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Magnetic resonance imaging techniques for risk stratification in cardiovascular disease

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Chapter 12

Comparison of myocardial infarct size assessed with contrast-enhanced magnetic resonance imaging and left ventricular function and volumes to predict mortality in patients with healed myocardial infarction

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Abstract

Currently, left ventricular (LV) ejection fraction (EF) and/or LV volumes are the established predictors of mortality in patients with coronary artery disease (CAD) and severe LV dysfunction. With contrast-enhanced magnetic resonance imaging (MRI), precise delineation of infarct size is now possible. The relative merits of LVEF/LV volumes and infarct size to predict long-term outcome are unknown. The purpose of this study was to determine the predictive value of infarct size assessed with contrast-enhanced MRI relative to LVEF and LV volumes for long-term survival in patients with healed myocardial infarction. Cine MRI and contrast-enhanced MRI was performed in 231 patients with healed myocardial infarction. LVEF and LV volumes were measured and infarct size was derived from contrast-enhanced MRI. Nineteen patients (8.2%) died during a median follow-up of 1.7 years (interquartile range 1.1–2.9). Cox proportional hazards analysis revealed that infarct size defined as spatial extent (hazard ratio [HR] 1.3, 95% confidence interval [CI] 1.1–1.6, chi-square 6.7, $p = 0.010$), transmurality (HR 1.5, 95% CI 1.1–1.9, chi-square 8.9, $p = 0.003$) or total scar score (HR 6.2, 95% CI 1.7–23, chi-square 7.4, $p = 0.006$), were stronger predictors of all-cause mortality than LVEF and LV volumes. In conclusion, infarct size on contrast-enhanced MRI may be superior to LVEF and LV volumes for predicting long-term mortality in patients with healed myocardial infarction.

Introduction

The main cause of death in patients with coronary artery disease (CAD) and severely depressed left ventricular (LV) function is end-stage heart failure, whereas sudden cardiac death is more common in patients with CAD and preserved or moderately depressed LV function (1-5). Risk stratification of patients with CAD is necessary for optimization of treatment. Previous studies showed that LV function and LV end-systolic volume (ESV) were the strongest predictors of cardiac death (6,7). However, other variables to optimize risk stratification are needed to identify patients at high risk for mortality among patients with preserved and moderately depressed LV function. 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 LV function (8). However, the prognostic value of infarct size determined with contrast-enhanced MRI in patients with healed myocardial infarction is unknown. Accordingly, this study examines the predictive value of infarct size assessed with contrast-enhanced MRI relative to LV function and volumes for long-term survival of patients with healed myocardial infarction.

Methods

Study population

This was a prospective, follow-up study that involved 2 hospitals. Consecutive patients (n = 231), referred for MRI to evaluate cardiac function and extent of scar tissue for clinical reasons, with a history of CAD and evidence of scar tissue on contrast-enhanced MRI were enrolled. Patients with myocardial infarction < 3 months before cardiac MRI were excluded. Other exclusion criteria were (supra-) ventricular arrhythmias, pacemakers, intracranial clips, and claustrophobia. Patient characteristics are listed in Table 1. 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 Medical Systems, Best, The Netherlands) equipped with powertrack 6000 gradients and 5-element cardiac synergy coil was used. 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 (9), 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. Geometric settings of baseline scans were stored and repeated for contrast-enhanced images to ensure matching of the same slices (and hence, myocardial segments).

Contrast-enhanced images were acquired approximately 15 minutes after bolus injection of gadolinium diethylenetriamine penta-acetic acid (Magnevist, Schering, Berlin, Germany; 0.15 mmol/kg or 0.20 mmol/kg) with an inversion-recovery 3D 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 / ViewForum, Philips, Best, The Netherlands) (10). Papillary muscles were regarded as part of the ventricular cavity, and epicardial fat was excluded. LV ESV and LV end-diastolic volume (EDV) were calculated. Subsequently, ESV was subtracted from EDV and LV ejection fraction (EF) was calculated.

End-diastolic wall thickness (EDWT) was measured quantitatively at the center of the infarct region.

Contrast-enhanced images were scored visually by 2 experienced observers (blinded to other MRI and clinical data) using the 17-segment model as recently proposed (11). 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 to 26% to 50%, 3: hyperenhancement extending to 51% to 75%, and 4: hyperenhancement extending to 76% to 100% (12).

To quantify and define the extent/transmurality of scar tissue, the following definitions were used (13): 1) Spatial (circumferential) extent: the number of affected segments; 2) transmurality: the number of segments with a segmental scar score of 3 or 4; 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 all-cause mortality, which was defined as death caused by end-stage heart failure or acute myocardial infarction, sudden cardiac death, and noncardiac death. Myocardial infarction was defined by clinical presentation, elevated cardiac enzyme levels and/or typical changes on electrocardiography. Sudden cardiac death was defined as unexpected

natural death from a cardiac cause within 1 hour from the onset of symptoms, in a person without any prior condition that would appear fatal (14).

Statistical analysis

Most continuous variables had non-normal distribution (as evaluated by Kolmogorov-Smirnov tests). For reasons of uniformity, summary statistics for all continuous variables are therefore presented as medians together with the 25th and 75th percentiles. 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 analysed using Wilcoxon-Mann-Whitney tests or Fisher's exact tests, as appropriate.

We aimed to study to what extent MRI results were associated with all-cause mortality. For this purpose, three Cox proportional hazards regression models were constructed, with spatial extent (first model), transmurality (second model) and the total scar score (third model) as main exposure, and age, LV function, LV dimensions, diabetes mellitus, hypertension, diuretic usage and statin usage as confounding factors. The latter variables appeared to be associated with all-cause mortality at the $p < 0.10$ 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 (HR) with their corresponding 95% confidence intervals (CI) are reported.

All the continuous variables were assessed for linearity by entering a transformed variable in addition to the variable of interest. The natural logarithm and square transformations were used. A significant change in the -2 log-likelihood was considered as a sign of non-linearity, otherwise the linearity assumption was accepted. All variables met the linearity assumption. To check the proportional hazard assumption (i.e., that the hazard ratio for two 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 all-cause mortality. Therefore, in a post-hoc analysis, the study population was divided in two groups, based on the observed median value of the spatial extent, and 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.

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; 231 patients with scar tissue on contrast-enhanced MRI were included (106 at the Leiden University Medical Center, The Netherlands and 125 at the German Heart Institute, Germany). All patients had evidence of CAD on angiography and 84% had a previous myocardial infarction; 16% had a clinically unrecognized myocardial infarction. MRI was performed more than two years after infarction in 52% of the patients.

MRI variables

MRI findings are summarized in Table 2. Median LVEF in the total study population was 43% (30-55%). LVEF was significantly higher in survivors than in non-survivors. Median LV ESV and LV EDV were significantly lower in survivors than in non-survivors. No difference in EDWT values between survivors and non-survivors was detected.

By definition, all patients had evidence of scar tissue on contrast-enhanced MRI. The median spatial extent, transmurality and total scar score were significantly higher in non-survivors than in survivors.

Clinical outcome of patients during follow-up

The median duration of follow-up was 1.7 years (1.1–2.9); 19 patients (8.2%) died during follow-up. Fourteen patients (6.1%) died of end-stage heart failure, 2 patients (0.9%) died of sudden cardiac death, 1 patient (0.4%) died after acute myocardial infarction, and noncardiac death was reported in 2 patients (0.9%). Seventy-one patients (31%) underwent revascularization after MRI. None of these revascularized patients died during follow-up.

Predictors of mortality

As demonstrated in Table 3, LVEF, LV ESV, LV EDV, spatial extent, transmurality of scar tissue, total scar score, diabetes mellitus, hypertension, diuretic usage and statin usage were significantly associated with all-cause mortality. Diuretic usage, but not statin usage, was as true confounder for the relation between infarct size and all-cause mortality (Table 4). After adjustment for multiple (true or potential) confounders (see Methods section), infarct size defined as spatial extent, transmurality and total scar score remained important outcome determinants (Tables 5A-C). In fact, in any of the three models, infarct size (as indicated by different MRI measurements) appears to be a stronger predictor (based on the observed chi-square value) of all-cause mortality than LVEF and LV volumes. Even when the LVEF and LV volumes were entered separately in the models, the spatial extent of scar tissue on MRI remained the strongest predictor.

The spatial extent of scar tissue on contrast-enhanced MRI was used to separate patients at high risk (spatial extent larger than or equal to the median 6, n = 116) from those at low risk (spatial extent < 6, n = 115) for mortality. Indeed, 3-year mortality in high-risk patients was 20.0% versus 2.4% in their low-risk counterparts (p = 0.005; Figure 1).

Table 1. Baseline clinical variables.

Variables	Total population (n = 231)	Survivors (n = 212)	Non-survivors (n = 19)	P-value
Age (years)	64 (58, 69)	64 (57, 69)	67 (61, 75)	0.1
Men	201 (87)	184 (87)	17 (89)	1.0
Diabetes mellitus	41/222 (18)	34/204 (17)	7/18 (39)	0.029
Hypertension	125/221 (57)	120/203 (59)	5/18 (28)	0.013
Hypercholesterolemia *	175/225 (78)	163/206 (79)	12/19 (63)	0.1
Smoker	103/219 (47)	95/202 (47)	8/17 (47)	1.0
Previous myocardial infarction	193 (84)	176 (83)	17 (89)	0.7
Q wave	109 (47)	98 (46)	11 (58)	0.3
Infarct location	34/109 (31)	31/98 (32)	3/11 (27)	1.0
anterior/inferior	75/109 (69)	67/98 (68)	8/11 (73)	
Numbers of coronary arteries narrowed on angiogram				
1-vessel disease	24 (10)	23 (11)	1 (5)	0.7
2-vessel disease	67 (29)	62 (29)	5 (26)	
3-vessel disease	140 (61)	127 (60)	13 (68)	
Medications				
β-Blockers	176/225 (78)	164/206 (80)	12/19 (63)	0.1
Calcium channel blocker	47/224 (21)	42/205 (20)	5/19 (26)	0.6
ACE inhibitor	177/225 (79)	163/206 (79)	14/19 (74)	0.6
Oral anticoagulant	222/226 (98)	203/207 (98)	19/19 (100)	1.0
Statin	191/225 (85)	180/206 (87)	11/19 (58)	0.003
Nitrate	69/224 (31)	61/205 (30)	8/19 (42)	0.3
Diuretic	106/224 (47)	90/205 (44)	16/19 (84)	0.001

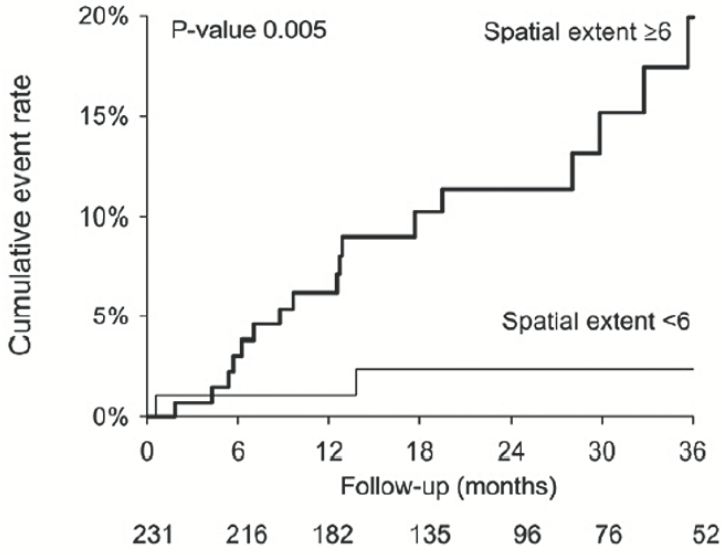
Continuous data are expressed as median (interquartile range).
Categorical data are expressed as n/total patients with complete data (%).
* Total cholesterol >200 mg/dl.
ACE: angiotensin converting enzyme.

Table 2. Baseline MRI variables.

MRI variables	Total population (n = 231)	Survivors (n = 212)	Non-survivors (n = 19)	P-value
LVEF (%)	43 (30, 55)	43 (32, 56)	27 (17, 41)	< 0.001
LV ESV (ml)	109 (69, 189)	103 (69, 179)	212 (122, 343)	< 0.001
LV EDV (ml)	197 (158, 258)	191 (154, 250)	283 (223, 414)	< 0.001
End-diastolic wall thickness (mm)	4.3 (3.1, 5.5)	4.3 (3.1, 5.5)	3.9 (3.2, 5.0)	0.4
Spatial extent	6 (4, 8)	6 (4, 8)	8 (6, 13)	< 0.001
Transmurality	3 (1, 5)	2 (1, 4)	5 (3, 8)	0.008
Total scar score	0.8 (0.5, 1.3)	0.8 (0.5, 1.2)	1.3 (0.8, 1.8)	0.004

Data are expressed as median (interquartile range).
LV EDV: left ventricular end-diastolic volume, LV ESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction.

Figure 1.



Kaplan-Meier curve analysis showing the difference in mortality when patients are stratified according to a large extent of scar tissue (spatial extent ≥ 6) or a small extent of scar tissue (spatial extent < 6) on contrast-enhanced MRI.

Table 3. Univariable analysis for prediction of all-cause mortality.

MRI variables	Hazard ratio	95% confidence interval	Chi-square	P-value
LVEF	0.95/%	0.92–0.98	9.4	0.002
LV ESV	1.07/10 ml	1.04–1.1	20	< 0.001
LV EDV	1.08/10 ml	1.04–1.1	19	< 0.001
Spatial extent	1.3/unit	1.2–1.6	16	< 0.001
Transmurality	1.3/unit	1.1–1.5	9.1	0.003
Total scar score	4.0/unit	1.7–9.4	10	0.002
End-diastolic wall thickness	0.82/mm	0.61–1.1	1.5	0.2
Clinical variables				
Age /10 years	1.55	0.93–2.6	2.8	0.09
Men	0.99	0.23–4.3	0.0	1.0
Diabetes mellitus	3.1	1.2–8.0	5.4	0.020
Hypertension	0.32	0.11–0.89	4.8	0.029
Hypercholesterolemia *	0.48	0.19–1.2	2.3	0.1
Smoker	1.0	0.40–2.7	0.0	0.9
Previous myocardial infarction	1.5	0.35–6.7	0.3	0.6
Q wave	1.3	0.54–3.4	0.4	0.5
Number of coronary arteries narrowed on angiogram #				
2-vessel disease	1.8	0.21-15	0.3	0.6
3-vessel disease	2.0	0.27-16	0.5	0.5
Medications				
β-Blocker	0.49	0.19–1.2	2.3	0.1
Calcium channel blocker	1.5	0.54–4.2	0.6	0.4
ACE inhibitor	0.75	0.27–2.1	0.3	0.6
Oral anticoagulant †				
Statin	0.27	0.11–0.68	7.8	0.005
Nitrate	1.5	0.62–3.8	0.9	0.4
Diuretic	7.2	2.1–25	9.7	0.002

* Total cholesterol >200 mg/dl.
# Increased risk of mortality as compared to 1-vessel disease.
† No events were reported in the patients who did not use oral anticoagulants.
LV EDV: left ventricular end-diastolic volume, LV ESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction.

Table 4. Relation between diuretic usage, statin usage and infarct size on contrast-enhanced magnetic resonance imaging.

	Patients using diuretics	Patients not using diuretics	P-value
Spatial extent	7 (5, 9)	5 (4, 7)	< 0.001
Transmurality	4 (2, 5)	2 (0, 4)	< 0.001
Total scar score	1.1 (0.7, 1.4)	0.7 (0.4, 1.1)	< 0.001
	Patients using statins	**Patients not using statins**	**P-value**
Spatial extent	6 (4, 8)	7 (5, 9)	0.2
Transmurality	3 (1, 5)	2 (1, 4)	0.8
Total scar score	0.8 (0.5, 1.3)	0.8 (0.6, 1.1)	0.8

Data are expressed as median (interquartile range).

Table 5. Multivariable Cox proportional hazards model for prediction of all-cause mortality.

	Hazard ratio	95% confidence interval	Chi-square	P-value
A. Model 1, using the spatial extent as variable of scar tissue on contrast-enhanced MRI.				
Spatial Extent	1.3	1.1–1.6	6.7	0.010
LVEF	1.04/%	0.96–1.1	0.8	0.4
LV ESV	0.90/10 ml	0.67–1.2	0.4	0.5
LV EDV	1.2/10 ml	0.89–1.5	1.2	0.3
Age	1.5/10 years	0.77–2.9	1.4	0.2
Diuretic usage	5.0	1.3–19	5.7	0.017
Statin usage	0.45	0.16–1.3	2.3	0.1
Diabetes mellitus	1.6	0.55–4.7	0.9	0.4
Hypertension	0.40	0.13–1.2	2.8	0.1
B. Model 2, using the transmurality as variable of scar tissue on contrast-enhanced MRI.				
Transmurality	1.5	1.1–1.9	8.9	0.003
LVEF	1.06/%	0.97–1.2	1.5	0.2
LV ESV	0.85/10 ml	0.62–1.2	1.0	0.3
LV EDV	1.3/10 ml	0.95–1.7	2.5	0.1
Age	1.5/10 years	0.81–2.8	1.7	0.2
Diuretic usage	4.6	1.2–18	5.0	0.025
Statin usage	0.24	0.08–0.79	5.5	0.019
Diabetes mellitus	1.04	0.33–3.2	0.0	1.0
Hypertension	0.26	0.09–0.79	5.7	0.017

C. Model 3, using the total scar score as variable of scar tissue on contrast-enhanced MRI.				
Total scar score	6.2	1.7–23	7.4	0.006
LVEF	1.06/%	0.97–1.2	1.5	0.2
LV ESV	0.86/10 ml	0.63–1.2	0.9	0.3
LV EDV	1.2/10 ml	0.93–1.6	2.2	0.1
Age	1.4/10 years	0.76–2.7	1.2	0.3
Diuretic usage	4.8	1.2–19	5.2	0.023
Statin usage	0.27	0.08–0.88	4.8	0.029
Diabetes mellitus	1.1	0.38–3.6	0.0	0.8
Hypertension	0.30	0.10–0.91	4.6	0.033

The different models use the different variables for scar tissue on contrast-enhanced MRI.
LV EDV: left ventricular end-diastolic volume, LV ESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction.

Discussion

The main finding in this study is that myocardial infarct size on contrast-enhanced MRI, expressed as either spatial extent, transmurality of scar tissue or total scar score is a stronger predictor of long-term mortality than LV function and/or LV volumes in patients with healed myocardial infarction.

MRI has emerged as a reliable non-invasive technique for assessment of scar tissue in patients with CAD (12,15). Kim et al. (16) validated the value of contrast-enhanced MRI to detect scar tissue in an animal model. In addition, previous studies demonstrated good correlation between infarct size on contrast-enhanced MRI and peak release of creatinine kinase-MB (12,17).

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 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.

Assessment of scar tissue using contrast-enhanced MRI also plays an important role in chronic CAD. Kim et al. (15) evaluated patients with chronic ischemic LV dysfunction and reported that an increasing transmurality of scar tissue was significantly related with absence of functional recovery after revascularization.

Survivors of acute myocardial infarction are at increased risk of subsequent fatal and nonfatal cardiovascular events (19). Early studies demonstrated that total cardiac enzyme release, as an indicator of the extent of myocardial necrosis, is related with short- and long-term prognosis after myocardial infarction (20,21). Subsequent studies demonstrated that the degree of LV dysfunction correlates well with mortality and is useful in risk stratification of patients after acute myocardial infarction (22,23). White et

al. (7) evaluated 605 patients after acute infarction, with a mean follow-up of 78 months (range 15-165 months), showing the powerful prognostic value of LVEF and LV ESV. More recently, Sharir et al. (6) demonstrated in a large population (n = 2686 patients) that post-stress LVEF on gated single-photon emission computed tomography (SPECT) imaging was the best predictor of cardiac death. Accordingly, LVEF and/or LV volumes have become the established predictors for mortality in patients with CAD. Indeed, patients with severe LV dilatation and remodeling are at high risk of development of heart failure. In patients with severe heart failure (New York Heart Association class III to IV) annual mortality is high (1,3) and the main cause of death is progressive pump failure (1-4). In mild heart failure (New York Heart Association class II), the overall annual mortality ranges from 5% to 15%, with a relatively high percentage of sudden cardiac deaths (2,5). Although the precise mechanism underlying lethal ventricular arrhythmias is not clear, it has been demonstrated that scar tissue may serve as a substrate for these arrhythmias (24,25).

Recent data have identified scar tissue and severely depressed LVEF (derived from gated SPECT) as important predictors of death or ventricular arrhythmias in patients with CAD (26). Wu et al. (27) studied 44 patients with cine and contrast-enhanced MRI and found that infarct size was directly related with cardiovascular complications after myocardial infarction, whereas LV volumes and LVEF had no significant predictive value for clinical outcome. A more recent study of Bello et al. (28) demonstrated that infarct size determined with contrast-enhanced MRI was superior over LVEF for identification of patients with a substrate for inducible ventricular tachycardia. In addition, Yan et al. (29) demonstrated that the extent of the peri-infarct zone characterized by contrast-enhanced MRI provides incremental prognostic value beyond LVEF and LV ESV. Based on the studies discussed above (27-30), it is conceivable that scar tissue may be superior over LVEF and LV volumes for prediction of all-cause mortality because of its additional value to predict death due to ventricular arrhythmias in patients with preserved or moderately depressed LV function, who are not likely to die of heart failure. Indeed, preliminary data revealed that infarct size on contrast-enhanced MRI was a better predictor for survival as compared to LVEF in patients with recent myocardial infarction (8). This observation agrees with the current results in 231 patients with healed myocardial infarction, identifying the extent of scar tissue on contrast-enhanced MRI as a better predictor for all-cause mortality than LV function and/or dimensions. A further explanation for the superior prognostic value of scar tissue over LVEF and/or LV volumes could be that the extent of scar tissue is a direct marker of infarct size, whereas LVEF only indirectly reflects myocardial damage (28).

Several limitations of the present study need to be addressed. First, the small number of mortality endpoints precludes exclusion of all potential confounding factors and the present conclusion requires confirmation in substantially larger patient groups. Diuretic usage was associated with relatively poor MRI results (i.e., extensive scar tissue) and

with increased mortality, and hence acted as true confounder. Most likely, diuretic usage is a substitute for severe heart failure, and thus reflects a poor clinical condition caused by LV dysfunction, rather than that the usage itself should be considered the cause of mortality. Simultaneously, patients who have developed heart failure have a larger extent of myocardial damage. It is important to note, however, that the prognostic value of MRI variables was maintained after adjustment for diuretic usage. Statin usage was also associated with poor prognosis. However, statin users and non-users had similar MRI results (Table 4). Thus, statin usage did not act as confounder, and did not influence the relation between MRI results and the primary endpoint.

Second, the power of the study is limited because of the small number of events. Furthermore, the small number of events does not permit distinction between heart failure death and sudden cardiac death. Larger studies with subsequently higher event rates are needed to confirm that infarct size on contrast-enhanced MRI is superior to LV function and volumes in predicting mortality and to further assess the value of infarct size as a predictor of mode of death. Also, the duration of follow-up was limited, and studies with longer follow-up are needed.

Third, not only viability and scar tissue are important for prognosis, but also stress-inducible ischemia is a relevant factor. In order to provide the full picture on jeopardized myocardium (viability and ischemia), contrast-enhanced MRI should be combined with stress-rest perfusion MRI. Future studies are needed to verify this hypothesis.

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