JACC: CARDIOVASCULAR IMAGING VOL. 6, NO. 1, 2013

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcmg.2012.08.010

Dynamic Nature of Nonculprit Coronary Artery Lesion Morphology in STEMI

A Serial IVUS Analysis From the HORIZONS-AMI Trial

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OBJECTIVES The authors sought to report the temporal stability of an untreated, nonculprit lesion phenotype in patients presenting with ST-segment elevation myocardial infarction (STEMI).

BACKGROUND The temporal stability of the untreated, nonculprit lesion phenotype has been studied using intravascular ultrasound-virtual histology (IVUS) in patients with stable ischemic heart disease, but not in STEMI patients.

METHODS As part of a formal substudy of the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, baseline and 13-month follow-up IVUS was performed in 99 untreated nonculprit lesions in 63 STEMI patients. Lesions were classified as pathological intimal thickening (PIT), IVUS–derived thin-cap fibroatheroma (TCFA), thick-cap fibroatheroma (ThCFA), fibrotic plaque, or fibrocalcific plaque.

RESULTS The frequency of TCFA increased from 41% at baseline to 54% at follow-up, whereas ThCFAs decreased from 41% to 34% and PIT decreased from 16% to 8%. Among the 41 lesions classified at baseline as TCFA, at follow-up, 32 (78%) were still classified as TCFA, whereas 9 (22%) were classified as ThCFAs or fibrotic plaques. An additional 21 lesions at follow-up were newly classified as TCFA, developing from either PIT or ThCFA. TCFA at baseline that evolved into non-TCFAs trended toward a more distal location than TCFA that did not change ($p = 0.12$). In lesions classified as TCFA, the minimum lumen area (MLA) decreased from 8.1 (interquartile range [IQR]: 7.4 to 8.8) mm^2 at baseline to 7.8 (IQR: 7.2 to 8.4) mm^2 at follow-up, $p < 0.05$; this was associated with an increase in percent necrotic core at the MLA site (14% [IQR: 12 to 16] to 19% [IQR: 17 to 22], $p < 0.0001$) and over the entire length of the lesion (14% [IQR: 12 to 16] to 18% [IQR: 17 to 20], $p < 0.0001$).

CONCLUSIONS Untreated nonculprit lesions in STEMI patients frequently have TCFA morphology that does not change during 13-month follow-up and is accompanied by a decrease in MLA and an increase in necrotic core. (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI]; NCT00433966) (J Am Coll Cardiol Img 2013;6:86–95) © 2013 by the American College of Cardiology Foundation

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Autopsy data suggest that rupture of an atheromatous plaque with superimposed thrombosis is the cause of most acute coronary syndromes (ACS) and sudden cardiac death (1–3). A thin-cap fibroatheroma (TCFA) with a large lipid-rich necrotic core (NC) is particularly prone to rupture and result in coronary artery thrombotic occlusion (4–7). Furthermore, 3-vessel imaging studies in patients with ACS have shown that the incidence of secondary plaque rupture in nonculprit lesions is fairly common (8). Intravascular ultrasound-virtual histology (IVUS) provides quantitative and qualitative information about plaque composition and lesion phenotype, including plaques prone to cause events (9–12), and may therefore be useful to assess serial plaque composition evolution. A previous IVUS study in patients, mostly with stable ischemic heart disease, demonstrated that the IVUS lesion phenotype can evolve and, specifically, that virtual histology–derived thin-cap fibroatheromas (TCFA) can develop and/or heal within 1 year (13). No such studies have been performed in patients with ACS. In the present study, therefore, we used serial (baseline and follow-up) IVUS to assess the dynamic nature of nonculprit coronary artery lesion morphology in patients with ST-segment elevation myocardial infarction (STEMI), in particular to evaluate the development and evolution of TCFA.

METHODS

Study population. HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) was a prospective, open-label, multicenter, dual-arm, 2 × 2 factorial randomized trial in patients with STEMI. The 2 randomization arms consisted of: 1) the direct thrombin inhibitor bivalirudin alone versus heparin plus a glycoprotein IIb/IIIa inhibitor (1:1 randomization); and 2) TAXUS EXPRESS paclitaxel-eluting stents versus otherwise equivalent EXPRESS bare-mental stents (3:1 randomization) (Boston Scientific, Natick, Massachusetts). The present study cohort consists of 63 patients (99 lesions) with serial IVUS examinations of at least 1 untreated nonculprit lesion in a native coronary artery at baseline and at follow-up that were studied at Charitė University Medicine Berlin (Campus Benjamin Franklin, Berlin, Germany) where the ethics committee approved the protocol, and written informed consent was obtained from all patients.

Clinical follow-up. Clinical follow-up was performed at 30 days, 6 months, 1 year, 2 years, and 3 years. Routine angiographic (with or without IVUS) follow-up was performed at 13 months or earlier if a clinical event occurred. Pre-specified endpoints included ischemia-driven revascularization and the composite of major adverse cardiac events (death, reinfarction, stroke, or stent thrombosis). An independent clinical events committee (Cardiovascular Research Foundation [CRF], New York, New York) that was masked to treatment assignment adjudicated all adverse events from original source documents and procedural angiograms.

IVUS image acquisition. After intracoronary nitroglycerin, a phased-array, 20-MHz, 3.2-F IVUS catheter (Eagle Eye, Volcano Corporation, Rancho Cordova, California) was placed into the distal coronary artery and pulled back to the aorto-ostial junction using an R-100 motorized catheter pullback device (Volcano Corporation) at a speed of 0.5 mm/s. During pull back, grayscale IVUS was recorded, raw radiofrequency data were captured at the top of the R-wave, and reconstruction of the color-coded map by an IVUS data recorder was performed (In-Vision Gold, Volcano Corporation). The grayscale IVUS and captured radiofrequency data were written onto a CD-R or DVD-R and sent to an independent IVUS core laboratory (CRF) for quantitative and qualitative analyses.

Grayscale and IVUS analyses. Off-line grayscale and IVUS analyses were performed using: 1) QCU-CMS (Medis, Leiden, the Netherlands) for contouring; 2) pcVH 2.1 software (Volcano Corporation) for contouring and data output; and 3) proprietary qVH software (qVH 2.5, developed and

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndromes
CRF = Cardiovascular Research Foundation
CSA = cross-sectional area
DC = dense calcium
EEM = external elastic membrane
FF = fibrofatty
FT = fibrotic tissue
IVUS = intravascular ultrasound-virtual histology
MI = myocardial infarction
MLA = minimum lumen area
NC = necrotic core
OCT = optical coherence tomography
PIT = pathological intimal thickening
STEMI = ST-segment elevation myocardial infarction
TCFA = thin-cap fibroatheroma
ThCFA = thick-cap fibroatheroma

Sankyo; serves on the advisory board for Regado Biosciences; and is a consultant for AstraZeneca, Abbott, Johnson & Johnson, Merk Sharp & Dohme, and Maya Medical. Dr. Stone is a consultant for Volcano Corporation. Dr. Maehara has received speaker's fees from St. Jude Medical; and grant support from Boston Scientific. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received February 24, 2012; revised manuscript received August 13, 2012, accepted August 21, 2012.