Stress Cardiac MR Imaging Compared with Stress Echocardiography in the Early Evaluation of Patients Who Present to the Emergency Department with Intermediate-Risk Chest Pain¹

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Purpose:

To compare the utility and efficacy of stress cardiac magnetic resonance (MR) imaging and stress echocardiography in an emergency setting in patients with acute chest pain (CP) and intermediate risk of coronary artery disease (CAD).

Materials and Methods:

Written informed consent was obtained from all patients. This HIPAA-compliant study was approved by the institutional review board for research ethics. Sixty patients without history of CAD presented to the emergency department with intermediate-risk acute CP and were prospectively enrolled. Patients underwent both stress cardiac MR imaging and stress echocardiography in random order within 12 hours of presentation. Stress imaging results were interpreted clinically immediately (blinded interpretation was performed months later), and coronary angiography was performed if either result was abnormal. CAD was considered significant if it was identified at angiography (narrowing >50%) or if a cardiac event (death or myocardial infarction) occurred during follow-up (mean, 14 months $\pm$ 5 [standard deviation]). McNemar test was used to compare the diagnostic accuracy of techniques.

Results:

Stress cardiac MR imaging and stress echocardiography had similar specificity, accuracy, and positive and negative predictive values (92% vs 96%, 93% vs 88%, 67% vs 60%, and 100% vs 91%, respectively, for clinical interpretation; 90% vs 92%, 90% vs 88%, 58% vs 56%, and 98% vs 94%, respectively, for blinded interpretation). Stress cardiac MR imaging had higher sensitivity at clinical interpretation (100% vs 38%, $P = .025$), which did not reach significance at blinded interpretation (88% vs 63%, $P = .31$). However, multivariable logistic regression analysis showed stress cardiac MR imaging to be the strongest independent predictor of significant CAD ($P = .002$).

Conclusion:

In patients presenting to the emergency department with intermediate-risk CP, adenosine stress cardiac MR imaging performed within 12 hours of presentation is safe and potentially has improved performance characteristics compared with stress echocardiography.

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In the United States, the number of patients presenting to the emergency department (ED) with chest pain has increased in the past decade and has been estimated to exceed 8 million patients per year (1). The evaluation of these patients is challenging and is aimed at the identification of those at increased risk for future cardiac events because of underlying coronary artery disease (CAD). Electrocardiographic changes and the serial assessment of cardiac biomarkers are valuable in such patients; however, approximately 50% of patients with acute coronary syndromes will have nondiagnostic or normal electrocardiograms at initial imaging, and up to 3% of patients may experience adverse cardiac events within 30 days despite normal troponin levels (2–4). Studies have shown that approximately 3%–5% of patients with acute myocardial infarction (MI) or unstable angina are erroneously discharged from the ED, which results in increased mortality (5). Early stress testing in the ED may have an important role in the care of patients who present with chest pain, as it facilitates expedient diagnosis and risk stratification in patients suspected of having CAD (6,7).

Advances in Knowledge

- In patients with acute chest pain and intermediate risk of coronary artery disease (CAD), a comprehensive cardiac MR imaging protocol incorporating adenosine stress perfusion imaging is safe, quick, and accurate when performed within 12 hours after presentation.
- At multivariate logistic regression analysis, stress cardiac MR imaging was the strongest predictor of significant CAD and had independent value over traditional cardiac risk factors.
- At both clinical and blinded interpretation, specificity, accuracy, and positive and negative predictive values were similar between stress cardiac MR imaging and stress echocardiography.

Stress echocardiography is an established method used to detect CAD, with reported sensitivity of 75%–80% and specificity of 85%–90% (8–10). A negative stress echocardiogram has been shown to portend an excellent prognosis, with a chance of death lower than 1% per year (11). More recently, a multicomponent cardiac magnetic resonance (MR) examination that included adenosine stress perfusion imaging was shown to enable accurate diagnosis of CAD in various clinical settings (12–16). However, data concerning the value of stress cardiac MR imaging in patients seen in the ED is limited, particularly in comparison with other stress modalities and in the early hours after presentation. The aim of the current study was to compare the utility and efficacy of stress cardiac MR imaging with the utility and efficacy of stress echocardiography in an emergency setting in patients with acute chest pain (CP) and intermediate risk of CAD.

Materials and Methods

Population

We prospectively recruited patients who were seen in the ED between October 2002 and December 2003 and who presented with acute chest discomfort and were deemed to have intermediate risk of CAD. Intermediate risk was defined as (a) one or more CAD risk factors in a man older than 40 years or a woman older than 50 years or (b) two or more risk factors in a man older than 30 years or a woman older than 40 years (17). Risk factors

included hypertension, hyperlipidemia, diabetes mellitus, current smoker, and a family history of MI before age 55. Patients with only atypical chest pain were generally excluded from the study. Patients with intermediate risk were chosen to eliminate those with a very low probability of having CAD in whom stress testing would not be needed to discharge them directly from the ED and to increase the prevalence of CAD in the study population, as the prevalence in all patients presenting to the ED with chest pain has been reported to be as low as 5% (18). Patients at highest risk for CAD in whom stress testing would be inappropriate, such as those with elevated cardiac enzyme levels or with electrocardiographic ST-segment changes consistent with ongoing infarction or ischemia, were excluded. To reduce spectrum bias and to provide the best estimates of sensitivity and specificity, we also excluded patients with known CAD, including those with a prior MI and those who had undergone prior revascularization procedures. Other exclusion criteria were aortic stenosis with a mean gradient of 40 mmHg or more, second-degree or higher atrioventricular block, pregnancy, hemodynamic or clinical

Implications for Patient Care

- In patients with acute chest pain who present to the emergency department, adenosine stress perfusion cardiac MR imaging is safe, quick, and accurate.
- In this clinical setting, stress cardiac MR imaging had performance characteristics that were similar to, if not potentially better than, those of stress echocardiography.

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Abbreviations:

CAD = coronary artery disease
CP = chest pain
ED = emergency department
MI = myocardial infarction

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Conflicts of interest are listed at the end of this article.

instability, noncardiac medical problems that could lead to hospital admission, and standard contraindications to MR imaging.

Written informed consent was obtained from all patients. The study was compliant with the Health Insurance Portability and Accountability Act and was approved by the institutional review board for research ethics. Details regarding the study protocol, follow-up, and stress echocardiography are given in Appendix E1 (online). The truth standard for the presence of significant CAD was prespecified and was a composite endpoint based on invasive coronary angiography findings and cardiac events during follow-up (Appendix E1 [online]).

Stress Cardiac MR Imaging

Acquisition.—The stress cardiac MR imaging examination has been described previously (12,14). It consisted of four components that were performed in the following order: (a) cine imaging was performed with the patient at rest to assess LV function, (b) adenosine gadolinium first-pass imaging was performed to assess stress perfusion, (c) repeated first-pass imaging without adenosine was performed at least 15 minutes later to assess rest perfusion, and (d) delayed-enhancement (or late-gadolinium-enhanced) imaging was performed to assess MI.

Cardiac MR imaging was performed with a 1.5-T imager (Avanto; Siemens, Malvern, Pa) and phased-array receiver coils. Details of the individual components are as follows: Cine images were acquired in multiple short-axis (every 10 mm throughout the entire left ventricle) and three long-axis views by using a steady-state free-precession sequence (repetition time msec/echo time msec, 3.0/1.5; temporal resolution, 35–40 msec; section thickness, 6 mm; intersection gap, 4 mm; flip angle, 60°; in-plane resolution, approximately 1.7×1.4 mm). After cine imaging, the patient table was moved partially outside the imager to enable direct patient observation and full access. Adenosine ($140 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) was infused with continuous electrocardiographic and blood pressure monitoring

for approximately 3 minutes. At 2.5 minutes into the infusion, the patient was repositioned in the imager, and he or she underwent first-pass perfusion imaging during infusion of gadolinium-containing contrast material (0.075 mmol per kilogram of body weight, Gadoversetamide; Mallinckrodt, St Louis, Mo) followed by a 50-mL saline flush; both were infused at a rate of 4 mL/sec. Typically, four short-axis views (matched to cine locations excluding the most basal and apical views) were obtained per heartbeat by using a saturation-recovery gradient-echo sequence, as described previously (2.4/1.1; delay time, 90–110 msec; temporal resolution, 110–125 msec; voxel size, $3.0 \times 1.8 \times 8.0$ mm; acceleration factor, two) (12,14). Patients were asked to hold their breath during the left ventricular perfusion phase, and images were visualized in real-time on the user interface display. Rest perfusion imaging was performed by using the same sequence settings and the same contrast material dose at least 15 minutes later. Finally, delayed-enhancement imaging was initiated 5 minutes after rest perfusion imaging by using a segmented inversion recovery sequence (9.5/3.8; section thickness, 6 mm; intersection gap, 4 mm; flip angle, 25°; in-plane resolution 1.8×1.4 mm) in the same imaging plane used for cine imaging, with inversion time manually adjusted to null normal myocardium (19).

Analysis.—For both the immediate clinical interpretation and the blinded interpretation, images were read qualitatively by two experienced readers in consensus; a previously designated third reader was consulted in cases of interpretive discordance (R.J.K., J.F.H., I.K.; level III trained in cardiac MR imaging with 20, 5, and 5 years of experience, respectively). The specific algorithm described by Klem et al (12) was used to define an abnormal stress cardiac MR imaging study. In brief, evidence of a stress perfusion defect or of delayed enhancement was considered an abnormal finding, unless there were matched stress and rest perfusion defects without evidence of delayed enhancement. The latter was considered

to represent artifactual perfusion defects. The criterion for a perfusion defect was a persistent delay in first-pass myocardial enhancement on more than three consecutive images. Cine findings were considered when perfusion results were equivocal (abnormal wall motion with equivocal stress perfusion was classified as abnormal overall).

For the blinded interpretation, cardiac MR images were placed in random order with identity markers removed. To reduce the potential for observer bias, images from 60 patients not enrolled in the study were included in the randomization. Blinded interpretation was performed twice, weeks apart. The first interpretation was performed with all components available to the readers. The second was performed with only individual components available (cine alone, stress and rest perfusion alone, delayed-enhancement cardiac MR imaging alone) to assess the independent value of the individual components of stress cardiac MR imaging.

Statistical Analysis

Continuous data are reported as mean $\pm$ standard deviation, or in cases in which the distribution was not normal, as the median and 25th and 75th percentiles. The 95% confidence limits presented for measures of diagnostic test performance are based on the Clopper-Peterson exact method for binomial proportions (SAS; SAS Institute, Cary, NC). Comparisons were made by using two-sample *t* tests for continuous data and χ^2 tests for discrete data. The McNemar test was used to compare the sensitivity, specificity, and accuracy of techniques. Differences between positive and negative predictive values of techniques were made by using regression modeling (20). Multivariable logistic regression analysis was performed to assess the independent value of traditional cardiac risk factors and the results of stress imaging. Because of the number of events, the analysis used the total number of cardiac risk factors at baseline rather than individual factors (21,22). The total number of cardiac risk factors at baseline ranged from zero to six and was defined as the

number of the following risk factors that were present: (a) age of more than 40 years for men and more than 50 years for women, (b) diabetes, (c) hypertension, (d) hyperlipidemia, (e) current tobacco use, and (f) family history of MI prior to age 55 years. Results are presented as the odds ratio for model variables and as the likelihood ratio for the overall model. Statistical tests were two tailed; $P < .05$ indicated a significant difference. S-Plus software (version 8.0; Insightful Software, Seattle, Wash) was used to perform statistical comparisons and logistic regression analyses. The authors are solely responsible for the design and conduct of this study, all study analyses, and drafting, editing, and the final content of the article.

Results

Patient Characteristics, Flow, and Outcome

Of the 68 patients enrolled in this study, 60 completed the study. Five withdrew consent before imaging, and three could not undergo cardiac MR imaging (two because of large body circumference, one because of claustrophobia). The mean age was 55 years $\pm$ 10 (52 years $\pm$ 9 in men, 57 years $\pm$ 11 in women; $P = .093$), 33 (55%) of the patients were women, and patients had on average 2.3 risk factors for CAD (Table 1).

Figure E1 (online) outlines the flow of patients. In 14 patients, results of one or both stress imaging tests were abnormal at immediate clinical interpretation; these patients were admitted to the hospital and underwent invasive coronary angiography in accordance with the prespecified protocol. Acute MI was not diagnosed in any of the admitted patients; eight of the patients had angiographically significant CAD, and six had single-vessel disease. The remaining 46 patients were discharged and followed up for clinical events. All were followed up for at least 6 months (mean, 14 months $\pm$ 5), and none were lost to follow-up. During the follow-up period, two patients had recurrent chest pain and underwent further cardiac evaluation. Both

had normal coronary arteries at invasive angiography. No patient had an adverse cardiac event (death or MI) or was found to have significant CAD during the follow-up period. Thus, all 46 patients who had negative findings at clinical interpretation of both stress cardiac MR images and stress echocardiograms had an uneventful follow-up, and we determined they had true-negative findings for significant CAD.

Overall, baseline clinical characteristics were not markedly predictive of patients in whom a diagnosis of significant CAD would be made (Table 1). While patients with CAD were more likely to be taking aspirin and angiotensin-converting enzyme inhibitors and there was a trend toward a lower high-density lipoprotein cholesterol level and nonspecific ST-T wave electrocardiographic changes, most characteristics, including high-sensitivity C-reactive protein level, were similar in patients with CAD and those without CAD.

Stress Testing

All patients fully completed the stress cardiac MR imaging protocol. Imaging time was less than 50 minutes in all patients, and there were no adverse events or complications associated with adenosine administration. Similarly, all patients completed stress echocardiography without adverse events, with 53 (88%) undergoing an exercise treadmill stress test and seven (12%) undergoing a dobutamine stress test. Forty-four (73%) reached their target heart rate. All stress tests yielded images that were of diagnostic quality, and none of the results were excluded from analysis.

For the two separate readings (clinical and blinded), concordance in the interpretations was high and similar for stress cardiac MR imaging (87%) and stress echocardiography (92%). When we compared stress cardiac MR imaging with stress echocardiography, the concordance was slightly lower at 82% for both clinical and blinded interpretation.

Diagnostic Performance

The diagnostic performance of stress cardiac MR imaging and stress

echocardiography is shown in Table 2. At both clinical and blinded interpretation, the specificity, accuracy, and positive and negative predictive values were similar between stress cardiac MR imaging and stress echocardiography (92% vs 96%, 93% vs 88%, 67% vs 60%, and 100% vs 91%, respectively, for clinical interpretation; 90% vs 92%, 90% vs 88%, 58% vs 56%, and 98% vs 94%, respectively, for blinded interpretation). Stress cardiac MR imaging had higher sensitivity at both clinical (100% vs 38%, $P = .025$) and blinded (88% vs 63%, $P = .31$) interpretation, but the difference was not significant for the blinded interpretation. The Figure shows an example of an abnormal stress cardiac MR imaging test. In this patient, we used invasive coronary angiography to verify the presence of significant CAD. In the patients with significant CAD missed at stress echocardiography, five of five patients had single-vessel disease at clinical interpretation and three of three patients had single-vessel disease at blinded interpretation. Additionally, two of five patients at clinical interpretation and one of three patients at blinded interpretation did not reach the target heart rate. There was no difference between the diagnostic accuracy of stress echocardiography performed with exercise and that of stress echocardiography performed with dobutamine ($P = .14$). A summary of the findings in the 14 patients with abnormal stress test findings at clinical interpretation is shown in Table E1 (online).

The diagnostic performance of the individual components of stress cardiac MR imaging at blinded interpretation is given in Table 3. Stress perfusion images read in isolation had lower sensitivity, specificity, and accuracy than did those read in the composite reading with the prespecified interpretation algorithm (75% vs 88% [$P = .56$], 73% vs 90% [$P = .007$], and 73% vs 90% [$P = .008$], respectively). Both cine imaging at rest and delayed-enhancement imaging had low sensitivity (38%), but the latter had very high specificity (98%). When any abnormality at stress cardiac MR imaging (whether abnormal resting wall motion,

Table 1

Baseline Characteristics

Characteristic	Entire Group (n = 60)	Patients with CAD (n = 8)*	Patients without CAD (n = 52)	P Value
Age (y) [†]	54.6 ± 10.1	57.1 ± 9.5	54.3 ± 10.3	.47
Female sex	33 (55)	2 (25)	31 (60)	.12
Cardiac history				
Diabetes mellitus	8 (13)	2 (25)	6 (12)	.29
Hypertension	36 (60)	5 (63)	31 (60)	>.99
Cigarette smoker	10 (17)	1 (13)	9 (17)	>.99
Hypercholesterolemia	22 (37)	3 (38)	19 (37)	>.99
Family history of CAD	21 (35)	3 (38)	18 (35)	>.99
No. of CAD risk factors [†]	2.3 ± 1.2	2.6 ± 0.9	2.3 ± 1.2	.40
Other medical history				
Renal disease	3 (5)	0 (0)	3 (6)	>.99
Peripheral vascular disease	1 (2)	0 (0)	1 (2)	>.99
Gastroesophageal reflux disease	17 (28)	4 (50)	13 (25)	.21
Cerebrovascular accident or transient ischemic attack	5 (8)	2 (25)	3 (6)	.13
Chronic obstructive pulmonary disease	7 (12)	1 (13)	6 (12)	>.99
Body mass index [†]	28.8 ± 5.0	28.2 ± 4.5	28.9 ± 5.1	.70
Medications				
Statins	10 (17)	2 (25)	8 (15)	.61
β-blockers	13 (22)	1 (13)	12 (23)	.67
Aspirin	18 (30)	5 (63)	13 (25)	.045
Angiotensin-converting enzyme inhibitors	17 (28)	5 (63)	12 (23)	.035
Diuretics	17 (28)	2 (25)	15 (29)	>.99
Calcium channel blocker	6 (10)	0 (0)	6 (12)	.58
Blood tests				
High-sensitivity C-reactive protein level [‡]	0.36 (0.13–0.87)	0.31 (0.14–0.58)	0.37 (0.12–0.96)	.71
Total cholesterol level (mg/dL) [§]	196 ± 44	187 ± 28	197 ± 45	.57
Low-density lipoprotein cholesterol level (mg/dL) [§]	112 ± 37	96 ± 36	115 ± 37	.23
High-density lipoprotein cholesterol level (mg/dL) [§]	50 ± 16	40 ± 11	51 ± 16	.08
Triglyceride level (mg/dL)	161 ± 93	180 ± 102	157 ± 93	.56
White blood cell count (×10 ³ /μL) ^{†#}	7.0 ± 1.7	6.8 ± 1.9	7.0 ± 1.7	.74
Twelve-lead electrocardiography				
Heart rate (beats per minute) [†]	73 ± 13	76 ± 21	73 ± 12	.66
Nonspecific ST-segment changes	15 (25)	4 (50)	11 (21)	.08
Nonspecific T-wave changes	10 (17)	3 (38)	7 (13)	.09
Sinus rhythm	60 (100)	8 (100)	52 (100)	>.99

Note.—Unless otherwise indicated, data are numbers of patients, and data in parentheses are percentages.

* CAD defined by x-ray coronary angiography or cardiac event during follow-up (see text).

[†] Data are mean ± standard deviation.

[‡] High-sensitivity C-reactive protein level was measured in 42 patients. Data are medians, and data in parentheses are the interquartile range.

[§] To convert to International System of Units (millimoles per liter), multiply by 0.02586.

^{||} To convert to International System of Units (millimoles per liter), multiply by 0.01129.

[#] To convert to International System of Units (×10⁹/L), multiply by 1.

stress perfusion defect, or the presence of delayed enhancement) was considered positive, the sensitivity was 100%; however, specificity was reduced to 60%.

Diagnostic performance was not significantly changed with either stress imaging test when significant CAD was defined as narrowing of more than

70% rather than as narrowing of more than 50%. The sensitivity, specificity, and accuracy of stress cardiac MR imaging compared with those of stress echocardiography were 100% versus 43% ($P = .046$), 91% versus 96% ($P = .26$), and 92% versus 90% ($P = .76$), respectively, for clinical interpretation

and 86% versus 71% ($P = .56$), 89% versus 92% ($P = .48$), and 88% versus 88% ($P = .76$), respectively, for blinded interpretation.

Multivariable Logistic Regression Analysis

To examine whether stress testing added incremental value to traditional cardiac

Table 2

Diagnostic Performance of Stress Cardiac MR Imaging and Echocardiography

Interpretation and Modality	Sensitivity (%)	Specificity (%)	Accuracy (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Clinical interpretation					
Stress cardiac MR imaging	100 (8/8) [63, 100]	92 (48/52) [82, 98]	93 (56/60) [84, 98]	67 (8/12) [35, 90]	100 (48/48) [93, 100]
Stress echocardiography	38 (3/8) [9, 76]	96 (50/52) [87, 100]	88 (53/60) [77, 95]	60 (3/5) [15, 95]	91 (50/55) [80, 97]
P value	.025	.41	.37	.79	NA*
Blinded interpretation					
Stress cardiac MR imaging	88 (7/8) [47, 100]	90 (47/52) [79, 97]	90 (54/60) [79, 96]	58 (7/12) [28, 85]	98 (47/48) [89, 100]
Stress echocardiography	63 (5/8) [24, 91]	92 (48/52) [81, 98]	88 (53/60) [77, 95]	56 (5/9) [21, 86]	94 (48/51) [84, 99]
P value	.31	.71	.76	.90	.36

Note.—Data in parentheses are raw data. Data in brackets are 95% confidence intervals.

* NA = not applicable. P value cannot be calculated since all subjects with negative cardiac MR imaging perfusion findings did not have significant CAD (narrowing >50%).

Example of an abnormal stress cardiac MR imaging (CMR) study. Cardiac MR imaging (left panel) shows a subendocardial perfusion defect in the inferior wall (white arrow) during adenosine infusion that is not present at rest. Delayed-enhancement imaging reveals no infarction in this territory. Resting wall motion was normal at cine cardiac MR imaging and echocardiography (right panel). There was no evidence of an inducible wall motion abnormality at dobutamine stress echocardiography. Invasive coronary angiography (bottom inset panel) showed 100% stenosis of the right coronary artery (solid black arrow) with retrograde filling from the collateral vessels (dashed arrow).

risk factors, multivariable regression analysis was performed by using three separate models. In each model, the total number of cardiac risk factors was a covariate along with the results of stress cardiac MR imaging in model A, stress echocardiography in model B, and both stress cardiac MR imaging and stress echocardiography in model C. In these models, the blinded stress test interpretations (and not the clinical

interpretations) were used to separate out the value of stress imaging. Table 4 shows the results, and in each of the three models only the covariate or covariates of stress imaging were independent predictors of significant CAD. Stress cardiac MR imaging was a stronger predictor of significant CAD than was stress echocardiography, as shown by the higher odds ratio in model C (56.6 vs 15.7) and the better overall

fit of model A compared with that of model B (χ^2 , 21.2 vs 12.1).

Discussion

In this prospective study of patients with chest pain who presented to the ED, the main finding is that a cardiac MR imaging protocol incorporating adenosine stress perfusion imaging is safe, quick, and accurate when performed within

Table 3

Diagnostic Performance of Individual Cardiac MR imaging Components

Blinded Interpretation	Sensitivity (%)	Specificity (%)	Accuracy (%)
Adenosine perfusion	75 (7/8) [35, 97]	73 (47/52) [59, 84]	73 (44/60) [62, 85]
Cine (resting WMA)	38 (3/8) [9, 76]	83 (43/52) [70, 92]	77 (46/60) [64, 87]
Delayed enhancement	38 (3/8) [9, 76]	98 (51/52) [94, 100]	90 (54/60) [79, 96]
Any abnormality	100 (8/8) [63, 100]	60 (31/52) [45, 73]	65 (39/60) [52, 77]

Note.—Data in parentheses are raw data. Data in brackets are 95% confidence intervals. WMA = wall motion abnormality.

Table 4

Logistic Regression Models Utilizing Blinded Stress-Imaging Interpretations

Model and Variable	Model χ^2	Model <i>P</i> Value	Odds Ratio	Variable <i>P</i> Value
Model A: Clinical with stress cardiac MR imaging	21.2	<.001	...	...
Total no. of cardiac risk factors	...	...	1.17	.11
Stress cardiac MR imaging	...	...	63.4	<.001
Model B: Clinical with stress echocardiography	12.1	.002	...	...
Total no. of cardiac risk factors	...	...	1.18	.69
Stress echocardiography	...	...	19.0	.001
Model C: Clinical with both stress tests	26.3	<.001	...	...
Total no. of cardiac risk factors	...	...	0.87	.81
Stress cardiac MR imaging	...	...	56.6	.002
Stress echocardiography	...	...	15.7	.04

12 hours after presentation. At multivariate analysis, stress cardiac MR imaging was the strongest predictor of significant CAD and had independent value over traditional risk factors. Additionally, stress cardiac MR imaging had performance characteristics that were similar to, if not better than, those of stress echocardiography.

The present study extends the findings of previous investigations (21–25). Both Kwong et al (23) and Cury et al (21) showed the value of cardiac MR imaging in patients seen in the ED. However, in these studies, researchers performed only rest perfusion imaging since the studies involved patients at higher risk (eg, several had acute non-ST segment elevation myocardial infarction). Ingkanisorn et al (22) performed adenosine stress cardiac MR imaging and used a similar composite endpoint based on coronary angiography and clinical events during follow-up. However,

stress testing was performed up to 72 hours after presentation. Thus, safety and feasibility data are not directly comparable with those in the current study, in which patients underwent stress cardiac MR imaging directly in the ED within 12 hours of presentation. Moreover, there was no comparison with a separate stress imaging modality. Similar to the Ingkanisorn et al study, the investigations by Lerakis et al (24) and Vogel-Claussen et al (25) yielded encouraging findings regarding the utility of stress cardiac MR imaging; however, the former is a retrospective analysis and the latter included only 27 patients.

In the current study, we did not enroll patients with a very high likelihood of CAD (ie, documented CAD history) because it is well established that such pretest referral (spectrum) bias can inappropriately increase test sensitivity, specificity, or both (26). Hence, our study population was different from

that of prior cardiac MR imaging studies in patients seen in the ED. Lastly, our study is distinctive in that we prospectively specified that an immediate interpretation of stress imaging findings would inform the ED triage decision. Correspondingly, we focused on a quick cardiac MR imaging protocol with only essential components and an interpretation based on rapid visual assessment (12). Prior investigations did not use cardiac MR imaging results to inform patient care (21–23). In this respect, our study enabled better validation of the utility of stress cardiac MR imaging for practical clinical use in a real-life setting.

Although our study did not strictly focus on patient outcome, the results build on the excellent reports from Ingkanisorn et al (22) and Lerakis et al (24). In the ED setting, a false-negative finding (ie, missing disease) is more important than a false-positive finding, and it is reassuring that the negative predictive value of stress cardiac MR imaging at clinical interpretation was 100% (blinded interpretation, 98%). Thus, all patients with normal findings at clinical interpretation of stress cardiac MR images had an excellent prognosis, as no diagnoses of an adverse event were made during 14 months $\pm$ 5 of follow-up.

Both stress cardiac MR imaging and stress echocardiography performed well in this study with respect to specificity and accuracy; however, stress echocardiography appeared to have lower sensitivity. Although the sensitivity of stress echocardiography has been reported to be as high as 85% in prior studies (9,27), those studies are not directly comparable with the present study, which focused on an ED population with intermediate risk of CAD. Most prior studies in which researchers investigated the diagnostic performance of stress echocardiography included patients with known CAD. It is well known that excluding such patients (as in the current study) leads to lower sensitivity of stress echocardiography (28). Furthermore, it is notable that in the current study, 100% of patients with

CAD missed at stress echocardiography had single-vessel disease. Prior stress echocardiography investigations have shown distinctly lower test sensitivity for single-vessel disease when compared with sensitivity for multi-vessel disease. For instance, Quiñones et al (29) reported sensitivity of 58% for single-vessel disease and 94% for three-vessel disease. The mechanism for the improved sensitivity of stress cardiac MR imaging over that of stress echocardiography may lie in the well-known temporal order of the ischemic cascade, in which abnormal perfusion precedes abnormal function (30). Additionally, Leong-Poi et al (31) showed perfusion defects are larger than functional defects, and both spatial and temporal differences are amplified in single-vessel disease as compared with multivessel disease.

This study is limited by its relatively small sample size, and a larger study is needed to confirm the improvement, if any, in the sensitivity of stress cardiac MR imaging. Nonetheless, multivariable regression analysis showed the independent value of stress cardiac MR imaging, and it was the strongest predictor of significant CAD. Given the low prevalence of CAD in our cohort (13%) and the relatively high specificity (and accuracy) of both stress tests, this study has insufficient power to enable detection of meaningful differences in specificity, accuracy, and negative predictive value. It is important to note that three (5%) patients could not undergo cardiac MR imaging because of limitations due to either body habitus or claustrophobia. The rate of patients unable to undergo MR imaging because of body habitus is low (21,23,25), but this is a practical disadvantage of stress cardiac MR imaging. Adenosine was used for stress cardiac MR imaging, but different methods (exercise or dobutamine) were used for stress echocardiography, which could have influenced the results. Advances in cardiac MR imaging and echo technology, such as those achieved with recent clinical use of 3-T cardiac MR imaging and three-dimensional echocardiography, may lead to different findings than those in the current study. Finally, we

note that patients underwent coronary angiography when the results of either stress cardiac MR imaging or stress echocardiography were abnormal at immediate clinical interpretation. We chose this study design to enable some patients with normal stress imaging results (from one modality) to undergo angiography and thereby reduce post-test verification bias (32). Nonetheless, many patients had normal results for both stress tests and did not undergo coronary angiography. Thus, we also required systematic patient follow-up to track clinical events and additional cardiac work-up. We surmised that our definition of a true-negative finding, which required both initial stress interpretations to be negative and follow-up to be negative, would lead to a very low rate in which patients with clinically meaningful CAD would be missed. Our finding that none of the patients who were discharged from the ED experienced clinical events or were found to have significant CAD at subsequent cardiac work-up during follow-up is consistent with this hypothesis. Nonetheless, in the current investigation, clinical outcome is used as a surrogate for anatomic CAD, and this should be considered a limitation of the study.

In conclusion, the results of this study support the feasibility, safety, and accuracy of stress perfusion cardiac MR imaging in the ED. In addition, stress cardiac MR imaging showed added value over traditional clinical indexes used for ED triage and had performance characteristics at least as good as those of stress echocardiography. The potential for improvement in test sensitivity over that provided by stress echocardiography will require further evaluation in a larger population.

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