The Diagnostic Accuracy of 64-Slice Computed Tomography Coronary Angiography Compared With Stress Nuclear Imaging in Emergency Department Low-Risk Chest Pain Patients

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Study objective: We compared the accuracy of multidetector computed tomography (CT) coronary angiography with stress nuclear imaging for the detection of an acute coronary syndrome or 30-day major adverse cardiac events in low-risk chest pain patients.

Methods: This was a prospective study of the diagnostic accuracy of myocardial perfusion imaging and multidetector CT in low-risk chest pain patients. The target condition was an acute coronary syndrome (confirmed >70% coronary stenosis on coronary artery catheterization) or major adverse cardiac events within 30 days. Patients were low risk by Reilly/Goldman criteria and had negative serial ECGs and cardiac markers. All had both rest/stress sestamibi nuclear imaging and multidetector CT. Patients with abnormal stress nuclear imaging results (reversible perfusion defects) or multidetector CT results (stenosis >50% or calcium score >400) were considered for cardiac catheterization, and those with discordant results had a greater than 30-day reevaluation (including ECG) by a cardiologist. All were followed up for evidence of major adverse cardiac events within 30 days by review of hospital records and structured telephone interview. Primary outcomes were the accuracy of multidetector CT and myocardial perfusion imaging for the detection of an acute coronary syndrome and 30-day major adverse cardiac events.

Results: Of the 92 patients, 7 (8%) were excluded because of uninterpretable multidetector CT scans. Of the remaining 85 study patients (49±11 years, 53% men), 7 (8%) were found to have the target condition, with all having significant coronary stenosis (88±9%) and none having myocardial infarction or major adverse cardiac events during 30 days. Stress nuclear imaging results were negative in 72 (85%) patients, and multidetector CT results were negative in 73 (86%) patients. The sensitivity of stress nuclear imaging was 71% (95% confidence interval [CI] 36% to 92%), and multidetector CT was 86% (95% CI 49% to 97%), and the specificity was 90% (95% CI 81% to 95%) and 92% (95% CI 84% to 96%), respectively. The negative predictive value of stress nuclear imaging and multidetector CT was 97% (95% CI 90% to 99%) and 99% (95% CI 93% to 100%), respectively, and the positive predictive value was 38% (95% CI 18% to 64%) and 50% (95% CI 25% to 75%), respectively.

Conclusion: The accuracy of multidetector CT is at least as good as that of stress nuclear imaging for the detection and exclusion of an acute coronary syndrome in low-risk chest pain patients. [Ann Emerg Med. 2007;49:125-136.]
Rapid advances in multidetector computed tomographic (CT) technology have allowed noninvasive coronary artery imaging. Studies comparing 64-slice multidetector CT with invasive coronary angiography have shown that multidetector CT performs well in the detection of significant coronary stenosis, with sensitivities ranging from 82% to 95% and specificities of 82% to 98%. The presence of coronary calcification in patients with acute chest pain has also been shown to be predictive of future cardiac events. However, there are no studies that compare the ability of multidetector CT to detect an acute coronary syndrome with traditional stress nuclear imaging in low-risk chest pain patients.

**Goals of This Investigation**

Our study objective was to compare the diagnostic accuracy of multidetector CT with traditional stress nuclear imaging for the detection of an acute coronary syndrome in ED low-risk chest pain patients.

**MATERIALS AND METHODS**

This was a prospective institutional review board–approved study comparing the diagnostic accuracy of multidetector CT and radionuclide rest/stress imaging in a convenience sample of low-risk chest pain patients. Study patients received a multidetector CT and a radionuclide stress test, thus allowing each patient to serve as his or her own control.

**Setting and Selection of Participants**

The setting of this study was a suburban teaching hospital with an annual ED census of 115,894 visits per year. The department included a 21-bed ED observation unit that has been operational for more than 10 years and is fully staffed by attending emergency physicians. A “low-risk” chest pain diagnostic protocol is used in the ED observation unit. All study patients had negative serial ECG and cardiac marker results in the ED and ED observation unit, as described below.

Patients were identified as study candidates by the initial emergency physician and then screened by trained research staff at their admission to the ED observation unit. Patient screening took place from 7:00 PM Sunday through 5:00 PM Friday (according to research staff and CT availability). Patients were excluded from the study if they had positive initial cardiac marker results or new ischemic ECG changes. Patients were also excluded from the study if they were younger than 18 years, pregnant, had known coronary artery disease (≥30% coronary stenosis), existing cardiomyopathy, congestive heart failure with an ejection fraction less than or equal to 45%, a contraindication to iodinated contrast or β-blocking drugs, atrial fibrillation or markedly irregular rhythm, renal insufficiency (creatinine ≥1.5 mg/dL), or had received CT imaging or contrast within the past 48 hours. Screening and data collection by trained research assistants began at study enrollment and occurred prospectively.

Patients were first treated in the ED and found to have symptoms suggestive of an acute coronary syndrome. “Suggestive” symptoms were included because up to one third of patients with an acute coronary syndrome do not present with chest pain. Suggestive symptoms included discomfort,
burning, and dyspnea. The term “chest pain” is used as a simplified descriptor of these patients. With criteria previously validated by Reilly et al., patients were identified as “low risk” according to their symptoms, examination results, and initial ECG findings. By these criteria, low-risk patients had no ECG evidence of acute infarction or ischemia (including new left bundle branch block), no pain that was worse than usual angina or like a previous myocardial infarction, no recent revascularization, no rales above both bases, and a systolic blood pressure that was greater than 110 mm Hg. In the ED, patients also had an initial chest radiograph and an initial set of cardiac markers (CK-MB and troponin I) to screen for non–ST-segment-elevation myocardial infarction or other major nonacute coronary syndrome conditions such as pneumothorax or pneumonia.

Study patients were admitted to the ED observation unit for the chest pain diagnostic protocol. The protocol consisted of cardiac monitoring and serial ECG and cardiac marker tests (CK-MB fraction, troponin I, and myoglobin) 4 hours after ED arrival. Positive test results were defined as dynamic ischemic ECG changes, positive CK-MB mass and index, or positive troponin I level. Patients whose myoglobin result was positive or whose CK-MB level was normal but doubled had a repeated ECG, CK-MB, and troponin I test 8 hours after ED arrival. If these results were negative, the patient then received an appropriate stress test, with sestamibi stress nuclear imaging, as well as a multidetector CT coronary angiography. To reduce the likelihood of β-blocker-induced chronotropic incompetence during stress testing, most patients (87%) underwent stress nuclear imaging before multidetector CT. The treating emergency physician, in concurrence with a consulting cardiologist, was provided with stress nuclear imaging and multidetector CT clinical readings. They selected patient management according to these combined results. It was not thought to be appropriate or necessary, so we chose to also follow a clinical outcome as a reference standard for disease or a surrogate marker of disease. The clinical outcome was major adverse cardiac events, for which all patients were followed up for at least 30 days from the index visit. Major adverse cardiac events was defined as an acute coronary syndrome, as defined above, the development of new Q waves on subsequent ECGs, new congestive heart failure or cardiogenic shock, major dysrhythmias (high-grade atrioventricular block, ventricular tachycardia, ventricular fibrillation), cardiac arrest, or death from an acute coronary syndrome.

Patients received a rest/stress nuclear imaging protocol. For rest imaging, a weight-adjusted dose of 99mTc-sestamibi (8 to 10 mCi) was injected, followed by image acquisition 10 minutes after injection. Two or more hours after rest injection, patients underwent symptom-limited standard exercise treadmill testing or a pharmacologic stress (dipyridamole intravenous injection at a dose of 0.57 mg/kg during 4 minutes) protocol. At peak exercise, a weight-adjusted dose of 99mTc-sestamibi (25 to 40 mCi) was injected, followed by image acquisition 30 minutes after injection. Patients with equivocal or probably abnormal supine stress nuclear imaging study results underwent prone imaging to minimize attenuation artifacts. The ECG response to exercise was categorized as either nonischemic or ischemic (>1 mm flat or downsloping ST-segment depression or sustained ventricular tachycardia). The clinical response to the emergency physician, in concurrence with a consulting cardiologist, was provided with stress nuclear imaging before multidetector CT. The treating emergency physician, in concurrence with a consulting cardiologist, was provided with stress nuclear imaging and multidetector CT clinical readings. They selected patient management according to these combined results. It was not thought to be appropriate or necessary, so we chose to also follow a clinical outcome as a reference standard for disease or a surrogate marker of disease. The clinical outcome was major adverse cardiac events, for which all patients were followed up for at least 30 days from the index visit. Major adverse cardiac events was defined as an acute coronary syndrome, as defined above, the development of new Q waves on subsequent ECGs, new congestive heart failure or cardiogenic shock, major dysrhythmias (high-grade atrioventricular block, ventricular tachycardia, ventricular fibrillation), cardiac arrest, or death from an acute coronary syndrome.

Data Collection and Processing

The collection of data for all patient characteristics and study outcomes occurred prospectively and began at study enrollment with a standardized case report form. Data were collected by trained research assistants or study physicians. Data validity was cross-checked with double data entry methods.

The target conditions being tested for in this study were an acute coronary syndrome on the index visit and major adverse cardiac events within 30 days of the index visit. Acute coronary syndromes encompass any of 3 conditions: an ST-segment-elevation myocardial infarction, a non–ST-segment-elevation myocardial infarction, and unstable angina. Because serial testing essentially excludes the first 2 conditions, the primary condition being tested for was unstable angina. Defining unstable angina according to symptoms alone is problematic and would lead to several false-positive cases. Alternatively, stress nuclear imaging results could not be used as a reference standard because stress nuclear imaging itself is an imperfect test, and in this study it was being compared with multidetector CT for their respective abilities to detect an acute coronary syndrome. In this study, patients with positive testing suggestive of unstable angina underwent cardiac catheterization for confirmation of the diagnosis. As such, unstable angina was defined by cardiac catheterization showing at least 70% coronary artery stenosis. Coronary stenosis was confirmed by quantitative coronary angiography (QuantCor Quantitative Coronary Angiography, Pie Medical Systems, Masstricht, Netherlands). Catheterization of all low-risk patients was not thought to be appropriate or necessary, so we chose to also follow a clinical outcome as a reference standard for disease or a surrogate marker of disease. The clinical outcome was major adverse cardiac events, for which all patients were followed up for at least 30 days from the index visit. Major adverse cardiac events was defined as an acute coronary syndrome, as defined above, the development of new Q waves on subsequent ECGs, new congestive heart failure or cardiogenic shock, major dysrhythmias (high-grade atrioventricular block, ventricular tachycardia, ventricular fibrillation), cardiac arrest, or death from an acute coronary syndrome.

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exercise was categorized as either nonischemic or ischemic (typical angina pectoris during exercise). Hemodynamic characteristics, including age-adjusted heart rate response, and Duke treadmill score were also recorded.

Qualitative and semiquantitative visual analysis was made by a board-certified nuclear physician using a 17-segment model, according to previously published methods. Each of the 17 segments was classified into a qualitative severity scale. All study images were read by a nuclear physician involved in the patients’ care and later by a second blinded nuclear physician. Both were blinded to multidetector CT results. Discordant readings were adjudicated by consensus with a third physician. Images were classified as abnormal or probably abnormal if there were significant reversible perfusion defect(s) and normal or probably normal if reversible defects were not present.

All patients were scanned on a 64-slice multidetector CT scanner (Sensation 64 Cardiac; Siemens Medical Systems, Forchheim, Germany), as previously described. Patients were given 50 to 100 mg of atenolol 1 hour before multidetector CT imaging or intravenous metoprolol (5 to 30 mg) as needed to achieve a target pulse rate less than or equal to 65 beats/min. Nitroglycerin 0.4 mg sublingual was given 1 minute before image acquisition. Pulse rate, ECG, and blood pressure were monitored before, during, and after imaging. An initial unenhanced scan was performed for calcium scoring. A contrast-enhanced scan (Visipaque; GE Healthcare, Waukesha, WI) was obtained using 100 mL of contrast injected through an antecubital vein at 5 mL/s, followed by 20 mL of contrast injected at 3 mL/s, followed by a 40-mL saline solution chaser. Timing was performed with a program sensing a threshold of 20 Hounsfield units in a region of interest in the aorta, using a single breath-hold cranial-to-caudal acquisition (aortic arch to inferior heart border). The scan parameters were $32 \times 0.6$ mm collimation with dual focal spots per detector row, tube rotation time 330 ms, table feed/rotation 3.8 mm, tube voltage 120 mV, effective mAs 750 to 850, pitch 0.2, volumetric CT dose index 59 mGy. Tube current modulation was used to decrease tube output during ECG systole in the majority of patients. ECG-gated data sets were reconstructed automatically at 65% and 55% of the R-R cycle length, and additional reconstruction windows were created after examination of data sets if motion artifacts were present. In addition, 2-mm- and 3-mm-thick reconstruction data sets were created with skin-to-skin field-of-view coverage for evaluation of the lung parenchyma and mediastinum.

Calcium scores were analyzed with SYNGO software (Siemens Medical Systems). Multidetector CT angiograms were analyzed on a 3-dimensional workstation (Aquarius; TeraRecon, San Mateo, CA). Scans were analyzed by a board-certified cardiologist with level 3 clinical competence in cardiovascular CT imaging who was unaware of the clinical data and blinded to the results of the stress nuclear imaging. A 15-segment model of the coronary tree was used. Each lesion was identified by using maximum intensity and multiplanar reconstruction techniques transversely and along multiple longitudinal axes. Lesions were classified by a qualitative severity scale: 0 = no stenosis, 1 = 1% to 25% stenosis, 2 = 26% to 50% stenosis, 3 = 51% to 70% stenosis, 4 = 71% to 99% stenosis, 5 = total occlusion. Multidetector CT stenosis of greater than 50% was classified as positive. Multidetector CT was also classified as positive if there was coronary calcium encroachment on the lumen in transaxial multiplanar reconstructions greater than 50% or a coronary artery calcium score greater than 400. Patients with uninterpretable images were excluded from this study.

Sensitivity, specificity, positive predictive value, and negative predictive value were determined for CT and stress nuclear imaging separately, including 95% confidence intervals (CIs). Patients with the reference outcome are shown separately from patients without for demographics, ECG data, stress nuclear imaging, and CT data. With few reference outcome patients, statistical comparisons were not completed between these 2 groups. Statistical analyses were completed using SAS version 9.1 (SAS Institute, Inc., Cary, NC).

**RESULTS**

Patient enrollment occurred during 7 months, from September 2004 to March 2005. Throughout the study period, there were 68,367 ED visits, of which 2,182 patients (age 58±16 years; 46% men) were sent to the ED observation unit for the chest pain diagnostic protocol; 13% were subsequently admitted.

**Characteristics of Study Subjects**

Ninety-six patients were enrolled with consent during the study period. Four patients did not complete the protocol and were excluded. Reasons for exclusion included computer technical failure and no data acquisition (1), cancellation of CT (1), treadmill testing without nuclear imaging (1), and stress echo testing (1). Additionally, 7 patients’ CT angiography images were uninterpretable and were also excluded. Reasons for uninterpretable images were motion artifact (3), poor contrast to noise (2), machine artifacts (1), and ECG gating deficiency (1). No patients were excluded because of positive serial ECG or cardiac marker results preceding imaging. Follow-up information was obtained by structured review of hospital records for 30-day outcomes for all patients. Structured telephone interview was completed for 83 (98%) patients at a median interval of 76 days (range 54 to 91 days); the remaining 2 patients were queried in the hospital database and government death registry, with no reference outcomes identified. Both of these patients had normal multidetector CT and stress nuclear imaging results.

Among the 85 study patients with interpretable images, the average age was 49±11 years, with 53% being men (Table 1). Chest pain was the presenting chief complaint in 94% of patients. Admission ECG results were normal in 60% of patients, with T-wave flattening in 34% and Q waves present in...
5.9% of results. Patients had an average probability of acute cardiac ischemia of 23%±14% according to Acute Cardiac Ischemia Time Insensitive Predictive Instrument (ACI-TIPI) scores, and patients had an average Thrombolysis in Myocardial Infarction (TIMI) risk score of 0.8 (±0.8).²⁰⁻²²

Main Results

Overall, 7 patients (8%) met criteria for a final reference outcome, all with a acute coronary syndrome defined by significant coronary artery stenosis. No patients had myocardial infarction and no patients had subsequent 30-day major adverse cardiac events. All 7 underwent cardiac catheterization, 6 during infarction and no patients had subsequent 30-day major adverse outcome, all with an acute coronary syndrome defined by Acute Cardiac Ischemia Time Insensitive Predictive Instrument (ACI-TIPI) score, 83% of patients were low risk and 17% were intermediate risk. Sestamibi perfusion imaging result was abnormal in 11% of patients, probably abnormal in 5%, probably normal in 34%, and normal in 51%. Of patients with a positive reference outcome, imaging result was abnormal or probably abnormal in 5 of 7 patients (71%). Eight patients had normal perfusion imaging results but achieved a submaximal pulse rate (average 74% predicted maximal pulse rate), with 1 of these having significant coronary artery stenosis (Table 4).

Eighty-seven percent of patients underwent stress nuclear imaging before multidetector CT. The average pulse rate before preparation for multidetector CT was 74±12 beats/min. In preparation for multidetector CT imaging, oral atenolol (88±22 mg) was initiated in the ED in 13 patients (12%), and intravenous metoprolol (27±17 mg) was administered in the multidetector CT holding area in 75 patients (88%) before scan acquisition. There were no adverse events related to β-blockade or iodinated contrast administration. Coronary calcium score was greater than 100 in 9 (11%) patients, with 2 of these having significant coronary artery stenosis. Of the seventy-six patients (89%) with calcium scores less than 100, 5 had significant coronary artery stenosis. Multidetector CT found greater than 100 in 9 (11%) patients, with 2 of these having significant coronary artery stenosis. Of the seventy-six patients (89%) with calcium scores less than 100, 5 had significant coronary artery stenosis. Multidetector CT found greater than 100 in 9 (11%) patients, with 2 of these having significant coronary artery stenosis. Of the seventy-six patients (89%) with calcium scores less than 100, 5 had significant coronary artery stenosis. Multidetector CT found greater than 100 in 9 (11%) patients, with 2 of these having significant coronary artery stenosis. Of the seventy-six patients (89%) with calcium scores less than 100, 5 had significant coronary artery stenosis. Multidetector CT found greater than 100 in 9 (11%) patients, with 2 of these having significant coronary artery stenosis. Of the seventy-six patients (89%) with calcium scores less than 100, 5 had significant coronary artery stenosis. Multidetector CT found greater than 100 in 9 (11%) patients, with 2 of these having significant coronary artery stenosis. Of the seventy-six patients (89%) with calcium scores less than 100, 5 had significant coronary artery stenosis.
artery found on cardiac catheterization. The multidetector CT image quality in this patient was limited by poor contrast opacification and significant background noise (Figure 4). Of the 65 patients (76%) with less than 25% stenosis on multidetector CT, none were found to have significant coronary artery disease (Figure 2). In comparing multidetector CT with cardiac catheterization, of 12 patients who had cardiac catheterization, 7 had coronary stenosis greater than 70%, with CTA being positive (>50% stenosis) in 6 of these 7 cases and falsely negative in 1 (discussed above). Of the 5 catheterization cases that did not have greater than 70% coronary stenosis (or 30-day clinical outcomes), CTA result was positive in 3 and negative in 2.

LIMITATIONS

This study has several important limitations to consider. Using the results of the multidetector CT and stress nuclear imaging to determine who would undergo angiography or who would have a follow-up appointment may have introduced an incorporation bias. Because we did not feel it ethical to withhold test results from those treating patients, knowledge of multidetector CT or stress nuclear imaging results may have also introduced a referral bias. Because cardiac catheterization did not occur in all low-risk patients, there is an inherent referral bias based on positive noninvasive diagnostic test results. This bias has been well reported for both stress ECG and stress nuclear testing. If the accuracy of multidetector CT is comparable to coronary catheterization, as has been suggested in preliminary studies, then performing both stress nuclear imaging and multidetector CT on all patients may have decreased referral bias. Correcting for this bias would decrease the sensitivity of each test. Attempts to minimize this were made using 30-day clinical outcomes. The use of a surrogate clinical marker, instead of an invasive criterion standard, is another limitation. However, this approach is reasonable in studies of diagnostic tests in which the prevalence of disease is low. Limiting the study to patients who agree to participate and to hours in which research assistants could enroll patients made the study population a convenience sample, and this may have introduced sampling bias. However, in comparing all chest pain observation unit patients with study patients, the 2 groups were comparable in terms of their admission rate (13% versus 14%) and percentage of male patients (46% versus 53%), with overlap in age distributions (58±16 years versus 49±11 years). Exclusion of patients with uninterpretable images may have overestimated the diagnostic accuracy for multidetector CT. Our rate of uninterpretable studies (8%), however, is consistent with the average rates cited in the literature. The relatively small sample size of this study limits the ability to fully address safety. Feasibility was not addressed by this study; a cohort study would be needed for that. Finally, issues of cost, length of stay, clinical impact, or long-term

Figure 1. Combined outcome of multidetector CT and stress nuclear imaging in the detection of an acute coronary syndrome. Positive multidetector CT: Luminal stenosis >50% in any segment or CAC >400. Positive stress nuclear imaging: Significant reversible perfusion defects present. MDCT, multidetector computed tomography; SNI, stress nuclear imaging; ACS, acute coronary syndromes.
prognosis was not addressed in this study. These issues and the relative clinical value of multidetector CT, relative to traditional stress nuclear imaging, would be better answered by a randomized controlled study. These are fertile areas for future studies.

Table 2. Summary of patients with discordant test results.

<table>
<thead>
<tr>
<th>Age, Sex</th>
<th>TIMI Risk</th>
<th>ACI-TIPI</th>
<th>Stress ECG</th>
<th>Stress Nuclear Result</th>
<th>PMHR %, Duke Score</th>
<th>CAC</th>
<th>MDCT</th>
<th>Re-evaluation or Coronary Artery Catheterization*</th>
<th>30-Day MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDCT negative, SNI positive (no cardiac catheterization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>44 F</td>
<td>1</td>
<td>3</td>
<td>Neg</td>
<td>Possible ischemia</td>
<td>102, Low</td>
<td>0</td>
<td>Normal</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>67 M</td>
<td>1</td>
<td>30</td>
<td>Neg</td>
<td>Possible ischemia</td>
<td>105, Intermediate</td>
<td>47</td>
<td>LAD 1%–25% stenosis</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>34 M</td>
<td>0</td>
<td>7</td>
<td>Pos</td>
<td>Normal perfusion</td>
<td>89, Intermediate</td>
<td>0</td>
<td>Normal</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>53 M</td>
<td>1</td>
<td>23</td>
<td>Neg</td>
<td>Possible ischemia</td>
<td>73, Intermediate</td>
<td>0</td>
<td>LAD 25%–50%</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>58 F</td>
<td>0</td>
<td>49</td>
<td>Neg</td>
<td>Possible ischemia</td>
<td>104, Low</td>
<td>0</td>
<td>Normal</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>MDCT negative, SNI positive (cardiac catheterization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58 M</td>
<td>1</td>
<td>43</td>
<td>Neg</td>
<td>Moderate ischemia</td>
<td>95, Low</td>
<td>6</td>
<td>Normal</td>
<td>Normal†</td>
<td>Neg</td>
</tr>
<tr>
<td>46 M</td>
<td>2</td>
<td>25</td>
<td>Neg</td>
<td>Moderate ischemia</td>
<td>74, Intermediate</td>
<td>15</td>
<td>RCA 25%–50%</td>
<td>RCA 95%†</td>
<td>Pos</td>
</tr>
<tr>
<td>MDCT positive, SNI negative (no cardiac catheterization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>47 M</td>
<td>1</td>
<td>N/A†</td>
<td>Neg</td>
<td>Normal</td>
<td>103, Low</td>
<td>0</td>
<td>Small PDA 50% stenosis</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>63 F</td>
<td>0</td>
<td>36</td>
<td>Neg</td>
<td>Normal</td>
<td>107, Low</td>
<td>0</td>
<td>RCA 50%–75% stenosis</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>63 F</td>
<td>1</td>
<td>36</td>
<td>Neg</td>
<td>Normal</td>
<td>92, Low</td>
<td>194</td>
<td>Focal Ca+ LAD, RCA 50%</td>
<td>Neg*</td>
<td>Neg</td>
</tr>
<tr>
<td>MDCT positive, SNI negative (cardiac catheterization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60 M</td>
<td>2</td>
<td>43</td>
<td>Neg</td>
<td>Normal</td>
<td>73, Low</td>
<td>92</td>
<td>RCA 25%–50%</td>
<td>RCA 30%</td>
<td>Pos</td>
</tr>
<tr>
<td>48 M</td>
<td>0</td>
<td>7</td>
<td>Pos</td>
<td>Probable Normal</td>
<td>88, Low</td>
<td>0</td>
<td>LAD 50%–75% Diag &gt;75%</td>
<td>RCA 90%†</td>
<td>Pos</td>
</tr>
<tr>
<td>40 M</td>
<td>1</td>
<td>7</td>
<td>Neg</td>
<td>Normal</td>
<td>99, Low</td>
<td>1</td>
<td>RCA 50%–75%</td>
<td>RCA 40%†</td>
<td>Neg</td>
</tr>
</tbody>
</table>

LAD, Left anterior descending; RCA, right coronary artery; PDA, posterior descending artery; Diag, diagonal branch artery.

*Reevaluation: return visit for medical history or examination findings suggestive of ACS or MACE and repeated ECG test to detect evidence of ACS/MACE. Additional testing not indicated in any cases.
†Underwent cardiac catheterization 1 year after study enrollment because of recurrent chest pain. Single-vessel mild disease (LAD 40% proximal) noted.
‡Catheterization results.
§ACI-TIPI score not applicable, because of baseline ECG repolarization abnormalities.

Table 3. Myocardial perfusion imaging and multidetector CT accuracy (n=85).

<table>
<thead>
<tr>
<th>Imaging Method</th>
<th>Sensitivity (n)</th>
<th>Specificity (n)</th>
<th>PPV (n)</th>
<th>NPV (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress nuclear imaging (95% CI)</td>
<td>71% (5/7) (36%-92%)</td>
<td>90% (70/78) (81%-95%)</td>
<td>38% (5/13) (18%-64%)</td>
<td>97% (70/72) (90%-99%)</td>
</tr>
<tr>
<td>Multidetector CT (95% CI)</td>
<td>86% (6/7) (49%-97%)</td>
<td>92% (72/78) (84%-96%)</td>
<td>50% (6/12) (25%-75%)</td>
<td>99% (72/73) (93%-100%)</td>
</tr>
</tbody>
</table>

DISCUSSION

This study shows that multidetector CT has accuracy that is comparable to that of stress nuclear imaging for the detection of an acute coronary syndrome in ED low-risk chest pain patients. As such, it appears to be a reasonable alternative to stress nuclear imaging in a “low-risk” ED chest pain population after negative serial ECG and cardiac marker results.

During the last 2 decades, there has been a progressive evolution in the management of ED chest pain patients at risk for an acute coronary syndrome. Traditionally, these patients were admitted to an inpatient hospital bed for 2 to 3 days to complete a diagnostic evaluation that usually consisted of serial enzyme levels, ECG results, and stress testing. Subsequently, chest pain observation units were developed to provide accelerated diagnostic protocols for chest pain patients.4,26,27 Compared with traditional admission, these protocols have been shown to decrease the length of stay to roughly half a day, decrease cost, and lead to fewer missed myocardial infarctions,
with comparable clinical outcomes.\textsuperscript{5,28-32} With this approach, roughly 80% of these patients are discharged home after completion of their protocol. The advent of multidetector CT coronary angiography offers to take this evolution 1 step farther with a technology that appears to be as accurate as stress nuclear imaging.

Recently, there has also been an evolution in cardiac CT imaging. Early studies suggested that normal to minimal coronary artery calcification alone was sufficient to accurately risk-stratify ED patients with acute chest pain, with reported sensitivities of 96% to 100% for the detection of significant cardiac events.\textsuperscript{10} Five of the 7 patients in the current study with catheterization-proven severe coronary artery disease had coronary artery calcification scores less than 100, and 2 had no detectable coronary calcium (ie, CAC=0). Not surprisingly, these 5 patients were young (average age 48.6 years) but with multiple coronary risk factors. These findings suggest that the addition of multidetector CT coronary angiography to CAC score alone is an important and necessary adjunct for the triage of this low-risk, often younger, patient population. Early studies of multidetector CT were done using 16-slice CT machines and have been followed by studies using 64-slice CT machines. We recently reported the accuracy of 64-slice multidetector CT compared with invasive coronary angiography in the detection of greater than 50% stenosis and found multidetector CT to be 95% sensitive and 90% specific.\textsuperscript{6} In that study population, significant stenosis was present in 57% of patients. Bayes’ theorem has been used to describe how a test may perform differently, depending on the prevalence of disease in the population to which it is applied. According to this principle, the current study adds to the evaluation of multidetector CT imaging by evaluating its diagnostic performance in a “low-prevalence” population. In the current study, the prevalence of coronary stenosis was 8%, and multidetector CT was able to identify 86% of patients (6/7) with disease, with a specificity of 92%, which suggests that multidetector CT performs well in both high- and low-prevalence populations.

The accuracy of stress nuclear imaging in our study (sensitivity 71%, specificity 92%) was slightly lower than that reported in the literature. Previous reports have demonstrated that the selective addition of stress nuclear imaging to a comprehensive ED chest pain evaluation protocol excludes

### Table 4. Stress imaging results.

<table>
<thead>
<tr>
<th>Stress imaging results</th>
<th>Reference Positive, N = 7 (8%)</th>
<th>Reference Negative, N = 78 (92%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stress test performed (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graded exercise stress test</td>
<td>6 (86)</td>
<td>71 (91)</td>
</tr>
<tr>
<td>Persantine</td>
<td>1 (14)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td><strong>Stress ECG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise duration, min</td>
<td>7.5±2</td>
<td>9.1±2</td>
</tr>
<tr>
<td>Peak pulse rate, beats/min</td>
<td>132±42</td>
<td>155±26</td>
</tr>
<tr>
<td>Percentage age-adjusted maximum pulse rate</td>
<td>84±9</td>
<td>95±8</td>
</tr>
<tr>
<td>Submaximal pulse rate, No. (%)</td>
<td>3 (43)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Ischemic ST changes, No. (%)</td>
<td>2 (29)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Ischemic clinical response, No. (%)</td>
<td>3 (43)</td>
<td>19 (24)</td>
</tr>
<tr>
<td><strong>Duke score (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>4 (57)</td>
<td>59 (76)</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>2 (29)</td>
<td>13 (17)</td>
</tr>
<tr>
<td><strong>Stress nuclear imaging protocol results (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal perfusion (reversible defect)</td>
<td>5 (71)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Probably abnormal perfusion*</td>
<td>0</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Probably normal</td>
<td>2 (29)</td>
<td>27 (35)*</td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>43 (55)</td>
</tr>
</tbody>
</table>

*Includes 1 patient with normal perfusion and positive clinical and electrocardiographic ischemic response.
†Includes 8 patients with normal perfusion and submaximal pulse-rate response.

![Figure 2. Dual-axis distribution of multidetector CT stenosis percentage and patients with a positive catheterization (number at end of bar).](image-url)
acute coronary syndrome with a sensitivity of 99% and specificity of 87%. Our diagnostic accuracy, however, is comparable to a recent stress nuclear imaging meta-analysis of 19 studies that reported a sensitivity and specificity of 87% and 73%, respectively, for detection of greater than 50% catheterization-proven stenosis. Our lower sensitivity is likely attributed to the overall low prevalence of disease (7 ACS-positive cases), as well as our decision to define patients with normal stress perfusion (without ECG or clinical evidence of ischemia) and submaximal pulse rate response as “probably normal” studies. One of the 2 false-negative stress nuclear imaging results occurred in a patient who achieved 74% peak predicted pulse rate (while receiving long-term β-blocker therapy), whereas the other occurred in a patient with stenosis (70%) localized to a large diagonal branch vessel.

Multidetector CT and stress nuclear imaging technologies differ in that stress nuclear imaging provides “physiologic” perfusion information intended to identify anatomic coronary stenosis, whereas multidetector CT shows “anatomic” coronary stenosis without perfusion data. Recent developments suggest that multidetector CT may ultimately be capable of providing both perfusion and anatomic information. However, we did not find that the lack of perfusion information limited the ability of multidetector CT to identify patients with an acute coronary syndrome. Additionally, multidetector CT is capable of identifying aortic dissection or pulmonary embolus by modifying the scan protocol and contrast dosing. In fact, this “triple rule-out” protocol was used on a discretionary basis in 35 of the 85 study patients; none were found to have major acute pathology. For suboptimal image quality, stress nuclear imaging offers an advantage because patients may be reimaged while the isotope remains active, with different positioning and acquisition techniques to overcome poor-quality images. Unfortunately, reimaging multidetector CT patients involves repeated doses of contrast and radiation, making reimaging less feasible. It is hoped that, as multidetector CT technology matures, this will be less of a problem.

Although others have reported good diagnostic outcomes in chest pain protocols in which a stress ECG is done without imaging, we chose to compare multidetector CT against both stress ECG and stress nuclear information. In our study, performing a stress ECG without imaging would have missed 5 of the 7 patients found to have an acute coronary syndrome. Because this is a new technology, we also thought that it was safest to perform serial cardiac marker and ECG tests in combination with imaging, rather than imaging alone. Further studies may disprove the need for this combination. We concur with the American Heart Association advisory committee about the need for testing beyond serial markers in a low-risk chest pain population. We had previously found that serial cardiac marker levels identified only 19% of acute coronary syndrome patients in this “low-risk” population, whereas stress imaging identified 60% of these acute coronary syndrome patients. Recent studies suggest that cardiac marker protocols of 2 hours or 90 minutes are effective in ruling out myocardial necrosis. It is possible that combining these rapid marker protocols with multidetector CT will allow the emergency physician to provide a completed evaluation in 2 to 5 hours while the patient remains within the ED. This combined approach merits further study.

Although our reference outcome was defined as any patient with an acute coronary syndrome and 30-day major adverse cardiac events, all positive reference outcomes were cardiac catheterization stenosis greater than 70%. Because no patients had 50% to 70% stenosis, using a catheter stenosis greater than 50% would not have changed our results. We assume that this stenosis caused the symptoms that prompted the patient to seek treatment and accounted for the patient’s unstable angina. In this study, there were also 8 patients with discordant multidetector CT and stress nuclear imaging results who did not undergo cardiac catheterization according to their overall clinical characteristics.
None of these patients had highly abnormal multidetector CT or stress nuclear imaging results, and none were found to have evidence of a missed diagnosis on follow-up.

From the results of this study and previous studies comparing multidetector CT with cardiac catheterization, it seems prudent to consider further testing, such as additional stress nuclear imaging, for any patient with greater than 25% stenosis on multidetector CT or any patient with a coronary artery calcium score greater than 100.6 It also seems reasonable to consider cardiac catheterization of any patient with greater than 70% stenosis on multidetector CT.

In defining an acute coronary syndrome, we chose to use objective findings, such as coronary stenosis, rather than a broader clinical diagnosis of unstable angina. This approach has been encouraged in a consensus document on standardized reporting criteria for studies of an acute coronary syndrome.14 This approach may have resulted in fewer patients with an acute coronary syndrome because some patients diagnosed with “unstable angina” are diagnosed according to their medical history alone. However, we believed that the combination of multidetector CT and stress nuclear imaging results with rigorous 30-day outcomes provided a more reliable study diagnosis.

In conclusion, in this prospective study of ED low-risk chest pain observation unit patients, multidetector CT performed at least as well as stress nuclear imaging in the detection and exclusion of an acute coronary syndrome after myocardial infarction had been ruled out.

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REFERENCES


