In Vivo Magnetic Resonance Evaluation of Atherosclerotic Plaques in the Human Thoracic Aorta
A Comparison With Transesophageal Echocardiography

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Background—The structure and composition of aortic atherosclerotic plaques are associated with the risk of future cardiovascular events. Magnetic resonance (MR) imaging may allow accurate visualization and characterization of aortic plaques.

Methods and Results—We developed a noninvasive MR method, free of motion and blood flow artifacts, for submillimeter imaging of the thoracic aortic wall. MR imaging was performed on a clinical MR system in 10 patients with aortic plaques identified by transesophageal echocardiography (TEE). Plaque composition, extent, and size were assessed from T1-, proton density–, and T2- weighted images. Comparison of 25 matched MR and TEE cross-sectional aortic plaque images showed a strong correlation for plaque composition ($\chi^2=43.5, P<0.0001; 80\%$ overall agreement; $n=25$) and mean maximum plaque thickness ($r=0.88, n=25; 4.56\pm0.21$ mm by MR and $4.62\pm0.31$ mm by TEE). Overall aortic plaque extent as assessed by TEE and MR was also statistically significant ($\chi^2=61.77, P<0.0001; 80\%$ overall agreement; $n=30$ regions).

Conclusions—This study demonstrates that noninvasive MR evaluation of the aorta compares well with TEE imaging for the assessment of atherosclerotic plaque thickness, extent, and composition. This MR method may prove useful for the in vivo study of aortic atherosclerosis. (Circulation. 2000;101:2503-2509.)

Key Words: atherosclerosis • magnetic resonance imaging • aorta • echocardiography • plaque

A natomy studies have shown that the amount of atherosclerotic plaque in the thoracic aorta directly correlates with the degree of atherosclerotic disease in the coronary arteries.1 Furthermore, thoracic aortic atherosclerosis is a stronger predictor of coronary artery disease (CAD) than conventional risk factors2 and is also a marker of increased mortality,3 stroke, and visceral thromboembolic events.4 Examination of the descending thoracic aorta by transesophageal echocardiography (TEE)5 and by fast computed tomography (CT)6 is used to predict CAD and cardiovascular risk.6,7

MR is a noninvasive imaging modality that can visualize and characterize the composition of carotid atherosclerotic plaques in vivo based on MR signal intensity.8,9 The principal challenges associated with MR imaging of thoracic aorta are obtaining sufficient sensitivity for submillimeter imaging and exclusion of artifacts due to respiratory motion and blood flow. This study presents the use of an MR imaging method for the assessment of atherosclerotic plaque size, extent, and composition in the thoracic aorta. The results show that the MR findings compare well with those obtained from TEE imaging. Therefore, MR may be a powerful noninvasive imaging tool for directly detecting aortic atherosclerotic plaques.

Methods

Patients
From a cohort of patients referred for TEE to rule out a cardiac or aortic source of thromboemboli, 10 patients (average age 63.6 years; range 31 to 82 years; 8 men, 2 women; 3 with peripheral emboli, 4 with transient ischemic attacks, and 3 with stroke) were identified with evidence of atherosclerotic plaques ($\geq 2$ mm in thickness) in the descending thoracic aorta. MR imaging was performed in these patients after informed consent in a form approved by the institutional review board. All patients received warfarin anticoagulation between TEE and MRI. MR imaging was conducted without knowledge of the specific TEE results for each patient.

Transesophageal Echocardiography
TEE was performed by a physician (T.N. or M.G.) using a 7-MHz multiplane probe (ATL HDI 300 or Sequoia, Acuson). All patients were mildly sedated with Demerol (Sanofi Winthrop) and/or Versed (Roche Laboratories). With the patient in the lateral decubitus position, the TEE probe was advanced toward the level of the
diaphragm (typically 40 to 45 cm from the incisors), then a gradual pullback was performed. For each patient, all images were recorded on super VHS videotape in real time for display and evaluation. During the real-time examination, the position of aortic plaques (≥2 mm in thickness) with respect to the TEE probe (distance from dental incisors and origin of the left subclavian artery) and extent of each plaque were carefully recorded for later analysis. Images were obtained in the horizontal and vertical planes. However, only horizontal-plane TEE images were compared with the MR images.

MR Imaging

MR was performed on a 1.5-T Signa (General Electric Medical Systems) Echospeed (capable of delivering 2.2 G/cm with a rise time of 184 μs) or cardiovascular MR system (capable of delivering 4.0 G/cm with a rise time of 147 μs). Images were obtained with fast gradient-echo, conventional spin-echo (SE), and optimized double-inversion-recovery fast spin-echo (FSE) sequences. A body coil was used for excitation. A 4-element (2 anterior elements and 2 posterior elements) phased-array coil was used for signal reception to obtain an improved signal-to-noise ratio.10 Patients were positioned supine, and ECG electrodes were attached to trigger data acquisition.

Fast gradient-echo images were acquired initially in the coronal and sagittal planes. Transverse SE T1-weighted (T1W) ECG-gated images of the entire descending thoracic aorta were obtained with respiratory compensation, 20-cm field-of-view (FOV), 256 × 160 to 192 acquisition matrix, no phase wrap, 2-signal averaging (NSA), ±16-kHz receiver bandwidth, 5-mm-thick slices with no interslice gap, repetition time (TR) of 1 RR interval, and echo time (TE) of 12 ms. Suppression of the blood flow signal in the aorta was achieved by use of spatial presaturation pulses superior and inferior to the imaging slice. The images were acquired without chemical shift suppression, and the aortic wall thickness was initially assessed during image acquisition with the console software as the images were collected. However, when the aortic wall was <3 mm in maximum thickness, imaging was repeated with the chemical shift suppression pulse to suppress the signal from periaortic fat. This improved visualization of the small atherosclerotic plaques.11

Proton density–weighted (PDW) and T2-weighted (T2W) images transverse to the descending thoracic aorta were obtained by an ECG-gated double-inversion-recovery–optimized FSE sequence. Imaging was performed during free breathing (16 to 32 heartbeats per slice). When necessary, imaging was performed during short periods of suspended respiration of 16 heartbeats per slice. Breath-holding was confirmed by a bellows respiratory monitor.

The double-inversion-recovery magnetization preparation pulses ensured that signal from flowing blood was adequately suppressed.12 The flow-inversion pulses were placed before the period of fast flow, and data acquisition occurred during the period of slow flow. This process maximized flow suppression due to outflow and minimized artifacts due to vessel motion. The delay time or inversion time (TI) for the double-inversion preparatory pulses was determined close to the null point of the blood signal. TI is based on the T1 relaxation value of the blood and the TR interval:

\[ T1 = -T1 \left( \frac{1 + e^{-TR/T1}}{2} \right) \]

With TR = 2, RR = 1000 ms (heart rate = 60 bpm), and T1 = 1200 ms, from the Equation, TI is 625 ms.

The FSE sequence used short radiofrequency pulses generated with the Shinnar-LeRoux algorithm,13 enabling an echo spacing (ESP) as short as 4.4 ms. The short ESP allowed the use of long echo-train (ETL) data acquisition without the disadvantage of T2 relaxation blurring. The imaging parameters were as follows: TR = 2 RR intervals, TE = 12 ms (PDW) and TE = 60 ms (T2W), 20-cm FOV, 5-mm slice thickness, no interslice gap, 256 × 256 acquisition matrix, no phase wrap, 2 NSA, 32 to 64 ETL, ±54-kHz receiver bandwidth, and chemical shift suppression (when necessary). A data acquisition window of 140 to 280 ms was achieved. All images (PDW and T2W) were acquired with a resolution of 0.78 × 0.78 × 5 mm³. Fifteen to 25 slices were used to cover the entire thoracic aorta. Total examination time was 45 to 60 minutes.

Data Analysis

Image Matching

MR images were carefully matched (visually and anatomically) with the chosen TEE cross sections with the dental incisors and origin of the left subclavian artery used as landmarks. After agreement on MR and TEE section alignment, one investigator (Z.A.F.) analyzed the MR data and another (T.N.) analyzed the TEE data independently.

Atherosclerotic Plaque Characterization

The American Heart Association (AHA) classification, types IV through VI,14 was used for grading plaques. Briefly, type IV/Va (fibrolipid), type Vb (calcified), type Vc (fibrotic), and type VI (thrombotic with or without fissure) were identified.

Atherosclerotic plaque grading by TEE was based on the echogenicity and morphological appearance of the atherosclerotic plaque, as previously described.6,7 Lipid components were defined as echolucent regions within the plaque that were not attributable to attenuation and dense reflections. Fibrocellular components were defined as hyperechogenic reflections within the plaque presented by dense echoes without acoustic shadowing. Thrombotic plaques had irregularities of the plaque luminal surface and had a laminated or “layered” appearance, with variable echogenicity and sometimes a thin border of relative echolucency.7

Atherosclerotic plaque characterization by MR was based on the signal intensities and morphological appearance of the plaque on T1W, PDW, and T2W images, as validated previously.8 Lipid components were defined as hypointense regions within the plaque on both T1W and PDW images and as hypointense images on T2W images. Fibrocellular components were defined as hyperintense regions of the plaque on T1W, PDW, and T2W images. Calcium deposits were defined as bright reflections with acoustic shadowing. Thrombotic plaques had marked irregularities on the luminal surface and were considered hyperintense (signal intensity less than most fibrocellular components) regions within the plaque on T1W9 and PDW images and variable on T2W images.8,11 Because of the improved flow suppression of the double-inversion-recovery FSE sequence (PDW and T2W imaging) compared with the conventional SE with radiofrequency presaturation pulses (T1W imaging), the differentiation between slow flow and plaque was determined only from the PDW and T2W images.

Atherosclerotic Plaque Extent

The descending thoracic aorta, from the origin of the left subclavian artery to the diaphragm, was divided into 3 equal segments (proximal, mid, and distal) on both TEE and MR data sets. We therefore obtained from all the data recorded by TEE and MR a total of 30 segments from our 10 patients. The plaque extent in each segment was graded on TEE and MR images according to the percent of the luminal surface involved by plaque: normal (0%), mild (0 to 25%), moderate (25% to 75%), and severe (>75%). Maximal extent of plaque involvement was evaluated for each segment of aorta using all available TEE and MR PDW images.

Maximum Plaque Thickness

Electronic calipers were used to measure maximum plaque thickness on the TEE and MR matched slices in the transverse view as the distance between the aortic border and the point of greatest luminal protrusion. The MR PDW images were used because of higher signal-to-noise ratios. The average of all MR slices from each segment was used.

Statistical Analysis

The findings were analyzed with χ² tests, 2-tailed paired Student’s t tests, and simple linear regression with 95% CIs (StatView, Abacus Corp). The comparison between the TEE and MR measurements for
maximum plaque thickness was evaluated further by the approach of Bland and Altman by calculating the mean (d) and SD (σd) of the difference. From these data, the limits of agreements (d−2σd and d+2σd) were calculated. Values are expressed as mean±SEM. A P value <0.05 was considered statistically significant.

Results

Before patient imaging, 6 young asymptomatic subjects (mean age 27 years; range 25 to 32 years; 3 men) were used for parameter optimization for aortic imaging with the double-inversion-recovery FSE sequence. Some of the parameters that were modified and optimized include ESP, ETL, acquisition matrix size, FOV, slice thickness, receiver bandwidth, TE, NSA, inversion slice thickness, and chemical shift suppression pulses. The images were assessed qualitatively, and the parameters that best visualized the aortic wall were chosen.

A typical image of the descending thoracic aorta in a normal subject is shown in Figure 1. This image demonstrates the results obtained with the optimized double-inversion-recovery FSE sequence, with excellent flow suppression. The normal aortic wall appears thin and of uniform thickness in both the ascending and descending aorta (Figure 1).

The MR imaging protocol described in Methods was kept constant for all patients except when image quality was severely compromised by respiratory motion artifacts. Then, breath-holding was used (3 of 10 patients). Also, in 2 patients, a chemical shift suppression pulse was used to improve visualization of small atherosclerotic plaques (<3 mm maximum thickness).

Table 1. Thoracic Aortic Plaque Characterization by TEE and MR

<table>
<thead>
<tr>
<th>TEE</th>
<th>MR</th>
<th>IV/Va</th>
<th>Vb</th>
<th>Vc</th>
<th>VI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV/Va</td>
<td>10</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Vb</td>
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<td>4</td>
<td>0</td>
<td>0</td>
<td>5</td>
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<td>Vc</td>
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<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>

MR and TEE aortic cross sections were graded according to AHA classifications. There was 80% overall agreement between TEE and MR classification (χ²=43.50, P<0.0001; n=25).

All aortic plaques that were identified by TEE were also detected by MR (100%). Each of the 25 plaques was characterized according to the AHA criteria given in Methods. Comparison of the TEE and MR characterization showed 80% (20 of 25 segments) overall agreement (Table 1). There was a statistically significant correlation between the TEE and MR data for plaque characterization (χ²=43.50, P<0.0001; n=25).

Plaque Extent

There was 80% (24 of 30 segments) overall agreement between TEE and MR findings (Table 2). There was a strong correlation between the TEE and MR findings for plaque extent (χ²=61.77, P<0.0001; n=30).

A patient with severe diffuse disease in the descending thoracic aorta is shown in Figure 4. The MR images show aortic plaques with different morphological and compositional characteristics.

Maximum Plaque Thickness

The 25 TEE and MR matched cross-sectional aortic plaque images were used for the study of maximum plaque thickness. Mean maximum plaque thickness as measured by TEE and MR was 4.62±0.31 and 4.56±0.21 mm, respectively. The difference was not statistically significant (P=0.68). There was a strong correlation between maximum plaque thickness measurements with both imaging modalities (correlation coefficient 0.88, n=25). Results from the Bland-Altman analysis are presented in Figure 5. As shown in Figure 5, the mean and SD of the difference were small (d=0.056 mm and σd=0.66 mm), and >95% of the differences were within the limits of agreement (−1.27 and 1.38 mm).
Discussion

In the present study, we evaluated the descending thoracic aortic wall using a fast MR technique that allows in vivo imaging of atherosclerotic plaque. We demonstrated that MR can assess aortic plaque composition, extent, and size. The MR findings closely correlated with TEE (the current noninvasive clinical “gold standard”) examination in the same patients.

Autopsy\(^1\) and TEE\(^2\) studies have shown that thoracic aortic atherosclerosis is a significant marker for coronary disease. In fact, parameters such as aortic wall thickness, luminal irregularities, and plaque composition are strong predictors of future vascular events.\(^7,17\) For example, using TEE, the French Study of Aortic Plaques in Stroke (FAPS) investigators\(^7,17\) found a significantly increased risk of all vascular events (stroke, myocardial infarction, peripheral embolism, and cardiovascular death) for patients who had noncalcified aortic plaques $\geq 4$ mm in thickness. These noncalcified plaques were thought to be lipid-laden plaques (AHA types IV/Va), which in coronary arteries are considered to be prone to rupture and thrombosis.\(^18\)

MR imaging has several advantages over currently available cardiovascular risk factor assessment methods and imaging modalities. MR is safe and noninvasive. Adult MR exams usually do not require injections, sedation, or anesthesia. Although not demonstrated in the present study, MR can detect atherosclerotic plaques at all locations in the aorta, including the aortic root,\(^11\) ascending aorta, and aortic arch, as
well as the descending thoracic and abdominal aorta. Examination of the carotid and peripheral arteries, brain, myocardium, and even the epicardial coronary arteries (Figures 3 and 4) may be performed during the same session. However, MR examination can be limited by claustrophobia, some arrhythmias and irregular heart rhythms, and implanted metallic devices.

Ex vivo aortic, carotid, peripheral, and coronary artery plaque characterization with MR is well validated. It was shown that MR accurately discriminates among the different plaque components of the carotid arteries in vivo using high-resolution T1W, T2W, and PDW images. A recent study by Moody and colleagues showed that carotid artery thrombus in patients with a recent stroke can be visualized with T1W MR.

Prior MR methods for clinical aortic imaging were hampered by severe blood flow and respiratory artifacts. This study demonstrates that the use of double-inversion-recovery–optimized FSE MR sequence with a short ESP value and rapid image acquisition limits these artifacts. Although not demonstrated in the present study, mobile plaque components may be evaluated with fast cine MR imaging or real-time MR imaging.

In the present study, there was good agreement between TEE and MR assessment of aortic plaque type (Table 1), plaque extent (Table 2), and maximum plaque thickness (Figure 5). In fact, there was 80% overall agreement between MR and TEE findings for both plaque type and extent. This compares well with a recent study showing 73% agreement between aortic plaques imaged in vivo with TEE and pathological findings after resection. The differences between TEE and MR assessments may be due to several factors. Three of the patients received warfarin anticoagulation between TEE and MRI. The data show that for these patients, the maximum plaque thickness was higher on TEE than on MRI, and this may be due to anticoagulant therapy between the time of TEE and MRI. Artifacts occur frequently with TEE, thus limiting the number of aortic image slices that could be compared with the corresponding MR images. Aortic calcification may make TEE assessment difficult as well. Moreover, there are several ultrasound parameters (eg, system gain and axial and lateral resolution) that interfere with accurate atherosclerotic plaque characterization by TEE. Finally, ultrasound is not a discriminator of chemical composition; thus, it is difficult to differentiate AHA type VI

<table>
<thead>
<tr>
<th>MR</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
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<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Mild</td>
<td>4</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>3</td>
<td>30</td>
</tr>
</tbody>
</table>

There was 80% overall agreement between TEE and MR findings ($\chi^2=61.77; P<0.0001$).

Figure 4. T2W MR images from patient with severe diffuse disease in descending thoracic aorta. Plaques are different in appearance and characteristics from one location to another. Insets in each panel represent magnified view of descending thoracic aorta. A, Type Vc (fibrotic) plaque. B, Type Vb (calcified) plaque. C and D, Lipid-rich plaques (type IV/Va). MR images are 5 mm thick and acquired with no interslice gap and are displayed cephalad (A) to caudal (D). Origin of right coronary artery (RCA) is clearly seen taking off from aortic root (Ao). Arrows in insets indicate plaque and its components.
from types IV/Va plaques with TEE, because both thombus and lipid components are echolocan.

With TEE, the anterior half of the aortic cross section is often not adequately visualized because the portion adjacent to the esophagus is usually out of focus. Air in the trachea and left bronchus limits visualization with TEE of the upper (distal) part of the ascending aorta and the proximal arch. For these reasons, we limited the comparison between MR and TEE to the descending thoracic aorta.

CT appears to be useful for the detection of protruding aortic atheroma, especially in areas not visualized by TEE. Although CT (fast spiral or electron beam) can detect calcification, this method lacks the capability for the detection of atherosclerotic plaque composition seen with MR. Although CT is a noninvasive technique, it requires exposure to ionizing radiation and usually necessitates the injection of a contrast agent for vascular imaging. Therefore, this technique, like TEE, is not suitable for routine and repeated patient assessments.

Although the number of patients in our study was limited, many different types of atherosclerotic plaques were detected with MR. Presumably, AHA type I, II, and III plaques were also present in the study group and were not identified by either MR or TEE because of the in-plane spatial resolution and contrast-to-noise ratios available. In the plaque classification analysis, type IV and Va plaques were grouped (IV/Va) because according to the AHA classification, types IV and Va differ only in their collagen content and therefore cannot be differentiated by either MR or TEE. Improvement in signal-to-noise ratio and spatial resolution and enhancement in image contrast could eventually allow the imaging of AHA type I through III aortic plaques and differentiation between AHA types IV and Va.

Our study is limited in its detection of thrombus. For example, the signal from intraplaque thrombus changes with time. Therefore, new MR contrast techniques such as diffusion imaging may prove more sensitive and accurate in the detection of thrombus. In addition, the use of respiratory motion compensation techniques such as MR navigators could further reduce respiratory motion artifacts and alleviate the use of breath-holding altogether.

Interobserver and intraobserver reliability of MR imaging, as well as sensitivity and specificity of our proposed criteria, must be documented in a larger number of patients. There is a potential for misregistration and measurement errors between the MR and TEE images. We carefully matched (visually and anatomically) the MR images with the corresponding TEE cross-sectional images using external anatomic structures as fiducial references. Our matching procedure is prone to error and is a limitation of this study. Computer-aided registration and 3D reconstruction methods can improve on this limitation and improve the measurement. In addition, studies that examine the cost-effectiveness of MR examination are needed.

In conclusion, we have demonstrated that MR is a method for direct noninvasive assessment of aortic atherosclerotic plaque thickness, extent, and composition. MR may allow the serial evaluation of progression and therapy-induced regression of atherosclerotic plaques.

Acknowledgments

This study was supported in part by National Institutes of Health grants P50HL54469 and R01HL61801. We acknowledge the help of Karen Metroka, Stella Palentia, and Mary Ann Whelan-Gales in patient selection and recruitment. We thank John Abela and Paul Wisdom for help in MR imaging.

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Circulation. 2000;101:2503-2509
doi: 10.1161/01.CIR.101.21.2503

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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