Noninvasive Detection of Coronary Artery Stenosis Using Contrast-Enhanced Three-Dimensional Breath-Hold Magnetic Resonance Coronary Angiography

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OBJECTIVES The purpose of this study was to evaluate a contrast-enhanced three-dimensional (3D) breath-hold magnetic resonance (MR) technique for detection of coronary artery stenoses.

BACKGROUND The accuracy of previously published MR coronary angiography protocols varies widely. Recently, coronary artery imaging using T1-shortening contrast agent has become possible, but so far there are no data concerning its clinical application.

METHODS Magnetic resonance coronary angiography was performed in 50 patients with suspected coronary artery disease. Magnetic resonance data acquisition using an ultrafast 3D gradient-echo sequence lasted over 32 heartbeats within one single breath-hold. Twenty milliliters of gadopentetate dimeglumine was injected at a flow rate of 1 ml/s for two successive studies covering the main coronary arteries in single-oblique planes. Stenosis assessment by MR was compared with significant (diameter stenosis > 50%) stenoses on X-ray angiography.

RESULTS Two hundred sixty-eight of 350 artery segments (76.6%) could be evaluated. Left circumflex coronary artery was only evaluable in 50% of cases by MR. In the evaluable segments, 48 of 56 stenoses and 193 of 212 nonstenotic segments were correctly classified by MR. On a patient basis, MR correctly identified 34 of 36 patients with and 8 of 14 patients without significant coronary stenoses as demonstrated by X-ray angiography (sensitivity 94.4%, specificity 57.1%).

CONCLUSIONS Oblique projection contrast-enhanced MR coronary angiograms obtained within one single breath-hold permit identification of patients with coronary stenoses in the proximal and mid segments of the major coronary arteries with satisfactory accuracy.

Since the early 1990s, magnetic resonance (MR) coronary angiography has been emerging as a noninvasive tool for coronary artery imaging (1–4). However, serious difficulties arise from the small size of coronary arteries, cardiac and respiratory motion, the highly tortuous course of the vessels and their close relationship to pericardial fat and cardiac chambers. Currently available MR techniques have specific limitations. Two-dimensional (2D) techniques, which are based on the acquisition of multiple parallel or oblique sections, require multiple breath-holds for a complete investigation of a single coronary artery. This may be strenuous for patients suffering from impaired cardiac or respiratory function. More importantly, misregistrations of contiguous sections due to inconsistent breath-hold positions frequently create interpretative difficulties (5–7). Three-dimensional (3D) respiratory gated techniques permit acquisition of volumetric data sets of the heart, which consist of contiguous sections (8,9). Nevertheless, their drawbacks include long scan times, as well as image degradation due to inconsistent breathing patterns and patient movement. In addition, in-plane and through-plane saturation effects may lead to low vessel-to-background contrast and contrast-to-noise ratio, respectively (10–14). In order to acquire a 3D data set within a single breath-hold, repetition time (TR) has to be dramatically reduced, resulting in high signal bandwidth and a low signal-to-noise ratio (SNR). To overcome this problem, it is possible to use a T1-shortening contrast agent to improve contrast between blood and the surrounding tissue. So far, contrast-enhanced MR angiography has been successfully applied to visualize peripheral vessels (15). Recently, the visualization of coronary arteries and bypass grafts has also become possible using contrast-enhanced MR angiography (16–22). A technique that combines ultrafast data acquisition within one single breath-hold and improved SNR by a T1-shortening contrast agent may be appropriate for clinical use. In this article, we present initial data to detect coronary artery stenoses using a contrast-enhanced, ultrafast 3D breath-hold technique.

METHODS Subjects. Fifty patients (40 men and 10 women) were studied. Their mean age was 60.7 years (range 42 to 76 years). Their average weight was 81.3 kg. All patients were...
admitted to our institution for diagnostic coronary angiography due to clinically suspected coronary artery disease. Patients with arrhythmias, in unstable clinical condition, with contraindications to MR imaging (e.g., cardiac pacemakers, other ferromagnetic implants or claustrophobia) and with contraindications to the administration of MR contrast agent (e.g., chronic obstructive pulmonary disease and chronic renal insufficiency) were excluded. All patients gave written, informed consent. The study was approved by the institutional review board. Conventional invasive coronary angiography was performed by independent investigators within three days after MR imaging according to standard techniques. All selected patients were included in the analysis.

**MR imaging.** All subjects were examined in supine position on a 1.5 T whole body scanner (VISION; Siemens AG, Erlangen, Germany) with gradient overdrive (maximum gradient strength 25 mT/m, gradient rise time 12 μs/mT/m, maximum slew rate 80 mT/m/s). A circular polarized body array coil was used for signal reception to increase SNR. Nitroglycerin (0.8 mg sublingually) was applied before MR angiography to achieve coronary vasodilation. The imaging protocol for contrast-enhanced breath-hold MR angiography consisted of four steps. Data acquisition was electrocardiographically triggered and each imaging sequence was performed within one breath-hold in inspiration. The first step was to determine the position of the heart and to guide placement of the following acquisitions using three coronal and four transversal Turbo FLASH (fast low angle shot) scout images (TR/echo time [TE]/flip angle = 4.2 ms/2.3 ms/10°, slice thickness 8 mm, field of view 400 mm, matrix 128 by 256). In a second step, the contrast agent transit time was determined using a turbo FLASH sequence (sequential single-slice acquisition, TR/TE/flip angle = 5.8 ms/2.4 ms/15°, slice thickness 8 mm, field of view 350 mm, matrix 128 by 256). The sequence provided 30 parasagittal images of the thoracic aorta, one image per second, and was started after rapid bolus injection of 2-ml gadopentetate dimeglumine and an 8-ml saline flush (Fig. 1). Based on these images, a signal intensity curve of a region of interest in the ascending aorta was obtained. The time to peak enhancement was considered to represent the contrast agent transit time (Fig. 1). In a third step, the course of the coronary arteries was localized in order to guide positioning of the imaging slabs for the coronary angiography (Fig. 2). Nine dark-blood transaxial images were obtained at the level of the aortic root using a single-shot turbo spin-echo HASTE (half-Fourier turbo spin echo) sequence (TR/TE/flip angle = 4.2 ms/43
ms/150°, slice thickness 6 mm, field of view 350 mm, matrix 128 by 256). Finally, MR coronary angiography was performed within one single breath-hold in inspiration using an ultrafast, electrocardiographically triggered 3D gradient-echo sequence (TR/TE/flip angle = 4.2 ms/1.6 ms/25°) (18,19). Two imaging slabs were acquired in oblique sagittal orientation along the course of the left main and left anterior descending coronary artery (LM) and the left anterior descending coronary artery (LAD) and along the right coronary artery (RCA) and the left circumflex coronary artery (LCX), respectively. A volume of 48-mm thickness with oblique orientation was divided into 16 contiguous partitions of 3-mm thickness. Using zero filling, the data were interpolated to 32 partitions of 1.5 mm each. With a field of view of 200 × 320 mm² and a matrix size of 140 by 256, the spatial resolution was 1.4 × 1.25 × 1.5 mm³. One half of k-space in the phase-encoding direction (70 lines) was acquired within each heartbeat. Phase encoding started in the center of k-space after a fat saturation pulse to suppress signal from perivascular tissue. Each partition was acquired over two consecutive heartbeats with a diastolic acquisition window of 70 × 4.2 ms = 294 ms. For 16 partitions, 32 heartbeats were required to acquire the complete 3D data set. An additional presaturation pulse after the fat saturation pulse covering the anterior chest wall was used to avoid wrap-around artifacts. Before acquisition of each imaging slab, 20-ml gadopentetate dimeglumine (0.5 mol/liter, MAGnevist; Schering AG, Berlin, Germany) was injected manually into a cubital vein by a 22-gauge intravenous line. Contrast agent was injected at a rate of 1 ml/s and data acquisition was started with a delay according to the formula proposed by Prince et al. (15): scan delay = transit time + injection time/2 − expected scan time/2.

**Data evaluation.** All MR images were evaluated independently by two investigators blinded to the findings of the patient’s conventional coronary angiograms. The image sets were analyzed based on the original source images and on maximum intensity projections, which were rendered using a commercially available software package (NUMARIS 3.31A; Siemens Medical Systems, Erlangen, Germany). The following segments were evaluated: LM (segment 5 according to the system of the American Heart Association [23]), and the proximal and mid segments of LAD (segments 6 and 7 and the first half of segment 8, respectively), LCX (segments 11 and 13) and RCA (segments 1 and 2). The following classification was used for visual assessment: significant stenosis (more than 50% diameter reduction) or occlusion, absence of significant stenosis or occlusion or impossibility to evaluate. Side branches and distal segments were not included in the evaluation. According to previous studies, a segmental reduction or signal loss in the MR image was considered to represent a significant coronary artery stenosis or occlusion (3,5–7,10–14). For analysis, both source and reconstructed images were accepted, but stenoses or occlusions seen only on the reconstructed images were rejected. In case of disagreement between the two observers, images were reviewed again and a final assessment was made in consensus. After separate evaluation of MR and coronary angiography images by independent observers, agreement between location of stenoses for MR and conventional coronary angiography was assessed.

**Coronary angiography.** In all patients, coronary angiography was performed by the transfemoral Judkins approach. Angiograms were documented on cine film or in digitized format and evaluated by visual assessment by two cardiologists who were independent of the MR investigators. Diameter reductions exceeding 50% were considered to represent significant stenoses. In case of disagreement be-
agreement between observers was achieved in 95% of cases without joint reading, and Cohen’s kappa was 0.90.

**RESULTS**

By conventional invasive contrast angiography, evaluation of all of the coronary artery segments was possible. Thirty-six of 50 (72%) patients had X-ray evidence of significant (diameter stenosis > 50%) coronary artery disease: 20 with one-vessel disease, 9 with two-vessel disease and 7 with three-vessel disease. In all patients, MR coronary angiography was performed without complications. None of the patients experienced nausea or other adverse reactions to the contrast agent. The mean time of the investigation, including all preparations for scanning, was 19 ± 5 min per patient. Forty-one of 50 (82%) patients were able to sustain the 32-heartbeat breath-hold. Of the 350 coronary artery segments (LM, proximal and mid parts of LAD, LCX and RCA), 268 (76.6%) coronary artery segments could be evaluated, whereas 82 (23.4%) were considered impossible to evaluate because of reduced image quality (Table 1). In eight patients, the LCX was outside the imaging volume. In the evaluable 268 segments, 48 of 56 significant coronary artery stenoses or occlusions and the absence of significant stenosis or occlusion in 193 of 212 segments were correctly determined by MR coronary angiography (see Table 1 and Figs. 3 and 4). On a patient basis, MR coronary angiography was able to detect the presence of any significant coronary artery stenoses or occlusions in 34 of 36 patients and to correctly exclude significant stenosis or occlusion in 8 of 14 patients (Table 2). This corresponds to a sensitivity of 94.4%, a specificity of 57.1%, a positive predictive value of 85% and a negative predictive value of 80%. In MR, interobserver agreement was achieved for 250 of 268 evaluable segments (93.3%). Cohen’s kappa was 0.85, indicating close agreement between observers. In conventional angiography, agreement between the observers was achieved in 95% of cases without joint reading, and Cohen’s kappa was 0.90.

**DISCUSSION**

Since the first report in 1987 by Paulin et al. (25), MR coronary angiography has been evolving rapidly. However, visualization of the coronary arteries with diagnostic image quality to detect or rule out coronary artery stenoses remains challenging. The reported accuracies of published MR coronary angiography protocols vary widely, from 38% to 90% (3,5–7,10–14). For that reason, with the exception of visualization of anomalous coronary arteries (26,27), MR coronary angiography is considered an investigational technique in current U.S. and European task force reports (28,29).

**Contrast-enhanced MR coronary angiography.** We evaluated a new contrast-enhanced ultrafast 3D gradient-echo technique that combines the advantages of ultrafast 3D data acquisition within one single breath-hold with an optimized SNR using a T1-shortening contrast agent. So far, comparable contrast-enhanced techniques have been successfully used for imaging of the thoracic and abdominal aorta, visceral, pulmonary and renal arteries as well as aortocoronary bypass grafts (15–17). First approaches and feasibility studies of contrast-enhanced MR coronary angiography have recently been published (18–22). However, there are no data on its clinical use in the detection of coronary artery stenosis. Moreover, in the present investigation and in contrast to previous studies, the imaging volume was positioned in oblique sagittal sections along the anatomical long axis of the coronary arteries. This approach has so far only been applied in 2D breath-hold coronary imaging and in a recent 3D protocol using echoplanar imaging (30,31). In contrast to conventional transaxial slab orientation, it permits visualization of long vessel segments in a single image. Because the blood signal in contrast-enhanced MR angiography relies mainly on the T1-shortening effect instead of on the inflow, saturation effects, which affect time-of-flight sequences especially if the vessel course is not perpendicular to the imaging plane, are avoided. Additionally, the coronary arteries can be visualized making use of the higher

**Table 1.** Results of Coronary Artery Segment Classification and Stenosis Assessment by Contrast-enhanced Magnetic Resonance Coronary Angiography Compared With Conventional Invasive Angiography (n = 350)

<table>
<thead>
<tr>
<th>Coronary Artery</th>
<th>True-positive</th>
<th>True-negative</th>
<th>False-positive</th>
<th>False-negative</th>
<th>Evaluation Impossible</th>
</tr>
</thead>
<tbody>
<tr>
<td>LM</td>
<td>1</td>
<td>38</td>
<td>1</td>
<td>0</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>LAD proximal</td>
<td>17</td>
<td>22</td>
<td>2</td>
<td>1</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>LAD mid</td>
<td>5</td>
<td>32</td>
<td>3</td>
<td>0</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>LCX proximal</td>
<td>2</td>
<td>21</td>
<td>4</td>
<td>2</td>
<td>21 (42%)</td>
</tr>
<tr>
<td>LCX mid</td>
<td>2</td>
<td>17</td>
<td>1</td>
<td>1</td>
<td>29 (58%)</td>
</tr>
<tr>
<td>RCA proximal</td>
<td>12</td>
<td>31</td>
<td>4</td>
<td>1</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>RCA mid</td>
<td>9</td>
<td>32</td>
<td>4</td>
<td>3</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>193</td>
<td>19</td>
<td>8</td>
<td>82 (23.4%)</td>
</tr>
</tbody>
</table>

LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LM = left main coronary artery; RCA = right coronary artery.
in-plane resolution as compared with 3D techniques based on the acquisition of axial cross sections, where the vessel course is often orthogonal to the imaging slab.

Clinical findings. We found a high sensitivity for detection of coronary artery stenoses and occlusions, if sufficient image quality could be obtained. In comparison with previous studies to detect coronary artery stenoses using the 3D respiratory gated technique, our results show higher values for sensitivity, whereas specificity was reduced due to false-positive results caused by artifacts created by breathing, motion or incorrect timing of contrast medium (10–14). Most stenoses that were not detected were located in the LCX and RCA. For the LCX, an explanation may be that this coronary artery is situated a further distance from the reception profile of the body array coil than the other coronary arteries, resulting in lower signal intensity. False-positive results were mainly due to small vessel sizes because

<table>
<thead>
<tr>
<th>Type of Imaging</th>
<th>Presence of Significant Stenosis</th>
<th>Absence of Significant Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic Resonance Coronary Angiography</td>
<td>34</td>
<td>6</td>
</tr>
<tr>
<td>Conventional Invasive Angiography</td>
<td>2</td>
<td>8</td>
</tr>
</tbody>
</table>

Figure 3. (A) Maximum intensity projection MR image shows contrast-enhanced MR coronary angiography of the left circumflex coronary artery (arrow) and of the right coronary artery containing a proximal stenosis (arrowhead). (B) Corresponding invasive coronary angiogram with a subtotal proximal stenosis of the right coronary artery (arrow). MR = magnetic resonance.

Figure 4. (A) Maximum intensity projection MR image shows contrast-enhanced MR coronary angiography with stenosis of the proximal left anterior descending coronary artery (arrow). (B) Corresponding invasive coronary angiogram with a long distance stenosis of the left anterior descending coronary artery (arrow). MR = magnetic resonance.
of partial volume effects of the neighboring tissues, as reported in previous studies using other imaging protocols (3,5–7,10–14). The main drawback of current MR coronary angiography seems to be that 23.4% of all coronary artery segments had to be excluded from evaluation because of inadequate image quality, especially the LCX, which was evaluable only in 50% of cases. The following reasons may be responsible for the high number of un evaluable coronary segments. Image degradation occurs if patients are unable to hold their breath until the end of the measurement leading to considerable image blurring. In addition, the LCX and the RCA move more rapidly in diastole than the left anterior descending coronary artery (32), which may contribute to the higher percentage of insufficient image quality and false-positive results in these two vessels. Finally, due to the method’s relatively crude spatial resolution, small vessels are difficult to depict with diagnostic quality.

Rationale for future improvements. Our study shows that with the use of the described technique, a high number of significant coronary artery lesions could be exactly classified. However, before the method can be applied as a diagnostic tool in a clinical setting, the number of studies that cannot be evaluated due to impaired image quality will have to be reduced. To achieve this, several issues need to be addressed. More careful instruction and preparation should permit more patients to hold their breath for the full scanning period. In addition, the heart rate in patients with severe bradycardia may be medically increased to shorten the overall image acquisition time. Moreover, improvement of scanner gradient systems (33), novel sequence techniques such as partial Fourier data acquisition (18), simultaneous acquisition of spatial harmonics technique (34) and optimization of the interval in the cardiac cycle that is used for image acquisition may permit data acquisition with reduced motion artifacts, improved spatial resolution, shortened time intervals for data acquisition and increased volume coverage of the imaging slabs. Additionally, image contrast may be improved by optimization of the contrast agent injection mode to guarantee coincidence of central parts of k-space sampling with the highest concentration in the coronary arteries, and by the use of more efficient coils. Finally, intravascular contrast agents may offer greater relativity and a longer data acquisition window compared with conventional extravascular contrast agent (21,22).

Study limitations. Stenosis evaluation was limited only to the proximal and mid segments of the main coronary arteries. Distal segments and side branches were excluded because of their small diameters, which do not permit reliable imaging with the spatial resolution MR scanners currently provide. Otherwise, partial volume effects would lead to an unacceptable number of false-positive results. Because lesions in distal segments and side branches may be the target of revascularization, this may hinder the current clinical application of the method. Second, no attempt was made to differentiate between significant stenoses and total occlusions of coronary arteries. Because partial volume effects may cause a subtotal stenosis to appear as a total occlusion, it may be impossible to differentiate whether such a coronary lesion represents a subtotal stenosis or a total occlusion with filling of the distal segments by collateral flow. For clinical decision making, however, mistaking total occlusions for significant stenoses would be irrelevant in most cases, because both conditions usually require further invasive study. Moreover, breath-holding during the image acquisition period in our study was performed at end inspiration. In a recent study, it was shown that at end inspiration, motion of the diaphragm during suspended breathing was more complex than at end expiration (35). Therefore, it has to be evaluated whether there is reduced blurring of images during suspended breathing at end expiration. Finally, in our study, two oblique imaging slabs were used to cover the course of the main coronary arteries. However, the complete course of the coronary arteries was not in all cases covered by these two slabs. To achieve complete coverage of the coronary tree, it seems to be necessary to perform successive studies made up of four or more imaging slabs with different positions.

Conclusions. In the present study, contrast-enhanced breath-hold MR coronary angiography was evaluated for the first time for detection of significant coronary artery lesions. With the technique used, the 3D imaging volume can be freely oriented along any desired course of the coronary arteries. Magnetic resonance coronary angiography could be successfully performed in the majority of cases. A high sensitivity for detection of patients with significant coronary artery lesions, provided there is adequate image quality, may make this method a clinically useful test in the future. Moreover, the imaging protocol presented is not as time-consuming as 3D respiratory gated approaches, and therefore more suitable for use in a clinical setting. However, further research must be directed toward reducing the number of studies with nondiagnostic image quality. Once this goal has been achieved, contrast-enhanced MR coronary angiography may replace a substantial number of invasive coronary angiographies documenting exclusion of significant coronary lesions.

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