Coronary Multidetector Computed Tomography in the Assessment of Patients With Acute Chest Pain

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Background—Noninvasive assessment of coronary atherosclerotic plaque and significant stenosis by coronary multidetector computed tomography (MDCT) may improve early and accurate triage of patients presenting with acute chest pain to the emergency department.

Methods and Results—We conducted a blinded, prospective study in patients presenting with acute chest pain to the emergency department between May and July 2005 who were admitted to the hospital to rule out acute coronary syndrome (ACS) with no ischemic ECG changes and negative initial biomarkers. Contrast-enhanced 64-slice MDCT coronary angiography was performed immediately before admission, and data sets were evaluated for the presence of coronary atherosclerotic plaque and significant coronary artery stenosis. All providers were blinded to MDCT results. An expert panel, blinded to the MDCT data, determined the presence or absence of ACS on the basis of all data accrued during the index hospitalization and 5-month follow-up. Among 103 consecutive patients (40% female; mean age, 54 ± 12 years), 14 patients had ACS. Both the absence of significant coronary artery stenosis (73 of 103 patients) and nonsignificant coronary atherosclerotic plaque (41 of 103 patients) accurately predicted the absence of ACS (negative predictive values, 100%). Multivariate logistic regression analyses demonstrated that adding the extent of plaque significantly improved the initial models containing only traditional risk factors or clinical estimates of the probability of ACS (c statistic, 0.73 to 0.89 and 0.61 to 0.86, respectively).

Conclusions—Noninvasive assessment of coronary artery disease by MDCT has good performance characteristics for ruling out ACS in subjects presenting with possible myocardial ischemia to the emergency department and may be useful for improving early triage. (Circulation. 2006;114:2251-2260.)

Key Words: angina ▪ atherosclerosis ▪ imaging ▪ prognosis ▪ tomography

Early and accurate triage of patients presenting with acute chest pain to the emergency department (ED) remains difficult because chest pain history,1,2 a single set of biochemical markers for myocardial necrosis,3,4 and the initial 12-lead ECG alone or in combination cannot identify a group of patients who can be safely discharged without further diagnostic testing.5,6 Although risk prediction algorithms such as the acute cardiac ischemia time-insensitive predictive instrument7 have improved the ability to risk stratify patients, the threshold to admit chest pain patients remains low.

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As a consequence, >60% of patients with chest pain who are admitted to the hospital do not turn out to have acute coronary syndromes (ACS).8,9 This overtriage has enormous economic implications for the US healthcare system, estimated at $8 billion in annual costs.10 Despite this conservative practice, the rate of missed diagnosis of ACS remains unacceptably high (2% to 8%).11–13 Thus, there is a clear need to improve the early triage of patients with acute chest pain.

Because coronary artery disease (CAD) is the major underlying cause of ACS,14,15 a noninvasive method that quickly and accurately excludes the presence of CAD could substantially improve the ability to triage patients with chest pain. Noninvasive coronary 64-slice multidetector computed tomography (MDCT) angiography accurately detects significant coronary artery stenosis compared with invasive coronary angiography, with sensitivities and specificities between 91% and 100%.16,17; it is also highly sensitive (84% to 92%) for detecting coronary atherosclerotic plaque compared with intracoronary ultrasound.18 Preliminary data from a separate...
TABLE 1. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
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<tbody>
<tr>
<td>Age &gt;18 y</td>
<td>Age &lt;18 y</td>
</tr>
<tr>
<td>&gt;5 min of chest pain within the previous 24 h</td>
<td>No prior history of myocardial infarction</td>
</tr>
<tr>
<td>No or nondiagnostic ECG changes</td>
<td>Prior myocardial infarction</td>
</tr>
<tr>
<td>Normal initial cardiac biomarkers</td>
<td>Prior PCI or CABG</td>
</tr>
<tr>
<td>Admitted to rule out myocardial infarction through standard care protocols</td>
<td>Prior angioplasty or coronary bypass surgery</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>Readmit for ACS during index hospitalization</td>
</tr>
<tr>
<td>Ability to perform a breathhold of 10–15 s</td>
<td>patients hospitalized &gt;5 days</td>
</tr>
</tbody>
</table>

Exclusion criteria

- Elevated troponin-I or creatine kinase-MB levels in the initial blood sample obtained in the ED
- New diagnostic ECG changes (ST-segment elevation or depression >1 mm or T-wave inversion >4 mm in >2 anatomically contiguous leads)
- Hemodynamic or clinical instability (systolic blood pressure <80 mm Hg, clinically significant atrial or ventricular arrhythmias, persistent chest pain despite therapy)
- Known allergy to iodinated contrast agent
- Serum creatinine >1.3 mg/dL
- Metformin treatment, hyperthyroidism
- Inability to provide informed consent
- Perceived interference with standard clinical care of patients

pilot study suggest that coronary MDCT can be performed safely in patients with acute chest pain. We conducted a blinded, prospective study to assess computed tomography (CT) angiographic patterns of CAD—any coronary atherosclerotic plaque and significant stenosis—in patients who were being admitted for chest pain and who had negative initial cardiac biomarkers and a nondiagnostic ECG on presentation. We further examined whether these computed tomographic angiography (CTA) characteristics were associated with risk of ACS and whether they provide incremental value to standard cardiovascular risk factors and standard clinical risk assessment.

Methods

Patients

ROMICAT (Rule Out Myocardial Infarction using Computer-Assisted Tomography) was conducted as a prospective observational cohort study of consecutive adult patients presenting to the ED with acute chest pain in whom initial ED evaluation was inconclusive and who were awaiting admission to the Massachusetts General Hospital. Intake was performed on weekdays from 7 AM to 7 PM from May to July 2005. The inclusion and exclusion criteria are shown in Table 1. All eligible patients who agreed to enroll underwent coronary MDCT angiography before admission to the hospital floor.

All physicians, including those in the ED, who were involved in the standard clinical care of the patients were blinded to the result of MDCT imaging. Patients received standard clinical care to rule out ACS during their index hospitalization, including serial ECGs and cardiac biomarkers, and subsequent cardiac testing, eg, exercise testing, stress perfusion imaging, or cardiac catheterization, as deemed clinically indicated. Our institutional review board approved this study. All patients provided written consent.

Interventions

CT Coronary Angiography: Data Acquisition

CT imaging was performed with a 64-slice CT scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany). All patients with a heart rate >60 bpm received a β-blocker (intravenous metoprolol, 5 to 20 mg) unless their systolic blood pressure was <100 mm Hg or other contraindications were present. All image acquisitions were performed during a single breathhold in inspiration.

After a test bolus of 15 mL contrast agent (Iodhexol 320 g/cm³, Visipaque, General Electric Healthcare, Princeton, NJ) to determine optimal timing, a contrast agent was injected intravenously at a rate of 5 mL/s to ensure homogeneous contrast enhancement of the entire coronary artery tree. Images were acquired with 64×0.6-mm slice collimation, a gantry rotation time of 330 ms, tube voltage of 120 kV, and an effective tube current of 850 mA using ECG-correlated tube current modulation.

Transaxial images were reconstructed with a slice thickness of 0.75 mm and increments of 0.4 mm with a retrospectively ECG-gated half-scan algorithm with a temporal resolution of 165 ms. Images were initially reconstructed at 65% of the cardiac cycle. If necessary, additional reconstructions were performed to minimize motion artifacts. Reconstructed CT data sets were made anonymous and transferred to an offline workstation (Leonardo, Siemens Medical Solutions).

Outcomes

The primary goal of the present study was to determine the CT angiographic pattern of CAD, defined as the presence and extent of coronary atherosclerotic plaque and the presence of significant coronary artery stenosis, in patients with and without ACS. Additional goals were to compare the CT angiographic patterns of CAD in patients at differing levels of risk of ACS as assessed by the ED caregivers at the time of triage and to examine whether the CT-based information on plaque provided incremental value to standard risk factors and clinical risk assessment.

Traditional Risk Factor Assessment

We prospectively collected data about each patient’s demographics, risk factor profile, and clinical course, including onset of symptoms, presentation to the ED, triage decision in the ED, transfer to the hospital floor, and hospital discharge. Medical records were reviewed to obtain data on all diagnostic tests. The presence of risk factors was established from actual measurements obtained during hospitalization (ie, hypertension, hypercholesterolemia, and diabetes mellitus).

Clinical Outcomes

Risk Stratification

To clinically characterize the risk of patients for ACS, ED caregivers (attending, n = 71; fourth-year resident, n = 32) provided an estimate of the probability of having ACS for each patient (0% to 100%) at the time of initial triage (patient history, risk factors, clinical presentation). We stratified patients into low (0% to 33%), moderate (34% to 66%), and high (67% to 100%) pretest probability. We stratified the level of care as medicine or cardiology floors, monitored cardiology floors, and prolonged stay in the ED.

Diagnosis of ACS During Index Hospitalization

ACS was defined as either an acute myocardial infarction (ST-elevation myocardial infarction or non–ST-elevation myocardial infarction) or unstable angina pectoris according to the American College of Cardiology/American Heart Association guidelines. Table 2. To establish this diagnosis, an outcome panel of 2 physicians (1 cardiologist and 1 ED physician) reviewed the patient data forms and medical records pertaining to the hospital admission of enrolled patients. The reviewers were blinded to the findings of CT coronary angiography. Disagreement was solved by consensus, which included an additional cardiologist. CT coronary angiography data were not used to define ACS.

Follow-Up

A follow-up phone call using a standardized questionnaire was conducted 5.2±0.3 months (mean±SD) after discharge to determine the occurrence of major cardiovascular adverse events, defined as recurrent ischemic chest pain resulting in myocardial infarction, coronary revascularization, or cardiac death.
TABLE 2. Definitions of ACS

| ST-segment elevation myocardial infarction | A new finding of ST-segment elevation of >0.1 mm in at least 2 anatomically contiguous leads and elevated serial levels of troponin-I (>0.09 ng/mL) |
| Non-ST-segment elevation myocardial infarction | A new finding of ST-segment depression of >0.1 mm or T-wave inversion of at least 0.4 mm in at least 2 anatomically contiguous leads or symptoms consistent with AMI, either or both criteria in association with elevated serial levels of troponin-I (>0.09 ng/mL) |

Unstable angina pectoris

Clinical symptoms suggestive of ACS (typical chest discomfort or equivalent) with an unstable pattern of chest pain (at rest, new onset, or crescendo angina) coinciding with objective evidence of myocardial ischemia in stress perfusion imaging, dobutamine or stress echocardiography, and/or coronary angiography demonstrating a >50% epicardial coronary stenosis

Data derived from References 20, 21, and 33.

CT Angiographic Patterns of CAD: Coronary Atherosclerotic Plaque and Significant Stenosis

Two experienced observers who were blinded to patient name and clinical characteristics independently evaluated all CT data sets separately. Assessment was performed on original axial source images: thin-slice maximum intensity projections and multiplanar reformatted images orthogonal and parallel to the vessel centerline.

CT data sets were assessed for the presence of significant luminal obstruction ≥50% diameter reduction in cross-sectional images (which corresponds to >≈70% stenosis in planimetric invasive coronary angiography) and any coronary atherosclerotic plaque within all coronary segments, including side branches, using a modified 17-segment model.23 Coronary segments were identified relative to the origin of side branches. For stenosis, the outcome was determined as stenosis detected, stenosis excluded, or stenosis not ruled out.

Coronary atherosclerotic plaque was classified as noncalcified and/or calcified plaque as described previously14,24: noncalcified plaque was defined as any discernible structure that could be assigned to the coronary artery wall, with a CT attenuation below the surrounding contrast-enhanced coronary lumen but above the surrounding epicardial fat in at least 2 independent planes. Disagreement with respect to the presence of stenosis or plaque was resolved by joint reading or, if no consensus could be reached, by a third expert reader.

Interobserver agreements for the detection of any plaque per patient and per segment (Cohen’s κ = 0.92 and 0.81, respectively) and for the detection of stenosis per patient (Cohen’s κ = 0.82) were excellent.

Statistical Analysis

We calculated accuracy, sensitivity, and specificity with 95% confidence intervals (CIs) for the predictor variables of significant coronary artery stenosis and any coronary atherosclerotic plaque by coronary CTA, as well as the positive predictive value (PPV) and negative predictive value (NPV) of these variables for the adjudicated discharge diagnosis of ACS. In assessing the test characteristics for stenosis, we counted both patients in whom stenosis was detected and those in whom a stenosis could not be ruled out as positive cases.

Univariated associations between baseline variables with the clinical diagnosis of ACS were examined through the use of Student t test for continuous variables and χ2 test for categorical variables. We used the Mantel-Haenszel trend test to assess whether the patients’ event risk or CT angiographic patterns of CAD were different between patients at low, intermediate, or high risk for ACS by standard clinical risk assessment.

CT angiographic patterns of CAD: coronary atherosclerotic plaque and significant stenosis

We performed multivariate regression analysis to determine whether information on the extent of coronary atherosclerotic plaque added incremental value to information available at initial triage to predict ACS in patients who had any atherosclerotic plaque on MDCT. Separate models were used to determine the incremental value of plaque to traditional risk factors and clinical risk assessment. The first model initially contained traditional risk factors (age, gender, and history of CAD, plus all other variables with P < 0.05 in univariate analysis) and ACS. In a next step, we added the extent of plaque defined as the number of coronary segments with any plaque1–17 as a continuous variable to the model. In a second model, we initially examined the association between clinical risk of ACS as assessed by the ED caregiver (as a categorical variable: low, intermediate, and high pretest probability). In a next step, we added the extent of plaque to the model. In this model, the group with low pretest probability served as the reference group. All analyses were repeated, excluding patients with known CAD. Model fit was assessed through the use of likelihood ratios (LR) and c statistic, which is equivalent to the area under the receiver-operating characteristics curve.25 To facilitate interpretation of the intercept, we centered the amount of segments with plaque to 1 and centered the age to the mean age of patients. A value of P < 0.05 was considered to indicate statistical significance. All analyses were performed with SAS (version 8, SAS Institute Inc, Cary, NC).

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

Results

Patient Population

During the 3 months of recruitment, we screened 305 patients (131 women, 43%). Of these, 123 consecutive patients met all study eligibility criteria and were deemed capable of providing informed consent (Figure 1). Of the 106 patients (86%) who agreed to participate, 103 successfully underwent coronary MDCT; they form the study cohort (83 white, 20 black; see Table 3). Among eligible patients, those who were protocol eligible but did not sign informed consent were older.
(60.8±12.5 versus 53.8±12.2 years; P<0.03) but similar in gender distribution compared with enrolled patients (40% versus 43% women, respectively; P=0.85).

**Time and Safety of CTA**

CT imaging was performed an average of 3.7±2.3 hours after presentation to the ED. CTA was not completed in 3 patients (2.8%) because of nausea after test bolus, claustrophobia, and extravasation of contrast (n=1 each). The average time for the CT procedure, including patient preparation, was 12±1 minutes. The mean CT scan time was 13.6±2.2 seconds; the mean contrast dose was 78±11 mL. Average time for the interpretation of CT images was 10±8 minutes (range, 3 to 29 minutes).

**Clinical Outcomes**

**Diagnosis of ACS During Index Hospitalization**

The average time from symptom onset to presentation in the ED was 3.8±3.7 hours (range, 0.3 to 17.6 hours). The mean length of stay in the ED was 7.4±6.9 hours. A total of 90 patients were admitted to medicine or cardiology floors; 9 patients were admitted to monitored cardiology floors; and 4 patients had a prolonged stay in the ED. The average hospital length of stay was 33.8±33.3 hours (range, 6.7 to 170.8 hours).

All 103 patients received standard clinical care to rule out ACS. Overall, 14 patients (14%) were diagnosed with ACS: 5 had an acute MI, and 9 had unstable angina pectoris. In the 14 patients with ACS, objective evidence of significant coronary disease or myocardial ischemia was demonstrated through selective invasive coronary angiography (n=5), positive biomarkers (n=5), stress perfusion imaging (exercise or adenosine) (n=8), and/or dobutamine stress echocardiography (n=2).

In the remaining 89 patients (86%), ACS was ruled out. For most of the 89 patients in whom ACS was ruled out by standard clinical care, the hospital course was characterized by serial troponins and ECGs over the first 24 hours, followed by stress testing the following day. These patients underwent a total of 70 procedures, including exercise treadmill testing (n=3), stress perfusion imaging with exercise or adenosine (n=57), dobutamine stress echocardiography (n=5), and selective invasive coronary angiography (n=3). In the entire study population, a total of 8 invasive coronary angiograms were performed during index hospitalization. Compared with invasive coronary angiography, coronary CTA correctly detected a significant coronary artery stenosis in 5 patients (all had MI) and correctly ruled out the presence of significant CAD in 3 patients.

**Follow-Up**

Telephone follow-up was completed in 81 of the 89 patients (91%) who did not have an ACS during the index hospitalization. None of these patients reported suffering a major cardiovascular adverse event.

**CT Angiographic Patterns of CAD in Patients With and Without ACS**

**Coronary Atherosclerotic Plaque**

The presence of coronary atherosclerotic plaque in each of the 17 segments could be excluded in 41 patients (40%). None of these patients was determined to have an ACS (NPV, 100%; 95% confidence interval [CI], 0.93 to 1.00). In 62 patients (21 women; mean age, 58±13 years), coronary atherosclerotic plaque was detected (Figure 2), including all 14 patients with ACS (PPV, 23%; 95% CI, 0.13 to 0.35). The mean number of coronary segments with plaque was signifi-

![Figure 2. Coronary CTA of a 52-year-old female patient with history of type 2 diabetes mellitus, hypertension, and hyperlipidemia who presented to the ED with 30 minutes of substernal chest pain. A, Axial 3-mm maximum-intensity projection of the left main (arrowhead) and left anterior descending (arrow) coronary artery, demonstrating the presence of calcified and noncalcified plaque. RVOT indicates right ventricular outflow tract.](image-url)
icantly higher in subjects with ACS (n=14) compared with subjects without ACS (n=48) (9.1±4.5 versus 4.5±3.2, respectively; \( P<0.001 \)) (see Table 2).

**Significant Coronary Artery Stenosis**
The presence of a significant coronary artery stenosis (>50% luminal narrowing) could be excluded in 73 patients (71%). None of these patients had ACS during the index hospitalization (NPV, 100%; 95% CI, 0.96 to 1.00). In 13 patients, a significant stenosis was detected; 8 of these patients had ACS (Figure 3). In 17 patients, the presence of a significant stenosis could not be excluded because of previous stent placement (n=7), severe calcification (n=8), poor signal-to-noise ratio (n=1), or tachycardia (n=1). Six of these patients had ACS. Thus, a significant stenosis either was detected or could not be excluded in 30 patients (29%), corresponding to a specificity of 82% and a PPV of 47% (95% CI, 0.72 to 0.89 and 0.28 to 0.66, respectively). If patients with previous stent placement were excluded from analysis, the PPV increased to 61% (14 of 23) (Table 4).

**Incremental Value of CTA Extent of Coronary Atherosclerotic Plaque to Traditional Risk Factors and Clinical Risk Assessment**
The average clinical pretest probability for ACS as assessed by ED staff at the time of triage was 30±26%. The pretest probability was low in 68 patients (66%), moderate in 26 patients (25%), and high in 9 patients (9%) and was significantly higher in patients with ACS (n=14) compared with patients without ACS (n=48) (48±24% versus 27±30%; \( P=0.005 \)). The ACS event rate was significantly different between these risk categories (6 of 68 [9%], 5 of 26 [19%], and 3 of 9 [33%] for low, intermediate, and high pretest probability, respectively; \( P=0.02 \)). The prevalence of any plaque was 53% in patients with low, 69% in patients with moderate, and 89% in patients with high pretest probability (\( P=0.02 \)).

Multivariate logistic regression analyses demonstrated the incremental value of the extent of plaque to traditional risk factors (Table 5) and clinical estimates of the probability of ACS by the ED caregiver (Table 6). Both initial models containing either traditional risk factors or the categorized clinical estimates of probability of ACS did not predict ACS (LR, 8.41; \( P=0.13 \); c statistic, 0.73; and LR, 1.94; \( P=0.38 \); c statistic, 0.61). Adding the extent of plaque as a continuous variable improved both the model with traditional risk factors (LR, 23.27; \( P=0.0007 \); c statistic, 0.89) and the model with the categorized clinical estimates of probability of ACS (LR, 19.1; \( P=0.0003 \); c statistic, 0.86). Similar results were seen after exclusion of patients with known history of CAD for the model containing traditional risk factors. However, being at high risk by clinical assessment became a significant predictor (\( P=0.04 \)) in the model containing plaque and clinical risk assessment as a categorical variable.

The average increase in odds of having ACS for every additional segment with plaque was 1.58 (95% CI, 1.18 to 2.10) in the model with traditional risk factors and 1.49 (95% CI, 1.19 to 1.87) in the model with categorized clinical estimates of probability of ACS.

**Figure 3.** A, B, Coronary CTA of a 39-year-old man presenting to the ED with episodic chest pain for ~2 weeks before admission. A, Selective coronary angiography of the left circumflex artery (LCX) demonstrating a significant stenosis of the mid LCX (black arrow) between the first obtuse marginal branch (OM1) and the takeoff of the second obtuse marginal branch (OM2), B, Orthogonal views through the mid LCX demonstrating a large, partly calcified atherosclerotic plaque (black arrow) causing a significant stenosis at the level of the mid LCX before the origin of the OM2 branch with nearly complete obliteration of the coronary lumen. LAD indicates left anterior descending coronary artery.

**Discussion**
In the present study of patients who presented with acute chest pain to the ED in whom initial triage was inconclusive, we found that the absence of coronary artery plaque or significant stenosis on noninvasive coronary MDCT angiography has an excellent NPV for the subsequent diagnosis of ACS. Furthermore, in those patients with CAD on CT, the extent of coronary atherosclerotic plaque provided incremen-
We demonstrated that 64-slice coronary CTA permits a rapid, noninvasive assessment of CAD in the setting of acute care, with an average procedure time of 12 minutes. The procedure was safe and well tolerated, with 97% of patients completing the test without any associated major adverse events.

We also demonstrated that CTA patterns of CAD—presence of any coronary atherosclerotic plaque and significant

<table>
<thead>
<tr>
<th>TABLE 4. Diagnostic Accuracy of CT-Based Detection of Significant Coronary Artery Stenosis (&gt;50%) and Presence of Any Coronary Plaque to Predict ACS During Index Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=103)</td>
</tr>
<tr>
<td>Sensitivity</td>
</tr>
<tr>
<td>Plaque</td>
</tr>
<tr>
<td>95% CI</td>
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<tr>
<td>n of N</td>
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<tr>
<td>Stenosis*</td>
</tr>
<tr>
<td>95% CI</td>
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<tr>
<td>n of N</td>
</tr>
</tbody>
</table>

Excluding patients with a proven history of CAD (prior stenting or bypass grafting) (n=93)

| Plaque       | 1.00        | 0.49  | 0.19  | 1.00 |
| 95% CI       | 0.74–1.00   | 0.38–0.60 | 0.09–0.32 | 0.93–1.00 |
| n of N       | 10/10       | 41/83 | 10/52 | 41/41 |
| Stenosis*    | 1.00        | 0.85  | 0.46  | 1.00 |
| 95% CI       | 0.74–1.00   | 0.76–0.92 | 0.24–0.68 | 0.96–1.00 |
| n of N       | 10/10       | 71/83 | 10/22 | 71/71 |

*Positive cases include subjects in whom a stenosis was detected (n=13) or could not be excluded (n=17).

<table>
<thead>
<tr>
<th>TABLE 5. Logistic Regression in 62 Patients With Any Coronary Atherosclerotic Plaque as Detected by MDCT</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Intercept</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Female gender</td>
</tr>
<tr>
<td>History of CAD</td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>Smoking</td>
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</tbody>
</table>

Model for a probability of ACS containing traditional risk factors and extent of plaque†

| Intercept                | $-3.82$               | 1.18            | 10.54          | ... | ...                |
| Plaque                   | $0.45$                | 0.15            | 9.72           | 0.002 | 1.58 (1.18–2.10)   |
| Age                      | $-0.02$               | 0.04            | 0.17           | 0.68 | 0.99 (0.92–1.06)   |
| Female gender            | $-1.71$               | 1.12            | 2.35           | 0.13 | 0.18 (0.02–1.6)    |
| History of CAD           | $-0.47$               | 1.02            | 0.21           | 0.65 | 0.63 (0.09–4.6)    |
| Hypertension             | $0.33$                | 1.00            | 0.11           | 0.74 | 1.4 (0.2–10)       |
| Smoking                  | $0.47$                | 0.84            | 0.31           | 0.58 | 1.6 (0.31–8.27)    |

Model for a probability of ACS containing traditional risk factors and extent of plaque, excluding those patients with a history of CAD‡

| Intercept                | $-3.95$               | 1.39            | 8.01           | ... | ...                |
| Plaque                   | $0.43$                | 0.15            | 7.89           | 0.005 | 1.54 (1.14–2.1)    |
| Age                      | $-0.02$               | 0.05            | 0.23           | 0.63 | 0.98 (0.89–1.07)   |
| Female gender            | $-1.38$               | 1.14            | 1.48           | 0.22 | 0.25 (0.03–2.32)   |
| Hypertension             | $0.37$                | 1.06            | 0.12           | 0.72 | 1.45 (0.18–11.51)  |
| Smoking                  | $0.76$                | 0.93            | 0.66           | 0.42 | 2.14 (0.34–13.31)  |

*Initial model includes age and gender and those risk factors with $P<0.05$ in univariate analysis: LR, 8.41 with 5 df ($P=0.13$); c statistic, 0.73.
†Model adding the extent of plaque: LR, 23.27 with 6 df ($P=0.0007$); c statistic, 0.89.
‡Model similar to second model but excluding those patients with a history of CAD (n=10): LR, 16.67 with 5 df ($P=0.005$); c statistic, 0.88.
TABLE 6. Logistic Regression in 62 Patients With Any Coronary Atherosclerotic Plaque as Detected by MDCT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient Estimate</th>
<th>Standard Error</th>
<th>Wald $\chi^2$</th>
<th>$P$</th>
<th>Odds Ratio with 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-1.61</td>
<td>0.45</td>
<td>12.95</td>
<td></td>
<td>1.92 (0.5–7.44)</td>
</tr>
<tr>
<td>Intermediate vs low risk</td>
<td>0.65</td>
<td>0.69</td>
<td>0.9</td>
<td>0.34</td>
<td>1.92 (0.5–7.44)</td>
</tr>
<tr>
<td>High vs low risk</td>
<td>1.1</td>
<td>0.86</td>
<td>1.65</td>
<td>0.2</td>
<td>3.00 (0.56–16.07)</td>
</tr>
<tr>
<td>Model for a probability of ACS by clinical risk assessment*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Intercept</td>
<td>-3.84</td>
<td>0.94</td>
<td>16.66</td>
<td></td>
<td>1.82 (0.37–9.0)</td>
</tr>
<tr>
<td>Intermediate vs low risk</td>
<td>0.6</td>
<td>0.82</td>
<td>0.54</td>
<td>0.46</td>
<td>1.9 (0.25–14.32)</td>
</tr>
<tr>
<td>High vs low risk</td>
<td>0.64</td>
<td>1.03</td>
<td>0.39</td>
<td>0.53</td>
<td>1.9 (0.25–14.32)</td>
</tr>
<tr>
<td>Plaque</td>
<td>0.4</td>
<td>0.12</td>
<td>12.1</td>
<td>0.0005</td>
<td>1.49 (1.19–1.87)</td>
</tr>
<tr>
<td>Model for a probability of ACS by clinical risk assessment and extent of plaque†</td>
<td></td>
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</tr>
<tr>
<td>Intercept</td>
<td>-4.22</td>
<td>1.11</td>
<td>14.39</td>
<td></td>
<td>3.14 (0.49–20.01)</td>
</tr>
<tr>
<td>Intermediate vs low risk</td>
<td>1.14</td>
<td>0.94</td>
<td>1.46</td>
<td>0.23</td>
<td>32.36 (1.1–940.47)</td>
</tr>
<tr>
<td>High vs low risk</td>
<td>3.48</td>
<td>1.72</td>
<td>4.09</td>
<td>0.04</td>
<td>32.36 (1.1–940.47)</td>
</tr>
<tr>
<td>Plaque</td>
<td>0.4</td>
<td>0.13</td>
<td>90.6</td>
<td>0.002</td>
<td>1.49 (1.15–1.93)</td>
</tr>
</tbody>
</table>

*Initial model includes the clinical risk as assessed by the ED caregiver defined as low (reference group), intermediate, or high: LR, 1.94 with 2 df ($P<0.003$); c statistic, 0.61.
†Model adding plaque: LR, 19.1 with 3 df ($P=0.0003$); c statistic, 0.86.
‡Model similar to second model, excluding those patients with a history of CAD.

stensosity—are significantly different between patients with and without ACS. Moreover, our data indicate that the absence of both significant coronary artery stenosis and any plaque (in 71% and 40% of patients) accurately excluded ACS (both NPVs, 100%). The high NPV suggests that coronary CTA may be most useful for facilitating early and accurate discharge of patients with acute chest pain and inconclusive initial ED evaluation. However, patients with previous stent placement or bypass surgery may currently not benefit from coronary CTA because a stenosis often cannot be ruled out.

Because ACS is rare in the absence of plaque, MDCT may identify a group of patients who can be sent home safely on the basis of the CT findings. However, in the presence of plaque, the CT result must be interpreted in the context of the patient’s clinical presentation. We demonstrated that in this subgroup, the extent of plaque added incremental value in predicting risk of ACS over both traditional risk factors and clinical risk assessment in separate models (c statistic, 0.73 versus 0.89 and 0.61 versus 0.86 for traditional risk factors and clinical risk assessment, respectively). In fact, both models explained the variability in ACS in our population and clinical risk assessment, respectively). In fact, both models explained the variability in ACS in our population only after the addition of the extent of plaque, whereas the initial models did not (LR, 8.41; $P=0.13$ versus LR, 23.27; $P=0.0007$; and LR, 1.94; $P=0.38$ versus LR, 19.1; $P=0.0003$).

These findings further support the notion that coronary MDCT is incremental to current risk stratification and may significantly improve triage of these patients. In addition, assessing the extent of CAD may be a feasible approach to estimating the risk of ACS in the 17% of patients in whom detecting stenosis remained indeterminate.

Ultimately, the clinical utility of coronary CTA for triage of chest pain patients will depend on the prevalence of ACS and CAD, the proportion of indeterminate CT exams, the cost of the test, and the number of patients who can complete the protocol or who have relative contraindications to undergoing CTA such as asthma or renal failure. Using coronary CTA in patients at very low risk (including patients who would otherwise be sent home) who have a prevalence of ACS <2% would not be cost-effective. We selected patients in whom the ED physicians had decided to rule out myocardial ischemia in the hospital despite the absence of ischemic evidence on ECG and negative initial biomarkers. Our data suggest that this patient population, with an adjudicated ACS rate of 14%, is one in which coronary CTA not only could improve triage but also may be cost-effective. With 34% of our study population at moderate or high risk of ACS as assessed by the ED caregiver (Figure 4), the clinical suspicion for ACS was high enough to justify further assessment of an alternative test that may facilitate early and safe exclusion of CAD such as coronary MDCT.

The need to improve the diagnostic workup for chest pain patients in the ED setting has led to extensive investigations of other noninvasive imaging modalities over the last decades. Several studies have demonstrated value with early exercise tolerance test alone, stress echocardiography, and rest myocardial perfusion imaging with technetium-99m in the ED evaluation of patients with chest pain. For some of these modalities (ie, single photon emission computed tomography), extensive observational data led to randomized trials and a class 1A recomm
mendation regarding its use for the triage of patients with acute chest pain. Similarly, we believe that CTA, which shows great promise as a diagnostic modality in this setting, merits further serious investigation.

The present study has several limitations. First, our statistical power was limited by the small number of events; it is this population, however, in whom more accurate early diagnostic testing has been shown to be useful for preventing and shortening overall hospital admission rates. A larger observational study is needed to replicate our findings and to further examine the relationships between traditional risk factors and CTA characteristics and their comparative strengths in predicting risk of ACS. Second, our strict exclusion criteria may have resulted in a study population that is healthier than the average population with chest pain. However, given that the prevalence of CAD may be higher in the general population, the proportion of patients with acute chest pain who could benefit from coronary CTA may be substantially higher than our study suggests. Although we believe that using the clinical decision making of acute-care providers following standard clinical care guidelines at our institution targets the population in whom coronary CTA can improve triage effectively, this may vary by institution, affecting the number of patients eligible for this type of study, their spectrum of disease, and the test characteristics of MDCT. Furthermore, 1 of the major limitations of MDCT technology is the potentially harmful effect of radiation exposure. Thus, in this study, we consistently used ECG-correlated tube current modulation, a technique that restricts the full tube current to the diastolic phase of the cardiac cycle and reduces the radiation exposure by up to 50%, resulting in an estimated effective dose of 6 to 11 mSv, comparable to stress perfusion imaging (8 to 10 mSv). Finally, the availability of MDCT is currently limited, and further studies are needed to determine whether it will be a clinically useful and cost-effective resource that should become more widely available.

Conclusions

CTA patterns are different between patients with and without acute coronary syndromes and provide information incremental to traditional risk factors and clinical risk assessment in predicting risk of ACS among patients presenting with acute chest pain to the ED. The absence of coronary artery plaque or stenosis on noninvasive coronary MDCT angiography has a high NPV for the subsequent diagnosis of ACS. These data lay the foundation for larger observational studies and randomized clinical trials that will determine whether coronary CTA may improve the ability to quickly and accurately triage patients with chest pain and has the potential to substantially reduce hospital admissions.

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Disclosures

None.

References


CLINICAL PERSPECTIVE

State-of-the-art coronary multidetector computed tomographic angiography (CTA) enables the detection of significant coronary artery stenoses with high sensitivity and specificity, and qualitative assessment of the presence and extent of coronary atherosclerotic plaque is in good agreement with intravascular ultrasound. Most analyses to date have involved stable patients already scheduled for catheterization; how CTA performs in patients with suspected acute coronary syndromes (ACS) in the emergency department has not been studied. Current risk stratification of such patients with acute chest pain is imperfect, often leading to unnecessary admission and a significant economic burden. The present observational study provides a first glimpse of the clinical utility of coronary CTA by demonstrating that the CTA patterns of coronary artery disease are different in patients with and without ACS. Our analysis and results, which are similar to earlier studies using rest technetium-99m single photon emission computed tomography myocardial perfusion imaging in this setting, suggest that noninvasive assessment of coronary artery disease by CTA has good performance characteristics for ruling out ACS in subjects presenting with possible myocardial ischemia to the emergency department. The ability to demonstrate the absence of coronary artery plaque noninvasively may prove to be key for patient management decisions. Moreover, in the present study, the extent of coronary artery disease predicted the likelihood ACS independently and incrementally to traditional risk factors and clinical judgment. These data provide the impetus for randomized clinical trials that will examine whether coronary CTA may improve the ability to quickly and accurately triage patients with chest pain and safely reduce unnecessary hospital admissions.
Coronary Multidetector Computed Tomography in the Assessment of Patients With Acute Chest Pain
Udo Hoffmann, John T. Nagurney, Fabian Moselewski, Antonio Pena, Maros Ferencik, Claudia U. Chae, Ricardo C. Cury, Javed Butler, Suhny Abbara, David F. Brown, Alex Manini, John H. Nichols, Stephan Achenbach and Thomas J. Brady

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/content/114/25/e651.full.pdf

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In the article, “Coronary Multidetector Computed Tomography in the Assessment of Patients With Acute Chest Pain” by Hoffmann et al, which published in the November 21, 2006, issue (Circulation. 2006;114:2251–2260), there was an error in Figure 4. Under “MDCT-derived patterns of CAD,” in the “Intermediate” row, “Plaque” subcategory, the number for “Stenosis detected” should be 8. This figure has been corrected in the PDF. The authors regret this error.

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