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# Prognostic Value of Myocardial Infarct Size and Contractile Reserve Using Magnetic Resonance Imaging

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**Objectives** Our aim was to assess the predictive value of myocardial infarct size assessed with late gadolinium-enhanced (LGE) magnetic resonance imaging (MRI) in medically treated patients with chronic myocardial infarction relative to contractile reserve on low-dose dobutamine magnetic resonance (DSMR) for long-term event-free survival.

**Background** Information on the relative merits of scar tissue and contractile reserve to predict long-term prognosis in patients with chronic myocardial infarction is lacking.

**Methods** A total of 177 patients with known coronary artery disease and scar tissue on LGE MRI were enrolled. Left ventricular (LV) functional parameters at rest and during low-dose DSMR were assessed, and the wall motion score index was calculated.

**Results** Eleven patients (6.2%) suffered an event during follow-up (average 20.3 months). Infarct size was a stronger predictor of events than LV ejection fraction and LV volumes at rest and during low-dose DSMR. Myocardial infarct size was used to separate patients at high risk (spatial extent ≥6 segments, n = 98) from those at low risk (spatial extent <6 segments, n = 79) for mortality. In the subgroup of patients at high risk, transmurality of infarct was not a predictor of events. However, the presence of contractile reserve (n = 63) was associated with a significantly higher number of events (12.7%) compared with no change in wall motion score index (6.7%; n = 15; p = 0.008).

**Conclusions** Myocardial infarct size on LGE MRI is a stronger predictor of clinical outcome than contractile reserve in medically treated patients with myocardial infarction. In patients with large myocardial scar, the presence of contractile reserve is more important for the prediction of events than scar tissue. (J Am Coll Cardiol 2009;54:1770–7) © 2009 by the American College of Cardiology Foundation

In early studies, left ventricular ejection fraction (LVEF) and left ventricular end-systolic volume (LVESV) have been demonstrated to be the strongest predictors of cardiac death (1,2). Preliminary findings in patients with acute myocardial infarction and moderate left ventricular (LV) dysfunction showed that infarct size assessed with late gadolinium-enhanced (LGE) magnetic resonance imaging (MRI) was a better predictor of adverse clinical outcome than LVEF (3).

In a previous study, it was shown that myocardial infarct size on LGE MRI, expressed as spatial extent, transmurality of scar tissue, or total scar score is a stronger predictor of events than LVEF and/or LV volumes in patients with chronic myocardial infarction (4).

However, low-dose dobutamine stress testing with echocardiography (5)—and more recently MRI—has been used for many years to detect contractile reserve (indicating hibernating myocardium) (6,7) and has been found to be superior for the prediction of functional recovery after revascularization than LGE (8). The presence of contractile reserve has also been demonstrated to have prognostic value: pooled analysis of 11 studies using dobutamine echocardiography demonstrated that patients with contractile reserve who underwent revascularization had good clinical outcome, whereas patients with contractile reserve who were treated medically had a high event rate (9). Information on the relative merits of scar tissue and contractile reserve to predict long-term prognosis in patients with chronic myocardial infarction is lacking.

Accordingly, this study evaluated the relative merits of scar tissue on LGE MRI and contractile reserve on low-dose dobutamine magnetic resonance (DSMR) for the

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prediction of long-term outcome of patients with chronic myocardial infarction who were treated medically.

## Methods

**Study population and design.** This was a prospective, follow-up study that involved 2 hospitals (German Heart Institute, Berlin, Germany and Leiden University Medical Center, Leiden, the Netherlands). Consecutive patients (n = 177) with chronic coronary artery disease were enrolled between 2000 and 2004, who were clinically referred for MRI to assess cardiac function, contractile reserve (using low-dose dobutamine), and the extent of scar tissue using LGE MRI (4). The patients in the current study were also included in a previous study evaluating the prognostic value of infarct size relative to LV function/volumes (4), whereas the current study evaluates the relative merits of hibernation and infarct size for prediction of prognosis. Patients with myocardial infarction <3 months before cardiac MRI were excluded. Other exclusion criteria were contraindications for MRI (noncompatible biometallic implants or claustrophobia, known arrhythmias) or contraindications for administration of dobutamine (severe arterial hypertension [≥220/120 mm Hg], unstable angina pectoris, significant aortic stenosis [aortic valve gradient >50 mm Hg or aortic valve area <1 $cm^2$], complex cardiac arrhythmias, significant hypertrophic obstructive cardiomyopathy, myocarditis, endocarditis, and pericarditis) (10). The study was approved by the local ethics committees of both institutions, and informed consent was obtained.

**MRI.** A 1.5-T Gyroscan ACS-NT/Intera MRI scanner (Philips Healthcare, Best, the Netherlands) equipped with a powertrack 6000 gradients and a 5-element cardiac synergy coil was used in both institutions. Patients were positioned in the supine position. Images were acquired during breath-holds of approximately 15 s using vectorcardiography gating.

The heart was imaged from apex to base, with 10 to 12 imaging levels (dependent on the heart size) in the short-axis view using a balanced, fast-field echo sequence with parallel imaging (sensitivity encoding [SENSE], acceleration factor 2). Typical parameters were a field of view of 400 × 400 $mm^2$, matrix of 256 × 256 pixels, slice thickness of 10.00 or 8.00 mm, no slice gap, flip angle of 50°, time to echo of 1.82 ms, and time to repeat of 3.65 ms. Temporal resolution was 25 to 39 ms.

Low-dose DSMR (continuous infusion of 10 μg/kg bodyweight per minute for 3 min) was performed in every patient. Magnetic resonance parameters were identical at rest and low-dose DSMR.

LGE images were acquired approximately 15 min after bolus injection of gadolinium diethylene triamine pentacetic acid (Magnevist, Bayer-Schering, Berlin, Germany; 0.15 mmol/kg [Leiden University Medical Center] or 0.20 mmol/kg [German Heart Institute]) with an inversion-recovery 3-dimensional spoiled gradient echo sequence; inversion time was determined with real-time plan scan. Typical parameters were a field of view of 400 × 400 $mm^2$, matrix of 256 × 256 pixels, slice thickness of 5.00 mm, overlapping slices (50%), flip angle of 15°, time to echo of 1.36 ms, and time to repeat of 4.53 ms.

**MRI analysis.** To determine global function, endocardial borders were outlined manually on short-axis cine images with previously validated software (MASS, Medis, the Netherlands, or ViewForum, Philips Healthcare) (11). Papillary muscles were regarded as part of the ventricular cavity, and epicardial fat was excluded. LVESV and left ventricular end-diastolic volume (LVEDV) were calculated. Subsequently, LVESV was subtracted from LVEDV and LVEF was calculated. End-diastolic wall thickness was measured quantitatively at the center of the infarct region.

For each of the 17 segments at rest and stress, LV wall motion was assessed with a visual scoring system in which 0 = normal wall motion, 1 = mild hypokinesia, 2 = severe hypokinesia, 3 = akinesia, and 4 = dyskinesia. Wall motion score index (WMSI) during each stage of the protocol was defined as the cumulative sum of individual segments scores divided by the number of interpreted segments. The change (delta) in WMSI and LV function from rest to low-dose DSMR was recorded. On a per-patient base, a decrease in WMSI was defined as contractile reserve (hibernation) and an increase as ischemia.

LGE images were scored visually by 2 experienced observers (blinded to other MRI and clinical data) using a 17-segment model (12). Each segment was graded on a 5-point scale (segmental scar score), with 0, absence of hyperenhancement; 1, hyperenhancement of 1% to 25% of LV wall thickness; 2, hyperenhancement extending from 26% to 50%; 3, hyperenhancement extending from 51% to 75%; and 4, hyperenhancement extending from 76% to 100% (13).

To quantify and define the extent/transmurality of scar tissue, the following definitions were used (14): 1) spatial (circumferential) extent, the number of affected segments; 2) nontransmurality, the number of segments with a segmental scar score of 1 or 2, and transmurality, the number of segments with a segmental scar score of 3 or 4; and 3) total scar score, summed segmental scar scores per patient divided by 17 (which reflects the damage per patient).

**Follow-up.** The long-term follow-up was performed by chart review and telephone contact. No patients were lost to follow-up. The primary end point was the occurrence of events, which were defined as cardiac death (caused by

**Abbreviations and Acronyms**

- **CI** = confidence interval
- **DSMR** = dobutamine magnetic resonance
- **LGE** = late gadolinium enhancement
- **LV** = left ventricle/ventricular
- **LVEDV** = left ventricular end-diastolic volume
- **LVEF** = left ventricular ejection fraction
- **LVESV** = left ventricular end-systolic volume
- **MRI** = magnetic resonance imaging
- **WMSI** = wall motion score index

end-stage heart failure, acute myocardial infarction, or sudden cardiac death) and noncardiac death and nonfatal myocardial infarction (4). Patients who underwent revascularization after MRI were censored since the purpose of this study was to determine the relative merits of scar tissue and contractile reserve in medically treated patients. Myocardial infarction was defined by clinical presentation, elevated cardiac enzyme levels, and/or typical changes on electrocardiography.

**Statistical analysis.** Statistical analysis was performed using SPSS for Windows (version 12.0.1, SPSS Inc., Chicago, Illinois). All continuous parameters are given as mean ± SD or median (25% to 75% percentile). Categorical data are summarized as frequencies and percentages. Differences in baseline characteristics between patients who reached the primary end point and those who did not were analyzed using Wilcoxon Mann-Whitney test for continuous variables and chi-square test for dichotomous variables.

We aimed to study to what extent MRI results were associated with events. For this purpose, all MRI data with a value of $p < 0.1$ (in a comparison between patients with and without the occurrence of events) were eligible. Cox proportional hazards regression models were constructed for MRI variables, with spatial extent of scar as main exposure, and LVEF and LV dimensions, total number of dysfunctional segments at rest, and WMSI at rest as confounding factors. The latter variables appeared to be associated with events at a value of $p < 0.1$ level in univariable analysis (and we had to limit the number of covariables because of the relatively small number of end point events). Unadjusted and adjusted hazard ratios with their corresponding 95% confidence intervals (CIs) are reported. To check the proportional hazard assumption (i.e., that the hazard ratio for 2 subjects with fixed predictors is constant over time) log(_log[survival probability]) for different categories was plotted against time to ensure that the curves were reasonably parallel. In general, all proportionality assumptions were appropriate. After adjustment for multiple confounders (discussed in the previous text), spatial extent as determined by MRI appeared significantly related with events. Therefore, in a post-hoc analysis, the study population was divided into 2 groups, based on the observed median value of the spatial extent of scar. Patients were stratified according to a large extent of scar tissue (spatial extent ≥6 segments) or a small extent of scar tissue (spatial extent <6 segments) on LGE. The survival of both cohorts was further analyzed by the method of Kaplan-Meier. Difference in survival over time was evaluated by a log-rank test. Patients with ≥6 segments with scar (n = 98) were stratified according to transmurality of scar (more nontransmural infarcted segments or more transmural infarcted segments on LGE) and the presence of recruitable myocardium (hibernation or ischemia) at low-dose dobutamine stimulation. The chi-square test was used to compare the event rates in both groups. For all tests, a value of $p < 0.05$ was considered statistically significant. All tests were 2-sided.

## Results

**Study population.** Clinical data are presented in Table 1; 177 patients presenting LGE were included (n = 111 at the German Heart Institute Berlin and n = 66 at the Leiden University Medical Center).

**Table 1 Clinical Data**

| Variable | Total Population (n = 177) | Events | | p Value |
|---|---|---|---|---|
| | | Yes (n = 11) | No (n = 166) | |
| Age (yrs) | 64 (57–68) | 67 (58–70) | 64 (57–68) | 0.306 |
| Men | 155 (88%) | 10 (91%) | 145 (87%) | 0.731 |
| Diabetes mellitus | 16% | 27% | 16% | 0.316 |
| Hypertension | 58% | 27% | 60% | 0.032 |
| Hypercholesterolemia | 85% | 64% | 87% | 0.036 |
| Smoker | 49% | 46% | 49% | 0.831 |
| Previous Q-wave MI | 54% | 55% | 54% | 0.989 |
| Extent of CAD (on angiogram) | | | | |
| 1-vessel disease | 13% | 0% | 16% | |
| 2-vessel disease | 29% | 30% | 29% | 0.196 |
| 3-vessel disease | 58% | 70% | 55% | |
| Medications | | | | |
| Beta-blocker | 80% | 73% | 81% | 0.522 |
| Calcium channel blocker | 22% | 36% | 21% | 0.231 |
| ACE inhibitor | 78% | 64% | 79% | 0.239 |
| Aspirin/warfarin | 99% | 100% | 99% | 0.798 |
| Statin | 86% | 46% | 89% | <0.001 |
| Nitrate | 32% | 27% | 32% | 0.785 |
| Diuretic | 39% | 73% | 37% | 0.018 |

Continuous data are expressed as median (interquartile range); categorical data are expressed as percent of patients with complete data.
ACE = angiotensin-converting enzyme; CAD = coronary artery disease; MI = myocardial infarction.

**Clinical outcome of patients during follow-up.** The average duration of follow-up was 20.3 ± 13.3 months, median: 18 months (10; 33); 11 patients (6.2%) suffered from an event during follow-up. Eight patients (4.5%) had cardiac death, and noncardiac death was reported in 2 patients (1.1%). One patient (0.5%) developed myocardial infarction during follow-up. Furthermore, 11 patients (6.2%) were hospitalized during follow-up because of ventricular arrhythmias (n = 7, 4.0%) or unstable angina (n = 4, 2.3%). Fifty-five patients (31.1%) underwent revascularization after MRI and were censored at the time of revascularization.

**MRI variables.** MRI findings are listed in Table 2. Median LVEF in the total study population was 45% (25th to 75th percentile, 35% to 57%). LVEF was significantly higher in patients without events than in patients with events. Median LVESV and LVEDV were significantly lower in patients without events than in patients with events. No significant difference in end-diastolic wall thickness values between patients without events and patients with events was detected. The WMSI was significantly lower in patients without events than patients with events at rest, but not at low-dose dobutamine. We found no significant difference for change in WMSI between patients without events and patients with events. The median spatial extent of scar tissue was significantly higher in patients with events than in patients without events.

**Predictors of events.** As demonstrated in Table 1, hypertension, hypercholesterolemia, and use of diuretics were significantly higher in patients without events than in patients with events, and the use of statins was less common. Diuretic and statin usage were significantly associated with events (Table 3). However, neither diuretic usage, nor statin usage, was a true confounder for the relation between spatial extent of scar tissue and events (Table 4).

**Table 3 Univariate Analysis for Prediction of Events**

| MRI Variable | Hazard Ratio | 95% Confidence Interval | p Value |
|---|---|---|---|
| LV function | | | |
| LVEF (%) | 0.966 | 0.925–1.009 | 0.117 |
| LVESV (ml) | 1.007 | 1.001–1.013 | 0.032 |
| LVEDV (ml) | 1.007 | 1.000–1.014 | 0.044 |
| No. of dysfunctional segments | 1.178 | 1.017–1.363 | 0.029 |
| WMSI at rest | 3.077 | 1.087–8.707 | 0.034 |
| WMSI at stress | 2.796 | 0.903–8.658 | 0.075 |
| Scar | | | |
| Spatial extent | 1.271 | 1.064–1.518 | 0.008 |
| Clinical variables | | | |
| Hypertension | 2.475 | 0.649–9.435 | 0.184 |
| Hypercholesterolemia | 3.251 | 0.945–11.178 | 0.061 |
| Medications | | | |
| Diuretics | 5.259 | 1.390–19.898 | 0.014 |
| Statins | 0.166 | 0.050–0.548 | 0.003 |

p values are unadjusted.
Abbreviations as in Table 2.

As demonstrated in Table 3, LVESV, LVEDV, the number of dysfunctional segments at rest and WMSI at rest, but not at stress, and spatial extent of scar tissue were significantly associated with events. LVEF was not related with the occurrence of events.

After adjustment for multiple (true or potential) confounders (see the Methods section), infarct size defined as spatial extent remained the most important outcome determinant (Table 5). Infarct size appears to be a stronger predictor of events than LVEF and LV volumes.

Next, patients were separated according to the extent of scar (patients with large myocardial infarction = patients at high risk, spatial extent ≥6 segments, n = 98) and were compared with patients with small myocardial infarction = patients at low risk (spatial extent <6 segments, n = 79) for

**Table 2 Magnetic Resonance Imaging Data**

| Variable | Total Population (n = 177) | Events | | p Value |
|---|---|---|---|---|
| | | Yes (n = 11) | No (n = 166) | |
| LV function | | | | |
| LVEF (%) | 45 (35 to 57) | 40 (21 to 46) | 45 (35 to 58) | 0.026 |
| LVESV (ml) | 101 (66 to 141) | 133 (102 to 294) | 98 (65 to 138) | 0.002 |
| LVEDV (ml) | 186 (150 to 233) | 225 (173 to 372) | 184 (149 to 230) | 0.004 |
| End-diastolic wall thickness (mm) | 4.3 (3.1 to 5.7) | 5 (2.4 to 5.8) | 4.3 (3.1 to 5.7) | 0.786 |
| No. of dysfunctional segments at rest | 6 (3 to 8.5) | 10 (6 to 13) | 5 (3 to 8) | 0.003 |
| WMSI at rest | 0.71 (0.29 to 1.06) | 1.06 (0.47 to 1.65) | 0.65 (0.29 to 1.06) | 0.017 |
| WMSI at stress | 0.59 (0.24 to 1.06) | 0.94 (0.29 to 1.53) | 0.59 (0.23 to 1.06) | 0.067 |
| Δ WMSI | −0.06 (−0.23 to 0.00) | −0.12 (−0.29 to 0.06) | −0.06 (−0.19 to 0.00) | 0.134 |
| Scar | | | | |
| Spatial extent | 6 (4 to 8) | 8 (6 to 13) | 6 (4 to 7) | 0.001 |
| Transmurality | 3 (1 to 5) | 3 (1 to 8) | 3 (1 to 5) | 0.277 |
| Total scar score | 0.76 (0.44 to 1.27) | 1 (0.53 to 1.65) | 0.76 (0.41 to 1.23) | 0.195 |

Data are expressed as median (interquartile range).
LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; WMSI = wall motion score index.

**Table 4** Relation Between Diuretic Usage, Statin Usage, and Infarct Size (Spatial Extent of Scar Tissue) on LGE MRI

| Scar | Patients Using Diuretics | Patients Not Using Diuretics | p Value |
|---|---|---|---|
| Spatial extent | 7 (4–9) | 5 (3–7) | 0.116 |
| | **Patients Using Statins** | **Patients Not Using Statins** | |
| Spatial extent | 6 (4–8) | 6 (4–9) | 0.536 |

Data are expressed as median (interquartile range).

events. The 4-year cumulative event rate was significantly higher in patients with a spatial extent of scar ≥6 segments (p = 0.03) (Fig. 1).

In the patient group at high risk for events (spatial extent of scar ≥6 segments), those with more nontransmural infarcted segments had a nonsignificant higher event-rate (12.5%, n = 40) than those with more transmural infarcted segments (8.6%, n = 58) (p = 0.53). However, the presence of contractile reserve during low-dose dobutamine (n = 63) was associated with a significantly higher number of events (12.7%) compared with no change in WMSI (6.7%, n = 15, p = 0.008) or increase in WMSI (ischemia) (5.0%, n = 20, p = 0.008). At univariate analysis, contractile reserve was the only predictor of events in this patient population (chi-square 4.0, 95% CI: 1.1 to 15.1, p = 0.04), whereas ischemia, no response to low-dose DSMR, and scar transmurality did not predict outcome (chi-square 0.7, 95% CI: 0.1 to 5.8, p = 0.08; chi-square 0.8, 95% CI: 0.1 to 6.2, p = 0.8; chi-square 2.1, 95% CI: 0.6 to 6.7, p = 0.2 [nontransmural scar]; and chi-square 2.0, 95% CI: 0.6 to 6.4, p = 0.3 [transmural scar], respectively). The chi-square value was not significantly different between patients with more nontransmural infarcted segments and patients with more transmural infarcted segments (p = NS). However, the chi-square value was significantly higher in patients showing contractile reserve as compared with ischemia (p < 0.001) or no response (p < 0.001) during low-dose dobutamine stimulation (Fig. 2).

## Discussion

The main finding in this study is that myocardial infarct size on LGE MRI is a stronger predictor of clinical outcome

**Table 5** Multivariable Cox Proportional Hazard Model for Prediction of Events

| MRI Variable | Hazard Ratio | 95% Confidence Interval | p Value |
|---|---|---|---|
| Scar spatial extent | 1.303 | 1.026–1.655 | 0.030 |
| LVEF (%) at rest | 1.102 | 0.972–1.250 | 0.130 |
| LVESV (ml) at rest | 1.029 | 0.980–1.080 | 0.252 |
| LVEDV (ml) at rest | 0.987 | 0.949–1.026 | 0.501 |

This model is using the spatial extent as variable of scar tissue on late gadolinium-enhanced magnetic resonance imaging.
Abbreviations as in Table 2.

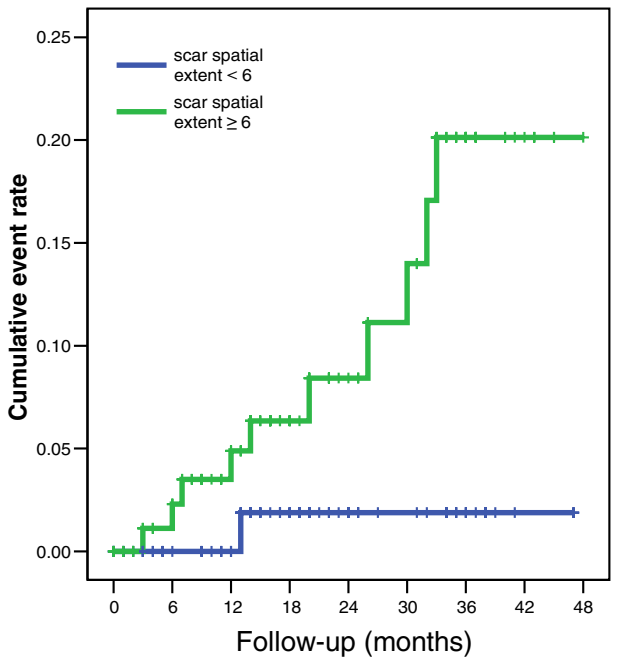


**Figure 1** Prognostic Value of Myocardial Infarct Size

Kaplan-Meier curve analysis (48 months) showing the difference in cumulative event rate when patients are stratified according to a large extent of scar tissue (spatial extent ≥6 segments) or a small extent of scar tissue (spatial extent <6 segments) on late gadolinium-enhanced magnetic resonance imaging. p = 0.03.

than contractile reserve (hibernation) on low-dose DSMR in medically treated patients with chronic myocardial infarction. In patients with large myocardial scar, however, the presence of contractile reserve on low-dose DSMR is more important for the prediction of events than scar tissue on LGE MRI.

**Importance of scar tissue.** There is growing clinical evidence that tissue characterization with LGE MRI provides information valuable to patient outcome (15). Separate clinical reports demonstrate the unique and important prognostic value of microvascular obstruction identified on LGE imaging in patients who experienced a recent myocardial infarction (16,17). Wu et al. (16) studied patients with acute myocardial infarction and demonstrated that infarct size determined by LGE MRI directly relates to long-term prognosis in contrast to LV volumes and LVEF. Assessment of infarct size using LGE MRI can also predict functional recovery after acute myocardial infarction: Gerber et al. (18) evaluated 20 patients after acute myocardial infarction with LGE MRI and myocardial tagging and noted that improvement in circumferential shortening was inversely related to the regional extent of hyperenhancement on LGE images.

The prognostic value of infarct size has also been demonstrated in patients with chronic myocardial infarction. In previous work, we demonstrated in 231 patients with

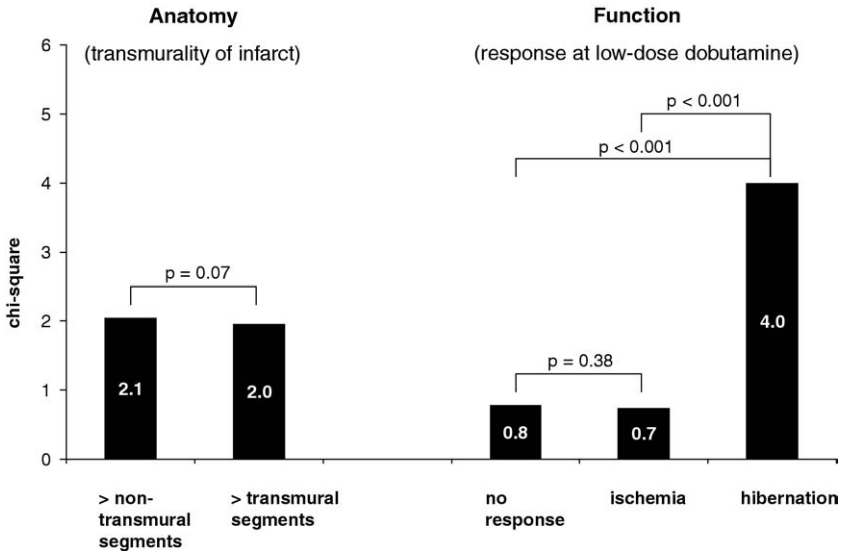


**Figure 2** **Prognostic Value: Contractile Reserve Versus Infarct Size**

Bar graphs illustrating the incremental prognostic value (depicted by chi-square value on the y-axis) of low-dose dobutamine in patients with large myocardial infarction (≥6 segments with scar).

chronic myocardial infarction that the extent of scar tissue on LGE MRI was a stronger predictor of events than LV function and/or dimensions (4).

In addition, recent data have identified scar tissue and severely depressed LVEF as important predictors of death or ventricular arrhythmias in patients with coronary artery disease (19). Bello et al. (20) showed that infarct size, determined with LGE MRI was superior to LVEF for identification of patients with a substrate for inducible ventricular tachycardia. Yan et al. (21) demonstrated that the extent of the peri-infarct zone characterized by LGE MRI provides incremental prognostic value beyond LVEF and LVESV. Another study in patients with chronic myocardial infarction found that infarct heterogeneity on LGE MRI was strongly related to inducibility for monomorphic ventricular tachycardia during electrophysiological or device testing (22).

Furthermore, LGE MRI was able to characterize occult myocardial scar consistent with myocardial infarction in diabetic patients without clinical evidence of myocardial infarction and provided significant prognostic value (23). Finally, Kim et al. (24) studied 185 patients with suspected coronary artery disease but without a history of clinical myocardial infarction using MRI and showed that the presence of non–Q-wave myocardial infarction was a strong predictor of mortality.

**Importance of contractile reserve (hibernation).** Low-dose DSMR enables detection of hibernation by assessment of contractile reserve in dysfunctional segments in response to dobutamine stimulation. Previous studies reported on the predictive value of low-dose DSMR for functional recovery in patients with acute myocardial infarction (7,25). Dendale et al. (7) studied 26 patients with an acute myocardial infarction using low-dose DSMR and concluded that the presence of contractile reserve predicts recovery of function after revascularization with 80% accuracy. Baer et al. (26,27) evaluated this technique in patients with chronic myocardial infarction and demonstrated that low-dose DSMR can also adequately predict improvement of LV function after revascularization.

However, information on the predictive value of low-dose DSMR for clinical outcome in patients with depressed LVEF is lacking. Nonetheless, previous 2-dimensional echocardiographic studies using low-dose dobutamine stimulation demonstrated that the presence of contractile reserve in patients with chronic myocardial infarction relates to long-term prognosis (28–30). Rizzello et al. (28) studied 128 patients with chronic myocardial infarction using echocardiography and undergoing revascularization and concluded that the presence of contractile reserve was associated with a favorable prognosis after revascularization. In addition, Sawada et al. (31) reported in 98 patients who underwent low-dose dobutamine echocardiography and subsequent revascularization that patients with larger areas with contractile reserve had favorable clinical outcome. Furthermore, multivariable analysis showed that the extent of contractile reserve had incremental prognostic value for long-term clinical outcome over clinical information and resting LV function.

A pooled analysis of 11 studies using dobutamine echocardiography (9) demonstrated that patients with contractile reserve who underwent revascularization had a good prognosis (annual event rate 6%), whereas patients with contractile reserve who were treated medically had a poor outcome

(annual event rate 17%). These results indicate that revascularization of hibernating myocardium may prevent future ischemic events or ventricular arrhythmias (9). Alternatively, patients with hibernating myocardium who are treated medically are at high risk for events. The results of the present study confirm that the presence of contractile reserve (hibernation) in medically treated patients with large myocardial infarction is associated with a significantly higher event rate compared with patients without contractile reserve.

**Scar tissue versus contractile reserve.** Kaandorp et al. (32) performed a head-to-head comparison between LGE and low-dose DSMR in 48 patients with chronic myocardial infarction and observed that the majority of segments with minimal scar tissue on LGE MRI showed contractile reserve on low-dose DSMR, whereas contractile reserve was practically absent in segments with transmural scar tissue on LGE MRI. However, in segments with an intermediate amount of scar tissue, an intermediate proportion of the segments (42%) showed contractile reserve during low-dose DSMR, suggesting additional value of low-dose DSMR for prediction of functional recovery in these segments. Indeed, Wellnhofer et al. (8) studied 29 patients with chronic myocardial infarction before and after revascularization and demonstrated that assessment of contractile reserve with low-dose DSMR was superior to scar quantification for the prediction of functional recovery, especially in segments with nontransmural scar tissue.

Until now, however, information on the relative value of scar tissue and contractile reserve (using LGE MRI and low-dose DSMR) for the prediction of clinical outcome was lacking. The results of the present study suggest that scar tissue (on LGE MRI) is more important than contractile reserve on low-dose DSMR for the prediction of events in medically treated patients with chronic myocardial infarction. However, in patients with large myocardial scar, contractile reserve (hibernation) is a better predictor of events than scar tissue on LGE MRI.

**Study limitations.** A limitation of the present study is that the extent of myocardial ischemia was not evaluated using high-dose dobutamine magnetic resonance. Accordingly, further MRI studies are needed to assess the prognostic value of integrated assessment of ischemia using high-dose dobutamine stimulation, hibernation, and scar tissue. Furthermore, segmental wall motion was visually analyzed, and additional studies evaluating myocardial strain using quantitative assessment of wall motion by MRI tagging combined with rapid post-processing algorithms may overcome this limitation (33,34). In addition, myocardial strain may have prognostic value since strain assessment enables evaluation of border zone function, which has been related to inducibility of monomorphic ventricular tachycardia (35). Furthermore, the small number of events in patients with small myocardial infarcts (<6 segments) limits the evaluation of the prognostic value of hibernation relative to scar transmurality in these patients. Larger studies with subsequently higher event rates are needed to clarify the relative merits of scar transmurality and hibernation in patients with small myocardial infarcts. Finally, evaluation of infarct tissue heterogeneity using LGE MRI (21,22,36) also enables prediction of events, and future studies are needed to evaluate the prognostic value of infarct tissue heterogeneity compared with hibernation and total infarct size.

## Conclusions

Myocardial infarct size on LGE MRI is a stronger predictor of clinical outcome than contractile reserve on low-dose DSMR in medically treated patients with chronic myocardial infarction. In patients with large myocardial scar, however, the presence of contractile reserve (hibernation) is more important for the prediction of events than scar tissue. Larger studies are needed to confirm the results of the present study.

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**Key Words:** cardiac magnetic resonance ■ prognosis ■ delayed enhancement ■ contractile reserve.