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Adverse Cardiovascular Events Arising From Atherosclerotic Lesions With and Without Angiographic Disease Progression

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OBJECTIVES The aim of this study was to use angiography and grayscale and intravascular ultrasound–virtual histology to assess coronary lesions that caused events during a median follow-up period of 3.4 years.

BACKGROUND Vulnerable plaque-related events are assumed to be the result of substantial progression of insignificant lesions.

METHODS In the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, 697 patients with acute coronary syndromes underwent treatment of all culprit lesions followed by 3-vessel imaging to assess the natural history of culprit and untreated nonculprit (NC) lesions. Future adverse cardiovascular events adjudicated to NC lesions were divided into those with versus without substantial lesion progression (SLP) (≥20% angiographic diameter stenosis increase).

RESULTS NC lesion events occurred in 72 patients, 44 (61%) with and 28 (39%) without SLP. Myocardial infarctions (n = 6) occurred only in patients with SLP. Conversely, patients without SLP presented only with unstable or increasing angina requiring rehospitalization. Lesions with versus without SLP occurred later (median time to event 401 vs. 223 days, $p = 0.07$); were less severe at baseline (median diameter stenosis 26.4% vs. 53.8%, $p < 0.0001$) but more severe at the time of the event (mean diameter stenosis 73.8% vs. 56%, $p < 0.0001$); and had comparable baseline median plaque burden (68.7% vs. 70.1%, $p = 0.17$), minimum luminal area (3.7 vs. 4.0 mm^2, $p = 0.60$), and intravascular ultrasound–virtual histology phenotype (83.3% vs. 90.9%, $p = 0.68$; classified as fibroatheromas at baseline).

CONCLUSIONS NC lesions responsible for future cardiovascular events showed angiographic increase during 3.4 years of follow-up, whereas SLP underlay many but not all of them. NC events due to lesions with SLP were angiographically less severe and presented with a delayed time course but were otherwise indistinguishable from NC events that were not associated with SLP. (J Am Coll Cardiol Img 2012;5:S95–105) © 2012 by the American College of Cardiology Foundation

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Most cases of sudden cardiac death and myocardial infarction (MI) are believed to arise from plaque rupture or surface erosion with subsequent thrombotic coronary occlusion of angiographically mild lesions ("vulnerable plaques"). The thin-cap fibroatheroma (TCFA), a metabolically active lesion with a large lipid-rich necrotic core and thin fibrous cap, is regarded as the most common type of rupture-prone and thrombosis-prone plaque (1–7). Angiographically, such lesions frequently undergo rapid progression in stenosis severity after plaque rupture, which may result in a spectrum of syndromes, ranging from sudden coronary occlusion with catastrophic symptoms to asymptomatic plaque progression (8–10).

See page S106

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)
CSA = cross-sectional area
DS = diameter stenosis
EEM = external elastic membrane
IVUS = intravascular ultrasound
MACE = major adverse cardiac event
MI = myocardial infarction
NC = nonculprit
SLP = substantial lesion progression
TCFA = thin-cap fibroatheroma
VH = virtual histology

The PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study investigated the natural history of atherosclerosis using multimodality intravascular imaging in vivo in patients presenting with acute coronary syndrome (ACS) (11–18). After treating all responsible culprit lesions, coronary angiography of the entire coronary tree and grayscale and radiofrequency intravascular ultrasound (IVUS)–virtual histology (VH) imaging of the proximal 6 to 8 cm of all 3 coronary arteries was performed, after which patients were followed for a median of 3.4 years on optimal medical therapy. Angiography was repeated in patients who had events during the follow-up period. Baseline and event-related coronary angiograms were compared to identify lesions responsible for unanticipated future events, which could occur either at the site of original treatment (culprit lesion–related events) or at untreated sites (nonculprit [NC] lesions). No prior study has examined how frequently future adverse cardiovascular events are indeed associated with angiographic substantial lesion progression (SLP) from NC lesions. We therefore sought to assess the frequency and predictors of angiographic SLP (the classic vulnerable plaque as defined by Naghavi et al. [19,20]) leading to NC lesion–related events in the contemporary era after the interventional management of ACS.

METHODS

Study population. In the PROSPECT study, 697 patients with ACS (unstable angina with electrocardiographic changes, non–ST-segment elevation MI, or recent ST-segment elevation MI) were enrolled from 37 sites in the U.S. and Europe. The study was approved by the institutional review boards of the participating institutions, and written informed consent was obtained from all patients. The pre-specified primary end point was the occurrence of major adverse cardiac events (MACEs), the composite of cardiac death, cardiac arrest, MI, or rehospitalization due to unstable or progressive angina. On the basis of follow-up angiography, events were adjudicated as occurring at initially treated sites (culprit lesions) or at previously untreated coronary segments (NC lesions). If follow-up angiography was not performed, the location was classified as indeterminate.

Coronary angiography. All baseline angiograms were prospectively analyzed without knowledge of subsequent events. Angiographic qualitative and quantitative analysis of the entire coronary tree was performed at the Angiographic Core Laboratory of the Cardiovascular Research Foundation (New York, New York) using proprietary methods modified from Medis CMS software version 7.0 (Medis Medical Imaging Systems, Leiden, the Netherlands). Every 1.5 mm of vessel length, the reference diameter, minimal luminal diameter, and diameter stenosis (DS) were recorded. Analysis of all angiographic lesions with ≥30% visual DS was also pre-specified. NC lesions were divided into those with and those without SLP, prospectively defined as a ≥20% increase in the quantitative coronary angiographic DS between baseline and follow-up.

Grayscale and IVUS-VH imaging and analyses. Grayscale and radiofrequency IVUS of the left main and proximal 6 to 8 cm of each major epicardial coronary artery was performed using a phased-array, 20-MHz, 3.2-F IVUS catheter (Eagle Eye, Volcano Corporation, Rancho Cordova, California) that was placed into the distal coronary artery after intracoronary administration of 0.2 mg nitroglycerin and withdrawn to the aorto-ostial junction using motorized catheter pullback at 0.5 mm/s. During pullback, grayscale IVUS images were recorded, raw radiofrequency data were captured at the top of the R-wave, and reconstruction of the color-coded map by an IVUS-VH data recorder was performed (In-Vision Gold and S5, Volcano Corporation).

Offline grayscale and IVUS-VH analysis were performed by: 1) QCU-CMS software (Medis Medical Imaging Systems) for contouring; 2) pcVH 2.1 software (Volcano Corporation) for contouring