The management of patients with suspected acute coronary syndrome (ACS) in the emergency department (ED) still remains a challenge, even with current diagnostic modalities, because ACS constitutes a broad classification of clinical status that includes ST-elevation myocardial infarction (MI), non-ST elevation MI (NSTEMI) and unstable angina (UA). In a relatively small population of patients with ACS the diagnosis and therapeutic strategy are clearly established on the basis of the ECG and initial cardiac enzyme concentrations. However, although cardiac enzymes are sensitive markers of MI, by definition, they are not sensitive to UA and furthermore, diagnosing ACS by cardiac enzymes may require 4–12 h to have elapsed after the onset of ACS. Echocardiography and myocardial perfusion single-photon emission computed tomography (SPECT) have incremental diagnostic value, but they are still insensitive for the diagnosis of UA.

The recent introduction of multislice computed tomography (MSCT) with its high spatial resolution has allowed direct visualization of the coronary arteries. MSCT is capable of not only detecting significant coronary artery stenoses and occlusions but also evaluating the texture of coronary artery plaques and myocardial perfusion status. The diagnosis of acute coronary syndrome (ACS), especially non-ST-elevation myocardial infarction and unstable angina in the emergency department (ED) still remains a challenge. Multislice computed tomography (MSCT) allows assessment of not only coronary artery stenoses and occlusions, but also assessment of coronary artery plaques and myocardial perfusion status.

Methods and Results MSCT was performed in 31 patients who were admitted to the ED because of chest pain persisting at least 30 min and non-diagnostic ECG changes and normal serum enzyme concentrations. Using MSCT, ACS was defined by coronary artery stenosis \( \geq 75\% \) accompanied by computed tomography (CT)-low-density plaques, and/or by the presence of myocardial perfusion defects. ACS was confirmed by coronary stenosis \( \geq 75\% \) by coronary angiography and/or subsequent elevation of troponin I concentration. In total, 22 patients were diagnosed as having ACS. MSCT detected stenoses with CT-low-density plaques in 21 and non-transmural myocardial perfusion defect in 3 patients. There was 1 false-positive and 1 false-negative result. The sensitivity and specificity of MSCT to identify ACS was 95.5% and 88.9%, respectively.

Conclusion MSCT provides diagnostic operating characteristics suitable for triage of patients with ACS in the ED. (Circ J 2005; 69: 1047–1051)

Key Words: Acute coronary syndrome; Emergency department; Multislice computed tomography

T he management of patients with suspected acute coronary syndrome (ACS) in the emergency department (ED) still remains a challenge, even with current diagnostic modalities, because ACS constitutes a broad classification of clinical status that includes ST-elevation myocardial infarction (MI), non-ST elevation MI (NSTEMI) and unstable angina (UA). In a relatively small population of patients with ACS the diagnosis and therapeutic strategy are clearly established on the basis of the ECG and initial cardiac enzyme concentrations. However, although cardiac enzymes are sensitive markers of MI by definition, they are not sensitive to UA and furthermore, diagnosing ACS by cardiac enzymes may require 4–12 h to have elapsed after the onset of ACS. Echocardiography and myocardial perfusion single-photon emission computed tomography (SPECT) have incremental diagnostic value, but they are still insensitive for the diagnosis of UA.

The recent introduction of multislice computed tomography (MSCT) with its high spatial resolution has allowed direct visualization of the coronary arteries. MSCT is capable of not only detecting significant coronary artery stenoses and occlusions but also evaluating the texture of coronary artery plaques and myocardial perfusion status. Because ACS is a consequence of rupture of lipid-rich plaques and subsequent thrombus formation detecting rupture-prone, vulnerable plaques would be the most reliable diagnostic procedure in patients with suspected ACS. In addition, the presence of myocardial perfusion defects on contrast-enhanced myocardial images should confirm the diagnosis of ACS. We, therefore prospectively evaluated the diagnostic accuracy of MSCT in patients with suspected ACS, using a combined assessment of coronary artery stenosis, plaque texture and the myocardial perfusion status.

Methods

Patients After obtaining informed consent, we prospectively studied 34 patients who presented to the ED between July 2002 and December 2004 with chest pain. MSCT scans were performed as early as possible after resolution of chest pain. Inclusion criteria were (1) >30 min of chest pain compatible with myocardial ischemia within 6 h of presentation, (2) normal or non-diagnostic ECG changes, and (3) normal initial concentrations of serum troponin-I (\( \leq 0.1 \text{ng/ml} \)), creatine kinase (CK, \( \leq 253 \text{mIU/ml} \) for men and \( \leq 182 \text{mIU/ml} \) for women) and CK-MB (\( \leq 25 \text{mIU/ml} \)).
nary stenosis in the prior angiographic study, the presence of ST elevation, anginal symptoms, use of nitrites and elevated serum cardiac enzymes. Medical exclusion criteria included ST-elevation MI, pregnancy, previous history of MI and severe congestive heart failure (unable to lie flat). MSCT exclusions included previous history of allergy to iodine, cardiac arrhythmias (atrial fibrillation, frequent supraventricular or ventricular premature contractions), renal dysfunction (serum creatinine >1.5 mg/dl) and severe left ventricular dysfunction assessed by echocardiography (left ventricular ejection fraction <30%), and severe coronary artery calcification, which was defined by the presence of computed tomography (CT)-high-density mass (<250 Hounsfield units (HU)) occupying more than 50% of the vessel area. Conventional coronary angiography was performed within 24h of the onset of chest pain in all patients using Judkin’s technique.

Definition of ACS

Because the enrolled patients did not fulfil the definition of ACS established by the American College of Cardiology and the American Heart Association (ACC/AHA) which is based on ECG and enzymatic criteria, NSTEMI was retrospectively defined as a subsequent increase in troponin-I (>0.1 ng/ml) with a temporal pattern consistent with acute MI and/or a ≥75% epicardial coronary artery stenosis on subsequent coronary angiograms. Confirmation of UA required ≥75% coronary artery stenosis or positive abnormal stress ECG-gated SPECT using a rest 201thalium/stress 99mTc-tetrofosmin dual-isotope separate acquisition protocol performed during hospitalization or in the subsequent 2- to 4-week follow-up period.

MSCT

MSCT was performed prior to angiography in all patients using either a SOMATOM Volume Zoom (4-detector-row, Siemens, Germany) with a collimation 1.0 mm, table feed 1.5 mm/rotation, 140 kV, 320 mA and gantry rotation time 500 ms or an Aquilion 16 (Toshiba Medical, Tokyo, Japan) with a collimation 0.5 mm, table feed 3.2–4.2 mm/rotation, 140 kV, 102 mA and gantry rotation time 400 ms. The scan protocol and image reconstruction method have been reported previously. Briefly, metoprolol (20–80 mg) was given 60 min prior to the scan in order to reduce the heart rate to enable performance of the single-phase algorithm. Nitroglycerin (Myocel Spray 0.3 mg, Toa Eiyo, Tokyo, Japan) was also administered sublingually 5 min prior to the scan. Following determination of contrast transit time from the cubital vein to the ascending aorta by injecting 15 ml of nonionic contrast medium (Iomeron 300 or 350 100 ml syringe, Eisai, Tokyo, Japan), the remaining contrast medium (85 ml) was injected at 2.6–2.8 ml/s. Image reconstruction was made with a reconstruction window (250 ms for a 4-detector-row equipment and 200 ms for a 16-detector-row equipment) positioned immediately before the atrial contraction period, which could be recognized by the peak of the P wave on the monitor ECG. The reconstructed data were transferred to a computer workstation (3D Virtuoso, Siemens, Germany for the SOMATOM Volume Zoom and M 900 quadra, AMIN, Tokyo, Japan for the Aquilion 16) for post-processing the volume rendering, curved and cross-sectional multiplanar reformation images. The presence of coronary artery plaques was carefully inspected on the axial and multiplanar reformation images. Plaques containing CT density <500 HU were considered as soft plaques. In patients with multiple coronary artery plaques, CT density measurements were performed on the plaque at the lesion of maximum stenosis. Myocardial perfusion defect was defined as an area that did not enhance as brightly as the surrounding myocardium on at least 5 consecutive multiplanar or axial images at 1 mm intervals. To accept a perfusion defect as a definite abnormality, there had to be coronary artery stenoses or plaques in a matching location. Definition of ACS by MSCT included the presence of coronary stenosis ≥75% on curved multiplanar reformation images with soft plaques and/or the presence of a myocardial perfusion defect. The radiation dose for our MSCT protocol was estimated to be 4–5 mSv for 4-detector-row and 7–8 mSv for 16-detector-row equipment.

Statistics

All the data are presented as mean ± standard deviation. Sensitivity and specificity of MSCT to detect ACS were calculated in the standard fashion. Cohen’s k was used to assess interobserver variations in the MSCT determination of coronary stenosis.

Results

MSCT scans with sufficient image quality for evaluation of stenoses and plaques were obtained in 31 patients; 3 patients were excluded from the study because they had severe coronary artery calcification that hampered the assessment of stenosis. Thus, the study group comprised these 31 patients (Table 1). All patients had a TIMI risk score ≤2. Fourteen patients had a subsequent elevation of troponin I concentration. Significant coronary artery stenosis was detected in 21 patients. Using an enzymatic and angiographic definition, NSTEMI was diagnosed in 14 patients; 8 patients were diagnosed as having UA on coronary angiography (n=7) and positive exercise myocardial perfusion SPECT during a 6-week follow-up period (n=1); 9 patients did not show significant coronary stenoses or occlusions on angiography and their serial serum troponin concentrations and exercise myocardial perfusion SPECT were normal.

Table 2 Scan Parameters

<table>
<thead>
<tr>
<th></th>
<th>4-slice CT (n=26)</th>
<th>16-slice CT (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>51±5</td>
<td>55±8</td>
</tr>
<tr>
<td>End</td>
<td>55±7</td>
<td>59±4</td>
</tr>
<tr>
<td>Contrast transit time (s)</td>
<td>21±3</td>
<td>19±2</td>
</tr>
<tr>
<td>z-axis coverage (mm)</td>
<td>105±4</td>
<td>112±9</td>
</tr>
<tr>
<td>Breath hold time (s)</td>
<td>35±2</td>
<td>34±5</td>
</tr>
</tbody>
</table>

CT, computed tomography.
Fig 1. A 48-year-old man with non-ST-segment elevation myocardial infarction. Volume rendering (A) and curved multiplanar reformation (B) images show stenosis in the distal portion of the left circumflex artery (arrows). An axial image (C) shows stenosis with a CT-low-density plaque (42 HU, arrow). A short-axis image of the left ventricle (D) shows a thin-layered subendomyocardial contrast defect in the infero-lateral left ventricular wall (arrows). Coronary angiography (E) shows patent left circumflex artery but a large thrombus (arrows).

Fig 2. A 33-year-old man with unstable angina. Volume rendering image (A) shows stenosis in the left anterior descending artery (arrow) and a cross-sectional multiplanar reformation (MPR) image (B) shows high-grade stenosis with a CT-low-density plaque (44 HU, arrow). Cross-sectional MPR image of the left main coronary artery (C) also exhibits mild stenosis with a CT-low-density plaque (14 HU, arrow). Coronary angiography demonstrates high-grade stenosis in the left descending artery (white arrow) and mild stenosis in the left main coronary artery (black arrow).

Fig 3. False-positive MSCT result in a patient with vasospastic angina. Volume rendering (A) and curved multiplanar reformation (B) images show stenosis in the proximal portion of the right coronary artery (arrows). Coronary angiography shows no stenosis (C), but spasm was provoked after acetylcholine injection (D, arrow).
MSCT was performed in all patients without complications related to ß-blocker or contrast medium. The scanning parameters are listed in Table 2. MSCT scans were completed within 15 min and image processing required 10–20 min depending on the complexity of the coronary artery status. The whole MSCT procedure from administration of ß-blocker to completion of image analysis required less than 120 min in all patients. Cohen’s ω was 0.92, indicating a good interobserver agreement in the coronary artery stenosis measurements by MSCT. MSCT detected significant coronary artery stenosis in 13 patients with NSTEMI and in these patients, the stenosis was unexceptionally accompanied by soft plaques. The CT density of the plaque was 23.5±22.4 HU (−32 to 48 HU). In 3 of the patients with NSTEMI, there was a thin-layered subendocardial contrast defect in the myocardial territory supplied by the culprit coronary artery (Fig 1). In the 8 patients diagnosed with UA, MSCT detected significant coronary artery stenosis associated with soft plaques (CT density 38.4±6.9 HU (28–47 HU)). Thus, MSCT detected ACS in 21 patients (sensitivity 95.5%). The MSCT and angiographic images in a patient with NSTEMI are shown in Fig 2. On the other hand, MSCT gave negative results for 8 of the 9 patients without ACS (specificity 88.9%). In these 9 patients, the follow-up myocardial perfusion SPECT was normal, and they had no ischemic episodes in the follow-up period of 4 weeks. In 1 patient in whom MSCT gave a false-positive result (initial coronary angiography was normal), the repeat coronary angiography performed 2 weeks after admission documented spasm in the proximal portion of the right coronary artery after provocation by intracoronary injection of acetylcholine (Fig 3).

**Discussion**

The present study shows the feasibility of MSCT in the ED for detecting patients with ACS who did not manifest ECG and enzymatic evidence. The goal of non-invasive imaging in the era of sensitive serum enzymes needs additive clinical value over infarct detection. Cardiac enzymes only detect the presence of myocardial necrosis, which represents only a fraction of ACS, and they are insensitive to UA. Although echocardiography can detect the regional wall motion abnormality that may persist for hours after transient ischemia, a phenomenon that is known as myocardial stunning, its sensitivity to detect ACS is limited, especially when the chest pain resolves. Myocardial perfusion SPECT is the most developed imaging modality for patient triage in the ED and although its sensitivity is excellent for the detection of infarction, particularly with the 99mTc tracers, it is insensitive for detection of UA. For example, in a cohort of more than 1,000 patients with acute chest pain, normal images were acquired in 7 of 32 patients with ACS (22%) and in a multicenter trial of 102 patients with typical chest pain, but non-diagnostic ECG, only 3 of 15 patients with UA had abnormal myocardial perfusion SPECT. More recently, Abbott et al reported that 144 of 2,601 patients with acute chest pain (6%) had false-negative results based on serum enzymes and rest myocardial perfusion SPECT using 99mTc-sestamibi. Because rupture of vulnerable plaque and the subsequent thrombosis is the cause of ACS, direct visualization of ruptured plaques and coronary artery obstruction or narrowing is the ultimate goal of using a diagnostic imaging modality for patients suspected of having ACS. Although the spatial resolution of currently available MSCT equipment is unsatisfactory for distinguishing ruptured plaques from non-ruptured plaques, MSCT can accurately detect coronary artery stenoses and occlusion as well as plaque texture, by measuring the CT density of the plaque. In a previous study from our laboratory, the plaque CT density in the infarct-related coronary artery in patients with ACS was exceptionally lower than 48 HU (−12 to 48 HU), whereas it was higher than 46 HU (46–101 HU) in patients with stable angina. Komatsu et al also demonstrated that plaque with a CT density less than 50 HU corresponded to angiographically detected yellow plaque, another marker of vulnerable plaques, with a sensitivity of 80% and specificity of 87% in infarct-related arteries. These studies suggest that in the majority of patients with ACS the plaques in the infarct-related artery can be identified by measuring the CT density. Myocardial perfusion defect, as documented by the presence of non-contrast enhanced ventricular myocar-dium, is also evidence of infarction. With its high spatial resolution, MSCT may be more sensitive than myocardial perfusion SPECT for detecting subendocardial myocardial ischemia. However, in the present study population only 3 of 14 (21%) patients with NSTEMI exhibited a contrast defect in the subendomyocardium. This insensitivity can be explained by our patient selection based on the absence of increased cardiac enzyme concentrations.

**Study Implications**

The revised ACC/AHA guidelines for the management of patients with UA and NSTEMI has encouraged rapid decision-making by the physician in the diagnosis of UA and NSTEMI, using evidence-based standards for risk stratification, prognostic use of biologic markers, and proper use of antiplatelet and antithrombotic therapy. Missing the diagnosis of ACS doubles the risk-adjusted mortality. Despite an initial risk assessment using ECG and cardiac enzymes, approximately 2% of patients with ACS are inappropriately discharged home from the ED. On the other hand, aggressive, invasive procedures are not fully justified because they may expose patients with a low likelihood of ACS to angiography-related complications and excessive medical expense. Our study, which targeted patients with a low likelihood of ACS, suggests that MSCT can be the first-choice imaging modality because of its noninvasiveness and low medical expense.

**Study Limitations**

The foremost limitation is the small patient population enrolled. Moreover, our diagnostic criteria for ACS was based on indirect evidence including enzyme elevation, angiographic coronary stenosis and positive exercise myocardial perfusion SPECT test result. Intravascular ultrasound or coronary angioscopy should have been performed to confirm ruptured plaque and subsequent thrombus formation.

The present study utilized 2 different types of MSCT equipment with different slice thicknesses to define soft plaques. The definition of soft plaques (<50 HU) has been established with 4-slice and 8-slice CT equipment. Although a direct comparison between plaque CT densities derived from a 4-slice scanner and those from a 16-slice scanner in the same individuals has not been made previously, it is plausible that the thinner the slice thickness the lower the plaque CT density (far less than 50 HU) that would be obtained because the thinner slice would have
less partial volume effect because of the contrast-enhanced, adjacent tissue. A revised definition of soft plaques for 16-slice and 64-slice equipment is warranted.

The temporal resolution of MSCT is limited and the majority of patients require administration of β-blockers prior to the scan in, which may cause vasospasm and lead to a false-positive MSCT results, as occurred in one of the present patients.

As mentioned previously, direct visualization of coronary artery plaque rupture and subsequent thrombosis would be the most reliable method of establishing the diagnosis of ACS. Future improvements in the spatial resolution of MSCT by increasing the number of detectors or by introducing flat panel detectors will enable assessment of these morphological alterations.

These limitations aside, our study indicates that MSCT provides diagnostic operating characteristics suitable for triage of patients with ACS in the ED.

References