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Cardiac Magnetic Resonance With T2-Weighted Imaging Improves Detection of Patients With Acute Coronary Syndrome in the Emergency Department

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Background—Cardiac magnetic resonance (CMR) imaging permits early triage of patients presenting to the emergency department with acute chest pain but has been limited by the inability to differentiate new from old myocardial infarction. Our objective was to evaluate a CMR protocol that includes T2-weighted imaging and assessment of left ventricular wall thickness in detecting patients with acute coronary syndrome in the emergency department.

Methods and Results—In this prospective cohort observational study, we enrolled patients presenting to the emergency department with acute chest pain, negative cardiac biomarkers, and no ECG changes indicative of acute ischemia. The CMR protocol consisted of T2-weighted imaging, first-pass perfusion, cine function, delayed-enhancement magnetic resonance imaging, and assessment of left ventricular wall thickness. The clinical outcome (acute coronary syndrome) was defined by review of clinical charts by a consensus panel that used American Heart Association/American College of Cardiology guidelines. Among 62 patients, 13 developed acute coronary syndrome during the index hospitalization. The mean CMR time was 32 ± 8 minutes. The new CMR protocol (with the addition of T2-weighted and left ventricular wall thickness) increased the specificity, positive predictive value, and overall accuracy from 84% to 96%, 55% to 85%, and 84% to 93%, respectively, compared with the conventional CMR protocol (cine, perfusion, and delayed-enhancement magnetic resonance imaging). Moreover, in a logistic regression analysis that contained information on clinical risk assessment (c-statistic=0.695) and traditional cardiac risk factors (c-statistic=0.771), the new CMR protocol significantly improved the c-statistic to 0.958 ($P < 0.0001$).

Conclusions—The present study indicates that a new CMR protocol improves the detection of patients with acute coronary syndrome in the emergency department and adds significant value over clinical assessment and traditional cardiac risk factors. (*Circulation*. 2008;118:837-844.)

Key Words: magnetic resonance imaging ■ angina ■ myocardial infarction ■ diagnosis

The accurate triage of patients presenting with acute chest discomfort is a common and challenging problem in the emergency department (ED). It is estimated that in the United States, >5 million patients per year are evaluated in the ED for chest pain or other symptoms suggestive of an acute coronary syndrome (ACS)¹; however, a large number of these patients presenting with chest pain will be determined to have a nonnegligible risk for an ischemic cause of their symptoms. In this group, initial biomarkers of cardiac injury and ECG changes can be nondiagnostic.^{2,3} Because the consequences of the premature discharge of patients at risk for coronary events can be catastrophic, the threshold used to determine whether to admit these patients is low, and many unnecessary admissions occur of

patients without ACS.⁴ Approximately 30% of patients admitted for suspected myocardial infarction (MI) are eventually diagnosed with ACS.⁵ On the other hand, 2% to 4% of patients with chest pain discharged from hospital EDs experience an ACS within 30 days.^{4,6} A possible strategy to triage these patients includes the early use of cardiovascular imaging for rapid diagnosis and appropriate management.

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Kwong et al⁷ reported that cardiac magnetic resonance (CMR) has diagnostic capability suitable for triage of patients with chest pain in the ED. However, the inability to differ-

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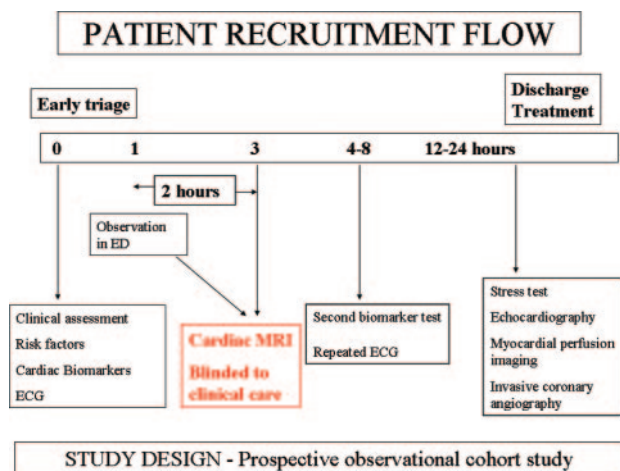


Figure 1. Patient recruitment flow through the trial.

entiate acute from chronic myocardial infarction limited the value of CMR and other cardiac imaging modalities in this setting.

A recent report demonstrated that CMR with delayed enhancement and T2-weighted (T2W) imaging (which detects associated myocardial edema) accurately differentiates acute from chronic lesions in patients with established MI.⁸ The addition of T2W edema-sensitive images can potentially identify initial myocardial edema and differentiate acute versus chronic MI in the acute setting. In addition, it is well known that patients with chronic MI have left ventricular (LV) wall thinning. Our hypothesis was that a comprehensive CMR protocol that used cine wall motion, rest first-pass myocardial perfusion (FP-MRI), T2W images, LV wall thickness (LVWT) analysis, and delayed-enhancement imaging (DE-MRI) could significantly increase the detection of ACS compared with existing triage strategies in patients presenting with chest pain in the ED.

Methods

Patient Population

In the present prospective cohort observational study, we enrolled 87 patients presenting to the ED with acute chest pain (within 12 hours of onset), negative initial cardiac biomarkers, and no ECG changes suggestive of acute myocardial ischemia (Figure 1). The setting was a 78 000–annual visit ED in an urban academic medical center. All patients were awaiting admission to the hospital for a rule-out MI protocol. As part of the inclusion criteria, to eliminate the very-low-risk population of patients with acute chest pain who are discharged directly from the ED, we included only patients who were being admitted to the hospital. Other inclusion criteria were as follows: age >18 years, sinus rhythm, ability to perform a breath hold of 10 to 15 seconds, and negative serum pregnancy for women of childbearing potential. The exclusion criteria included elevated troponin I or creatine kinase-MB levels in the initial blood sample obtained in the ED; new diagnostic ECG changes (ST-segment elevation or depression >1 mm or T-wave inversion >4 mm in >2 anatomically contiguous leads); hemodynamic or clinical instability; perceived interference with standard clinical care of patients; and general contraindications to MRI. Recruitment was performed consecutively on weekdays from 7 AM to 7 PM over a 4-month period. All eligible patients who agreed to enroll underwent CMR before admission to the hospital floor (n=62 patients). All physicians, including those in the ED, who were involved in the standard clinical care of the patients were blinded to the result of the CMR examination. Patients

received standard clinical care to rule out ACS during their index hospitalization, including serial ECGs and cardiac biomarkers, and subsequent cardiac testing, eg, exercise testing, stress perfusion imaging, or cardiac catheterization, as deemed indicated clinically. The institutional review board approved this study, and all patients provided written consent.

CMR Examination

All subjects were examined on a 1.5-Tesla magnet located in the ED (Signa HDx, GE Healthcare, Milwaukee, Wis) that had an 8-element, phased-array cardiac coil. The cardiac MRI protocol consisted of T2W imaging, FP-MRI, cine LV function, and DE-MRI. After the localizers were applied, cine images in the 2- and 4-chamber views were acquired. A breath-hold, black-blood, T2W double-inversion recovery sequence with a fat-saturation pulse was performed in 4 short-axis slices with the following parameters: repetition time, 2 R-R intervals; echo time, 100 ms; echo train length, 20; matrix, 256×256; field of view, 32 to 34 cm; slice thickness, 12 mm; and number of excitations, 1. Subsequently, a breath-hold FP-MRI myocardial perfusion image was acquired with a hybrid gradient echo-planar imaging pulse sequence, described elsewhere,⁹ during a bolus injection of 0.1 mmol/kg of gadopentetate dimeglumine (Gd-DTPA; Schering AG, Berlin, Germany) via an infusion pump (Medrad, Indianola, Pa) at 5 mL/s, followed by 20 mL of saline flush, which allowed the acquisition of 5 to 8 slices in the short-axis view, depending on the heart rate. A second bolus of Gd-DTPA was injected (0.1 mmol/kg IV at 2 mL/s). Although the gadolinium was washing out of the myocardium, cine images were acquired with a steady-state free precession technique in the short-axis view (10 to 12 slices). Approximately 10 minutes after the second gadolinium injection, DE-MRI was obtained by use of an inversion-recovery prepared, gated, fast-gradient echo pulse sequence by an adiabatic 3D technique, followed by a 2D technique if necessary, which covered the base to the apex of the LV. During the study, ECG, heart rate, and respiration were monitored continuously.

Outcomes

The primary goal of the present study was to test the hypothesis that a new MRI protocol with T2W images could increase the diagnostic accuracy of CMR to detect patients with and without ACS. Additional goals were to examine whether the MRI information provided incremental value to the initial clinical risk assessment performed by ED caregivers at the time of triage and to the information provided by standard risk factors, and finally, to compare the diagnostic accuracy of the different MRI sequences for the detection of ACS patients.

Clinical Outcomes

We prospectively collected data about each patient's demographics, risk factor profile, and clinical course, including clinical presentation to the ED and hospital discharge. Medical records were reviewed to obtain data about all diagnostic tests.

Risk Stratification

To clinically characterize the risk of patients for ACS, ED caregivers provided an estimate of the probability of having ACS for each patient at the time of initial triage on the basis of the patient's history, risk factors, and clinical presentation. A subjective scale ranging from 0% to 100% was used, depending on the probability of the ED caregiver's clinical assessment for considering a patient to have an ACS. We stratified patients as having a low (0% to 33%), moderate (34% to 66%), or high (67% to 100%) pretest probability of having an ACS.¹⁰

Traditional Risk Factor Assessment

The presence of risk factors was established from actual measurements obtained during the hospitalization (ie, hypertension, hypercholesterolemia, and diabetes mellitus). The total number of traditional cardiac risk factors (TCRFs) was defined as the number of the following that were present: advanced age (>45 years for men and >55 years for women), hypercholesterolemia or statin use, hyper-

tension, diabetes mellitus, family history of coronary artery disease, tobacco use, and history of previous MI. Thus, the TCRF ranged from 0 to 7.

Diagnosis of ACS During Index Hospitalization

ACS was defined as either an acute MI (ST-elevation MI [STEMI] or non-STEMI [NSTEMI]) or unstable angina pectoris according to the American Heart Association/American College of Cardiology guidelines.¹ To establish this diagnosis, an outcome panel of 2 experienced ED physicians reviewed the patient data forms and medical records pertaining to the hospital admission of all enrolled patients. The reviewers were blinded to the findings of CMR. Disagreement was solved by consensus, and if necessary, an additional cardiologist was included.¹¹ CMR data were not used to define ACS.

MRI Analysis

Two experienced observers, who were blinded to the patient's name and to all clinical data, evaluated all CMRs by consensus. CMR was initially interpreted qualitatively for each MRI technique individually in different sessions (at least 1 week apart). Next, CMR was interpreted by combining cine function, FP-MRI, and DE-MRI, similar to the study by Kwong et al,⁷ herein referred to as the standard CMR protocol. Finally, the blinded readers incorporated all MRI data together (T2W images, cine function, FP-MRI, DE-MRI, and LVWT analysis), herein referred to as the new CMR protocol. If necessary, disagreement was resolved by a third expert reader. Assessment was performed on a dedicated workstation (ADW 4.2, GE Healthcare).

MRI images were assessed for the following: (1) Presence or absence of myocardial edema, with T2W images; (2) presence or absence of myocardial perfusion defects, with FP-MRI; (3) presence or absence of regional and global wall motion abnormalities; (4) presence or absence of delayed hyperenhancement; and (5) presence or absence of LV wall myocardial thinning. Myocardial segments were assigned to the 3 major coronary artery territories according to the American Heart Association's standardized myocardial segmentation.¹²

T2W images were considered abnormal if increased signal was observed within the myocardium. Increased signal was defined as a signal intensity greater than the mean signal intensity plus 2 SD of normal myocardium. Care was taken to not include the LV cavity, particularly toward the apex and apical level of the LV, where slow flow can lead to increase signal within the LV cavity. If necessary, T2W images were matched with the cine images for a clear delineation of the LV endocardial border in the comprehensive analysis. Cine images were considered abnormal if any wall motion abnormality (hypokinesia, akinesia, or dyskinesia) was present. The criterion used for perfusion defects in FP-MRI was a persistent delay in the enhancement pattern during the first pass of the contrast media through the myocardium, observed on at least 5 consecutive temporal images and at least 2 contiguous slices. MI was defined as an area with hyperenhancement in the DE-MRI consistent with a coronary distribution. LV thinning was defined if the LVWT was less than 6 mm during end diastole in a corresponding segment with regional wall motion abnormality or delayed hyperenhancement.

First, in the individual MRI technique analysis, a patient was defined as positive for ACS if the individual MRI pulse sequence was positive by the criteria described above. Second, the standard CMR protocol (cine, perfusion, and delayed enhancement) was considered positive if any of the 3 sequences were positive. Third, the criteria used for the new CMR protocol (T2W, cine, perfusion, delayed enhancement, and LVWT) for positive ACS were increased signal in T2W images, which indicated the presence of myocardial edema, or if abnormal cine regional wall motion abnormality, perfusion defect, or delayed hyperenhancement was found, in addition to preserved LV wall myocardial thickness. A patient was considered to have a prior MI and no ACS at the index hospitalization if the new CMR protocol demonstrated the presence of delayed hyperenhancement, negative T2W images, and LV wall thinning at end diastole. A patient was considered to have no ACS or prior MI if all MRI sequences were normal.

Statistical Analysis

Results are expressed as sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy with 95% confidence interval (CI) of use of the normal approximation method,¹³ with the expert clinical panel's adjudication of presence or absence of ACS as the reference standard. The diagnostic accuracy for each individual MRI technique was calculated. The diagnostic accuracy of the standard CMR protocol, which involved cine, perfusion, and delayed enhancement, was compared by McNemar test with a new CMR protocol that added T2W imaging and LVWT evaluation. Univariate associations between baseline variables with the clinical diagnosis of ACS were examined with Student *t* test for continuous variables and χ^2 test for categorical variables.

We performed multivariable regression analysis to determine whether information from the new CMR protocol that included T2W images added incremental value to information available at initial triage by clinical risk assessment and a combined score of total TCRFs to predict ACS. Separate models were used to determine the incremental value of CMR findings to those of initial clinical risk assessment and traditional risk factors. The first model initially contained clinical risk assessment as assessed by the ED caregiver (as a categorical variable of low, intermediate, or high pretest probability). In this model, the group with a low pretest probability served as the reference group. In a next step, we added the total number of TCRFs (range 0 to 7) rather than considering individual risk factors. In the final step, we added the new CMR protocol with T2W images to the model. Model fit was assessed with an area under the receiver operating characteristic curve, which is equivalent to the c-statistic.¹⁴ To test whether information on TCRF or CMR improved the model fit for the baseline model, differences in the $-2 \log$ likelihood statistics were calculated. A probability value of <0.05 was considered to indicate statistical significance. All analyses were performed with SAS (version 8, SAS Institute Inc, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Patient Population

Of the 87 patients who fulfilled the inclusion criteria, 16 declined to participate in the study, and 9 were excluded either owing to claustrophobia ($n=5$) or because the MRI system located in the ED was not available within the initial hours that the patient presented to the ED because of other urgent clinical MRI studies, such as for stroke ($n=4$). Thus, a total of 62 patients (42 men, mean age 58 ± 14 years) completed the MRI study and participated in the final analysis. The mean CMR scan time was 32 ± 8 minutes. All patients completed the CMR examination without complications. Patient characteristics are summarized in Table 1.

Clinical Outcomes

Diagnosis of ACS During Index Hospitalization

Thirteen patients (21%; 95% CI 11% to 31%) developed ACS during index hospitalization according to the consensus expert panel. Nine patients were diagnosed with unstable angina and 3 with non-STEMI, and 1 patient presented with unstable angina in the ED (negative ECG and cardiac enzymes) but progressed to STEMI during the second day of hospitalization. Invasive cardiac catheterization was performed in all 13 patients with a final diagnosis of ACS and in 1 patient without ACS, which revealed coronary arteries without significant narrowing. In 92% of the patients with ACS (12 of 13), a significant coronary obstruction ($>70\%$ of

Table 1. Clinical Characteristics of 62 Patients and Comparison of Patients With and Without ACS

	All Patients (n=62)	ACS Patients (n=13)	Non-ACS Patients (n=49)	P
Age, y, mean±SD	57.7±14.1	65.5±12.5	55.6±13.9	0.23
Advanced age, n (%) [*]	47 (75)	13 (100)	34 (69.3)	0.02
Male gender, n (%)	42 (67.7)	9 (69.2)	33 (67.3)	0.89
BMI, kg/m ² , mean±SD	28.2±3.2	29.8±3.2	28.2±41.1	0.76
Diabetes mellitus, n (%)	9 (14.5)	5 (38.5)	4 (8.1)	0.02
Hypertension, n (%)	38 (61.2)	9 (69.2)	29 (50.1)	0.73
Dyslipidemia or statin use, n (%)	32 (51.6)	9 (69.2)	23 (46.9)	0.26
Family history of CAD, n (%)	23 (37.0)	5 (38.5)	18 (36.7)	0.90
History of CAD, n (%) [†]	22 (33.8)	6 (46.1)	16 (32.7)	0.56
Current smoking, n (%)	9 (14.5)	2 (15.3)	7 (14.2)	0.92
Total No. of CAD risk factors	2.8	3.7	2.6	0.001

BMI indicates body mass index; CAD, coronary artery disease.

^{*}Age >45 years in men and >55 years in women.

[†]Previous MI with percutaneous coronary intervention or coronary artery bypass grafting.

the lumen) was found. Among these 12 patients, 7 had 1-vessel disease, 4 had 2-vessel disease, and 1 had 3-vessel disease. The only patient with a final diagnosis of ACS who demonstrated nonobstructive lesions during invasive angiography (stenoses <50%) had increased cardiac enzymes 6 hours after the CMR and new ECG changes compatible with myocardial ischemia that developed late during hospitalization.

Eight patients received percutaneous coronary intervention, and 2 patients needed coronary artery bypass grafting during hospitalization. Three patients with NSTEMI and 1 with STEMI had increased cardiac enzymes in a later stage of initial presentation during the hospital course (6±2 hours after a positive MRI). Stress imaging was performed in 5 ACS patients during hospitalization, with demonstration of ischemia in all 5. MRI correctly identified the ischemic blood supply area in 11 of 13 ACS patients as seen by invasive angiography, single-photon emission computed tomography (CT), and ECG. In 49 non-ACS patients, 20 had a stress nuclear test performed during hospitalization that was negative for perfusion defects. One had a negative invasive cardiac catheterization, and ACS was ruled out for the other 28 patients by standard clinical care during the hospital course with serial troponins and ECGs over the first 24 hours, followed by exercise stress testing the next day. Twelve patients

among the total of 62 were classified as having a prior documented MI by invasive angiography, single-photon emission CT, or ECG plus clinical history according to the panel composed of 2 physicians blinded to MRI results. Four of these patients had a new ACS, and 8 were deemed to have no ACS.

MRI Patterns to Detect ACS

The mean LV ejection fraction was 63±11% for all patients, 56±13% for ACS patients, and 65±8% for non-ACS patients. Diagnostic accuracy characteristics for the individual CMR techniques (cine MRI, FP-MRI, DE-MRI, and T2W images) and the analysis of LVWT to detect patients with ACS are demonstrated in Table 2.

The standard CMR protocol (cine, perfusion, and DE-MRI) demonstrated 85% sensitivity, 84% specificity, 58% positive predictive value, and 95% negative predictive value, with overall diagnostic accuracy of 84%. The addition of T2W imaging and the evaluation of LVWT to the MRI algorithm resulted in increased specificity and an increased positive predictive value (from 84% to 96% and from 58% to 85%, respectively, compared with the standard CMR protocol; Table 3). The sensitivity remained the same, with a slight increase in the negative predictive value. The overall diag-

Table 2. Comparison of Diagnostic Accuracy of Individual MRI Parameters to Detect Patients With ACS

	Sensitivity	Specificity	PPV	NPV
Cine MRI-RWM	0.85 (11/13)	0.86 (42/49)	0.56 (9/16)	0.91 (42/46)
Perfusion	0.77 (10/13)	0.92 (45/49)	0.71 (4/14)	0.94 (45/48)
DE-MRI	0.62 (8/13)	0.84 (41/49)	0.5 (8/16)	0.89 (41/46)
T2W	0.69 (9/13)	1.0 (49/49)	1.0 (9/9)	0.92 (49/53)
Cine MRI-LVWT	1.0 (13/13)	0.1 (5/49)	0.25 (13/57)	1.0 (5/5)

Values in parentheses indicate No. of patients who were treated according to the gold standard/total No. of patients.

PPV indicates positive predictive value; NPV, negative predictive value; and RWM, regional wall motion.

Table 3. Comparison of Diagnostic Accuracy Between Standard CMR Protocol (Cine+Perfusion+DE-MRI) and a New CMR Protocol (T2W, Cine, LVWT, Perfusion, and DE-MRI) for Detection of Patients With ACS

	Cine+Perfusion+ DE-MRI	Cine+Perfusion+DE-MRI+ T2W+LVWT
Sensitivity	85% (11/13)	85% (11/13)
Specificity	84% (41/49)	96% (47/49)
PPV	58% (11/19)	85% (11/13)
NPV	95% (41/43)	96% (47/49)
Accuracy	84% (52/62)	93% (58/62)

Values in parentheses indicate No. of patients who were treated according to the gold standard/total No. of patients.

PPV indicates positive predictive value; NPV, negative predictive value.

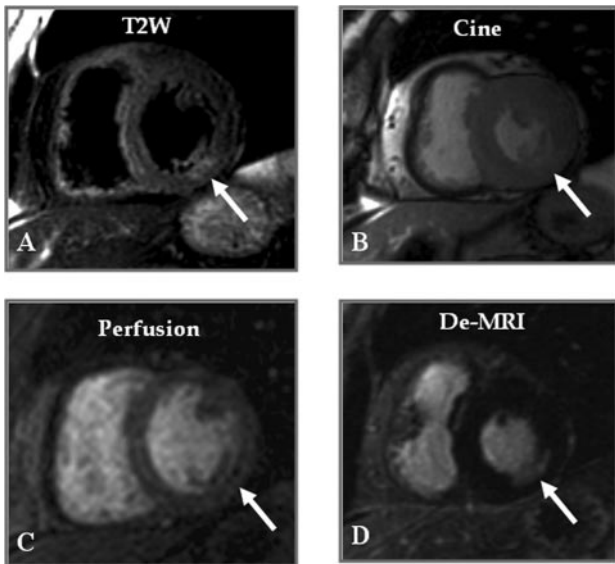


Figure 2. Example of a patient with NSTEMI. CMR was performed in a 63-year-old male 1 hour after his arrival at the ED with initial normal cardiac enzymes; it revealed a small area of T2 hyperintensity (A) in the inferolateral wall (myocardial edema) with associated subtle hypokinesis (B), a resting perfusion defect (C), and delayed hyperenhancement (D; myocardial necrosis) in the same area (arrows). Troponin level was elevated 7 hours after CMR. Invasive angiogram revealed triple-vessel disease with a 95% stenosis in the posterolateral branch.

nostic accuracy of the new CMR protocol was significantly higher than that of the standard CMR approach (93% versus 82%, $P < 0.01$). This improvement was mainly achieved by the correct detection of patients with previous MI (6 of 8) and no current ACS at index hospitalization (negative T2W plus LV wall thinning). In all 4 patients with a final diagnosis of MI (3 with NSTEMI and 1 with STEMI), CMR showed positive hyperintensity by T2W (myocardial edema) and delayed hyperenhancement (myocardial necrosis; Figure 2). These findings were observed before cardiac enzyme elevation (6 ± 2 hours). Among 9 patients with a final diagnosis of unstable angina, CMR showed T2W hyperintensity in 5 (Figure 3) and delayed enhancement in 2.

Incremental Value of CMR to TCRFs and Initial Clinical Risk Assessment

The average clinical pretest probability for ACS was assessed by ED staff at the time of triage as low in 26 patients (42%), moderate in 26 patients (42%), and high in 10 patients (16%), with an average of $44 \pm 22\%$. ACS event rates in the low-, moderate-, and high-probability categories were 2 of 26 (8%), 9 of 26 (35%), and 2 of 10 (20%), respectively.

In multivariate logistic regression analyses, the new CMR protocol was a significant predictor of ACS independent of information on clinical risk assessment and TCRFs. Although the initial clinical assessment was not a significant predictor of ACS ($P = 0.08$), the c-statistic for this baseline model was 0.695. The additional information on TCRFs significantly improved the model for the detection of ACS compared with the baseline model (0.77 versus 0.70, $\chi^2 = 4.48$, $P = 0.04$); however, TCRFs did not significantly predict ACS (odds ratio 1.88, 95% CI 0.99 to 3.58 per risk factor, $P = 0.05$). With

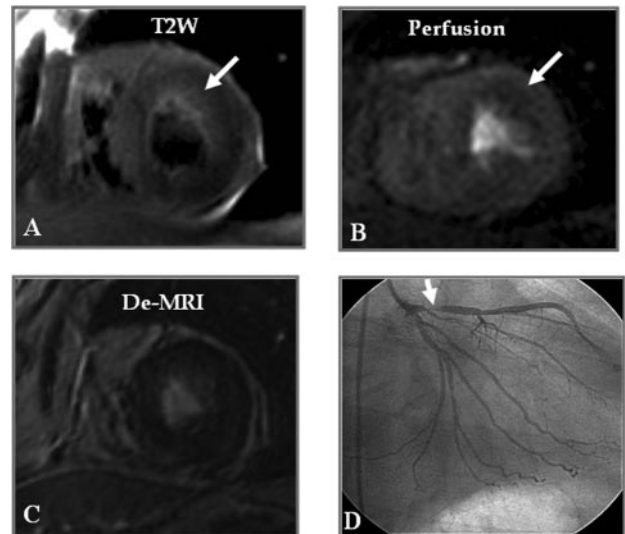


Figure 3. Example of a patient with unstable angina. CMR was performed 2 hours after the patient arrived at the ED and revealed an area of T2 hyperintensity (A) in the anterior wall (myocardial edema) with an associated resting perfusion defect (B) in the same area (arrows) but without evidence of delayed hyperenhancement (C). Stress single-photon emission CT revealed inducible ischemia in the anterior wall. Cardiac enzymes remained normal. Invasive coronary angiography demonstrated a 90% stenosis in the proximal left anterior descending coronary artery (D), which was treated with percutaneous coronary intervention.

the addition of CMR to the baseline model, the c-statistic improved to 0.913 ($\chi^2 = 30.7$, $P < 0.0001$), and CMR was a significant predictor of ACS (odds ratio 106.9, 95% CI 13.27 to 862.4, $P < 0.0001$). Moreover, the addition of information from CMR to the model that contained the clinical risk assessment and TCRFs improved the model significantly (c-statistic 0.958, $\chi^2 = 28.6$, $P < 0.0001$), and CMR remained a significant predictor of ACS (odds ratio 129.4, 95% CI 11.8 to >999.9 ; Figure 4). Thus, subjects with a positive CMR had a 129-times higher likelihood of ACS than those with a normal CMR after adjustment for initial clinical risk assessment and TCRFs.

Discussion

The evaluation of patients presenting to the ED with acute chest pain remains a challenge, particularly in those with initially negative cardiac enzymes and a nondiagnostic ECG. We demonstrated that the addition of CMR in the evaluation of these patients is highly accurate for the detection of patients with ACS and provides incremental value to initial clinical risk assessment and traditional risk factors. Previous studies^{7,15} demonstrated the safety and feasibility of a CMR-based approach in the assessment of patients presenting to the ED with chest pain. Although good diagnostic test characteristics were reported, the performance of CMR was limited by its inability to differentiate prior MI from new ACS. We addressed this inherent difficulty by adding an additional pulse sequence (T2W) that allows for imaging of myocardial edema, the hallmark of acute injury, and assessment of LVWT to identify patients with chronic infarct (Figure 5). This new approach improved the overall accuracy of CMR (Table 3), with improvement in the specificity and positive

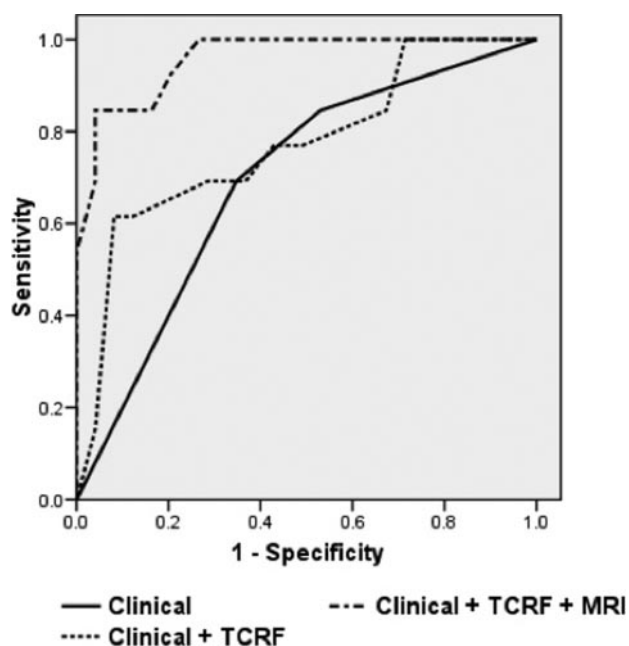


Figure 4. Receiver operating characteristic curves showing the predicted probabilities as derived from multivariable logistic regression analysis of different diagnostic strategies for the detection of patients with ACS. Area under the receiver operating characteristic curve for initial clinical assessment (solid line) was 0.695 and improved to 0.771 ($P=0.03$) with the addition of TCRFs. The addition of information from the new CMR protocol to the model improved the receiver operating characteristic curve to 0.958 ($P<0.0001$).

predictive value (from 84% and 58% to 96% and 85%, respectively). In the comparison between the individual MRI parameters (Table 2), T2W imaging allowed 100% specificity but 69% sensitivity. On the other hand, LVWT analysis allowed poor specificity (10%) but excellent sensitivity (100%). One can assume from these data that if T2W is positive, the patient has ACS (positive predictive value 100%), and conversely, if LV thinning is present, the patient does not have ACS and has had a prior chronic MI (negative predictive value 100%), which demonstrates that this information is complementary. Another advantage in the present study is that the MRI system is located directly in the ED facility, which provides a unique setting to perform these examinations in a timely fashion.

Ingkanisorn et al¹⁶ determined the diagnostic value of adenosine CMR in 135 patients who presented to the ED with chest pain. Adenosine CMR perfusion abnormalities had 100% sensitivity and 93% specificity for detection of significant coronary artery disease, and an abnormal CMR added significant prognostic value in predicting a future diagnosis of CAD, MI, or death over that of clinical risk factors. The present study is similar in that it showed that an abnormal CMR added significant diagnostic value in the detection of patients with ACS over that of initial clinical risk assessment and TCRFs. Although both CMR protocols performed better than conventional clinical assessment and TCRFs, the study protocol has the advantage of not requiring pharmacological (adenosine) stress testing in a population with acute chest pain and only initially negative troponin. On the other hand,

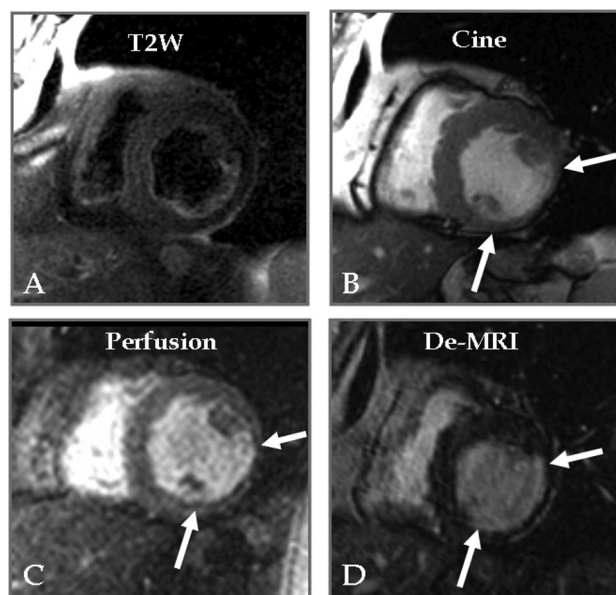


Figure 5. Example of a patient with prior chronic MI in whom ACS was excluded by index hospitalization. This patient was a 61-year-old male with prior history of MI and stent placement in the left circumflex artery. CMR demonstrated an area of LV thinning (B), perfusion defect (C), and subendocardial delayed hyperenhancement (D) in the inferolateral and inferior walls consistent with a chronic myocardial infarct. Note that the T2W image (A) was negative for edema within the myocardium but revealed a hyperintense signal within the LV cavity due to slow flow.

a disadvantage of the present protocol is that 2 patients with unstable angina were missed, and the addition of MRI stress perfusion imaging could have overcome this limitation.

Other noninvasive diagnostic imaging modalities exist that are useful in the evaluation of patients presenting to the ED with acute chest pain, including contrast echocardiography,^{17,18} single-photon emission CT–myocardial perfusion imaging,^{19,20} and most recently, coronary CT angiography.^{10,21,22} Although these imaging modalities are useful in excluding ACS (because of their high negative predictive value), they are not entirely helpful in identifying patients with true ACS and thereby refining patient management in those who need more aggressive treatment, because they are limited by low to intermediate positive predictive values. The present CMR approach with T2W data provided detection of myocardial edema, which not only enabled the differentiation of patients with and without ACS but also provided insights into further characterization of the specific subsets of ACS (unstable angina and NSTEMI). Specifically, we were able to differentiate patients with acute from chronic MI and those with unstable angina (and no MI) from those with acute NSTEMI. In fact, this could be a “CMR signature” of unstable angina: an area of signal hyperintensity on the T2W images (myocardial edema) without evidence of delayed hyperenhancement (MI; Figure 3). The detection of patients with unstable angina, as described, is of particular interest, because this subset of patients is the most challenging to identify.

We also found that in all cases with MI, CMR revealed edema by T2W images and delayed hyperenhancement, which indicated myocardial necrosis, that preceded elevation

of cardiac enzymes. The ability of a CMR with T2W images to rapidly identify chest pain patients with unstable angina and NSTEMI and correctly highlight myocardial areas at risk could help lead to a prompt and targeted revascularization strategy.

The present study has a few limitations. First, it had a small sample size. Second, a mismatch existed between the number of patients presenting to EDs with chest pain nationwide and the number of EDs that have the capability to perform and interpret these types of examinations. In addition, T2W–fast spin echo is a pulse sequence with an inherently lower signal-to-noise ratio than other CMR sequences, such as delayed enhancement. Because of this, although it was quite specific for acute injury, the detection of myocardial edema had a modest sensitivity (9 of 13 cases). Another technical limitation of this pulse sequence relates to the fact that areas of slow flow in the LV cavity, particularly the apex, will present with increased signal intensity and can mimic areas of myocardial edema. However, although this is a theoretical possibility, we did not find this to be a problem in the present study, because the specificity was excellent (96%). Moreover, a recently described MRI pulse sequence can increase confidence in the detection of myocardial edema in patients with AMI and warrants further investigation.²³

In conclusion, the present study supports the feasibility of CMR in the ED, because CMR demonstrated a high diagnostic accuracy for the detection of patients with true ACS. The addition of T2W imaging and the evaluation of LVWT to the conventional CMR protocol improved diagnostic performance for detection of ACS by improving the differentiation of acute and chronic MI. In addition, CMR demonstrated additional value over that of the initial clinical risk assessment and TCRFs. Future studies will need to confirm these observations in a larger trial, determine the impact of CMR in clinical decision making, and assess the cost-effectiveness of CMR in the ED setting.

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Disclosures

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CLINICAL PERSPECTIVE

Cardiac magnetic resonance (CMR) is emerging as an alternative noninvasive diagnostic test for rapid and accurate assessment of patients with acute chest pain who present to the emergency room, particularly for patients with intermediate risk of developing an acute coronary syndrome. We demonstrated that CMR with T2-weighted imaging and left ventricular wall thickness analysis provided not only high diagnostic accuracy for detection of patients with acute coronary syndrome but also allowed the differentiation of patients with acute versus old myocardial infarction. Furthermore, the CMR changes presented before the rise of cardiac enzymes in patients with non–ST-segment myocardial infarction (6 ± 2 hours), and the combination of T2-weighted imaging, a signature of myocardial edema, and delayed hyperenhancement, which represents myocardial necrosis, allowed further characterization as unstable angina or non–ST-segment myocardial infarction. Finally, the CMR data provided significant incremental value over initial clinical assessment and traditional cardiac risk factors (odds ratio 129.4, 95% confidence interval 11.8 to >999.9). These data suggest that a 30-minute CMR protocol is feasible and accurate in the emergency department setting. Future studies will need to determine the impact of CMR in clinical decision making and assess the cost-effectiveness of CMR in the emergency department setting.