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A Randomized Controlled Trial of Multi-Slice Coronary Computed Tomography for Evaluation of Acute Chest Pain

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- Objectives** This study sought to compare the safety, diagnostic efficacy, and efficiency of multi-slice computed tomography (MSCT) with standard diagnostic evaluation of low-risk acute chest pain patients.
- Background** Over 1 million patients have emergency center evaluations for acute chest pain annually, at an estimated diagnostic cost of over \$10 billion. Multi-slice computed tomography has a high negative predictive value for exclusion of coronary artery stenoses.
- Methods** We randomized patients to MSCT (n = 99) versus SOC (n = 98) protocols. The MSCT patients with minimal disease were discharged; those with stenosis >70% underwent catheterization, whereas cases with intermediate lesions or non-diagnostic scans underwent stress testing. Outcomes included: safety (freedom from major adverse events over 6 months), diagnostic efficacy (clinically correct and definitive diagnosis), as well as time and cost of care.
- Results** Both approaches were completely (100%) safe. The MSCT alone immediately excluded or identified coronary disease as the source of chest pain in 75% of patients, including 67 with normal coronary arteries and 8 with severe disease referred for invasive evaluation. The remaining 25% of patients required stress testing, owing to intermediate severity lesions or non-diagnostic scans. During the index visit, MSCT evaluation reduced diagnostic time compared with SOC (3.4 h vs. 15.0 h, $p < 0.001$) and lowered costs (\$1,586 vs. \$1,872, $p < 0.001$). Importantly, MSCT patients required fewer repeat evaluations for recurrent chest pain (MSCT, 2 of 99 (2.0%) patients vs. SOC, 7 of 99 (7%) patients; $p = 0.10$).
- Conclusions** Multi-slice computed tomographic coronary angiography can definitively establish or exclude coronary disease as the cause of chest pain. However, inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations. (Study of Coronary Artery Computed Tomography to Diagnose Emergency Chest Pain CR; <http://clinicaltrials.gov/ct/show/NCT00273832?order=1>; NCT00273832) (J Am Coll Cardiol 2007;49:863-71) © 2007 by the American College of Cardiology Foundation



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Failure to diagnose myocardial ischemia as the cause of acute chest pain has serious public health consequences and causes substantial malpractice litigation. Although over 50% of acute chest pain cases represent non-cardiac conditions, symptoms are often atypical and clinical presentations frequently overlap, contributing to the challenge of rapidly establishing a correct diagnosis (1-4). Accordingly, emergency department (ED) chest pain units employ standard of care (SOC) "rule-out myocardial infarction" diagnostic algorithms with serial electrocardiograms

and cardiac enzymes followed by rest and/or stress-imaging studies (5-10). This approach has reduced diagnostic error but is time consuming, expensive, and not always definitive.

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Multi-slice computed tomographic angiography (MSCT) provides high-resolution coronary angiograms noninvasively. Previous studies established that coronary MSCT is highly accurate for delineation of the presence and severity of coronary atherosclerosis (11-15). Its high negative predictive value for exclusion of significant coronary artery stenoses makes it potentially attractive for evaluation of a low-risk chest pain population. Accordingly, this study in ED patients with acute chest pain was designed to

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Abbreviations and Acronyms

ECG = electrocardiogram

ED = emergency department

MACE = major adverse cardiac event

MSCT = multi-slice computed tomography

SOC = standard of care

compare the diagnostic safety, efficacy, and efficiency of 2 diagnostic strategies: initial MSCT angiography versus a SOC nuclear stress testing protocol.

Methods

We enrolled 203 patients presenting to the ED between March 2005 and September 2005 with acute chest pain who

were deemed “low-risk.” Eligibility criteria included: 1) chest pain or angina equivalent symptoms compatible with ischemia during the past 12 h; 2) age ≥ 25 years; and 3) a prediction of a low risk of infarction and/or complications according to established criteria (16,17). Exclusion criteria included: 1) known coronary artery disease; 2) electrocardiograms diagnostic of cardiac ischemia and/or infarction (significant Q waves, ST-segment deviations >0.5 mm, or T-wave inversion); 3) elevated serum biomarkers including creatine kinase-MB, myoglobin, and/or cardiac troponin I on initial and 4-h testing; 4) previously known cardiomyopathy, with estimated ejection fraction $\leq 45\%$; 5) contraindication to iodinated contrast and/or beta-blocking drugs; 6) atrial fibrillation or markedly irregular rhythm; 7) body

mass index ≥ 39 kg/m²; 8) renal insufficiency (creatinine ≥ 1.5 mg/dl); and 9) computed tomography imaging or contrast administration within the past 48 h. After determination that the time 0-h and 4-h electrocardiograms and serum biomarkers were normal, patients were randomized to either the MSCT or SOC protocols (Fig. 1). Enrollment was done 24 h/day, although MSCT and SPECT scanners were available only between 7:00 AM and 6:00 PM; waiting time until scanners were available and the costs incurred thereby were included in this analysis. The Human Investigation Committee of William Beaumont Hospital approved the study, and all patients gave informed consent.

MSCT angiography protocol. The MSCT coronary angiography was performed according to previously published methods (14). If not already receiving beta-blocking drugs, patients were administered atenolol 50 to 100 mg orally and/or metoprolol 5 to 30 mg intravenously to achieve a heart rate <65 beats/min. However, no patient was excluded from the MSCT exam because of heart rate above this target. Nitroglycerin 0.4 mg sublingual was given 1 min before image acquisition.

Imaging was performed on a 64-slice MSCT scanner (Sensation 64 Cardiac, Siemens Medical Systems, Forchheim, Germany). An initial non-enhanced electrocardiogram-gated scan was acquired for calcium scoring. A contrast-enhanced

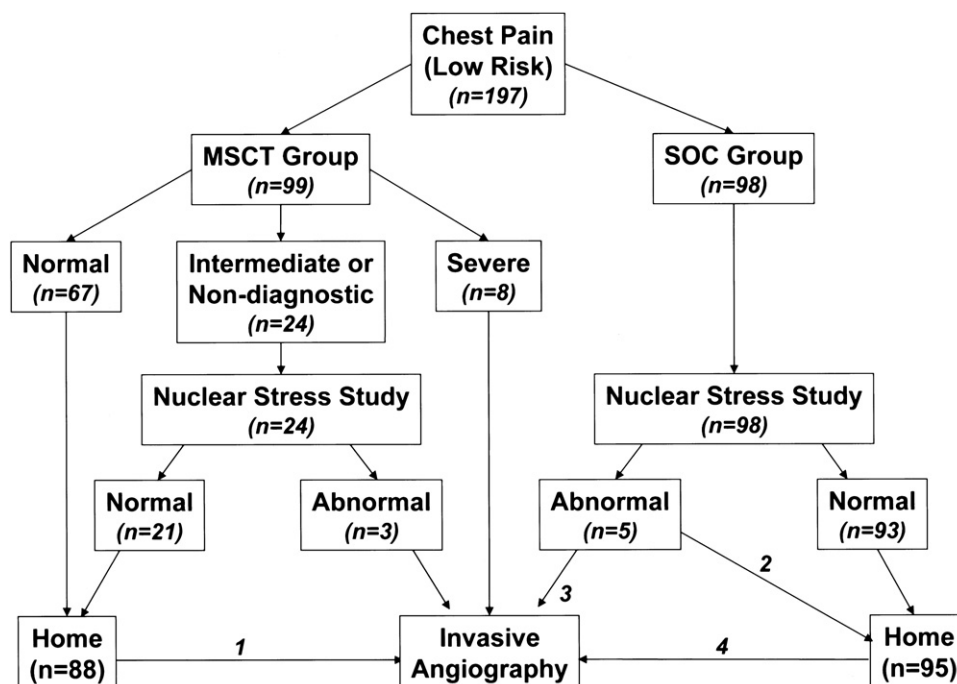


Figure 1 Study Algorithm

In this diagnostic algorithm, patients in the multi-slice computed tomography (MSCT) group with normal scans were eligible for immediate discharge. Patients with severe stenosis on MSCT (over 70%) were referred for invasive angiography, whereas those with intermediate lesions or nondiagnostic scans were referred for nuclear stress scans. Patients in the standard diagnostic group underwent nuclear stress scans and were eligible for discharge if normal or referred for invasive angiography if abnormal. SOC = standard of care diagnostic evaluation.

scan was obtained with 60 to 100 ml of contrast (Visipaque, GE Healthcare, Waukesha, Wisconsin) injected through an antecubital vein at 5 ml/s followed by 20 ml injected at 3 ml/s followed by a 40-ml saline chaser, with scan parameters as previously described (14). Estimated effective radiation dose was 13 milliSieverts (mSv) for men and 18 mSv for women. Electrocardiogram-gated datasets were reconstructed automatically at 65% of the R-R cycle length, with additional reconstructions as needed. Further 2-mm-thick and 3-mm-thick reconstruction data sets were reconstructed for evaluation of the mediastinum and lungs, which were read on an emergency basis by radiology department physicians.

Angiographic analyses. The MSCT scans were analyzed according to previously published methodology (14), by a single experienced observer blinded to other findings (J.G., M.G., or G.R.). The MSCT angiographic analysis was performed employing a previously described 15-segment model of the coronary tree (18). Lesions were classified by the maximal luminal diameter stenosis according to a qualitative severity scale: 0 = no stenosis, 1 = 1% to 25% stenosis, 2 = 26% to 50%, 3 = 51% to 70%, 4 = 71% to 99%, and 5 = total occlusion.

In those patients referred for invasive angiography, a single blinded observer performed quantitative angiographic analysis of stenosis severity with an automated edge-detection system (QuantCor.QCA, Pie Medical Systems, Maastricht, the Netherlands).

SOC diagnostic protocol. Patients underwent serial electrocardiograms and cardiac biomarkers (creatinine kinase-MB, troponin I, and myoglobin; Advia Centaur assay, Bayer Healthcare, Tarrytown, New York) at 4 and 8 h after their baseline studies. Cardiac biomarker results were classified as abnormal for: creatine kinase-MB >5 ng/ml, troponin I ≥ 1.5 ng/ml, and myoglobin ≥ 98 ng/ml.

Standard same-day rest-stress myocardial perfusion single-photon emission computed tomography imaging (nuclear stress testing) was performed according to established methodology (19). Stress test findings were categorized according to standard criteria, including: 1) symptoms (typical angina pectoris during exercise); 2) electrocardiographic response (>1 mm flat or downsloping ST-segment depression 80 ms after the J point or >1 mm of ST-segment elevation 80 ms after the J point or sustained ventricular tachycardia); and 3) single-photon emission computed tomography evidence of perfusion defects with qualitative and semiquantitative visual analysis and a standard 17-segment model (20). Nuclear stress test results were categorized as: 1) definitely normal, 2) probably normal, 3) probably abnormal, or 4) definitely abnormal.

Clinical decision algorithms. Clinical decisions regarding further testing and treatment were governed as outlined in Figure 1. In patients undergoing MSCT angiography: 1) if there were no coronary arterial narrowings >25% or calcium score over 100 Agatston U, patients were eligible for immediate discharge home; 2) patients with stenosis >70% were referred for invasive coronary angiography; and 3)

patients with intermediate lesions (stenosis 26% to 70% or calcium score over 100 Agatston U) or non-diagnostic scans (e.g., severe coronary calcifications, excessive motion artifact, or poor contrast-to-noise signals) underwent nuclear stress testing. In patients randomized to the SOC protocol: 1) those with normal serial electrocardiograms, cardiac biomarkers, and stress test were eligible for immediate discharge home; 2) patients who developed electrocardiogram (ECG) abnormalities, elevated biomarkers, or abnormal nuclear stress studies were referred for invasive angiography. For patients for whom the investigational protocol specified invasive angiography in either arm, investigators telephoned the patient's ED physician to recommend catheterization; however, the final clinical decision for invasive angiography was determined by the consulting cardiologist, as dictated by the hospital Human Investigation Committee of William Beaumont Hospital.

Data analysis. DIAGNOSTIC PERFORMANCE. We compared the evaluation strategies with respect to the following measures of diagnostic performance:

1. Safety, defined as absence of test complications and 6-month major adverse cardiovascular events (MACE) including cardiac death, acute myocardial infarction, or unstable angina.
2. Diagnostic efficacy, defined as the clinical ability of the primary testing strategy to correctly and definitively establish or exclude coronary artery disease as the cause of chest pain during the index visit, without requiring repeat cardiovascular testing over a 6-month follow-up period. In patients undergoing catheterization, a clinical diagnosis was judged correct if supported by the results of quantitative invasive angiography. For other patients, a clinically correct diagnosis was supported by the presence or absence of MACE events during the index visit or 6-month follow-up period. A primary diagnosis was considered definitive if no late repeat cardiovascular testing was ordered to verify that diagnosis, as determined by examination of hospital and office records after the 6-month follow-up period. Invasive angiography was not considered a repeat test if it was recommended by the primary diagnostic strategy.
3. Efficiency, measured as time to diagnosis (from randomization until completion of MSCT or nuclear scan interpretation) and costs during the index ED visit. To derive the ED cost of care, total patient charges in the ED calculated by the hospital billing department were multiplied by the hospital's ED cost-to-charge ratio. For patients undergoing both MSCT and nuclear stress testing, the additional stress testing time and costs were added to such cases. For patients randomized during periods when neither scanner was available (6:00 PM to 7:00 AM), the time and costs associated with waiting until scanners were available were included in the end point diagnostic time and costs.

Table 1 Demographic Analysis

Demographic Data	MSCT Group n = 99	Standard Diagnostic Group n = 98	p Value
Age (mean), yrs	48 ± 11 (47)	51 ± 12 (50)	0.08
Male	42 (43%)	56 (57%)	0.05
Weight (median), lbs	187 ± 43 (180)	191 ± 48 (188)	0.69
BMI	29 ± 5 (28)	29 ± 5 (28)	0.78
hsCRP at baseline (mean)	n = 71, 0.6 ± 1.9 (0.3)	n = 71, 0.6 ± 1.0 (0.3)	0.66
Hx hypertension	38 (39%)	37 (38%)	0.88
Hyperlipidemia	33 (34%)	37 (38%)	0.55
DM	8 (8.2%)	12 (12.2%)	0.35
Family history of early coronary disease	39 (40%)	43 (44%)	0.56
Current smoker	15 (15%)	20 (20%)	0.35
ASA in past 7 days	24 (24%)	28 (29%)	0.52
Chest pain in last 24 h	75 (77%)	64 (65%)	0.08
TIMI risk score, mean ± SD (median)	1.24 ± 0.8 (1.0)	1.33 ± 0.8 (1.0)	0.30
Goldman Riley criteria			
0—Very low risk	98 (100%)	97 (99.0%)	1.00
1—Low risk	0 (0%)	1 (1.0%)	
2—Moderate risk	0 (0%)	0 (0%)	

ASA = aspirin; BMI = body mass index; DM = diabetes mellitus; hsCRP = high-sensitivity C-reactive protein; Hx = history of; TIMI = Thrombolysis In Myocardial Infarction.

Statistical methods. To assign patients to each study arm, the study statistician created a randomization scheme in blocks ranging in size from 8 to 22, allowing for periodic balancing of the 2 randomization arms. The size of the block varied to prevent researchers’ knowledge of the next assignment at any given time. The SAS software version 9.1 (SAS Institute, Cary, North Carolina) was used for generating the randomization scheme.

Categorical variables were examined with a chi-square test where appropriate (expected frequency >5); otherwise a Fisher exact test was used. Data that were not normally distributed are shown as median and 25th to 75th percentiles. Other continuous variables are shown as mean ± 1 SD followed by the median. All continuous variables were examined with a Wilcoxon rank test, a non-parametric approximation on the basis of the ranks of the observations. SAS version 9.1 (SAS Institute) was used for all analyses.

Results

Patient population. Of 203 patients enrolled, 197 completed the full protocol (99 MSCT and 98 SOC). Demographic variables were comparable between the groups, with the exception of age, which was significantly lower in the MSCT group (Table 1). Among 461 patients screened for this study, 10% of potential enrollees refused consent, while 46% of patients were excluded owing to: history of pulmonary disease sufficient to preclude beta-blocker usage (18%); allergy to contrast, iodine, or shellfish (12%); history of coronary artery disease (10%); atrial fibrillation (4%); and other exclusions (2%).

Diagnostic performance: safety. There were no test complications in any MSCT patient. Minimal or no coronary

disease was found in 67 (67.7%) patients (Figs. 1 and 2) who were discharged home. In 24 of 99 (24.2%) cases, MSCT showed either intermediate coronary disease (26% to 70% stenosis, n = 13) or non-diagnostic scans (n = 11), requiring nuclear stress testing; of these, 21 of 24 (87.5%) patients had negative stress scans and were discharged (Table 2). Overall, 88 of 99 (88.9%) patients in the MSCT group were directly discharged home from the ED during the index visit; importantly, none of these patients suffered MACE events during the index ED visit or over the 6-month follow-up period.

In the SOC group, 93 of 98 (94.9%) patients had normal nuclear scans and were discharged. Of 5 (5.1%) patients with abnormal stress scans, 3 underwent early invasive angiography, whereas 2 others were discharged for outpatient follow-up by physician preference. There were no test complications in any patient. Overall, 95 of 98 (96.9%) SOC group patients were discharged home from the initial ED visit, and there were no MACE events in these patients during the 6-month follow-up period.

Diagnostic performance: efficacy. **INVASIVE ANGIOGRAPHIC CORRELATIONS AND CLINICAL OUTCOMES.** In the MSCT group, 12 of 99 (12.1%) patients underwent invasive angiography for MSCT abnormalities (Table 2), including 7 cases with MSCT finding of significant coronary stenosis ≥70% in at least 1 coronary segment (Fig. 3), 1 case with a lesion of 50% to 70% (who had a positive stress scan as well), and 1 case with a malignant coronary anomaly. By quantitative invasive angiography, 8 of 9 (88.9%) of these cases were true positives, whereas 1 of 9 (11.1%) cases was a false positive. Thus, among the MSCT group of patients undergoing catheterization, the MSCT test itself was angiographically verified in 8 of 9 (88.9%) cases. Among the 8

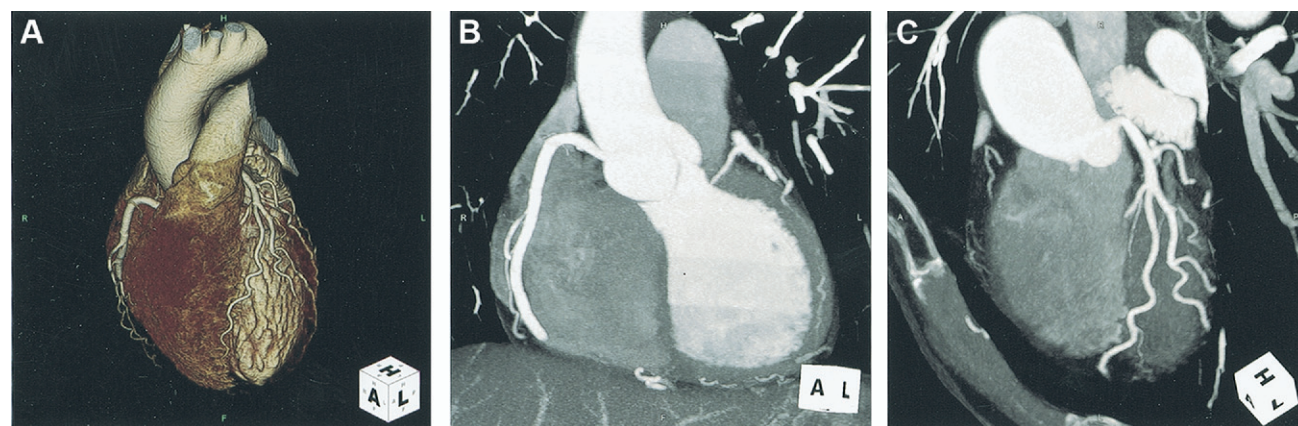


Figure 2 MSCT Images From a Patient With Normal Coronary Arteries

Panel A depicts the left anterior descending (LAD) and right coronary arteries (RCA) by volume-rendering technique.

Panel B depicts the RCA, and **panel C** depicts the LAD in maximum intensity projections. MSCT = multi-slice computed tomography.

true positive patients, 4 underwent percutaneous coronary intervention, 2 underwent coronary artery bypass surgery, and 2 others were treated medically.

Importantly, MSCT alone was not considered adequate for diagnosis in 24 of 99 (24.1%) cases, owing either to lesions of unclear hemodynamic significance (stenosis = 26% to 70%) in 13 patients or to nondiagnostic quality scans in 11 others; all such patients underwent nuclear stress scans according to the predefined protocol. Overall, 2 such patients ultimately required invasive angiography for nondiagnostic MSCT scans together with a positive stress scan; both such cases were false positive stress studies. Another patient was a true negative, with a nondiagnostic MSCT scan, negative stress scan, and a negative late invasive angiogram. As previously mentioned, 1 patient from this group had an “intermediate” 50% to 70% MSCT lesion, a positive stress scan, and a positive invasive angiogram.

Among all MSCT patients, on an intention-to-treat basis, there were 8 of 12 (67.7%) true positive cases, 3 of 12 (25%) false positive cases, and 1 of 12 (8.3%) true negative cases; yielding an overall accuracy of 9 of 12 (75%) for cases that came to catheterization. An additional 87 of 99 (87.9%) MSCT group patients were discharged home as normal without catheterization but remained clinically negative for coronary disease during the 6-month follow-up period. Combining angiographic and clinical results for the MSCT group, 96 of 99 (97.0%) patients were judged to have a clinically correct diagnosis.

Among the SOC patients, 7 of 98 (7.1%) patients underwent invasive angiography, 3 cases as part of the primary diagnostic strategy and 4 of 98 (4.1%) cases during the 6-month follow-up period owing to recurrent chest pain. Of these, 1 of 7 (14.3%) patients was a true positive and underwent percutaneous coronary intervention, 2 of 7 (28.6%) patients were false positives, and 4 of 7 (57.1%) patients were true negatives, yielding an overall accuracy of

5 of 7 (71.4%) for cases that underwent catheterization. Another 89 of 98 (90.8%) SOC group patients were discharged home as normal without catheterization but remained clinically negative for coronary disease during the 6-month follow-up period. Combining angiographic and clinical results for the SOC group, 96 of 98 (98.0%) patients were judged to have a clinically correct diagnosis.

On the basis of the previous text, a similarly high proportion of patients in both groups had a correct clinical diagnosis (MSCT group 96 of 99 [97.0%] patients vs. SOC group 96 of 98 [98.0%] patients, $p = 1.0$).

Late cardiovascular evaluations. During the 6-month follow-up period, in both groups, a similar number of patients judged normal during their index visit required office or ED visits for recurrent chest pain (MSCT group 8 of 99 [8.1%] patients vs. SOC 8 of 98 [8.1%], $p = 1.0$). The MSCT patients underwent fewer repeat non-invasive cardiovascular evaluations compared with the SOC group (MSCT 1 of 99 [1.0%] patients vs. SOC 3 of 98 [3.1%] patients, $p = 0.37$) and were hospitalized less frequently for late catheterizations (1 of 99 [1.0%] vs. 4 of 98 [4.1%] patients, $p = 0.21$). Combining these 2, the number of cases requiring late cardiovascular re-evaluation was higher in the SOC group (MSCT group 2 of 99 [2.0%] vs. SOC 7 of 98 [7.1%] patients, $p = 0.10$), but these results did not reach statistical significance. Overall, the proportion of patients with an “effective” diagnosis that was both clinically correct and definitive was high in both groups (MSCT group, 94 of 99 [94.9%] patients vs. SOC group, 89 of 98 [90.8%] patients, $p = 0.26$).

Diagnostic performance: efficiency. The median diagnostic time (randomization to definitive diagnosis) was significantly shorter for patients undergoing MSCT (3.4 h [25th to 75th percentile 2.3 h to 14.8 h] vs. 15.0 h [25th to 75th percentile 7.3 h to 20.2 h], $p < 0.001$) (Table 3). Even though neither MSCT nor nuclear stress scans were avail-

Table 2 Early and 6-Month Clinical Outcomes

	MSCT n = 99	Standard of Care n = 98	p Value
Index visit outcomes			
Test complications	0 (0%)	0 (0%)	NA
Direct ED discharges	88 (88.1%)	95 (96.9%)	0.03
Acute myocardial infarction	0 (0%)	0 (0%)	NA
Death	0 (0%)	0 (0%)	NA
In-hospital diagnostic cath	11 (11.1%)	3 (3.1%)	0.03
Positive cath	9 (9.1%)	1 (1%)	0.02
In-hospital PCI	3 (3.0%)	1 (1.0%)	0.62
In-hospital CABG	2 (2.0%)	0 (0%)	0.50
6-month outcomes			
Test complications	0 (0%)	0 (0%)	NA
Unstable angina	0 (0%)	0 (0%)	NA
Myocardial infarction	0 (0%)	0 (0%)	NA
Death	0 (0%)	0 (0%)	NA
Late ED R/O ischemia	6 (6.1%)	6 (6.1%)	1.00
Late office R/O ischemia	2 (2.0%)	2 (2.0%)	1.00
Late diagnostic cath	1 (1.0%)	4 (4.1%)	0.21
Late stress/MSCT test	1 (1.0%)	3 (2.0%)	0.37
Cath cumulative	12 (12%)	7 (7.1%)	0.24
True-positive cumulative	8/12 (67.7%)	1/7 (14.3%)	0.06
True-negative cumulative	1/12 (8.3%)	4/7 (57.1%)	0.04
False-positive cumulative	3 (25%)	2 (28.5%)	1.00
False-negative cumulative	0 (0%)	0 (0%)	NA
Cath-accuracy cumulative	9 (75%)	5 (71.4%)	1.00
Clinically correct diagnosis	96/99 (97.0%)	96/98 (98.0%)	1.00
Late tests cumulative	2 (2.0%)	7 (7.1%)	0.10
Diagnostic efficacy	94/99 (94.9%)	89/98 (90.8%)	0.26
PCI cumulative	4 (4.0%)	1 (1.0%)	0.37
CABG cumulative	2 (2.0%)	0 (0%)	0.50

CABG = coronary artery bypass grafting; Cath = cardiac catheterization/invasive coronary angiography; ED = emergency department; MSCT = multi-slice computed tomography; PCI = percutaneous coronary intervention; R/O = rule out.

able from 6:00 PM until 7:00 AM, patients randomized in those hours still had consistently faster diagnostic evaluations by MSCT.

Patients undergoing MSCT also had significantly lower ED costs of care. Although the cost of a MSCT procedure versus a nuclear stress study was similar (\$507 vs. \$538), the median cost of care for MSCT was less, primarily owing to reduced length of stay (\$1,586 [25th to 75th percentile \$1,413 to \$2,059] vs. \$1,872 [25th to 75th percentile \$1,727 to \$2,069], $p < 0.001$).

Discussion

Observations from this study of patients with “low-risk” acute chest pain provide the basis to compare the strengths and weaknesses of diagnostic evaluation by MSCT angiography versus traditional nuclear stress testing. The present results demonstrate that both diagnostic strategies are safe and ultimately highly effective in establishing a clinically correct diagnosis over a 6-month follow-up period. The major advantage of MSCT angiography is on the basis of its ability to rapidly and accurately delineate the absence of coronary artery disease or the presence of severe stenoses,

thereby establishing an immediate diagnosis in nearly 75% of cases, which facilitates more rapid discharge. However, MSCT angiography also has limitations, particularly with regard to cases with inadequate image quality and owing to inability to determine the physiological significance of coronary lesions judged to be of intermediate severity.

Acute chest pain prompts 6 million patients annually to undergo ED evaluation to exclude acute coronary syndromes (21). Alarming, up to 8% of patients with acute coronary syndromes are misdiagnosed and inappropriately discharged home (1–4). In “low-risk” patients (i.e., those with initially normal electrocardiograms and cardiac enzymes), only a minority actually suffers from myocardial ischemia (17). However, because of the consequences of failure to diagnose acute coronary syndromes, it is standard practice to evaluate all such patients with serial electrocardiograms and cardiac enzymes over 8 to 12 h, followed by a rest and/or stress-imaging study (9,10,22). This approach is time-consuming and resource-intensive, incurring an estimated cost of \$10 to \$12 billion annually in this country alone (6,22).

Our findings confirm that MSCT can serve as the definitive evaluation in the vast majority of such “low-risk” cases. By virtue of its ability to accurately delineate normal coronary arteries (the majority of cases) or severe stenoses, the MSCT scan alone was able to immediately identify or exclude coronary disease as the cause of chest pain in nearly 75% of cases. Although further testing was required in cases with intermediate lesions or scans of insufficient diagnostic quality, ultimately the MSCT strategy arrived at a correct and definitive diagnosis in 95% of cases. Multi-slice computed tomography also demonstrates noncardiac thoracic pathology, including pericardial disease, aortic dissection, and acute pulmonary embolism (23). However, MSCT has potential limitations. One concern is the potential for unnecessary catheterizations (and even revascularization procedures), related to the inability of MSCT to provide physiological coronary blood flow data that, in lesions judged moderate and therefore of unclear hemodynamic significance, might lead to an “oculo-stenotic reflex” procedure. Other disadvantages of MSCT include exposure to radiation and iodinated contrast (24,25). Although rest-stress nuclear scanning also provides radiation exposure, it does not require iodinated contrast. Fast or irregular rhythms are another limitation, despite use of beta-blocking drugs. Overall, inadequate diagnostic quality scans occurred in 10% of cases, due to motion, coronary calcification, or obesity. Such cases required a second radiation exposure from rest-stress nuclear scanning, as did an additional 14% of cases with “intermediate” lesions (26% to 70% stenoses on MSCT), whereas none of the SOC patients required double radiation doses for initial evaluation. Also, 4 of 99 (4.0%) MSCT patients with either nondiagnostic scans or intermediate grade stenoses required invasive angiography as well, resulting in a third radiation exposure. Alternatively, patients with nondiagnostic or intermediate MSCT results

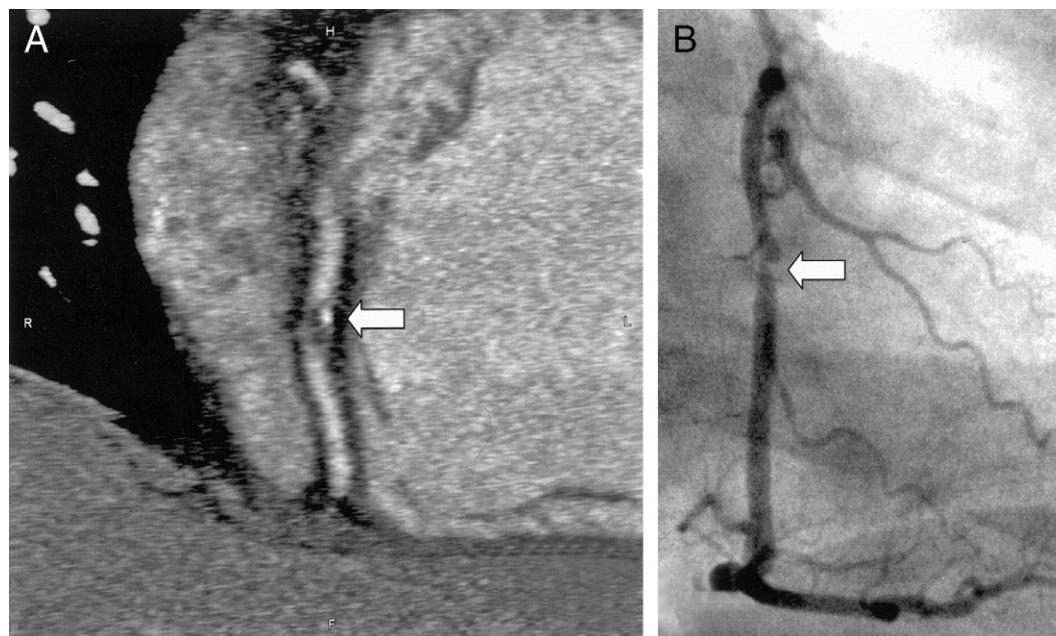


Figure 3 Comparative MSCT Images and Invasive Angiograms in a Patient With Severe (>70%) Coronary Stenosis

The appearance of a severe stenosis in the mid-right coronary artery identified by multi-slice computed tomography (MSCT) (**A**, arrow) is concordant with the appearance on invasive angiography (**B**, arrow).

could undergo stress echocardiography or stress magnetic resonance imaging to avoid repeat radiation exposure from nuclear scanning.

The traditional “rule-out myocardial infarction” protocol is known to be overall reasonably accurate, safe, and is widely available for application. One advantage compared with MSCT is that it provides myocardial perfusion data, thereby offering insights regarding the physiological significance of coronary stenoses. Thus, this approach might minimize catheterizations and potentially mitigate unnecessary revascularization procedures. However, as emphasized by the present results, this diagnostic strategy has

significant limitations as well, including false positive studies (9). Furthermore, the rest-stress imaging approach takes longer to complete and might incur more costs.

These results are consistent with recently published studies documenting the accuracy of MSCT coronary angiography for delineation of the presence and severity of coronary artery disease (11–15). The present randomized results also are consonant with and extend those of recent small nonrandomized studies of MSCT angiography for evaluation of acute chest pain (23,26).

Study limitations. It is important to consider limitations pertinent to the methods of this study. More MSCT

Table 3 Diagnostic Efficiency

	All Combined n = 197	ED Arrival 12 AM to 6 AM n = 23	ED Arrival 6 AM to 12 PM n = 80	ED Arrival 12 PM to 6 PM n = 72	ED Arrival 6 PM to 12 AM n = 22
MSCT	99	11 (11.1%)	41 (41.4%)	37 (37.4%)	10 (10.1%)
SOC	98	12 (12.2%)	39 (39.8%)	35 (35.7%)	12 (12.2%)
Rand to diagnosis (h)					
MSCT arm	3.4 (2.3–14.8)	3.3 (2.3–3.7)	2.5 (2.1–3.4)	13.8 (2.6–19.5)	10.0 (2.9–12.0)
SOC arm	15.0 (7.3–20.2)	8.2 (7.4–9.1)	8.6 (6.1–21.0)	19.1 (15.7–20.7)	13.8 (7.3–15.4)
p value	<0.001	<0.001	<0.001	0.01	0.29
ED Cost (\$)					
MSCT arm	1,586 (1,413–2,059)	1,520 (1,427–2,049)	1,437 (1,345–1,729)	1,706 (1,474–2,076)	1,604 (1,526–2,511)
SOC arm	1,872 (1,727–2,069)	1,748 (1,702–1,792)	1,750 (1,643–2,078)	1,995 (1,880–2,141)	1,834 (1,743–1,878)
p value	<0.001	0.10	<0.001	0.01	0.14

Given are the medians followed by the (25th–75th) percentiles.

Rand = randomization; SOC = standard of care; other abbreviations as in Table 2.

patients underwent invasive angiography and revascularization during the index hospital stay. The decision to undergo angiography was in part protocol-driven but ultimately governed by decisions of the patient's personal physician. Although the vast majority of MSCT cases undergoing invasive study had severe disease confirmed by selective coronary angiography, concerns must be raised regarding the potential for unnecessary invasive procedures. A significantly higher number of MSCT patients had angiographically proven coronary disease compared with the standard arm; although not clinically evident during the 6-month follow-up period, whether true disease was missed in the SOC group is not certain. The results of each non-invasive protocol was used to refer patients for the invasive angiography by which it was judged, thereby constituting a potential inherent referral bias, in particular with regard to false negative cases. We sought to minimize this by using a 6-month follow-up period to detect clinical coronary disease in patients judged to be normal. There are other methodological issues to consider that might limit the applicability of the present results. Although the MSCT strategy proved to be a more time- and cost-effective strategy, at least during the index ED visit, our analysis did not include "global" costs or time incurred from protocol-driven invasive procedures or those related to additional cardiovascular testing during the follow-up period. Also, the present study did not address the comparative value of alternative "standard-of-care" non-invasive strategies employing ECG-only stress testing, stress echocardiography, or rest-only nuclear scanning (10,22). It is also important to note that the present patients were at "low risk" for acute coronary syndromes. Therefore, caution must be applied when extrapolating these findings to patients with higher risk, including those with known coronary disease, particularly those with ischemic ECG changes or positive cardiac biomarkers as well as those with coronary stents that obscure lumen assessment by MSCT. Finally, because low-risk patients inherently have low event rates and the number of patients in our study was small, there were few patients who underwent invasive angiography or had MACE events, making it difficult to evaluate the true incidence of false positive and false negative MSCT findings.

In summary, these results illustrate the strengths and weaknesses of MSCT coronary angiography as a diagnostic tool in acute low-risk chest pain patients. In the majority of cases, MSCT definitively and noninvasively establishes or excludes coronary artery disease as the cause of chest pain. However, this approach has significant limitations, particularly with regard to its inability to determine the physiological significance of coronary lesions judged to be of intermediate severity as well as in cases with inadequate image quality. Future studies will be necessary to determine how best to use this diagnostic technique.

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