Coronary Arterial Plaque Characterized by Multislice Computed Tomography Predicts Complications Following Coronary Intervention

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SUMMARY

Background: A reliable, noninvasive assessment of plaque configuration would constitute an important step forward for predicting complications following percutaneous coronary intervention (PCI). Multislice computed tomography (MSCT) holds promise with respect to allowing for differentiation of coronary lesion configuration. However, it has not yet been clarified whether the characteristics of coronary artery plaque measured by MSCT predict complications after PCI. The aim of this study was to investigate the relationship between plaque configuration and complications after coronary intervention in patients with stable angina pectoris.

Methods: MSCT was performed in patients with angina pectoris who were scheduled for PCI prospectively, and 26 patients (70 ± 11 years, 18 males) with coronary artery plaque in a stenotic coronary artery measured by MSCT were recruited for this study. Thirty-five plaques in the stenotic coronary lesions were divided into 3 groups based on the CT density as soft, intermediate, and hard, and were compared with the complications after PCI.

Results: The soft plaque group before PCI ($n = 11$) was significantly associated with the appearance of slow flow ($n = 4$) or a compromised side branch ($n = 1$) after PCI, whereas the hard plaque group before PCI ($n = 17$) was associated with the appearance of dissection ($n = 2$) or perforation ($n = 1$) after PCI ($P = 0.004$). The intermediate plaque group ($n = 7$) had only one complication, a compromised side branch ($n = 1$).

Conclusion: Coronary arterial plaque characterized by MSCT can predict intervention-related complication. It may be important for the risk stratification of the patients scheduled to undergo PCI to investigate plaque configuration by MSCT. (Int Heart J 2007; 48: 25-33)

Key words: Multislice computed tomography (MSCT), Percutaneous coronary intervention (PCI), Coronary plaque

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Received for publication September 13, 2006.

Revised and accepted December 4, 2006.

PERCUTANEOUS coronary intervention (PCI) is increasingly utilized in the treatment of coronary artery disease. Despite its numerous benefits, serious and potentially life-threatening complications of PCI can occur, including slow flow phenomenon,^{1,2)} and coronary dissection and perforation.^{3,4)} PCI, which depends upon mechanical dilatation of the artery or ablation of atherosclerotic plaque, is requisitely associated with plaque rupture,^{5,6)} plaque fracture, intimal splitting, localized media dissection, and frank perforation.³⁾ Therefore, the reliable detection of coronary artery lesions and evaluation of atherosclerotic coronary plaque would constitute an important step forward in risk stratification of patients with coronary artery disease scheduled to undergo PCI.

Conventional cine coronary angiography (CAG) has been the standard for evaluating the extent of coronary artery disease. However, CAG underestimates the extent of coronary atherosclerosis, and does not provide information on coronary artery plaque texture. Multislice computed tomography (MSCT) is now being used for noninvasive coronary angiography. MSCT permits visualization of the coronary artery lumen and detection of stenosis with high accuracy.⁷⁾ Furthermore, MSCT has the capability to visualize the coronary artery wall and assess whether the various components of atherosclerotic plaque are calcified, predominately fibrous, or contain a large lipid pool.⁸⁻¹⁰⁾ However, it is not yet clear whether or not the characteristics of coronary plaque measured by MSCT are associated with the complications of PCI. We hypothesized that the CT density of plaque in a stenotic coronary artery can predict complications after PCI.

METHODS

Patients and study protocol: The study population consisted of 26 patients with chronic stable angina due to at least one high grade stenosis in the left anterior descending coronary artery (LAD), circumflex artery (LCX), or the right coronary artery (RCA) scheduled for PCI. The angiographic criteria for enrollment in the study included a lesion with a stenosis of $> 75\%$ and the absence of severe vessel angulations ($> 90\%$) in the proximal vessel segments. Angiographic exclusion criteria were left main stem disease, total occlusions, vessel diameter < 2.0 mm, and bypass lesions. Clinical exclusion criteria were renal failure (creatinine > 1.5 mg/dL), unstable angina pectoris, acute myocardial infarction, known allergic reactions to contrast media, or advanced heart failure (New York Heart Association III to IV). According to the study protocol, MSCT of the heart was performed within 1 week prior to the intervention.

Coronary intervention: The transfemoral Judkins technique was used for all interventions. Before coronary intervention, all patients received a bolus of 10,000 IU of unfractionated heparin intra-arterially. Coronary interventions

included balloon expansion, stent implantation, and directional coronary atherectomy. All patients were receiving aspirin 100 mg/dL for at least 24 hours before the procedure. Selective angiography was performed in multiple views before and after intervention. All events occurring during the procedure were recorded, especially those adverse events that could indicate myocardial ischemia. An event included chest pain of duration > 5 minutes, prolonged alterations of electrocardiographic parameters over a period of 5 minutes, appearance of transitory slow flow (TIMI flow I, II that, in all cases, reverted following intracoronary administration of nitroglycerin), compromised lateral branches following the stent implant (narrow lateral branches of < 2 mm diameter that, because of their low numbers, do not require other treatments),¹¹⁾ and appearance of coronary angiographic dissections provoked during the angioplasty and which persisted after implantation of the stent without coronary flow compromise. Finally, the TIMI 3 flow rate was obtained at the end of the procedure. Ticlopidine hydrochloride was given at the dose of 200 mg per day thereafter along with aspirin 100 mg per day.

MSCT protocol: MSCT was performed according to the protocol described in a previous study¹²⁾ using a SOMATOM Volume Zoom (4-detector-row, Siemens AG, Germany). Medications were not discontinued prior to the MSCT study. The patients were given metoprolol (20-60 mg p.o.) 60 minutes prior to the MSCT scan to achieve a heart rate less than 65 beats/min so that the single phase algorithm (reconstructing one image by single cycle) could be performed. Sublingual nitroglycerin (0.6 mg) was also administered 5 minutes before the start of MSCT scanning. 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 10 mL of contrast medium (OMNIPAQUE 350 mg/mL, GE Healthcare, NJ, USA) was injected intravenously at 3.0 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 4×2.5 mm, slice thickness 10 mm, 80 kV, 60 mA, 0.5 sec/rotation, up to 30 second duration/2 second step). The remainder of the contrast medium (90 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 (collimation 4×1.0 mm, slice thickness 1.25 mm, 120 kV, 225 mA, table feed 1.5 mm/rotation, 0.5 sec/rotation, 5 sec/rotation, up to 30 second duration/2 second step, slice thickness 1.0 mm, table feed 1.5 mm/rotation), which allowed temporal resolution of 250 ms and spatial resolution of 0.6 mm on the horizontal axis. The ECG was digitized and continuously monitored during the scan period.

CT angiography and measurement of CT density in coronary artery: The raw

data of the scans were reconstructed using a single-phase algorithm in all the patients as described in a previous study.¹³⁾ The end of the reconstruction window (250 ms) was positioned at the peak of the P wave on the monitoring ECG by inputting the absolute time (ms) backward from the next R waves. 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. 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. On the axial or cross-sectional MPR images, an ROI greater than 1.0 mm² was placed on at least 4 randomly selected points within each plaque, and the lowest CT density was defined as the minimum plaque density. 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 plaque causing the maximum coronary luminal narrowing.

The mean CT density of calcified plaque or hard plaque was defined as more than 120 Hounsfield Units (HU), while the mean density measured within "lipid rich" or "soft" plaque as less than 50 HU, and intermediate plaque as 50-120 HU.⁸⁾

Statistical analysis: All statistical analyses were performed using SYSTAT version 11 (SYSTAT Software, Inc, Richmond, California). For continuous variables, Student's *t* test or ANOVA was used to identify whether intergroup differences were significant. Continuous variables are presented as the mean $\pm$ standard deviation. For discrete variables, the chi-square test was used to test significance. A *P* value < 0.05 was considered significant.

RESULTS

Patients characteristics and CT density of plaque: The patient characteristics are summarized in Table I. MSCT scans were performed in 26 patients with stable angina pectoris. Of these, 16 patients (61.5%) had a history of diabetes mellitus, 10 (38.5%) a history of hyperlipidemia, and 13 (50%) a history of myocardial infarction. All scans showed sufficient image quality for analysis and no patient was excluded.

A total of 35 plaques were detected and analyzed with respect to lesion configuration. The mean CT density of the plaques was 256 ± 367 HU. Eleven lesions were considered to be soft plaques, 7 intermediate plaques, and 17 hard or calcified plaques.

Table 1. Patient Characteristics

	Patients (<i>n</i> = 26)
Age	70 ± 11 years
Male gender	18 (69.2%)
Current smoker	12 (46.2%)
History of diabetes mellitus	16 (61.6%)
History of hyperlipidemia	10 (38.5%)
History of hypertension	12 (46.2%)
Familial history	3 (11.5%)
History of myocardial infarction	13 (50%)

Figure 1. A 71-year-old man showing a stenotic coronary artery with a soft plaque on MSCT (Figure 1A) and IVUS (Figure 1B). A transient slow flow occurred immediately after directional coronary atherectomy that was implicated in a severe stenotic lesion of the proximal LAD coronary artery on the angiographic findings (Figure 1C).

Case presentations: The coronary angiography, MSCT, and intravascular ultrasound (IVUS) results in 2 patients with stable angina pectoris are presented in Figures 1 and 2. Case 1 was a 71-year-old man who had a stenotic coronary artery with soft plaque (Figure 1). In MSCT, he had severe stenosis and plaque of low CT density in the proximal lesion of the LAD artery. The mean CT attenuation in a standard ROI into the plaque was low density with -47 ± 6.0 HU. In IVUS, this plaque was considered to be attenuation plaque because the echogenicity of the plaque lesion was lower than the surrounding tissue with acoustic shadow from plaque. A transient slow flow occurred immediately after directional coronary atherectomy that was involved in a severe stenotic lesion of the proximal LAD coronary artery. Case 2 was an 82-year-old man who had a stenotic coronary artery with hard plaque (Figure 2). MSCT revealed severe stenosis and a low CT density plaque in the mid portion of the LCX coronary artery. The mean CT atten-

Figure 2. An 82-year-old man showing a stenotic coronary artery with a hard plaque on MSCT (Figure 2A). A perforation that occurred immediately after PCI with stent implantation was implicated in a severe stenotic lesion of the LCX coronary artery on the angiographic findings (Figure 2B).

Table II. Lesion Characteristics and Complications after PCI

Number of lesions <i>n</i> = 35	Soft plaque group (<i>n</i> = 11)	Intermediate plaque group (<i>n</i> = 7)	Hard plaque group (<i>n</i> = 17)	<i>P</i> (χ^2 test)
Location of culprit lesions (LAD/LCX/RCA)	10/1/0	4/1/2	5/5/7	NS
TIMI flow grade before PCI (0/1/2)	2/1/8	0/1/6	3/3/11	NS
Adverse event				
Chest pain	4 (36.4%)	0 (0%)	0 (0%)	< 0.01
Transient slow flow	4 (36.4%)	0 (0%)	0 (0%)	< 0.01
ECG alterations	4 (36.4%)	0 (0%)	0 (0%)	< 0.01
Side branch compromised	1 (9.1%)	1 (14.3%)	0 (0%)	NS
Dissection	0 (0%)	0 (0%)	2 (11.8%)	NS
Perforation	0 (0%)	0 (0%)	1 (5.9%)	NS

LAD indicates left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; PCI, percutaneous coronary intervention; and NS, not significant.

uation in a standard ROI into the plaque was high with 734.8 ± 37 HU. A perforation occurred immediately after PCI with stent implantation which was involved in a severe stenotic lesion of the LCX coronary artery.

Lesion characteristics and complications after PCI: As summarized in Table II, 4 of 11 lesions with soft plaque before PCI had an appearance of slow flow after PCI and 1 lesion had a side branch compromised. On the contrary, 2 of 17 patients with hard plaque before PCI had a dissection of the involved lesion after PCI and 1 patient had a perforation of a coronary artery. One of 7 lesions with intermediate plaque had a side branch compromised. The soft plaque group before PCI was significantly associated with the appearance of slow flow or side branch compromise after PCI, whereas the hard plaque group before PCI was associated with the appearance of dissection or perforation after PCI ($P = 0.004$). The CT densities of

plaque in the lesions with slow flow and a side branch compromised after PCI were significantly lower compared to those in the lesions without the complication of PCI, and the CT density of plaque in the lesions with dissection and perforation after PCI was the highest (25.1 ± 41.8 HU, 257.1 ± 377.8 HU, and 712.1 ± 180.7 HU, $P < 0.05$).

DISCUSSION

The major findings in the present study were that the soft plaque measured by MSCT was associated with an appearance of slow flow after PCI while the hard plaque was associated with a dissection of the involved lesion or a perforation after PCI. Thus, coronary arterial plaque characterized by MSCT predicts intervention-related complication.

PCI is the most common strategy for treating stenotic coronary artery disease. However, PCI fails to achieve TIMI-III flow in 12% to 30% of cases because of the slow flow/no-reflow phenomenon,¹⁴⁾ or results in iatrogenic coronary dissection in up to 30% cases or perforation in 0.5% cases.³⁾ The mechanisms of slow flow/no-reflow phenomenon have not been clarified, but recently, there has been a report that distal protection devices may be effective in preventing distal embolization.¹⁵⁾ Kotani, *et al*¹⁴⁾ demonstrated that no-reflow during PCI in patients with acute coronary syndrome is not just attributable to the thrombus burden but also to plaque components of the atheromatous lesions. There was a shift in intraluminal particulate matter from thrombotic to atherosclerotic debris comparing pre-PCI to post-PCI aspirate, especially in no-reflow lesions. In particular, most no-reflow lesions improved when this intraluminal atherosclerotic debris was removed. Their results suggest that slow flow/no-reflow phenomenon might be caused by mechanical residual plaque disruption of lipid rich (atheromatous core) atheroma with secondary platelet and fibrin accumulation termed soft plaque or attenuation plaque.¹⁶⁻¹⁸⁾ On the other hand, dissection of a coronary artery after PCI is frequently adjacent to hard plaque including calcification,¹⁹⁾ and is believed to be related to the development of high internal shear stress at the edge of a hard plaque undergoing balloon expansion.²⁰⁾ In the present study, the relationship between the characteristics of plaque before PCI was evaluated using MSCT, and the differences in plaque configuration predicted an appearance of slow flow or dissection after PCI.

Although IVUS is an excellent method for defining plaque from the histological and immunohistochemical findings,²¹⁾ it is invasive and the stenotic coronary artery must be overcome with these catheters to use IVUS in the ideal way.²²⁾ Furthermore, geometric distortion can degrade the cross-sectional images of the vessel wall.²³⁾ MSCT also permits the visualization of coronary atherosclerotic

plaque noninvasively. There is growing evidence that the presence, amount, and composition of noncalcified coronary atherosclerotic plaque and the degree of coronary remodeling in proximal segments can be assessed by MSCT with a good correlation to IVUS.²⁴⁻²⁶⁾ MSCT accurately detects calcified or mixed plaque with sensitivities and specificities above 90%. On the other hand, MSCT has the potential to further stratify noncalcified plaque into fibrous plaque and lipid-rich plaque, but is less accurate for the detection of soft plaques than that of hard plaque, with sensitivities and specificities ranging from 60% to 85%.²⁷⁾ Therefore, we confirmed the soft plaque by IVUS just immediately before PCI when the soft plaque was detected using MSCT. In the present study, we decided the characterization of plaque from CT density into coronary artery using MSCT as described in a previous study,⁸⁾ and plaque configurations could be compared to the complications after PCI.

Furthermore, it may be important to perform MSCT before selecting a strategy for PCI.

Study limitation: Visualization of the coronary artery using the current temporal resolution of 250 ms is only available at low heart rates, and the use of beta-blocker is essential at present for artifact free visualization of the coronary artery. Therefore, the spatial resolution decreases and the accuracy of the morphological assessment may be sacrificed. However, Sato, *et al* also reported the detection of coronary plaque using MSCT by means of the same method.¹³⁾

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