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Mechanisms of Very Late Bioresorbable Scaffold Thrombosis

The INVEST Registry

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ABSTRACT

BACKGROUND Very late scaffold thrombosis (VLScT) occurs more frequently after bioresorbable scaffold (Absorb BVS 1.1, Abbott Vascular, Santa Clara, California) implantation than with metallic everolimus-eluting stents.

OBJECTIVES The purpose of this study was to elucidate mechanisms underlying VLScT as assessed by optical coherence tomography (OCT).

METHODS The INVEST (Independent OCT Registry on Very Late Bioresorbable Scaffold Thrombosis) registry is an international consortium of investigators who used OCT to examine patients with VLScT.

RESULTS Between June 2013 and May 2017, 36 patients with 38 lesions who had VLScT underwent OCT at 19 centers. VLScT occurred at a median of 20 months (interquartile range: 16 to 27 months) after implantation. At the time of VLScT, 83% of patients received aspirin monotherapy and 17% received dual-antiplatelet therapy. The mechanisms underlying VLScT were (in descending order) scaffold discontinuity (42.1%), malapposition (18.4%), neoatherosclerosis (18.4%), underexpansion or scaffold recoil (10.5%), uncovered struts (5.3%), and edge-related disease progression (2.6%). Discontinuity (odds ratio [OR]: 110; 95% confidence interval [CI]: 73.5 to 173; $p < 0.001$), malapposed struts (OR: 17.0; 95% CI: 14.8 to 19.7; $p < 0.001$), and uncovered struts (OR: 7.3; 95% CI: 6.2 to 8.8; $p < 0.001$) were more frequent in the thrombosed than the nonthrombosed scaffold regions. In 2 of 16 patients with scaffold discontinuity, intercurrent OCT before VLScT provided evidence of circularly apposed scaffold struts with minimal tissue coverage.

CONCLUSIONS The leading mechanism underlying VLScT was scaffold discontinuity, which suggests an unfavorable resorption-related process, followed by malapposition and neoatherosclerosis. It remains to be determined whether modifications in scaffold design and optimized implantation can mitigate the risk of VLScT. (Independent OCT Registry on Very Late Bioresorbable Scaffold Thrombosis [INVEST]; NCT03180931) (J Am Coll Cardiol 2017;70:2330–44)

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Fully bioresorbable coronary scaffolds were introduced to overcome the limitations of metallic stents associated with permanent caging of the arterial wall aiming to restore vessel physiology, as well as to mitigate the long-term risk of device-related adverse events, including restenosis and stent thrombosis (1). Early results from 6 randomized controlled trials comparing the Absorb bioresorbable vascular scaffold (BVS) with metallic everolimus-eluting stents (EES) showed similar clinical outcomes up to 1 year (2–7). More recently, longer-term follow-up of the ABSORB II trial suggested an increased risk of scaffold thrombosis at 3 years (8). In addition, the AIDA (Amsterdam Investigator-Initiated Absorb Strategy All-comers Trial), which compared BVS with metallic EES in an all-comer population, reported a higher risk of target-vessel myocardial infarction and early, late, and very late device thrombosis at a median follow-up of approximately 2 years after BVS implantation (9).

SEE PAGE 2345

Meta-analyses of these trials, which included more than 5,000 patients with follow-up beyond 1 year, consistently showed that BVS is inferior to EES in terms of target-lesion failure, myocardial infarction, and target-lesion revascularization in the absence of differences in mortality. Of note, the relative risk of scaffold thrombosis was more than 3 times higher with BVS than with EES during extended follow-up, with a concerning 10-fold increased relative risk of very late scaffold thrombosis (VLScT) between 1 and 2 years after BVS implantation (10–15).

Mechanisms underlying early scaffold thrombosis are largely consistent with observations previously reported with metallic bare-metal stents (BMS) and drug-eluting stents (DES), including procedural factors such as acute device underexpansion, malapposition, incomplete lesion coverage, and residual dissections (16,17). Conversely, the principal causes underlying VLScT remain largely unknown, and as a result, the translation of mechanistic insights into modifications of the implantation procedure or device iterations to address specific components in scaffold design, polymer composition, and degradation is lacking. VLScT is a clinical manifestation of particular concern because it is responsible for a considerable proportion of device-related myocardial infarctions and could impact the need for extended-duration dual-antiplatelet therapy (DAPT) (18).

Because of its high spatial resolution (10 to 20 μm), optical coherence tomography (OCT) has become the imaging modality of choice for the investigation of coronary device failures including thrombosis and is of particular value to investigate time-dependent changes after scaffold implantation (19–21). Against this background, the INVEST (Independent OCT Registry on Very Late Bioresorbable Scaffold Thrombosis) registry was conducted by an independent international consortium of investigators to investigate the mechanisms underlying VLScT as assessed by OCT in the largest worldwide cohort to date.

ABBREVIATIONS AND ACRONYMS

3D = 3-dimensional
ACS = acute coronary syndrome(s)
BMS = bare-metal stent(s)
BVS = bioresorbable vascular scaffold
DAPT = dual-antiplatelet therapy
DES = drug-eluting stent(s)
EES = everolimus-eluting stent(s)
OCT = optical coherence tomography
PCI = percutaneous coronary intervention
PSP = pre-dilation, sizing, and post-dilation
QCA = quantitative coronary angiography
RVD = reference vessel diameter
VLScT = very late scaffold thrombosis

METHODS

STUDY POPULATION. Patients enrolled in the INVEST registry had to fulfill the following criteria: (1)

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