank-sum test was used for comparisons involving variables that were not normally distributed. Categorical variables were compared with the χ² test. A 2-sided value of P<0.05 was considered significant.

Survival curves were created with the Kaplan–Meier method; the log-rank test was used to compare survival between patients with and without DE. For the survival analysis, the end point for each patient was either death (ascertained from the Social Security Death Index) or cardiac transplantation. Single-variable analysis identified 17 variables with values of P<0.2; these variables were included in an analysis that used the Cox proportional-hazards model with a stepwise Cox regression method. Results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). The proportional-hazards assumption used in the Cox regression analysis was verified by plotting the cumulative hazard function for each covariate. For the categorical covariates that were proportional, the curves would not intersect. Continuous covariates were categorized to carry out this verification. A 2-sided value of P<0.05 was considered statistically
significant. All statistical analyses were performed with SAS 8.2 (SAS Institute Inc, Cary, NC). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

## Results

Of the 905 patients who met the inclusion criteria for the study, 48 were excluded from analysis because they had incomplete demographic data or because they were international patients whose vital status we could not confirm. No other patients were excluded. Thus, our final sample comprised 857 patients (567 men; age, 59.1 ± 13.6 years; Table 1).

The mean LVEF of the entire study cohort was 40.6 ± 16.7%. During follow-up, patients were more likely to reach the primary end point if they had CAD; these patients were generally older and male and had lower LVEF. The majority of patients without documented CAD had no DE. In contrast, 79% of patients with CAD had some DE (Figure 2).

During the median follow-up period of 4.4 years, 252 patients reached the end point of death (n = 230) or cardiac transplantation (n = 22). After CVMRI, 101 patients underwent PCI, 238 underwent cardiac surgery (eg, coronary artery bypass grafting, valvular surgery, ventricular assist device placement), and 158 underwent AICD/BiVPM placement. Patients with CAD underwent more cardiac operations than patients without CAD (57.5; P < 0.0001), but there was no intergroup difference in the number of AICD/BiVPM placements or cardiac transplantations.

In the group with CAD, patients who underwent cardiac surgery had a lower median LVEF than those who did not (37% [lower and upper quartiles, 25% to 51%] versus 40% [lower and upper quartiles, 27% to 54%]; P = 0.04), although the median scar index was similar (1.59 [lower and upper quartiles, 1.2 to 2.06] versus 1.53 [lower and upper quartiles, 1.06 to 2.18]; P = 0.55). Neither LVEF nor scar index differed significantly between CAD patients who underwent PCI and those who did not.

Kaplan–Meier analysis (Figure 3 and Table 2) revealed a significant association between the presence of DE and poorer adjusted transplant-free survival. Because of the survival impact of PCI and cardiovascular procedures and the potential influence of DE-MRI findings on the decision to revascularize, these procedures were included in the multivariable analysis despite their lack of apparent impact in preliminary analysis.

Traditional prognosticators (eg, congestive heart failure [CHF], LVEF < 30%, and age) were all significantly associated with a reduced likelihood of transplant-free survival.

### Table 1. Demographic Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With CAD (n=642)</th>
<th>Patients Without CAD (n=215)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>61.7 ± 11.7</td>
<td>51.3 ± 16.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>455 (71)</td>
<td>122 (57)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>EDV, mL*</td>
<td>193 (150, 256)</td>
<td>178 (133, 260)</td>
<td>0.06</td>
</tr>
<tr>
<td>ESV, mL*</td>
<td>117 (73, 190)</td>
<td>85 (54, 160)</td>
<td>0.0002</td>
</tr>
<tr>
<td>LVEF, %*</td>
<td>39 (26, 52)</td>
<td>52 (33, 60)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>LV mass, g*</td>
<td>136 (111, 173)</td>
<td>125 (95, 161)</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>285 (44)</td>
<td>28 (13)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>CHF, n (%)</td>
<td>357 (56)</td>
<td>72 (33)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>493 (77)</td>
<td>64 (30)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>82 (13)</td>
<td>11 (5)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>PVD, n (%)</td>
<td>176 (27)</td>
<td>16 (7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Creatinine, mg/dL*</td>
<td>1.1 (0.9, 1.3)</td>
<td>1.0 (0.9, 1.2)</td>
<td>0.004</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>275 (43)</td>
<td>31 (14)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Scar index,*†</td>
<td>1.56 (1.12, 2.08)</td>
<td>1.00 (1.00, 1.00)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>211 (33)</td>
<td>41 (19)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

EDV indicates end-diastolic volume; ESV, end-systolic volume; and PVD, peripheral vascular disease. Data are presented as median (upper quartile, lower quartile) when appropriate.

*Variable was not normally distributed.
† Scar index is the sum of each patient’s scar scores in all myocardial segments divided by 17.

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group who survived to each time point.

Table 2. Number and Percentage of Transplant-Free Patients in Each Group Who Survived to Each Time Point for Figure 3

<table>
<thead>
<tr>
<th>Years Survived</th>
<th>Patients without DE, n (%)</th>
<th>Patients with DE, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>310 (100)</td>
<td>547 (100)</td>
</tr>
<tr>
<td>1</td>
<td>284 (91.6)</td>
<td>456 (83.4)</td>
</tr>
<tr>
<td>3</td>
<td>268 (86.5)</td>
<td>392 (71.7)</td>
</tr>
<tr>
<td>5</td>
<td>261 (84.1)</td>
<td>352 (64.4)</td>
</tr>
<tr>
<td>7</td>
<td>258 (83.2)</td>
<td>347 (63.4)</td>
</tr>
</tbody>
</table>

Figure 3. Adjusted Kaplan–Meier transplant-free survival analysis for patients with (+) and without (−) DE. Table 2 lists the number (and percentage) of transplant-free patients in each group who survived to each time point.

(17) Scar index independently predicted death/transplantation in the multivariable model (HR, 1.26; 95% CI, 1.02 to 1.55; \( P=0.033 \)). Similarly, scar index independently predicted death/transplantation in the CAD group (HR, 1.33; 95% CI, 1.05 to 1.68; \( P=0.018 \)).

Traditionally, patients with LVEF \( \geq 50\% \) are considered to have “preserved” systolic function. When LVEF of 50% was used as a cutoff in the entire study cohort (with and without DE), the HR of death/transplantation in the presence of any DE was 1.61 (95% CI, 1.15 to 2.25; \( P=0.005 \)). The entire study cohort was risk stratified according to the presence or absence of DE and LVEF <50% or \( \geq 50\% \) (Figure 4 and Table 4). In patients with LVEF \( \geq 50\% \), the presence of DE predicted a worse outcome than the absence of DE. A similar pattern was observed in patients with LVEF <50%. Patients with LVEF <50% and with DE had the worst outcome. Importantly, patients with LVEF \( \geq 50\% \) and DE had survival characteristics similar to those of patients with LVEF <50% and no DE.

Among patients without documented CAD (n=215), 37 had DE, of whom 19 had only midmyocardial DE (which was detected only in the non-CAD group). Multivariable analysis indicated that in these patients, scar index significantly predicted death/transplantation (HR, 5.65; 95% CI, 1.74 to 18.30; \( P=0.004 \)). CHF was the other significant predictor (Table 3). For patients with a scar index \( \geq 1 \) (ie, any degree of DE), the HR of death/transplantation was 2.19 (95% CI, 1.13 to 4.23; \( P=0.020 \)), and the only other significant predictor of death/transplantation was CHF (HR, 4.81; 95% CI, 2.39 to 9.69; \( P<0.0001 \)). Thus, among non-CAD patients, DE was associated with poorer transplant-free survival (Figure 5 and Table 5).

Discussion

CVMRI has become an important noninvasive tool for assessing patients with LV dysfunction. Advances in CVMRI methods permit robust, highly accurate, and highly reproducible estimates of global LV function and myocardial fibrosis. Impaired LVEF (the adoption of optimal medical and device therapies notwithstanding) remains a strong predictor of long-term survival in CAD patients.2–4,18

Although an accurate estimate of LVEF alone is clinically useful, CVMRI provides additional clinically valuable information. Specifically, the DE-MRI technique is a simple, noninvasive method of reliably identifying and quantifying myocardial fibrosis with spatial resolution hitherto unavailable in clinical practice.7,8,10,11,13

Several studies have clearly demonstrated the prognostic value of LVEF, although only a few have assessed the prognostic value of CVMRI-identified irreversible myocardial damage for patient survival. In a study of 44 patients with acute infarction, Wu et al19 used a technique related to the DE-MRI technique described here and found that a larger degree of infarction was associated with a higher risk of postinfarct complications, including cardiac death, CHF, stroke, and reinfarction. Likewise, Bello et al20 showed in a cohort of 48 CAD patients that infarct mass and LV infarct surface area are better predictors of the inducibility of ventricular tachycardia (VT) than LVEF. Yan et al16 similarly noted that in patients with documented CAD (mean LVEF, 44%), the extent of the peri-infarct zone as measured by DE-MRI significantly predicts post–myocardial infarction mortality after adjustment for traditional prognosticators, including LVEF.

Recent studies show that DE-MRI can provide important prognostic information about patients without known CAD. Kwong et al15 studied 195 patients (mean LVEF, 54%) with no documented history of myocardial infarction or ischemic disease. During a median follow-up period of 16 months, the presence of DE had significant prognostic value above and beyond established risk factors for major adverse cardiac events and cardiac mortality. Even small amounts of DE-MRI technique described here and found that a larger degree of infarction was associated with a higher risk of postinfarct complications, including cardiac death, CHF, stroke, and reinfarction. Likewise, Bello et al20 showed in a cohort of 48 CAD patients that infarct mass and LV infarct surface area are better predictors of the inducibility of ventricular tachycardia (VT) than LVEF. Yan et al16 similarly noted that in patients with documented CAD (mean LVEF, 44%), the extent of the peri-infarct zone as measured by DE-MRI significantly predicts post–myocardial infarction mortality after adjustment for traditional prognosticators, including LVEF.

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Our most important finding was that even in the presence of traditional cardiovascular prognosticators, DE was a strong, independent predictor of death/transplantation. Furthermore, our results emphasize that the combination of LVEF and DE carries independent prognostic information.

Specifically, in patients with low LVEF (<30%), who already had increased mortality risk, survival was worse when DE was present. Finally, the risk of death/transplantation increased progressively as the extent of DE increased.

Although the precise mechanism linking increased mortality risk to myocardial scar or DE is unknown, several groups have proposed possible mediators. Zipes and Wellens have suggested that myocardial scar can act as a substrate for ventricular tachyarrhythmia that could lead to sudden death. Others have hypothesized that viable myocardium adjacent to myocardial scar could give rise to reentry pathways for the development of VT.22 We found that survival improved significantly in patients who received AICD/BiVPM therapy. Assomull et al14 have suggested that even in patients with nonischemic cardiomyopathy but without CAD, DE may be responsible for the reentrant mechanism of ventricular tachyarrhythmia. This might explain why AICD improves survival in patients with nonischemic cardiomyopathy but without CAD.23

Although we did not obtain data on cause of death, other investigators have indicated that DE could be a substrate for malignant ventricular arrhythmias.16,20 In fact, the recently initiated Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation (DETERMINE) trial (http://clinicaltrials.gov/ct2/show/NCT00487279) is designed to investigate whether initiated Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation (DETERMINE) trial (http://clinicaltrials.gov/ct2/show/NCT00487279) is designed to investigate whether AICD is effective in reducing sudden death in patients with nonischemic cardiomyopathy.
prognostic implications of DE may suggest a role for DE-MRI in patient risk stratification, and DE-MRI could potentially identify higher-risk patients who may benefit from more aggressive interventions.

Bello et al.,20 who investigated the relationship between infarct mass and VT, found that patients with polymorphic VT had an infarct mass of 20% of the LV and that patients with monomorphic VT had an infarct mass of 26% of the LV. The authors concluded that infarct mass predicts VT inducibility better than LVEF and hypothesized that myocardial infarction size characterized by DE-MRI could also be a better predictor of sudden death than LVEF. The results of our study also indicate that the greater the amount of scar is, the greater the risk of death/transplantation is.

In our patients without CAD, the presence of DE predicted an increase in death/transplantation after adjustment for other, traditional risk factors. In these patients, coronary angiograms revealed mild (ie, <50%) or no stenosis, or the patient had a negative stress test. The mean LVEF of these patients was 52%, (range, 33% to 60%), and all were treated by their attending physicians as having nonischemic cardiomyopathy. In addition, the DE in these patients was not found in the coronary artery distribution typical of ischemic cardiomyopathy. Although one could argue theoretically that these patients have underlying CAD, that the DE was caused by embolization, or that there was recanalization of infarct-related coronary artery, it should be noted that the degree of LV dysfunction in many of these patients could not be explained solely by underlying CAD. Recently, McCrohon et al24 reported that patients diagnosed with dilated cardiomyopathy can have DE patterns similar to those of patients with CAD and myocardial infarction. When these authors included midmyocardial enhancement in their multivariable model, CHF and the presence of any hyperenhancement were the only significant predictors of death/transplantation. Our findings were in concordance with the above-mentioned results14–16 in that the presence of DE was a strong predictor of cardiovascular mortality.

Traditionally, patients with relatively preserved LVEF (eg, ≥50%) have been considered to be at lower risk for adverse events than patients with LV systolic dysfunction. In the 310 patients with preserved LVEF in our study cohort, the presence of any DE significantly increased the risk of death/transplantation after adjustment for potential confounding variables. Thus, DE-MRI could be a useful, noninvasive risk stratification tool in patients with preserved LVEF. Such risk stratification could lead one to adopt more aggressive treatment strategies than otherwise may have been considered.

CVMRI is inherently suited to the detection of myocardial scar because of its high in-plane spatial resolution of 1.5 to 2 mm. Previous studies7,8,10,11 have shown that nuclear techniques such as single-photon emission computed tomography and positron emission tomography are excellent for detecting transmural scar but are inferior to CVMRI in detecting subendocardial scar. These findings further emphasize the importance of CVMRI as a tool for accurately assessing the degree and extent of myocardial injury and potentially helping clinicians to identify patients with a higher risk of death.

**Study Limitations**

Our study had the limitations inherent to retrospective analysis. Additionally, patients referred for CVMRI at our tertiary care center were likely to be at higher-than-normal risk because of their underlying cardiac conditions; this high level

<table>
<thead>
<tr>
<th>Years Survived</th>
<th>Patients without DE and with EF ≥50%, n (%)</th>
<th>Patients without DE and with EF &lt;50%, n (%)</th>
<th>Patients with DE and with EF ≥50%, n (%)</th>
<th>Patients with DE and with EF &lt;50%, n (%)</th>
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<td>145 (92.3)</td>
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<td>147 (95.8)</td>
<td>147 (95.8)</td>
<td>143 (91.1)</td>
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</tr>
</tbody>
</table>

**Table 5. Number and Percentage of Transplant-Free Patients in Each Group Who Survived to Each Time Point for Figure 5**
of risk was reflected by our mortality rate of \( \approx 27\% \) during the follow-up period.

Death and cardiac transplantation were chosen as the only end points; we did not record direct cause of death or other, “softer” end points such as revascularization or hospital admission. All-cause mortality is a clinically relevant and commonly used end point in survival studies and should be equally relevant for a study of the DE-MRI technique.

Our findings could have been influenced by the patients’ DE results because the presence of viable myocardium could have made the treating physicians more inclined to revascularize the patients percutaneously or surgically; however, this possibility seems unlikely because scar indexes were similar in patients who underwent coronary revascularization (surgical or percutaneous) and those who did not. Additionally, our analysis included potential confounding variables, including revascularization and placement of AICD/BiVPM, which are known to improve survival.

The degree of myocardial scar (as identified by DE on CVMR) was assessed qualitatively, which is the most common approach used clinically. Previous studies have shown that qualitative assessments provide estimates of global scar burden that are clinically comparable to the estimates provided by quantitative analysis. Moreover, qualitative assessments provide a rapid and reliable measure of irreversible myocardial damage that is easily extrapolated to routine clinical practice.27,28

There were only a few patients with DE (including mid-myocardial DE) in the non-CAD group, perhaps too few to allow any definitive conclusion to be drawn about the usefulness of DE-MRI in such patients. Nonetheless, various studies have shown that DE predicts mortality in patients with or without CAD.14–16

Conclusions

Our findings suggest that the degree of DE detected by CVMRI is a strong and independent predictor of all-cause mortality/cardiac transplantation, even in the presence of traditional, well-known prognosticators. More extensive DE appears to be associated with worse outcomes. Furthermore, even in patients with DE and relatively preserved LVEF (\( \approx 50\% \)), DE-MRI can provide additional discriminatory information, predicting poorer survival in this subset of patients. Our findings, if confirmed in prospective studies, suggest that DE-MRI, which has spatial and contrast resolution superior to those of other currently available noninvasive modalities, could make a unique contribution to patient risk stratification beyond those made by traditional prognosticators.

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Disclosures

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References


15. Kwong RY, Chan AK, Brown KA, Chan CW, Reynolds HG, Tsang S, Davis RB. 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. Circulation. 2006;113:2733–2743.


Delayed-enhancement magnetic resonance imaging (DE-MRI) is increasingly being used for myocardial variability assessment because it is reproducible, has high spatial and contrast resolution, and can be performed without exposing patients to ionizing radiation. To date, there are only a few reports on the prognostic value of DE-MRI. In the present study, a total of 857 patients who underwent DE-MRI were followed up for a median of 4.4 years. The primary end point was composite all-cause mortality and cardiac transplantation. The degree of DE was assessed qualitatively and was expressed as the scar index. We found that the presence of DE predicted worse transplant-free survival. Scar index was a significant independent predictor of death/cardiac transplantation even after adjustment for traditional prognosticators. In patients with preserved systolic function (ejection fraction \( \geq 50\% \)), those with DE had poor outcomes, similar to patients with systolic dysfunction and no DE. Our findings support prior, smaller studies showing that DE is an independent predictor of death (or cardiac transplantation). The precise causes of death in our patients with DE were not determined; however, DE is postulated to be a substrate for ventricular tachyarrhythmia. If our findings are confirmed in prospective studies investigating the prognostic value of DE-MRI, this imaging technique could potentially be used as a novel clinical tool for identifying at-risk patients, giving clinicians prognostic capability beyond that provided by traditional risk factors.
Prognostic Significance of Delayed-Enhancement Magnetic Resonance Imaging: Survival of 857 Patients With and Without Left Ventricular Dysfunction

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