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Predictors of Plaque Rupture Within Nonculprit Fibroatheromas in Patients With Acute Coronary Syndromes

The PROSPECT Study

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ABSTRACT

OBJECTIVES The study sought to examine the relative importance of lesion location versus vessel area and plaque burden in predicting plaque rupture within nonculprit fibroatheromas (FAs) in patients with acute coronary syndromes.

BACKGROUND Previous studies have demonstrated that plaque rupture is associated with larger vessel area and greater plaque burden clustering in the proximal segments of coronary arteries.

METHODS In the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study 3-vessel grayscale and radiofrequency-intravascular ultrasound was performed after successful percutaneous coronary intervention in 697 patients with acute coronary syndromes. Untreated nonculprit lesion FAs were classified as proximal (<20 mm), mid (20 to 40 mm), and distal (>40 mm) according to the distance from the ostium to the maximum necrotic core site.

RESULTS Overall, 74 ruptured FAs and 2,396 nonruptured FAs were identified in nonculprit vessels. The majority of FAs (73.6%) were located within 40 mm of the ostium, and the vessel area and plaque burden progressively decreased from proximal to distal FA location (both $p < 0.001$). In a multivariate logistic regression model, independent predictors for plaque rupture included the distance from the ostium to the maximum necrotic core site per millimeter (odds ratio [OR]: 0.86; 95% confidence interval [CI]: 0.76 to 0.98; $p = 0.02$), plaque burden per 10% (OR: 2.05; 95% CI: 1.63 to 2.58; $p < 0.0001$), vessel area per mm^2 (OR: 1.14; 95% CI: 1.11 to 1.17; $p < 0.0001$), calcium (OR: 0.09; 95% CI: 0.05 to 0.18; $p < 0.0001$), and right coronary artery location (OR: 2.16; 95% CI: 1.25 to 3.27; $p = 0.006$). By receiver-operating characteristic analysis, vessel area correlated with plaque rupture stronger than either plaque burden ($p < 0.001$) or location ($p < 0.001$).

CONCLUSIONS Large vessel area, plaque burden, proximal location, right coronary artery location, and lack of calcium were associated with FA plaque rupture. The present study suggests that among these variables, vessel area may be the strongest predictor of plaque rupture among non–left main coronary arteries. (PROSPECT: An Imaging Study in Patients With Unstable Atherosclerotic Lesions [PROSPECT]; NCT00180466) (J Am Coll Cardiol Img 2015;8:1180–7)

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Previous pathologic studies have demonstrated that plaque rupture with thrombosis is the major mechanism leading to acute coronary syndromes (1-4). Lesions with high-risk characteristics, including thin-cap fibroatheromas (TCFAs) and plaque rupture, cluster predominantly in the proximal coronary segment of the left anterior descending artery (LAD) and more diffusely throughout the right coronary artery (RCA) (5-8). Vessel area, shear stress, and other anatomic features contribute to this pattern of longitudinal distribution (7-11); however, whether proximal location independently determines the risk of plaque rupture has remained unclear (7,8). The present study aims to investigate the predictors of plaque rupture among fibroatheromas within nonculprit lesions by using the 3-vessel grayscale and intravascular ultrasound (IVUS)-virtual histology (VH) data from the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study.

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METHODS

PATIENT POPULATION AND PROTOCOL. The enrollment criteria and the methodology of the PROSPECT study have been previously described in detail (12). In brief, 697 patients with acute coronary syndromes underwent grayscale and IVUS-VH examination of the proximal 6 to 8 cm of all the 3 coronary vessels after successful percutaneous coronary intervention of culprit lesions and other severe stenoses. The study was approved by the institutional review board or medical ethics committee at each participating center, and all patients signed written informed consent (12). Of 697 patients enrolled in the PROSPECT study, 454 patients with at least 1 fibroatheroma in a nonculprit vessel comprised the current study population.

QUANTITATIVE ANALYSIS OF CORONARY ANGIOGRAPHY AND IVUS. Imaging was performed using a synthetic aperture array, 20 MHz, 3.2-F catheter (Eagle Eye, Volcano Corporation, Rancho Cordova, California). During a motorized catheter pullback at 0.5 mm/s, grayscale IVUS was recorded, and radiofrequency data were captured gated to the R-wave (In-Vision Gold, Volcano Corporation). Qualitative and quantitative coronary angiographic assessment of the entire length of the coronary tree was performed at an independent core laboratory (Cardiovascular Research Foundation, New York, New York) using a proprietary methodology modified from standard Medis CMS software version 7.0 (Leiden, the Netherlands); this analysis included each major epicardial coronary artery and every side branch >1.5 mm in diameter. This 3-vessel angiographic analysis served as a roadmap to identify each lesion on the basis of longitudinal axis location (mm). Detailed angiographic, grayscale, and IVUS-VH methodology have been described previously (13). All IVUS images were also analyzed at an independent core laboratory (Cardiovascular Research Foundation). Off-line grayscale and IVUS-VH analyses were performed using: 1) QCU-CMS (Medis) for contouring; 2) pcVH 2.1 software (Volcano Corporation) for contouring and data output; and 3) proprietary qVH software for segmental qualitative assessment and quantitative data output.

A lesion was defined as a segment with ≥3 consecutive frames with ≥40% plaque burden. A fibroatheroma was defined as >10% confluent necrotic core (NC) and was subclassified as TCFA-VH, calcified thick-cap fibroatheroma (CaThCFA), and non-CaThCFA (13). A plaque

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve
CaThCFA = calcified thick-cap fibroatheroma
EEM = external elastic membrane
IVUS = intravascular ultrasound
LAD = left anterior descending artery
LCX = left circumflex artery
NC = necrotic core
RCA = right coronary artery
ROC = receiver-operating characteristic
TCFA = thin-cap fibroatheroma
VH = virtual histology

TABLE 1 Baseline Characteristics of Patients With Nonculprit Vessel Fibroatheromas

Age, yrs	58.6 (51.5–67.5)
Men	80.2 (364/454)
Diabetes mellitus	17.9 (81/452)
Insulin requiring	2.2 (10/452)
Metabolic syndrome	49.9 (221/443)
Current cigarette use	47.3 (211/446)
Hypertension	48.3 (218/451)
Hyperlipidemia	45.5 (190/418)
Prior myocardial infarction	11.3 (51/450)
Family history of coronary artery disease	46.1 (185/401)
Framingham score	7.0 (5.0–9.0)
Prior percutaneous coronary intervention	10.8 (49/453)
Clinical presentation	
ST-segment elevation myocardial infarction	29.5 (134/454)
Non–ST-segment elevation myocardial infarction	66.5 (302/454)
Unstable angina with electrocardiogram changes	4.0 (18/454)
Body mass index, kg/m^2	28.1 (25.4–31.6)
Total cholesterol, mg/dl	172.0 (148.0–200.0)
Low-density lipoprotein cholesterol, mg/dl	101.4 (80.2–129.6)
High-density lipoprotein cholesterol, mg/dl	38.6 (34.0–46.0)
Triglycerides, mg/dl	125.5 (88.6–177.1)
Hemoglobin A1c, %	5.8 (5.3–6.2)
Estimated creatinine clearance, ml/min	99.2 (75.3–125.4)
High-sensitivity C-reactive protein, mg/dl	7.7 (2.5–18.8)
Statin at admission	46.7 (212/454)
Aspirin at admission	72.7 (330/454)
Clopidogrel at admission	62.3 (283/454)
Number of diseased epicardial coronary arteries	
1	24.7 (110/446)
2	44.2 (197/446)
3	31.2 (139/446)

Values are median (interquartile range) or % (n/N).