Clinical and Angiographic Characteristics of Patients Likely to Have Vulnerable Plaques

Analysis From the PROSPECT Study

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OBJECTIVES This study sought to determine the clinical and angiographic variables that would identify patients with high-risk "vulnerable" coronary plaques.

BACKGROUND In the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, in patients successfully treated for acute coronary syndrome (ACS), plaque composition, plaque burden, and minimal luminal area as detected by 3-vessel radiofrequency intravascular ultrasound (IVUS) imaging were associated with an increased risk of developing future events from untreated atherosclerotic lesions (vulnerable plaques). Whether baseline demographic and angiographic findings can be used to identify patients most likely to have vulnerable coronary plaques has not been examined.

METHODS On the basis of 3-vessel radiofrequency IVUS imaging, patents in the PROSPECT trial were classified in 2 groups according to whether or not one or more untreated high-risk plaques were present, defined as having ≥2 high-risk features (a thin-cap fibroatheroma, plaque burden ≥70%, and/or minimal luminal area ≤4 mm^2).

RESULTS The high-risk group (those with one or more high-risk lesions) had higher Framingham risk score (7.5 ± 3.4 vs. 6.9 ± 3.3; p = 0.04), more extensive coronary artery disease, and more nonculprit lesion–related cardiovascular events during the 3-year follow-up (hazard ratio: 2.63; 95% confidence interval: 1.62 to 3.66; p < 0.0001). However, demographic factors had poor discrimination in detecting high-risk patients (area under the curve 0.55), and discrimination was only slightly improved when angiographic variables were entered into the model (area under the curve 0.64).

CONCLUSIONS Clinical and angiographic characteristics had poor predictive accuracy in identifying patients with untreated high-risk plaques related to future adverse events. This finding highlights the potential value of comprehensive 3-vessel imaging assessment (either invasive or noninvasive) to evaluate plaque phenotype for more accurate risk stratification of patients admitted with ACS. (J Am Coll Cardiol Img 2013;6:1263–72) © 2013 by the American College of Cardiology Foundation

ntravascular ultrasound (IVUS) with radio-frequency backscatter analysis provides visualization of the entire vessel wall; assessment of the luminal, outer vessel wall, and plaque dimensions; and reliable semiautomated detection of plaque components and quantification of their burden (1,2). This imaging modality is therefore useful in the research of atherosclerosis (3,4). Several studies used serial backscatter analysis of IVUS signal examinations to assess changes in the composition of the plaque and the effect of pharmaceutical treatment (5–7). In the recently reported PROSPECT

(Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, 3-vessel IVUS–virtual histology (VH) imaging was used to evaluate the prognostic implications of the composition of the plaque and its burden in patients admitted with acute coronary syndrome (ACS) (6). Consistent with prior pathological studies, the PROSPECT trial demonstrated that plaque composition, as well as burden, were predictors of future cardiovascular events (6,8).

The 3 characteristics in the PROSPECT trial that were associated with future adverse lesion-specific cardiovascular events, namely plaque burden, minimal luminal area, and thin-cap fibroatheroma (TCFA) as defined by IVUS-VH, required 3-vessel catheter-based interrogation for identification, a procedure not without risk (6). Several studies have shown that the composition and extent of atheroma are associated with cardiovascular risk factors and that they differ in patients admitted with different clinical presentations (3,9–12). Therefore, baseline demographics or a combination of clinical and angiographic variables may allow detection of patients who have lesions with plaque features related to an increased risk for cardiovascular events, possibly allowing a targeted approach to imaging. The aim of the present analysis was therefore to identify clinical and angiographic characteristics related to the high-risk plaques in the PROSPECT study and to construct a model that will allow accurate detection of patients with a vulnerable plaque phenotype.

METHODS

Study population. The design, inclusion and exclusion criteria, and endpoints and definitions of the

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

CRP = C-reactive protein

EEM = external elastic membrane

IVUS = intravascular ultrasound

MACE = major adverse cardiac events

MLA = minimum lumen area

QCA = quantitative coronary angiography

TCFA = thin-cap fibroatheroma

VH = virtual histology

PROSPECT study have already been described in detail (6). The PROSPECT trial included 697 patients admitted for an acute coronary event (i.e., ST-segment elevation myocardial infarction, non–ST-segment elevation myocardial infarction, or unstable angina) who had successful percutaneous coronary intervention in all culprit lesions. The studied patients underwent coronary angiography and 3-vessel grayscale and IVUS-VH (Volcano Corp., San Diego, California) imaging of the proximal 6- to 8-cm coronary segments using a synthetic aperture array, 20 MHz, 3.2-Fr catheter (Eagle Eye, Volcano Corp.), after intracoronary nitroglycerin administration.

Data analysis. The acquired angiographic, IVUS, and IVUS-VH data were transferred to an independent core laboratory (Cardiovascular Research Foundation, New York, New York) and analyzed, blinded to the baseline and clinical characteristics. Quantitative coronary angiographic (QCA) analysis was performed, with the use of the software Medis CMS (version 7.0, Leiden, the Netherlands) in the entire length of the coronaries and the side branches that had a reference diameter >1.5 mm. All stenoses >30% on coronary angiography were analyzed, and the following metrics were obtained: lesion length, reference diameter, minimal lumen diameter, and diameter stenosis. Lesions related to the event were characterized as culprit and the rest as nonculprit lesions.

IVUS and IVUS-VH analysis was conducted with the use of QCU-CMS (Medis) software for contouring, pcVH 2.1 (Volcano Corp.) for contouring and data output, and proprietary software (qVH, Cardiovascular Research Foundation) for segmental qualitative and quantitative output. The external elastic membrane (EEM) and the lumen borders were detected at approximately every 0.5-mm interval (depending on the heart rate and the R-R interval) and used to determine the EEM area, lumen area, and plaque area and burden (defined as $100 \times$ plaque area/EEM area). Nonculprit IVUS lesions were defined as >3 consecutive IVUS frames visualizing segments with a plaque burden ≥40%. IVUS-VH allows characterization of 4 different plaque components that are portrayed in a color-coded map, with the red corresponding to the necrotic core, green to fibrous tissue, light green to fibrofatty, and white to dense calcium. Based on its compositional traits, each lesion was classified as TCFA, thick-cap fibroatheroma, pathological intimal thickening, fibrotic plaque, and fibrocalcific plaque (2).

The IVUS-derived independent lesion characteristics, which were associated with future adverse