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Clinical Outcome of Nonculprit Plaque Ruptures in Patients With Acute Coronary Syndrome in the PROSPECT Study

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OBJECTIVES The aim of this study was to report the frequency, patient and lesion-related characteristics, and outcomes of subclinical, nonculprit plaque ruptures in the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study.

BACKGROUND Plaque rupture and subsequent thrombosis is the most common cause of acute coronary syndrome (ACS). Secondary, subclinical, nonculprit plaque ruptures have been seen in both stable patients and patients with ACS; however, reports of the natural history of these secondary plaque ruptures are limited.

METHODS After successful stenting in 697 patients with ACS, 3-vessel grayscale and intravascular ultrasound virtual histology (IVUS-VH) was performed in the proximal-mid segments of all 3 coronary arteries as part of a prospective multicenter study.

RESULTS Among 660 patients with complete IVUS data, 128 plaque ruptures were identified in 105 nonculprit lesions in 100 arteries from 93 patients (14.1%). Although the minimum lumen area (MLA) was similar, the plaque burden was significantly greater in nonculprit lesions with a plaque rupture compared with nonculprit lesions without a plaque rupture (66.0% [95% confidence interval: 64.5% to 67.4%] vs. 56.0% [95% confidence interval: 55.6% to 56.4%]; $p < 0.0001$). IVUS-VH analysis revealed that a nonculprit lesion with a plaque rupture was more often classified as a fibroatheroma than a nonculprit lesion without a plaque rupture (77.1% vs. 51.4%; $p < 0.0001$). Independent predictors of a plaque rupture were lesion length (per 10 mm; odds ratio: 1.30; $p < 0.0001$), plaque burden at the MLA site (per 10%; odds ratio: 2.56; $p < 0.0001$), vessel area at the MLA site (per 1 mm^2; odds ratio: 1.13; $p < 0.0001$), and VH–thin-cap fibroatheroma (odds ratio: 1.80; $p = 0.016$). During 3 years of follow-up, the incidence of overall major adverse cardiac events did not differ significantly between the patients with and patients without subclinical, nonculprit plaque ruptures.

CONCLUSIONS Secondary, nonculprit plaque ruptures were seen in 14% of patients with ACS and were associated with a fibroatheroma phenotype with a residual necrotic core but not with adverse outcomes if patients were treated with optimal medical therapy as part of a multicenter study. (Providing Regional Observations to Study Predictors of Events in the Coronary Tree [PROSPECT]; NCT00180466) (J Am Coll Cardiol Img 2014;7:397–405) © 2014 by the American College of Cardiology Foundation

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The most common cause of an acute coronary syndrome (ACS) is rupture of an atherosclerotic lesion followed by acute luminal thrombosis (1,2). Pathological studies have suggested that the precursor of a ruptured plaque is a thin-cap fibroatheroma (TCFA). Although in vivo studies of TCFAs and their evolution into a ruptured plaque are rare, intravascular ultrasound (IVUS) studies (3,4) have reported that a plaque rupture occurs not only in culprit lesions but also in nonculprit or secondary atherosclerotic plaques in patients with ACS. Reports of the natural history of these secondary plaque ruptures are limited and include only small numbers of patients (5–7). The present study uses the 3-vessel IVUS data from the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study to assess the prevalence, clinical features, angiographic appearance, IVUS–virtual histology (VH) morphology, and clinical outcomes of nonculprit plaque ruptures in patients with ACS.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome
CI = confidence interval
CSA = cross-sectional area
IVUS = intravascular ultrasound
MACE = major adverse cardiac event(s)
MLA = minimum lumen area
TCFA = thin-cap fibroatheroma
ThCFA = thick-cap fibroatheroma
VH = virtual histology

METHODS

Patient selection and protocol. The enrollment criteria and methodology of the PROSPECT study have been described in detail (8). Briefly, 697 patients with ACS (ST-segment elevation myocardial infarction >24 h, non–ST-segment elevation myocardial infarction, or unstable angina with electrocardiographic changes) underwent coronary angiography and multimodality intracoronary imaging of the proximal 6 to 8 cm of all 3 coronary arteries after treatment of the culprit lesion and any other planned interventions. Patients were then followed up for a median of 3.4 years to relate subsequent events to the morphologies of the lesions detected at baseline. Medications, including dual antiplatelet therapy and statin therapy, were recorded at discharge and during follow-up. The study was approved by the institutional review board or medical ethics committee at each participating center, and all patients signed written informed consent. Of 697 patients enrolled in the PROSPECT study, 660 patients with complete grayscale and IVUS-VH data comprised the current study population.

Quantitative coronary angiography and IVUS. Intracoronary imaging, both grayscale and IVUS-VH, was performed with the use of a synthetic aperture array, 20-MHz, 3.2-F catheter (Eagle Eye, InVision Gold, Volcano Corp., Rancho Cordova, California) with motorized catheter pullback (0.5 mm/s). Baseline angiographic as well as grayscale and IVUS-VH images were analyzed at the Cardiovascular Research Foundation (New York, New York) in a core laboratory that was blinded to the clinical outcomes. Off-line grayscale and IVUS-VH analyses of all imaged segments were performed prospectively at an independent IVUS core laboratory at the Cardiovascular Research Foundation by investigators who were blinded to the angiographic analysis and to the clinical events. Detailed angiographic and grayscale and IVUS-VH methodology has been described previously (9).

An IVUS nonculprit lesion was defined as a plaque burden of ≥40% in at least 3 consecutive frames. Lesions were considered separate if there was a ≥5-mm-long segment with <40% plaque burden between them. A plaque rupture was defined as a cavity that communicated with the lumen with an overlying residual fibrous cap fragment (Fig. 1). One lesion could have multiple plaque ruptures. Rupture sites separated by ≥3 consecutive frames (approximately 1.5 mm) of artery containing smooth lumen contours and no cavity were considered to represent discrete and separate plaque ruptures.

On the basis of IVUS-VH, plaque components were categorized as dense calcium, fibrous tissue, fibrofatty plaque, or necrotic core and reported as percentages of total plaque areas and volumes. Lesions were then classified by IVUS-VH as 1 of the following: VH-TCFA, thick-cap fibroatheroma (ThCFA), pathological intimal thickening, fibrotic plaque, or fibrocalcific plaque, as previously

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