Value of Magnetic Resonance Imaging for the Noninvasive Detection of Stenosis in Coronary Artery Bypass Grafts and Recipient Coronary Arteries

Susan E. Langerak, PhD; Hubert W. Vliegen, MD; J. Wouter Jukema, MD; Patrik Kunz, PhD; Aeilko H. Zwinderman, PhD; Hildo J. Lamb, PhD; Ernst E. van der Wall, MD; Albert de Roos, MD

Background—Magnetic resonance imaging (MRI) is a potential noninvasive diagnostic tool to detect coronary artery bypass graft stenosis, but its value in clinical practice remains to be established. We investigated the value of MRI in detecting stenotic grafts, including recipient vessels.

Methods and Results—We screened for inclusion 173 consecutive patients who were scheduled for coronary angiography because of recurrent chest pain after coronary artery bypass grafting (CABG). We studied 69 eligible patients with 166 grafts (81 single vein, 44 sequential vein, and 41 arterial grafts). MRI with baseline and stress flow mapping was performed. Both scans were successful in 80% of grafts. Grafts were divided into groups with stenosis ≥50% (n=72) and ≥70% (n=48) in the graft or recipient vessels. Marginal logistic regression was used to predict the probability for the presence of stenosis per graft type using multiple MRI variables. Receiver operator characteristics (ROC) analysis was performed to assess the diagnostic value of MRI. Sensitivity (95% confidence interval)/specificity (95% confidence interval) in detecting single vein grafts with stenosis ≥50% and ≥70% were 94% (86 to 100)/63% (48 to 79) and 96% (87 to 100)/92% (84 to 100), respectively.

Conclusions—MRI with flow mapping is useful for identifying grafts and recipient vessels with flow-limiting stenosis. Flow scans could be obtained in 80% of the grafts. This proof-of-concept study suggests that noninvasive MRI detection of stenotic grafts in patients who present with recurrent chest pain after CABG may be useful in selecting those in need of an invasive procedure. (Circulation. 2003;107:1502-1508.)

Key Words: magnetic resonance imaging ▪ stenosis ▪ bypass

Coronary artery bypass grafting (CABG) is a frequently performed surgical procedure worldwide. In 1998, an estimated 336,000 patients underwent such a procedure in the United States.1 Subsequent graft disease, especially vein graft disease, is an important issue in cardiology, as reflected by the increasing number of patients who present with recurrent angina after CABG.2

Coronary angiography is the gold standard to evaluate the status of the grafts and recipient vessels. However, this invasive procedure includes x-ray exposure, hospitalization, and a small risk of complications.3 Consequently, noninvasive alternative diagnostic methods are preferable for detecting grafts and coronary arteries with significant luminal narrowing.

MRI allows the noninvasive evaluation of both graft morphology and function. By using MR angiography and MR flow mapping, patent grafts can be differentiated from occluded grafts, but the detection of graft stenosis, especially stenosis in recipient vessels (coronary arteries distal from the graft anastomosis) has remained difficult.4–10

Extensive work in native coronary arteries has been performed with the use of MRI, demonstrating its ability to distinguish patent from occluded coronary arteries,11,12 to detect stenosis in proximal coronary arteries,13–15 and to quantify flow.16–18 To our knowledge, no studies have focused on the value of MRI in detecting stenotic vein grafts and recipient vessels. Recently, a fast MR flow sequence was validated, and this method allowed accurate flow measurements in vitro and in grafts.19,20

The purpose of this study was to assess the value of MRI with baseline and stress flow measurements in detecting grafts including recipient vessels with stenosis in patients who present with recurrent chest pain after CABG.

Methods

Patients

We screened 173 consecutive CABG patients who had been referred for coronary angiography because of recurrent chest pain...
for potential inclusion from March 1999 to January 2001. Adenosine-related exclusion criteria were chronic obstructive pulmonary disease (17 patients) and second or third degree atrioventricular block (5 patients).21,22 MR-related exclusion criteria consisted of metallic devices (14 patients), unstable angina (4 patients), atrial fibrillation (5 patients), irregular cardiac rhythm (5 patients), claustrophobia (5 patients), inability to lie flat (1 patient), and logistic reasons (14 patients), leaving 103 patients to be included. MR flow mapping was performed remote from the stented area. Informed consent was obtained in 71 out of 103 patients. Patients were not allowed to have caffeine-containing beverages on either of the examination days. The medical ethics committee of our institution approved the study protocol.

All 71 patients underwent MRI in addition to coronary angiography. In 2 patients, artifacts from sternal wires prevented adequate cardiac imaging. Data from the resulting 69 patients (age 65.9 ± 8.7 years) are presented. Patients were not allowed to have caffeine-containing beverages on either of the examination days. The medical ethics committee of our institution approved the study protocol.

Coronary Angiography
Coronary angiography was performed using the femoral approach with the Seldinger technique. To standardize vasomotor tone, a 0.3-mg bolus of nitroglycerine was injected into all grafts before visualization of the grafts and recipient vessels. When visual analysis of the grafts and recipient vessels revealed stenosis >20%, quantitative coronary analysis (QCA) was performed (Medis, Heart Core). According to the most severe stenosis, grafts were divided into 2 groups, one with stenosis severity ≥50% and one with stenosis severity ≥70%.

MR Imaging
A 1.5 Tesla Gyroscan ACS-NT MR scanner (Philips Medical Systems) equipped with Powertrack 6000 gradients (25 mT · m⁻¹, 100 mT · m⁻¹ · ms⁻¹), cardiac research software patch, and 5-element cardiac synergy coil was used. A survey scan was performed before coronary angiography in 41 patients (2.3 ± 2.0 days) and after coronary angiography in 28 patients (9.3 ± 13.8 days). No change in the patients’ clinical status was observed between the procedures.

MR Image Analysis
Patent vascular structures are identified as bright signal by gradient-echo MRI, whereas occluded grafts are not visualized on consecutive MRI slices.10 Consequently, nonvisualized grafts were scored as occluded (zero flow). Flow analysis was performed using the FLOW software package (Medis). Flow scans consisted of paired modulus and phase images in consecutive time
frames of 23 ms. A region of interest of 2 × 2 reconstructed pixels was placed in the center of each phase image, and the mean velocity of 4 pixels was defined as peak velocity for that heart phase. The mean peak velocity over the entire cardiac cycle was defined as average peak velocity (APV, cm/s), and the highest peak velocities during systole and diastole were defined as systolic peak velocity (SPV, cm/s) and diastolic peak velocity (DPV, cm/s) respectively (Figure 2). The ratio between DPV and SPV was called diastolic-to-systolic velocity ratio (DSVR). Velocity reserve (CVR) was calculated as the ratio between stress and baseline APV.

Statistical Analysis

Grafts were divided into 4 groups: single vein, sequential vein, single arterial, and sequential arterial grafts. Heart rate and blood pressure at baseline versus stress were compared by paired Students’ t test. A probability value < 0.05 was considered statistically significant. Receiver-operator characteristic (ROC) analyses were used in each graft type to determine the diagnostic performance of each velocity parameter for detecting stenosis severity ≥50% or ≥70% (univariate analysis).

Marginal logistic regression was performed to predict the probability for the presence of stenosis ≥50% or ≥70% for baseline and combined baseline and stress parameters. Velocity parameters were included in the multivariate analysis when univariate analysis revealed a significant ROC area. Variables of the regression equation were used to define a graft specific model, which was used to calculate the probability for the presence of stenosis in grafts with recipient vessels. ROC analysis was performed and jack-knife estimates of sensitivity and specificity were reported at the optimal cutoff point in probability. The optimal cutoff was chosen as the point closest to the top left, preferring high sensitivity. Finally, the diagnostic value of MRI for ROC analysis. Sixteen out of 81 single vein grafts supplied the LAD, 25 the LCX, and 40 the RCA region. Thirty-six grafts were not visualized in their expected course and were considered occluded. Velocity mapping was performed in 130 grafts.

QCA results regarding stenosis severity are depicted in Table 2. Forty-one out of 166 (25%) grafts or recipient vessels were occluded. From the 36 nonvisualized grafts or recipient vessels, QCA revealed 6 without significant stenosis, 30 with stenosis ≥50%, 27 with stenosis ≥70%, and 25 occluded grafts or recipient vessels. This resulted in a sensitivity and specificity of 61% (25/41 grafts) and 91% (114/125 grafts), respectively, for conventional gradient-echo MRI in detecting occlusions in grafts or recipient vessels.

### TABLE 1. Patient Characteristics

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>69</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female, n</td>
<td>58/11</td>
</tr>
<tr>
<td>Age, y*</td>
<td>65.9 ± 8.7 (43–79)</td>
</tr>
<tr>
<td>Time after bypass graft surgery, y*</td>
<td>9.3 ± 5.4 (0–22)</td>
</tr>
<tr>
<td>Total grafts/studied grafts, n</td>
<td>177/166</td>
</tr>
<tr>
<td>Prior myocardial infarction, n</td>
<td>41</td>
</tr>
<tr>
<td>Subendocardial infarction</td>
<td>22</td>
</tr>
<tr>
<td>Transmural infarction</td>
<td>19</td>
</tr>
<tr>
<td>Risk factors, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>53 (77)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36 (52)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>9 (13)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>13 (19)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>42 (61)</td>
</tr>
<tr>
<td>Medication, n (%)</td>
<td></td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>66 (96)</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>48 (70)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>53 (77)</td>
</tr>
<tr>
<td>Statins</td>
<td>55 (80)</td>
</tr>
<tr>
<td>ß-blocking agents</td>
<td>44 (64)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>22 (32)</td>
</tr>
<tr>
<td>AT II antagonist</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>17 (25)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Other</td>
<td>35 (51)</td>
</tr>
<tr>
<td>ACE indicates angiotensin-converting enzyme; AT, angiotensin.</td>
<td></td>
</tr>
</tbody>
</table>

*Values are given as mean ± SD (range).

### TABLE 2. Graft Characteristics Based on Quantitative X-Ray Coronary Analysis

<table>
<thead>
<tr>
<th>Coronary Artery Bypass Grafts</th>
<th>Total</th>
<th>Stenosis ≥50%</th>
<th>Stenosis ≥70%</th>
<th>Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studied grafts</td>
<td>166</td>
<td>72</td>
<td>48</td>
<td>41</td>
</tr>
<tr>
<td>Single vein grafts</td>
<td>81</td>
<td>39</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Sequential vein grafts</td>
<td>44</td>
<td>23</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Single arterial grafts</td>
<td>27</td>
<td>8</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Sequential arterial grafts</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; AT, angiotensin.
vessels. A sensitivity of 75% and specificity of 91% was found for the assessment of graft occlusion alone.

**Adenosine Side Effects**
Baseline and stress MR flow measurements were both successful in 104 out of 130 (80%) grafts. Despite a successful stress flow scan, baseline flow mapping was unsuccessful in 2 grafts. Stress flow mapping was not possible in 24 grafts (18%) because of adenosine-related side effects. Side effects during adenosine infusion were reported in 45 out of 69 patients (65%) and included chest pain, dyspnea, facial flush, and headache. Side effects disappeared within 2 minutes after the infusion had stopped.

**Hemodynamics and Scan Duration**
Average ± SD baseline heart rate during MRI was 62.8 ± 9.9 beats per minute (bpm) and increased to 75.5 ± 11.4 bpm (*P < 0.001*) during stress. Systolic and diastolic blood pressures during MRI at baseline (systolic 136.0 ± 22.1 mm Hg; diastolic 71.1 ± 10.6 mm Hg) and during stress (systolic 135.9 ± 26.0 mm Hg, *P = 0.47*; diastolic 71.2 ± 10.4 mm Hg, *P = 0.86*) were similar. Mean breath-hold duration was 19.6 ± 3.1 sec for completed baseline flow scans and 16.3 ± 2.7 sec for completed stress flow scans.

**Single and Sequential Vein Grafts**
ROC analysis showed the best univariate predictive values for stress velocity parameters to detect stenotic single vein grafts or recipient vessels as reflected by larger ROC areas (Table 3). The optimal cutoff point (sensitivity/specificity) to differentiate single vein grafts with and without a stenosis ≥70% was 13.58 cm/s (91%/62%) for stress APV, 21.29 cm/s (91%/52%) for stress SPV, 20.86 cm/s (91%/74%) for stress DPV, 1.02 (96%/78%) for stress DSVR, and 1.43 (91%/78%) for the CVR. In sequential vein grafts, the best univariate predictive values to identify stenosis were obtained for stress APV and DPV. To detect sequential vein grafts with stenosis ≥70%, higher cutoff points for stress APV and DPV (sensitivity/specificity) were found as compared with single vein grafts; they were 22.47 cm/s (82%/62%) for stress APV and 38.67 cm/s (88%/62%) for stress DPV.

Multivariate analysis in single vein grafts showed the best diagnostic value of MRI using all baseline and stress velocity parameters (Table 3). This resulted in a sensitivity/specificity of 94%/63% (ROC area 0.90) and sensitivity/specificity of 96%/92% (ROC area 0.96) for detecting single vein grafts or recipient vessels with stenosis ≥50% and ≥70%, respectively (Table 4 and Figure 3). No difference in the diagnostic value of MRI was demonstrated in detecting stenotic single vein grafts to the LAD (ROC areas: 1.00, *P < 0.001*), LCX (ROC areas: 0.96, *P < 0.001*), and RCA (ROC areas: 0.97, *P < 0.001*) regions. There might have been insufficient power for this comparison. In sequential vein grafts, all velocity parameters except the DSVR and CVR were included in multivariate analysis, yielding ROC areas of 0.87 and 0.88 for detecting stenosis ≥50% and ≥70%, respectively (Table 3). Sensitivity/specificity for detecting sequential vein grafts or recipient vessels with luminal stenosis ≥50% was 91%/82%. These values were 94%/71% for identifying sequential vein grafts or recipient vessels with stenosis ≥70% (Table 4 and Figure 3).

**Single and Sequential Arterial Grafts**
Multivariate analysis of all baseline and stress velocity parameters in single arterial grafts revealed ROC areas of
0.96 (0.86 to 1.00; \(P<0.005\)) and 0.90 (0.74 to 1.00; \(P=0.07\)) for detecting stenosis \(\geq 50\%\) or \(\geq 70\%\). Because of the limited number of stenotic sequential arterial grafts, ROC analyses were not performed.

### Discussion

The present study shows that in a population suitable for adenosine infusions, MRI velocity measurements may be useful for detecting flow-limiting lesions in bypass grafts and recipient vessels in patients presenting with chest pain after CABG.

#### Value of MRI Velocity Parameters

Multiple velocity parameters in a graft specific regression model revealed the best value of MRI in detecting stenotic single and sequential vein grafts. The graft specific models seem to be very promising but should be tested in a second group of patients to predict the probability of significant graft stenosis when MRI velocity values of that graft are available. A prospective study using the cutoff values of the patients with regard to these factors (Table 1), velocity reserve allowed differentiation between single vein grafts with and without stenosis \(\geq 50\%\) or \(\geq 70\%\) as reflected by ROC areas of 0.81 and 0.89. In sequential vein grafts, the velocity reserve could not differentiate between grafts with and without stenosis \(\geq 50\%\) or \(\geq 70\%\) (ROC area 0.66 to 0.71). This implies that a single distal stenosis in a sequential graft will hardly impair proximal flow capacity during maximal hyperemia, as distal flow through other graft anastomoses preserves proximal flow. Although the velocity reserve alone does not have an adequate diagnostic value in detecting stenotic sequential vein grafts, multivariate analysis of combined baseline and stress velocity parameters showed acceptable ROC areas.

#### Clinical Implications

The need for a noninvasive diagnostic tool with a high sensitivity for selecting patients with a stenotic graft or recipient vessel is underlined by the substantial part (40%) of the currently studied CABG patients who underwent diagnostic coronary angiography without showing lesions that required further intervention. In an ideal scenario, these CABG patients have been labeled as “normal” before coronary angiography, such that invasive analysis was deferred. Noninvasive tests, such as myocardial perfusion scintigraphy and dobutamine stress echocardiography, provide valuable strategies for the detection of myocardial ischemia and viability in patients with coronary artery disease. The advantage of the presented MRI approach is the selection of grafts in the need of further invasive analysis and revascularization to alleviate myocardial ischemia.

#### Study Limitations

Although MRI seems reliable in detecting grafts and recipient vessels with significant stenosis, there are a number of patients who had to be excluded from the study. The main reasons were MRI- and adenosine-related. Adenosine-induced side effects prohibited the performance of stress testing in 20% of the grafts. However, baseline MRI allowed detection of stenotic single and sequential vein grafts as reflected by ROC areas of 0.76 to 0.88.

We applied conventional 2-dimensional gradient-echo scans to visualize grafts. A good diagnostic value of these gradient-echo scans was found in detecting graft occlusion (sensitivity 75%, specificity 91%). These values were in the range of previously described values. Conventional gradient-echo MRI included a low sensitivity but good specificity when occlusions in recipient vessels were included. Thus, conventional MR sequences alone are not suitable to evaluate distal parts of grafts and recipient vessels. Therefore, we combined conventional gradient-echo MRI with flow mapping. Incorporating more ad-
advanced MR angiography techniques\textsuperscript{15,35,36} with flow mapping will probably further improve outcome.

Left ventricular dysfunction, hypertrophy, or dilation are confounding parameters that may affect graft function in addition to the presence of luminal narrowing. Because of time restrictions, we were not allowed to perform additional scans assessing these clinical parameters. Future studies using faster scans may allow a comprehensive evaluation of myocardial ischemia.

Acknowledgments

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References


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