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OCT Analysis in Patients With Very Late Stent Thrombosis

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OBJECTIVES We report optical coherence tomography (OCT) findings in 33 patients who presented with very late stent thrombosis (VLST) after either drug-eluting stent (DES) or bare-metal stent (BMS) implantation.

BACKGROUND VLST is a potentially life-threatening complication, but the underlying mechanisms remain unclear.

METHODS In 33 patients (27 DES- and 6 BMS-treated lesions) with definite VLST, OCT images were acquired before either thrombus aspiration or intravascular ultrasonography (IVUS) imaging.

RESULTS The median duration from implantation was 61.5 months in the DES group and 109.1 months in the BMS group. In the overall cohort, combining DES and BMS, 94% showed intraluminal thrombi. VLST was associated with in-stent neointimal rupture in 23 patients (70%); 22 had thrombi near the site of neointimal rupture. Stent malapposition was observed in 14 (42%) lesions, but only 9 of them showed thrombi at the site of stent malapposition; moreover, 6 (18%) stented segments with malapposition also had neointimal rupture. Only 2 (6%) lesions had no evidence of neointimal rupture or malapposition. Stent fracture was detected in 3 DES-treated lesions, all with concomitant neointimal rupture. Compared with lesions without neointimal rupture, lesions with neointimal rupture showed a higher frequency of ST-segment elevation myocardial infarction (65% vs. 20%, respectively, $p = 0.040$) as well as a higher peak creatine kinase-myocardial band level (163.1 ng/ml vs. 15.7 ng/ml, respectively, $p = 0.017$).

CONCLUSIONS OCT imaging indicated that advanced neoatherosclerosis with neointimal rupture and thrombosis was the most common mechanism of definite VLST and was associated with a high frequency of ST-segment elevation myocardial infarction. (J Am Coll Cardiol Img 2013;6:695–703)
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Very late stent thrombosis (VLST) is a catastrophic complication that occurs beyond 1 year from stent implantation with a steady frequency of 0.6% per year thereafter in drug-eluting stents (DES) (1). However, the precise mechanisms of VLST are the subject of debate. Previous pathologic studies report that delayed arterial healing characterized by persistent fibrin deposition and poor endothelialization is the primary substrate of late DES thrombosis (2,3). Studies by Cook et al. (4,5) and a meta-analysis by Hassan et al. (6) suggest that late stent malapposition with expansive vascular remodeling is more frequent after DES implantation than that with bare-metal stent (BMS) implantation and is associated with VLST. An in vivo study by Guagliumi et al. (7) shows that optical coherence tomography (OCT) detected uncovered stent struts are independently associated with late DES thrombosis. Finally, de novo in-stent neoatherosclerosis induced by chronic inflammation and abnormal vascular responses has been suggested as an additional mechanism of VLST (8–10).

ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)

DES = drug-eluting stent(s)

EEM = external elastic membrane

IQR = interquartile range

IVUS = intravascular ultrasonography

MLA = minimal lumen area

OCT = optical coherence tomography

STEMI = ST-segment elevation myocardial infarction

TCFA = thin-cap fibroatheroma

VLST = very late stent thrombosis

We previously reported grayscale intravascular ultrasonography (IVUS) findings of VLST suggesting that stent malapposition was unique to DES-related VLST, while in-stent neointimal rupture was found in both BMS and DES with VLST (8). However, grayscale IVUS is limited both in its ability to characterize the neointima and to accurately identify uncovered stent struts, stent coverage, or stent–vessel wall malapposition. Thus, we report high-resolution OCT findings in 33 patients who presented with VLST.

METHODS

Subjects. From February 2009 to September 2011, a total of 55 consecutive patients (36 DES and 19 BMS lesions) presented with definite VLST (beyond 1 year after stent placement) at the Asan Medical Center, Seoul, Korea. Angiographic evidence of definite stent thrombosis was based on Academic Research Consortium criteria (11). Furthermore, we included only those patients presenting with acute myocardial infarction or patients presenting with unstable angina who had stent thrombosis documented by thrombectomy. Exclusion criteria were hemodynamic instability, balloon pre-dilation, or thrombectomy prior to OCT examination; inability of the OCT ImageWire or DragonFly catheter (LightLab Imaging, Inc., Westford, Massachusetts) to cross the lesion into the distal vessel due to tight stenosis or severe tortuousity; or presence of left main lesions or saphenous vein graft lesions. In addition, before April 2011, OCT examination using the proximal occlusive technique could not be carried out in lesions located near the ostium. Thus, OCT imaging was performed with 36 patients. After excluding 3 patients whose image quality was poor, we included 33 patients with 33 VLST lesions (27 DES and 6 BMS) in the current study. The DES-VLST group included 22 lesions with the Cypher stent (Cypher Select, Cordis, Johnson & Johnson, Miami, Florida), 3 with Taxus stents (Boston Scientific Corp., Natick, Massachusetts), 1 with Xience stent (Abbot Vascular, Santa Clara, California), and 1 with Pico Elite stent (amg International GmbH, Raesfeld-Erle, Germany). Baseline C-reactive protein was measured before the procedure. All patients signed written informed consent prior to the study.

Angiographic analysis. Qualitative and quantitative angiographic measurements were taken using standard techniques with automated edge detection algorithms (CAAS-5, Pie-Medical, Maastricht, the Netherlands) in the angiographic analysis center of the CardioVascular Research Foundation, Seoul, Korea (12).

OCT imaging and analysis. All OCT images were acquired before thrombus aspiration or IVUS imaging. Before April 2011, OCT images were acquired using the proximal occlusive technique, the 0.019-inch ImageWire, and a commercially available system (LightLab Imaging, Inc.). The artery was cleared of blood by continuous flushing with iodixanol 370 (Visipaque, GE Health Care, Cork, Ireland) at a flow rate of 3.0 ml/s (13). Since April 2011, OCT images have been acquired using a nonocclusive technique with the C7XR system (LightLab Imaging, Inc.).

Strut-level OCT analysis was performed every 3 frames (every 0.45 mm in images obtained at 3 mm/s pullback using the occlusive technique or every 0.55 mm in images obtained at 20 mm/s pullback using the nonocclusive technique).

Struts were classified as uncovered when a tissue layer on the endoluminal surface was not visible. Struts were classified as malapposed if the distance from the endoluminal surface of the strut to the adjacent lumen contour was greater than the sum of the metal and polymer thickness, not related to a side branch. Thus, the cutoff points of malapposition used for each stent type were 130 μm for the Taxus paclitaxel-eluting stent; 160 μm for the

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