Coronary artery disease (CAD) is the leading cause of death in the United States, accounting for 600,000 deaths per year. Cardiac catheterization is an expensive and invasive investigation requiring the use of iodinated contrast agent and x-rays, but is the gold standard for assessment of coronary artery stenosis. It may cause local, cerebral and cardiac complications or even death. Up to 20% of conventional coronary angiographic investigations lead to negative results. Various attempts have been made to visualize and assess coronary arteries with alternative, less invasive methods, such as electron beam tomography (EBT), echocardiography, and magnetic resonance imaging (MRI).

MRI is a widely available non-invasive method with fewer risks and lower cost than cardiac catheterization. MRI is known as a reliable diagnostic tool for several cardiac indications. Small vessels in other regions of the body, such as cerebral or renal arteries, can be examined by MRI with high diagnostic accuracy. However, MRI of coronary arteries still remains a major challenge because of respiratory motion and cardiac motion, as well as the small diameter and tortuous configuration of the coronary arteries. Different two-dimensional (2D) protocols using the breath-hold technique for the visualization of coronary arteries have been employed. However, only a limited volume can be examined with high spatial resolution during a single breath-hold. Thus, only...
a portion of the coronary arteries can be continuously visualized.

Recent developments allow respiratory gating by the non-invasive measurement of diaphragm motion with navigator echoes. With a combination of cardiac and respiratory gating, a complete, continuous examination of the heart without breath-hold is possible in a three-dimensional (3D) technique. Patients with severe respiratory disease can be examined with this technique. Complete visualization of the main coronary arteries may be possible with high spatial resolution, since the acquisition time is not limited by the length of a breath-hold.

Only studies with small populations have been reported on the use of the 3D respiratory-gated navigator echo technique in the examination of coronary arteries, either without blinded reading or with exclusion of a portion of the examined subjects. Thus, various results were found in comparing the diagnostic accuracy of MR coronary angiography (MRCA) with conventional catheter angiography (CCA). Three-dimensional MRCA may fail in a part of a study population. Therefore, some studies exclude examinations without success from a comparison with CCA and present results only of successful investigations. However, there is no study that analyzes the varying image quality of coronary arteries and its impact on the reliability in the assessment of coronary artery stenoses.

In our study, the visualization quality of coronary arteries in healthy volunteers and patients with CAD was investigated as well as the value of navigator echo respiratory gating in the assessment of coronary artery stenosis. We determined sensitivity and specificity first for all examined coronary vessels and afterward for vessels with high image quality, both after evaluation by two blinded readers.

**METHODS**

Twenty healthy volunteers (mean age, 26 ± 4.3 years) and twenty patients (mean age, 64.9 ± 7.7 years) with proximal coronary artery stenosis were investigated with a cardiac-gated and retrospective-respiratory gated (navigator echo) 3D-gradient echo sequence. Informed consent to perform MR angiography of coronary arteries was obtained from healthy volunteers and consecutive patients referred for elective conventional coronary angiography. All patients underwent conventional coronary angiography 10 days before or after MR examination.

We used a superconducting, 1.5 Tesla whole body System (Vision, Siemens AG, Erlangen, Germany) and a phased-array body coil with four channels. The subjects were studied in the supine position. The navigator echo pulse sequence included ECG gating and retrospective respiratory gating. Two navigators were positioned on the dome of the right diaphragm in sagittal and parasagittal orientation with an angulation of 30°. Three transverse 3D slabs were positioned in transversal orientation with an overlap of 12 mm, a thickness of 48 mm and 24 partitions. The first slab was localized with its center on the level of coronary artery origin, with the two following slabs below. The field of view was 250–300 mm depending on the subject’s anatomy and the matrix was 256 x 160, resulting in a spatial resolution of 1.2 mm x 1.4 mm x 2 mm. The scan parameters included a TE of 2.7 ms, 5 acquisitions and a TR of 7.4 ms. The flip angle varied during the acquisition. In order to suppress the fatty tissue surrounding the coronary arteries, a spectral fat saturation was used. No contrast material was used for this study.

The conventional coronary angiograms were reviewed by two cardiologists who were blinded to the MR imaging data in a consensus reading. From their results, only hemodynamically significant lesions (> 50% of luminal diameter) were considered. The following arterial vessel segments were compared with magnetic resonance coronary angiography: main stem; proximal segment of the left anterior descending coronary artery (LAD); left circumflex artery (LCX) and right coronary artery (RCA), and middle segment of the LAD, LCX and RCA.

A standard definition of human coronary artery anatomy was used. The left main has a single segment. The LAD is separated into three segments. The proximal segment of the LAD extends from its origin at the left main to the first septal perforating artery, the middle segment of the LAD extends from the first to the third septal perforating artery and the distal segment extends from the third septal perforating artery to the cardiac apex. A fourth segment distal of the cardiac apex was excluded from our evaluation. The proximal segment of the RCA extends from the origin to the first of the three largest acute marginal branches. The middle segment extends from the first to the third acute marginal branch. The distal segment extends from the third acute marginal branch to the posterior descending branch. The LCX is divided in three segments by the first and second marginal branches. Coronary anatomy tends to be somewhat variable, but it was possible in all cases to identify segments corresponding to the standard by coronary arteriograms.

Curved MPR reconstructions were performed for visualization of the main stem and the main coronary arteries. The image quality was analyzed for the main stem and for three defined segments in each coronary artery after MPR reconstruction. A grading system including six scores was used for the assessment of visualization quality (5 = completely identified; 4 = completely identified with minor luminal irregularities; 3 = completely identified, but with major luminal irregularities; 2 = incompletely identified, but more than 2/3 of segment visualized; 1 = incompletely identified, but more than 1/3 of segment visualized; 0 = incompletely identified, less than 1/3 of segment visualized). Fat saturation was analyzed with a grading
system of five (4 = excellent, homogenous; 3 = good, slightly heterogenous; 2 = moderate, heterogenous; 1 = bad, only patches; 0 = none or water saturated) and motion artifacts were analyzed with a grading system of six (5 = none; 4 = few, not obscuring anatomy; 3 = moderate, obscuring small vessels; 2 = severe, partially obscuring proximal coronaries; 1 = very severe, completely obscuring proximal coronaries; and 0 = maximal, cardiac anatomy obscured).

The assessment of coronary artery stenoses was performed by two experienced readers who were blinded to the results from the conventional coronary angiography. Single slices and curved MPR reconstructions were used for evaluation of MRCA. An independent reading and a consensus reading were performed.

The mean and standard deviation for the score of image quality in vessel visualization, fat saturation and motion artifacts were calculated for patients and healthy volunteers. Sensitivity and specificity were determined for the detection of stenoses. The Kappa-value was determined with a 95% confidence level.

**RESULTS**

In healthy volunteers and patients, four hundred coronary artery segments were analyzed for quality of visualization. The image quality was variable for individual coronary artery segments. The percentage of coronary artery segments with a score of at least 3 (i.e., completely identified, but with major luminal irregularities) or better is shown in Table 1.

The mean value of image quality scores was dependent on the localization in the proximal, middle or distal part of the coronary arteries (Figure 1). The value decreased from proximal to distal, probably due to narrowing of the anatomical vessel diameter and limited spatial resolution of the pulse sequence used.12

For the evaluation of fat saturation and motion artifacts, mean and standard deviation (SD) were calculated for each score. No significant difference was found between healthy volunteers and patients (student’s t-test). The mean score for quality of fat saturation was 2.90 (SD, 0.82) for volunteers and 3.18 (SD, 0.80) for patients. The mean score for motion artifacts was 3.88 (SD, 0.92) for volunteers and 3.55 (SD, 0.93) for patients.

Since the results of a new MR technique can be dependent on the investigators’ experience, a learning curve was calculated for all consecutively examined subjects. An increasing image quality was found (Figure 3) that was significant for healthy volunteers, but not for patients ($p = 0.05$).

Fifty-three hemodynamically significant (> 50%) stenoses were found using conventional coronary angiography. Five stenoses were localized in the main stem, twenty-two in the LAD, ten in the LCX and sixteen in the RCA. Twenty-nine of 53 lesions were localized in proximal segments, eighteen in mid segments and one in the distal segments of the LAD, LCX and RCA.

Reader 1 had an overall sensitivity of 82% and specificity of 42%, while Reader 2 had an overall sensitivity of 65% and specificity of 53%. The consensus reading had a sensitivity of 73% and specificity of 50%. The results were analyzed for each vessel and segment (Table 2). In most vessel segments, the results of Reader 1 and Reader 2 showed a higher sensitivity than specificity. Distal coronary artery segments were excluded from a comparison with conventional coronary angiography because of small vessel diameter, poor image quality score and small number of stenoses diagnosed by conventional coronary angiography in this location in the examined population.

A variable image quality was found for different subjects and different vessels. Therefore, sensitivity and specificity were also calculated only in vessels with a visualization quality of ≥ 3 (segment completely identified with major luminal irregularities). Reader 1 found sensitivity of 93% and specificity of 43%; Reader 2 found

<table>
<thead>
<tr>
<th>Segment</th>
<th>Volunteers</th>
<th>Patients</th>
<th>Score of At Least 3</th>
<th>Score of At Least 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main stem</td>
<td>2.90</td>
<td>2.85</td>
<td>67%</td>
<td>72%</td>
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<tr>
<td>LAD proximal third</td>
<td>3.50</td>
<td>3.10</td>
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<td>71%</td>
</tr>
<tr>
<td>LAD mid segment</td>
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<td>45%</td>
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<tr>
<td>LAD distal third</td>
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<td>1.25</td>
<td>17%</td>
<td>21%</td>
</tr>
<tr>
<td>RCX proximal third</td>
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<td>3.10</td>
<td>51%</td>
<td>65%</td>
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<tr>
<td>RCX mid segment</td>
<td>1.88</td>
<td>2.50</td>
<td>27%</td>
<td>45%</td>
</tr>
<tr>
<td>RCX distal third</td>
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<td>10%</td>
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<tr>
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<td>3.62</td>
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</tr>
<tr>
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<td>3.30</td>
<td>32%</td>
<td>51%</td>
</tr>
<tr>
<td>RCA distal third</td>
<td>0.53</td>
<td>1.45</td>
<td>25%</td>
<td>25%</td>
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</tbody>
</table>

SD = standard deviation; LAD = left anterior descending coronary artery; RCX = right circumflex artery; RCA = right coronary artery
Figure 1. Mean of image quality score of coronary artery segments in magnetic resonance coronary angiography: Healthy volunteers. LAD = left anterior descending coronary artery; RCX = right circumflex artery; RCA = right coronary artery; 1/3 = proximal third of vessel; 2/3 = mid-third of vessel; 3/3 = distal third of vessel.

Figure 2. Mean of image quality score of coronary artery segments in magnetic resonance coronary angiography: Patients with proximal coronary artery stenosis. LAD = left anterior descending coronary artery; RCX = right circumflex artery; RCA = right coronary artery; 1/3 = proximal third of vessel; 2/3 = mid-third of vessel; 3/3 = distal third of vessel.

Figure 3. The learning curve: Image quality as a function of time for volunteers and patients.
sensitivity of 69% and specificity of 61%. The consensus reading had a sensitivity of 79% and a specificity of 54%. Results for vessels and segments are shown in Table 3. We performed this evaluation in order to achieve results comparable to other studies, wherein only parts of vessels were used for comparison with conventional coronary angiography. In contrast to other studies, we clearly defined the excluded vessel segments by an image quality score and we present both an overall evaluation and a selected evaluation of sensitivity and specificity when comparing MRCA to catheter angiography.

**DISCUSSION**

Different techniques for the imaging of coronary arteries using MRA have been reported. In earlier studies, 2D breath-hold methods were employed including a series of 2D slices, which are necessary for the visualization of coronary arteries because of the small vessel caliber and tortuous anatomy. Therefore, only parts of a coronary vessel can be imaged within one 2D slice; partial volume effects make a reliable assessment of coronary artery stenoses difficult. Since multiple breath-holds result in acquisitions in more or less different positions of the heart, attempts were made to get a continuous visualization of the coronary arteries; respiratory gating was combined with a 2D technique. In order to improve spatial resolution and to prevent partial volume averaging, 3D data acquisition techniques with respiratory gating were used. Due to longer scan times, respiratory gating is essential for this type of image acquisition.

Oshinsky et al. used a 2D technique with a respiratory monitoring belt and a navigator echo for respiratory gating. They found better image quality by respiratory gating than by breath-hold imaging. Navigator echo gating provided better image quality than the use of a monitoring belt. McConnell et al. studied different respiratory suppression methods with a varying number and location of navigators. They found superior image quality during navigator gating compared with breath...
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hold and respiratory-bellows gated imaging. No significant difference in image quality was found in four different navigator locations, but the shortest scan time was found by positioning the navigators on the right diaphragm. Therefore, in our study we used a retrospective-gated 3D MR technique for visualization of the coronary arteries with two navigators positioned on the dome of the right diaphragm with an angulation of 30°.

Previous studies compared the results of conventional coronary angiography with MRCA in the assessment of hemodynamically significant (> 50%) coronary artery stenoses. In 1994, Duerrinckx et al.6 used a 2D coronary angiography with MRCA in the assessment of the right diaphragm with an angulation of 30°. Therefore, in our study we used a retrospective-gated 3D MR technique for visualization of the coronary arteries with two navigators positioned on the dome of the right diaphragm with an angulation of 30°.

Pennell et al.15 used a 2D gradient echo imaging technique with a fat saturation and reported a sensitivity of 62% and a specificity between 37% and 82% depending on the localization of stenoses.

Muller et al.16 also used a 3D acquisition with navigator echo technique and fat suppression in 54 stenoses, diagnosed by coronary angiography. They found a sensitivity of 83% and a specificity of 93% when they excluded 5 out of 35 patients because of motion artifacts. Muller et al. used a respiratory gating technique with 3D acquisition and navigator echo measurement, similar to this study. However, they used two or three 3D slabs with a thickness of only 32 mm. Therefore, only a limited proximal portion of the coronary arteries could be visualized and the analysis of stenoses only in proximal coronary segments regardless to stenoses in mid segments may have improved the results. In our study, we found lower sensitivity and much lower specificity in the evaluation of nearly the same number of stenoses, both for the two independent blinded readers and for consensus reading. However, the voxel size in our study was even lower than in the study of Muller et al.

Pennell et al.15 used a 2D gradient echo imaging technique with fat suppression. Eighty-five percent of 47 stenoses in proximal and mid segments of the coronaries were detected by MRCA. However, no attempt was made to quote specificity in Pennell’s study.

Post et al.16 found a low sensitivity of 38% and a high specificity of 95% using a 3D gradient echo with respiratory gating. Twenty-one hemodynamically significant stenoses were diagnosed by conventional coronary angiography. Our study included 20 patients with 54 stenoses. Our results with relatively high sensitivity and inferior specificity values indicate that retrospective respiratory-gated 3D MRCA may be useful as a screening test for coronary artery stenosis. However, our results may be biased by high pre-test probability of stenoses since only patients with coronary heart disease scheduled for coronary angiography were included in this dial.

The variable image quality of retrospective respiratory-gated 3D MRCA is a major limitation. The pulse sequence used is T1 weighted, but it works with an inflow effect to enhance the signal in coronary vessels. Also, an increasing flip angle is used to shorten scan time and prevent saturation effects during rapid data acquisition. A similar technique by Fellner et al.17 was described in the assessment of renal arteries as the 3D tilted optimized nonsaturation excitation (TONE) technique. The T1/T2 contrast, which is dependent on variable presaturation and movement of protons by coronary flow or cardiac motion can change within a 3D slab. Therefore, soft plaques and the vessel wall may have a signal intensity similar to blood flow; this may decrease sensitivity.

Post et al.16 suggest that the length of TE may have an influence on sensitivity and specificity, and they recommend using a longer TE than they did (TE = 2.9 ms), which may lead to higher SI in vessels. They expect to improve sensitivity by the use of a longer TE. In contrast to Post et al., we found higher sensitivity but lower specificity using a TE of 2.7 ms, which is even shorter than the TE used by Post et al.

When good image quality is achieved with retrospective-gated 3D MRCA, the main epicardial arteries are almost fully visualized. However, orientation of the vessels in relation to the imaging plane may have a major impact on signal intensity within the vessels, which is dependent on inflow effects. The tortuous course of the coronaries results in changing inplane and throughplane orientation within the 3D slab. Therefore, signal intensity variations may mimic vessel stenosis.

When the coronaries are not surrounded by epicardial fat, it may be difficult to differentiate them from adjacent tissue. Epicardial veins may be confused with coronary arteries, but it is possible to differentiate veins from arteries with the use of single slices and MPR reconstructions. Collateral and reverse flow can make it impossible to diagnose a complete occlusion only with a navigator echo sequence. Additional investigation with a velocity encoding technique may solve this problem.14 This technique was not applied in our study.

Another difficulty of MRCA is the small vessel diameter and the limited spatial resolution with a voxel size of about 1.2 mm x 1.4 mm x 2 mm, which is high compared to other MRCA sequences reported (1998, Woodwar, Li D, Haacke E, et al.). Even if voxel size in retrospective respiratory-gated 3D MRCA is smaller than in other MRCA techniques, spatial resolution still does not allow visualization of distal segments of the coronaries with adequate image quality. Dodge et al.12 report on luminal diameters determined by conventional coronary angiography to be 4.4 mm for the left main, 3.6 mm for proximal segments of the LAD, 3.0 mm for proximal segments of the RCA and 3.4 mm for proximal segments of the LCX. For distal segments of the LAD, RCA and LCX they found diameters of 1.8 mm, 2.0 mm and 2.5 mm, respectively. These findings were obtained from normal men with a balanced coronary artery anatomy. It is not surprising that the decrease of image quality from
proximal to distal segments of the coronary arteries correlates with smaller vessel diameters.

Movement of the coronary arteries during the cardiac cycle represents another problem. We used a time window of 178 ms for data acquisition in mid diastole, where we expected high flow in the coronary arteries. In order to achieve good results, data have to be acquired with minimal movement of the coronaries. Poncelet et al. demonstrated a substantial movement of the distal part of the LAD within a narrow temporal window during diastole. Maximal flow in the RCA is not only reported during mid diastole but also during late systole and early diastole. However, data acquisition during late systole would create additional motion artifacts.

SI in the coronary vessels may be improved by contrast agent application. However, Gadolinium-chelates are not useful for contrast enhancement within the vessel lumen when ECG and respiratory-gated 3D acquisition are employed, since the blood half-life of these compounds is so short in relation to the total acquisition times. Intravascular contrast agents, however, may be advantageous for enhancing intravascular signal.

Various other methods for non-invasive assessment of the coronary arteries are under investigation, such as contrast-enhanced electron beam tomography (EBT) moshage and echocardiography. EBT is also useful for the detection and quantification of coronary artery calcification. EBT and echocardiography, as well as MRCA, are methods of an evolving state and no studies comparing these methods with each other are available.

In order to make MRCA a reliable diagnostic tool, further improvements are required. This includes improvement of ECG triggering, e.g., by the use of fiber optic cables, which are less sensitive to artifacts induced by RF and a constant magnetic field. Improvements of respiratory gating may be possible; the retrospective respiratory gating could be replaced by prospective real-time gating, which is possible if a linear phase shift processing of the navigator profile is employed. Another way of shortening scan time by a prospective real-time navigator gating is narrowing the acceptance window and adapting it during data acquisition, since the mean of the diaphragm end-expiratory position can significantly change. Currently, non-invasive respiratory-gated 3D MRCA is already superior to 2D techniques and respiratory bellows gating in visualizing the main coronary arteries.

In our trial, retrospective respiratory-gated 3D MRCA had a high sensitivity and a low specificity for the detection of proximal coronary artery stenoses. If these results are confirmed on larger patient collectives and if further technical improvements can be achieved, this technique might be applied as a non-invasive screening test for CAD.

REFERENCES