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LETTERS TO THE EDITOR

Delayed Plaque Enhancement by CT Angiography

High-risk coronary atherosclerotic plaques that are believed to lead to acute coronary events usually demonstrate 2 distinct features on computed tomography (CT) angiography: low (<30 HU) attenuation presumably representing the necrotic core and positive remodeling (plaque area/reference area, >1.1) of the affected vascular segments (1). Plaques that lack these 2 features are less commonly associated with subsequent adverse coronary events. In addition to low attenuation and remodeling, the identification of other characteristics of high-risk plaque, such as inflammation and neovascularization, are not amenable to standard CT angiography (2).

By a molecular targeting strategy, intravenous administration of a CT angiographic contrast agent comprising iodinated nanoparticles dispersed with surfactant has been employed to image macrophages and inflammation in atherosclerotic plaques (3). On the other hand, coronary plaque neovascularization has been reported with contrast-enhanced ultrasound and cardiac magnetic resonance (4,5) but not by CT. Because microvessels are below the threshold of spatial resolution of CT, we hypothesized that serial CT acquisitions at a short imaging interval following contrast injection should allow analysis of plaque enhancement as a marker of neovascularization.

We investigated 13 patients with stable angina (63.5 ± 10.3 years, all men, body mass index 24.4 ± 2.1 kg/m^2). The study was approved by the ethics and human research subjects review committee; delayed enhancement protocols, incremental radiation dose, and the research components of the study were discussed with patients and they voluntarily consented to participate in the study. All patients were in sinus rhythm and atenolol (25 mg) was administered orally or propranolol (2 to 10 mg) intravenously before the CT procedure to achieve a heart rate <60 beats/min (mean 51.1 ± 4.9 beats/min; range: 43 to 60 beats/min). Coronary CT angiography was performed using a 320-row area detector CT (Toshiba, Ohtawara, Japan) with prospectively ECG-gated axial single-beat acquisition at 75% of R-R, 320 × 0.5 mm collimation, 175 ms temporal resolution, and 120 kV tube voltage. Mean tube current per acquisition was 119 ± 21.0 mA and mean radiation exposure was 7.9 ± 1.6 mSv for both acquisitions combined. The injection rate of contrast agent was determined as the patient's weight × 0.06 ml/s and scanning started when arrival of the contrast medium in the left ventricle was visually confirmed. Without a second contrast injection, and using identical parameters, data acquisition was repeated after an interval of 3 min.

Contrast-enhanced coronary CT angiography in the 13 patients demonstrated 8 coronary segments showing 2 features of high-risk plaques (i.e., positive remodeling and low attenuation plaques). In 13 segments, although a plaque was identified, the lesions did not show both characteristic features of high-risk plaques. In all plaques, CT attenuation was obtained through the minimum CT value from 5 circular regions (area 1 mm^2) of interest. By using landmarks, such as calcifications and/or side branches, attenuation measurements were repeated at exactly the same location in the datasets obtained 3 min after contrast injection. Contrast washout between the initial and delayed CT datasets was determined as a percent value both for all plaques (early plaque attenuation − delayed plaque attenuation)/(early plaque attenuation) and for the ascending aortic lumen (early aortic attenuation − delayed aortic attenuation)/(early aortic attenuation). Table 1 demonstrates the observed values. There was no significant difference in the CT attenuation of the aortic lumen in 8 patients with and 11 patients without high-risk coronary plaque, indicating similar kinetics of contrast enhancement in the 2 groups. However, the washout of contrast from high-risk plaques after 3 min (−8.0 ± 6.1%) was significantly lower than the washout from plaques without high-risk morphology (4.1 ± 8.0%, $p < 0.005$) (Figs. 1A and 1B). A possible explanation for this observation may be intraplaque neovascularization with different contrast enhancement patterns in stable and high-risk coronary atherosclerotic lesions. Further investigation of this phenomenon is warranted.

Shinichiro Fujimoto, MD, PhD,* Takeshi Kondo, MD, PhD, Takahide Kodama, MD, PhD, Shinichi Takase, MD, Jagat Narula, MD, PhD

Table 1. Delayed Plaque Enhancement Characteristics

	Plaques With High-Risk CT Features (n = 8)	Plaques Without High-Risk CT Features (n = 11)	p Value
No. of plaques	8	13	
Ascending aorta (mean per patient)			
Early attenuation	393.4 ± 40.9	382.0 ± 55.5	NS
Delayed attenuation	96.1 ± 7.2	97.4 ± 7.1	NS
Washout	75.5 ± 1.8	74.1 ± 3.9	NS
Coronary plaque (mean per plaque)			
Early attenuation	16.6 ± 8.2	69.4 ± 21.5	<0.0001
Delayed attenuation	48.5 ± 29.6	54.8 ± 26.2	NS
Washout	−8.0 ± 6.1	4.1 ± 8.0	<0.005

Values are mean ± SD.
CT = computed tomography.

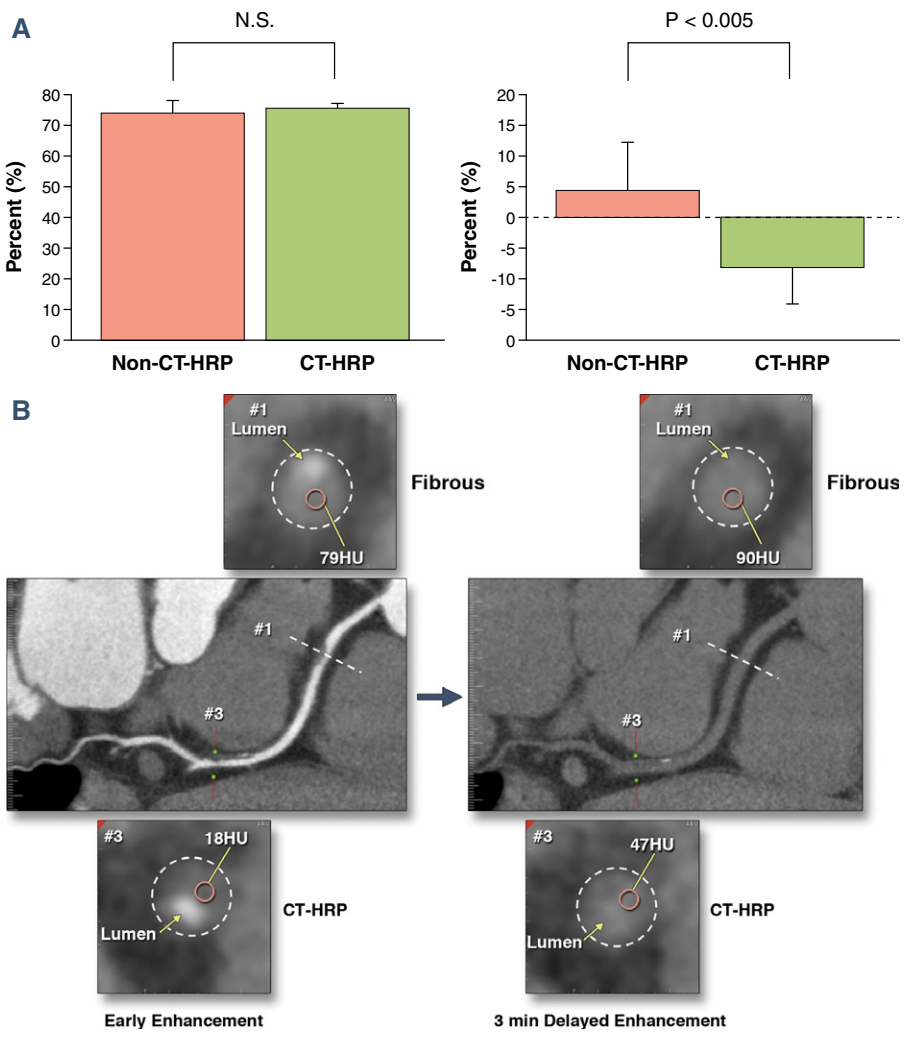

Figure 1. Comparison of Contrast Washout Between Early and Delayed CT and a Representative Case of Coronary Plaque Delayed Enhancement

(A) Comparison of contrast washout between early and delayed computed tomography (CT) acquisitions in the aortic lumen **(left)** and within coronary atherosclerotic plaque **(right)** in lesions with high-risk morphology and lesions without such features. **(B)** Delayed enhancement of a high-risk coronary plaque. A 61-year-old male, with coronary risk factors (family history, hypertension, dyslipidemia, and smoking) underwent coronary CT angiography that revealed a stenosis with 75% luminal diameter reduction and associated plaque without high-risk features in the proximal right coronary artery. In addition, a second lesion with positive remodeling and low initial CT attenuation (high-risk morphology) was found in the distal right coronary artery. Percent contrast washout was −2.4% in the proximal lesion and −6.3% in the distal lesion. CT-HRP = computed tomography verified high-risk plaque (positive remodeling >1.3 and low attenuation plaque <30 HU).

*Department of Cardiology, Takase Clinic, 885-2 Minami-orui, Takasaki 370-0036, Japan. *E-mail: s-fujimo@tj8.so-net.ne.jp*

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Pre-Dismissal Surveillance Echocardiography Second Day After TAVR

Transcatheter aortic valve implantation (TAVI) has been recognized as an alternative treatment for high-risk surgical patients