Quantification of Myocardial Area at Risk With T2-Weighted CMR
Comparison With Contrast-Enhanced CMR and Coronary Angiography

Jeremy Wright, MBBS,*‡ Tom Adriaenssens, MD,† Steven Dymarkowski, MD, PhD,* Walter Desmet, MD, PhD,† Jan Bogaert, MD, PhD*
Leuven, Belgium; and Brisbane, Australia

OBJECTIVES We sought to quantify the myocardium at risk in reperfused acute myocardial infarction (AMI) in man with T2-weighted (T2W) cardiac magnetic resonance (CMR).

BACKGROUND The myocardial area at risk (AAR) is defined as the myocardial tissue within the perfusion bed distally to the culprit lesion of the infarct-related coronary artery. T2W CMR is appealing to retrospectively determine the myocardial AAR after reperfused AMI. Data on the utility of this technique in humans are limited.

METHODS One hundred eight patients with successfully reperfused ST-segment elevation AMI were studied between 1 and 20 days after percutaneous coronary intervention (PCI). We compared the volume of hyperintense myocardium on T2W CMR with the myocardial AAR determined by contrast-enhanced CMR with infarct endocardial surface length (ESL) and AAR estimated by conventional coronary angiography with the BARI (Bypass Angioplasty Revascularization Investigation) risk score.

RESULTS The volume of hyperintense myocardium on T2W CMR (mean 32 ± 16%, range 3% to 67%) was consistently larger than the volume of myocardial infarction measured with contrast-enhanced images (mean 17 ± 12%, range 0% to 55%) (p < 0.001). Myocardial salvage ranged from −4% to 45% of the left ventricular myocardium (mean 14 ± 10%). The AAR determined by T2W CMR compared favorably with the infarct ESL (r = 0.77) with contrast-enhanced CMR, and there was moderate correlation between the BARI angiographic risk score and infarct ESL (r = 0.42). The time between PCI and CMR did not cause a significant difference in the volume of T2W hyperintense myocardium (r = 0.11, p = 0.27) or the calculated volume of salvaged myocardium (r = 0.12, p = 0.23).

CONCLUSIONS T2W CMR performed early after successfully reperfused AMI in humans enables retrospective quantification of the myocardial AAR and salvaged myocardium. (J Am Coll Cardiol Img 2009;2:825–31) © 2009 by the American College of Cardiology Foundation
The myocardial area at risk (AAR) is defined as the myocardial tissue within the perfusion bed that is distal to the culprit lesion of the infarct-related coronary artery. In humans, the portion of the AAR that is irreversibly injured (i.e., infarcted) ranges from 0% (aborted infarction) to as much as 88% (1). The proportion of the AAR that survives—the salvaged myocardium—is dependent on multiple factors including time to reperfusion, ischemic pre-conditioning, collateral flow, distal embolization, reperfusion injury, and microvascular dysfunction. Because the extent of myocardial salvage determines final infarct size, quantification of myocardial salvage is an appealing method for the assessment of the efficacy of different therapies for acute myocardial infarction (AMI).

However, quantification of AAR remains challenging. Fluorescent microspheres are the reference standard for measuring the AAR in animal studies. In humans, the most widely used technique is single-photon emission computed tomography (SPECT), but there are many drawbacks to its widespread use. These include 24-h isotopy availability, additional radiation exposure for the patient and the operator, and suboptimal spatial resolution. Cardiac magnetic resonance (CMR) is an attractive technique to noninvasively quantify the AAR. First, infarct endocardial surface length (ESL) measured with contrast-enhanced CMR has recently been described as a measure of AAR (2).

Assuming the widely accepted “wave front phenomenon” of irreversible injury during coronary artery occlusion (3), AAR is estimated by measuring the circumferential extent of endocardial necrosis (as a percentage of total left ventricular [LV] endocardial circumference) on contrast-enhanced magnetic resonance images. The results compared favorably with 2 angiographic risk score estimates of AAR (2). Second, it has been demonstrated that T2-weighted (T2W) CMR, or “edema-weighted” imaging in animal models and patients, performed after myocardial infarction can retrospectively identify the AAR (4,5). The purpose of this study was to quantify AAR in patients with reperfused AMI with T2W CMR and to compare results with both angiographic risk scores and infarct ESL.

**METHODS**

**Patient population.** One hundred thirty-four patients with ST-segment elevation AMI and successful PCI were prospectively enrolled between May 2003 and October 2007. Patients were included if they had cumulative ST-segment elevation of 6 mm or more, PCI between 2 and 24 h after symptom onset, and significant LV dysfunction (hypokinesia of at least 3 contiguous myocardial segments). Exclusion criteria included pulmonary edema, cardiogenic shock, prior coronary artery bypass grafting, significant renal dysfunction (glomerular filtration rate <60 ml/min/1.73 m²), or other major comorbidities. One hundred nineteen consecutive patients underwent CMR during the in-hospital phase. This study comprises 108 of the 119 patients in whom T2W CMR-derived AAR quantification was able to be performed. We obtained informed written consent from all patients, and the study was approved by the ethics review board of the Gasthuisberg University Hospital, Leuven, Belgium.

**CMR imaging.** The CMR studies were performed on a 1.5-T system (Intera, Philips Medical Systems, Best, the Netherlands) with commercially available CMR software, electrocardiographic triggering, dedicated cardiac surface coils, and inspiratory breath holds. After determining the cardiac axes by the ethics review board of the Gasthuisberg University Hospital, Leuven, Belgium.

The CMR studies were performed on a 1.5-T system (Intera, Philips Medical Systems, Best, the Netherlands) with commercially available CMR software, electrocardiographic triggering, dedicated cardiac surface coils, and inspiratory breath holds. After determining the cardiac axes

**A B B R E V I A T I O N S  
A N D A C R O N Y M S**

AAR = area at risk  
AMI = acute myocardial infarction  
CMR = cardiac magnetic resonance  
ESL = endocardial surface length  
FOV = field of view  
LV = left ventricle/ventricular  
PCI = percutaneous coronary intervention  
SPECT = single-photon emission computed tomography  
T2W = T2-weighted  
TE = echo time  
TIMI = Thrombolysis In Myocardial Infarction  
TR = repetition time
follows: TR: 4.5 ms; TE: 1.3 ms; flip angle: 15°; 20 contiguous slices, slice thickness: 5 mm; matrix: 128 × 256; and FOV: 350 mm. Images were obtained 10 to 20 min after contrast administration, and the inversion time was tailored to null signal from normal myocardium.

**Image analysis.** All CMR images were analyzed on an offline workstation (ViewForum, Philips Electronics, Best, the Netherlands), and the results are the consensus of 2 experienced observers blinded to the angiographic data (S.D. and J.B.). To avoid interpretation bias, T2W images and contrast-enhanced CMR images were presented separately to the readers in a random way, respecting an interval of 3 days between readings. Moreover, CMR readers were blinded to the clinical and angiographical data. Endocardial and epicardial borders were delineated on the end-diastolic and -systolic short-axis slices for quantification of LV volumes, function, and mass. The AAR was quantified on the T2W images by delineation of myocardium with signal intensity 2 SDs above the mean signal obtained in the remote noninfarcted myocardium. If present, a central core of hypointense signal within the area of increased signal intensity (hemorrhagic infarction) was included in the AAR (6,7). Increased signal intensity from the blood pool adjacent to the endocardium due to slow flow was excluded. The volume of T2W increased signal intensity was normalized for LV mass and expressed as a percentage. Myocardial infarction was quantified by delineation of the areas of hyperenhancement on the contrast-enhanced CMR images and was also normalized for LV mass. If present, the dark subendocardial zone in the center of the hyperenhancement (microvascular obstruction) was included in the infarct volume. The infarct ESL was calculated as the percentage of summed lengths of endocardial hyperenhancement/total LV endocardial surface length (again, the hypoenhanced surface of microvascular obstruction was included in the infarct).

**Coronary angiography.** Cardiac catheterization with selective injection of right and left coronary arteries was performed before PCI. The angiograms were retrospectively assessed independently by 2 angiographers (not present at the PCI) blinded to the CMR data (J.W. and T.A.). The anatomic area at risk distally to the culprit lesion in the infarct-related artery was estimated with the adapted angiographic BARI (Bypass Angioplasty Revascularization Investigation) scoring system (8). Right ventricular marginal branches, atrial branches, and septal branches of the posterior descending coronary artery were excluded from the analysis. All remaining terminating coronary arteries were qualitatively graded from 0 to 3 on the basis of relative length. The BARI risk score was defined as the percentage of the sum scores of the vessels distal to the culprit lesion divided by the total LV score. Noninfarct-related artery stenoses did not contribute to the AAR (Fig. 1). Consensus between angiographers was used for subsequent analysis. When the Thrombolysis In Myocardial Infarction (TIMI) flow grade was >0 before PCI, the culprit vessel was verified by the 12-lead electrocardiogram and left ventriculography in 2 orthogonal planes.

**Statistical analysis.** Continuous data are reported as mean ± SD, and categorical data are reported as frequencies and percentages. Correlations between continuous variables were assessed with Pearson’s correlation coefficient r. The technique proposed by Bland and Altman was used to compare T2W AAR and BARI risk score with infarct ESL. Discrepancies between T2W AAR and infarct ESL correlated to clinical factors with Pearson’s r (continuous variables) and 1-way analysis of variance for categorical variables. All tests were 2-tailed, and statistical significance was accepted at p < 0.05. Data were analyzed with SPSS version 15.0 (SPSS Inc., Chicago, Illinois).

**RESULTS**

The demographic data of the 108 patients are presented in Table 1. The culprit vessel was the left anterior descending coronary artery in 48 (44%) patients, the left circumflex coronary artery in 12 (11%), and the right coronary artery in 48 (44%) patients. All patients had a region of increased signal intensity detected on T2W CMR (Fig. 2). Three patients had no increased signal on contrast-enhanced CMR (aborted infarcts), and 4 patients had evidence of prior infarction (in different vascular territories) on contrast-enhanced CMR. Microvascular obstruction was identified in 69 patients, range 0 to 80 g (mean 6.3 ± 10.7 g). Time from symptom onset to PCI ranged from 120 to 720 min (mean 250 ± 139 min). The CMR was usually performed within 1 week of PCI, range 22 to 496 h (mean 93 ± 64 h).

**Comparison of infarct size and (T2W AAR).** Infarct size ranged from 0% to 55% of the LV myocardium (mean 17 ± 12%). The T2W AAR ranged from 3%
to 67% (mean 32 ± 16%). The T2W AAR was significantly larger than infarct size (p < 0.001) (Fig. 3). The single exception was a patient with a modest-sized infarct (11% of LV myocardium) who had CMR 166 h after PCI. There was no correlation between the T2W AAR and the delay between PCI and CMR (r = 0.11, p = 0.27). Myocardial salvage ranged from 4% to 45% of the LV myocardium (mean 14 ± 10%). There was no correlation between myocardial salvage and the time from onset of symptoms to PCI (r = 0.11, p = 0.29) or between myocardial salvage and the delay between PCI and CMR (r = 0.12, p = 0.23).

**Comparison of different measures of area at risk.** The BARI risk score ranged from 14% to 48% of the LV myocardium (mean 31 ± 7.6%). There was moderate correlation between the BARI risk score and infarct ESL (r = 0.42, p < 0.001). There was strong correlation between T2W AAR and infarct ESL (r = 0.77, p < 0.001) (Fig. 4). The correlation between T2W and infarct ESL was significantly stronger than the correlation between BARI and infarct ESL (r = 0.77 vs. 0.42, Z = 3.99, p = 0.0003).

Bland-Altman analysis demonstrated that the agreement between T2W AAR and infarct ESL (mean difference 7.8 ± 10.0%) was similar to the

---

**Table 1. Patient Demographic Data**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
<td>91:17</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>59 ± 11</td>
</tr>
<tr>
<td>Hypertensive subjects (%)</td>
<td>35 (32)</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>62 (57)</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>73 (68)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Family history of coronary artery disease (%)</td>
<td>53 (49)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>4</td>
</tr>
<tr>
<td>Pre-hospital thrombolysis (%)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>TIMI flow grade before PCI (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>61 (57)</td>
</tr>
<tr>
<td>I</td>
<td>9 (8)</td>
</tr>
<tr>
<td>II</td>
<td>20 (18)</td>
</tr>
<tr>
<td>III</td>
<td>18 (17)</td>
</tr>
<tr>
<td>Multivessel disease (%)</td>
<td>58 (53)</td>
</tr>
<tr>
<td>Peak CK (U/l)</td>
<td>2,507 ± 1,843</td>
</tr>
<tr>
<td>Peak CKM (µg/l)</td>
<td>253 ± 194</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>159 ± 34</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>82 ± 24</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>49 ± 8</td>
</tr>
</tbody>
</table>

Data are n (%) ± SD or mean unless otherwise stated.

CK = creatine kinase; CKM = creatine kinase mass; LV = left ventricular; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

---

**Figure 1. Hemorrhagic Myocardial Infarction in a 69-Year-Old Man**

Coronary angiography before (A) and after (B) percutaneous coronary intervention, T2-weighted (T2W) cardiac magnetic resonance (CMR) (C). Left anterior oblique cranial view shows a proximal left anterior descending coronary artery (LAD) occlusion with thrombotic appearance (A). Presence of 60% stenosis on mid left circumflex coronary artery and 40% stenosis on the fourth inferolateral branch. Successful reperfusion of LAD (B). The T2W CMR shows area of increased signal intensity in anterior- septal left ventricular wall with hypointense core consistent with post-reperfusion intramyocardial hemorrhage (C). The BARI (Bypass Angioplasty Revascularization Investigation) risk score is 43.5%, T2W area at risk 48.7%.
agreement between BARI and infarct ESL (mean difference 7.3 ± 11.2%) (Fig. 5).

**Discrepancies between T2W AAR and infarct ESL.**
There was no significant correlation of the differences between T2W AAR and infarct ESL with time to reperfusion, time between PCI and CMR, LV ejection fraction, or infarct size. The mean difference between T2W AAR and infarct ESL did not seem to be predicted by TIMI flow grade before PCI, the culprit vessel, or single-versus multi-vessel disease (Table 2).

**DISCUSSION**

This study demonstrates that it is possible to quantify the volume of myocardium that has increased signal intensity on T2W CMR after AMI in humans. Animal studies have demonstrated that this portion of the myocardium correlates closely with the AAR as measured by fluorescent microspheres (4) and is thought to encompass reversibly and irreversibly injured myocardium. Contrast-enhanced CMR with late (or delayed) imaging for quantification of irreversible myocardial injury has been extensively validated in acute and chronic settings (9–11). Thus, comparing the volume of delayed enhancement with the volume of T2W AAR it is possible to determine the proportion of myocardium that has been salvaged.

The T2W CMR has long been considered technically challenging, due to the long echo times required and reduced spatial resolution and signal-to-noise ratios. Current pulse sequences with dedicated cardiac coils have largely overcome these problems. We found that it was possible to achieve diagnostic image quality in 108 of 119 patients.

Friedrich et al. (12) recently reported the feasibility of quantifying salvaged myocardium at risk in reperfused AMI. Our study confirms their findings and strengthens the validity of the technique by comparison with 2 other measures of myocardial area at risk (i.e., infarct ESL and BARI angiographic risk score). Infarct ESL is a recently described novel technique for estimating the area at risk (2) and is measured on contrast-enhanced CMR.
CMR images. In our study, T2W AAR and infarct ESL showed good correlation across the entire range of infarct sizes ($r = 0.77$). The Bland-Altman plot demonstrated a bias of 8% toward T2W AAR with SD 10%. This bias is in keeping with the observations of Lee et al. (1) of a small lateral border of at-risk but viable myocardium at the lateral edges of the infarcted myocardium. The SD we observed is consistent with the findings of Aletras et al. (4) in animals—their Bland-Altman analysis of T2W AAR versus fluorescent microspheres demonstrated a bias of 0.4% with SD of 9%.

We observed no relationship between myocardial salvage and time to reperfusion ($r = 0.11, p = 0.29$). Friedrich et al. (12) found myocardial salvage had a weak (although statistically significant) negative correlation with time between onset of symptoms and reperfusion ($r = -0.37$). Within the limitations of the small study size and mean time to reperfusion of 4 h, these observations are consistent with factors other than time to reperfusion having a significant influence on the volume of myocardial salvage.

The angiographic BARI risk score has recently been validated as a measure of myocardium at risk, by comparison with infarct ESL (2). We found only moderate correlation between BARI risk score and infarct ESL, in contrast to the results reported by Ortiz-Perez et al. (2). This might be due in part to different study populations, because Ortiz-Perez et al. (2) only studied patients with TIMI flow grade 0 before PCI. Additionally, the BARI risk score does not take into account stenoses in noninfarct-related vessels or collateral vessel flow. Moreover, it should be emphasized that inferior infarcts not infrequently extend to the right ventricular inferior wall (13). Because T2W AAR and infarct ESL measurements were limited to the LV, this might at least partially explain the poor agreement with BARI AAR estimates. In the absence of a reference standard (e.g., microspheres), these issues are difficult to resolve.

The optimal timing for measurement of T2W AAR and myocardial salvage is unknown. On the one hand, reperfusion injury (14) is thought to increase the volume of irreversibly injured myocardium within the first 48 h after restoration of epicardial coronary artery flow; thereafter, infarct shrinkage will reduce the volume of delayed enhancement over the next 6 to 8 weeks (9). On the other hand, edema will resolve over time. In our study CMR was performed between 1 and 20 days (mean and median 4 days). Despite this variation we observed the T2W AAR to be consis-
tently larger than infarct size measured with contrast-enhanced CMR. The only patient with T2W AAR less than infarct size was an 82-year-old man. Though unproven, the likely cause is prior infarction due to the same culprit vessel. The delay between PCI and CMR did not cause systematic differences in the measured T2W AAR or myocardial salvage, although serial studies of individual patients were not performed.

**CONCLUSIONS**

It is possible to retrospectively quantify the myocardium at risk and salvaged myocardium after reperfused ST-segment elevation AMI with T2W CMR. This should enable new insights into reperfusion therapy and contribute to clinical decision-making.

Reprint requests and correspondence: Dr. Jan Bogaert, Department of Radiology, Gasthuisberg University Hospital, Herestraat 49, B-3000 Leuven, Belgium. E-mail: jan.bogaert@uz.kuleuven.ac.be.

### REFERENCES

3. Reimer KA, Jennings RB. The “wavefront phenomenon” of myocardial ischaemic cell death. II. Transmural progression of necrosis within the framework of ischemic bed size (myocardium at risk) and collateral flow. Lab Invest 1979;40:633–44.

**Key Words:** area at risk ■ cardiac magnetic resonance ■ myocardial infarction ■ edema.