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ORIGINAL INVESTIGATIONS

Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events in Mid-Term Follow-Up

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ABSTRACT

BACKGROUND Coronary computed tomography angiography (CTA)-verified positive remodeling and low attenuation plaques are considered morphological characteristics of high-risk plaque (HRP) and predict short-term risk of acute coronary syndrome (ACS).

OBJECTIVES This study evaluated whether plaque characteristics by CTA predict mid-term likelihood of ACS.

METHODS The presence of HRP and significant stenosis (SS) of ≥70% were evaluated in 3,158 patients undergoing CTA. Serial CTA was performed in 449 patients, and plaque progression (PP) was evaluated. Outcomes (fatal and nonfatal ACS) were recorded during follow-up (mean 3.9 ± 2.4 years).

RESULTS ACS occurred in 88 (2.8%) patients: 48 (16.3%) of 294 HRP(+) and 40 (1.4%) of 2,864 HRP(−) patients. ACS was also significantly more frequent in SS(+) (36 of 659; 5.5%) than SS(−) patients (52 of 2,499; 2.1%). HRP(+)/SS(+) (19%) and HRP(+)/SS(−) (15%) had higher rates of ACS compared with no-plaque patients (0.6%). Although ACS incidence was relatively low in HRP(−) patients, the cumulative number of patients with ACS developing from HRP(−) lesions (n = 43) was similar to ACS patients with HRP(+) lesions (n = 45). In patients with serial CTA, PP also was an independent predictor of ACS, with HRP (27%; $p < 0.0001$) and without HRP (10%) compared with HRP(−)/PP(−) patients (0.3%).

CONCLUSIONS CTA-verified HRP was an independent predictor of ACS. However, the cumulative number of ACS patients with HRP(−) was similar to patients with HRP(+). Additionally, plaque progression detected by serial CTA was an independent predictor of ACS. (J Am Coll Cardiol 2015;66:337–46) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

BMI = body mass index

CABG = coronary artery bypass graft

CAD = coronary artery disease

CI = confidence interval

CTA = computed tomography angiography

FPP = feature-positive plaque

HR = hazard ratio

HRP = high-risk plaque

IQR = interquartile range

IVUS = intravascular ultrasound

LAP = low attenuation plaque

PCI = percutaneous coronary intervention

PIT = pathological intimal thickening

PP = plaque progression

PR = positive remodeling

RI = remodeling index

SAP = stable angina pectoris

SS = significant stenosis

TCFA = thin-cap fibroatheroma

ThCFA = thick-cap fibroatheroma

Coronary computed tomography angiography (CTA) allows noninvasive assessment of luminal stenosis, as well as plaque morphology (1-4). Several reports have confirmed CTA's diagnostic accuracy for identifying significantly obstructive disease, and the severity of such stenosis was also predictive of major adverse cardiac events (5-7). Additionally, lesions predictive of major adverse cardiac events demonstrate positive remodeling (PR) and low attenuation plaque (LAP) (8,9). Noncalcified plaques with ≤30 Hounsfield unit (HU) densities identified by CTA correlate closely with intravascular ultrasound (IVUS)-verified necrotic cores in coronary atherosclerotic plaques (2). Although the presence of PR and LAP was associated with the development of acute coronary syndrome (ACS) during 2-year follow-up in our previous study (10), the mid-term prognosis on the basis of CTA findings has not been reported. In the present study, we extended the follow-up period to investigate the relationship between CTA-verified high-risk plaque (HRP) and the incidence of ACS in mid-term follow-up. In patients with serial CTA, the association between plaque progression (PP) and ACS was also evaluated.

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METHODS

We enrolled 4,423 consecutive patients who underwent CTA for suspected or known coronary artery disease (CAD) from March 2003 to May 2011. Of these, 1,265 patients were excluded from analysis, including 604 patients who underwent coronary artery bypass graft (CABG) surgery before CTA or scheduled CABG on the basis of CTA findings, 590 patients lacking 1-year follow-up, 37 ACS patients post-CTA wherein the culprit lesions could not be identified, and 34 patients where ACS occurred at restenotic lesions. All plaques were analyzed in the remaining 3,158 patients for the study, which was performed at Fujita Health University, Nagoya Memorial Hospital, and Imai Outpatients Clinic; the study protocol was approved by the Institutional Review Board and ethics committee. Dr. Narula has been associated with this project since 2003 and has guided the proceedings of this project with Dr. Ozaki.

Of 3,158 patients, 641 had serial CTA, of whom 192 patients were excluded from analysis because of CABG history (n = 126), a short interval between first CTA (CTA-1) and second CTA (CTA-2) of <30 days (n = 8), and a short available follow-up period of <30 days since CTA-2 (n = 58). The serial analysis involved the remaining 449 patients, including 80 (17.8%) who underwent CTA-2 for occurrence/recurrence of chest pain symptoms and 122 (49.0%) for follow-up after percutaneous coronary intervention (PCI). The remaining 247 patients underwent serial CTA evaluation at the request of treating physicians for follow-up.

The study endpoint was defined as ACS occurrence on the basis of the third universal definition of myocardial infarction (11) and the Canadian Cardiovascular Society grading of angina pectoris (12). Briefly, ACS was defined as ischemic discomfort presenting with elevated troponin levels and ischemic discomfort that was Canadian Cardiovascular Society class 3 or 4 without troponin elevation. The culprit lesion was determined by a combination of electrocardiographic, echocardiographic, and invasive coronary angiographic findings. There were 187 deaths (age 70.8 ± 8.5 years; male 79%; median follow-up 1.7 years; interquartile range [IQR]: 0.6 to 4.6 years) during follow-up: 7 sudden deaths, 30 cardiac deaths, and 150 noncardiac deaths. Of 30 cardiac deaths, 12 were ACS-related and 18 died from heart failure. Because we focused on coronary artery plaque characteristics of ACS, cardiac death only as a result of ACS was included as the event in this study.

Follow-up information was obtained from hospital chart review and supplemented by information obtained via mail. However, 590 patients did not follow up with our institution or reply to the mail. Compared with patients with complete follow-up, the patients lost to follow-up were younger (61.7 ± 13.0 years vs. 65.5 ± 11.1 years), less likely to be male (60.6% vs. 69.8%), and had less HRP (5.1% vs. 9.3%). Median follow-up duration of event-free survivors was 1,143 days (IQR: 702 to 2,081 days). One of the 3 cardiologists (M.S., Y.N., S.K.) blinded to CTA findings was responsible for reviewing patient charts and clinical presentations as well as defining the ACS culprit lesion.

CTA PROTOCOL/ANALYSIS. We used 320-slice CT (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan) and 64-slice CT (Aquilion 64, Toshiba Medical Systems; Brilliance CT 64-channel, Philips Healthcare, Cleveland, Ohio); older studies were performed with 16-slice CT (Aquilion 16, Toshiba Medical Systems). In patients without contraindications, oral metoprolol and/or intravenous landiolol was administered before imaging if the heart rate was >65 beats/min. Whenever possible, 0.4 mg sublingual nitroglycerin was administered 3 to 5 min before image acquisition. Tube voltage was 120 kV or 135 kV, and the maximal tube current