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Assessment of Coronary Artery Disease Using Magnetic Resonance Coronary Angiography

A National Multicenter Trial

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- Objectives** This national multicenter study determined the diagnostic performance of 1.5-T whole-heart coronary magnetic resonance angiography (MRA) in patients with suspected coronary artery disease (CAD).
- Background** Whole-heart coronary MRA using steady-state free precession allows noninvasive detection of CAD without the administration of contrast medium. However, the accuracy of this approach has not been determined in a multicenter trial.
- Methods** Using a 1.5-T magnetic resonance imaging unit, free-breathing steady-state free precession whole-heart coronary MRA images were acquired for 138 patients with suspected CAD at 7 hospitals. The accuracy of MRA for detecting a $\geq 50\%$ reduction in diameter was determined using X-ray coronary angiography as the reference method.
- Results** Acquisition of whole-heart coronary MRA images was performed in 127 (92%) of 138 patients with an average imaging time of 9.5 ± 3.5 min. The areas under the receiver-operator characteristic curve from MRA images according to vessel- and patient-based analyses were 0.91 (95% confidence interval [CI]: 0.87 to 0.95) and 0.87 (95% CI: 0.81 to 0.93), respectively. The sensitivity, specificity, positive and negative predictive values, and accuracy of MRA according to a patient-based analysis were 88% (49 of 56, 95% CI: 75% to 94%), 72% (51 of 71, 95% CI: 60% to 82%), 71% (49 of 69, 95% CI: 59% to 81%), 88% (51 of 58, 95% CI: 76% to 95%), and 79% (100 of 127, 95% CI: 72% to 86%), respectively.
- Conclusions** Non-contrast-enhanced whole-heart coronary MRA at 1.5-T can noninvasively detect significant CAD with high sensitivity and moderate specificity. A negative predictive value of 88% indicates that whole-heart coronary MRA can rule out CAD. (J Am Coll Cardiol 2010;56:983-91) © 2010 by the American College of Cardiology Foundation

Coronary artery disease (CAD) is the most frequent cause of death in developed countries (1), and the current gold standard for its detection is conventional X-ray coronary angiography (CAG). However, conventional CAG is expensive, potentially harmful, and associated with a small risk of serious complications. In addition, a considerable number of patients who undergo CAG have no evidence of clinically important CAD. Coronary computed tomography angiography is an inexpensive, noninvasive alternative to CAG for ruling out CAD. However, coronary computed tomography

angiography still requires radiation exposure and an iodinated contrast agent.

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Coronary magnetic resonance angiography (MRA) has emerged over the past decade as a possible noninvasive alternative for visualizing coronary arteries (2). A previous multicenter study using a target volume, turbo field echo method (3) showed that coronary MRA can reliably identify left main coronary artery (LM) stenosis or 3-vessel disease (3VD). Recently, steady-state free precession (SSFP) whole-heart coronary MRA has become the method of choice for coronary imaging at 1.5-T (4-7). Because of an intrinsically high blood signal intensity (8), the SSFP sequence can acquire whole-heart coronary MRA images without the need for magnetic resonance imaging (MRI) contrast medium. Several single-center studies evaluated the

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Abbreviations and Acronyms

- 3D** = 3-dimensional
- 3VD** = 3-vessel disease
- AUC** = area under the receiver-operator characteristic curve
- BMI** = body mass index
- CAD** = coronary artery disease
- CAG** = coronary angiography
- CI** = confidence interval
- HR** = heart rate
- LM** = left main coronary artery
- MDCT** = multidetector-row computed tomography
- MR** = magnetic resonance
- MRA** = magnetic resonance angiography
- MRI** = magnetic resonance imaging
- NPV** = negative predictive value
- PPV** = positive predictive value
- RCA** = right coronary artery

diagnostic performance of 1.5-T SSFP whole-heart coronary MRA for detecting significant coronary artery stenoses on X-ray CAG (9–11). However, to the best of our knowledge, no multicenter study has yet assessed the diagnostic value of 1.5-T whole-heart coronary MRA.

Consequently, this multicenter study determined the ability of whole-heart coronary MRA to detect significant obstructive CAD using conventional X-ray CAG.

Methods

Patients. We studied 138 patients with suspected CAD who presented with chest pain that suggested newly developed or recurrent coronary artery stenosis and were scheduled for X-ray CAG at 7 hospitals during the period August 2005 to December 2007. Exclusion criteria included patients with general contraindications to MRI (e.g., pacemakers, claustrophobia), acute coronary syndrome, atrial fibrillation, and previous coronary bypass graft surgery.

Table 1 summarizes the features of the 138 patients, of whom 95 (69%) were male and 43 (31%) were female (mean age 67 ± 9 years; range 39 to 87 years). The local institutional review board or local ethics committee of all participating hospitals approved the study, and all patients gave written informed consent to participate.

Acquisition of MRI data. We acquired magnetic resonance (MR) images using a 1.5-T MRI unit (Intera, Philips Medical Systems, Best, the Netherlands) with a 5-channel cardiac coil. Isosorbide dinitrate (5 mg) was administered sublingually to the patients before undergoing MRI. Beta-blockers were not used in this study. The tight-fitting abdominal belt was wrapped in all patients to suppress the motion of the diaphragm in relation to breathing. Initial survey images to determine the position of the heart and diaphragm and reference images to evaluate individual coil sensitivities for parallel imaging acquisition were obtained without holding the breath. Transaxial cine MR images were then acquired with an SSFP sequence while breathing freely (repetition time, 2.6 ms; echo time, 1.3 ms; flip angle, 60° ; field of view, $320 \times 320 \times 120$ mm; acquisition matrix, 128×128 ; cardiac phases, 50; SENSE factor, 3.0 in the anteroposterior direction; imaging time, 3 s) to determine the rest period of the right coronary artery (RCA). Patient-specific acquisition windows were set during either the

diastolic or systolic phase, depending on the phase of minimal motion of the RCA.

Free-breathing, navigator-gated whole-heart coronary MR angiograms were obtained using a 3-dimensional (3D), segmented SSFP sequence with radial k-space sampling (repetition time, 4.1 ms; echo time, 2.1 ms; flip angle, 80° ; excitations per cardiac cycle, 20 to 50; SENSE factor, 2.0; navigator gating window, ± 2.5 mm; no drift correction; field of view, $300 \times 300 \times 130$ mm; acquisition matrices, $224 \times 224 \times 75$; reconstruction matrices, $512 \times 512 \times 150$). Myocardial and venous blood signals were suppressed using T2 preparation. Spectral pre-saturation with inversion recovery was also applied to suppress epicardial fat signals. MRA data acquisition was terminated if the scan length exceeded 30 min.

Whole-heart coronary MRA analysis. Coronary MR images were transferred to a 3D PACS (picture archiving and communication system) server (Aquarius NET server, Tera-Recon, Inc., San Mateo, California). Two observers independently evaluated the whole-heart coronary MRA images using sliding thin-slab maximum intensity projection. The image quality of whole-heart coronary MRA was evaluated using the following scale: 1, poor (coronary vessel barely evident or noisy image); 2, moderate (coronary vessel visible but diagnostic confidence low); 3, good (coronary artery adequately visualized and diagnostic quality image); and 4, excellent (coronary artery clearly depicted). Results generated by 2 readers were averaged. The coronary arteries were visually screened for the presence or absence of significant luminal narrowing ($\geq 50\%$ diameter reduction) using an intention-to-read approach. All coronary arteries were in-

Table 1 Patient Characteristics

Characteristics	All Patients Who Underwent Coronary MRA (n = 138)	Patients With Successful Acquisition of Coronary MRA Images (n = 127)
Male/female	95/43	86/41
Age, yrs	67 ± 9	67 ± 9
Range	39–87	39–87
Heart rate, beats/min	68 ± 12	68 ± 12
Range	42–108	42–108
Body mass index, kg/m ²	24 ± 4	24 ± 4
Previous myocardial infarction	30 (22)	28 (22)
Coronary stent	15 (11)	14 (11)
Risk factors		
Hypertension	103 (75)	95 (75)
Hypercholesterolemia	64 (46)	61 (48)
Diabetes mellitus	46 (33)	41 (32)
Smoking	59 (43)	54 (43)
Family history of CAD	29 (21)	27 (21)
Stenosis on coronary angiography		
1-vessel disease	41 (30)	41 (32)
2-vessel disease	12 (9)	11 (9)
3-vessel disease	4 (3)	4 (3)

Data are expressed as mean \pm SD or n (%).
CAD = coronary artery disease; MRA = magnetic resonance angiography.

cluded for the evaluation regardless the image quality of coronary MRA to avoid overestimation of the diagnostic accuracy (12–14). Disagreement between the 2 observers was settled by a consensus reading. For receiver-operator characteristic curve analysis, 2 observers visually graded the likelihood of coronary artery stenosis on whole-heart coronary MR angiograms according to the following scale: 1, absent; 2, probably absent; 3, possibly present; 4, probably present; and 5, definitely present. Results for the 2 readers were averaged. The in-stent coronary lumen was not included in the analysis. To evaluate the impact of heart rate (HR) on image quality and diagnostic performance, the patients were divided into 2 groups based on HR as follows: group 1, HR <70 beats/min (n = 72, mean HR 60 ± 7.0 beats/min, range 42 to 68 beats/min) and group 2, HR ≥70 beats/min (n = 55, mean HR 78 ± 8.6 beats/min, range 70 to 108 beats/min). In addition, the impact of body mass index (BMI) on diagnostic performance was evaluated. The patients were divided into 2 groups based on BMI as follows: group 3, BMI <25 kg/m² (n = 83, mean BMI 22.0 ± 2.2 kg/m², range 15.8 to 24.8 kg/m²), and group 4, BMI ≥25 kg/m² (n = 44, mean BMI 27.5 ± 2.4 kg/m², range 25.1 to 40.4 kg/m²).

X-ray CAG and interpretation. An observer who was blinded to the results of whole-heart coronary MRA interpreted the conventional X-ray coronary angiograms in which coronary artery stenosis was evaluated using quantitative CAG software (QangioXA, Medis, Inc., Raleigh, North Carolina). Intracoronary administration of isosorbide dinitrate (2 to 3 mg) was performed in all patients before contrast injection. Significant coronary arterial stenosis was defined as a reduction in luminal diameter of ≥50%.

Statistical analysis. Based on the sensitivity of 82% and specificity of 90% in a patient-based analysis in a previous single-center study that assessed 113 patients with the prevalence of 45% (9), we estimated that a minimum of 127 subjects were required to reject the null hypothesis that either sensitivity or specificity is ≤70% with a p value <0.05.

The diagnostic accuracy of MRA was determined for lesions with a reference diameter of ≥2.0 mm on X-ray coronary angiograms regardless of the quality of images acquired from patients for whom MRI was completed. Data in subjects with successful MRA acquisitions (92%) underwent statistical analysis using SPSS software, version 11.5 (SPSS, Inc., Chicago, Illinois). Areas under receiver-operator characteristic curves were calculated to evaluate the diagnostic performance of whole-heart coronary MRA. Continuous values are presented as mean ± SD. Because the image quality score comprised skewed variables (according to the Shapiro-Wilk test), the differences between image quality scores of 2 groups were tested using the Mann-Whitney *U* test. The correlation between image quality score and HR and the level of agreement between the 2 raters with respect to the 5-point scale ratings for receiver-operator characteristic analysis were evaluated using Spearman's rank correlation. Sensitivity, specificity, positive pre-

dictive value (PPV), negative predictive value (NPV), and accuracy per patient, vessel, and segment analysis were calculated with a 95% confidence interval (CI). The level of agreement between the 2 raters with respect to the binary judgments was evaluated by the kappa value. The significance of differences in diagnostic performance between patients with an HR of <70 and ≥70 beats/min or a BMI <25 and ≥25 kg/m² was tested using the chi-square test for comparisons of cross tables. The number of subjects in whom the MR study could not be completed was not taken into account in the calculation of diagnostic performance. A p value <0.05 was considered statistically significant.

Results

Acquisition of whole-heart coronary MRA was completed in 127 (92%) of 138 patients with an average imaging time of 9.5 ± 3.5 min (range 2.4 to 19.2 min). The total study time including the pre-scan was <30 min in patients undergoing a successful study. The mean ± SD navigator efficiency was 37.4 ± 26.0%. Eleven patients for whom MRA images could not be acquired had an irregular breathing pattern or the position of the diaphragm drifted during the procedure. The average HR in the 138 patients was 68 ± 12 beats/min. Whole-heart coronary MRA was performed during diastole in 73% (93 of 127) (mean HR 65 ± 10 beats/min; mean acquisition window 131 ± 40 ms; mean imaging time 9.5 ± 3.7 min) and during systole in 27% (34 of 127) (mean HR 76 ± 13 beats/min; mean acquisition window 110 ± 52 ms; mean imaging time 9.2 ± 2.9 min) of the patients. Significant coronary artery stenosis was observed on X-ray coronary angiograms from 56 (44%) of the 127 patients in whom MR acquisition was completed. **Image quality of whole-heart coronary MRA.** Table 2 summarizes image quality scores in each coronary artery segment of whole-heart coronary MRA. No significant differences were found in the image quality scores between groups 1 and 2 (HR <70 and ≥70 beats/min, respectively) and in any segment (p values ranged from 0.06 to 0.98). Image quality scores did not significantly correlate with HR (Spearman's rank correlation: r = -0.04, p = 0.65).

Diagnostic accuracy of whole-heart coronary MRA. In a patient-based analysis, the area under the receiver-operator characteristic curve (AUC) of whole-heart coronary MRA was 0.87 (95% CI: 0.81 to 0.93) (Fig. 1) for the detection of significant coronary artery stenoses on X-ray angiography. The sensitivity, specificity, PPV, NPV, and accuracy for detecting patients with significant CAD were 88% (95% CI: 75% to 94%), 72% (95% CI: 60% to 82%), 71% (95% CI: 59% to 81%), 88% (95% CI: 76% to 95%), and 79% (95% CI: 72% to 86%), respectively (Table 3). The kappa value for the binary judgment was 0.73 (95% CI: 0.62 to 0.85) in the patient-based analysis. In a vessel-based analysis, the AUC of whole-heart coronary MRA was 0.91 (95% CI: 0.87 to 0.95) with Spearman's rank correlation coefficient

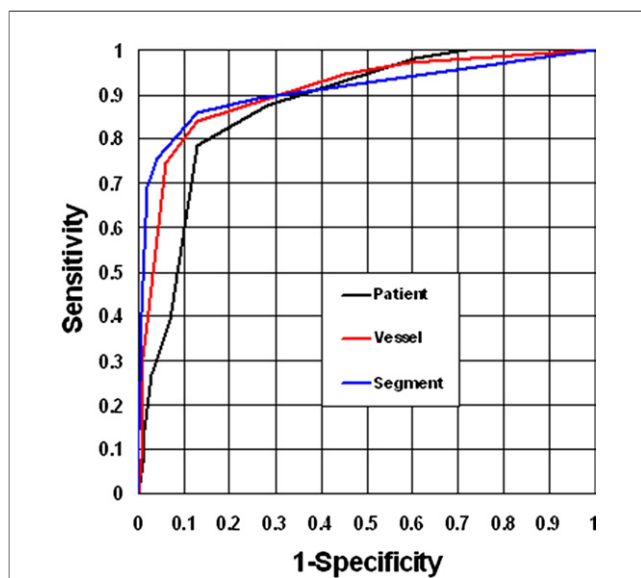
Table 2 Impact of High Heart Rate on Image Quality Score of Whole-Heart Coronary MRA

Artery	No. of Segments ≥ 2.0 mm	All Patients (n = 127)	Patients With HR <70 beats/min (n = 72)	Patients With HR ≥ 70 beats/min (n = 55)	p Value*
RCA					
1	127	3.8 \pm 0.3	3.8 \pm 0.4	3.7 \pm 0.3	0.08
2	126	3.7 \pm 0.4	3.8 \pm 0.4	3.7 \pm 0.4	0.06
3	123	3.7 \pm 0.4	3.7 \pm 0.4	3.7 \pm 0.4	0.55
4	106	3.1 \pm 0.6	3.1 \pm 0.7	3.2 \pm 0.5	0.6
LM					
5	127	3.8 \pm 0.3	3.8 \pm 0.3	3.8 \pm 0.3	0.98
LAD					
6	123	3.7 \pm 0.4	3.7 \pm 0.4	3.6 \pm 0.5	0.53
7	127	3.6 \pm 0.5	3.6 \pm 0.5	3.5 \pm 0.5	0.40
8	127	3.1 \pm 0.7	3.2 \pm 0.7	3.1 \pm 0.7	0.47
9	111	2.6 \pm 0.8	2.7 \pm 0.7	2.5 \pm 0.9	0.23
LCX					
11	127	3.4 \pm 0.5	3.4 \pm 0.6	3.4 \pm 0.5	0.67
12	112	2.4 \pm 0.8	2.3 \pm 0.8	2.4 \pm 0.8	0.76
13	125	3.2 \pm 0.7	3.3 \pm 0.7	3.2 \pm 0.7	0.38

Data are expressed as mean \pm SD. *p values represent significance of difference in image quality score of whole-heart coronary MRA between patients with heart rates of <70 and ≥ 70 beats/min.

HR = heart rate; LAD = left anterior descending artery; LCX = left circumflex coronary artery; LM = left main coronary artery; RCA = right coronary artery; other abbreviation as in Table 1.

between the 2 readers of 0.83 (Fig. 1). The sensitivity, specificity, PPV, NPV, and accuracy for detecting significant coronary artery stenosis were 83% (95% CI: 72% to 90%), 90% (95% CI: 86% to 93%), 67% (95% CI: 57% to 77%), 96% (95% CI: 92% to 98%), and 89% (95% CI: 86%

**Figure 1**

Receiver-Operator Characteristic Curves of 1.5-T Whole-Heart Coronary MRA for Detecting Significant Coronary Artery Stenosis

The area under the receiver-operator characteristic curve of 1.5-T non-contrast-enhanced whole-heart coronary magnetic resonance angiography (MRA) for detecting significant coronary artery disease is 0.87 (95% confidence interval [CI]: 0.81 to 0.93), 0.91 (95% CI: 0.87 to 0.95), and 0.91 (95% CI: 0.87 to 0.95) in patient-, vessel-, and segment-based analyses, respectively.

to 92%), respectively (Table 3). The kappa value for the binary judgment was 0.79 (95% CI: 0.72 to 0.87) in the vessel-based analysis. The individual AUC for the RCA, the left anterior descending artery including the LM and left circumflex artery were 0.91 (95% CI: 0.84 to 0.98), 0.92 (95% CI: 0.87 to 0.97), and 0.87 (95% CI: 0.75 to 0.99), respectively (Fig. 2). Spearman's rank correlation coefficient between the 2 readers was 0.85 in a patient-based analysis. The mean \pm SD rating for positive consensus judgments was 2.56 \pm 0.17. There were 3 segments for the negative consensus judgment and the mean \pm SD MR rating was 2.00 \pm 0.00. The sensitivity, specificity, PPV, NPV, and accuracy of whole-heart coronary MRA for detecting LM stenosis or 3VD were 89% (95% CI: 51% to 99%), 100% (95% CI: 96% to 100%), 100% (95% CI: 60% to 100%), 99% (95% CI: 95% to 100%), and 99% (95% CI: 98% to 100%). Figures 3 and 4 illustrate the detection of significant stenoses by whole-heart coronary MRA with correlation with X-ray CAG.

Impact of HR on diagnostic performance of whole-heart coronary MRA. Table 4 summarizes the diagnostic performance of whole-heart coronary MRA in patients with an HR <70 beats/min and those with an HR ≥ 70 beats/min. The sensitivity, specificity, PPV, and NPV did not significantly differ between the 2 groups at any level of analysis (patient, vessel, and segment).

Impact of BMI on diagnostic performance of whole-heart coronary MRA. Table 5 summarizes the diagnostic performance of whole-heart coronary MRA in patients with a BMI <25 kg/m² and those with a BMI ≥ 25 kg/m². No significant difference was observed between the values in the

Table 3 Diagnostic Accuracy of Whole-Heart Coronary MRA Compared With Radiographic Angiography

	n	Sensitivity	Specificity	PPV	NPV	Accuracy
Per patient	127	88 (49/56) [75-94]	72 (51/71) [60-82]	71 (49/69) [59-81]	88 (51/58) [76-95]	79 (100/127) [72-86]
Per vessel	381	83 (62/75) [72-90]	90 (276/306) [86-93]	67 (62/92) [57-77]	96 (276/289) [92-98]	89 (338/381) [86-92]
RCA	127	77 (17/22) [54-91]	90 (95/105) [83-95]	63 (17/27) [43-80]	95 (95/100) [88-98]	88 (112/127) [83-94]
LM	127	100 (6/6) [52-100]	100 (121/121) [96-100]	100 (6/6) [52-100]	100 (121/121) [96-100]	100 (127/127) [—]
LAD	127	91 (32/35) [76-98]	82 (75/92) [72-89]	65 (32/49) [50-78]	96 (75/78) [88-99]	84 (107/127) [78-91]
LCX	127	69 (11/16) [42-88]	97 (108/111) [92-99]	79 (11/14) [49-94]	96 (108/113) [90-98]	94 (119/127) [90-98]
Per segment	1,461	81 (73/90) [71-88]	98 (1,341/1,371) [97-99]	71 (73/103) [61-79]	99 (1,341/1,358) [98-99]	97 (1,414/1,461) [96-98]

Values are shown as percentages. Data are % (raw data) [95% confidence interval].

CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value; other abbreviations as in Tables 1 and 2.

2 groups, except for the PPV in a segment-based analysis (77% vs. 55%, $p = 0.03$).

Discussion

The present prospective, multicenter trial evaluated the diagnostic ability of non-contrast-enhanced whole-heart coronary MRA to detect significant coronary artery stenosis on X-ray CAG among patients with suspected CAD. We applied an intention-to-read approach without excluding segments with low image quality (12-14). Whole-heart coronary MRA demonstrated high sensitivity (88%), moderate specificity (72%), a moderate PPV (71%), and a high NPV (88%) with an AUC of 0.87 for detecting significant coronary artery stenosis. An NPV of 88% indicated that whole-heart coronary MRA is useful for ruling out CAD in

patients with suspected CAD and is thus useful for eliminating unnecessary X-ray CAG. In addition, a high NPV of 99% for detecting LM stenosis or 3VD was observed in the current multicenter study. Therefore, 1.5-T whole-heart coronary MRA reliably rules out LM stenosis or 3VD.

Until the development of the whole-heart approach, coronary MRA was performed by repeated acquisitions of a targeted volume of 3-cm thickness using a double oblique, 3D gradient echo sequence. One prospective multicenter study revealed that 3D coronary MRA using a gradient echo sequence and a target volume approach can accurately identify LM stenosis or 3VD. However, the clinical utility of target volume coronary MRA is limited by time-consuming 3-point planning, lengthy scanning time (70 min on average), and poor specificity (42%) when all vessels are analyzed (3).

The introduction of SSFP sequences allowed acquisition of a large 3D volume covering the entire heart without compromising the high blood signal of coronary arteries. Planning of the 3D volume for whole-heart coronary MRA is quite simple, and considerable time can be gained by eliminating 3-point planning. One study demonstrated that whole-heart coronary MRA can be performed in 30 min (7). The diagnostic accuracy of SSFP whole-heart coronary MRA was evaluated by several single-center studies (9-11), in which the sensitivity and specificity of whole-heart coronary MRA ranged from 78% to 96% and from 68% to 96%, respectively, for significant CAD. The sensitivity and specificity demonstrated in the current study are in line with these published results from single-center studies.

The use of a patient-specific acquisition window in the cardiac cycle can provide optimal temporal resolution for each patient, allowing the acquisition of diagnostic coronary MR images without the administration of beta-blockers, even in patients with a high HR (≥ 70 beats/min). This is one advantage of whole-heart coronary MRA over multi-detector computed tomography (MDCT) of coronary arteries in which a lower HR is often essential for high-quality images. In addition, whole-heart coronary MRA does not require exposure to ionizing radiation or the injection of iodinated contrast material, and high-density calcium does not cause beam-hardening artifacts (15).

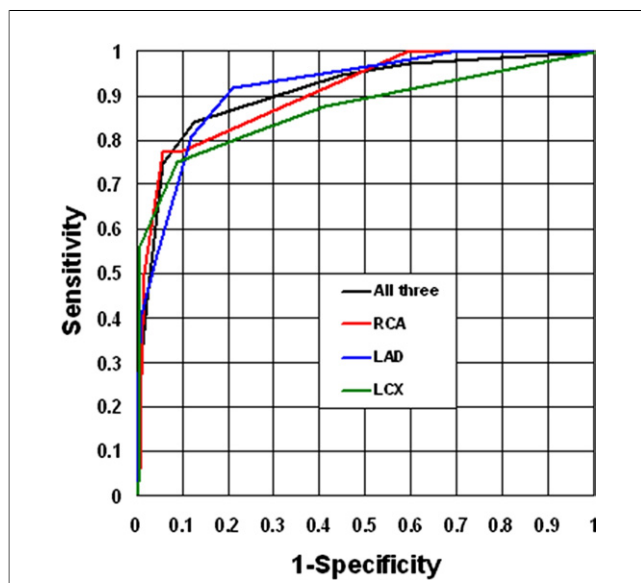


Figure 2 Receiver-Operator Characteristic Curves of 1.5-T Whole-Heart Coronary MRA for Individual Vessels

The area under the receiver-operator characteristic curve of 1.5-T non-contrast-enhanced whole-heart coronary MRA for detecting significant coronary artery disease is 0.91 (95% CI: 0.87 to 0.95) for all 3 vessels, 0.91 (95% CI: 0.84 to 0.98) for the right coronary artery (RCA), 0.92 (95% CI: 0.87 to 0.97) for the left anterior descending artery (LAD) (including the left main coronary artery), and 0.87 (95% CI: 0.75-0.99) for the left circumflex artery (LCX). Abbreviations as in Figure 1.

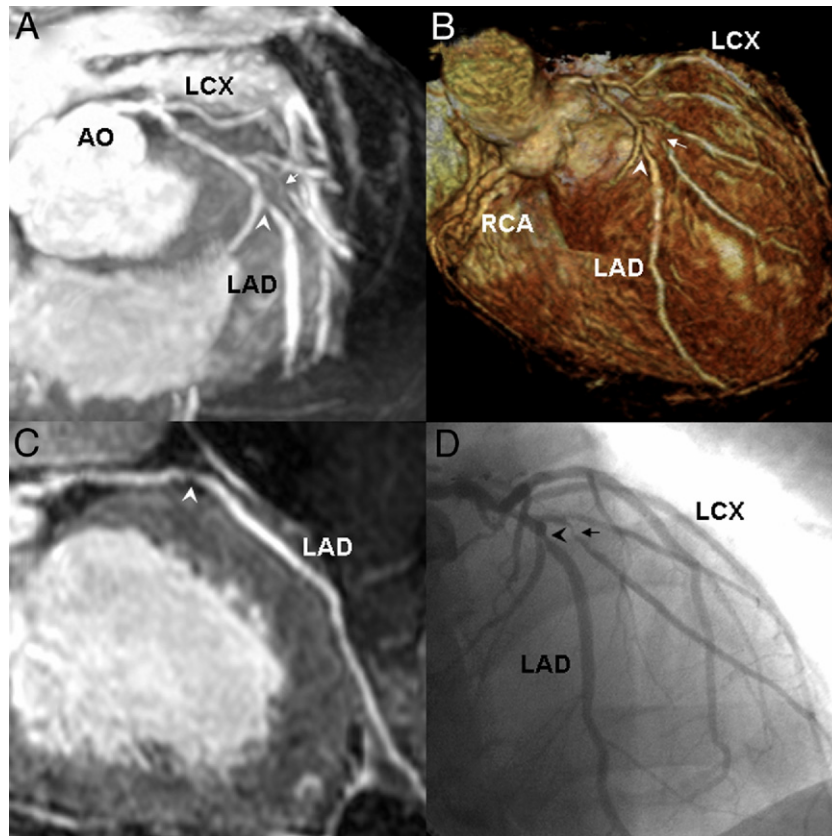


Figure 3 Noncontrast-Enhanced 1.5-T Whole-Heart Coronary MRA in a 58-Year-Old Man Presenting With Chest Pain on Effort

Sliding thin-slab maximum intensity projection image (A) and volume-rendered image (B) detect coronary artery stenoses in the LAD (arrowhead) and diagonal branch (arrow). Curved planar reconstruction image shows severe coronary artery stenosis in the LAD (C, arrowhead). Good agreement is observed between coronary MRA and X-ray coronary angiography (D). Black arrowhead in D indicates coronary artery stenosis in the LAD; black arrow in D indicates coronary artery stenosis in the diagonal branch. AO = aorta; other abbreviations as in Figures 1 and 2.

A recent multicenter study demonstrated that the AUC values of 64-row MDCT angiography for detecting significant coronary artery stenosis are 0.93 and 0.91 in patient- and vessel-based analyses, respectively (16). These AUC values are slightly higher than those of whole-heart coronary MRA in the current study. However, several patients (22% of entire study population) had to be excluded from the analysis in that MDCT multicenter trial due to heavy coronary calcification. Another prospective multicenter trial using 64-row MDCT showed sensitivity of 95%, specificity of 83%, a PPV of 64%, and an NPV of 99% for detecting luminal diameter narrowing of $\geq 50\%$ on invasive coronary angiograms (17). The NPV of 88% in this multicenter study was lower than that of 64-row MDCT. However, whole-heart coronary MRA can overcome heavy coronary arterial calcification and achieve sufficient diagnostic performance without the use of contrast medium and ionizing radiation. In this regard, 1.5-T whole-heart coronary MRA is preferable in patients with lower pretest probability of CAD compared with 64-row MDCT.

Contrast-enhanced whole-heart coronary MRA at 3.0-T has emerged as a means of improving the contrast-to-noise ratio compared with noncontrast-enhanced 1.5-T whole-heart coronary MRA (18,19). The diagnostic accuracy of 3.0-T contrast-enhanced whole-heart coronary MRA was recently evaluated in 69 patients with suspected CAD in a single-center trial (20). Although the acquisition time (9.0 ± 1.9 min) and study success rate (89.9%) were similar to those of our current study, the diagnostic performance of 3.0-T whole-heart coronary MRA seems to be quite promising, with 94.1% sensitivity and 82.1% specificity for detecting $\geq 50\%$ stenoses in the coronary arteries. However, due to increased field inhomogeneity and radiofrequency energy deposition at a high field strength, 3.0-T whole-heart coronary MRA relies on a double-dose infusion of a high-relaxivity contrast medium. The use of contrast medium increases the study cost and is associated with potential side effects, especially in patients with impaired renal function. Therefore, non-contrast-enhanced 1.5-T

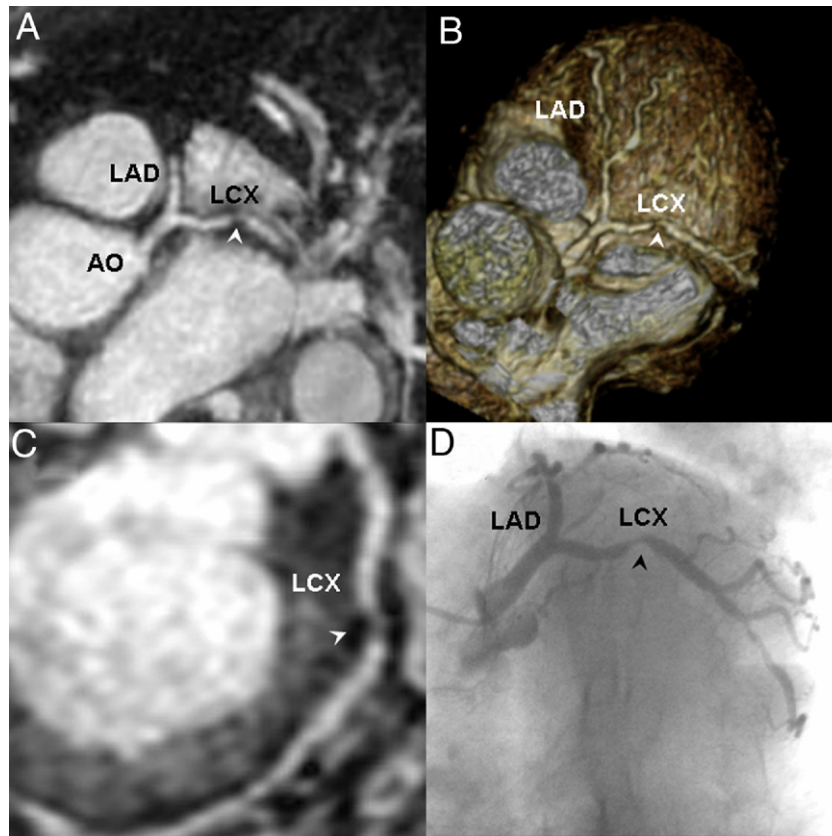


Figure 4 Noncontrast-Enhanced 1.5-T Whole-Heart Coronary MRA in a 66-Year-Old Woman

Significant coronary artery stenosis in the LCX (white arrowhead) is observed in the sliding thin-slab maximum intensity projection image (A), the volume-rendered image (B), and the curved planar reconstruction image (C), with good correlation with X-ray coronary angiography (black arrowhead) (D). Abbreviations as in Figures 1, 2, and 3.

SSFP MRA and contrast-enhanced 3.0-T MRA are not competing modalities and may have different indications. **Study limitations.** Our study population had a clinical indication for X-ray CAG and thus had a disease prevalence of 44%. Although 1.5-T whole-heart coronary MRA is a noninvasive examination with an NPV of 88%, as demonstrated here, this technology should not be considered for populations with a low prevalence of CAD (e.g., screening CAD in asymptomatic patients) at this time. The PPV,

which was 71% in the current patient population with a moderate to high pretest probability of CAD, will be reduced in individuals with low pretest probabilities. Therefore, screening asymptomatic individuals by coronary MRA would increase the potential for performing unnecessary coronary computed tomography angiography and/or CAG and incurring additional costs. MR images could not be acquired in approximately 8% of the patients. Because this was due to unstable breathing patterns or drift of the

Table 4 Impact of HR on Diagnostic Performance of Whole-Heart Coronary MRA

	n	Sensitivity	Specificity	PPV	NPV	AUC
HR <70 beats/min						
Patient-based analysis	72	85 (29/34) [68-98]	74 (28/38) [57-86]	74 (29/39) [58-86]	85 (28/33) [67-94]	0.90 [0.83-0.97]
Vessel-based analysis	216	77 (34/44) [62-88]	91 (157/172) [86-95]	69 (34/49) [54-81]	94 (157/167) [90-97]	0.89 [0.82-0.95]
Segment-based analysis	831	76 (42/55) [63-86]	98 (761/776) [97-99]	74 (42/57) [60-84]	98 (761/774) [97-99]	0.89 [0.83-0.95]
HR ≥70 beats/min						
Patient-based analysis	55	91 (20/22) [69-98]	70 (23/33) [51-84]	67 (20/30) [47-82]	92 (23/25) [72-99]	0.87 [0.78-0.96]
Vessel-based analysis	165	90 (28/31) [73-98]	89 (119/134) [82-93]	65 (28/43) [49-79]	98 (119/122) [92-99]	0.94 [0.90-0.98]
Segment-based analysis	630	89 (31/35) [72-96]	97 (580/595) [96-99]	67 (31/46) [52-80]	99 (580/584) [98-100]	0.94 [0.89-1.00]

Values are shown as percentages. Data are % (raw data) [95% confidence interval].

AUC = area under the receiver-operator characteristic curve; other abbreviations as in Tables 2 and 3.

Table 5 Impact of BMI on Diagnostic Performance of Whole-Heart Coronary MRA

	n	Sensitivity	Specificity	PPV	NPV	AUC
BMI <25 kg/m²						
Patient-based analysis	83	90 (37/41) [76-97]	74 (31/42) [58-86]	77 (37/48) [62-87]	89 (31/35) [72-96]	0.85 [0.77-0.93]
Vessel-based analysis	249	85 (47/55) [73-93]	91 (177/194) [86-95]	73 (47/64) [61-83]	96 (177/185) [91-98]	0.92 [0.87-0.97]
Segment-based analysis	955	84 (57/68) [72-91]	98 (870/887) [97-99]	77 (57/74) [66-86]	99 (870/881) [98-99]	0.92 [0.84-1.00]
BMI ≥25 kg/m²						
Patient-based analysis	44	80 (12/15) [51-95]	69 (20/29) [49-84]	57 (12/21) [34-77]	87 (20/23) [65-97]	0.91 [0.83-1.00]
Vessel-based analysis	132	75 (15/20) [51-90]	88 (99/112) [81-93]	54 (15/28) [34-72]	95 (99/104) [89-98]	0.89 [0.82-0.96]
Segment-based analysis	506	73 (16/22) [50-88]	97 (471/484) [95-99]	55 (16/29) [36-73]	99 (471/477) [97-99]	0.91 [0.86-0.96]

Values are shown as percentages. Data are % (raw data) [95% confidence interval].
BMI = body mass index; other abbreviations as in Tables 1, 3, and 4.

diaphragm position during the scan, the study success rate should be improved if imaging time can be reduced. The performance of whole-heart coronary MRA using 32-channel cardiac coils and a higher parallel imaging factor is currently under investigation from this perspective. Asian individuals were studied in this national multicenter study. Due to the lack of a large population study in the Asian countries including Japan, pretest probability of CAD was difficult to estimate in the patient group that we studied. In addition, the BMI of the patient population (average BMI = 24 ± 4 kg/m²) was relatively low for patients with CAD in a Western population. When we analyzed the impact of BMI on diagnostic performance of whole-heart coronary MRA, the AUC of 1.5-T whole-heart coronary MRA for detecting significant CAD was similar between the 2 groups (BMI <25 and ≥25 kg/m²) at any level of analysis (patient, vessel, and segment). However, it should be noted that the PPV in a segment-based analysis was significantly lower in patients with a BMI ≥25 kg/m² than in those with a BMI <25 kg/m², indicating that the diagnostic performance of coronary MRA is significantly influenced by BMI. For ruling out significant CAD, the NPV in a patient-based analysis was 89% in patients with a BMI <25 kg/m² and 87% in patients with a BMI ≥25 kg/m². For the prediction of LM stenosis or 3VD, the NPV was 99% in patients with a BMI <25 kg/m² and 100% in patients with a BMI ≥25 kg/m² in this study population. These results suggest that whole-heart coronary MRA is of value for noninvasive exclusion of significant CAD regardless of BMI. We used SENSE factor of 3 in the anteroposterior direction in all patients. In patients with higher BMIs, the imaging time of cine MRI to determine the rest period of the RCA may be increased from 3 s to 5 s using a reduced SENSE factor of 2. However, a slightly increased imaging time does not seem to become a major limitation in assessing the rest period of the RCA. A previous study by Jahnke et al. (21) demonstrated that radial k-space sampling leads to small vessel diameters in the images compared with Cartesian sampling. We did not compare vessel diameter between whole-heart coronary MRA and X-ray CAG in this study. Further study is required to determine the accuracy of MRA with radial k-space sampling for the measurement of vessel diameter. The current whole-heart coronary MRA approach is optimized for assessing luminal stenoses in the

coronary arteries and does not provide sufficient information regarding the presence and characteristics of atherosclerotic plaque in the coronary arterial wall.

Conclusions

Whole-heart coronary MRA noninvasively detected significant coronary artery stenosis with sensitivity of 88% and specificity of 72% in this multicenter trial. An NPV of 88% in a patient-based analysis indicates the potential role of whole-heart coronary MRA to rule out CAD in patients with chest pain. In addition, 1.5-T whole-heart coronary MRA reliably rules out LM stenosis or 3VD with a high NPV of 99%.

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Assessment of Coronary Artery Disease Using Magnetic Resonance Coronary Angiography: A National Multicenter Trial

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