Magnetic resonance imaging techniques for risk stratification in cardiovascular disease

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Chapter

13

Prognostic value of myocardial infarct size and contractile reserve using magnetic resonance imaging

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Abstract

Purpose
The purpose of this study was to assess the predictive value of myocardial infarct size assessed with contrast-enhanced magnetic resonance imaging (MRI) in medically treated patients with chronic myocardial infarction relative to contractile reserve (hibernation) on low-dose dobutamine MR (DSMR) for long-term event-free survival.

Methods
A total of 177 patients with known coronary artery disease and scar tissue on contrast-enhanced 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). Cox proportional hazard analysis revealed that the spatial extent of scar tissue was a stronger predictor of events than LV ejection fraction (LVEF) and LV volumes at rest and during low-dose DSMR. The spatial extent of scar tissue on contrast-enhanced MRI was used to separate patients at high risk (spatial extent ≥ the median 6, n = 98) from those at low risk (spatial extent < 6, n =79) for mortality. In the subgroup of 98 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 patients, p = 0.008).

Conclusions
Myocardial infarct size on contrast-enhanced MRI is a stronger predictor of clinical outcome than contractile reserve 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 (on contrast-enhanced MRI).

Introduction

In early studies, left ventricular (LV) ejection fraction (LVEF) and LV 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 LV dysfunction showed that infarct size assessed with contrast-enhanced 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 contrast-enhanced 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 contrast-enhanced MRI (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 contrast-enhanced MRI and contractile reserve on low-dose dobutamine MR (DSMR) for the 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 contrast-enhanced 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

(non-compatible biometallic implants or claustrophobia, known arrhythmias), or contra-indications for administration of dobutamine (severe arterial hypertension [≥ 220/120 mmHg], unstable angina pectoris, significant aortic stenosis [aortic valve gradient > 50 mmHg 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.

Magnetic resonance imaging: data acquisition

A 1.5T Gyroscan ACS-NT/Intera MRI scanner (Philips Healthcare, Best, The Netherlands) equipped with powertrack 6000 gradients and 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 seconds using vector electrocardiographic 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 (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 minutes) was performed in every patient. Magnetic resonance parameters were identical at rest and low-dose DSMR.

Contrast-enhanced images were acquired approximately 15 minutes after bolus injection of gadolinium DTPA (Magnevist, Bayer-Schering, Berlin, Germany; 0.15 mmol/kg [Leiden University Medical Center] or 0.20 mmol/kg [German Heart Institute Berlin]) 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.

Magnetic resonance imaging: data analysis

To determine global function, endocardial borders were outlined manually on short-axis cine images with previously validated software (MASS, Medis, Leiden, The Netherlands or ViewForum, Philips, Best, The Netherlands) (11). Papillary muscles were regarded as part of the ventricular cavity, and epicardial fat was excluded. LVESV and LV end-diastolic volume (LVEDV) were calculated. Subsequently, LVESV was subtracted from LVEDV and LVEF was calculated. End-diastolic wall thickness (EDWT) 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: 0: normal wall motion, 1: mild hypokinesia, 2: severe hypokinesia, 3: akinesia, 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.

Contrast-enhanced 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) non-transmurality, 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 endpoint was the occurrence of events, which were defined as cardiac death (caused by 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 and 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 (release 12.0.1; SPSS Inc., Chicago, Illinois, USA). All continuous parameters are given as mean ± standard deviation (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 endpoint 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 p-value < 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 the p < 0.1 level in univariable analysis (and we had to limit the number of covariables because of the relatively small number of endpoint events). Unadjusted and adjusted hazard ratios with their corresponding 95% confidence intervals (CI) 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 previously), 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 contrast-enhanced MRI. 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 patients) were stratified according to transmurality of scar (more non-transmural infarcted segments or more transmural infarcted segments on contrast-enhanced MRI) 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, p < 0.05 was considered statistically significant. All tests were 2-sided.

Results

Study population
Clinical data are presented in Table 1; 177 patients were included (111 at the German Heart Institute Berlin, Germany; and 66 at the Leiden University Medical Center, The Netherlands).

Table 1. Baseline clinical variables.

Variables	Total population (n = 177)	Patients with events (n = 11)	Patients without events (n = 166)	P-value
Age (years)	64 (57, 68)	67 (58, 70)	64 (57, 68)	0.306
Men	88	91	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-vesesl disease	58	70	55	
Medications				
ß-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 % of study population.
ACE: angiotensin converting enzyme, MI: myocardial infarction, CAD: coronary artery disease.

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 (7 patients, 4.0%) or unstable angina (4 patients, 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 EDWT

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.

Table 2. Baseline MRI variables.

Variables	Total population (n = 177)	Patients with events (n = 11)	Patients without events (n = 166)	P-value
LVEF (%)	45 (35, 57)	40 (21, 46)	45 (35, 58)	0.026
LV ESV (ml)	101 (66, 141)	133 (102, 294)	98 (65, 138)	0.002
LV EDV (ml)	186 (150, 233)	225 (173, 372)	184 (149, 230)	0.004
End-diastolic wall thickness (mm)	4.3 (3.1, 5.7)	5 (2.4, 5.8)	4.3 (3.1, 5.7)	0.786
No. of dysfunctional segments at rest	6 (3, 8.5)	10 (6, 13)	5 (3, 8)	0.003
WMSI at rest	0.71 (0.29, 1.06)	1.06 (0.47, 1.65)	0.65 (0.29; 1.06)	0.017
WMSI at stress	0.59 (0.24, 1.06)	0.94 (0.29, 1.53)	0.59 (0.23; 1.06)	0.067
Δ WMSI	-0.06 (-0.23, 0.00)	-0.12 (-0.29, -0.06)	-0.06 (-0.19; 0.00)	0.134
Scar tissue				
Spatial extent	6 (4, 8)	8 (6, 13)	6 (4, 7)	0.001
Transmurality	3 (1, 5)	3 (1, 8)	3 (1, 5)	0.277
Total scar score	0.76 (0.44, 1.27)	1 (0.53, 1.65)	0.76 (0.41, 1.23)	0.195

Data are expressed as median (interquartile range).
LV EDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction, WMSI: wall motion score index.

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).

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.

Table 3. Univariate analysis for prediction of events.

Variables	Hazard ratio	95% confidence interval	P-value
LV function			
LVEF (%)	0.966	0.925-1.009	0.117
LV ESV (ml)	1.007	1.001-1.013	0.032
LV EDV (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

LV EDV: left ventricular end-diastolic volume, LV ESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction, WMSI: wall motion score index. P-values are unadjusted.
No.of dysfunctional segments

Table 4. Relation between diuretic usage, statin usage, and infarct size (spatial extent of scar tissue) on contrast-enhanced MRI.

	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).

After adjustment for multiple (true or potential) confounders (see 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.

Table 5. Multivariable Cox proportional hazard model for prediction of events:

MRI variables	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
LV ESV (ml) at rest	1.029	0.980-1.080	0.252
LV EDV (ml) at rest	0.987	0.949-1.026	0.501

This model uses the spatial extent as variable of scar tissue on contrast-enhanced MRI. LV ESV: left ventricular end-systolic volume, LVEDV: left ventricular end-diastolic volume, LVEF: left ventricular ejection fraction.

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

Figure 1.
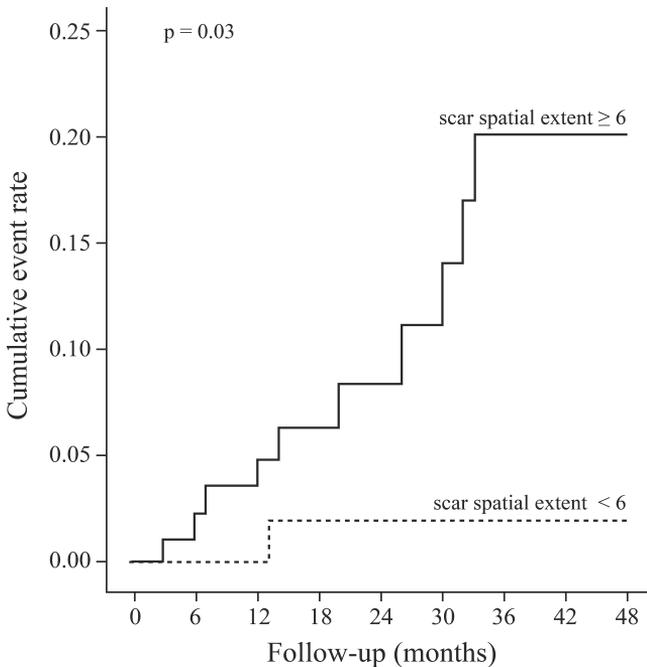
Kaplan-Meier curve analysis (48 months) showing the difference in cumulative event rate when patients are stratified according to a large extent of scar tissue (spatial extent ≥ 6 segments) or a small extent of scar tissue (spatial extent < 6 segments) on contrast-enhanced MRI.

In the patient group at high risk of events (spatial extent of scar ≥ 6 segments) those with more non-transmural infarcted segments had a non-significant 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, CI 1.1-15.1, p = 0.04), whereas ischemia, no response to low-dose DSMR and scar transmurality did not predict outcome (chi-square 0.7, CI 0.1-5.8, p = 0.08; chi-square 0.8, CI 0.1-6.2, p = 0.8; chi-square 2.1, CI 0.6-6.7, p = 0.2 [non-transmural scar], chi-square 2.0, CI 0.6-6.4, p = 0.3 [transmural scar], respectively). The chi-square value was not significantly different between patients with more non-transmural 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 (Figure 2).

Figure 2.
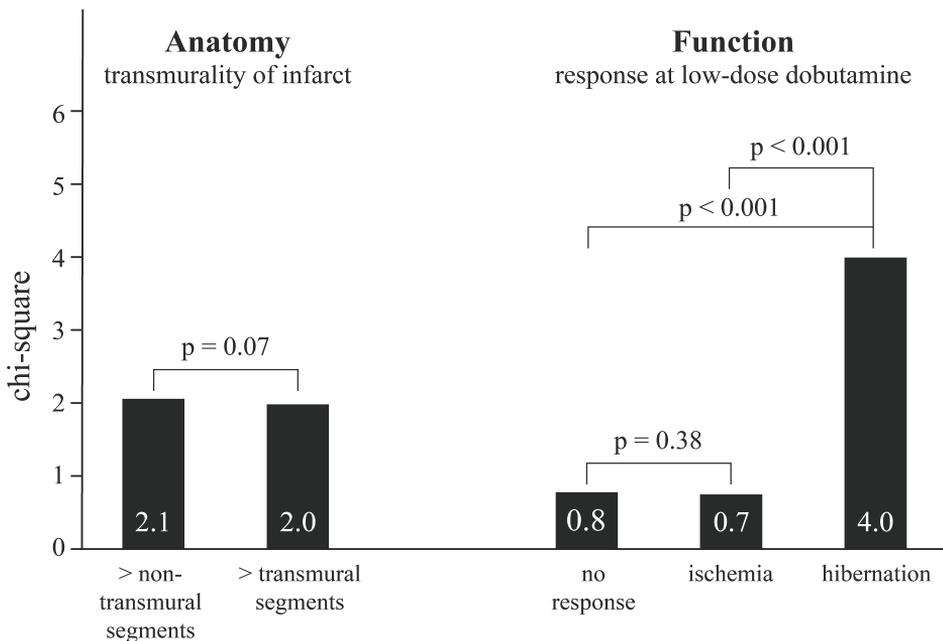
Bar graphs illustrating the incremental prognostic value (depicted by chi-square value on the y-axis) of low-dose dobutamine in patients with large myocardial infarction (≥ 6 segments with scar).

Discussion

The main finding in this study is that myocardial infarct size on contrast-enhanced MRI is a stronger predictor of clinical outcome 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 contrast-enhanced MRI.

Importance of scar tissue

There is growing clinical evidence that tissue characterisation with contrast-enhanced MRI provides information valuable to patient outcome (15). Separate clinical reports demonstrate the unique and important prognostic value of microvascular obstruction identified on contrast-enhanced MRI in patients who experienced a recent myocardial infarction (16,17). Wu and co-workers (16) studied patients with acute myocardial infarction and demonstrated that infarct size determined by contrast-enhanced MRI directly relates to long-term prognosis in contrast to LV volumes and LVEF. Assessment of infarct size using contrast-enhanced MRI can also predict functional recovery after acute myocardial infarction: Gerber et al. (18) evaluated 20 patients after acute myocardial infarction with contrast-enhanced MRI and myocardial tagging and noted that improvement in circumferential shortening was inversely related to the regional extent of hyperenhancement on contrast-enhanced 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 chronic myocardial infarction that the extent of scar tissue on contrast-enhanced 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 contrast-enhanced 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 contrast-enhanced MRI provides incremental prognostic value beyond LVEF and LVESV. Another study in patients with chronic myocardial infarction found that infarct heterogeneity on contrast-enhanced MRI was strongly related with inducibility for monomorphic ventricular tachycardia during electrophysiological or device testing (22).

Furthermore, contrast-enhanced 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). Rizello 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 favourable prognosis after revascularization. In addition, Sawada and co-workers (31) reported in 98 patients who underwent low-dose dobutamine echocardiography and subsequent revascularization that patients with larger areas with contractile reserve had favourable 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.

Pooled analysis of 11 studies using dobutamine echocardiography 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%) (9). 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 of 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 contrast-enhanced MRI and low-dose DSMR in 48 patients with chronic myocardial infarction and observed that the majority of segments with minimal scar tissue on contrast-enhanced MRI showed contractile reserve on low-dose DSMR, whereas contractile reserve was practically absent in segments with transmural scar tissue on contrast-enhanced 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 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 non-transmural scar tissue.

Until now however, information on the relative value of scar tissue and contractile reserve (using contrast-enhanced MRI and low-dose DSMR) for the prediction of clinical outcome was lacking. The results of the present study suggest that scar tissue (on contrast-enhanced 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 contrast-enhanced MRI.

Limitations

A limitation of the present study is that the extent of myocardial ischemia was not evaluated using high-dose DSMR. 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 with 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 contrast-enhanced MRI (21,22,36) also enables prediction of events, and future studies are needed to evaluate the prognostic value of infarct tissue heterogeneity compared to hibernation and total infarct size.

Conclusions

Myocardial infarct size on contrast-enhanced 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 however needed to confirm the results of the present study.

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Chapter