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Diagnostic Performance of Stress Cardiac Magnetic Resonance Imaging in the Detection of Coronary Artery Disease

A Meta-Analysis

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Objectives The purpose of our study was to conduct an evidence-based evaluation of stress cardiac magnetic resonance imaging (MRI) in the diagnosis of coronary artery disease (CAD).

Background Stress cardiac MRI has recently emerged as a noninvasive method in the detection of CAD, with 2 main techniques in use: 1) perfusion imaging; and 2) stress-induced wall motion abnormalities imaging.

Methods We examined studies from January 1990 to January 2007 using MEDLINE and EMBASE. A study was included if it: 1) used stress MRI as a diagnostic test for CAD (≥50% diameter stenosis); and 2) used catheter X-ray angiography as the reference standard.

Results Thirty-seven studies (2,191 patients) met the inclusion criteria, with 14 datasets (754 patients) using stress-induced wall motion abnormalities imaging and 24 datasets (1,516 patients) using perfusion imaging. Stress-induced wall motion abnormalities imaging demonstrated a sensitivity of 0.83 (95% confidence interval [CI] 0.79 to 0.88) and specificity of 0.86 (95% CI 0.81 to 0.91) on a patient level (disease prevalence = 70.5%). Perfusion imaging demonstrated a sensitivity of 0.91 (95% CI 0.88 to 0.94) and specificity of 0.81 (95% CI 0.77 to 0.85) on a patient level (disease prevalence = 57.4%).

Conclusions In studies with high disease prevalence, stress cardiac MRI, using either technique, demonstrates overall good sensitivity and specificity for the diagnosis of CAD. However, limited data are available regarding use of either technique in populations with low disease prevalence. (J Am Coll Cardiol 2007;50:1343–53) © 2007 by the American College of Cardiology Foundation

Noninvasive imaging for the evaluation of coronary artery disease (CAD) is currently largely performed by: 1) anatomical imaging, such as coronary multidetector computed tomography or coronary magnetic resonance angiography, which directly visualize the arteries; or 2) functional imaging, such as single-photon emission tomography (SPECT) or echocardiography, which evaluate the hemodynamic sequelae of coronary obstructive disease.

While the accuracy of these respective modalities has been assessed extensively, the diagnostic capabilities of stress cardiac magnetic resonance imaging (MRI), which appears promising given its excellent depiction of wall motion, high contrast, spatial resolution, and lack of ionizing radiation, has only been examined by studies of limited sample size. This has led to studies with wide confidence intervals (CIs) for sensitivity and specificity and potentially unreliable estimates of performance. Moreover, stress cardiac MRI is performed with 2 very different techniques: 1) dynamic first-pass perfusion imaging, which assesses for inducible perfusion defects, indicating impaired perfusion reserve; and 2) stress-induced wall motion abnormalities imaging, which evaluates for impairment of regional endocardial excursion and myocardial thickening, also indicating underlying ischemia. To overcome these issues and to provide an evidence-based evaluation of the clinical utility of stress MRI, we performed a comprehensive meta-analysis of all currently published studies comparing stress MRI with catheter-based X-ray angiography in the diagnosis of CAD.

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Abbreviations and Acronyms

CAD = coronary artery disease

LR = likelihood ratio

MRI = magnetic resonance imaging

SPECT = single-photon emission tomography

Methods

Data sources and searches. We searched MEDLINE and EMBASE for English and non-English literature published from January 1990 to January 2007 evaluating for the presence of CAD in native or non-native coronary arteries by stress MRI and catheter-based X-ray angiography in the same patients. The search included medical subject headings for magnetic resonance, perfusion, wall motion, and coronary angiography with the exploded term "coronary artery disease." Moreover, we evaluated bibliographies of retrieved articles, review articles, and textbooks. The retrieved studies were examined for potentially duplicate or overlapping data. Corresponding investigators were contacted for clarification when data were unclear or inadequate. Meeting abstracts provide insufficient information regarding their data, lack finality regarding the results, and were excluded.

Study selection. We included a study if: 1) it used stress MRI as a diagnostic test for obstructive CAD, with ≥50% diameter stenosis selected as the threshold for significant CAD, using catheter-based X-ray angiography as the reference standard; and 2) reported cases in absolute numbers of true positive, false positive, true negative, and false negative results or stated data adequate to derive this information. Studies were eligible regardless of whether they were referred for suspected or known CAD and regardless of technique used for stress MRI. Studies were excluded if: 1) performed in phantom-only models; 2) animals; 3) normal healthy volunteers without catheter-based X-ray angiography correlation; or 4) included <10 patients.

Data extraction and quality assessment. Two independent investigators performed data extraction. Inconsistencies were resolved by discussion and consensus. Data were recorded, as available, at the coronary territory level (left anterior descending, left circumflex, and right coronary arteries) and patient level. Study quality and applicability were assessed by a modified checklist based on the Quality Assessment Tool for Diagnostic Accuracy guidelines by 2 independent investigators, with discrepancies solved by consensus (1).

Data synthesis and statistical analysis. Categorical variables from studies are presented as percentages and continuous variables as mean values. The main analysis was performed at the patient level, as most studies provided this level of information. Secondary analyses were performed at the coronary territory level. We applied the bivariate mixed-effects regression model for treatment trial meta-analysis and modified for synthesis of diagnostic test data assuming binomial errors distribution for sensitivity and specificity (2,3). Between-study variability was assessed assuming correlated normally distributed random effects for logit (sensitivity) and logit (specificity) with the degree of correlation between studies predictive of an implicit threshold effect. We derived summary sensitivity and specificity as functions of the estimated model parameters with associated 95% CIs.

Estimate of clinical utility. The positive likelihood ratio (LR+) measures the likelihood that a positive (abnormal) stress MRI would be expected in a patient with CAD, whereas the negative LR (LR−) measures the likelihood that a negative (normal) stress MRI would be expected in a patient without CAD. As a measure of test performance, the LR has advantages over sensitivity and specificity as it changes with disease prevalence and can be used to calculate post-test probability. Positive likelihood ratio and LR− are defined with the following formulas: LR+ = sensitivity/(1 − specificity) and LR− = (1 − sensitivity)/specificity.

We examined clinical utility of each method by means of Bayes' theorem, where pretest probability = prevalence of disease and post-test probability = LR × pretest probability/[(1 − pretest probability) × (1 − LR)]. Assuming that the study samples are representative of the entire population, an estimate of the pretest probability of CAD can be calculated from the global or subgroup-specific prevalence of this disorder across the studies. The weighted mean percentage of CAD of the prevalence of CAD in patients who underwent stress MRI was used as the pretest probability. The post-test probability was evaluated by changing the pretest probability into pretest odds with the following equation: odds = probability/(1 − probability). The post-test odds were then derived by multiplying together the pretest odds and the LR. Finally, the post-test odds were converted to probabilities by utilizing the following equation: probability = odds/(odds + 1). These

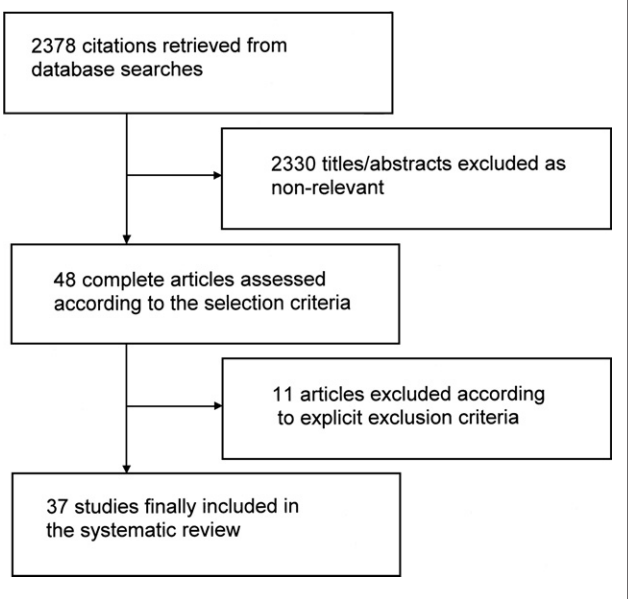

Figure 1 Flow Diagram of Review Process

Process of identification and selection of studies for inclusion in meta-analysis.

Table 1 Characteristics of Included Studies

Author (Ref. #)	Year	Journal	Patients (n)	Excluded	Men (%)	Mean Age, yrs (SD)	MRI (Brand) and Tesla	MRI Technique	MRI Sequence	Data Assessment	Stressor	Selection	Stenosis Definition (%)
al-Saadi et al. (4)	2000	*Circulation*	40	6	80	59 (11)	Philips 1.5-T	Perfusion	Inversion recovery single-shot turbo gradient-echo	Semiquantitative	Dipyridamole	Suspected CAD	≥75
al-Saadi et al. (5)	2002	*Journal of Cardiovascular Magnetic Resonance*	23	0	70	59 (8)	Philips 1.5-T	Perfusion	Inversion recovery single-shot turbo gradient-echo	Semiquantitative	Dobutamine	23 patients with CAD and 4 without CAD	≥75
Bunce et al. (6)	2004	*Journal of Cardiovascular Magnetic Resonance*	35	0	77	56 (NS)	Picker 1.5-T	Perfusion	Ultrafast gradient-echo	Semiquantitative	Adenosine	Suspected CAD	>50
Chiu et al. (7)	2003	*Radiology*	13	0	54	68 (NS)	Siemens 1.5-T	Perfusion	T1-weighted inversion-recovery true-FISP	Qualitative	Adenosine	Suspected CAD	>50
Cury et al. (8)	2006	*Radiology*	47	1	81	63 (5)	GE 1.5-T	Perfusion	Hybrid gradient-echo-planar	Qualitative	Dipyridamole	Suspected of having or known to have CAD	≥70
Doyle et al. (9)	2003	*Journal of Cardiovascular Magnetic Resonance*	199	15	0	59 (11)	Philips 1.5-T	Perfusion	Gradient-echo	Semiquantitative	Dipyridamole	Suspected CAD	≥70
Giang et al. (10)	2004	*European Heart Journal*	44	0	81	58 (NS)	GE 1.5-T	Perfusion	Hybrid echo-planar	Semiquantitative	Adenosine	Suspected CAD	≥50
Ibrahim et al. (11)	2002	*Journal of the American College of Cardiology*	25	NS	76	63 (13)	Philips 1.5-T	Perfusion	Ultra-fast hybrid	Semiquantitative	Adenosine	25 with documented CAD	>75
Ishida et al. (12)	2003	*Radiology*	104	0	78	66 (12)	GE 1.5-T	Perfusion	Gradient-echo sequence by using fast echo-planar readouts and interleaved notched saturation	Qualitative	Dipyridamole/ isometric handgrip exercise	Suspected CAD	≥70
Kawase et al. (13)	2004	*Osaka City Medical Journal*	50	0	58	67 (12)	Philips 1.5-T	Perfusion	Multislice turbo field echo with multishot echo-planar imaging	Qualitative	Nicorandil	Suspected CAD	>70
Klem et al. (14)	2006	*Journal of the American College of Cardiology*	95	3	49	58 (12)	Siemens 1.5-T	Perfusion	Hybrid of fast gradient-echo and echo-planar	Qualitative	Adenosine	Suspected CAD	≥70

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Table 1 Continued

Author (Ref. #)	Year	Journal	Patients (n)	Excluded	Men (%)	Mean Age, yrs (SD)	MRI (Brand) and Tesla	MRI Technique	MRI Sequence	Data Assessment	Stressor	Selection	Stenosis Definition (%)
Nagel et al. (15)	2003	*Circulation*	90	6	81	63 (8)	Philips 1.5-T	Perfusion	Turbo-gradient-echo/echo-planar imaging-hybrid	Semiquantitative	Adenosine	Suspected CAD	≥75
Okuda et al. (16)	2005	*Radiation Medicine*	33	0	88	60 (NS)	GE 1.5-T	Perfusion	Gradient-echo with echo-planar	Qualitative	Dipyridamole	Suspected CAD	≥75
Panting et al. (17)	2001	*Journal of Magnetic Resonance Imaging*	17	0	81	63 (9)	Surrey 0.5-T	Perfusion	Spin echo/echo-planar	Semiquantitative/ qualitative	Adenosine	Abnormal thallium SPECT scans	>50
Pilz et al. (18)	2006	*Clinical Research in Cardiology*	176	5	64	62 (12)	GE 1.5-T	Perfusion	Hybrid of fast gradient-echo and echo-planar acquisition imaging	Qualitative	Adenosine	Suspected CAD	>70
Plein et al. (19)	2004	*Journal of the American College of Cardiology*	71	3	79	57 (11)	Philips 1.5-T	Perfusion	T1-weighted saturation recovery segmented k-space gradient-echo pulse sequence combined with sensitivity encoding	Qualitative	Adenosine	Suspected CAD	≥70
Plein et al. (20)	2005	*Radiology*	92	10	74	58 (NS)	Philips 1.5-T	Perfusion	Saturation-recovery segmented k-space gradient-echo	Semiquantitative	Adenosine	Suspected CAD	>70
Rieber et al. (21)	2006	*European Heart Journal*	43	0	88	65 (8)	Siemens 1.5-T	Perfusion	T1-weighted saturation recovery turbo flash	Semiquantitative	Adenosine	Suspected CAD	>50/FFR
Sakuma et al. (22)	2005	*American Journal of Roentgenology*	40	0	70	65 (9)	Siemens 1.5-T	Perfusion	Saturation-recovery turbo fast low-angle shot	Qualitative	Dipyridamole	Suspected CAD	>70
Schwitter et al. (23)	2001	*Circulation*	48	1	85	58 (NS)	GE 1.5-T	Perfusion	Hybrid echo-planar	Semiquantitative	Dipyridamole	Suspected CAD	≥50
Sensky et al. (24)	2002	*International Journal of Cardiovascular Imaging*	30	0	90	62 (NS)	Siemens 1.5-T	Perfusion	Dynamic inversion recovery snapshot	Qualitative	Adenosine	Known CAD	>50
Takase et al. (25)	2004	*Japan Heart Journal*	102	0	83	66 (9)	GE 1.5-T	Perfusion	Hybrid of fast gradient-echo and echo-planar	Qualitative	Dipyridamole	Suspected CAD	>50

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Table 1 Continued

Author (Ref. #)	Year	Journal	Patients (n)	Excluded	Men (%)	Mean Age, yrs (SD)	MRI (Brand) and Tesla	MRI Technique	MRI Sequence	Data Assessment	Stressor	Selection	Stenosis Definition (%)
Thiele et al. (26)	2004	*International Journal of Cardiovascular Imaging*	20	0	65	64 (8)	Philips 1.5-T	Perfusion	Turbo gradient-echo with sensitivity encoding	Semiquantitative	Adenosine	Suspected CAD	≥70
Baer et al. (27)	1992	*American Journal of Cardiology*	23	0	96	60 (8)	Philips 1.5-T	Wall motion	Gradient-echo	Qualitative	Dipyridamole	Known CAD	>70
Baer et al. (28)	1994	*Radiology*	35	3	80	58 (10)	Philips 1.5-T	Wall motion	Gradient-echo	Qualitative	Dobutamine	35 patients with CAD	≥50
Hundley et al. (29)	1999	*Circulation*	41	NS	56	NS	GE 1.5-T	Wall motion	Gradient-echo sequence with k-space segmentation	Semiquantitative	Dobutamine and atropine	Poor acoustic windows on TTE	>50
Jahnke et al. (30)	2006	*Radiology*	40	0	75	63 (9)	Philips 1.5-T	Wall motion	4-dimensional k-t BLAST	Qualitative	Dobutamine	Suspected or known CAD	≥50
Nagel et al. (31)	1999	*Circulation*	172	NS	71	60 (9)	Philips 1.5-T	Wall motion	Gradient-echo	Qualitative	Dobutamine	Suspected CAD	≥50
Paetsch et al. (32)	2004	*Circulation*	79	0	66	61 (9)	Philips 1.5-T	Wall motion	Steady-state free precession	Qualitative	Dobutamine and atropine	Suspected or known CAD	>50
Paetsch et al. (32)	2004	*Circulation*	79	0	66	61 (9)	Philips 1.5-T	Perfusion	Turbo field echo	Qualitative	Adenosine	Suspected or known CAD	
Paetsch et al. (33)	2006	*European Heart Journal*	150	0	83	61 (10)	Philips 1.5-T	Wall motion	Steady-state free precession	Qualitative	Dobutamine	Suspected CAD	≥50
Pennell et al. (34)	1990	*British Heart Journal*	40	0	88	54 (NS)	Picker 0.5-T	Wall motion	Field echo even rephasing	Qualitative	Dipyridamole	Suspected CAD	NS
Pennell et al. (35)	1992	*American Journal of Cardiology*	25	0	74	52 (NS)	Picker 0.5-T	Wall motion	Gradient-refocused, velocity-compensated echo	Qualitative	Dobutamine	Suspected CAD	≥50
Rerkpattanapipat et al. (36)	2003	*American Journal of Cardiology*	27	0	86	62 (11)	GE 1.5-T	Wall motion	Gradient- echo	Qualitative	Exercise	Suspected CAD	>70
Schalla et al. (37)	2002	*Radiology*	22	0	80	60 (5)	Philips 1.5-T	Wall motion	Segmented k-space turbo gradient-echo echo-planar	Qualitative	Dobutamine	Suspected CAD	>75
van Rugge et al. (38)	1993	*Journal of the American College of Cardiology*	45	0	82	61 (9)	Philips 1.5-T	Wall motion	Gradient-echo	Qualitative	Dobutamine	Suspected CAD	>50
van Rugge et al. (39)	1994	*Circulation*	39	0	86	60 (NS)	Philips 1.5-T	Wall motion	Gradient-echo	Quantitative	Dobutamine	Suspected CAD	≥50
Zhao et al. (40)	1997	*Magnetic Resonance Imaging*	16	2	72	60 (7)	Siemens 1.5-T	Wall motion	Gradient-echo-segmented k-space	Qualitative and quantitative	Dipyridamole	Known CAD	≥70

CAD = coronary artery disease; echo = echocardiography; FFR = fractional flow reserve; FISP = fast imaging with steady-stage precession; MRI = magnetic resonance imaging; NS = not specified; SPECT = single-photon emission computed tomography; TTE = transthoracic echocardiography.

Table 2 Per Patient, Per Coronary Territory Analysis

	Analysis by Patient							Analysis by Coronary Territory						
Author (Ref. #)	n	TP (n)	FN (n)	FP (n)	TN (n)	Sensitivity	Specificity	n	TP (n)	FN (n)	FP (n)	TN (n)	Sensitivity	Specificity
MRI perfusion														
al-Saadi et al. (4)								102	54	6	7	35	0.90	0.83
al-Saadi et al. (5)								69	26	6	10	27	0.81	0.73
Bunce et al. (6)								105	26	9	20	50	0.74	0.71
Chiu et al. (7)								39	24	2	1	12	0.92	0.92
Cury et al. (8)	46	29	1	4	12	0.97	0.75	138	47	7	9	75	0.87	0.89
Doyle et al. (9)	184	15	11	35	123	0.57	0.78							
Giang et al. (10)	44	26	2	4	12	0.93	0.75							
Ibrahim et al. (11)								75	10	4	7	54	0.71	0.89
Ishida et al. (12)	104	69	8	4	23	0.90	0.85	312	109	21	32	150	0.84	0.82
Kawase et al. (13)	50	31	2	1	16	0.94	0.94	150	34	5	14	97	0.87	0.87
Klem et al. (14)	92	33	4	7	48	0.89	0.87	264	45	11	22	186	0.80	0.89
Nagel et al. (15)	84	38	5	4	37	0.88	0.90							
Okuda et al. (16)								94	42	7	5	40	0.89	0.85
Panting et al. (17)								51	27	8	3	13	0.77	0.81
Pilz et al. (18)	171	109	4	10	48	0.96	0.83							
Plein et al. (19)	68	54	2	2	10	0.96	0.83	204	72	17	27	88	0.81	0.77
Plein et al. (20)	82	52	7	6	17	0.88	0.74							
Rieber et al. (21)								42	11	2	3	26	0.85	0.90
Sakuma et al. (22)	40	17	4	6	13	0.81	0.68	120	23	10	11	76	0.70	0.87
Schwitter et al. (23)	47	32	5	3	7	0.86	0.70							
Sensky et al. (24)								86	66	5	6	9	0.93	0.60
Takase et al. (25)	102	71	5	4	22	0.93	0.85							
Thiele et al. (26)								60	21	7	1	31	0.75	0.97
MRI wall motion														
Baer et al. (27)	23	18	5	0	0	0.78		69	26	7	3	33	0.79	0.92
Baer et al. (28)*	32	27	5	0	0	0.84		64	36	11	0	17	0.77	1.00
Hundley et al. (29)	41	29	6	1	5	0.83	0.83							
Jahnke et al. (30)	40	25	3	3	9	0.89	0.75	120	23	5	13	79	0.82	0.86
Nagel et al. (31)	172	94	15	9	54	0.86	0.86							
Paetsch et al. (PI) (32)	79	48	5	10	16	0.91	0.62							
Paetsch et al. (WMA) (32)	79	47	6	5	21	0.89	0.81							
Paetsch et al. (33)	150	60	17	9	64	0.78	0.88							
Pennell et al. (34)	40	24	15	0	1	0.62	1.00							
Pennell et al. (35)	25	20	2	0	3	0.91	1.00							
Rerkpattanapipat et al. (36)	27	11	3	2	11	0.79	0.85							
Schalla et al. (37)	22	13	3	1	5	0.81	0.83							
van Rugge et al. (38)	45	30	7	0	8	0.81	1.00							
van Rugge et al. (39)	39	30	3	1	5	0.91	0.83							
Zhao et al. (40)								36	16	4	4	12	0.80	0.75

*Utilized 2 perfusion territories (left anterior descending coronary artery and combined left circumflex artery/right coronary artery).

FN = false negative; FP = false positive; MRI = magnetic resonance imaging; PI = perfusion imaging; TN = true negative; TP = true positive; WMA = wall motion abnormalities.

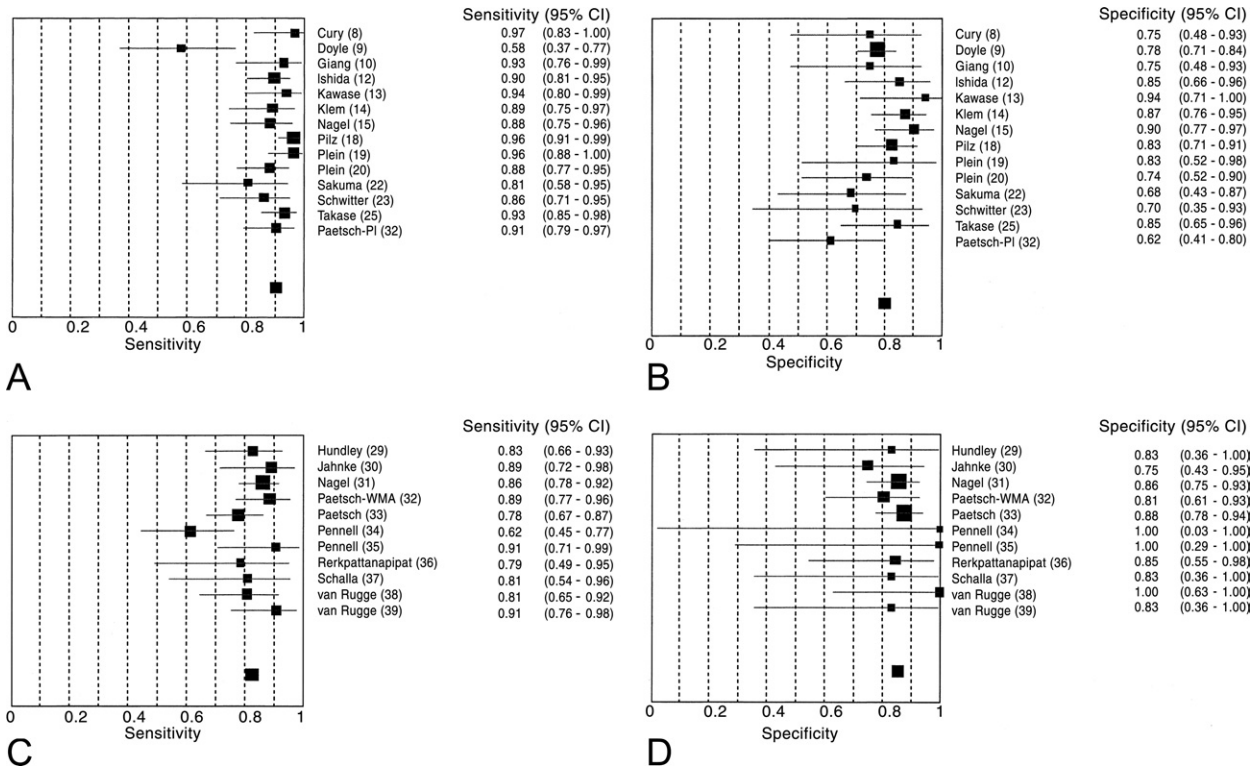

Figure 2 **Forest Plot of Sensitivity and Specificity**

(A, B) Forest plot of patient-level sensitivity and specificity of stress perfusion imaging compared with coronary angiography. **(C, D)** Forest plot of patient level sensitivity and specificity of stress-induced wall motion abnormalities imaging compared with coronary angiography. **Solid squares** = point estimate of each study (area indicates relative contribution of the study to meta-analysis); **horizontal lines** = 95% confidence interval (CI).

results are represented in a graph of conditional probabilities displaying the post-test probability of CAD, if the test was negative or positive, for a given pretest probability.

Assessment of heterogeneity. Heterogeneity of the results between the studies was assessed graphically by forest plots and statistically using the quantity I^2 that describes the percentage of total variation across studies attributable to heterogeneity rather than chance.

Statistical analyses were performed with Stata 9.0 (Stata Corp., Chicago, Illinois).

Results

The literature process is summarized in Figure 1. Database searches identified 48 potentially relevant citations. Thirty-seven studies were included, with 11 being excluded because: 1) they had overlapping data; or 2) it was not possible to calculate absolute figures from the presented data. Study and population characteristics of the included studies are summarized in Table 1 (4–40).

Data on diagnostic accuracy were available for the 37 studies with a total of 2,191 patients, with 14 comparisons (754 patients) using stress-induced wall motion abnormalities imaging and 24 comparisons (1,516 patients) using perfusion imaging. One study directly compared stress-induced wall motion abnormalities imaging and perfusion imaging in the same patients (79 patients) (32). Results of the individual studies on a per-patient and per-coronary territory level are summarized in Table 2.

Patient-level summary performance estimates. After pooling 14 datasets (1,183 patients after exclusion of 50 patients secondary to unsuccessful MRI), perfusion imaging demonstrated a sensitivity of 0.91 (95% CI 0.88 to 0.94) and specificity of 0.81 (95% CI 0.77 to 0.85), compared with catheter-based X-ray angiography (Fig. 2A). The prevalence of CAD in this group was 57.4% (679 of 1,183). After pooling 13 datasets (735 patients after exclusion of 5 patients secondary to unsuccessful MRI), stress-induced wall motion abnormalities imaging demonstrated a sensitivity of 0.83 (95% CI 0.79 to 0.88) and specificity of 0.86 (95% CI 0.81 to 0.91) for CAD at the subject level (Fig. 2B). The prevalence of CAD in this group was 70.5% (518 of 735). Overall, these summary estimates show good sensitivity and specificity for CAD at the patient level. Analysis of stress-induced wall motion abnormalities imaging with dobutamine or exercise as the stressor (excluding studies utilizing dipyridamole) demonstrates an improved sensitivity of 0.85 (95% CI 0.82 to 0.90) with a comparable specificity of 0.86 (95% CI 0.81 to 0.91).

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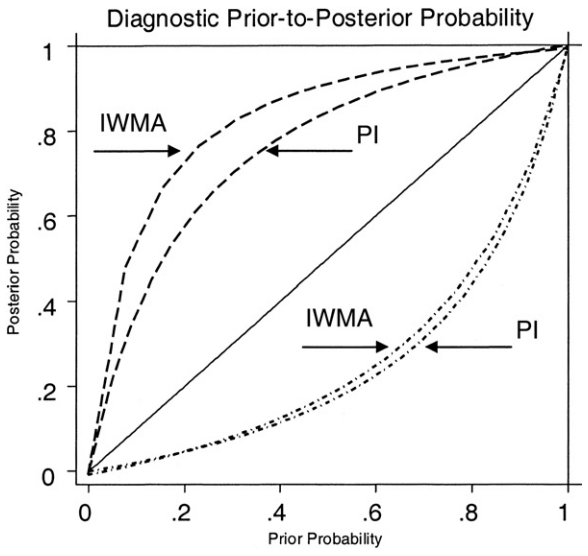

Figure 3 Plot of Conditional Probabilities for PI and IWMA

Post-test probabilities are shown as a function of pretest probability for patients with positive results on perfusion imaging (PI), positive results on wall motion abnormalities imaging (IWMA), negative results on PI, and negative results on IWMA.

Evaluating clinical utility, the positive LR for perfusion MRI is 5.10 (95% CI 3.92 to 6.28); the negative LR, 0.11 (95% CI 0.07 to 0.15). For stress-induced wall motion abnormalities imaging, the positive LR is 5.24 (95% CI 3.28 to 7.21); the negative LR, 0.19 (95% CI 0.15 to 0.24). Using the rule of thumb that for a diagnostic test to be useful it should have a high positive LR (>5) (i.e., good at ruling in a disease) and a low negative LR (<0.2) (i.e., good at ruling out disease), both methods are good at confirming and excluding CAD. For each test, Figure 3 shows the effect of a positive or negative result on pretest probabilities.

Coronary territory-level summary performance estimates. Per-coronary territory meta-analysis of perfusion imaging pooled 16 datasets with 1,911 coronary territories and demonstrated a sensitivity of 0.84 (95% CI 0.80 to 0.87) and specificity of 0.85 (95% CI 0.81 to 0.88). Per-coronary territory meta-analysis of stress-induced wall motion abnormalities imaging pooled 4 datasets with 289 coronary territories and demonstrated a sensitivity of 0.79 (95% CI 0.71 to 0.86) and specificity of 0.93 (95% CI 0.81 to 1.0), although notably limited by a small study size.

Assessment of heterogeneity. Analysis at the patient level demonstrated moderate heterogeneity in sensitivities between perfusion imaging studies ($I^2 = 0.44$, $p = 0.04$) and specificities between stress-induced wall motion abnormality studies ($I^2 = 0.73$, $p < 0.001$). At the coronary territory level, heterogeneity was present for between-study specificities for both perfusion ($I^2 = 0.62$, $p < 0.001$) and stress-induced wall motion abnormality studies ($I^2 = 0.85$, $p < 0.001$).

Quality grading by study is shown in Table 3.

Discussion

Stress MRI has recently emerged as a promising alternative to nuclear SPECT and stress echocardiography in the noninvasive functional evaluation of CAD. Our study examined the diagnostic performance data of stress MRI from multiple centers throughout the world describing populations with a relatively high prevalence of disease, 57% in the perfusion imaging group and 71% in the stress-induced wall motion abnormalities imaging group. At the patient level, we found that the 2 main techniques, perfusion imaging and stress-induced wall motion abnormalities imaging, used in stress MRI demonstrated similar good specificities (perfusion imaging: 81%, stress-induced wall motion abnormalities imaging: 86%) and sensitivities (perfusion imaging: 91%, stress-induced wall motion abnormalities imaging: 83%). With the exclusion of stress-induced wall motion abnormalities studies utilizing dipyridamole, which may be a less effective stressor for this technique, and inclusion of those with dobutamine or exercise, the sensitivity of wall motion imaging was improved (85%) without a notable change in the specificity (40). At the coronary territory level, perfusion imaging and stress-induced wall motion abnormalities imaging showed overlapping sensitivities and specificities that were good overall.

The wide range of prevalence of CAD in the examined studies likely reflects institutional referral patterns and clinical thresholds for imaging patients. As post-test probability depends on disease prevalence, practical use of the results relies on cognizance of CAD prevalence at any individual medical center. In our study, the summary sensitivities and specificities for perfusion imaging and stress-induced wall motion abnormalities imaging were attained in patients selected to undergo an invasive examination, catheter-based X-ray angiography, and thus had relatively high probability of CAD. This selection bias is illustrated by the high prevalence of disease in both technique populations. Limited empiric data are available in low disease prevalence populations, except in a few studies (9,14). Moreover, similar studies in a low-risk population would be difficult to conduct given the strong prognostic value of a negative stress MRI (41).

The diagnostic capabilities of stress MRI, especially with perfusion imaging, appear comparable if not superior to SPECT and stress echocardiography. Underwood et al. (42) examined 79 studies with 8,964 patients using SPECT in the diagnosis of CAD and found a sensitivity of 86% and specificity of 74%, with the caveat that the low specificity may be partially due to referral bias. Ishida et al. (12) directly compared perfusion imaging and SPECT in 69 patients who also underwent catheter-based X-ray angiography and found a significantly greater area under the receiver-operating characteristic curve for perfusion imaging compared with that in SPECT, and Sakuma et al. (22) found superior but not statistically significant diagnostic accuracy for perfusion imaging compared with that in SPECT in 40

Table 3 Quality Assessment

Author (Ref. #)	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Score
al-Saadi et al. (4)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
al-Saadi et al. (5)	Yes	No	Yes	NS	Yes	Yes	Yes	Yes	No	No	6
Bunce et al. (6)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Chiu et al. (7)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	6
Cury et al. (8)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Doyle et al. (9)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	8
Giang et al. (10)	Yes	Yes	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	9
Ibrahim et al. (11)	Yes	No	No	No	Yes	Yes	Yes	Yes	No	No	5
Ishida et al. (12)	Yes	Yes	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	9
Kawase et al. (13)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	8
Klem et al. (14)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
Nagel et al. (15)	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	No	7
Okuda et al. (16)	Yes	Yes	Yes	NS	Yes	Yes	Yes	No	No	No	6
Panting et al. (17)	Yes	No	No	No	NS	Yes	Yes	No	No	No	3
Pilz et al. (18)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
Plein et al. (19)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Plein et al. (20)	Yes	No	Yes	NS	Yes	Yes	Yes	Yes	Yes	No	7
Rieber et al. (21)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Sakuma et al. (22)	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	No	6
Schwitter et al. (23)	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Sensky et al. (24)	Yes	No	Yes	NS	NS	Yes	Yes	No	No	Yes	5
Takase et al. (25)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
Thiele et al. (26)	Yes	Yes	No	NS	Yes	Yes	Yes	Yes	No	Yes	7
Baer et al. (27)	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	7
Baer et al. (28)	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	8
Hundley et al. (29)	Yes	Yes	Yes	NS	Yes	Yes	Yes	Yes	Yes	No	8
Jahnke et al. (30)	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Nagel et al. (31)	Yes	Yes	Yes	NS	Yes	Yes	Yes	No	Yes	No	7
Paetsch et al. (32)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Paetsch et al. (33)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Pennell et al. (34)	Yes	Yes	Yes	NS	Yes	Yes	Yes	No	Yes	No	7
Pennell et al. (35)	Yes	Yes	Yes	NS	Yes	Yes	Yes	No	No	No	6
Rerkpattanapipat et al. (36)	Yes	Yes	Yes	NS	Yes	Yes	Yes	Yes	No	No	7
Schalla et al. (37)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8
van Rugge et al. (38)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
van Rugge et al. (39)	Yes	Yes	No	NS	Yes	Yes	Yes	No	Yes	Yes	7
Zhao et al. (40)	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	7

Item 1: Was the population clinically relevant, defined as a group of patients covering the spectrum of disease that is likely to be encountered in the current or future use of the test? Item 2: Was there complete verification by the reference standard? Item 3: Was there blinded interpretation of the test results? Item 4: Was there consecutive patient selection? Item 5: Was there prospective enrollment of patients? Item 6: Was there adequate description and quality of the imaging procedure? Item 7: Was the quality of the reference test technically adequate? Item 8: Was there adequate clinical description of the patient population? Item 9: Was the sample size ≥35 patients? Item 10: Was there adequate reporting of results, including summary and subgroup indexes of accuracy?
NS = not specified.

patients. The favorable capabilities of stress MRI, specifically perfusion imaging, are likely due to superior spatial resolution compared with that in SPECT allowing for the distinction between subendocardial and transmural defects, which is important because subendocardial perfusion defects can indicate ischemia at an early stage. Single-photon emission computed tomography also has the disadvantages of radiation exposure and attenuation artifacts. Although, notably, stress MRI, with perfusion imaging or stress-induced wall motion abnormalities imaging, can be limited by availability, claustrophobia, obesity, poor gating, and motion artifact, along with the use of pharmacologic stressors, and attaining the appropriate heart rate (for stress-induced wall motion abnormalities imaging). With regard to stress exercise echocardiography, Schuijf et al. (43) pooled 15 studies with 1,849 patients and found a weighted mean sensitivity and specificity of 84% and 82% for the detection of CAD, and a weighted mean sensitivity and specificity of 80% and 84% in 28 studies with 2,246 patients using dobutamine echocardiography. Nagel el al. (31) found stress-induced wall motion abnormalities imaging to have significantly higher sensitivity and specificity than dobutamine stress echocardiography in a study with over 170 patients.

The American College of Cardiology recently reported that stress cardiac MRI, with either technique, is indicated for detection of CAD in symptomatic patients with intermediate pretest probability, who have uninterpretable elec-

trocardiograms or are unable to exercise (44). They also stated that stress cardiac MRI is of uncertain usefulness in symptomatic patients with a high pretest probability of CAD. From our analysis, the clinical utility of stress cardiac imaging, using either technique, is most evident when the test is negative, decreasing the probability of CAD to at or below 20% in patients with low-to-intermediate pretest probability of CAD (<60%). A positive test appears more useful with intermediate-to-high pretest probabilities (>40%), where the post-test probability of disease would exceed approximately 80%. Consequently, our analysis supports the use of stress cardiac MRI in patients with intermediate pretest probability disease, as both a positive and negative test confer a relatively acceptable post-test probability of disease, while its role in high pretest probability of disease needs to be further evaluated, given the utility of a positive test but questionable usefulness if negative.

Our study contains several limitations. Significant heterogeneity was identified in multiple performance characteristics; thus the results and potential clinical application should be interpreted with caution. Not all of the included studies provided comprehensive data on the patient and coronary territory level, although numerous investigators were contacted to provide additional data. Moreover, limited or ambiguous information was provided by many studies regarding the number of examinations that were not interpretable, which can lead to false estimates of sensitivity and specificity. Future studies should be promoted to have more rigorous reporting of results. Publication bias, favoring studies with positive results, also confounds comprehensive evaluation. Quality assessment and data abstraction were performed by independent reviewers, with disagreement settled by consensus. Consequently, quantitative agreement between the reviewers could not be examined. An anatomy-based gold standard, catheter-based angiography was utilized, which is imperfect, particularly with regard to physiological information. Stress MRI technology has been evolving since the earliest studies and newer additional techniques, such as the addition of coronary magnetic resonance angiography, double contrast bolus technique, and delayed enhancement infarction imaging, which were utilized in only a small number of studies in the current meta-analysis, may further improve the diagnostic properties of stress MRI.

Conclusions

Stress perfusion MRI, with either perfusion imaging or wall-motion imaging, has good sensitivity and specificity in the diagnosis of CAD, in patients with a high prevalence of disease. However, we recommend cautious clinical application of the results, given the limited data available for a low disease prevalence population.

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