Fat-Suppressed Breath-Hold Magnetic Resonance Coronary Angiography

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Background. The ability to image the coronary arteries noninvasively would represent an advance in patient care. We have developed a magnetic resonance (MR) angiographic technique that allows the acquisition of complete images of coronary flow within a single breath-hold. By this method, the feasibility of noninvasive MR coronary angiography was evaluated in 25 subjects, including 19 healthy adult volunteers and six patients after diagnostic coronary angiography.

Methods and Results. Noninvasive MR coronary angiography was performed with a fat-suppressed ECG-gated gradient-echo sequence with k-space segmentation. Overlapping transverse sections were initially used to image coronary flow, with oblique images obtained after identification of proximal anatomy. The left main coronary artery was seen in 24 subjects (96%), with a mean diameter of 4.8 mm (range, 3.4–6.2 mm) and average length of 10 mm (range, 8–14 mm). The left anterior descending coronary artery was seen in 100% of subjects, with a mean proximal diameter of 3.6 mm (range, 2.6–4.3 mm) and for an average length of 44 mm (range, 28–93 mm). The left circumflex coronary artery was seen in 76% of subjects, with a mean proximal diameter of 3.5 mm (range, 2.6–4.3 mm) and for an average length of 25 mm (range, 9–42 mm). The right coronary artery was also identified in 100% of subjects, with a mean proximal diameter of 3.7 mm (range, 2.7–5.1 mm) and for an average length of 58 mm (range, 24–122 mm). Quantitative angiography of normal proximal segments demonstrated a good correlation with MR-determined lumen diameters (r=0.86, p<0.002). Occluded vessels in patients with coronary artery disease displayed an absence of flow signal distal to the occlusion, whereas vessels with significant angiographic stenoses demonstrated signal loss corresponding to the area of the stenosis, with visualization of the more distal vessel.

Conclusions. Breath-hold MR coronary angiography provides visualization of the major epicardial vessels. In the future, MR coronary angiography may provide a noninvasive means for the evaluation of patients with known or suspected coronary artery disease. (Circulation 1993;87:94–104)

KEY WORDS • angiography • magnetic resonance imaging • coronary artery disease

Cardiovascular disease remains the leading cause of death in the United States, with more than 1 million myocardial infarctions and 600,000 deaths per year attributed to coronary artery disease. The “gold standard” for the evaluation of coronary arteries is contrast angiography, with over 500,000 such procedures performed annually in the United States and up to 20% of these demonstrating no significant coronary artery disease. The ability to assess coronary artery blood flow noninvasively would represent an advance in patient care. Information regarding the coronary arteries would then be acquired with minimal risk, both for patients with suspected coronary disease and for follow-up in patients with known disease.

Magnetic resonance (MR) imaging is well suited for evaluating the heart, with excellent soft-tissue contrast without the need for vascular access or an exogenous contrast agent and the ability to acquire images in oblique sections. Initial attempts at MR imaging of the proximal coronary arteries met with limited success because of prolonged imaging times coupled with prominent cardiac and respiratory motion. More recently, magnetic resonance angiography (MRA) of arterial vessels of a caliber similar to that of the coronary arteries has been developed for clinical applications, including screening for intracranial aneurysms and renal artery stenosis. These gradient-echo techniques depict laminar flow as bright signal, whereas turbulence or absent flow are displayed as signal voids. Given the success of MR angiography for these applications, we sought to study the ability of MR to image coronary artery blood flow noninvasively. Previous studies from our laboratory have demonstrated that imaging of coronary flow in isolated and in vivo rodent hearts is feasible. We have modified this approach for use in humans and now apply this technique to a series of healthy volunteers and patients with known coronary artery disease to determine the feasibility of human MR coronary angiography.
FIGURE 1. Breath-hold transverse magnetic resonance sections 5 mm thick in a healthy volunteer at (panel A) the level of the proximal right coronary artery (RCA; white arrow) and (panel B) subsequent transverse section of RCA at a more inferior level (white arrow). LV, left ventricular cavity; RV, right ventricular cavity; Ao, aortic root.
Methods

Study Group

The study group consisted of 25 adult subjects, including 20 men and five women. Nineteen subjects were consenting volunteers, mean age, 28 years (range, 23–36 years), and six subjects were adults, age 43–68 years, with known coronary artery disease who underwent MR study after diagnostic coronary angiography. Angiography was planned in each case for the evaluation of chest pain. All volunteers were free of cardiovascular disease by history and physical examination. No volunteer was on any medication or used tobacco products.
Patients with coronary artery disease included those with an occluded proximal left anterior descending coronary artery (n=2), an occluded proximal right coronary artery (n=2), and significant stenosis (>70%) of the proximal right coronary artery (n=1) or left anterior descending coronary artery (n=1).
**FIGURE 3.** This page and facing page. Panel A: Transverse magnetic resonance section of the left main coronary artery (white arrow) continuing on into (panel B) the left anterior descending coronary artery (LAD; black arrows). Note the diagonal branches off the LAD (solid white arrow) and the great cardiac vein (open white arrow). Panel C: Transverse section of the left main coronary artery (white arrow) and LAD (black arrow) in another patient. Ao, aorta; RV, right ventricle.

**MR Imaging**

MR imaging was performed with a superconducting 1.5-T Magnetom SP whole-body imaging system (Siemens Medical Systems, Inc., Iselin, N.J.) with a standard planar elliptical spine coil used as radiofrequency receiver. ECG leads were placed on the subject's back, and subjects were placed in the prone position with the heart positioned directly above the surface coil. The
imaging technique consisted of a gradient-echo sequence with incremented flip angle series and k-space segmentation such that six or eight phase-encoding steps were acquired in rapid sequence, constituting one segment. Sixteen or 20 interleaved segments were acquired so as to complete the 120×256, 128×256, or 160×256 matrix. Because the epicardial coronary vessels are surrounded by epicardial fat, a chemical shift-selective fat saturation pulse was applied before each segment to nullify signal from fat and thus enhance signal from coronary flow. The sequence was gated to the patient's ECG, with an initial delay after the QRS complex to allow for image acquisition in mid-diastole. A repetition time of 13 msec and an echo time of 8 msec were used, resulting in an effective temporal resolution of 78–104 msec. For transverse imaging, a 5-mm slice thickness and 230-mm field of view were used (in-plane resolution of 1.4–1.9×0.9 mm). Oblique imaging was conducted with a 3-mm slice thickness and 240-mm field of view. Heart rate varied from 54 to 90 beats per minute, resulting in a typical scan time of 12–18 seconds and imaging within a single end-expiratory breath-hold.

A scout was first obtained in the sagittal section to identify thoracic structures, followed by ECG-gated breath-hold transverse images at the level of the aortic root. Sequential transverse images were obtained with 2–3-mm overlap over a 2–3-cm vertical distance. Oblique views were then obtained along the axis defined by the origins of the right and left main coronary arteries after flow through the proximal portion of the vessels had been identified. Total imaging time averaged less than 45 minutes per patient.

**MR Image Analysis**

Individual transverse or oblique images were stored on optical disk for later recall and analysis. The diameter of the proximal segment and the length of the observed coronary segment were assessed with an online software package and consensus of two observers.

**Quantitative Contrast Angiography**

Cine images of proximal vessels free of stenoses on contrast angiography (n=13) were optically magnified and compared with the 7F (2.3-mm-diameter) guiding catheter as a reference object using digital calipers (Fowler Ultra-Cal II).

**Statistical Analysis**

MR data on proximal vessel diameter were compared with digital caliper assessment of proximal contrast angiographic data by Student's paired t test, and the correlation of the two measurements was performed by least-squares linear regression.

All studies were performed within the guidelines of the hospital Committee on Clinical Investigations. Informed consent was obtained from all participants.

**Results**

The major epicardial vessels were visualized in all subjects. An example of a typical transverse MR image at the level of the origin of the right coronary artery is
shown in Figure 1A, with a subsequent transverse image at a more inferior level shown in Figure 1B. Oblique images along the major axis of the vessel identified in transverse section could then be obtained as shown in Figure 2A, with successive sections obtained to delineate deviations of the vessel into adjacent imaging sections (Figures 2B–2D). Contiguous segments of coronary vessels as distal as the bifurcation of the distal right coronary artery were often seen (Figure 2D). The left main coronary artery was visualized in both transverse and oblique sections (Figure 3A), whereas the left anterior descending coronary artery, diagonals, and cardiac veins were best identified on transverse sections (Figures 3A and 3B).

The left main coronary artery was seen in 24 (96%) of 25 subjects, the left anterior descending coronary artery in 25 (100%), the left circumflex coronary artery in 19 (76%), and the right coronary artery in 25 (100%). The average diameter and average length of observed coronary artery in volunteers and nondiseased vessels of patients with coronary artery disease are shown in Table 1. Quantitative angiography of normal proximal segments from the subgroup who underwent conventional contrast angiography demonstrated a good correlation with MR-determined lumen diameters ($r=0.86$, $p<0.002$; Figure 4), with no significant difference between the two measurements (contrast angiography, $4.1\pm0.9$ mm versus MR angiography, $4.3\pm0.9$ mm; $p=0.14$).

In addition to these major vessels, the diagonal branches of the left anterior descending coronary artery were identified in 20 subjects (80%) (Figure 3B), and the great cardiac vein was identified in 22 (88%) of 25 subjects (Figure 3B). Confirmation of arterial and venous flow was made by saturation of proton spins from blood (nullification of signal from the blood pool) in the aortic root and resultant loss of signal within the left main and left anterior descending coronary arteries but persistent signal in the cardiac vein.

 Occluded vessels in the six patients with coronary artery disease were visualized by MR as a total absence of flow signal distal to the area of occlusion (Figure 5). Patients with significant stenoses demonstrated signal loss in the area of the stenosis, with flow seen again in the more distal portion of the vessel (Figure 6).

**Discussion**

The ability to acquire information regarding coronary artery anatomy noninvasively would represent an improvement in the care of patients with known or suspected coronary artery disease. Our study demonstrates that despite their small caliber, tortuosity, and mobility, imaging of the proximal, mid, and distal epicardial coronary arteries is possible by breath-hold MR angiographic techniques. The method allows for the acquisition of a series of sections within a period of 30–45 minutes. Measured lumen diameter of angiographically normal segments compares favorably with that obtained from autopsy specimens and contrast angiography, in which the left main coronary artery is typically 4–6 mm in diameter and 10 mm in length and the proximal left anterior descending, circumflex, and right coronary arteries are typically 3–4 mm in diameter. Comparison of proximal coronary diameter in the subgroup of patients who underwent both MR coronary angiography and conventional contrast angiography demonstrated a good correlation, with MR slightly overestimating angiographically determined lumen diameter. This is probably because of a combination of partial volume averaging related to the lower MR spatial resolution and slight movement of the vessels during the imaging period.

The use of oblique imaging sections allows visualization of the proximal, mid, and distal segments of the right coronary artery, whereas transverse sections reliably image the left main and left anterior descending coronary artery from cardiac base to apex. The volunteer in whom the left main coronary artery was not visualized was a subject studied very early in our series, before our routine use of oblique imaging sections. The mid and distal left circumflex coronary arteries were less reliably seen, possibly as a result of their more distal location with respect to the surface coil or the need to use an oblique imaging section. Patients with angiographically documented obstruction to flow demonstrate an abrupt cessation of flow signal at the area corresponding to the obstruction as well as in the more distal lumen. Significant stenoses appear as a signal void at the area of stenosis, with visualization of the more distal vessel, consistent with local turbulence at the area of stenosis with laminar flow distally. Similar exaggerations are seen with two-dimensional MRA of other vessels with focal stenoses or occlusions. Since the MR coronary angiographic technique is insensitive to the direction of blood flow, however, the presence of extensive collaterals to a vessel distal to a total occlusion may yield results similar to those seen with focal stenoses.

The MR angiographic technique's sensitivity to differences between nonturbulent blood flow (appearing bright) and turbulent blood flow (appearing dark) would result in an imperfect concordance with contrast angiography. Minor luminal irregularities or ulcers/aneurysms may lead to significant local turbulence and resultant MR signal loss in the absence of an angiographically significant diameter narrowing. This ability of MR coronary angiography to detect areas of turbulence in the absence of an angiographically significant stenosis, however, may have clinical utility. Numerous pathological studies have documented extensive atherosclerosis distant from angiographically significant stenoses, whereas other studies have suggested that it is the mild-to-moderate stenosis that has the greatest potential to progress. Many of these progressive coronary lesions have eccentric shapes—lesions that would be

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<th>Table 1. Magnetic Resonance Angiography Assessment of Proximal Coronary Diameter and Length of Vessel Visualized</th>
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LM, left main coronary artery; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery.
expected to demonstrate turbulence or signal void on the MR coronary angiogram. Thus, the information gained from the MR angiogram, with its sensitivity to turbulence, has the potential to be more valuable for the assessment of mild-to-moderate stenoses than a conventional contrast angiogram.

Previous investigators have used MR for the assessment of coronary artery bypass graft patency. Spin-echo MR imaging, which gives detailed anatomic information, depicts rapidly moving blood as a signal void because of movement of excited spins out of the imaging plane between the 90° and 180° pulses and intravoxel dephasing. This technique has been used to classify a graft as patent or occluded on the basis of the identification of a patent graft lumen. In an analogous fashion, gradient-echo sequences, which use short repetition times and shallow flip angles, depicting positive signal with moving blood have been shown to be useful for the identification of patent reverse saphenous and internal mammary artery grafts. Coronary artery bypass grafts, however, are typically much larger than native vessels (up to twice the diameter), with less respiratory and cardiac motion associated with the proximal portion of graft. Less encouraging results have been obtained previously with attempts at native coronary artery imaging by conventional MR techniques, although the proximal coronary arteries have recently been visualized in some volunteers by subtraction techniques or three-dimensional angiograms formed by stacking two-dimensional planar images. With standard spin-echo and gradient-echo techniques, visualization of the coronary arteries has been erratic and often limited to the proximal vessel. This is probably caused by significant respiratory and cardiac motion during the cardiac cycle, including apex-to-base shortening and rotation and vessel tortuosity. Cardiac rotational and translational motion can be divided into four phases, with rapid movement during ventricular systole and less vigorous but still significant movement during rapid ventricular filling in early diastole and after atrial systole. Between these latter two events, however, is a period of relative diastasis, when there is little cardiac motion and little intracavitary blood flow but coronary blood flow is still high. Our use of an ultrafast breath-hold sequence allowed the elimination of respiratory motion by acquiring data during a single breath-hold, whereas cardiac motion and temporal resolution were minimized by image acquisition during diastole and the use of k-space segmentation, respectively. The method is adaptable to slower or more rapid heart rates; with a short RR interval, the number of phase-encoding steps acquired per QRS is reduced, and the number of segments is increased. Conversely, with significant bradycardia and long RR interval, the number of phase-encoding steps acquired per QRS could be increased, with a comparable total time for acquisition of each image. In theory, cardiac and respiratory motion can also be minimized by the use of combined cardiac and respiratory gating and more conventional spin-echo techniques, although this would result in prohibitively long scan times to image each level at the same time point within the cardiac cycle.

Echocardiography is the only other noninvasive technique that has also been used to image the coronary arteries. Two-dimensional transthoracic echocardiography has been successful at visualization of the left main and proximal right coronary arteries in 60–90% of patients, whereas imaging of the left anterior descending and circumflex arteries has proved more difficult despite advances in transducer and imaging technology. Difficulties for the transthoracic echocardiographic technique include unfavorable chest-wall configuration, chronic obstructive lung disease, and the small diameter and distal location of the vessels. More recently, transesophageal echocardiography, using high-frequency transducers and with lack of chest-wall interference, has been shown to be useful for the detection of left main coronary artery stenoses. Adequate images of the full length of the left main coronary artery and identification of the bifurcation are reported in 90% of subjects. Although this is encouraging, the incidence of left main coronary artery disease is relatively low. More recently, an intraoperative study demonstrated the potential utility of transesophageal echocardiography for delineating stenoses of the very proximal left anterior descending, left circumflex, and right coronary arteries.

Because the spatial resolution of MRA does not currently match that of contrast angiography, MR coronary angiography would not be expected to fully supplant diagnostic coronary angiography. Although there is a good correlation between the MR-estimated proximal vessel diameter and quantitative angiography, MR angiography slightly overestimated angiographic lumen diameter, probably because of partial volume effects and cardiac motion during the imaging period. At present, partial volume effects and signal dropout caused by turbulence preclude the use of quantitative MR coronary angiography to assess diameter stenoses, although the use of shorter echo times may help minimize signal loss and specially designed surface coils will enhance signal-to-noise ratio and permit better spatial resolution. Alternatively, black blood imaging methods could be applied that are insensitive to turbulence. The use of more rapid echo-planar imaging methods would serve to further minimize the effects of cardiac motion. Nonetheless, with further development and clinical testing, MR coronary angiography may come to provide a noninvasive alternative for the detection or exclusion of coronary artery disease of the major epicardial vessels in asymptomatic individuals with multiple risk factors for coronary disease or in patients with chest pain of uncertain cause. MR coronary angiography...
FIGURE 5. Panel A: Oblique magnetic resonance (MR) section from a patient with an occlusion of the proximal right coronary artery (RCA). Note the abrupt loss of signal (white arrow), which corresponded angiographically to the area of occlusion. No extension of the RCA was seen in adjacent sections. Panel B: Transverse MR section from a patient with an angiographic occlusion of the proximal left anterior descending coronary artery (white arrow) immediately after the first diagonal (black arrow). Ao, aorta; RV, right ventricle.

Phy may also help avoid misinterpretation of catheter-induced ostial right coronary artery spasm,27 assist in the screening of young adults involved in highly competitive sports for the presence of rare but sometimes fatal coronary artery anomalies,28,29 aid in the evaluation of patients requiring surgery primarily for valvular heart disease, and assist in the evaluation of patients with renal failure or other conditions associated with increased morbidity from coronary angiography. Moreover, MR coronary angiography may be combined with MR perfusion imaging30 along with anatomic and functional MR imaging to provide a comprehensive cardiac evaluation.
FIGURE 6. Panel A: Oblique magnetic resonance section of the right coronary artery (RCA) in a patient with a stenosis of the proximal vessel. Note the tapering of the proximal RCA and loss of signal (white arrow). Panel B: Corresponding coronary angiogram (right anterior oblique view) depicting a 90% diameter stenosis (large black arrow) of the proximal RCA corresponding to the area of signal loss shown in panel A. The vessel ostia (with catheter engaged) is also seen (small black arrow).
A limitation of the current technique is the relative dependence on a regular heart rate and patients’ holding their breath for 12–18 seconds. Frequent ventricular premature beats may cause acquisition of one or more series of phase-encoding steps during systole of the succeeding beat, resulting in image degradation. No subjects had difficulty holding their breath for the required time period, although this may be a problem for other individuals. If so, the use of a coarser matrix or an increased number of phase-encoding steps per QRS could be used.

In the future, MR coronary angiography may come to provide a unique, noninvasive means for the detection or exclusion of coronary artery disease involving the major coronary arteries in asymptomatic individuals with risk factors for coronary disease or in patients with suspected coronary artery disease. MR coronary angiography may also allow for periodic assessment of the efficacy of a medical or mechanical intervention used for the treatment of coronary artery disease.

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