Detection of Vein Graft Disease Using High-Resolution Magnetic Resonance Angiography

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Background—The application of previous magnetic resonance (MR) angiography techniques has enabled noninvasive differentiation between patent and occluded coronary artery bypass grafts. However, the detection of graft stenosis remains difficult. The purpose of our study was to determine the accuracy of high-resolution navigator-gated 3-dimensional (3-D) MR angiography in detecting vein graft disease.

Methods and Results—MR angiography was performed in addition to coronary angiography with quantitative coronary analysis in 56 vein grafts from 38 patients (mean age 66.6±9.3 years), who presented with recurrent chest pain after bypass surgery. Eighteen grafts showed a luminal stenosis ≥50%, 11 grafts a stenosis ≥70%, and 6 grafts were occluded. All MR angiograms were evaluated independently by 2 blinded observers, who scored the presence of graft occlusion and graft stenosis ≥50% and ≥70% with a confidence level of 1 to 10. MR image quality was judged as insufficient in 6 grafts and these were excluded. Receiver-operator characteristic analysis revealed an area under the curve of 0.89 and 0.89 for identifying graft occlusion, 0.81 and 0.87 for stenosis ≥50%, and 0.82 and 0.79 for stenosis ≥70% for the 2 observers, respectively. Interobserver agreement in assessing graft occlusion and stenosis ≥50% and ≥70% was 94% (κ=0.74, r=0.81), 72% (κ=0.40, r=0.66), and 82% (κ=0.53, r=0.72), respectively.

Conclusions—High-resolution navigator-gated 3-D MR angiography allows not only good differentiation between patent and occluded vein grafts but also the assessment of vein graft disease with a fair diagnostic accuracy. This approach offers perspective as a noninvasive diagnostic tool for patients who present with recurrent chest pain after vein graft surgery. (Circulation. 2002;105:328-333.)

Key Words: magnetic resonance imaging ■ stenosis ■ bypass ■ angiography
TABLE 1. Patient and Graft Characteristics

<table>
<thead>
<tr>
<th>Coronary artery bypass grafts</th>
<th>All</th>
<th>Good Image Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vein grafts</td>
<td>56</td>
<td>50</td>
</tr>
<tr>
<td>Single grafts</td>
<td>30</td>
<td>25</td>
</tr>
<tr>
<td>Sequential grafts</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>Number of graft stenosis ≥50%</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Number of graft stenosis ≥70%</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Number of occluded grafts</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

Medical history (n=38)

- Myocardial infarction in graft region 17 (45%)
- Hypercholesterolemia 26 (68%)
- Hypertension 20 (53%)
- Current smokers 6 (16%)
- Diabetes 5 (13%)

Current medication (n=38)

- Anticoagulation 35 (92%)
- Calcium-antagonists 25 (66%)
- Nitrates 28 (74%)
- Statins 29 (76%)
- Beta-blocking agents 22 (58%)
- Ace-inhibitors 10 (26%)
- Diuretics 8 (21%)
- Digoxin 2 (5%)
- Other 19 (50%)

Methods

Patients
Fifty-six vein grafts from 38 patients (mean age 66.6±9.3 years, range 43 to 81 years) who were scheduled to undergo x-ray coronary angiography because of recurrent chest pain after bypass surgery (8.2±5.4 years, range 0 to 21 years) were studied. High-resolution MR angiography scans were performed in these patients as part of a MR cardiac function protocol in which adenosine stress testing was performed.

Patients with stents in the graft or near the distal graft anastomosis were excluded. MR-related exclusion criteria were unstable angina, the presence of a pacemaker, atrial fibrillation, claustrophobia, and the inability to lie flat. Exclusion criteria for the function protocol were chronic obstructive pulmonary disease, sick sinus syndrome, and second or third degree atrioventricular block. In 19 patients, MR angiography was performed before coronary angiography (mean time 2.7±2.2 days) and in the other 19 patients MR angiography was done after coronary angiography (mean time 9.4±13.7 days). No clinical events occurred between both examinations. All patients gave informed consent, and the medical ethical committee in our hospital approved the study protocol. Patient and graft characteristics are depicted in Table 1.

X-Ray Coronary Angiography
Vascular access was obtained using the femoral approach with the Seldinger technique and a 6- or 7-French catheter. To standardize vasomotor tone in the native coronary arteries beyond the graft anastomosis, grafts were visualized after injection of a 0.3-mg bolus nitroglycerine selectively into the graft. This was part of the standard operating procedure to quantify luminal stenosis severity in native coronary arteries by quantitative coronary analysis (QCA). Visualization was done according to standardized projections (a right-anterior-oblique and left-anterior-oblique projection, 60° apart). Off-line computer-assisted QCA was performed by an independent corelab (Heart Core). According to QCA data, grafts were divided into 4 subgroups: patent grafts (0% to 99% luminal stenosis), grafts with ≥50% luminal stenosis, grafts with ≥70% luminal stenosis, and occluded grafts (100% luminal stenosis). The location of the graft stenosis was also scored as either in the graft origin or graft body.

MR Imaging
A 1.5 Tesla Gyroscan ACS-NT Philips MR scanner (Philips Medical Systems) with Powertrack 6000 gradients (25 mT/m, 100 mT/m/ms), cardiac research software patch (CPR 6), and 5-element cardiac synergy coil was used. One operator (S.E.L.) and a medical doctor for patient monitoring performed the MR examination. Because MRI was performed after x-ray coronary angiography in 19 patients, the operator was not blinded to angiographic results in these patients, although in most cases the exact diagnosis was not known. According to a previously described MR protocol to visualize native coronary arteries, 2 localizer scans were performed: (1) a multislice 2-D turbo-field-echo (TFE) survey scan to identify the right hemidiaphragm and rough cardiac structures, (2) followed by a transverse ECG-gated navigator-gated and corrected 3-D turbo-field echo-planar-imaging (TFEPI) scout to localize the vein grafts as they course from their origin to distally.

High-Resolution MR Angiography
Three anatomical landmarks in the graft, namely the origin and most apical level of the graft and the mid-distance between these points, were manually selected, and the computer calculated the double-oblique plane that fits these 3 points. This plane was used to plan the ECG-gated navigator-gated and corrected 3-D high-resolution TFE MR angiography scan. The pulse sequence consisted of a T2-preparation prepulse for muscle suppression, a rest slab for foldover suppression, navigator gating and tracking for freezing of the respiratory motion, a fat suppression prepulse, and finally, the image acquisition. Data were acquired in mid-diastole and end-diastole with an acquisition duration of 71 ms using a heart rate-dependent trigger delay. A low-high k-space-filling pattern was applied for data acquisition. The following scan parameters were used: repetition time of 7.1 ms, 10 α-pulses per shot, echo time of 1.9 ms, field-of-view of 360 mm, rectangular field-of-view of 75%, scan matrix of 512×512, scan percentage of 70%, and 20 overcontiguous slices of 3-mm thickness reconstructed to 1.5 mm, resulting in a spatial resolution of 0.7×1.00×1.5 mm.

MR Image Analysis
An experienced cardiologist and radiologist, who were blinded to the results of coronary angiography but informed about the surgical graft anastomosis, independently evaluated all MR angiograms. Image evaluation was performed on an Easy Vision Workstation (Philips Medical Systems) by analyzing the original slices of the 3-D data set and the multiplanar-reformat image (MPR). Using this postprocessing technique, the user navigates through the 3-D stack and interactively marks the graft along its course. MPR reconstructions were made without knowledge of angiographic results. Both observers preferred the use of source data as compared with the MPR image because the MPR image is a nonanatomical plane and dependent on knowledge of the individual who performs postprocessing.

Each observer judged for each MR angiogram the image quality: (1) blurring or major artifacts with poor vessel conspicuity, which is insufficient for diagnosis of graft stenosis; (2) minor blurring or artifacts and sufficient for diagnosis of graft stenosis without excellent graft visualization; and (3) excellent image quality with no blurring or artifacts and a high degree of vessel conspicuity. When image quality was scored as insufficient (score 1), the MR angiogram was excluded from further analysis by that observer. In the remaining angiograms for each observer, the presence of graft occlusion (100% luminal stenosis), ≥50% luminal stenosis, and ≥70% luminal stenosis was scored as present or not with a confidence level from 1 to 10 for subsequent receiver-operator characteristic (ROC) analysis. A score of 1 denotes 100% certainty of graft occlusion and a score of 10 refers to 100% certainty of graft...
were calculated. The interobserver agreement was determined by the change in luminal diameter before and within the signal void. In addition, the location of the graft stenosis on the MR angiogram was scored by each observer as either in the graft origin or graft body.

Statistical Analysis
To determine the diagnostic accuracy of MR angiography in identification of vein graft occlusion and disease, visual interpretations of all MR angiograms were compared with QCA data. Diagnostic properties of MR angiography were evaluated by ROC-analysis, in which the sensitivity is plotted against the complement of specificity for each specific cut-off value in confidence level. The optimal cut-off value for determination of sensitivity and specificity was chosen according to standard practice. In order to account for association between grafts within the same patient, robust variances were calculated. The interobserver agreement was determined by Cohen’s $\kappa$ statistic and correlation coefficient ($r$).

Results
Image quality was judged as insufficient by one observer in 6 out of 56 MR angiograms and these 6 grafts were excluded from further statistical analysis of the data from this observer. The excluded grafts were patent by QCA and one graft had a moderate stenosis between 50% to 70%. Statistical analysis of the visual scores from the other observer was performed in all 56 grafts and in the remaining 50 grafts.

The results of x-ray coronary angiography with QCA are shown in Table 1. Figures 1, 2, and 3 depict a MR angiogram with the accompanying x-ray coronary angiography of a normal vein graft, a patent vein graft with a moderate stenosis, and an occluded graft, respectively.

ROC analysis of the first observers’ interpretations revealed an area under the curve (AUC) of 0.89 for detecting occluded grafts, 0.87 for detecting graft stenosis $\geq$50%, and 0.79 for detecting graft stenosis $\geq$70% (Figure 4). Sensitivity and specificity for identifying graft occlusion, graft stenosis $\geq$50%, and graft stenosis $\geq$70% were 83/98%, 65/82%, and 73/87%, respectively, for the first observer (Table 2). For the second observer, the equivalent numbers were 83/100%, 82/88%, and 73/80%, respectively. The interobserver agreement was 94% ($\kappa=0.74$, $r=0.81$) for assessment of graft patency, 72% ($\kappa=0.40$, $r=0.66$) for detection of graft stenosis $\geq$50%, and 82% ($\kappa=0.53$, $r=0.72$) for detection of graft stenosis $\geq$70%.

In all grafts that were correctly scored as having a stenosis $\geq$50% by the first observer, the location of the stenosis as scored on the MR angiogram corresponded to the location by QCA. In one graft that was correctly scored as having a stenosis $\geq$50% by the second observer, the location of the stenosis as scored on the MR angiogram did not correspond to the location by QCA. In this graft, a 74% stenosis in the grafts revealed AUCs of 0.89 for detecting occluded grafts, 0.87 for detecting graft stenosis $\geq$50%, and 0.79 for detecting graft stenosis $\geq$70% (Figure 4). Sensitivity and specificity for identifying graft occlusion, graft stenosis $\geq$50%, and graft stenosis $\geq$70% were 83/98%, 65/82%, and 73/87%, respectively, for the first observer (Table 2). For the second observer, the equivalent numbers were 83/100%, 82/88%, and 73/80%, respectively. The interobserver agreement was 94% ($\kappa=0.74$, $r=0.81$) for assessment of graft patency, 72% ($\kappa=0.40$, $r=0.66$) for detection of graft stenosis $\geq$50%, and 82% ($\kappa=0.53$, $r=0.72$) for detection of graft stenosis $\geq$70%.

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origin was missed, and a stenosis $\geq 70\%$ in the graft body was incorrectly observed.

The duration of a MR angiography study in a patient with 2 vein grafts was approximately 1 hour, depending on the gating efficiency. Total MR examination includes patient preparation (10 minutes), planning and scanning of 2 localizer scans (10 minutes), and the high-resolution scan (15 to 20 minutes per graft). The feasible maximum duration of a MR imaging study from our experience is 1.5 hours. This implies that from a practical perspective the application of high-resolution MR angiography, by using the present MR technology, is limited to patients with a maximum of 4 vein grafts.

**Discussion**

Our findings confirm previous observations that MR angiography allows differentiation between patent and occluded vein grafts. The novel finding in the current study is that high-resolution MR angiography enables the assessment of vein graft stenosis severity with a fair diagnostic accuracy. To the best of our knowledge, this is the first study that addresses the value of MR angiography in assessing the severity of vein graft stenosis. High-resolution MR angiography offers perspective as a noninvasive diagnostic screening tool for patients who present with recurrent chest pain after bypass surgery.

**Previous Experience in MR Angiography of Grafts**

The first pioneers in the field of graft MR angiography used nonrespiratory-compensated, ECG-triggered, 2-D spin-echo,4-6 and gradient-echo techniques,6,19,20 and later on, breath-hold 2-D gradient-echo sequences with k-space segmentation were applied.21 When 2 successive proximal slices showed a patent vessel, it was concluded that the graft was patent. More recently, 3-D MR angiography techniques, such as gadolinium-enhanced breath-hold MR angiography sequence and navigator-gated MR angiography with 1-mm resolution, proved to be feasible in assessing graft patency over a longer course.7,8,22 The overall sensitivity and specificity of these techniques in detecting patent grafts varied from 88% to 98% and 72% to 100%, respectively. In the present study, we applied a technically improved high-resolution MR angiography sequence, which allowed the identification of vein graft occlusion with an at least as good sensitivity (83%) and specificity (98% to 100%) as previously obtained values with lower spatial resolution.4-8,19-22

The fact that our method has not much better diagnostic performance than the cruder approaches might be attributable to a difference in pretest probability of disease, patient selection, and inclusion criteria. For instance, the prevalence of graft occlusion in the older studies varied from 19% to 48%, which was considerably higher than the occlusion prevalence (11%) in the present study.

**Figure 4.** Receiver-operator characteristic (ROC) analysis was performed for the observers’ interpretation of graft occlusion and $\geq 50\%$ and $\geq 70\%$ luminal stenosis. The normal and dotted line represent the ROC curves for the first and second observer, respectively. The arrows indicate the optimal cut-off points for the first (●) and second observer (●).

**TABLE 2.** Diagnostic Accuracy of High-Resolution MR Angiography in Identifying Graft Occlusion and Graft Stenosis $\geq 50\%$ and $\geq 70\%$

<table>
<thead>
<tr>
<th></th>
<th>Observer 1</th>
<th>Observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Graft occlusion</td>
<td>83% (36–100%)</td>
<td>98% (88–100%)</td>
</tr>
<tr>
<td>Graft stenosis $\geq 50%$</td>
<td>65% (38–86%)</td>
<td>82% (65–93%)</td>
</tr>
<tr>
<td>Graft stenosis $\geq 70%$</td>
<td>73% (39–94%)</td>
<td>87% (73–96%)</td>
</tr>
</tbody>
</table>

Sensitivity and specificity are shown in percentage with confidence interval.
Despite the increased possibilities of earlier MR angiography studies to differentiate between patent and occluded grafts, even more distally in grafts, the detection of significant graft stenosis has remained difficult due to limitations in spatial resolution. In the present study, we first demonstrate the diagnostic properties of high-resolution 3-D MR angiography\textsuperscript{10,11} in detecting vein graft stenosis severity.

Study Limitations

The present study focused solely on vein grafts, because vascular clips that surround arterial grafts disturb the magnetic field homogeneity and demonstrate major artifacts. These artifacts prevent good visualization of arterial grafts with MR angiography and do not allow assessment of arterial graft patency at that level. Similarly, the visualization of the stent lumen has been jeopardized by artifacts. However, MR flow mapping can be performed in internal mammary artery grafts and stented vein grafts by selecting a scan plane either in between the vascular clips or proximal or distal from the stent.

Signal voids resulting from artifacts caused by vascular clips or stents can be differentiated from stenotic grafts because these artifacts extend outside the lumen. A pitfall in interpretation of 3-D angiographic data are that the vessel of interest courses out of the image volume, mimicking an occlusion and resulting in false-positive findings for graft occlusion. Therefore, a prerequisite for the diagnosis graft occlusion is that the last slice, in which the graft can be seen, is not at the border of the 3-D volume.

The image duration of the navigator-gated MR angiography scan is rather long compared with a breath-hold sequence. This limits the use of this sequence in a more comprehensive MR study that might include the assessment of left ventricular wall motion and perfusion at baseline and during pharmacological stress.

Nitroglycerine was given prior to x-ray coronary angiography to standardize vasomotor tone in the native vessels beyond the graft anastomosis for QCA. Because variations in vein graft lumen and vein graft spasms are a rarity postoperatively\textsuperscript{23} and the present study focused solely on grafts, no nitroglycerine was given prior to MR angiography. If small variations in graft lumen would occur over time, these would probably not affect the visual scoring of grafts.

Future Perspectives

In the present study, we focused on diagnostic properties of high-resolution MR angiography in detecting graft stenosis severity. To study the accuracy of this diagnostic tool in evaluating the status of coronary arteries in and beyond the distal graft anastomosis, additional MR angiography scans are required with optimal scan planning for the native right and left coronary artery. MR flow mapping\textsuperscript{6,24–26} in combination with MR angiography may be an alternative tool to study distal coronary arteries because baseline and stress flow in the proximal part of the graft is a functional measure of the entire vascular bed beyond the level of the flow measurement. Moreover, invasive studies have shown that lesion morphology does not necessarily reflect the functional graft status.

Therefore, a combined approach of MR angiography and flow mapping may further improve the results.

Intravascular contrast agents have been successfully applied in coronary MR angiography, leading to a considerable enhancement of the blood/muscle contrast compared with T2-preparation techniques\textsuperscript{27} and low-molecular Gadolinium compounds.\textsuperscript{28} Phase-2 clinical trials with these promising agents are currently in progress to examine the effect of intravascular contrast agents in the diagnostic performance of MR angiography in stenosis detection.

Conclusion

Our findings confirm previous observations that high-resolution MR angiography allows differentiation between patent and occluded vein grafts. However, the novel finding in the present study is that high-resolution MR angiography enables the assessment of vein graft stenosis severity with a fair diagnostic accuracy. This offers perspective for noninvasive screening of patients who present with recurrent chest pain after bypass surgery.

Acknowledgments

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References


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