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Atherosclerotic Plaque Characterization by 0.5-mm-Slice Multislice Computed Tomographic Imaging

— Comparison With Intravascular Ultrasound —

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Background It has been proposed that 0.5-mm-slice multislice computed tomography (MSCT) is a noninvasive tool for the detection of atherosclerotic plaque, but the validity of such an assessment has not been demonstrated by an invasive investigation. The present study was performed to compare the 0.5-mm-slice MSCT density of plaques with intravascular ultrasound (IVUS) findings.

Methods and Results Atherosclerotic plaques were characterized in 37 consecutive patients undergoing percutaneous interventions. Based on the IVUS echogenecity, the plaques were classified as soft (n=18), fibrous (n=40) or calcified (n=40). In these 98 plaques, 0.5-mm-slice MSCT plaque density was calculated in 443 regions-of-interest, including 331 lesional foci and 112 luminal cross-sections, and represented as Hounsfield units (HU). MSCT density of the 3 types of plaque was 11±12 HU, 78±21 HU, and 516±198 HU respectively. Computed tomography density of the (contrast-filled) lumen was 258±43 HU. There were statistically highly significant differences in the densitometric characteristics among the 4 groups (soft, fibrous, calcified plaque and lumen) by nonparametric Kruskal-Wallis test ($p<0.0001$).

Conclusions The IVUS-based coronary plaque configuration can be accurately identified by 0.5-mm slice MSCT. Noninvasive assessment of plaque characterization will ensure emphasis on the vessel wall beyond the vascular lumen. (*Circ J* 2007; **71:** 363–366)

Key Words: Computed tomography; Coronary artery; Intravascular ultrasound; Plaque characterization

Atherosclerotic plaque disruption accounts for at least two-thirds of acute coronary events. Plaques vulnerable to rupture are referred to as thin cap fibroatheroma and characterized pathologically as having large necrotic lipid cores covered with an inflamed and attenuated fibrous cap[1–8] In addition, small calcific concretions in the fibrous cap have been demonstrated to contribute to plaque instability[9,10] Reliable noninvasive detection and classification of coronary lesions would constitute an important step for risk stratification of patients with known or suspected coronary artery disease (CAD). Multislice computed tomography (MSCT) has been proposed as a noninvasive tool for the characterization of atherosclerotic plaque[11–21] Correlation between intravascular ultrasound (IVUS) characteristics of plaques and 1-mm-slice computed tomography (CT) density has been reported[22] but evaluation of small coronary plaques by 1-mm-slice CT is often less accurate because of the partial volume effect. Therefore, it seems prudent to examine the ability of 0.5-mm-slice MSCT for the detection of plaque defined by IVUS.

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Methods

Study Protocol

Thirty-seven consecutive patients (31 males, 6 females; mean age, 66±12 years) with angiographically documented CAD (17 patients with acute coronary syndrome (ACS) and 17 patients with stable angina) were scheduled for elective IVUS-guided percutaneous coronary intervention (PCI). 0.5-mm-slice MSCT of the heart was performed within the week prior to PCI. Patients with renal failure (creatinine >1.5 mg/dl), known allergic reactions to contrast medium, who were pregnant, had epilepsy, liver dysfunction (glutamic oxaloacetic and glutamic pyruvic transaminase values >3× reference value), or advanced heart failure (New York Heart Association III-IV) were not included. During PCI, IVUS was performed before the intervention to evaluate vessel wall characteristics proximal to and at the target lesion. In general, some of the culprit lesions had thrombus, especially those in patients with ACS. Because it is difficult to distinguish thrombus from soft plaque by IVUS, such culprit lesions were excluded from this study. Soft plaque and fibrous plaque that were observed in the same cross-sectional images as calcified plaque were also excluded from the assessment. To ensure that the identical plaques were assessed by the 2 techniques, landmarks such as the origin of side branches and their relation to target lesions were used and confirmed by 2 observers.

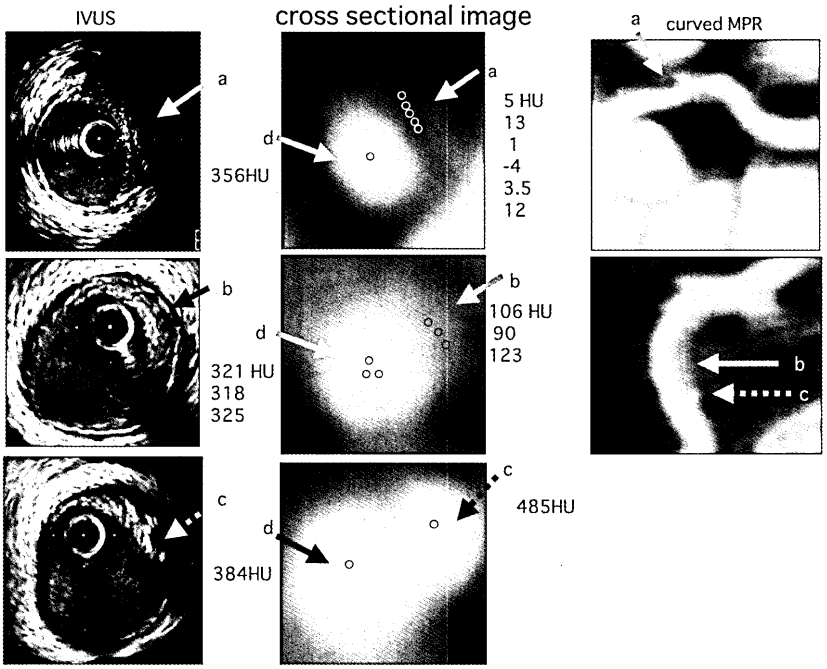

Fig 1. Plaque as assessed by IVUS and MSCT. (a) Soft plaque, (b) fibrous plaque, (c) calcified plauqe, (d) lumen. (Left) IVUS cross-sectional image. (Middle) MSCT cross-sectional images. CT density of soft plaque was –4–12 HU. CT density of fibrous plaque was 90–123 HU. CT density of calcified plaque was 485 HU. CT density of the lumen was 318–384 HU. (Right) MSCT curved MPR images. IVUS, intravascular ultrasound; MSCT, multislice computed tomography; HU, Hounsfield unit; CT, computed tomography; MPR, multiplanar reformation.

The study was approved by the institutional review board and the internal ethics committee and all patients voluntarily consented to participate in the study protocol.

IVUS and PCI

The percutaneous transfemoral approach was used for all interventions. Before PCI and IVUS, all patients received an intra-arterial bolus of 10,000 IU of heparin. Selective angiography was performed in multiple views before and after PCI. After passage of the guidewire across the target lesion, IVUS was performed under fluoroscopic guidance (Boston Scientific Corporation, with a 40-MHz transducer). Continuous ultrasound images were obtained with automatic catheter pull-back at the rate of 0.5 mm/s from approximately 20 mm distal to the lesion and ending at the guiding catheter. After obtaining the IVUS images, the ultrasound catheter was withdrawn and PCI was performed using standard practices.

Intracoronary atherosclerotic lesions resulting in at least 25% luminal narrowing were identified and characterized by IVUS. These plaques were classified as reported earlier[23] Briefly, soft plaques were identified as lesions with low echogenic acoustic signals and no structural characteristics. Calcific plaques demonstrated bright echoes that often obstructed the penetration of ultrasound, resulting in acoustic shadowing. Fibrous plaques were defined as lesions with intermediate echogenicity between soft and calcific plaques. The IVUS classification was performed by 1 observer unaware of the MSCT results, and was repeated by a second independent and blinded observer to account for reproducibility. In case of disagreement, the plaques were reevaluated for the consensus judgment.

MSCT

For 0.5-mm-slice MSCT, an Aquilion 16 (Toshiba Medical Systems, Japan) scanner was used, with collimation 16-slice×0.5 mm, detector pitch 3.2–3.6, and pixel size 0.39×0.39 mm. Rotation time was 400 ms, and tube current and voltage were 360 mA, 135 kV, respectively. Patients received atenolol 1 h before the CT scan if the heart rate was >60 beats/min. For the contrast-enhanced scan, 60 ml of contrast media (Omnipaque300, Daiichi Pharmaceutical Co, Tokyo, Japan) was injected at 3.0 ml/s, followed by 40 ml at 1.5 ml/s. This strategy also allowed the application of dedicated spiral algorithms that provided up to 75 ms of temporal resolution. The start of contrast-enhanced scanning was adapted to 'Sure start' images[24] All scans were performed during a single breath-hold. The raw data of the scans were reconstructed using algorithms optimized for retrograde ECG-gated multislice spiral reconstruction. The reconstructed image data was transferred to a computer workstation for post-processing (ZIO M900, Amin/ZIO, Japan). For plaque detection, cross-sectional and curved multiplanar reformation images were analyzed.

For densitometric characterization, plaques were selected according to the IVUS classification. Side branches were used as landmarks to detect the same plaque on the MSCT image as on the IVUS image. Multiple regions-of-interest (ROI) in each plaque and lumen were located on the cross-sectional image, and the density of the ROI measured (expressed by Hounsfield units (HU)). To confirm the accuracy of CT for evaluating plaque characteristics, the minimum size of the ROI was used in this study. Because the minimum pixel size is 0.39 mm, each ROI size was set at less than 0.39×0.39 mm. The densities of the ROIs in the lumen, next to soft, fibrous and calcified plaques, were compared.

Statistics Analysis

Continuous variables are described by mean and standard deviations. The nonparametric Kruskal-Wallis test was used to compare the mean of the density measurements of soft, fibrous, calcified plaque and lumen. P-values <0.05 were considered to identify significant differences. For evaluation of inter- and inter-observer and intra-observer variation in interpretation, CT findings were recorded by the observers blindly and analyzed by Cohen's kappa statistic. All analyses were done using the StatView statistical package (Abacus Concepts, Calabasus, CA, USA).

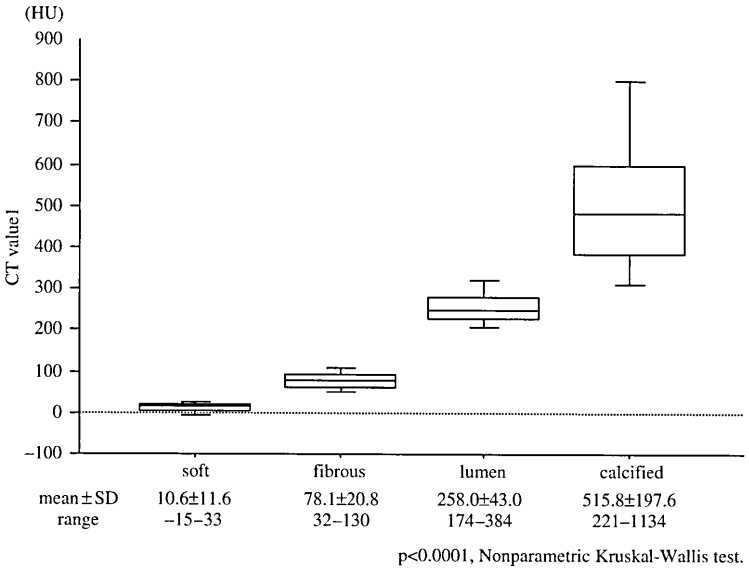

Fig 2. Comparison of plaque classfication (IVUS) and plaque density (MSCT). Box-and-whiskers plot showing mean±SD. Nonparametric Kruskal-Wallis test revealed a statistically significant difference of the plaque and lumen density as determined by MSCT among the 4 groups. IVUS, intravascular ultrasound; MSCT, multislice computed tomography; HU, Hounsfield unit; CT, computed tomography.

Results

All images were of sufficient quality for analysis and no patient was excluded. A total 98 plaques were examined by both methods, and 331 ROI were placed on the plaque and lumen on the MSCT images. Of the 331 ROI, 39 were located on soft plaque, 88 on fibrous plaque, 92 on calcified plaque and 112 were placed within the lumen (Fig 1). Using MSCT, soft plaque had a density of 10.6±11.6 HU (range, −15 to +33 HU), fibrous plaques were 78.1±20.8 HU (range, 32–130 HU), and calcified plaques were 515.8± 197.6 HU (range, 221–1,134 HU). The density of the lumen was evaluated as 258.0±43.0 HU (range, 174–384 HU) (Fig 2). There was a good agreement between (Cohen's kappa 87) and within (Cohen's kappa 89) observers for the number of plaques on the CT images. The nonparametric Kruskal-Wallis test revealed a statistically significant difference of both plaque and lumen density as determined by MSCT among the 4 groups ($p<0.0001$). There was no significant difference among the density of the lumen next to soft, fibrous and calcified plaque (244.0±58.5 HU, 274.2± 46.4 HU, 262.0±56.9 HU, respectively; $p=0.1881$).

Discussion

Our results indicate that the IVUS-based coronary plaque configuration is accurately reproduced by noninvasive 0.5-mm-slice MSCT examination. Using a 1-mm-slice CT scanner, Schroeder et al had earlier reported the density of soft (14±26 HU), fibrous (91±21 HU) and calcified plaques (419±194 HU)[19] which suggested that a density <50 HU should identify soft plaque from 50–119 HU-dense fibrous and >120 HU-dense calcified plaques. With 1.0-mm MSCT spatial resolution, there is a higher partial volume effect, especially on small images such as the coronary plaques. Kunimasa et al reported that the mean plaque CT density of IVUS-defined soft plaque was 33.7±16.9 HU and the upper limit of the CT density was 67.5 HU[21] In their study, plaque density was measured using >1 mm^2 of ROI on images acquired by 0.5-mm slice CT. In the present study, a minimum sized ROI was used. There was a higher partial volume effect in the larger ROI, even for images acquired with 0.5-mm slice CT. The lower partial volume effect with 0.5-mm-slice MSCT is expected tp offer better imaging characteristics. In the present study, a density <30 HU identified soft plaque and 31–150 HU identified fibrous plaque. The lumen density was calculated as 151–380 HU and calcified plaque as >220 HU. The density of the lumen and calcified plaque showed a significant overlap, and a density between 220 and 380 should be interpreted in cooperation with angiographic data. Compared with the data from 1-mm-slice CT, soft plaque on 0.5 mm CT had a lower density and calcified plaque had a higher density. These differences can be attributed to the partial volume effect and substantiate the superior image quality with the thinner slice. Because of insufficient spatial resolution CT is unable to evaluate the thickness of the fibrous cap, an additional component of rupture-prone, vulnerable coronary artery plaques. Thinner slices are needed to evaluate plaque characteristics more accurately. However, there are some disadvantages that need to be resolved with thinner slices, such as the need for a longer breath-hold, increased single to noise rate, and more radiation exposure. Neverthless, noninvasive assessment of plaque will allow an emphasis on the vessel wall beyond the vascular lumen.

Study Limitations

The present study lacks histologic confirmation of the MSCT findings. IVUS is the best available invasive technique and is used as the gold standard[23,25] Notably, it is difficult to differentiate thrombus from soft plaque by either imaging technique. In addition, IVUS and MSCT are unable to evaluate the thickness of the fibrous cap, because of insufficient spatial resolution. More detailed observations of plaque characteristics are needed in comparison with other modalities such as coronary angioscopy or optical coherent tomography. There are some limitations to the image quality with MSCT. CT density may vary depending on the contrast-enhanced lumen, although there was no significant difference between the density of the lumen next to soft, fibrous or calcified plaque. Images using helical scanning have blur, which may make spatial resolution worse, resulting in erroneous CT density. Finally, to ensure that the identical plaques were assessed by IVUS and CT, landmarks such as the origin of side branches and their relation to the target lesions were used and confirmed by 2 observers;

however, there is still the possibility of misunderstanding the location.

Conclusions

Our results indicate that the IVUS-based coronary plaque configuration is correctly identified by 0.5-mm-slice MSCT, which can classify plaques more accurately than 1-mm-slice MSCT. Noninvasive assessment of plaque characterization will allow an emphasis of the vessel wall.

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