Assessment of Myocardial Viability With Contrast-Enhanced Magnetic Resonance Imaging Comparison With Positron Emission Tomography

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Background—Recent studies indicate that MRI, after administration of gadolinium-diethylenetriamine pentaacetic acid, can identify nonviable areas in dysfunctional myocardium. We compared MRI hyperenhancement with PET as a gold standard for detection and quantification of myocardial scar tissue.

Methods and Results—Thirty-one patients with ischemic heart failure (ejection fraction, 28±9%) were imaged with PET and MRI. Scar was defined as regionally increased MRI signal intensity 20 minutes after injection of 0.2 mmol/kg gadolinium-diethylenetriamine pentaacetic acid and as concordantly reduced perfusion and glucose metabolism as defined by PET. Sensitivity and specificity of MRI in identifying patients and segments (n=1023) with matched flow/metabolism defects was 0.96 of 1.0 and 0.86 of 0.94, respectively. Eleven percent of segments defined as viable by PET showed some degree of MRI hyperenhancement. Defect severity score based on visual analysis was 44.3±9.1 for PET and 47.6±11.1 for MRI (r=0.91, P<0.0001). Quantitatively assessed relative MRI infarct mass correlated well with PET infarct size (r=0.81, P<0.0001). Furthermore, MRI hyperenhancement was a better predictor of scar tissue than end-diastolic and end-systolic wall thickness or thickening.

Conclusions—In severe ischemic heart failure, MRI hyperenhancement as a marker of myocardial scar closely agrees with PET data. Although hyperenhancement correlated with areas of decreased flow and metabolism, it seems to identify scar tissue more frequently than PET, reflecting the higher spatial resolution. Additional functional studies after revascularization are required to define the significance of small islands of scar detected by MRI. (Circulation. 2002; 105:162-167.)

Key Words: magnetic resonance ■ coronary disease ■ heart failure ■ hibernation

It is well established that impaired left ventricular (LV) function does not necessarily represent irreversible tissue injury, because contractile performance can improve after revascularization.1 Correct assessment of the extent of viable and nonviable myocardium in patients with severely reduced LV ejection fraction (EF) and chronic coronary artery disease (CAD) is important for clinical decision making, because perioperative mortality and morbidity of these patients are increased. However, it has been shown that patients with dysfunctional but viable myocardium profit most from revascularization.2 Detection of viability based on assessment of myocardial perfusion and glucose metabolism by PET is presently considered by many as the reference method.3 The extent of viable myocardium correlates with improved contractile performance after revascularization4,5 and affects both short-term6 and long-term7-9 prognosis. MRI, using gadolinium-based contrast agents, delineates irreversibly damaged myocardium8 and predicts areas that will not recover functionally after revascularisation.9 The aim of this study was to compare extent and location of hyperenhancement with nonviable tissue defined by PET in patients with chronic ischemic heart failure.

Methods

Patients

Thirty-one patients (26 men; 59±10 years of age) with CAD (angiography) and reduced LV function (EF<35%), assessed by echocardiography or contrast ventriculography and scheduled for a diagnostic PET study, were included in the study after giving informed consent. Twenty-six patients had documented (history, Q-waves, or elevated enzymes) myocardial infarction (14 anterior and 15 inferior). Twenty patients had 3-vessel, 7 had
on the basis of volumetric sampling of tracer uptake. Areas of normal, mismatched, and matched defects were calculated.

Extent of scar tissue was estimated using a 3-point scoring system, where −1 indicated viable tissue, −2 indicated nontransmural defect, and −3 indicated transmural defect. For each patient, the 33 segments were scored and the sum was calculated (minimum possible score, 33; maximum possible score, 99). Interobserver variability for MRI and PET was low ($r=0.95$, slope=0.80, $P<0.0001$ and $r=0.94$, slope=0.82, $P<0.0001$, respectively).

Global and Regional LV Function
LV volumes, mass, EF, and regional wall thickness in end diastole/end systole were calculated from MRI cine short-axis views. Regional wall motion was visually assessed within each of the 33 segments by 2 observers. It was graded as normokinetic, moderate hypokinetic, severe hypokinetic, and akinetic or dyskinetic.

Statistics
Mean and standard deviation (SD) are given for all continuous data. Using PET as the gold standard, sensitivity and specificity of detecting scar tissue were determined for MRI. Linear regression/Bland-Altman analysis was used for comparison of defect extent. One-way ANOVA and post hoc Bonferroni-corrected $t$ test, as well as receiver operating characteristic (ROC) analysis (SPSS Inc), was applied for assessment of hyperenhancement and wall thickness/thickening in differentiating scar from viable tissue. $P<0.05$ was considered statistically significant.

Results
MRI LV EF averaged $28\pm9\%$, mean LV mass was $135\pm31$ g, end-diastolic volume was $258\pm78$ mL, and end-systolic volume was $190\pm74$ mL.

Enhanced MRI and PET
Five patients (16%) had transmural and 4 patients (13%) had subendocardial hyperenhancement only, whereas 18 patients (58%) had a combination of both. Four patients (13%) showed no hyperenhancement. Eleven patients (35%) had a severe-matched and 7 patients (23%) had a mild-matched PET defect only. Ten patients (32%) showed a combination of both, and 3 patients (10%) were normal. Individual patient data are shown in Table 1. Sensitivity and specificity of MRI in detecting patients with scar tissue, defined by PET, were 0.96 and 1, respectively. In the single patient who did not show hyperenhancement, 1 segment had a severe and 2 segments had a mild-matched defect in PET. Figures 1 and 2 show patient examples of MRI hyperenhancement compared with PET results.

Location of Scar Tissue
Sensitivity and specificity for detecting transmural defects only were 0.86 and 0.94, respectively, and for detecting any defect (transmural or nontransmural) were 0.83 and 0.88, respectively. In 11% of segments defined as normal by PET, MRI showed hyperenhancement, whereas only 5% with a matched PET defect showed no hyperenhancement (Table 2). Fifty-five percent of segments with subendocardial hyperenhancement were classified as normal by PET. Of 34 segments showing a mismatch, reflecting hibernating myocardium in PET, 3 showed transmural, 8 showed nontransmural, and 23 showed no hyperenhancement.

The number of segments with scar tissue increased with the level of dysfunction. In segments with normokinesia, there
were 17 of 249; with moderate hypokinesia, there were 16 of 248; in severe hypokinesia, there were 44 of 277; and with dyskinesia and akinesia, there were 128 of 249 segments with scar tissue as assessed with PET. To assess influence of contractile performance, the results in akinetic and dyskinetic segments and severely and moderately hypokinetic segments were determined separately (Table 3). In normokinesia, of 6 segments with a transmural defect in PET, only 2 were detected by hyperenhancement, and of 11 segments with a nontransmural defect, only 2 were detected by hyperenhancement.

**Extent of Scar Tissue**

Visual scar score averaged 44.3±9.1 for PET and 47.6±11.1 for MRI, with a mean difference of 9%. A close correlation between both estimates was found \((r=0.91, \text{slope}=1.1, P<0.0001, \text{Figure 3})\).

Mean LV mass, derived from contrast MR images, was 135±31 g compared with the value of 132±28 g obtained from cine images \((r=0.94 \text{ with a mean difference of } 7\% \text{ and a slope of } 0.84, P<0.0001)\). Relative infarct size expressed as percent LV mass was 18±16%, which correlated well \((r=0.81, \text{slope}=0.70, P<0.0001)\) with quantitative measurements of 20±18% by PET expressed as percent defect of LV surface (Figure 3).

**Viability and Cardiac Function**

The extent of scar tissue showed a weak inverse correlation \((P=0.05)\) with EF \((r=-0.42)\) and with end-diastolic and end-systolic volumes \((r=0.32 \text{ and } r=0.41, \text{respectively})\). As shown in Table 4, there was a significant difference between...
end-diastolic and end-systolic wall thickness and wall thickening in viable segments compared with segments with transmural scar in PET ($P<0.001$). However, ROC analysis (Figure 4) revealed smaller area under the curve for wall thickness and thickening compared with hyperenhancement.

Discussion

The present study indicates that in patients with chronic CAD and severely reduced LV function, the MRI hyperenhancement technique is able to identify location and extent of nonviable tissue in close agreement with PET measurements provided by comparison of flow and glucose metabolism.

Dysfunctional but viable areas have a high likelihood of improving contractile performance after restoration of flow.

Estimation of perfusion and glucose metabolism by PET has been reported to accurately differentiate between viable and nonviable myocardial tissue in many studies and, thus, was used as reference method. Myocardial regions graded viable by PET are expected to improve contractile performance in 78% to 92% of cases. A recent comparison of various imaging modalities suggested that nuclear techniques, including PET, tend to overestimate tissue viability on the basis of functional recovery after revascularization, yielding lower specificity compared with techniques assessing contractile reserve. In cases of nontransmural scar formation, regional function may not recover despite the presence of residual tissue viability in the affected territory. Therefore, functional recovery may not be the only valid endpoint for evaluation of tissue viability. Prognosis may be altered without changing LV function by improving LV remodeling processes, promoting electrical stability, and reducing risk of subsequent fatal ischemic events. Besides scintigraphic and echocardiographic methods, MRI offers various parameters of tissue viability, such as wall thickness and wall thickening, and hyperenhancement. This study is, to our knowledge, the first direct comparison of MRI hyperenhancement with PET in patients with ischemic heart failure.

Hyperenhancement and Myocardial Viability

Several studies suggest that areas of hyperenhancement represent irreversible ischemic injury. Wesbey et al showed increased $T_1$ shortening in transiently ischemic canine myocardium compared with normal tissue. In a canine model, after varying length of coronary occlusion and reperfusion, the size and three-dimensional shape of hyperenhancement correlated closely with irreversible damage defined by triphenyltetrazolium chloride staining. In a clinical follow-up of 41 patients with ischemic ventricular dysfunction, segments that showed transmural hyperenhancement before revascularization did improve to a lesser extent than areas without transmural or nontransmural enhancement. However, the mechanism of Gd-DTPA retention in areas of chronic irreversible tissue damage remains largely unknown. In acute infarction, contrast wash-in and wash-out kinetic as well as altered myocyte and sarcolemmal membrane integrity may play an important role. Maes et al examined LV biopsies of patients with chronic wall motion abnormalities

### Table 3. Accuracy of MRI Hyperenhancement in Assessing Transmural or Both Transmural and Subendocardial Defects as Defined by PET in Relation to the Degree of Dysfunction

<table>
<thead>
<tr>
<th>Segments</th>
<th>Transmural</th>
<th></th>
<th>Transmural and Subendocardial</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>All</td>
<td>0.86</td>
<td>0.94</td>
<td>0.83</td>
</tr>
<tr>
<td>Akinetic</td>
<td>0.89</td>
<td>0.84</td>
<td>0.89</td>
</tr>
<tr>
<td>Severe hypokinetic</td>
<td>0.86</td>
<td>0.90</td>
<td>0.95</td>
</tr>
<tr>
<td>Moderate hypokinetic</td>
<td>1.00</td>
<td>0.98</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Table 4. Segmental Wall Thickness or Thickening (mm) Compared With Extent of Scar as Defined by PET

<table>
<thead>
<tr>
<th></th>
<th>v (n=767)</th>
<th>m (n=32)</th>
<th>nt (n=56)</th>
<th>T (n=137)</th>
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<tbody>
<tr>
<td>ED</td>
<td>7±2</td>
<td>6±2‡</td>
<td>5±2*</td>
<td></td>
</tr>
<tr>
<td>ES</td>
<td>9±3</td>
<td>8±2‡</td>
<td>8±4</td>
<td>5±2*</td>
</tr>
<tr>
<td>WT</td>
<td>2±2</td>
<td>2±2</td>
<td>0±1†</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

* $P<0.001$ vs v, m, and nt.
† $P<0.001$ vs v and nt.
‡ $P=0.006$ vs v.
and compared them with their PET findings. They found a significantly higher proportion of fibrosis in areas with a matched defect than in normal areas evidencing scar formation. This may lead to altered kinetic behavior and partition coefficient of Gd-DTPA as extracellular space increases. In our study, segments with hyperenhancement agreed closely with segments with matched defects. This is in concordance with the above studies.

Compared with 201TI imaging, a reduced accuracy of hyperenhancement in hypokinetic segments compared with akinetic segments for detecting scar tissue was found. As shown in Table 3, diagnostic accuracy of MRI did not change with the degree of dysfunction in our study when compared with PET. Different sequence parameters, such as an inversion prepulse as described by Simonetti et al and the higher dose of Gd-DTPA (0.1 vs 0.2 mmol/kg bw), may be important for signal intensity in areas with smaller proportion of scar tissue, which is suspected in segments with preserved wall motion. In normokinesia, a reduced sensitivity compared with PET was found. However, in these areas, scar tissue is not expected, and, therefore, defects in these segments might represent false-positive results by PET.

Visual assessment of MRI data tends to overestimate scar tissue compared with PET (Figure 2). Several reasons may account for this observation. First, MRI can delineate segments more accurately, because the border between hyperenhanced and normal areas is distinct, whereas in nongated PET images, the border between normal and defect areas is less well defined (Figure 2). Fifty-five percent of segments showing a subendocardial enhancement by MRI were classified as normal by PET. Because the assessment of wall thickness is limited by the spatial resolution of nongated PET, epicardial tracer activity may mask small subendocardial defects. Therefore, MRI might provide, with its better spatial resolution, a more subtle delineation of scar tissue than PET. Second, FDG is a marker for viability, whereas Gd-DTPA is considered a marker for scar tissue. Thus, a relatively small number of viable cells may show increased FDG uptake, indicating viability, whereas structural changes may already coexist and alter Gd-DTPA kinetics. Therefore, PET imaging may show viability in segments with hyperenhancement, depending on the relative contribution of viable and fibrotic tissue. Third, an increase in regional signal intensity (Gd-DTPA) may be easier to interpret than a regional comparison of flow and metabolism by PET. And, finally, all comparative studies have the potential for anatomical misalignment. Although short-axis views were used in both modalities, the visualization of the inferior interception of the ventricles is especially difficult in patients with extensive scar tissue, because regions are not always clearly definable in PET.

**Viability and Myocardial Function**

As expected, the proportion of segments with scar increased with severity of dysfunction. However, parameters like EF and end-diastolic and end-systolic volumes showed only a weak correlation with extent of scar. Regional wall thickness or thickening is reduced significantly with increasing myocardial damage. However, these wall-thickness parameters had only limited diagnostic value for differentiation between viable and scar tissue (Figure 4). In contrast to previous investigations, remodeling processes may have altered LV geometry in our patient population with severely dilated ventricles, so that these parameters did not allow the detection of viable myocardium.

**Study Limitations**

An improved contractile performance is commonly considered the gold-standard for assessing viable myocardium. We did not examine patients after revascularization. However, several clinical studies exist demonstrating the diagnostic value of PET criteria in predicting functional recovery and clinical outcome. In addition, a recent study by Kim et al showed the predictive value of MRI for functional recovery. It was the purpose of this study to compare results of the most sensitive technique presently available for assessing viability with extent and location of MRI hyperenhancement as a specific marker for scar tissue.

Only a few segments showed a mismatch in PET (hibernating myocardium, 34 of 1023). Therefore, we were not confident evaluating MRI findings in these segments. It is interesting to note that 68% of these segments showed no hyperenhancement, whereas transmural enhancement occurred in only 8% (Table 2). This suggests that hibernating myocardium was diagnosed correctly by MRI as viable in most cases. However, patients with higher incidence of
hibernation have to be examined before final conclusions can be drawn.

Conclusions
In patients with chronic CAD and severely reduced LV function, hyperenhancement 20 minutes after application of 0.2 mmol Gd-DTPA/kg bw correlated closely concerning location and extent with scintigraphically assessed infarct size using PET with NH3 for perfusion and FDG as a metabolic tracer. Results were independent of the severity of contractile dysfunction. Thus, the MRI hyperenhancement technique seems to be a promising diagnostic tool for detecting nonviable tissue in patients with advanced CAD.

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References