Usefulness of 64-slice multidetector computed tomography as an initial diagnostic approach in patients with acute chest pain

Sung-A Chang, MD, Sang Il Choi, MD, Eue-Keun Choi, MD, Hyung-Kwan Kim, MD, Jin-Wook Jung, MD, Eun Ju Chun, MD, Kyu-Seok Kim, MD, Young-Seok Cho, MD, Woo-Young Chung, MD, Tae-Jin Youn, MD, In-Ho Chae, MD, Dong-Ju Choi, MD, and Hyuk-Jae Chang, MD Seoul, Republic of Korea

Background Recently, multidetector computed tomography (MDCT) has been proposed as an accurate diagnostic tool to evaluate for coronary artery disease. However, the role of MDCT as part of the initial diagnostic for evaluating acute chest pain is less well established.

Methods We prospectively enrolled patients presenting with acute chest pain to the emergency department (ED) and risk stratified them based on the pretest probability for an acute coronary syndrome (ACS): (1) very low, (2) low, (3) intermediate, (4) high, and (5) very high or definite. After exclusion of very low and very high risk patients, 268 patients were randomized to either immediate 64-slice cardiac MDCT or a conventional diagnostic strategy. Number of admissions, ED and hospital length of stay (LOS), and major adverse cardiac events over 30 days of follow-up were compared between the strategies based on the pretest probability for ACS.

Results The number of patients ultimately diagnosed with an ACS did not differ between the 2 strategies. Emergency department LOS and total admissions were not different between strategies. Patients in the MDCT-based strategy had a decreased hospital LOS (P = .049) and fewer admissions deemed unnecessary (P = .007). Reductions in unnecessary admissions were more prominent in intermediate-risk patients (P = .015). None of the patients discharged from the ED in the MDCT-based strategy experienced major adverse cardiac events at follow-up.

Conclusion Use of an MDCT-based strategy in the ED as part of the initial diagnostic approach for patients presenting with acute chest pain is safe and efficiently reduces avoidable admissions in patients with an intermediate pretest probability for ACS. (Am Heart J 2008;156:375-83.)

Appropriate triage of patients with acute chest pain is one of the most important issues for physicians in the emergency department (ED). Considering the high morbidity and mortality of missed cases of acute coronary syndrome (ACS), the importance of accurate and efficient triage for these patients cannot be overstated. To date, the triage of patients with chest pain largely depends on the individual’s symptom history, serial electrocardiograms (ECG), and cardiac biomarkers.

However, a number of patients with ACS have nondiagnostic findings on their initial evaluation. Because of the limited capability of current diagnostic tools to define the etiology of acute chest pain, overcrowded state of ED and unnecessary admission increase and result in misappropriation of resources.

With rapid technical improvements, cardiac multidetector computed tomography (MDCT) permits noninvasive imaging of coronary anatomy with high accuracy and may also provide insight into noncoronary causes of chest pain. Recently, several observational studies have demonstrated that 64-slice MDCT in acute chest pain is safe, feasible, and facilitates early triage of acute chest pain in low-risk patients, primarily relying on their negative MDCT result. However, the appropriate use and timing of MDCT in the ED are still unclear and its role in patients with different risk profiles has not been studied yet. The aim of this study was to investigate in a prospective, randomized manner whether 64-slice MDCT as part of the initial diagnostic strategy decreases ED and hospital length of stay (LOS), admissions, and 30-day major adverse cardiac events...
(MACE) in patients presenting with chest pain stratified based on the pretest probability for ACS.

Methods

Study population

Patients older than 18 years presenting to the ED with acute chest pain syndrome were consecutively enrolled from May 2006 to February 2007. This study was performed in a 900-bed tertiary referral university hospital with on-site percutaneous coronary intervention and surgical backup 24 hours a day. Patients presenting to the ED were cared for by attending physicians trained in either emergency medicine or internal medicine.

Based on the initial history, physical examination, and ECG findings, patients were categorized into 5 different groups according to the pretest probability for having an ACS: (1) very low; (2) low; (3) intermediate; (4) high; (5) very high or definite (Table I). Patients deemed very low and very high risk were excluded from the study as they are less likely to need further diagnostic tests to risk stratify them into different treatment strategies. Additional exclusion criteria were (1) constant arrhythmia, (2) hemodynamic or clinical instability, (3) history of allergy to radio-contrast dye, (4) documented renal insufficiency, (5) pregnancy or women of childbearing age who are not using contraception, (6) contraindication to β-blockade, (7) and recent (<1 month) diagnostic workup for coronary disease as this may influence the treating physician’s diagnostic strategy.

Study protocol

After a comprehensive history and physical examination and timely review of the initial ECG, patients were stratified into 5 groups depending on the pretest probability for ACS. Eligible patients were randomly assigned to either an MDCT or conventional diagnostic strategy (control) (Figure 1). Patients randomized to the control group received an evidence-based diagnostic workup including serial ECGs, and cardiac biomarkers. Subsequent diagnostic tests, other than MDCT, and treatments were made at the discretion of the treating physician. Patients assigned to the MDCT-based strategy underwent CT scanning immediately after randomization, and results were made available immediately using electronic medical records and a picture archiving system. Subsequent studies and treatments were left to the discretion of the treating physician after results of the CT scan were made available. Neither treatment strategy was dictated by a hospital-established protocol for acute chest pain.

A month after the index ED visit, clinical status and cardiac events were assessed by individual interviews and using the hospital computer database. The study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital, and written informed consent was obtained from all patients.

Multidetector computed tomography protocol and image analysis

Intravenous esmolol, 10 to 30 mg (Jeil Pharm, Inc, Seoul, Korea), was administered to subjects with a baseline heart rate >65 beats per minute before imaging to achieve a heart rate of ≤65 beats per minute. All patients were scanned using a 64-slice MDCT scanner with a 0.42-second rotation time (Brilliance 64; Philips Medical Systems, Best, The Netherlands). An unenhanced ECG-gated CT scan was performed to assess for coronary artery calcification. Then, for the contrast enhanced coronary CT angiography studies, a bolus of 80 ml iomeprol (Iomeron 400; Bracco, Milan, Italy) was injected intravenously (4 mL/s) followed by a 50-mL saline flush. A region of interest was placed in the descending thoracic aorta, and scanning was automatically initiated once a selected threshold (150 HU) had been reached using a bolus tracking method. Tube current modulation was done on all participants in an attempt to decrease radiation exposure. The mean radiation exposure was 12.5 ± 2.0 mSv. Images were reconstructed in the mid-diastolic phase (75% of R-R interval) of the cardiac cycle. Additional reconstructions were performed if motion artifacts were present. Evaluation of left ventricular global and regional systolic function was assessed with 5-mm stacks by multiplanar reconstructions using a 2-phase reconstruction method.13

All MDCT data sets were analyzed with the clinical information by a single, experienced radiologist immediately after acquisition. Images were analyzed for technical factors, coronary artery calcium score (CACS), coronary artery stenosis, left ventricular ejection fraction, wall motion, and perfusion abnormalities, and extra-cardiac findings on a workstation (Brilliance; Philips Medical Systems). The Agatston method was used to quantify coronary artery calcification.14 Patients with previous coronary artery bypass grafting or stenting were excluded from CACS analysis. Coronary artery stenosis was estimated by multiplanar reconstruction with 0.6-mm slice thickness. A significant stenosis was defined quantitatively as >50% luminal narrowing on maximum intensity projection images or multiplanar reconstruction images. Image quality was evaluated on a per-segment basis and classified as good (no artifact), adequate (defined as the presence of image-degrading artifacts related to motion, calcification, or noise, but feasible for evaluation with moderate confidence), or poor (the presence of image-degrading artifacts resulting in a low confidence for accurate evaluation).

Data analysis

We prospectively gathered information on traditional risk factor profiles, ED and hospital LOS, and diagnosis at triage.
Traditional risk factors included hypertension, diabetes mellitus, smoking, dyslipidemia or use of statin, and family history of premature coronary artery disease (CAD). Final diagnosis was determined independently 1 month after discharge by 2 cardiologists. Any disagreements were resolved by consensus in the presence of another cardiologist. Acute coronary syndrome was defined as either an acute non-ST-segment elevation myocardial infarction (MI) or unstable angina according to the American College of Cardiology/American Heart Association guidelines. Acute chest pain derived from coronary spasm, as proven by provocative testing during angiography, was also designated as ACS. The term unnecessary admission was defined as a medical condition that should not have led to hospitalization, which was ultimately confirmed to be neither ACS nor any medical conditions requiring hospitalization for urgent care, for example, pulmonary embolism, aortic dissection, or pneumothorax. Unnecessary admissions were determined by consensus of the outcome panel. Emergency department LOS was calculated as the time from arrival in ED until discharge from the ED, or admission to an inpatient ward. Hospital LOS was calculated as the time from ED to discharge from the hospital. Major adverse cardiac event was defined as death from any cause, nonfatal MI, or target vessel revascularization.

Statistical analysis
All values are expressed as means ± SD or as number (percentages), and Student t test was used to compare the continuous variables with normal distribution. If >1 group was compared to the same control, the Bonferroni correction was applied. As the distributions of ED and hospital LOS were negatively skewed, summary statistics were presented as...
medians (interquartile ranges) and pairwise group comparisons were performed by Mann-Whitney U test. Pearson’s χ² test or Fisher exact test was applied to categorical variables. One-way analysis of variance with Sheffe’s post hoc test for parametric variables or linear-by-linear association for categorical variables was used to determine differences between 3 groups. All analyses were performed using SPSS version 13.0 (SPSS, Inc, Chicago, IL), and probability values of <.05 were considered statistically significant.

Results

Patient population

Of 280 eligible patients, 268 were enrolled after obtaining written informed consent (Figure 1). Two patients who discharged against medical advice were excluded from final analysis. The majority of patients were categorized as having either a low or intermediate probability for an ACS (21% high, 42% intermediate, and 37% low probability). Patients categorized as low probability were younger and had less history of hypertension, diabetes, dyslipidemia, and CAD than high-probability patients (Table II). There were no significant differences in patient baseline characteristics between the conventional and MDCT strategies (Table II).

Multidetector computed tomography image acquisition

The mean time from ED arrival to MDCT imaging was 1.67 ± 1.62 hours. Time for patient preparation and scanning was 15.2 ± 4.5 minutes and for image reconstruction and interpretation was 24.2 ± 3.7 minutes. Two patients developed a diffuse irritating skin rash after imaging which resolved spontaneously. Coronary artery image quality was classified as good in 92%, adequate in 6%, and poor in 2% on a segmental basis. Reasons for poor image quality were motion artifact (56%, 18/32 segments), blooming artifact (28%, 9/32 segments), or low contrast-to-noise ratio (16%, 5/32 segments).

Clinical outcomes

One hundred forty-four (54%) patients were discharged from the ED and 122 (46%) patients were hospitalized.
There was no difference in the number of patients ultimately diagnosed with an ACS between the 2 strategies (39/133 [29%] vs 39/133 [29%], \( P = 1.0 \)). There were fewer admissions in the MDCT-based strategy than in the conventional strategy (55/133 [41%] vs 67/133 [50%], \( P = .14 \)). There were fewer admissions deemed unnecessary in the MDCT-based strategy (4% vs 15%, \( P = .007 \)) (Figure 2).

In the conventional strategy, 57 (85.1%) of 67 admitted patients underwent invasive coronary angiography and 39 (58%) were ultimately diagnosed with an ACS. All the patients classified as having a high probability for ACS were admitted to the ward with no additional stress testing in the ED. Intermediate- and low-probability patients were often admitted for recurrent chest pain, positive cardiac biomarkers, or abnormal stress testing. If initial cardiac biomarkers were negative and there were no recurrent episodes of chest pain, most patients underwent stress testing while in the ED.

Twenty-eight intermediate-probability (50%) and 39 low-probability patients (80%) underwent stress testing. Overall, 67 (51%) patients underwent stress testing in the ED: exercise treadmill (n = 52), myocardial stress perfusion imaging (n = 11), and stress echocardiography (n = 4). The mean time from ED arrival to stress testing was 5.0 ± 3.3 hours.

In the MDCT-based strategy, 39 (71%) of 55 admitted patients were ultimately diagnosed with an ACS. Of the 55 admitted patients, at least one had a significant coronary artery stenosis (>50%) with or without perfusion or wall motion abnormality and 1 patient had a perfusion abnormality without significant stenosis on MDCT. Seven patients without MDCT findings of significant stenosis or perfusion or wall motion abnormalities were admitted owing to (1) positive cardiac enzymes (n = 2), (2) high clinical suspicion of coronary artery spasm (n = 3), and (3) to rule out ACS at the discretion of the treating physician (n = 2).

Ten patients (18.2%) were admitted with noncardiac pathology, and 6 (11%) diagnosed by MDCT. None of the patients treated with an MDCT-based strategy had further noninvasive stress testing while in the ED with only 13 patients (9.8%) having additional stress testing as an inpatient or outpatient.

In subgroup analysis, there were fewer admissions only in high-probability patients randomized to the MDCT-based strategy without a difference in unnecessary admission (Table III). Six patients, categorized as high probability, had no significant coronary stenosis on MDCT and were discharged from the ED. Of the 6 patients, one was diagnosed with hypertrophic cardiomyopathy and the remaining 5 reported no further symptoms or MACE at follow-up.

Reductions in unnecessary admissions were more prominent in patients with intermediate probability (20% for control vs 4% for the MDCT-based strategy, \( P = .015 \)). There were no differences in unnecessary admissions in low probability groups possibly because of the small number of patients admitted in both strategies (Table III).

**Emergency department and hospital LOS**

Emergency department LOS was not different between the conventional and MDCT strategies (4.8 [3.1-7.6] vs 4.6 [3.2-7.1] hours, \( P = .98 \)). In patients with intermediate probability for ACS, there was a nonsignificant trend toward decreased ED LOS in the MDCT-based strategy (6.0 [4.1-8.9] vs 4.5 [3.2-7.7] hours, \( P = .055 \)) (Figure 3, A). There were no differences in ED LOS between strategies in low- and high-risk patients.

Hospital LOS (time from ED presentation to hospital discharge) was decreased in the MDCT-based strategy compared with the conventional strategy for all patients studied (7.1 [4.1-9.7] vs 26.6 [4.8-131.1] hours, \( P = .049 \)). However, in subgroup analysis, hospital LOS was significantly decreased only in patients with a high probability for ACS (94.7 [56.9-159.9] vs 155.2 [95.5-266.1] hours, \( P = .036 \)) (Figure 3, B).

**Follow-up**

One-month follow-up was completed in all patients for MACE. One patient in the conventional strategy had...
experienced a nonfatal MI. There were no events in patients managed with the MDCT-based strategy. No patients experienced clinical or laboratory evidence of contrast-induced nephropathy during follow-up.

Multidetector computed tomography findings

In the MDCT-based strategy, there were 39 patients ultimately diagnosed with ACS. Not surprisingly, patients diagnosed with ACS had more significant coronary stenosis, greater prevalence of wall motional

Table IV. Cardiac MDCT findings in patients diagnosed with ACS vs non-ACS

<table>
<thead>
<tr>
<th>Coronary artery stenosis</th>
<th>Regional wall motion abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACS</td>
</tr>
<tr>
<td>Coronary artery stenosis</td>
<td></td>
</tr>
<tr>
<td>&lt;25%</td>
<td>0</td>
</tr>
<tr>
<td>25%-75%</td>
<td>10 (26)</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>29 (74)</td>
</tr>
</tbody>
</table>

Rest Perfusion abnormality

<table>
<thead>
<tr>
<th>Coronary artery calcium score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
</tr>
<tr>
<td>(+)</td>
</tr>
<tr>
<td>(-)</td>
</tr>
</tbody>
</table>

Data are expressed as number (%).

*Eleven patients with previous coronary artery bypass grafting or stenting were excluded from the analysis.
abnormalities and rest perfusion abnormalities, and more individuals with CACS > 100 (Table IV). All images were assessed for noncardiac findings that may or may not have been related to presenting symptoms. Individuals with serious findings (ie, aortic dissection) were immediately admitted and treated. The majority of patients with nonemergent noncardiac findings were discharged with follow-up as deemed necessary by the treating physician.

Discussion

In this study, we used a conventional or cardiac MDCT-based strategy to assist in the evaluation of patients presenting to the ED with acute chest pain after risk classification.

In most cases, MDCT could be successfully performed within 2 to 3 hours after arrival to the ED. Overall admissions and ED LOS were not different between the 2 strategies with a borderline significantly decreased hospital LOS. However, the MDCT-based strategy had fewer avoidable admissions predominantly in intermediate-risk patients who also had a borderline significantly decreased ED LOS. None of the patients discharged from the ED in the MDCT-based strategy and 1 in the conventional strategy experienced MACE at 30 days.

Impact of MDCT on triage in ED

In our study, triage of acute chest pain by immediate MDCT was feasible and safe. Although there were no differences in the primary outcome between the strategies, intermediate-risk patients randomized to MDCT had significantly fewer avoidable admissions, which is not surprising given the historical prevalence of ACS in this group. Multidetector computed tomography also reduced the number of total admissions by “ruling out” the presence of significant coronary artery stenosis in high-risk patients. However, these results are based on a short-term follow-up period; therefore we have to be prudent to interpret an impact factor of MDCT in high-probability patients. For low-risk patients, the number of admissions was low, consistent with prior studies; therefore the risk-to-benefit ratio for MDCT in this population needs to be carefully assessed given the potential harmful effect of radiation exposure.\textsuperscript{12,17}

Impact of MDCT on the length of ED and hospital stay

In contrast to previous reports,\textsuperscript{11} application of an MDCT-based strategy in the ED did not reduce ED LOS (3.2 [2.2-6.2] vs 4.7 [3.3-8.6], \( P = .14 \)). This was not surprising given that high-risk patients treated with the conventional strategy were rapidly transferred to coronary care unit rather than waiting for MDCT imaging results. Although previous reports showed a decrease in ED LOS, they excluded high-risk patients.\textsuperscript{11} Furthermore, intermediate- and low-risk patients, most of whom had negative cardiac biomarkers, underwent immediate exercise testing\textsuperscript{18,19} which might shorten ED LOS compared to the control patients in a previous study in which all the patients had the myocardial single photon emission computed tomography.\textsuperscript{11} In addition, the expectation to reduce ED LOS by MDCT relies on the excellent negative predictive value of MDCT.\textsuperscript{18} Application of MDCT results to clinical decision making would be easy if MDCT shows normal (or near normal) or severe (>75%) stenosis in symptomatic patients. However, imaging demonstrating intermediate lesions (25%-75%) may add diagnostic dilemma prolonging ED LOS.\textsuperscript{20} In our study, more than 70% of patients had intermediate lesion in which ED LOS was prolonged compared to insignificant (<25%) and significant (>75%) lesions (Figure 4). Therefore, the effect of MDCT on reducing ED LOS needs to be interpreted in the context of risk classification and lesion characteristics.

Hospital LOS was decreased in the MDCT-based strategy predominantly in high-risk patients. This is supposed to be largely responsible for the admission rate difference between strategies, as inhospital LOS (from admission to discharge) of admitted patients in high probability group did not differ between the 2 different strategies (152.9 [89.5-262.9] vs 108.9 [68.0-167.1], \( P = .18 \)).
Diagnostic value of MDCT in chest pain triage

Cardiac MDCT is also a useful modality to assess noncardiac abnormalities. In the present study, abnormal noncardiac findings were reported in some patients, which were related to the symptom or incidental findings. For patients with atypical chest pain, yet with multiple risk factors, MDCT provides a unique opportunity to differentiate cardiac from noncardiac causes of chest pain by directly evaluating coronary artery and surrounding structures, which is an additional advantage over conventional noninvasive modalities.

The diagnostic accuracy of cardiac MDCT for ACS, considering the final diagnosis as a gold standard, resulted in a sensitivity and specificity of 100% and 92.8%, respectively. Furthermore, there were no adverse events at 30 days in patients in the MDCT-based strategy discharged from the ED, highlighting the potential excellent negative predictive value of MDCT for future cardiac events.

On the other hand, MDCT is an anatomical imaging modality, and although it offers excellent coronary artery anatomy visualization, none of the MDCT findings specifically point to an ACS as patients with angina yet no coronary stenosis still have poor outcomes. In this context, use of MDCT should not replace careful clinical history taking highlighting the importance for studies to correlate MDCT findings and the clinical spectrum of ACS.

Study limitations

This study included relatively small numbers of patients, especially low-risk individuals who had significant MDCT findings. Therefore, the differences in admissions and LOS were seen only in subgroup analysis which decreases statistical power. Therefore, large-scale trials are needed to establish practical guidelines for the use of this new versatile modality. Second, as this study occurred in a setting of tertiary center, it should be prudent to extrapolate our results to patient care in nontertiary hospitals. Finally, the follow-up period was too short to assess future cardiac events in patients presenting with acute chest pain and was not the primary aim of this study.

Conclusions

Application of MDCT as part of the initial diagnostic approach for patients presenting with acute chest pain to the ED is safe, efficient, and reduces avoidable admissions in patients with an intermediate risk for ACS. The use of MDCT to assist in triage of acute chest pain in the ED needs to be applied in the context of the patient risk profile and available conventional diagnostic tests.

We are grateful for statistical assistance from the Medical Research Collaborating Center of Seoul National University Hospital.

References


ON THE MOVE?

Send us your new address at least 6 weeks ahead

Don’t miss a single issue of the journal! To ensure prompt service when you change your address, please photocopy and complete the form below.

Please send your change of address notification at least 6 weeks before your move to ensure continued service. We regret we cannot guarantee replacement of issues missed because of late notification.

JOURNAL TITLE:

Fill in the title of the journal here.__________________________________________________________

OLD ADDRESS:

Affix the address label from a recent issue of the journal here.

NEW ADDRESS:

Clearly print your new address here.

Name __________________________
Address _________________________
City/State/ZIP ____________________

COPY AND MAIL THIS FORM TO: Elsevier Subscription Customer Service
6277 Sea Harbor Dr
Orlando, FL 32887

OR FAX TO: 407-563-9661

OR PHONE: 1-800-654-2452
Outside the U.S., call 407-345-4000

OR E-MAIL: elspcs@elsevier.com