Evaluation of Plaque Texture by Means of Multislice Computed Tomography in Patients With Acute Coronary Syndrome and Stable Angina

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Background  In the present study, multislice spiral computed tomography (MSCT), which allows non-invasive assessment of coronary artery plaque, was used to compare the CT density of plaque between patients with acute coronary syndrome (ACS) and those with stable angina (SA).

Methods and Results  MSCT was performed in 20 patients with ACS (17 with acute myocardial infarction, 3 with unstable angina) and 22 patients with SA. The presence of the plaque was defined on the basis of multiplanar reformation and axial images. At least 4 regions of interest were then placed within the plaque and the minimum CT density was measured and expressed as Hounsfield units (HU). The number of plaques did not differ between the 2 groups, but the minimum CT density was significantly lower in patients with ACS (25±15 HU) than in those with SA (71±16 HU, range 46–101 HU, p<0.001). Similarly, the minimum plaque density was significantly lower in the culprit coronary segment (26±16 HU) than in the non-culprit segment (48±17 HU) in 15 ACS patients with multiple plaques.

Conclusion  MSCT can potentially differentiate vulnerable from stable plaque in patients with coronary artery disease, although long-term, prospective analysis is needed to establish the conclusion. (Circ J 2004; 68: 840–844)

Key Words:  Acute coronary syndrome; Coronary artery plaque; Multislice spiral computed tomography

Disruption of coronary artery plaque and subsequent thrombosis has been identified as a primary cause of acute coronary syndrome (ACS), which includes acute myocardial infarction and unstable angina, and thus, reliable noninvasive detection of plaque is extremely important in patients who have coronary risk factors.

Multislice spiral computed tomography (MSCT), which provides simultaneous acquisition of 4–16 sections and 0.4–0.5 s gantry rotation, has been recently developed and initial results indicate that this technique allows visualization of the coronary arteries in both normal subjects and patients with coronary artery disease. Moreover, Schroeder et al reported that MSCT can detect coronary artery plaques by demonstrating good agreement of plaque texture between the computed tomography (CT) density of the plaque and that observed by intracoronary ultrasound (ICUS): plaques with a low CT density (0–40 Hounsfield units (HU)) corresponded to those containing a lipid core, and plaques with a medium CT density corresponded to fibrous plaques. Previous pathological and ICUS studies have consistently documented that rupture-prone, vulnerable coronary artery plaques are characterized by the presence of a lipid-rich core and thin fibrous cap. Thus, we hypothesized that plaque vulnerability could be evaluated in patients with coronary artery disease by measuring the CT density, so we compared the CT density of the plaque in culprit lesions between patients with ACS and those with stable angina (SA), as well as the CT density between the ACS-related, culprit coronary segment and non-culprit segment in a series of patients with ACS who had multiple plaques.

Methods

Patients  Forty two patients (35 males, 7 females; mean age, 60±11.5 years (range: 32–78 years)) with angiographically documented coronary artery disease underwent MSCT. Patients who had undergone previous coronary artery bypass surgery or any kind of percutaneous coronary intervention, including stent implantation and percutaneous transluminal balloon angioplasty, were excluded, as were patients with atrial fibrillation, other supraventricular or ventricular arrhythmias, renal dysfunction (serum creatinine >1.5 mg/dl) or severe left ventricular dysfunction (left ventricular ejection fraction <30%). The final study group consisted of 20 patients (19 males, 1 female; age 54.7±12.3 years) with ACS (17 with acute myocardial infarction, 3 with unstable angina). There were 22 patients with SA (16 males, 6 females; mean age, 64.9±8.4 years). ACS was prospectively defined to satisfy guidelines established by the American College of Cardiology and the American Heart Association (ACC/AHA) with the following modifications. Possible or probable ACS required resting chest pain compatible with myocardial ischemia ≥30min duration, non ST-segment elevation myocardial infarction required abnormal serial troponin-T (>1.96 g/dl) with a
temporal pattern consistent with acute myocardial infarction. Confirmation of unstable angina required >50% luminal narrowing of the epicardial coronary artery on coronary angiography. There were 15 patients with ST-segment elevation myocardial infarction, 2 with non-ST-segment elevation myocardial infarction, and 3 with unstable angina. All the patients with ACS underwent coronary thrombolyis and achieved TIMI grade III coronary flow without further angioplasty procedures such as percutaneous transluminal balloon angioplasty, directional atherectomy or stent implantation. SA was defined by the presence of chest pain upon exercise, exercise-induced perfusion defect without abnormal myocardial perfusion at rest on rest 201Tl/stress 99mTc separate acquisition, dual-isotope myocardial perfusion single-photon emission computed tomography (MPS) and significant luminal narrowing (>50%) on subsequent diagnostic coronary angiography at the site of the artery that corresponded to the territory of reversible ischemia on MPS. Patients with a known history of previous myocardial infarction or perfusion abnormality at rest on MPS were excluded. The study was approved by the hospital’s ethical committee and informed consent was obtained from all patients.

**MSCT**

MSCT was performed within 2 weeks following coronary angiography in the patients with ACS and within 4 weeks prior to angiography in those with SA using a SOMATOM Volume Zoom (4-detector-row, Siemens, Germany). Medications were not discontinued throughout the angiographic and MSCT studies. Our MSCT scan protocol has been described previously.8 In brief, metoprolol (20–60 mg) or atenolol (25 or 50 mg) was administered orally 90–120 min prior to the MSCT scan to reduce the heart rate so that the single-phase algorithm (reconstructing one image by single cardiac cycle) could be performed. Sublingual nitroglycerin (0.3 mg) was also administered 5 min prior to the scan. All the image acquisitions were performed during inspiratory breathhold preceded by inhalation of oxygen (4 L/min) for 5 min. After imaging at the level of the carina tracheae and positioning the region of interest (ROI) in the center of the ascending aorta, a bolus of 15 ml of the contrast medium (Iomeron 300 100 ml syringe, Eisai and Optiray 320, Tyco Healthcare, Tokyo, Japan) was injected intravenously at 3.3 ml/s via a 20-gauge catheter placed in the cubital vein, and the time interval between contrast agent injection and the maximum enhancement within the ROI was measured (collimation 2.5 mm, 140 kV, 60 mA). The remainder of the contrast medium (85 ml) was then injected and the scan was started with a delay according to the previously determined contrast transit time. The volume data set for coronary artery imaging was acquired in spiral mode, with simultaneous acquisition of 4 parallel slices (slice thickness 1.0 mm, table feed 1.5 mm/rotation, 140 kV, 320 mA and gantry rotation time 500 ms), which allowed temporal resolution of 250 ms and spatial resolution of 0.6 mm on the horizontal axis. The patient’s ECG was digitized and continuously monitored during the scan period.

**Image Reconstruction and Postprocessing**

The raw data of the scans were reconstructed using a single-phase algorithm in all the patients as described previously. Retrospective ECG-gated image reconstruction was performed using a method developed in our laboratory.8 In brief, the end of the reconstruction window (250 ms) was positioned at the peak of the P waves on the monitoring ECG by inputting the absolute time (ms) backward from the next R waves. This technique has been shown to substantially reduce cardiac motion artifact (CMA) occurring during the periods of ventricular rapid filling and atrial contraction. The reconstructed image data of the CT angiography were transferred to a computer workstation (3D Virtuoso, Siemens, Germany) for post-processing. Following visual inspection of the volume rendered images, which depicted the gross configuration of the coronary artery lumen, the coronary artery plaques were carefully inspected on the basis of axial images, curved multiplanar reformation (MPR) images, and cross sectional MPR images (Fig 1). Coronary artery lesions were identified as atherosclerotic plaques when they occupied more than 50% of the coronary lumen and had a low-density CT appearance.10 To ensure that the identical lesions were assessed by angiography and MSCT, landmarks such as origin of side branches and the distance to the left coronary artery ostium or bifurcation were used. Calcified plaques as determined
by the CT signal density greater than 250 HU were not analyzed. On the axial or cross-sectional MPR images, the ROI greater than 1.0 mm$^2$ was placed on at least 4 randomly selected points within each plaque, the lowest CT density was defined as the minimum plaque density. The analysis was performed on 8 coronary artery segments: the left main coronary artery (LMCA), proximal portions of the left anterior descending artery (LAD, segments #6 and #7), the left circumflex artery (LCX, segments #11 and #13) and the right coronary artery (RCA, segments #1, #2 and #3). In patients with multiple coronary artery plaques, CT density measurements were performed on the plaque that was considered to be the culprit lesion on the basis of coronary angiography in the patients with ACS, and on the plaque causing the maximum coronary luminal narrowing in the patients with SA. In patients with ACS who had multiple plaques in the culprit segment, the plaque at the lesion of maximum stenosis was considered to be the culprit plaque. The number of plaques that exceeded 25% of the coronary luminal diameter was also determined. A comparison was also made between the plaque CT density in both the culprit and non-culprit segments in a selected series of ACS patients who had plaques in non-culprit coronary artery segments. When there were more than 2 plaques in the non-culprit segment, the average of the minimum plaque densities was defined as the density of the non-culprit plaques.

Statistics

Statistical analyses were performed using SPSS software (version 11.0) (SPSS Inc, Chicago, ILL, USA). Continuous variables were described by their means and standard deviations. Nonparametric Kruskal-Wallis test was used to compare the mean of the plaque density between the 2 groups and between the plaque density of culprit and non-culprit lesions. Percentages of those having multiple coronary plaques were compared between the 2 groups by Fisher’s exact test. Cohen’s kappa was calculated to assess interobserver agreement for determining the number of plaques per patient.

Results

MSCT scans with sufficient image quality for plaque evaluation were obtained without complications in all 42 patients. Both the gender ratio and incidence of coronary risk factors were comparable between the ACS and SA groups, although patients with ACS were significantly younger than those with SA (Table 1). The scan was generally completed within 10 min and post-processing and data evaluation required 15–30 min depending on the complexity of the coronary artery status. The heart rate increased during breathhold from 53.1±6.8/min to 58.0±6.7/min, the average contrast transit time was 22.0±3.8 s (range 17–32 s) and the z axis coverage ranged from 90 to 135 mm, which corresponded to the duration of breathholding for 30–45 s (Table 2).

Interobserver agreement on the number of plaques was achieved in 37 of the 42 patients (Cohen’s kappa 0.86). Overall, 138 plaques were detected (16 in the LMCA, 57 in the LAD, 21 in the LCX and 44 in the RCA) and the number of plaques was similar between the 2 groups (Table 3). In 15 patients (5 with ACS, 10 with SA), multiple plaques with different CT signals were detected in the same coronary artery segment and by definition, plaques in the region of maximum luminal narrowing were considered as culprit plaques in these patients. Fifteen of 20 patients with ACS had plaques in non-culprit segments. In the culprit lesions, the mean CT density of the plaque was 25±15 HU (12–48 HU) in the patients with ACS and 71±16 HU (46–101 HU) in the patients with SA. In 15 ACS patients who had plaques in non-culprit segments, the plaque CT density in the culprit segments and in non-culprit segments was 26±16 (12–48 HU) and 48±17 HU (17–74 HU), respectively (p<0.001). Plaques in patients with ACS and SA are shown in Figs 2 and 3, respectively. Nonparametric Kruskal-Wallis test revealed statistically significant differences in the CT density of the plaque in the culprit lesion between the 2 groups (p<0.001, Fig 4a) and between the plaques in culprit segments and those in non-culprit segments (n=15, p<0.01, Fig 4b) in patients with ACS.

Discussion

In the present study patients with ACS had plaques of lower CT density as compared to plaques in patients with SA. Moreover, the plaque CT density was lower in the culprit segments than in the non-culprit segments in the patients with ACS. These observations support the concept that patients with ACS are more likely to have vulnerable plaques characterized by a large lipid-rich core than patients with SA.11–13 Thus, MSCT not only non-invasively
Fig 2. MSCT and coronary angiographic images in a patient with unstable angina. Volume rendering (A), curved MPR (B) and angiographic (C) images consistently show high-grade luminal narrowing at the proximal portion of the right coronary artery (arrows). An axial image (C) demonstrates a plaque with low CT density (14±8 Hounsfield units).

Fig 3. MSCT images in a patient with stable angina. Volume rendering (A) and curved MPR (B) images show significant luminal narrowing (arrows). A cross-sectional image (C) exhibits a plaque with a relatively high CT density (65±15 Hounsfield units).

Fig 4. Comparison of the CT density of plaques between (a) patients with acute coronary syndrome (ACS) and stable angina (SA) and (b) between culprit segments and non-culprit segments in patients with ACS.
provides information about plaque texture, but also has the potential to predict future cardiac event in both patients with known coronary artery disease and those with multiple coronary risk factors. Because we did not perform ICUS, which is a domain for the tissue characterization of plaque, we could not evaluate the accuracy of MSCT for assessing plaque texture; however, a previous study by Schroeder et al clearly demonstrated excellent agreement between CT density and ICUS-derived plaque texture. In their report, soft plaques as determined by ICUS was characterized by a low CT signal density of 14±26HU (range −42–47HU), and fibrous plaques had 91±21HU (range 61–112HU). Furthermore, density measurements performed with a conventional single-slice CT scanner in plaques located in carotid arteries had similar results: plaque density of soft plaques and fibrous plaques was 39±12HU and 90±24HU, respectively. It deserves mentioning that in the 2 groups of patients in the present study there was little overlap in the plaque density of the culprit lesion, which implies that plaque measurement by MSCT has the potential to accurately predict future cardiac events in patients with a high coronary risk. A large-scale, prospective study is obviously needed to establish this conclusion. Unlike a previous angiographic study that demonstrated a close relationship between the number of plaques and future cardiac events, our data did not show a difference in the number of plaques between the 2 groups, which might be attributed to the different study modes (ie, prospective or retrospective) or to the insensitivity of angiography to detect plaques. For example, plaques accompanied by positive vascular remodeling may not be detected because angiography depicts only the silhouette of the internal lumen of the artery whereas CT can directly depict the plaque and external arterial wall.

Study Limitations

Our study was a retrospective study in which patients were designated into 2 groups on the basis of clinical status, not on the anatomical features of the plaque such as a lipid-rich core or disruption of the fibrous cap and subsequent thrombosis; hence, it has considerable limitations. A large-scale, prospective study is needed to clarify the efficacy of MSCT to predict the patient’s long-term outcome. In addition, direct comparison of the plaque detected by MSCT to that obtained by other imaging modalities such as ICUS or coronary angiography is essential to establish the accuracy of MSCT for evaluating plaque texture. We did not perform repeated MSCT examinations in patients with ACS, which might be useful for understanding the natural course of vulnerable plaque, because multiple MSCT scans may expose the patient to hazardous levels of radiation. The new generation magnetic resonance imaging, which has a 3 Tesla magnet and permits plaque visualization, might be superior to MSCT for that purpose. One might argue that ruptured plaques in patients with ACS are associated with thrombus on the surface of the plaque, resulting in erroneous CT density measurements. However, previous observations indicated that the CT density of blood is 55±5HU and that fresh thrombus is even more dense. Therefore, thrombus could be differentiated from plaques whenever the plaque CT density was less than 50HU. We excluded heavily calcified plaques from the analysis because the partial volume effect from calcification might have led to underestimation of plaque CT density. Although MSCT can detect coronary artery plaques and evaluate the plaque structure, more precise observation of the plaque, such as the lipid-rich core, fibrous cap or calcified sprinkles, by MSCT is still restricted because of the limited spatial resolution. However, future technical developments will enable direct visualization of these anatomical alterations.

References