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Assessment of Non-Calcified Coronary Plaques Using 64-Slice Computed Tomography: Comparison With Intravascular Ultrasound

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ABSTRACT

Background and Objectives: Non-invasive detection and characterization of plaque composition may constitute an important step in risk stratification and monitoring of the progression of coronary atherosclerosis. Multislice computed tomography (MSCT) allows for accurate, non-invasive detection and characterization of atherosclerotic plaques, as well as determination of coronary artery stenosis. The aim of this study was to determine the usefulness of MSCT for characterizing non-calcified coronary plaques previously classified by intravascular ultrasound (IVUS). **Subjects and Methods**: Seventy-one plaques were evaluated in 42 patients undergoing MSCT and IVUS. Coronary plaques were classified as hypoechoic or hyperechoic based on IVUS echogenicity. On MSCT, CT attenuation was measured using circular regions of interest (ROI) and represented as Hounsfield units (HU). **Results**: MSCT attenuation in hypoechoic plaques was significantly lower than it was in hyperechoic plaques (52.9 ± 24.6 HU vs. 98.6 ± 34.9 HU, respectively, $p < 0.001$). When comparing CT attenuation between hypoechoic and hyperechoic plaques, 60.2 HU was the cut-off value for differentiating between the two, with a 90.7% sensitivity and a 78.6% specificity. **Conclusion**: MSCT might be a useful tool for non-invasively evaluating the characteristics of coronary artery plaques. **(Korean Circ J 2009;39:95-99)**

KEY WORDS: Atherosclerosis; Coronary arteries; X-ray computed tomography.

Introduction

Atherosclerotic plaque disruption is the initiating event in at least two-thirds of all acute coronary events. Non-invasive detection and characterization of vulnerable plaques may constitute an important step in risk stratification and the monitoring of coronary atherosclerosis progression.[1)]

Intravascular ultrasound (IVUS) is currently the reference method for quantifying coronary atherosclerosis, and it is commonly used in the assessment of plaque composition. However, this method is invasive. Recently, multislice computed tomography (MSCT) has been proposed as an accurate, non-invasive means of assessing atherosclerotic plaques, as well as detecting coronary artery stenosis.[2)] Therefore, this method might hold promise in the prediction and evaluation of coronary heart disease.[3)] Some reports have shown that calcified, fibrous, and lipid-rich plaques exhibit significant differences in their mean computed tomography (CT) attenuation.[4-7)] In addition, this differentiation may be important in identifying plaques that are more prone to rupture. In this study, we tried to determine the usefulness of MSCT in the characterization of coronary plaques classified as non-calcified by IVUS.

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Subjects and Methods

Patient population

We enrolled 42 patients (20 males with a mean age of 66 ± 9 years) who had typical chest pain and underwent coronary angiography and IVUS. Invasive coronary angiography was performed within 4 weeks after MSCT coronary angiography. Twenty-seven patients (64%) had hypertension, 7 patients had diabetes mellitus (18%), and 6 patients had hyperlipidemia (14%) (Table 1).

Seventeen patients presented with unstable angina. Exclusion criteria included arrhythmias, contraindications to iodinated contrast agents, significant renal dysfunction, prior coronary intervention in the region of interest, acute myocardial infarction, and advanced heart failure.

Multislice computed tomography

Hypoechoic or hyperechoic plaques with calcified components in the same cross-sectional images were excluded from the assessment to rule out the influence of calcification within plaques. All patients were in sinus rhythm and received oral nitroglycerin to improve image quality. Patients with an initial heart rate of >70 beats/min received 10-40 mg of propranolol prior to MSCT imaging to decrease the heart rate to <70 beats/min. Approximately 60 mL of iodinated contrast agent was injected intravenously at a rate of 5 mL/sec, followed by a chaser bolus of 20 mL of normal saline. MSCT data were acquired using a 'Lightspeed VCT' 64-channel MSCT scanner (GE Healthcare, Milwaukee, WI, USA). Scan parameters were as follows: detector collimation of 64×0.625 mm, gantry rotation time of 350 ms, tube voltage of 120 kVp, tube current of 700 mAs, and pitch of 0.18-0.26. The position of the reconstruction window was initially placed at 75% of the cardiac cycle, but, if necessary, it was individually adapted by 10% increases or decreases to minimize motion artifacts. Images were transferred to a workstation (AW 4.3; GE Healthcare) and evaluated for atherosclerotic plaques. Axial reconstructions, maximal intensity projections, and multiplanar reformations were used to identify and assess lesions in the three coronary arteries.

Table 1. Characteristics of the patients

Variables	
Total Patients (n)	42
Male (%)	20 (48)
Age (yrs)	66±9
Heart rate (beat per minute)	56±4
Atherosclerotic risk factors (%)	
Diabetes mellitus	7 (18)
Hypertension	27 (64)
Hyperlipidemia	6 (14)
Current smoking	9 (21)
Prior CVA	3 (7)
Prior IHD	6 (14)
Clinical presentation (%)	
Stable angina	23 (55)
Unstable angina	17 (41)

CVA: cerebrovascular attack, IHD: ischemic heart disease

Intravascular ultrasound

IVUS was performed using a 40 MHz IVUS catheter (Atlantis pro40, Boston Scientific, Natick, MA, USA) and a motorized pullback at 0.5 mm/sec. Coronary plaques were classified as hypoechoic or hyperechoic based on IVUS echogenicity. Hypoechoic plaques were defined as those having an echogenicity lower than that of the adventitia. Hyperechoic plaques were defined as those producing echoes as bright as, or brighter than, adventitia without calcium.

Multislice computed tomography and Intravascular ultrasound

All coronary plaques were compared site-by-site. On IVUS, a single cross-sectional image was chosen that most closely corresponded to the location in which MSCT showed the greatest plaque area.

Anatomic cross-correlation between MSCT and IVUS was achieved using the side branch as a landmark and measuring the distance between branches on the MSCT images and IVUS, as well as taking into account plaque area and shape. In order to measure plaque attenuation on MSCT, we used the averaged value of three independent regions of interest (ROI) placed within the plaque on the cross-sectional image. The MSCT attenuation of the measured ROI was represented in Hounsfield units (HU) (Fig. 1). The minimum size of the ROI

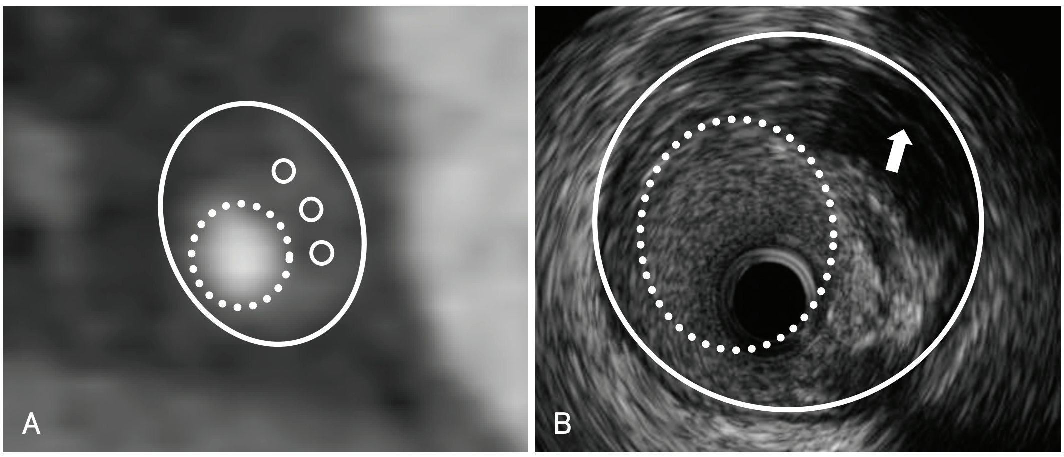

Fig. 1. Measurement of CT attenuation (A) in the plaque corresponding to IVUS (B) (arrow). The CT attenuation data was based on the mean value in different three sites. IVUS: intravascular ultrasound, CT: computed tomography.

(area <0.5 mm^2) was used to confirm the accuracy of MSCT in evaluating plaque characteristics.

Statistical analysis

Quantitative data are represented as means ± standard deviations. The non-parametric Kruskal-Wallis test was used to compare the mean densities of hypoechoic and hyperechoic plaques. Receiver operating characteristic (ROC) curves were constructed to determine optimal cut-off values. The accuracy in differentiating hypoechoic and hyperechoic plaques was determined. $P<0.05$ were considered statistically significant. Variability was calculated as the difference between the means of the two results and was expressed as the percentage of the mean.

Table 2. Distribution of plaques

Coronary segment	Number of lesions (n=71)
Left main (%)	3 (4.2)
Left Ant. descending coronary artery (%)	39 (54.9)
Proximal	22 (31.0)
Middle	17 (23.9)
Distal	0 (0)
Left circumflex coronary artery (%)	12 (16.9)
Proximal	6 (8.5)
Middle	5 (7.0)
Distal	1 (1.4)
Right coronary artery (%)	17 (23.9)
Proximal	10 (14.1)
Middle	5 (7.0)
Distal	2 (2.8)

Ant: anterior

Table 3. Plaques according to coronary artery

	LMA	LAD	LCX	RCA
Hypoechoic plaques	1	15	6	6
Hyperechoic plaques	2	24	6	11

p=0.863. LMA: left main coronary artery, LAD: left anterior descending coronary artery, LCX: left circumflex coronary artery, RCA: right coronary artery

Results

Distribution of plaques

Seventy-one plaques were analyzed. Thirty-nine (54.9%) plaques were located in the left anterior descending coronary artery (LAD), with 38 (54.8%) plaques located in the proximal segments (Table 2).

There was no significant difference in the number of hypoechoic and hyperechoic plaques according to the coronary artery (Table 3).

CT attenuation between hypoechoic and hyperechoic plaques

IVUS classified 28 lesions as predominantly hypoechoic and 43 lesions as hyperechoic (Fig. 2). The mean CT density measured within hypoechoic plaques on IVUS was 52.9±24.6 HU. In hyperechoic plaques, the mean CT attenuation was 98.6±34.9 HU. There was a statistically significant difference between hypoechoic and hyperechoic plaques ($p<0.001$) (Fig. 3). ROC curves showed discrimination between hypoechoic and hyperechoic plaques at 60.2 HU (sensitivity of 90.7%, specificity of 78.6%, and area of 0.892) (Fig. 4). However, there was some overlap between the CT densities measured in plaques classified as hypoechoic and hyper-echoic by IVUS. The intraobserver and interobserver variabilities were 1.32±2.44% and 2.51±1.97%, respectively.

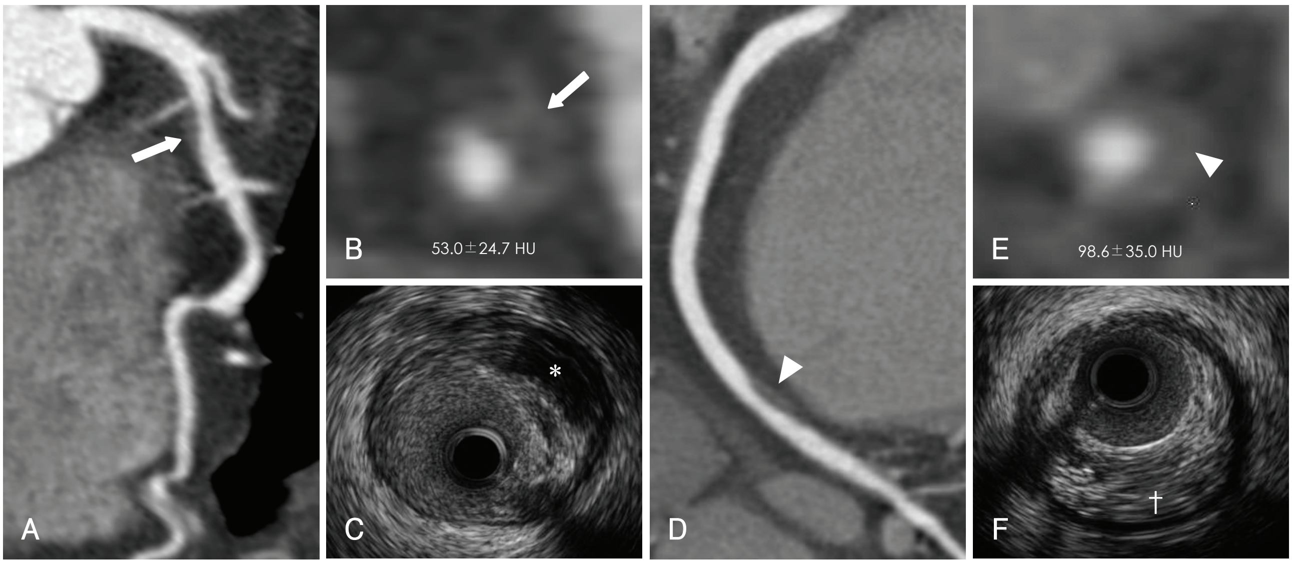

Fig. 2. Visualization of non-calcified plaques by MSCT and IVUS. The CT attenuation (arrow of A and B) of hypoechoic plaques on IVUS (*, C) was lower than the CT attenuation (arrow head of D and E) of hyperechoic plaques (†, F). MSCT: multislice computed tomography, IVUS: intravascular ultrasound, HU: Hounsfield units.

Discussion

The principal finding of this study was that the mean CT attenuation measured in non-calcified coronary atherosclerotic plaques was significantly different in hypoechoic and hyperechoic plaques. Acute coronary syndrome is caused by unstable plaques, which exist not in high grade stenosis sites, but in mild or moderate stenosis sites filled with lipid.[8)9)] Lipid-rich plaques are known to increase intimal wall shear stress compared with fibrous tissue and calcification and are known to be more unstable and vulnerable to rupture compared to other types of plaques.[10)] Yamagishi et al.[11)] reported that large eccentric plaques containing a lipid-rich echolucent zone on IVUS are at increased risk for instability, even though the lumen area is preserved. It is common for unstable plaques in coronary lesions with preserved lumen area to be missed on catheter coronary angiography (CAG). IVUS could identify unstable plaques in those lesions.[12)] However, this method is invasive. Therefore, non-invasive imaging tools that can reliably determine plaque morphology are important in identifying high-risk patients and enabling serial assessment during therapeutic intervention.[13)] In recent studies, MSCT has been proposed as just such a non-invasive tool for the characterization of atherosclerotic plaques and the correlation between IVUS characteristics of plaques and CT attenuation.[2)4)] On MSCT, the lipid-core of the plaque is easily characterized, with dark attenuation seen in the plaque.[14)]

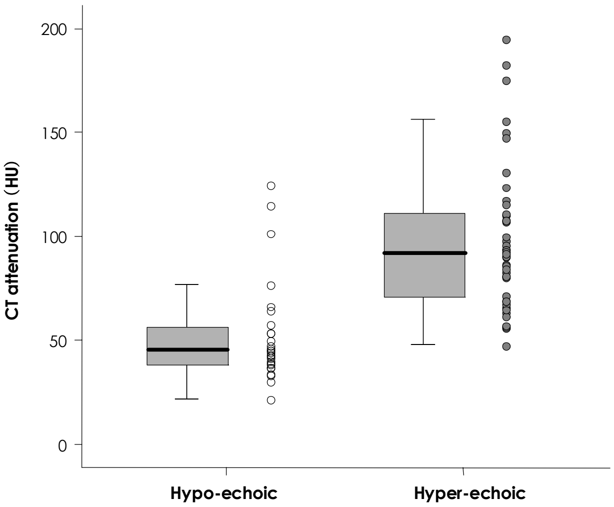

Fig. 3. Comparison of CT attenuation according to plaque echogenicity on IVUS. IVUS: intravascular ultrasound, HU: Hounsfield units.

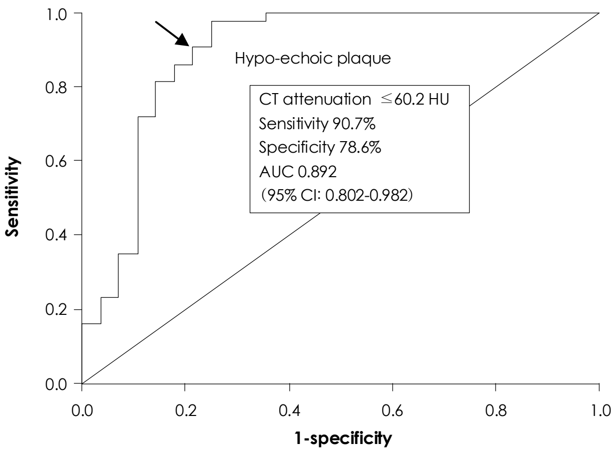

Fig. 4. A receiver operating characteristic curve of CT attenuation for predicting hypo-echoic plaques on IVUS. AUC: area under the curve, IVUS: intravascular ultrasound, CI: confidence interval.

Becker et al.[10)] used histologic classification to show that the mean CT attenuations of lipid-rich and fibrous-rich plaques were significantly different in human coronary arteries (47±9 and 104±28 HU, $p<0.01$). Schroeder et al.[16)] compared MSCT attenuation with histopathology and found that the CT attenuation of coronary artery plaques might be useful for characterizing plaque morphology. Recently, several authors have reported CT attenuation according to plaque echogenicity on IVUS. Pohle et al.[7)] studied the densities of hypoechoic (58±43 HU) and hyperechoic plaques (121±34 HU) using 16-slice MDCT. In the studies listed in Table 4, the mean CT attenuation of hypoechoic plaques was in the range of 14-71.7 HU, and the mean CT attenuation of hyperechoic plaques was in the range of 70-121 HU. Though there were differences in the ab-

Table 4. CT attenuations of hypoechoic and hyperechoic plaques (HU)

	Hypoechoic or soft	Hyperechoic or fibrous	Cut-off value	p	CT scanner
1. Estes et al. (1998)[6]	39±12	90±24	-	<0.001	1-slice
2. Schroeder et al. (2001)[4]	14±26	91±21	-	<0.0001	4-slice
3. Becker et al. (2003)[12]	47±9	104±28	-	<0.001	4-slice
4. Schroeder et al. (2004)[16]	42±22	70±22	60	<0.0001	4-slice
5. Leber et al. (2004)[5]	49±22	91±22	-	<0.02	16-slice
6. Carrascosa et al. (2006)[15]	71.5±31.1	116.3±35.7	88	<0.001	4-slice
7. Pohle et al. (2006)[7]	58±43	121±34	-	<0.001	16-slice
8. Rasouli et al. (2006)[13]	23±71	108±79	-	<0.0001	EB
9. Motoyama et al. (2007)[1]	11±12	78±21	-	<0.0001	16-slice
10. Iriat et al. (2007)[18]	38±33	94±44	-	<0.001	16-slice

HU: Hounsfield units, EB: electron beam

solute HU of CT attenuation according to the type of CT scanner, the CT attenuation was significantly different for hypoechoic and hyperechoic plaques.

Carrascosa et al.[15] suggested 88 HU as a cut-off value for classifying fibrous or soft plaques. Schroeder et al.[16] proposed 60 HU as a meaningful threshold for differentiating between hypoechoic and hyperechoic plaques on MSCT. Our ROC curves indicated that 60.2 HU was a better discriminating cut-off value between hypoechoic and hyperechoic plaques. However, there was an overlap of attenuation values between plaques, and there were some limitations, so further plaque characterization using MSCT might be needed.

Plaques are most frequently distributed in the proximal and mid-segments of the coronary arteries.[17] In our study, most of the plaques were distributed in the upper two-thirds of the coronary artery.

The major limitations of our study were a lack of histologic confirmation of the MSCT findings and the use of IVUS as the gold standard. There were also some limitations to the quality of images obtained with MSCT. CT density may be influenced by image noise, partial volume effect, and calcification, although a minimum-sized ROI was used to decrease the partial volume effect, and plaques with calcification were excluded from the analysis. Furthermore, only cross-sectional images were used to assess the plaque appearance on IVUS, and no volumetric assessment was performed. In addition, the averaged HU value within a certain ROI may not be sufficient to characterize plaque composition. Finally, even though landmarks such as side branches, plaque morphology, and the distance between branches were used to ensure the anatomic cross-correlation between MSCT and IVUS, the two studies still might not have been completely correlated.

In summary, we observed that the mean CT attenuation was significantly different for hypoechoic and hyperechoic plaques. CT attenuation might be a useful tool for evaluating coronary artery plaque characteristics non-invasively.

Acknowledgments

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