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Original article

Incremental prognostic value of coronary computed tomographic angiography high-risk plaque characteristics in newly symptomatic patients

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ABSTRACT

Background: The incremental prognostic value of the plaque features in coronary computed tomographic angiography (CTA) has not been well assessed. This study was designed to determine whether CTA high-risk plaques have prognostic value incremental to the Framingham risk score (FRS) and the severity of luminal obstruction.

Methods: A total of 628 newly symptomatic patients without known coronary artery disease underwent CTA. They were followed for a median of 677 days during which there were 26 cardiac events, including cardiac death, acute myocardial infarction, and hospitalization for unstable angina. Incremental prognostic value of adding plaque characteristics to the number of diseased vessels and the FRS was evaluated using 3 Cox models and net reclassification indexes.

Results: The discrimination index was significantly increased by adding the number of diseased vessels to the FRS (change in c-statistic from 65.8% to 78.6%, $p = 0.028$) but not significantly by further adding plaque characteristics (change in c-statistic from 78.6% to 80.0%, $p = 0.812$). However, improved model-fitting by adding plaque characteristics into the linear combination with risk score and the number of diseased vessels ($p = 0.007$ from likelihood ratio test) and the lowest value of Akaike's information criteria of that model indicated that plaque characteristics improved both predictive accuracy and discrimination perspective. More subjects reclassified by plaque characteristics were moved to directions consistent with their subsequent cardiac event status than in an inconsistent direction.

Conclusions: Evaluation of CTA plaque characteristics may provide incremental prognostic value to the number of diseased vessels and the FRS.

Introduction

Coronary computed tomographic angiography (CTA) may help predict future cardiovascular events [1–11]. It has been proposed that the extent of vascular involvement and plaque morphology is associated with major adverse coronary events. The high-risk plaque is characterized by positive remodeling (PR) and low-attenuation plaques (LAP) [12]; such 2-feature positive plaques (2FPP) were associated with a higher likelihood of acute coronary syndrome (>22%) in the ensuing 2 years, compared to 3.7% and 0.5% for 1FPP or 2 feature negative plaques (2FNP) [13]. However, the additive value of combining plaque characterization with luminal stenosis is not known. This study was designed to evaluate

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the incremental prognostic value of CTA plaque characterization to luminal stenosis and the Framingham Risk Score (FRS) in newly symptomatic patients referred for suspected coronary artery disease (CAD).

Methods

Study population

This is a single center retrospective study, and was approved by the ethics committee. The need for written informed consent from subjects was waived after the identification of the subjects was duly blocked. Between September 30, 2008 and April 30, 2011, one thousand five hundred and seventy-two consecutive subjects without known CAD (aged 35–74 years) underwent 64- or 320-row CTA for suspected CAD. Patients without coronary lesions and/or calcification ($N = 563$), and those who needed percutaneous coronary intervention or coronary artery bypass grafting within 30 days after CTA ($N = 252$), or had poor image quality scans ($N = 18$) were excluded. Clinical follow-up data were available for 628 of the remaining 739 subjects (85%), and were analyzed for the current study (Fig. 1).

Follow-up

Either clinical visits and/or telephone interviews were conducted for follow up. All reported events were verified by hospital records or contacts with the attending physician. The end point of the study was the occurrence of cardiac events defined as cardiac death, nonfatal myocardial infarction, or hospitalization for unstable angina. Death from a clearly non-cardiac cause was not counted as an event. All subjects without cardiac events and death were observed until April 30, 2012.

All cardiac events occurred within 2.1 years from the start of follow-up (>90% occurred within 2 years). We assessed whether the prediction of cardiac events within a relatively short interval (2.1 years) could be improved by adding CTA plaque morphology to the severity of CAD and the FRS.

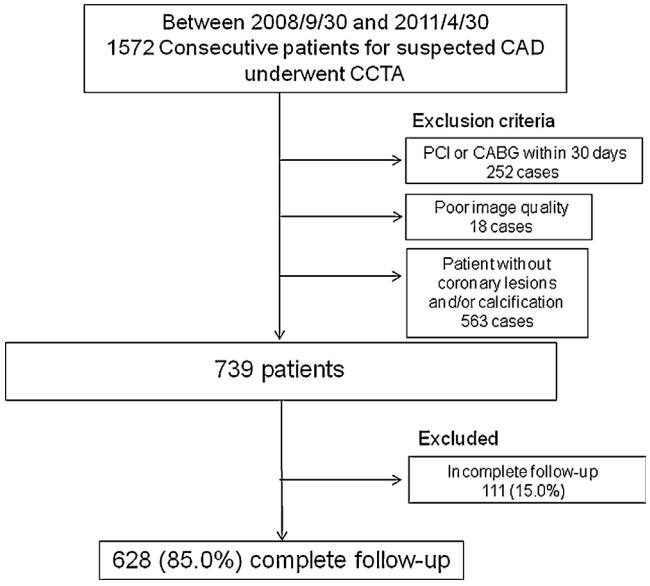

Fig. 1. Flow chart of the study population. CAD, coronary artery disease; CCTA, coronary CT angiography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

CTA acquisition

64-row multi-detector CT protocol

Subjects with a heart rate greater than 60 beats per minute received atenolol (25 mg) by mouth in the evening before the CT examination. Alternatively, heart rate control with a target of 60 beats per minute was achieved using 2–10 mg propranolol injected intravenously before data acquisition. The tube voltage for imaging (Aquilion 64, Toshiba Medical Systems Corporation, Tochigi-ken, Japan) was 120 kV. The tube current ranged from 400 to 600 mA; patients with a body mass index (BMI) of 22 were imaged at 440 mA, and for each 2-point increase or decrease in BMI, the tube current was increased by 10 mA. The gantry rotation time (0.35–0.45 s) and beam pitch (0.125–0.26) were determined by a manufacturer-based algorithm to optimize image quality. Imaging was performed from caudal to cranial.

Between 60 and 80 mL of iodinated contrast (300–370 mg iodine/mL) (Iopamiron-370, Bayer, Osaka, Japan; Omnipaque 300 and 350, Daiichi-Sankyo Inc, Tokyo, Japan), were injected (Stellant Dual Flow, Nihon Medrad K.K., Osaka, Japan) via an antecubital vein using a three-phase injection method: contrast alone (12 s), followed by an equal volume admixture of contrast and saline (9 s), and then saline only (2.5 s). The iodine load was weight based, and was timed using manual triggering when contrast arrived in the left ventricle.

320-row multi-detector CT protocol

Imaging for the second cohort paralleled the initial patients, with the following differences: the 320 mm × 0.5 mm scanner (Aquilion ONE, Toshiba Medical Systems Corporation) operated on the v4.51 software platform; and the craniocaudual field of view was tailored to the smallest exposure (10 cm, 12 cm, 12.8 cm, or 16 cm) that encompassed the heart. The default tube voltage was 120 kV. The tube current was modulated according to the patient's body habitus. Axial imaging had a gantry rotation time that ranged from 0.35 to 0.4 s per rotation. Based on prior experience with 64-detector row CTA, the electrocardiogram gating acquisition strategy was divided into 5 heart rate groups [14]. Contrast was injected via a two-phase protocol: contrast medium alone for 10 s, followed by saline for 8 s. The contrast and saline injection rates were calculated as the individual patient's mass in kilograms multiplied by 0.06 mL per second.

Image reconstruction

Half image reconstruction or segmental image reconstruction was performed in the slow filling phase and/or end-systolic phase using the "R + absolute time" method to generate images, and images with the lowest level of motion artifacts were selected on the 4-chamber cardiac cine CT.

CTA interpretation

For plaque detection, both cross-sectional and longitudinal curved multiplanar reformation images were analyzed. The coronary arteries were divided into 17 segments based on the recommendations of the American Heart Association (AHA) [15]. Coronary artery segments with a diameter of ≥2 mm were evaluated for the degree of stenosis. The percent ratio of the stenotic lumen to the normal vessel diameter proximal or distal to the stenosis was obtained and the percent degree of stenosis expressed. From still images taken from multiple projections, measurements were made in the angle showing the narrowest degree of stenosis. The degree of stenosis was evaluated by consensus of two experienced cardiologists who were unaware of the clinical data. Lesions with stenosis of >50% were defined as significant. The number of diseased vessels was defined as the