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Clinical research

Sequelae of acute myocardial infarction regarding cardiac structure and function and their prognostic significance as assessed by magnetic resonance imaging

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Infarct size;
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Right ventricular infarction;
Coronary heart disease

Aims Because of its high spatial resolution and tissue contrast, magnetic resonance imaging (MRI) was used to assess cardiac structure and function in a large population of patients with acute myocardial infarction (AMI).
Methods and results One hundred and ten patients were studied by MRI 6.1 ± 2.2 days after AMI. Infarct size (IS), persistent microvascular obstruction (PMO), left and right ventricular (LV/RV) volumes, and functions were measured. The same MRI measurements were repeated in 89 patients after a mean follow-up period of 225 ± 92 days. IS was 11.9 ± 7.3% of total LV muscle mass. PMO was detected in 51/110 (46.4%) patients and comprised 15.6 ± 8.5% of IS and 2.8 ± 2.3% of LV muscle mass. Papillary muscle infarct was seen in 26%, RV infarction in 16%, pericarditis in 40%, and pericardial effusion in 66% of the patients. During follow-up, there were 16 major adverse cardiac events (MACE) including seven deaths. IS, PMO, and amount of transmural infarction were predictive for LV adverse remodelling defined as >20% increase in LV end-diastolic volume. Multivariable analysis revealed LV end-diastolic volume, LV ejection fraction, and PMO as significant predictors for the occurrence of MACE.
Conclusion MRI is a highly sensitive and reliable tool to detect morphologic and functional sequelae of AMI providing baseline MRI parameters with relevant predictive power for LV adverse remodelling and occurrence of MACE.

Introduction

In principle, all cardiac structures may be involved in acute myocardial infarction (AMI), although in clinical practice infarct size (IS), left ventricular function (LVF), and the status of the infarct-related artery are of primary relevance and targets for therapy.[1] Echocardiography and left ventricular (LV) angiography are used to assess regional and global LVF and IS, which may be measured more precisely by radionuclide studies with 99mTc sestamibi[2] and positron emission tomography.[3,4] With the advent of contrast-enhanced magnetic resonance imaging (MRI) it became possible for the first time to visualize myocardial infarction directly *in vivo* with high spatial resolution.[5,6] Nearly

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half of all subendocardial infarcts detected by MRI elude the diagnosis by single photon emission computed tomography.[6]

In some patients, the 'no-reflow' or 'low-flow' phenomenon occurs despite early recanalization of the infarct-related artery by thrombolysis or coronary angioplasty,[7] most probably due to simultaneous damage and necrosis of both myocytes and capillaries in the centre of the infarct region. Experimental and clinical studies showed that microvascular obstruction (MO) is associated with greater myocardial damage and poorer global ventricular function in the early post-infarction phase.[8,9]

Right ventricular (RV) and pericardial involvement during AMI and their possible consequences are not in the main focus of treating patients with AMI, as these complications only become evident in case of a haemodynamic compromise, although a higher mortality has been reported in patients with RV infarction.[10,11] On the basis of clinical and echocardiographic data, pericarditis during AMI is associated with larger and transmural infarctions.[12,13] Both the true incidence of minor degrees of RV infarcts and pericarditis in patients with AMI in the era of revascularization therapy is unknown.

Owing to the high tissue contrast and spatial resolution of cardiac MRI, this study was performed in patients with AMI to discover infarct-related alterations of cardiac structure and function during the acute phase of myocardial infarction and the consequences of infarct healing on these parameters, including their prognostic significance.

Methods

Patients

One hundred and sixteen consecutive patients with AMI were enrolled between May 2001 and March 2003. Six patients were excluded from MR scanning (haemodynamic unstable condition in one, severe claustrophobia in three, refusal of MRI study in two). Patients with MR-incompatible implants were not considered for enrolment. In 108/110 patients with MRI, coronary angiography was performed. Eighty-one patients (73.6%) were treated by primary percutaneous coronary intervention (PCI) 6.5 ± 4.7 h after acute onset of symptoms, with stenting in 94%. Sixteen patients had a delayed PCI 2.8 ± 2.9 days after onset of AMI. The remaining 13 patients (two without coronary angiography because of small infarcts) were treated without PCI. All patients with primary PCI were directly admitted to our hospital. Twenty-three patients received IV thrombolysis, which was successful in six patients documented by regression of ST-segment elevation in subsequent electrocardiograms. These patients were referred to our hospital for cardiac catheterization after thrombolysis. After clinical stabilization, the patients were studied with MRI 6.1 ± 2.2 days (range 2–10 days) after the onset of AMI. Patients with previous myocardial infarction were enrolled if AMI was localized in another territory.

Follow-up MRI was planned in the range of 6–9 months after AMI and performed after a mean follow-up of 268 ± 94 days (median 251, lower quartile 195, upper quartile 308) in 89 patients with the identical protocol as before. The study protocol was approved by the local Ethics Committee. All subjects gave their written informed consent.

MRI protocol and data analysis

MRI was performed on a 1.5 T whole body scanner (Intera CV, Philips Medical Systems, Best, The Netherlands). To define the position and axis of the left ventricle, three short survey scans were performed. Parallel imaging was employed for all scans.[14] Resting LV and RV function was determined with cine images using a segmented k-space balanced fast-field-echo sequence (steady-state-free-precession) in short and long axis views in the true heart axis. Depending on the field-of-view, in-plane resolution was between 1.5×1.8 mm^2 and 2.3×1.8 mm^2 with a slice thickness of 10 mm for the functional scans. The short axis scans covered the whole LV and RV with 10–14 contiguous slices. LV- and RV- ejection fractions (EFS) and volumes were determined using short axis volumetry, as previously described.[15]

For the first-pass perfusion, a balanced turbo-field-echo sequence with three short axis slices per heartbeat (prospective triggering) and a selective saturation recovery pre-pulse (delay 130 ms) before each slice was used. Slice thickness was 10 mm. The typical in-plane resolution was 2.8×3.0 mm. In order to achieve post-contrast conditions comparable to a stress/rest perfusion protocol, this sequence was conducted twice with 0.1 mmol/kg body weight gadolinium-diethylene-triamine-pentaacetic acid, injected into an antecubital vein by a power injector (Medrad Spectris, Volkach, Germany) at a rate of 6 mL/s.

After 6–12 min, a late enhancement (LE) analysis using a 3D-gradient spoiled turbo fast-field-echo sequence with a selective 180° inversion recovery pre-pulse was acquired in the short axis covering the whole left ventricle (20–22 5 mm slices). Two to three long axis views with a similar 2D-sequence were additionally performed. An initial pre-pulse delay of 225 ms was applied and the measurement was repeated if contrast was not favourable with an adjusted pre-pulse delay. The typical examination time was 45–60 min.

Wall motion abnormalities were visually classified as hypo-, dys-, or akinetic and documented on the usual 17-segment model. Regional hypoperfusion on first-pass was visually assessed and documented using the same model. Infarct size (IS) was defined as an area of late hyper-enhancement on LE images of the AMI. Persistent microvascular obstruction (PMO) was defined as late hypo-enhancement within a hyper-enhanced region on LE images (*Figure 1*).[16] IS and PMO were quantified on the 3D-volume by manual delineation of the enhanced and unenhanced myocardium with different contours (MASS plus 5.0, Medis, Leiden, The Netherlands). PMO was included in the IS quantification. Papillary muscles were assigned to the myocardium and binary judged as infarcted or not. Pericarditis was defined as increased signal intensity of the pericardium post-contrast (*Figure 3*).[17–19] Pericardial effusion was diagnosed on cine steady-state-free-precession sequences. In uncertain cases, T1- and T2-weighted black blood turbo-spin-echo sequences (with and without fat saturation pre-pulse) were additionally performed to distinguish effusion from pericardium, epicardium, and epicardial fat.

Cardiac catheterization and ventriculography

A standard Judkins technique was used for coronary angiography. Routine LV angiography during AMI was not performed. Flow within the infarct-related artery was graded according to the standard TIMI criteria.[20]

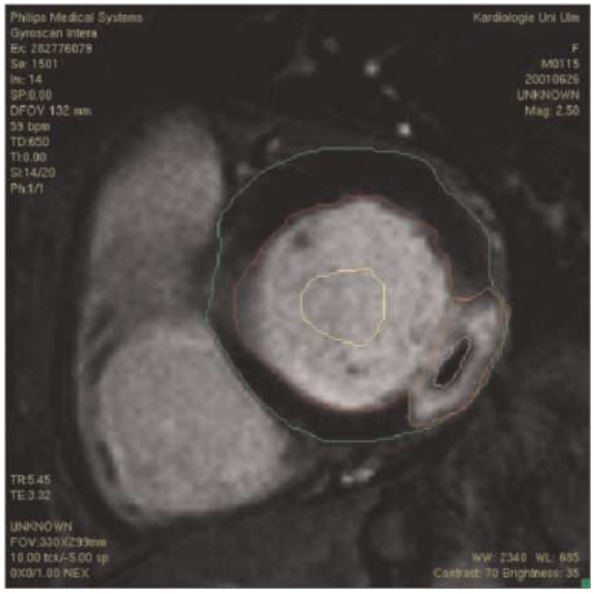

Figure 1 Single short axis basal slice in a patient with posterolateral myocardial infarction (inferior-right) with manual quantification of enhanced myocardium and PMO (dark central zone within the myocardium with the high signal-intensity posterolaterally).

Follow-up

Patients were followed by an intern questionnaire used previously[21] for CCS-status, medication, and major adverse cardiac events (MACE) at the time of the intended second MRI study. MACE were defined as death, myocardial infarction, re-hospitalization for cardiac failure, unstable angina, or revascularization [PCI or coronary artery bypass grafting (CABG)]. The follow-up interviewer was not aware of the results of the MRI studies.

Statistics

There was no sample size calculation. Summary values are expressed as means $\pm$ standard deviation. Categorical data were compared by the χ^2 test. Differences between means of continuous variables were analysed using the Student's *t*-test. We used the Holm method to account for type I error due to multiple testing.[22] Survival curves for MACE were calculated according to Kaplan–Meier. Statistical significance was tested with the log-rank test (Statistica version 6.0, StatSoft Incorporation, Tulsa, OK, USA). Pearson's correlation coefficients (r) were calculated with StatXact (version 6.0, Cytel Software Corporation, Cambridge, MA, USA) as exact test. All tests were two-sided. *P*-values below 0.05 were considered as statistically significant.

Subgroups of patients, differentiated by the presence or absence of PMO and according to the median of IS, were compared. We performed multivariable receiver operator characteristics (ROC) analysis (Matlab)[23] to test the diagnostic value in terms of adverse remodelling of following baseline MRI parameters: LV end-diastolic volume (EDV), LV end-systolic volume (ESV), LVEF, infarct localization (anterior vs. not anterior), amount of transmural infarction in per cent of total IS. Parameter combination was done using Fisher's discriminate. Adverse remodelling was defined as an increase in LVEDV from baseline to follow-up MRI measurement of $\geq$20% according to Mannaerts *et al.*[24] The best combination of three parameters was defined as being the one with the maximal area under the ROC curve. We performed a Cox regression to evaluate variables with potential impact on the occurrence of MACE. We included the baseline MRI parameters LVEDV, LVESV, LVEF, PMO, IS, and transmural infarction in per cent of total infarct. For reasons of co-linearity, variables with a correlation coefficient greater than 0.4 were not considered in the subsequent analysis. Survival curves were estimated by the Kaplan–Meier method. The log-rank test was used to compare survival curves from the groups of patients with and without PMO and for the groups of patients according to the median of IS. Confidence intervals for estimated event rates were calculated according to Altman *et al.*[25]

Results

Baseline clinical characteristics and the results of coronary angiography are shown in *Table 1*. Medication at discharge was: beta-blockers in 94.2%, ACE-inhibitors in 83.7%, acetylsalicylic acid in 98.1%, statins in 92.1%, and diuretics in 11.5% of cases. The MRI protocol could

Table 1 Baseline data

Number of patients	110
Patient age (years)	59.5 $\pm$ 12.6
Risk factors and history	
Male sex	96 (87.3)
Current smoker	58 (54.7)
Diabetes mellitus	16 (14.8)
Hypertension	65 (60.2)
Body mass index (kg/m^2)	27.1 $\pm$ 3.5
Previous myocardial infarction	24 (21.8)
Characteristics of AMI	
STEMI	60 (58.3)
Acute anterior infarction	56 (50.9)
Thrombolysis	23 (21.1)
Primary PCI	81 (73.6)
Maximal creatine kinase in-hospital (U/L)	954 $\pm$ 823
Maximal creatine kinase-MB in-hospital (U/L)	109 $\pm$ 104
Maximal troponin-I in-hospital (μg/L)	32.8 $\pm$ 56.6
Status of coronary arteries	
Cardiac catheterization	108 (98.2)
Culprit vessel	
Left anterior descending artery	57 (52.8)
Circumflex artery	24 (22.2)
Right coronary artery	27 (25.0)
TIMI flow	
Pre-PCI 0	50 (46.3)
Pre-PCI 1	31 (28.7)
Pre-PCI 2	18 (16.7)
Pre-PCI 3	9 (8.3)
Post-PCI 0	2 (2.0)
Post-PCI 1	1 (1.0)
Post-PCI 2	11 (11.2)
Post-PCI 3	84 (85.7)

Plus–minus values represent mean $\pm$ standard deviation.
CAD, coronary artery disease; STEMI, ST-elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction. Other values are presented as *n* (%).

be completed and evaluated in all 110 patients with sufficient diagnostic image quality of the functional, perfusion, and LE scans.

MRI results in the acute phase

The initial data obtained by MRI are listed in *Table 2*. LVEF was 28–80% and RVEF was 38–82%. LVEF and RVEF were normal, defined as EFs $\geq$60%, in 46 and 76%, respectively. IS comprised 0.7–32% of the total LV muscle mass (LVMM). PMO was detected in 51/110 (46.4%) of the patients and comprised 15.6 $\pm$ 8.5% (range 1.3–35.8%) of IS and 0.2–11.4% of LVMM. There was a significantly positive correlation between IS and PMO ($P < 0.00001$, correlation coefficient 0.754). Papillary muscle infarct was seen in 28 patients (25.5%), in two patients both papillary muscles were infarcted.

RV involvement by LE (*Figure 2*) was seen in 18 patients, generally not resulting in global functional impairment. Six out of these 18 patients had an RVEF <60% within the acute phase.

Signs of pericarditis were present in 44/110 (40.0%) patients (*Figure 3*) and pericardial effusion was seen in 72/110 (65.5%) patients. Both were present in 31/110 (28.2%), whereas 25/110 (22.7%) patients had neither pericardial effusion nor signs of pericarditis. The incidence of pericardial effusion did not differ between patients with and without signs of pericarditis. Patients with pericarditis suffered from significantly larger IS (15.0 $\pm$ 7.3 vs. 9.8 $\pm$ 6.7%, $P = 0.0002$) and a significantly larger amount of PMO (2.0 $\pm$ 2.6 vs. 0.8 $\pm$ 1.6%, $P = 0.0044$) compared with patients without pericarditis.

Table 2 Results of baseline MRI

Number of patients	110
Localization of AMI	
Anteroseptal	39 (35.5)
Anterior	4 (3.6)
Anterolateral	1 (0.9)
Lateral	10 (9.1)
Posterolateral	16 (14.5)
Inferior	24 (21.8)
Inferoseptal	9 (8.2)
Septal	3 (2.7)
Apical	4 (3.6)
Morphological data	
IS (%)	11.9 $\pm$ 7.3
PMO (%)	2.8 $\pm$ 2.3
RV infarction	18 (16.4)
RV abnormal wall motion	47 (42.7)
Infarction of papillary muscle	28 (25.5)
Pericardial enhancement	44 (40.0)
Local pericardial effusion	60 (54.5)
Circular pericardial effusion	12 (10.9)
Segments with abnormal wall motion, *n*	5.1 $\pm$ 2.4
Quantitative and functional parameters	
LVEF (%)	57.0 $\pm$ 10.7
LVEDV (mL)	144.7 $\pm$ 33.2
LVESV (mL)	63.3 $\pm$ 25.3
RVEF (%)	64.6 $\pm$ 7.6
RVEDV (mL)	126.9 $\pm$ 34.6

Plus–minus values represent mean $\pm$ standard deviation. Other values are presented as *n* (%).

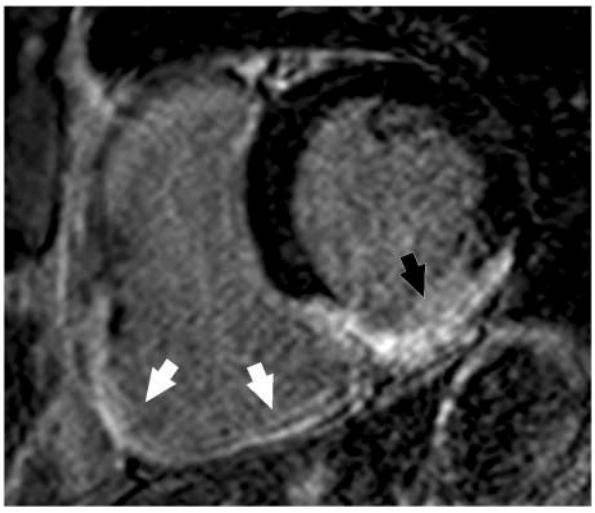

Figure 2 Basal short axis slice of the 3D-LE study in a patient with inferior AMI (black arrow) and major RV involvement (white arrows).

Subgroups

Baseline MRI morphologic and functional MRI parameters (RV- and LV-volumes, LVEF, PMO size, IS) did not statistically differ between the groups of patients with primary ($n = 81$) or delayed PCI ($n = 16$) or with non-interventional treatment ($n = 13$). However, patient numbers in all groups were low and the treatment options run from optimal to non-optimal.

Comparison of baseline data, MRI data as well as follow-up results between patients with and without PMO are given in *Table 3*. The following parameters were compared between the groups: LVEF and IS at baseline and at follow-up, maximal creatine kinase, and MACE. Patients with PMO had a significantly higher

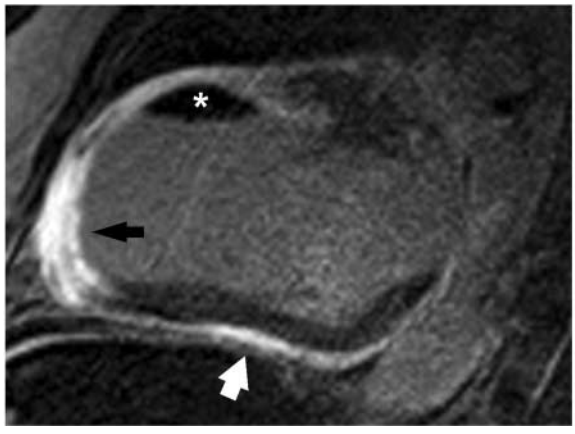

Figure 3 Two-chamber view with 2D-LE-study in a patient with anterior myocardial infarction (black arrow) and LE of the pericardium indicating pericarditis. Asterisk represents a LV thrombus.

Table 3 Comparison of subgroups with and without PMO at baseline MRI

	With PMO	Without PMO
Number of patients	51	59
Baseline data		
Maximal creatine kinase in-hospital (U/L)	1188 ± 937	757 ± 657
Maximal creatine kinase-MB in-hospital (U/L)	146 ± 109	79 ± 89
Troponin-I in-hospital (μg/L)	59.0 ± 73.2	11.2 ± 20.4
TIMI flow pre-PCI	0.8 ± 1.0	0.9 ± 1.0
TIMI flow post-PCI	2.8 ± 0.6	2.8 ± 0.5
MRI data		
IS (%)	16.2 ± 7.2	8.1 ± 5.1
IS at follow-up (%)	9.8 ± 5.4	6.1 ± 4.5
LVEF (%)	54.3 ± 10.1	59.3 ± 10.8
LVEF at follow-up (%)	61.0 ± 9.7	66.7 ± 8.1
LVEDV (mL)	147.8 ± 35.7	141.9 ± 30.9
LVEDV at follow-up (mL)	151.3 ± 38.0	140.9 ± 32.5
LVESV (mL)	69.3 ± 28.4	58.0 ± 22.1
LVESV at follow-up (mL)	61.5 ± 27.6	48.2 ± 20.1
RVEF (%)	64.9 ± 7.4	64.4 ± 7.9
RVEDV (mL)	122.6 ± 31.9	130.6 ± 36.7
RV LE, *n* (%)	11 (21.6)	7 (11.9)
Pericardial effusion, *n* (%)	38 (74.5)	34 (57.6)
Follow-up		
Cardiac death, *n* (%)	4 (7.8)	2 (3.4)
Major adverse cardiac events, *n* (%)	11 (21.6)	5 (8.5)

TIMI, thrombolysis in myocardial infarction.

Table 4 Comparison of subgroups according to IS at baseline MRI

	IS < median	IS ≥ median
Number of patients	55	55
Baseline data		
Maximal creatine kinase in-hospital (U/L)	639 ± 615	1275 ± 887
Maximal creatine kinase-MB in-hospital (U/L)	61 ± 72	160 ± 108
Troponin-I in-hospital (μg/L)	18.3 ± 41.8	48.6 ± 65.9
TIMI flow pre-PCI	1.1 ± 1.0	0.6 ± 0.9
TIMI flow post-PCI	2.8 ± 0.5	2.8 ± 0.6
MRI data		
IS (%)	6.0 ± 3.0	17.7 ± 5.6
IS at follow-up (%)	4.5 ± 2.7	11.4 ± 5.1
PMO (%)	0.1 ± 0.3	2.5 ± 2.5
LVEF (%)	61.1 ± 10.3	52.9 ± 9.5
LVEF at follow-up (%)	69.4 ± 6.2	58.4 ± 8.7
LVEDV (mL)	138.8 ± 29.0	150.5 ± 36.2
LVEDV at follow-up (mL)	133.8 ± 28.6	158.5 ± 37.6
LVESV (mL)	54.7 ± 21.8	71.9 ± 25.8
LVESV at follow-up (mL)	41.7 ± 14.7	67.8 ± 26.1
RVEF (%)	65.3 ± 7.0	63.9 ± 8.2
RVEDV (mL)	128.4 ± 32.3	125.4 ± 37.0
RV LE, *n* (%)	5 (9.1)	13 (23.6)
Pericardial effusion, *n* (%)	32 (58.2)	40 (72.7)
Follow-up		
Cardiac death, *n* (%)	2 (3.6)	4 (7.4)
Major adverse cardiac events, *n* (%)	6 (10.9)	10 (18.2)

TIMI, thrombolysis in myocardial infarction.

maximal creatine kinase, a significantly larger IS, and a lower LVEF both at baseline and at follow-up, and a trend towards a higher occurrence rate of MACE.

Table 4 details the study population according to the IS at baseline. The population with IS larger than its median had higher blood levels of cardiac enzymes, lower TIMI flow pre-PCI, larger PMO and LV volumes, lower LVEF, and a higher occurrence rate of MACE.

Follow-up results

In 92 patients, the MRI study was repeated with the same protocol as before, in three disregarded for technical reasons and in 89 evaluated with sufficient image quality. Sixteen patients had MACE. Seven patients died after discharge during follow-up: six from cardiac cause and one from end-stage metastatic colon cancer. In the other nine patients with MACE, a second MRI study was performed. Clinical follow-up data were obtained from all 103 surviving patients. One patient was lost, he was alive and free from cardiac events for at least 6 months after MRI. Eleven patients refused a second MRI study but were clinically followed and free from MACE. Clinical follow-up time was 225 ± 92 days (median 198, lower quartile 186, upper quartile 264).

In patients with both MRI measurements, IS decreased from 11.4 ± 7.2 to 7.8 ± 5.3% ($P < 0.00001$). IS was significantly smaller in patients without PMO when compared with patients with PMO, both at baseline (8.0 ± 5.2 vs. 15.5 ± 7.2%, $P < 0.00001$) and at follow-up (6.1 ± 4.5 vs. 9.8 ± 5.4%, $P = 0.00064$) (*Figure 4A*). In addition, shrinkage of IS was significantly higher in patients with PMO compared with patients without PMO (35.6 ± 22.7 vs. 22.0 ± 28.7%, $P = 0.017$). No PMO was seen at follow-up. LVEF and LVEDV increased and LVESV decreased during follow up (*Figure 4B–D*). The mean number of segments with wall motion abnormalities decreased from 5.0 ± 2.4 to 3.7 ± 2.5 ($P < 0.00001$). Values of MRI parameters between patients with and without PMO are given in *Table 3*.

The combination of the following three baseline MRI parameters was most predictive for the occurrence of adverse remodelling: IS, PMO, and transmural infarction. Maximizing both sensitivity and specificity on the ROC curve resulted in a sensitivity of 0.800 and a specificity of 0.846. The area under the ROC curve was 0.816 with a 95% confidence interval of 0.614–0.906.

Patients ($n = 6$) with cardiac death during follow-up had a lower LVEF (41.5 ± 8.3 vs. 58.1 ± 10.0%), a larger IS (15.7 ± 10.1 vs. 11.7 ± 7.2%), and a larger amount

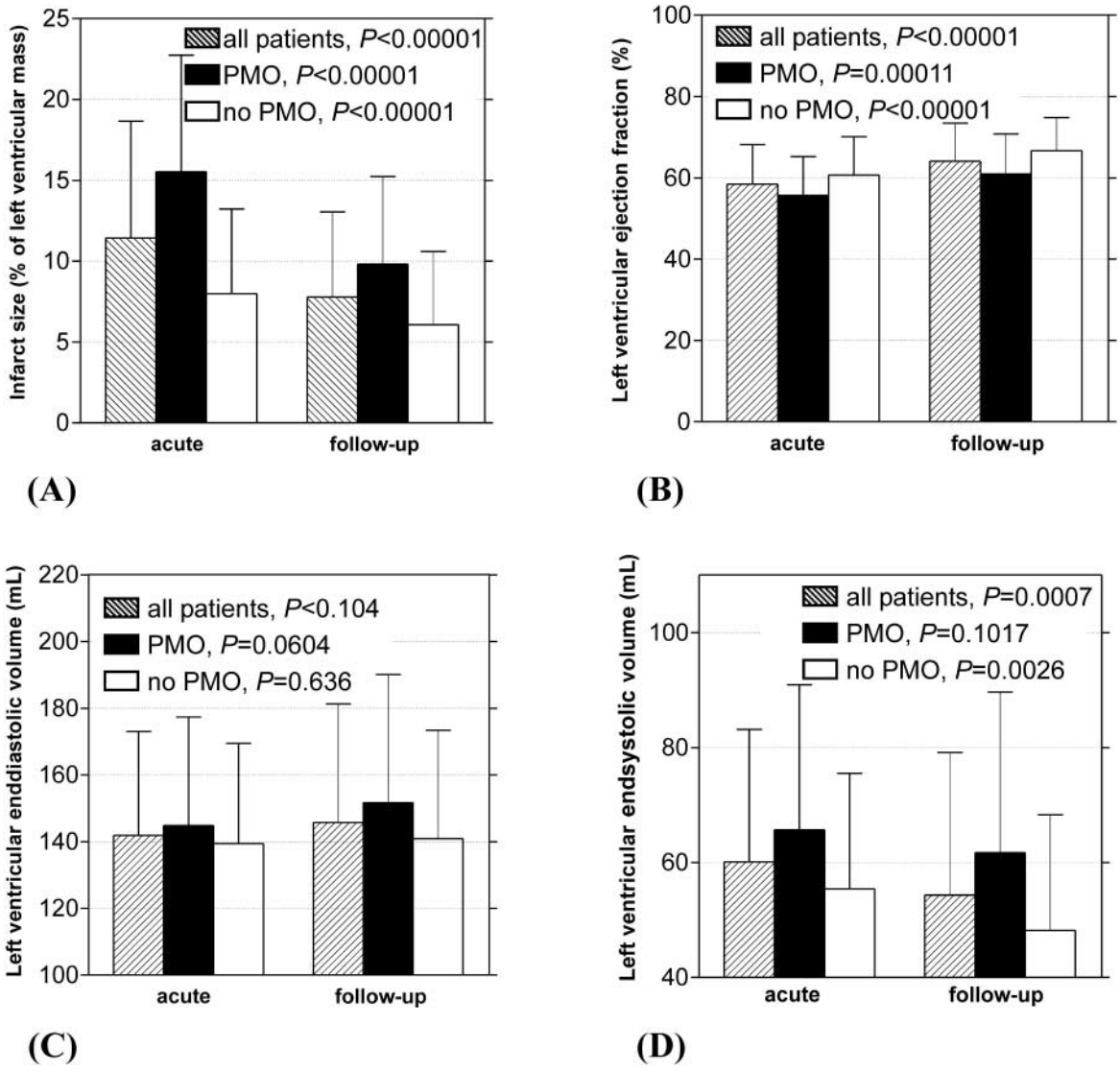

Figure 4 (*A*) Mean IS, (*B*) EF, (*C*) EDV, and (*D*) ESV of the LV during the the acute stage of AMI (acute) and at follow-up in the total cohort (all patients), in patients with (PMO+) and without PMO (PMO−). *P*-values compare acute stage vs. follow-up data in each of the three groups.

of PMO (3.6 ± 3.2 vs. 1.2 ± 2.2%) at baseline MRI compared with surviving patients.

Survival rate was significantly higher in the primary PCI group and delayed PCI group compared with the conservatively treated group (97.5, 93.8, and 61.5%, respectively; $P < 0.00001$).

Cox regression analysis revealed LVEF ($P = 0.0057$), LVEDV ($P = 0.038$), and PMO ($P = 0.044$) as significant predictors for the occurrence of MACE (total model $P = 0.0074$).

Kaplan–Meier survival curves revealed a significant better event-free survival for patients without PMO and a trend in patients with smaller IS (*Figure 5*). At 100 days' follow-up, the difference in occurrence of MACE between patients with and without PMO was 12.6% (95% confidence interval 1.4–23.8%) and in patients regarding median IS was 5.4% (95% confidence interval, −4.9–15.6%).

Discussion

This report describes the consequences of AMI on cardiac structure and function studied by MRI in a large group of 110 patients, in whom a near optimal treatment was performed. Not only were IS, PMO, and LV/RV function studied, but also further sequelae such as RV involvement, papillary muscle infarct, pericarditis, and pericardial effusion.

IS comprised a mean of 12% (0.7–32%) of LVMM and displayed a regular shrinkage of relative 28% at follow-up during optimal evidence-based drug therapy. Patients with larger infarcts by LE showed a higher LVESV, LVEDV, and a lower LVEF both at baseline and at follow-up MRI study, more pericardial effusion, and RV infarcts compared with patients with smaller IS.

PMO comprised 16% of IS and always disappeared on infarct healing. The significantly positive correlation

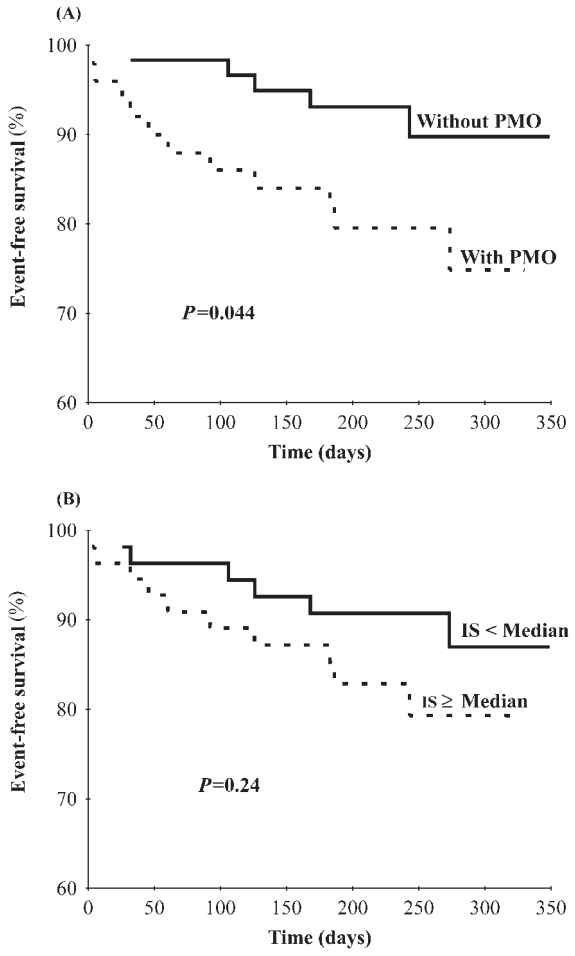

Figure 5 Kaplan–Meier survival curves for cumulative MACE in patient subgroups (*A*) with and without PMO and (*B*) with an IS of <median vs. ≥median of IS of LVMM.

between the extent of PMO and IS and the significantly higher shrinkage of IS in patients with PMO may be explained by a larger amount of necrosis in these patients resulting in a thinner fibrous scar and an increased amount of negative remodelling. The predictive impact of IS and PMO is strengthened by the finding that the combination of IS, PMO, and transmural infarction was most predictive for the occurrence of adverse remodelling. These results are not biased by ventricular remodelling *per se*, since this process should be completed after 5 months post-AMI, which was the shortest interval of the second MRI study in our series.

The earlier mentioned findings compare well with experimental and clinical data: the larger the infarct, the worse are the global and regional ventricular functions, and the higher the rate of LV remodelling and adverse events during follow-up of the patients.[26] In our study, survivors had, at baseline MRI measurement, a better cardiac function and a lower PMO and IS than patients suffering from cardiac death.

We defined MO as persistent late-hypo-enhancement within a hyper-enhanced area. Recently, Lund *et al.*[16] reported a high concordance between MO on first-pass enhancement MR images and MO on delayed enhancement MR images defined as late hypo-enhancement. They found a correlation of 0.71. The sensitivity of delayed enhancement MR images was 74% for the detection of MO with first-pass enhancement MR images used as the reference standard. They discussed that the difference could be explained by a filling of the early hypo-enhancement over time by contrast material, through collateral flow, or by slow diffusion. A contrast filling of an area accused to have MO implies the requirement of an at least minimal residual blood flow. If there is complete obstruction of the microvasculature (= no-reflow) due to thrombotic material within the vessel or due to tissue or vessel wall swelling after AMI, there has to be no contrast filling in this area over time. Here, our intention was to report on the amount of MO which is definitely not filled by contrast material, which focuses our analysis on severe cases with persistent contrast filling defects. In our study, all areas with late hypo-enhancement were surrounded by late hyper-enhancement, indicating a persistent area of non-perfusion compatible with severe PMO, which has been mentioned previously.[27,28] The impact of PMO is stressed by our results. The evidence of PMO was associated with an increased risk of the occurrence of MACE. Frequency of occurrence of MACE was 8.4% ($n = 5/59$) in patients without PMO and 21.6% ($n = 11/51$) in patients with PMO. In the multivariable analysis of MRI baseline parameters to predict adverse remodelling, the combination included PMO. In cox regression analysis, PMO was a predictor for the occurrence of MACE.

Wu *et al.*[9] analysed MO defined as early hypo-enhancement in 44 AMI patients (eight patients with primary PCI, 20 patients with elective PCI >48 h). In patients with MO, more cardiovascular events occurred than in those without MO and microvascular status predicted the occurrence of cardiovascular complications. The combined risk of cardiovascular death, re-infarction, congestive heart failure, or stroke increased with infarct extent (30, 43, and 71%, respectively) for small, mid-sized, and large infarcts. Even if the analysis was adjusted for IS, the presence of MO remained a prognostic marker for post-MI complications. In our study, LVEF, LVEDV, and MO were predictors for the occurrence of MACE.

The incidence of further morphologic sequelae was higher than expected: papillary muscle infarct was seen in 26%, RV involvement by LE in 17%, and by regional wall motion abnormalities in 43%. These patients had minor wall motion abnormalities within the septal part of the RV without a relevant functional impairment. These subtle findings were not yet described in the literature, which generally resumes that RV infarction correlates to ~50% to inferior infarction due to proximal RCA occlusion and becomes clinically relevant with cardiac failure. Bueno *et al.*[10] studied 198 elderly patients with inferior AMI receiving acute reperfusion therapy (PCI or thrombolysis) in only 25%. In the RV infarction group, mortality was 47% and cardiogenic shock occurred in 32%, compared with 10 and 5% for patients without RV infarction, respectively. Zehender *et al.*[11] reported a 31% in-hospital mortality rate in AMI

patients with RV infarction, compared with 6% in those without. Thrombolytic therapy was given in 36% of patients, who were admitted within 6 h after onset of AMI and $\leq$75 years old. In our study, RV infarction detected by LE was not associated with a worse outcome, although it was found predominantly in patients with larger infarcts. This may be due to the generally preserved RV performance due to early recanalization therapy. This is supported by the data of Giannitsis *et al*.[29] showing that in-hospital mortality after early recanalization therapy in patients with RV infarction is not increased when compared with patients without RV involvement.

Post-infarction pericarditis is known to occur with transmural or near transmural infarction and to be localized at the infarct's 'apex' on the epicardium,[12,13] whereas the post-MI syndrome (Dressler syndrome) does not require transmural infarction. Using MRI we observed a much higher incidence of pericarditis (40%) and pericardial effusion (66%) of subclinical degree without a significant influence on the acute clinical course of the patients.

Limitation

Comparison of MRI parameters between baseline and follow-up was performed in 81% of the study population, but did not include the 7 patients who died during follow-up and did not include the 11 asymptomatic patients who refused the second MRI. We performed baseline MRI in the range of day 2–10 after onset of AMI. Although, animal experiments revealed no change in size of myocardial infarction and MO at day 2 and 9 after AMI,[30] we basically cannot exclude changes in IS and size of PMO during these first days.

Conclusion

In conclusion, our study demonstrates the feasibility and great potential of MRI in AMI to detect the wide spectrum of infarct sequelae, to study pathophysiological processes and interrelations between structure and function, to follow post-interventional course and predict ventricular remodelling and to assess prognosis of AMI patients.

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