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Magnetic Resonance Imaging Delineates the Ischemic Area at Risk and Myocardial Salvage in Patients With Acute Myocardial Infarction

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Background—The area at risk (AAR) is a key determinant of myocardial infarction (MI) size. We investigated whether magnetic resonance imaging (MRI) measurement of AAR would be correlated with an angiographic AAR risk score in patients with acute MI.

Methods and Results—Bright-blood, T2-prepared, steady-state, free-precession MRI was used to depict the AAR in 50 consecutive acute MI patients, whereas infarct size was measured on gadolinium late-contrast-enhancement images. AAR was also estimated by the APPROACH and DUKE angiographic jeopardy scores and ST-segment elevation score. Myocardial salvage was calculated as AAR minus infarct size. Results are mean±SD unless specified otherwise. Patients were 61±12 years of age, 76% had an ST-segment elevation MI, and 20% had a prior MI. All underwent MRI 4±2 days after initial presentation. The relation between MRI and the APPROACH angiographic estimates of AAR was similar (overall size relative to left ventricular mass was 32±12% vs 30±12%, respectively, $P=0.33$), correlated well ($r=0.78$, $P<0.0001$), and had a 2.5% bias on Bland-Altman analysis. The DUKE jeopardy score underestimated AAR relative to infarct size and was correlated less well with MRI ($r=0.39$, $P=0.0055$). ST-segment elevation score underestimated infarct size in 19 subjects (50%) and was not correlated with MRI ($r=0.27$, $P=0.06$). Myocardial salvage varied according to Thrombolysis in Myocardial Infarction flow grade at the end of angiography/percutaneous coronary intervention ($P=0.04$), and Thrombolysis in Myocardial Infarction flow grade was a univariable predictor of myocardial salvage ($P=0.011$). In multivariable analyses, infarct size was predicted by T2-prepared, steady-state, free-precession MRI ($P<0.0001$).

Conclusions—T2-prepared, steady-state, free-precession MRI delineates the AAR and enables estimation of myocardial salvage when coupled with a measurement of infarct size. **(*Circ Cardiovasc Imaging*. 2010;3:527-535.)**

Key Words: myocardial infarction ■ MRI ■ edema ■ myocardial ischemia

Salvaging threatened myocardium during acute coronary occlusion is a key therapeutic objective. The extent of myocardium subject to ischemia, also known as the myocardial area at risk (AAR), is a determinant of infarct size (IS) and prognosis.[1,2] Therefore, identification of the ischemic AAR may provide useful information for clinical and research purposes.

Clinical Perspective on p 535

Although it is possible to image the AAR with single-photon emission computed tomography in research studies, determination of initial AAR and myocardial salvage in routine clinical practice has not been feasible.[3] Preclinical validation studies have shown that cardiac magnetic resonance imaging (MRI) may now enable AAR delineation and estimation of salvage.[4] Because changes in myocardial water content and mobility are an early consequence of ischemia,[5] alterations in proton transverse relaxation times enable depiction of myocardial edema by MRI.[6] Given that edema formation corresponds to the ischemic AAR,[7] which is typically greater than IS, edema imaging by MRI represents a noninvasive approach to AAR estimation.

T2-weighted MRI has considerable potential to guide management after acute MI.[8–11] Because several variables beyond AAR modulate IS, we hypothesized that multivariable analysis of clinical, angiographic, and MRI parameters would reveal the relative strengths of these factors in predicting AAR, IS, and myocardial salvage. Thus, the specific aim of this study was to validate that the ischemic AAR can be measured in patients by T2-weighted MRI. Our first hypothesis was that AAR derived by T2-weighted MRI should be correlated with angiographic estimates of AAR. Our second hypothesis was that T2-weighted MRI could delineate the

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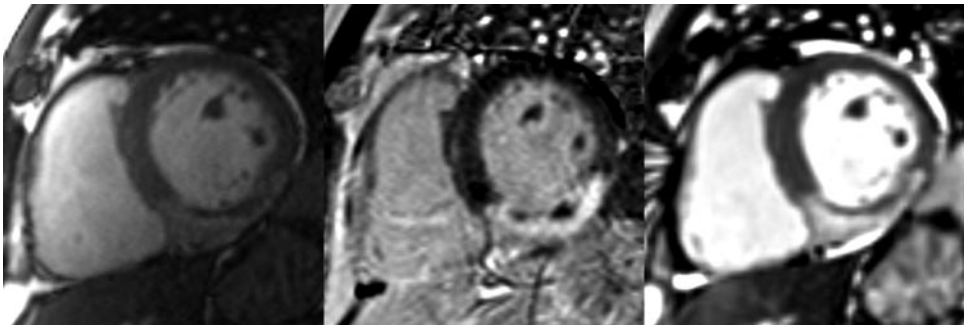

Figure 1. Matched diastolic cardiac MRI (left, cine MRI; middle, phase-sensitive inversion-recovery image; right, T2-weighted SSFP) obtained in a 57-year-old man 1 week after primary PCI to the right coronary artery for an acute inferior STEMI. Post-PCI culprit artery flow was reduced (TIMI flow grade 1). Transmural infarction (as revealed by late gadolinium enhancement, middle) corresponds to transmural edema (bright-blood, T2-weighted SSFP, right). Absolute AAR and salvage in this patient were 29% and 6%, respectively. The central dark zones within the infarct territory represent MVO complicated by hemorrhage.[28]

ischemic AAR in MI patients, including those with prior MI, as determined by history and catheter and ECG data determining the infarct-related artery. Thus, we used T2-weighted MRI to determine AAR in 50 consecutive patients with acute MI.

Methods

Patient Population and Acute MI Management

Fifty consecutive patients who underwent invasive management for acute MI at a community hospital and who also had T2-weighted MRI were analyzed. No patients were excluded owing to poor image quality. Exclusion criteria represented standard contraindications to MRI and an estimated glomerular filtration rate <30 mL/min per 1.73 m^2. This research was approved by the institutional review board of the National Heart, Lung, and Blood Institute, Bethesda, Md.

MI was defined according to a history of symptoms consistent with acute myocardial ischemia, with or without ST-segment elevation, on the ECG associated with a typical rise of troponin I concentration.[12] Cardiogenic shock was determined on the basis of the following criteria: acute heart failure consistent with Killip class IV and/or a systolic blood pressure $\leq$90 mm Hg despite a fluid challenge, together with signs of tissue hypoperfusion.[13]

Acute MI management followed contemporary guidelines.[12] Aspiration thrombectomy, direct stenting, antithrombotic drugs, and other therapies were administered according to clinical judgment. Opening pulse pressure was recorded at the beginning of the catheter laboratory procedure.

MRI Acquisition and Analyses

MRI was performed on a Siemens Magnetom Espree (Erlangen, Germany) 1.5-T scanner with 12 surface-coil elements. The MRI protocol included steady-state free-precession (SSFP) cine MRI, T2-prepared SSFP edema MRI,[4] and delayed-enhancement, phase-sensitive inversion-recovery sequences.[14] Sample images are shown in Figure 1.

We used bright-blood, T2-weighted MRI[4] to avoid bright rim artifacts associated with black-blood T2-weighted turbo spin echo MRI.[4] A T2-prepared, single-shot SSFP sequence with parallel techniques to reduce imaging duration was used to repetitively acquire an interleaved T2-weighted image and a proton density–weighted reference middiastolic image every 2 RR intervals[4] by prospective ECG gating. The proton density–weighted image was used for surface-coil correction. Typical imaging parameters were as follows: bandwidth=977 Hz per pixel, echo time/repetition time=1.6 ms/3.2 ms, flip angle=60° to 90°, and T2 preparation echo time=60 ms. Parallel imaging (rate 2) was used. Temporal resolution within the cardiac cycle was 175 ms. The in-plane resolution was typically 1.9×2.5 mm^2 with a 6-mm slice thickness. Eight respiratory motion–corrected images were obtained per acquisition.

Microvascular obstruction (MVO) was defined as a dark zone on early delayed-enhancement imaging 1, 3, 5, and 7 minutes after contrast injection and within an area of late gadolinium enhancement. MI was imaged by a segmented phase-sensitive, inversion-recovery, turbo fast low-angle shot,[14] starting $\approx$9 minutes after intravenous injection of 0.15 mmol/kg Gd-DTPA (Magnevist, Berlex). Typical imaging parameters were as follows: bandwidth=140 Hz per pixel, echo time/repetition time=4.2 ms/8.7 ms, readout flip angle=25°, field of view=360×270 mm, in-plane spatial resolution=1.4×2.2 mm (matrix=256×125), 25 views per segment, and slice thickness=6 mm.

MR Image Analyses

All MR images were analyzed on a Siemens Leonardo workstation by a level 3 trained cardiologist blinded to the patients' history and outcomes. Left ventricular (LV) dimensions, volumes, and ejection fraction were quantified by computer-assisted planimetry.

Standardized Measurements of T2-Weighted AAR

Hyperintense zones on T2-weighted MR images were first reviewed by 2 cardiologists who were blinded both to the angiographic data and clinical history to ensure consensus agreement on the affected territory. Each observer measured AAR independently. LV endo- and epicardial borders were delineated. The window setting was defined as the sum of the mean myocardial signal intensity of the unaffected area plus 2 SDs for this area. The level setting was set at the mean signal intensity of the unaffected area. The jeopardized LV AAR was defined as the percentage of LV volume delineated by the hyperintense zone on T2-weighted images. Interobserver variability in AAR measurement was evaluated with data from 8 ($\approx$15% of overall cohort) randomly selected subjects.

Infarct Size

IS was measured on contrast-enhanced images with validated software[15,16] and expressed as a percentage of total LV mass. MVO regions were included within the infarct area. Transmural extent of infarction was categorized qualitatively on a typical 5-point scale.

Myocardial Salvage

Myocardial salvage, as estimated by MRI, was calculated by subtracting the percentage of IS from the percentage of AAR.

Angiographic Jeopardy Scores and Coronary and Collateral Flow Grades

The jeopardy score from Duke University[1] and the lesion score from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH)[2] provided angiographic estimates of the AAR.[17] All angiograms were analyzed by 2 interventional cardiologists independent of the MRI analyses. The percentage of jeopardized myocardium distal to the infarct-related artery on the index angiogram was calculated for the APPROACH lesion score and Duke Jeopardy Score.

Table 1. Clinical Characteristics of Acute MI Patients Who Underwent Invasive Management and in Whom MRI Was Performed During the Index Admission

	All	STEMI	Non-STEMI	*P*
No. of patients	N=50	n=38 (76%)	n=12 (24%)	
Mean±SD age, y	61±12	58±11	66±12	0.050
Male	38 (76)	29 (76)	9 (75)	0.93
History, n (%)				
MI	10 (20)	5 (13)	5 (42)	0.031
Diabetes mellitus	11 (22)	9 (24)	3 (25)	0.61
Hypertension	21 (42)	14 (37)	7 (58)	0.19
Cigarette smoking	13 (26)	11 (29)	2 (17)	0.40
Previous angina	12 (24)	6 (16)	6 (50)	0.016
Chronic heart failure	4 (8)	1 (3)	3 (25)	0.013
Dyslipidemia	37 (74)	27 (71)	10 (83)	0.40
PCI	3 (6)	1 (3)	2 (17)	0.074
CABG	4 (8)	1 (3)	3 (25)	0.013
Presenting characteristics				
Cardiogenic shock	4 (8)	4 (11)	0	0.24
Mean±SD pulse pressure, mm Hg	49±22	47±21	54±23	0.35
Median (IQR) peak troponin I, μg/L	30.1 (8.8, 76.4)	41.0 (18.7, 95.1)	6.0 (4.2, 13.0)	0.0005
Median (IQR) time from onset of symptoms to PCI, h	5.4 (3.1, 15.4)	4.6 (3.0, 11.8)	32 (8.4, 72)	0.0057
Median (IQR) door-to-balloon time, h	1.8 (1.0, 3.2)	1.6 (0.9, 2.2)	6.5 (3.4, 48)	0.0034
ECG on admission				
Sum of ST-segment elevation	…	4 (6, 10)	…	…
ST-segment elevation jeopardy score	…	18.2±7.3	…	…
Drug therapy, n (%)				
Aspirin	50 (100)	38 (100)	12 (100)	1.00
Glycoprotein IIb/IIIa inhibitor	26 (52)	23 (60)	3 (25)	0.032
Prior clopidogrel therapy	12 (24)	10 (26)	2 (17)	0.50
β-blocker	50 (100)	12 (100)	38 (100)	1.00

CABG indicates coronary artery bypass graft; IQR, interquartile range. Other abbreviations are as defined in text.

The Rentrop classification was used to evaluate coronary collateral supply.[18] The Thrombolysis in Myocardial Infarction (TIMI) flow classification was used to grade culprit artery flow at initial angiography and at the end of the procedure.[19]

Biochemical Assessment of Infarct Size

Peak troponin I (AccuTnI; Beckman Coulter) was used as a biochemical measure of IS.

ECG Assessment of IS

Because the extent of ST-segment elevation at presentation is a reasonable predictor of the extent of myocardial injury,[20] we also used the admission ECG with the most extensive ST-segment elevation as a reference measure for percent of jeopardized myocardium.[20]

Statistical Analyses

Normality was confirmed or excluded by the Shapiro-Francia test. Mean (SD) values and medians (interquartile ranges) were calculated. Correlations (*r*) between normally and nonnormally distributed variables were tested by Pearson's or Spearman's methods, respectively. All tests were 2 tailed. Between-group comparisons of normally distributed, continuous data were undertaken with a Student *t* test or ANOVA. Between-group comparisons of nonnormally distributed data were performed with a Mann–Whitney test. A Fisher's exact test was used to assess the difference in proportions.

Univariable regression models were constructed to determine the predictors of MRI-derived AAR, IS, and salvage. Linearity assumptions were satisfied for variables entered into the univariable and multivariable models. Relations were described by the correlation coefficient (*r*) and β estimate with 95% CIs. A multivariable model was constructed for predictors of IS. Variables that were measures of IS (eg, troponin I) or that are consequences of MI (eg, LV volumes and function) were not included in the multivariable model for IS. Univariable predictors significant at a level of $P<0.1$ were entered into the multivariable model. In the multivariable model for IS, the proportion of variability accounted for by each variable was expressed as the coefficient of determination (R^2), and β coefficient (continuous data) for a given increment of the covariate is reported along with the associated probability value.

A significance level of 5% was used in all tests. No adjustments were made to probability values to account for multiple testing. All statistical analyses were performed with STATA version 7 (Stata Corp, College Station, Tex).

Results

Fifty acute MI patients (mean±SD age, 61±12 years; 76% with an ST-segment elevation MI [STEMI]) underwent MRI 4±2 days after initial management between January 23, 2006, and February 12, 2008 (Tables 1 through 3).

Characteristics of Selected Patient Groups

Compared with patients without prior MI, patients with prior MI (n=10, or 20%) had a higher frequency of non-STEMI (50% vs 18%, $P=0.031$) and prior coronary revascularization

Table 2. Cardiac Catheter Laboratory Findings and Outcomes

	All	STEMI	Non-STEMI	*P*
No. of patients	N=50	n=38 (76%)	n=12 (24%)	
Angiographic characteristics, n (%)				
Multivessel coronary artery disease*	29 (58)	22 (58)	7 (58)	0.98
Emergent procedure	41 (80)	34 (89)	7 (58)	0.014
Infarct-related territory				0.11
Right	15 (30)	14 (36)	1 (8)	
Left anterior descending	31 (62)	22 (58)	9 (75)	
Circumflex	4 (8)	2 (5)	2 (17)	
Rentrop's collateral grade				0.80
0	32 (64)	24 (63)	8 (67)	
1	5 (10)	4 (10)	1 (8)	
2	11 (22)	9 (24)	2 (17)	
3	2 (4)	1 (3)	1 (8)	
TIMI flow grade (first view)				0.23
0	31 (62)	25 (66)	6 (50)	
1	4 (8)	4 (10)	0	
2	6 (12)	3 (8)	3 (25)	
3	9 (18)	6 (16)	3 (25)	
Postprocedure TIMI flow grade				0.20
0	5 (10)	2 (5)	3 (25)	
1	3 (6)	3 (8)	0	
2	15 (30)	12 (32)	3 (25)	
3	27 (54)	21 (55)	6 (50)	
Invasive management				0.062
PCI	43 (86)	34 (89)	9 (75)	
CABG	3 (6)	2 (5)	1 (8)	
PCI and CABG	2 (4)	2 (5)	0	
Angiography without intervention	2 (4)	0	2 (17)	
Aspiration thrombectomy	13 (26)	11 (29)	2 (17)	0.40
Angiographic risk scores				
Mean±SD APPROACH lesion score	30±12	31±12	26±10	0.16
Median (IQR) Duke jeopardy score	17 (17, 33)	17 (17, 33)	21 (17, 33)	0.83

CABG indicates coronary artery bypass graft; IQR, interquartile range. Other abbreviations are as defined in text.

Multivessel coronary artery disease was defined according to the presence of 2 or more arteries with stenoses of at least 50% of the reference vessel diameter, by visual assessment.

(40% vs 8%, $P=0.008$). Baseline TIMI flow ($P=0.06$) and collateral grades ($P=0.09$) tended to be higher in patients with prior MI, whereas TIMI flow grades after percutaneous coronary intervention (PCI) were similar between groups.

Compared with patients without a history of revascularization, patients with prior revascularization had a lower LV ejection fraction (43±16% vs 52±9%, $P=0.030$) and lower TIMI flow grades after PCI ($P=0.017$).

Cardiac MRI Findings

The cardiac MRI findings are summarized in Table 3. Figure 1 shows a representative MRI image of MI. The 95% CIs of agreement for AAR estimation by 2 independent observers were −12% and 15%. There was no evidence of bias ($P=0.14$). Myocardial salvage was greater in patients with a history of MI (19±10%) compared with patients without prior MI (12±8%, $P=0.022$). AAR, IS, and salvage in patients with a history of prior revascularization were similar to MRI findings in patients without prior revascularization.

Agreement Between Localization of Edema and Infarction

In 48 patients (96%), there was good agreement between bright-blood, T2-weighted MRI and acute infarct localization for the culprit artery revealed by coronary angiography.

Relations Between MRI-Derived AAR and Other Jeopardy Scores

The relations between MRI and the APPROACH angiographic estimates of AAR were similar (overall size relative to LV mass, 32±12% vs 30±12%, respectively; $P=0.33$). In all MI patients, AAR derived by T2-weighted MRI was correlated strongly with the APPROACH lesion score ($r=0.78$, $P<0.0001$) and moderately correlated with the Duke jeopardy score ($r=0.54$, $P=0.0001$; Table 4). When further restricted to patients with first STEMI and no prior coronary artery bypass graft, there was a similar correlation between AAR derived by T2-weighted MRI and the APPROACH lesion score ($r=0.74$, $P<0.0001$).

Table 3. Cardiac MRI Findings

	All	STEMI	Non-STEMI	*P*
No. of patients	N=50	n=38 (76%)	n=12 (24%)	
LV dimensions and function, mean±SD				
LV ejection fraction, %	51±11	51±10	51±15	0.94
End-diastolic volume index, mL/m^2	84±25	84±24	86±29	0.77
End-systolic volume index, mL/m^2	43±20	42±18	45±28	0.74
Left atrial volume index, mL/m^2	44±14	42±14	43±14	0.68
LV mass, g/m^2	69±18	69±17	70±22	0.80
Late gadolinium enhancement, n (%)				
No. of affected territories per patient				0.013
1	46 (92)	37 (97)	9 (75)	
2	4 (8)	1 (3)	3 (25)	
Wall motion score index	1.4 (1.2, 1.7)	1.4 (1.2, 1.6)	1.2 (1.0, 1.9)	0.39
Transmurality, n (%)				
Transmural	34 (68)	26 (68)	8 (67)	0.91
Mean±SD acute IS, %	18.8±12.4	21.4±12.5	10.7±8.1	0.0016
MVO	42 (84%)	32 (84%)	10 (83%)	0.94
Edema imaging				
Mean±SD AAR, %	32.2±11.9	34.7±11.3	24.3±10.8	0.0074
Myocardial salvage				
Mean±SD % salvage (%AAR−%IS)	13.5±8.6	13.4±8.4	13.7±9.8	0.78

The relation between IS measured by contrast-enhanced MRI and AAR measured by T2-weighted MRI provides a check for internal consistency, as AAR is expected to be greater or equal to infarct size. Forty-six (92%), 44 (88%), 35 (70%), and 19 (50%) patients had an AAR greater or equal to infarct size when AAR was estimated by T2-weighted MRI, the APPROACH lesion score, the Duke jeopardy score, and an ST-segment elevation myocardial jeopardy score, respectively (Figure 2). The relation between IS and AAR was most constricted when measured by MRI and least constricted when estimated by the ECG.

In STEMI patients (n=38), AAR estimated by T2-weighted MRI was correlated with the APPROACH lesion score (r=0.79, P<0.0001) and Duke jeopardy scores (r=0.54, P=0.0005). In patients with index MI (n=40; Figure 3), there was a good correlation between T2-weighted MRI and the APPROACH lesion score AAR estimates. On Bland-Altman analysis, there was a 2.5% bias (P=0.1), with 95% CIs of 19.6% to −14.6%. The correlation between T2-weighted MRI and the Duke jeopardy score AAR estimates was weaker and demonstrated a bias of 6.7% (P<0.01), with 95% CIs of 31.6% to −18.2% on Bland-Altman analysis.

Table 4. Univariable Predictors of MRI-Derived Percent AAR in All MI Patients (N=50)

Variable: Univariable Predictors of AAR	*r*	β Estimate	95% CI	*P* Value
APPROACH lesion score, %	0.78	0.79	0.60, 0.97	<0.0001
Duke jeopardy score, %	0.54	0.51	0.28, 0.74	0.0001
ST-segment elevation jeopardy score, mm	0.35	0.57	0.06, 1.07	0.028
STEMI	0.37	10.36	2.91, 17.82	0.007

Relations Between AAR, IS, and Salvage by MRI and Other Measures of Infarct Severity

Compared with patients with nontransmural MI, patients with transmural MI had a larger mean AAR (35±11% vs 25±12%, P=0.0037) and a larger mean IS (23±12% vs 11±9%, P=0.0007) by MRI, whereas myocardial salvage was similar in each group (P=0.5). Moderate correlations were also observed between MRI-derived AAR and peak troponin I concentration (r=0.55, P<0.0001). The ST-segment elevation score was not correlated with MRI (r=0.27, P=0.06).

Hemodynamic and Microvascular Factors Associated With AAR, IS, and Salvage

Persistent Flow to the Ischemic Territory Influences IS and Myocardial Salvage

Mean IS fell with increasing TIMI flow grade at baseline angiography (P=0.02), and the sum of collateral and TIMI flow influenced IS (Table 5). Postprocedure TIMI flow grade influenced myocardial salvage (Table 6 and Figure 4). AAR was greater in patients with MVO (34±11%) compared with patients without MVO (21±10%, P=0.0047). IS was also greater in patients with MVO (21±12%) compared with patients without MVO (9±10%, P=0.013).

Predictors of AAR, IS, and Salvage

The univariable predictors of percent AAR, percent IS, and percent salvage in all MI patients are shown in Tables 4, 5, and 6, respectively. AAR was predicted by angiographic and ECG jeopardy scores and by presentation with STEMI (Table 4). Myocardial salvage was predicted by coronary angiographic flow grades before and after angiography/PCI and by prior history of MI (Table 6).

A multivariable model of IS was constructed with univariable predictors that were prospectively determined as poten-

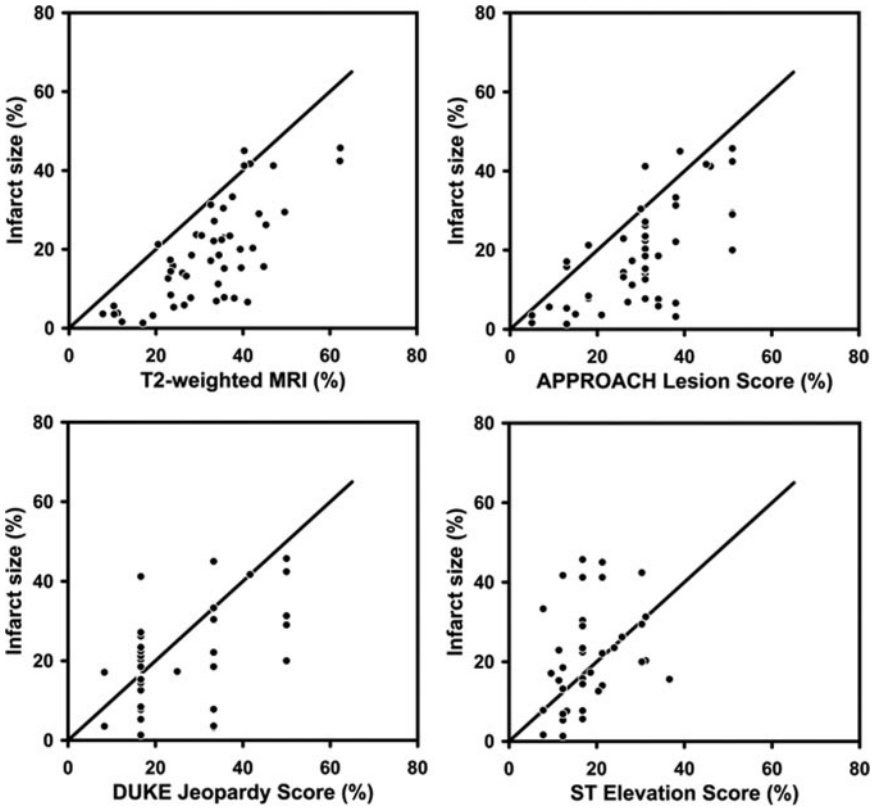

Figure 2. Scatterplots with lines of identity for the relations between IS measured by MRI vs (1) AAR derived by bright-blood, T2-weighted MRI (r=0.74, P<0.0001); (2) the APPROACH lesion score (r=0.66, P<0.0001); (3) the Duke jeopardy score (r=0.39, P=0.0055); and (4) an ST-segment elevation jeopardy score (r=0.27, P=0.06; n=38 patients). Because IS is physiologically a subset of the AAR, the expected relation between AAR and infarct size involves all points at or below the line of identity.

tial determinants of MI rather than consequences of MI. In this model (Table 5), IS was predicted by T2-weighted MRI-derived AAR (for a 1% change, the β estimate was 0.69; 95% CI, 0.46 to 0.92; P<0.0001) and by TIMI flow grade after PCI (−3.83; 95% CI, 7.28 to −0.38; P=0.031).

Discussion

Our main findings are summarized as follows. First, AAR by T2-weighted MRI was well correlated with angiographic measures of myocardial jeopardy, such as the APPROACH lesion score. Second, measurement of AAR and IS in the early postinfarct period enabled estimation of myocardial salvage in all patients, regardless of presentation type or past history of MI. Third, in a multivariable analysis, IS was predicted by MRI-derived AAR and also by the sum of coronary and collateral artery flow grades at initial angiography.

Determination of initial AAR and myocardial salvage has several applications for clinical and research purposes; however, measurement of these variables has limited feasibility.[3] Whereas AAR measurement is possible after technetium perfusion tracer injection during coronary occlusion,[21] this approach has been difficult to implement in both clinical practice and in large multicenter studies. MRI may now enable AAR delineation and estimation of salvage. First, recent technical advances have overcome problems due to signal drop-off[4] and cardiorespiratory motion.[22] Second, AAR measurements by T2-weighted MRI have been validated in reperfused[7] and nonreperfused[23] MI. Third, because MVO and intramyocardial hemorrhage may cause AAR to be underestimated by MRI,[24] our approach to image analyses was designed to minimize this problem. Fourth, our study was prospectively performed in a broad range of patients with acute MI. Previous studies have had several exclusion criteria,[17] such as symptoms >24 hours from PCI, history of prior MI, signs of clinical instability,[9] or persistent TIMI flow at angiography. To enhance the applicability of our findings to clinical practice, we included all MI patients who would consent to MRI, regardless of presentation type or success of reperfusion. Our results indicate that T2-weighted MRI enables AAR estimation, even in patients with a second MI. In line with our first hypothesis, we found that AAR estimated by T2-weighted MRI was a predictor of the APPROACH lesion score, which is an anatomic and prognostically validated measure of the extent of myocardial jeopardy. Additionally, AAR was a multivariable predictor of IS.

Correlations and limits of agreement between T2-weighted MRI and the angiographic estimates of AAR leave questions regarding which answer is correct. The Bland-Altman analysis suggests either that T2-weighted MRI overestimates AAR or that the APPROACH lesion score underestimates AAR, or some combination of these 2 factors. However, the relations between IS derived by MRI and AAR derived by MRI, the APPROACH lesion score, the Duke jeopardy score, and the ST-segment elevation jeopardy score (Figure 2) provide an independent metric to help resolve these possibilities. As IS is physiologically a subset of the AAR, the expected relation between AAR and IS involves all points at or below the line of identity. Of all metrics analyzed, T2-weighted MRI had the fewest underestimations of AAR (1 underestimate), APPROACH was almost as good on this metric (5 underestimates), and the Duke jeopardy and the

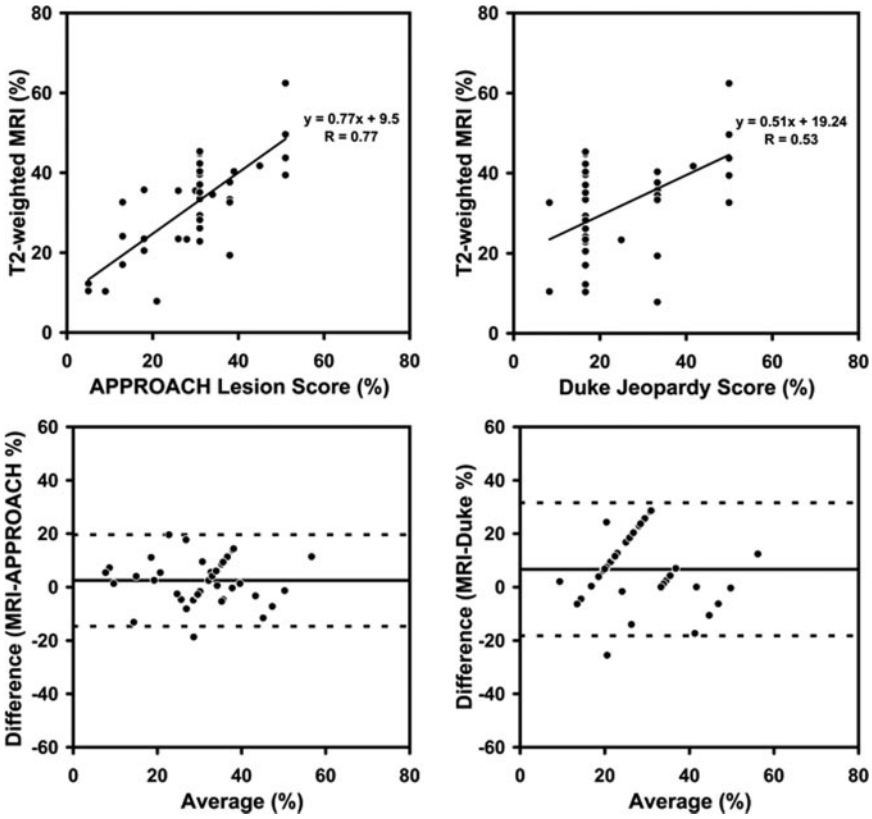

Figure 3. Relations between AAR derived by T2-weighted MRI and the APPROACH and Duke angiographic scores in STEMI and non-STEMI patients without a history of prior MI (n=40). Bland-Altman analysis revealed a 2.5% bias and 95% CIs between 19.6% and −14.6% for MRI vs APPROACH. Bland-Altman analysis revealed a 6.7% bias and 95% CIs between 31.6% and −18.2% for MRI vs Duke jeopardy score.

ST-segment elevation scores underestimated AAR in 10 and 19 cases, respectively. Although these data cannot unequivocally resolve which method provides the best measurement of AAR, all analyses indicate that T2-weighted MRI provides a good measure of AAR.

Consistent with previous studies in which salvage has been measured by nuclear perfusion imaging[25] and also with what might be expected from a biological perspective, coronary flow grades at baseline and after the procedure were predictors of salvage derived by MRI. Furthermore, given the pathophysiologic importance of no reflow,[26] which is also a determinant of IS,[27] we also found that AAR and IS were larger in patients with MVO compared with those with no evidence of microvascular injury. These results were also observed in analyses restricted to STEMI patients.

We confirmed the recent observations by Ortiz-Pérez et al,[17] who demonstrated that IS estimated by MRI closely matched angiographic estimates of jeopardy in a group of patients undergoing primary angioplasty for a first MI. Our results extend this analysis, as AAR derived by T2-weighted

Table 5. Predictors of MRI-Derived Percent IS (N=50)

Variable	*r*	β Estimate	95% CI	*P* Value
Univariable predictors of IS				
AAR by MRI, %	0.74	0.76	0.56, 0.96	<0.0001
APPROACH lesion score, %	0.67	0.70	0.47, 0.93	<0.0001
Duke jeopardy score, %	0.39	0.48	0.23, 0.72	0.0055
STEMI	0.39	10.7	2.98, 18.42	0.008
Sum of Rentrop's collateral grade and TIMI flow grade at initial angiography	−0.38	−3.80	−6.58, −1.01	0.009
Pulse pressure, mm Hg	−0.35	−0.21	−0.38, −0.04	0.019
Insulin therapy	0.33	9.7	0.89, 18.51	0.032
Postprocedure TIMI flow grade, 0/1, 2, 3	−0.28	−4.41	−9.0, 0.18	0.059
Multivariable predictors of IS				
AAR	…	0.69	0.46, 0.92	<0.0001
Sum of collateral and baseline TIMI flow grades at initial angiography	…	−1.87	−4.00, 0.26	0.084
Post-PCI TIMI flow grade	…	−3.83	−7.28, −0.38	0.031

The R^2 value for the multivariable model was 0.69. Variables that were prospectively determined as potential determinants of MI (eg, AAR) rather than consequences of MI (eg, ejection fraction, LV volumes) were tested.

Table 6. Univariable Predictors of MRI-Derived Percent Myocardial Salvage (N=50)

Univariable Predictors of Myocardial Salvage	*r*	β Estimate	95% CI	*P* Value
Postprocedure TIMI flow grade, 0/1, 2, 3	0.35	4.07	0.96, 7.18	0.011
Prior MI	0.31	6.06	0.68, 11.43	0.028
Sum of collateral and baseline TIMI flow grades at initial angiography	0.30	2.03	0.02, 4.03	0.047

MRI represents all of the ischemic territory, including viable and infarcted myocardium, permitting estimation of myocardial salvage. Our results extend those of Carlsson et al[25] and O'Regan et al,[28] who used black-blood, T2-weighted MRI to estimate myocardial salvage in MI patients. This method may be less applicable to clinical practice, because it has a lower diagnostic accuracy than does bright-blood, T2-weighted SSFP.[4]

Confirming our second hypothesis, T2-weighted MRI enabled delineation of the acute infarct territory in patients with prior MI. This is consistent with the observations of Abdel-Aty et al,[9] who found that T2-weighted, black-blood MRI combined with delayed enhancement permitted discrimination of acute versus chronic MI with a specificity of 96% in 57 infarct zones when evaluated by 2 blinded observers. Prior MI was also a predictor of myocardial salvage. One explanation for this result may be due to a preconditioning effect from chronic myocardial ischemia or enhanced coronary flow grades related to collateral artery supply.[29]

Several other observations merit comment. We found that coronary flow grade at initial angiography, represented by the sum of the TIMI and Rentrop collateral flow grades, was a negative multivariable predictor of IS, which is consistent with previous observations.[17,21] Our study extends these earlier findings because pre- and postprocedure coronary flow grades were also predictors of myocardial salvage derived by MRI. Our results add to the role of MRI in postinfarct imaging, where the utility of MRI to discriminate acute from chronic MI[9] and to depict adverse characteristics, such as LV remodeling,[30] has already been established. To our knowledge, T2-weighted SSFP methods are being developed by several MRI vendors.

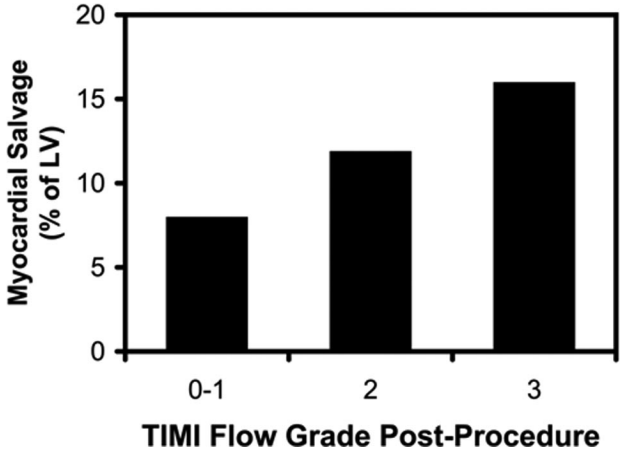

Figure 4. Myocardial salvage by MRI according to postprocedure TIMI flow grade (n=50) show stepwise increases in salvage related to the increasing amounts of postprocedural TIMI flow.

We also found that there was a fairly wide scatter for AAR estimates by ECG or the Duke angiographic risk score compared with the APPROACH lesion score or contrast-enhanced MRI (Figure 3). Although all of these variables were correlated with AAR estimated by T2-weighted MRI, the magnitude of the differences in AAR estimates between the variables (agreement) varied and appeared best for contrast-enhanced MRI and worst for ECG.

Conclusions

Our findings indicate that MRI can delineate the ischemic AAR and quantify myocardial salvage in MI patients, including those with prior MI. Our results are relevant to clinical practice, because MRI is the only method that can provide an AAR estimate without using radiation. Because angiographic estimates of AAR are either time-consuming or not normally used clinically, our findings open the door to measurement of myocardial salvage after acute MI not only for clinical research purposes but also for routine clinical practice. Future studies are required in larger patient groups to further evaluate these observations.

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Disclosures

None.

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CLINICAL PERSPECTIVE

The extent of myocardium subject to ischemia, also known as the myocardial area at risk (AAR), is a determinant of infarct size (IS) and prognosis. Therefore, identification of the ischemic AAR may provide useful information for clinical and research purposes. We investigated whether magnetic resonance imaging (MRI) measurement of AAR would be correlated with an angiographic AAR risk score in 50 consecutive patients with acute myocardial infarction (MI) treated at a community hospital. Bright-blood, T2-prepared, steady-state, free-precession MRI was used to depict the AAR, whereas IS was measured in late gadolinium-enhancement images. AAR was also estimated by the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease and Duke angiographic jeopardy scores. Myocardial salvage was calculated as AAR minus IS. We found that AAR measured by T2-weighted MRI was correlated well with angiographic measures of myocardial jeopardy. Measurement of AAR and IS in the early postinfarct period enabled estimation of myocardium salvage in all patients, regardless of presentation type or past history of MI. In multivariable analysis, IS was predicted by MRI-derived AAR. Our results have potential clinical importance for the following reasons. Bright-blood, T2-weighted MRI can delineate the ischemic AAR and quantify myocardial salvage in MI patients, including those with prior MI. MRI is the only method that can provide an AAR estimate without using radiation. Because angiographic estimates of AAR are time-consuming and not normally used clinically, our findings open the door to measurement of myocardial salvage after acute MI, not only for clinical research purposes but also for routine clinical practice.