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Optical Coherence Tomography Findings in Bioresorbable Vascular Scaffolds Thrombosis

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Background—Everolimus-eluting bioresorbable vascular scaffolds have been developed to improve late outcomes after coronary interventions. However, recent registries raised concerns regarding an increased incidence of scaffold thrombosis (ScT). The mechanism of ScT remains unknown.

Methods and Results—The present study investigated angiographic and optical coherence tomography findings in patients experiencing ScT. Fifteen ScT (14 patients, 79% male, age 59±10 years) occurred at a median of 16 days (25%–75% interquartile range: 1–263 days) after implantation. Early ScT (<30 days) occurred in 8 cases (53%). Possible causal factors in these patients included insufficient platelet inhibition in 2 cases and procedural factors (scaffold underexpansion, undersizing, or geographical miss) in 4 cases. No obvious cause could be found in 2 early ScT. In late (>1 month) and very late (>1 year) ScT (respectively, 5 and 2 cases), 5 scaffolds showed intimal neovessels or marked peristrut low-intensity areas. Scaffold fractures were additionally found in 2 patients, and scaffold collapse was found in 1 patient with very late ScT. Extensive strut malapposition was the presumed cause for ScT in 1 case. One scaffold did not show any morphological abnormality. Thrombectomy specimens were analyzed in 3 patients and did not demonstrate increased numbers of inflammatory cells.

Conclusions—The mechanisms of early ScT seem to be similar to metallic stents (mechanical and inadequate antiplatelet therapy). The predominant finding in late and very late ScT is peristrut low-intensity area.

Key Words: bioresorbable vascular scaffold ■ optical coherence tomography ■ percutaneous coronary intervention ■ peristrut low-intensity area ■ scaffold thrombosis ■ stent thrombosis

Stent thrombosis (ST) is an uncommon but devastating adverse event after percutaneous coronary intervention (PCI).[1] Various factors influence the likelihood of ST, such as patient-related characteristics, procedural and lesion characteristics, the presence of acute coronary syndrome, or the premature discontinuation of antiplatelet therapy.[2–6] Experiences with early generation drug-eluting stents (DES) demonstrated the crucial impact of pathological vessel healing and hypersensitivity reactions to one of the components of the stent in the genesis of late ST.[4,6,7] To decrease the incidence of these phenomena, the technology evolved from more biocompatible DES to fully bioresorbable vascular scaffolds (BVS).

Among BVS, the everolimus-eluting Absorb BVS (Abbott Vascular, Santa Clara, CA) are the most commonly implanted. Based on the evidence of safety demonstrated in early trials,[8–10] Absorb BVS have been subsequently launched to unrestricted clinical use in August 2012 in Europe. To date, >60 000 patients have been treated. Although the recently presented randomized Absorb II[11] and EverBio-2[12] trials suggest similar efficacy compared with DES, some concerns about an increased rate of scaffold thrombosis (ScT) arose. Indeed, the Gauging Coronary Healing With Bioresorbable Scaffolding Plaforms in Europe (GHOST-EU) registry reported a 2.1% incidence of definite ScT at 6 months.[13] Along with this evidence, isolated small case series were reported, describing possible pathophysiological mechanisms of ScT and its putative therapeutic options.[14–16]

Optical coherence tomography (OCT) imaging has proved instrumental in identifying the mechanisms of scaffold failure and vessel healing after BVS implantation. Therefore, the aim of this study was to investigate the structural findings in patients presenting with ScT at our institutions.

Methods

Patient Population

Between December 2012 and October 2014, 26 patients had definite ScT after BVS implantation at our institutions. Since January 2014, a protocol

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WHAT IS KNOWN

- Thrombosis of bioresorbable vascular scaffolds has been reported recently.
- Intravascular imaging, such as optical coherence tomography and intravascular ultrasound, can provide information as to the mechanism(s) of stent thrombosis.

WHAT THE STUDY ADDS

- We identified a relationship between early scaffold thrombosis to mechanical factors, such as underexpansion, undersizing, and geographical miss, as well as to inadequate antiplatelet treatment.
- The predominant optical coherence tomography finding in late and very late scaffold thrombosis is peristrut low-intensity area, which may be the correlate of vascular edema, thus enhancing vascular vulnerability.

was implemented to perform OCT before emergency PCI in patients presenting with ScT. During this time period, 14 consecutive patients in whom definite ScT occurred were investigated by OCT and constitute the study population for this report. Clinical data were collected in an anonymized way with the approval of the local Ethics Committees.

Bioresorbable Vascular Scaffold

All included patients were treated with the ABSORB (Abbott Vascular, Abbott Park, IL) BVS version 1.1. BVS became available for all-comer use in June 2012 in Fribourg, in May 2012 in Mainz, and in July 2013 in Luzern.

Definition of Scaffold Thrombosis

ScT was defined in analogy to the definitions for ST proposed by the Academic Research Consortium in 2007.[1] Thus, the presence of a thrombus that originated in the scaffold or its 5 mm proximal or distal margins on angiographic or intravascular examination and the presence of either (1) acute onset of ischemic symptoms, (2) new ECG changes that suggest ischemia, (3) typical rise and fall in cardiac biomarkers, or a combination of the latter defined ScT. Nonocclusive thrombi on angiographic examination were defined as noncalcified filling defect or lucency surrounded by contrast material seen in multiple projections, or persistence of contrast material within the lumen, or a visible embolization of intraluminal material downstream. Occlusive thrombi were considered with a Thrombolysis in Myocardial Infarction flow of 0 or 1 either intrascaffold or proximal to a scaffold up to the most adjacent proximal side branch or main branch (if originates from the side branch). On OCT, ScT was identified as mass attached to the luminal surface or floating within the lumen of the scaffold or its 5 mm proximal and distal margins.[17] Timing of ScT was defined according to the Academic Research Consortium criteria for ST as early (<30 days after implantation), late (>30 days to 1 year after implantation), and very late (>1 year after implantation).

Quantitative Coronary Angiography

Coronary angiograms were recorded digitally at baseline after index procedure and at the time of ScT. All analyses were performed at the angiographic core laboratory of the University and Hospital of Fribourg. QCA were computed with dedicated software (CAAS II; Pie Medical Imaging, Maastricht, The Netherlands) that uses automated edge detection. Quantitative measurements included reference vessel diameter, minimal luminal diameter, percent diameter stenosis (calculated as 100×[reference vessel diameter−minimal luminal diameter]/reference vessel diameter), and lesion length.

OCT Acquisition and Analysis

OCT images were acquired before emergency PCI. After the diagnostic angiography, 200 μg of intracoronary nitroglycerin was administered. OCT was performed with the Optis Ilumien system (St Jude Medical, MN) according to manufacturer guidelines using the Dragonfly Duo OCT Imaging Catheter with motorized pullback (25 mm/s) and the nonocclusive flushing technique. Images of the scaffold and of the reference segments 10 mm proximal and distal of the scaffold were acquired. OCT pullbacks were registered on CD-ROM and assessed offline by 2 assessors using dedicated software (Lightlab Imaging, St. Jude Medical, MN).

Quantitative measurements were performed at intervals of 0.6 mm whenever quality image allowed for it and comprised the cross-sectional area (CSA) of the external elastic membrane (mm^2) and the lumen (mm^2) of reference and treated segments. In addition, the mean and minimal scaffolds CSA (mm^2) were recorded. Neointimal hyperplasia was calculated as scaffold CSA minus in-scaffold lumen CSA. Incomplete scaffold apposition (ISA) was defined as a lack of contact of at least 1 strut at a distance of ≥163 μm to the underlying vessel wall in the absence of a side branch with evidence of blood flow behind the strut. ISA CSA was defined as in-scaffold lumen CSA minus scaffold CSA. Scaffold expansion index was calculated in dividing the minimal scaffold CSA by the mean proximal and distal lumen CSA. Scaffold underexpansion was defined as a stent expansion index 0.8. Undersizing was defined as the employment of a scaffold whose deployment at implantation pressure resulted in an incomplete stent apposition with a distance of >100 μm of the abluminal stent edge from the adjacent vessel wall.

Neoatherosclerosis was defined as the presence of either (1) fibrocalcific plaques (signal-poor regions with sharply delineated upper and lower borders) or (2) lipid-rich plaques (diffusely bordered, signal-poor regions) on the luminal side of scaffold struts.[18] Because they share the same OCT appearance (homogenous, highly backscattering lesions devoid of OCT signal-poor regions) and histology, no discrimination was made between fibrotic plaques and neointima. Neovessels were defined as sharply delimitated signal-poor lacunae that extended over multiple contiguous frames. Peristrut low-intensity areas (PSLIA) were defined according to Otake et al as homogenously appearing, nonsignal-attenuating zones around struts of lower intensity than the surrounding tissue.[19] Peristrut intensity was measured at the midstrut at 150 μm depth from the lumen and at equal distance between 2 contiguous struts based on intensity of the key component of the cyan, magenta, yellow, key/black (CYMK) color model based on raw cross-sectional images. PSLIA in each patient was judged as either present or absent by 3 independent observers. Two observers performed ratings on 2 different occasions to allow the assessment of intraobserver reliability. Scaffold fracture was suspected in case of altered scaffold geometry appearing as 2 overlapping rows of at least 2 contiguous struts on a portion of the circumference in the absence of scaffold overlap or lack of circumferential struts.

Thrombus Harvesting, Histopathologic Sampling, and Analysis

Before emergency PCI, patients underwent thrombus aspiration followed immediately by OCT acquisition of the affected scaffold segment as already published.[6] In brief, if the hemodynamic status allowed, sublingual or intracoronary nitroglycerin was administered (0.2–0.3 mg), and an angiogram with the use of a 6F guiding catheter was performed to identify the site of thrombotic scaffold occlusion. Then, a 0.014-inch coronary guidewire was passed through the affected scaffold, followed by aspiration of thrombus with the use of specifically designed manual aspiration catheters. Harvested thrombus was passed through a 40-μm Becton Dickinson Cell Strainer filter and fixed in 4% neutral buffer formalin. Paraffin blocks of the thrombotic material were sectioned on a rotary microtome and stained with hematoxylin–eosin, Movat

pentachrome, and Luna stains. All sections were examined by light microscopy for platelets, fibrin, red blood cells, plaque constituents, and inflammation. In addition, 5 high-power fields (×40) demonstrating the greatest severity of inflammation were selected for quantitative analysis. Total white blood cell (WBC) and eosinophil counts were performed and summed for the selected 5 high-power fields. Data were recorded as total WBCs and total eosinophils. The severity of the inflammation was graded on the basis of a 3-tiered scale defined as (1) mild (<100 WBCs per high-power field), (2) moderate (101–300 WBCs per high-power field), and (3) severe (>300 WBCs per high-power field).

Statistical Analysis

Statistical analysis was primarily descriptive. Categorical variables are presented as absolute counts and percentages, and continuous variables are presented as means and standard deviations or medians with 25th to 75th percentiles. For illustrative purposes, comparisons between early ScT and late/very late ScT were performed using the Wilcoxon rank-sum test. Inter-rater reliability was assessed using Fleiss's kappa and intraobserver reliability using Cohen's kappa. All statistical analyses were performed using dedicated software (Stata version 13; StataCorp LP, College Station, TX) at a 2-tailed significance level of α=0.05.

Results

Baseline Patient Characteristics

A total of 14 patients who had 15 ScT underwent OCT before emergency PCI and were included in the present study. Mean age was 59±10 years, and 79% (n=11) of patients were men. Smoking and hypertension were the most prevalent risk factors found in 71% (n=10) of patients. Five (36%) patients had undergone PCI before BVS implantation. ST-elevation myocardial infarction was the most frequently encountered indication for index procedure (50%; n=7). Mean left ventricular ejection fraction was 48±10%. Further baseline characteristics are outlined in Table 1.

Table 1. Baseline Patient Characteristics (n=14)

Male, n (%)	11 (79)
Age, years±SD	59±10
Hypertension, n (%)	10 (71)
Diabetes mellitus, n (%)	2 (14)
Smoking, n (%)	10 (71)
Dyslipidemia, n (%)	8 (57)
Family history, n (%)	4 (29)
Previous MI, n (%)	1 (7)
Previous PCI, n (%)	5 (36)
Previous CABG, n (%)	1 (7)
Indication at index procedure	
Stable angina, n (%)	2 (14)
Silent ischemia, n (%)	0 (0)
Acute coronary syndrome	12 (86)
Unstable angina, n (%)	3 (21)
NSTEMI, n (%)	2 (14)
STEMI, n (%)	7 (50)
LVEF, % ±SD	48±10
Multivessel disease, n (%)	6 (43)

CABG indicates coronary artery bypass grafting; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non–ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; and STEMI, ST-elevation myocardial infarction.

Angiographic and Procedural Characteristics at Index Procedure

Baseline angiographic and procedural characteristics are summarized in Table 2. Four (27%) patients presented with total coronary occlusion. Mean minimal luminal diameter was 0.82±0.77 mm and mean diameter stenosis was 79±20%. The median number of implanted BVS per lesion was 1 [25%–75% interquartile range: 1–1]. BVS overlap was present in 2 (13%) patients. Final in-scaffold minimal luminal diameter was 2.59±0.42 mm. All patients showed a Thrombolysis in Myocardial Infarction flow of 3 after BVS implantation.

Scaffold Thrombosis

Timing

Fifteen ScT occurred at a median of 16 days [25%–75% interquartile range: 1–263 days]. There were 8 (53%) early ScT (median: 3 days) of whom 3 (20%) were acute and 5 (33%) subacute. ScT occurred late (median: 243 days) in 5 (33%) cases and very late (573 days) in 2 (14%) cases.

Qualitative OCT Findings

Table 3 provides information on antiplatelet medication, implanted devices, target vessel, presentation at index procedure, and the presumed underlying mechanism of ScT in the individual patients as assessed by qualitative OCT interpretation.

Early ScT were presumably because of insufficient platelet inhibition in 2 (13%) cases and procedural factors (scaffold underexpansion, undersizing, or geographical miss) in 4 (27%) cases. No obvious cause was found in 2 (13%) early ScT. Exemplary images of undersizing and underexpansion are shown in Figure 1.

In late and very late ScT, 5 (33%) scaffolds showed intimal neovessels or marked PSLIA as demonstrated in Figure 2. Intraobserver reliability for PSLIA showed perfect

Table 2. Lesion Characteristics at Index Procedure (N=15)

Target coronary artery	
LAD, n (%)	6 (40)
LCX, n (%)	2 (13)
RCA, n (%)	7 (47)
Lesion length, mm	17.2±7.5
Reference vessel diameter, mm	2.76±0.44
Minimal luminal diameter, mm	0.82±0.77
Diameter stenosis, %	79±20
Number of scaffolds per lesion	1 (1–1)
Total scaffold length, mm	26±14
Scaffold diameter, mm	3.1±0.3
Scaffold overlap, n (%)	2 (13)
Post-procedural characteristics	
Final in-scaffold minimal luminal diameter, mm	2.59±0.42
Final in-scaffold diameter stenosis, %	12±7
TIMI flow	3 (3–3)

Values are expressed in mean±SD (standard deviation) or median with interquartile range (in brackets). LAD indicates left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; and TIMI, Thrombolysis in Myocardial Infarction.

Table 3. Narratives of 15 ScT

ID No.	Time to ScT, days	Presumed Cause for ScT	Indication for Index PCI	Treated Vessels	Target Vessel	No. of BVS in Target Lesion	BVS Diameter, mm	BVS Length, mm	P2Y12 Inhibitor
1	0	Patient did not receive DAPT/Undersized scaffold with ISA	STEMI	1	RCA	1	3.5	18	Prasugrel
2	0	Calcified lesion	UA	1	LAD	1	3	12	Prasugrel
3	0	Regional miss—de novo stenosis proximal to scaffold left untreated	STEMI	1	RCA	1	3	18	Ticagrelor
4	1	Calcified lesion, asymmetrical apposition, fracture	Stable Angina	1	LAD	1	3	28	Prasugrel
5	4	Insufficient platelet inhibition,* scaffold underexpansion	STEMI	1	LAD	1	3	18	Ticagrelor/ Clopidogrel
6	6	Undersized scaffold with ISA	STEMI	1	RCA	1	2.5	28	Ticagrelor
7	8	Underexpansion, calcified lesion	NSTEMI	1	LAD	1	2.5	18	Ticagrelor
8	16	Organized thrombus in distal scaffold	UA	2	LCX	1	2.5	28	Clopidogrel
9	73	No mechanistic explanation	UA	2	RCA	2	3	56	Prasugrel
10	104	Focal restenosis after bifurcation, neovessels, ruptured restenosis	STEMI	1	LAD	1	3.5	28	Prasugrel
11	243	PSLIA, long scaffold fracture;	NSTEMI	1	RCA	2	3	56	Prasugrel
12	263	PSLIA, neovessels	Stable Angina	2	LAD	1	3	28	Prasugrel
13	349	ISA, PSLIA, BVS recoil?	STEMI	1	RCA	2	3	28	Prasugrel
14	562	PSLIA, ISA, asymmetrical scaffold and fracture	STEMI	1	RCA	1	3.5	12	Prasugrel
15	584	PSLIA, scaffold collapse	NSTEMI	1	LAD	1	3.5	12	Ticagrelor

BVS indicates bioresorbable vascular scaffold; DAPT, dual antiplatelet therapy; ISA, incomplete scaffold apposition; LAD, left anterior descending artery; LCX, left circumflex artery; NSTEMI, non–ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PSLIA, peristrut low intensity area; RCA, right coronary artery; ScT, scaffold thrombosis; STEMI, ST-elevation myocardial infarction; and UA, unstable angina.

*Insufficient platelet inhibition: Ticagrelor was stopped on day 3 after scaffold implantation and Clopidogrel was started on day 4 (75 mg, no loading). In the evening of day 4, the patient sustained ScT.

(kappa=1.0; P<0.001) agreement, and interobserver reliability showed almost perfect (kappa=0.86; P<0.001) agreement. Scaffold fractures were additionally found in 2 (13%) and scaffold collapse additionally in 1 (7%) of latter patients. Extensive strut malposition was the presumed cause for ScT in 1 (7%) case. One (7%) scaffold did not show any abnormalities at the time point of thrombosis. Postprocedural OCTs (after final treatment) were analyzed in 6 (40%) cases, and the volume

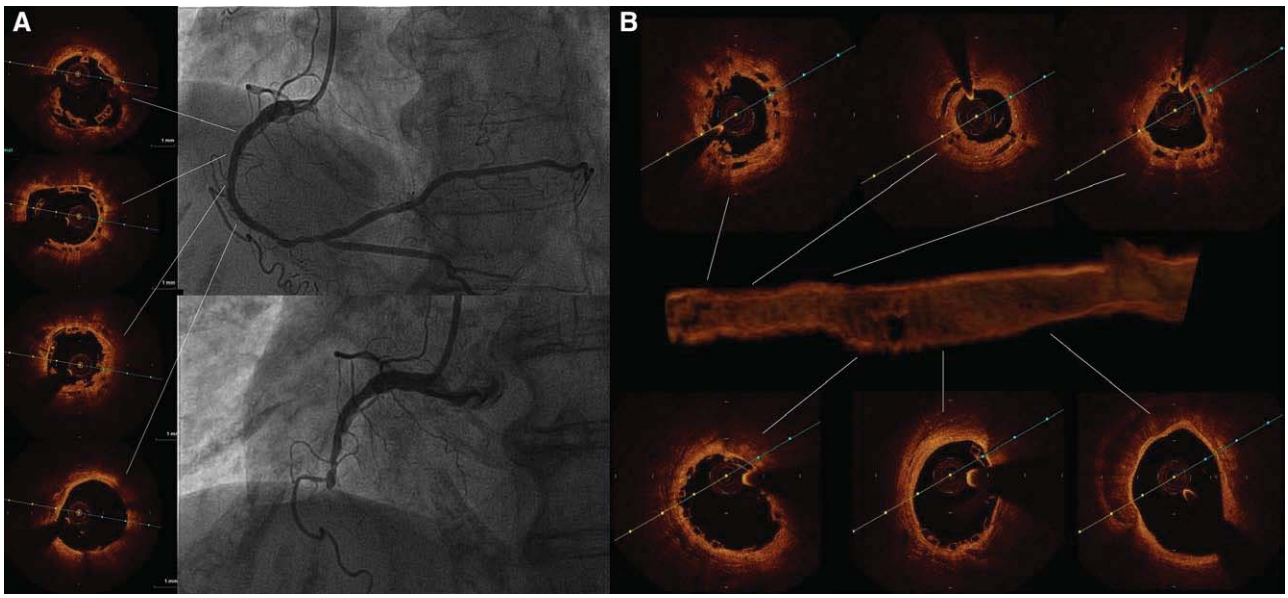

Figure 1. Early scaffold thrombosis (ScT). **A**, ScT 6 days after scaffold implantation for inferior ST-elevation myocardial infarction. Optical coherence tomography revealed undersizing in the proximal part of the scaffold as the key mechanism for ScT. **B**, ScT 8 days after scaffold implantation for non–ST-elevation myocardial infarction. Optical coherence tomography revealed underexpansion as the key mechanism for ScT: 3D reconstruction demonstrates an underexpanded distal segment with good expansion in the proximal segment of the scaffold.

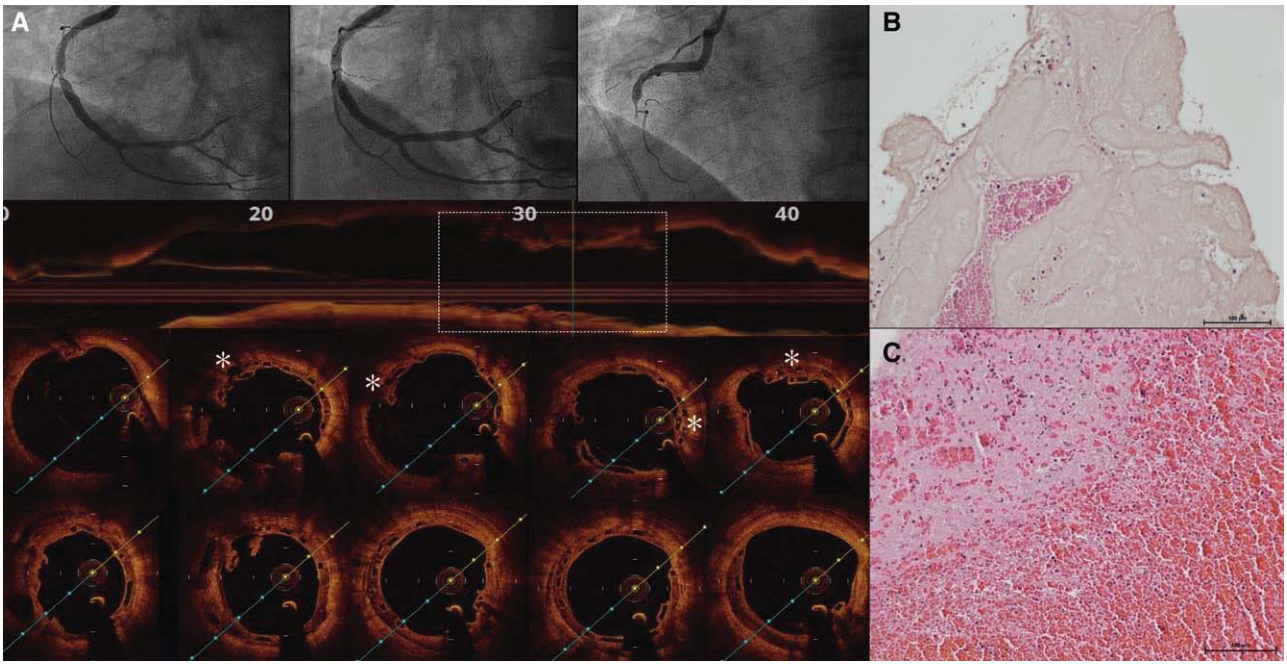

Figure 2. Very late scaffold thrombosis (ScT). **A**, Angiographic and optical coherence tomography (OCT) findings in a 55-year-old man who presented with ScT 562 days after scaffold implantation. The OCT demonstrates diffuse peristrut low-intensity area (PSLIA) and strut discontinuities (*) along the scaffold length. **B** and **C**, Histological sections of harvested thrombus showed fragments of platelet-rich thrombus with rare signs of acute and chronic inflammation, including scarce eosinophils (**B**) and regions of organized thrombus with high amount of trapped red cells but no excess amount of inflammatory cells (**C**). Histology: H&E staining ×200.

of residual thrombus computed (Table 4). No new evidence regarding the underlying mechanism of ScT was gathered.

Quantitative OCT Findings

Quantitative OCT analysis was conducted in all affected segments and is outlined in Table 5. Mean scaffold CSA was 6.5±1.9 mm.^{2} Two (13%) segments presented a minimal scaffold CSA of <4 mm.^{2} Mean scaffold expansion index was 0.95±0.36, with 9 (60%) of segments presenting an index <0.8. When comparing early ScT with late and very-late ScT, the mean scaffold expansion index was not significantly smaller in early ScT (0.88±0.12) versus late and very late ST (1.04±0.15, P=0.56). Any ISA was found in 8 (53%) segments. Latter presented a mean maximal ISA CSA of 1.3±1.3 mm^2 and a mean maximal ISA length of 3.4±4.1 mm. Moderate neointimal hyperplasia was present in 6 out of 7 patients presenting with late and very late ScT. One patient presented with focal restenosis that ruptured and lead to ScT. None of the remaining patients, in whom the neointima was homogenous (4 patients with bright tissue and 1 patient with signal-poor tissue extending abluminally beyond the scaffold struts), presented OCT findings consistent with neoatherosclerosis. In these patients, the mean neointima hyperplasia–CSA per analyzed frame was 1.3±1.0 mm.^{2} Finally, a lower light intensity (higher Key component) was found in segments from patients presenting with late and very late ScT (20±16%) in comparison with patients presenting with early ScT (13±9%, P<0.001). This phenomenon is demonstrated in Figure 3.

Histopathologic Findings

A total of 3 thrombectomy specimens were submitted for histopathologic analysis. Qualitative histopathologic analysis of the thrombi showed fragments of fibrin and platelet-rich thrombus with variable numbers of trapped red blood cells (Figure 2). None of the 3 thrombi demonstrated any significant acute or chronic inflammatory reaction. Of note, the number of eosinophils were within the normal range.

Discussion

This study used OCT imaging to explore BVS failure in 15 ScT. The main findings are that (1) OCT findings are distinctive in early ScT versus late or very late ScT, (2) early ScT is mostly related to inadequate antithrombotic regimen and implantation technique; and (3) late ScT is associated with lower peristrut light intensity (a surrogate marker of edema), neovessel formation, and scaffold fracture.

Early ScT: Undersizing and Underexpansion

Several reports have identified undersizing as a key factor for ST in both bare-metal stents and DES.[20–23] In 2 out of 8 patients sustaining early ScT, we identified undersizing as the key mechanism. In the case shown in Figure 1, a 2.5 mm scaffold was implanted in a vessel with a diameter >3.5 mm. Not surprisingly, both patients with undersizing were treated for ST-elevation myocardial infarction during the index procedure. It is well known that blood levels of potent vasoconstrictors, such as endothelin-1 and neuropeptide Y, are markedly elevated in patients with ST-elevation myocardial infarction, and although this has been mainly linked to microcirculatory dysfunction in the literature,[24,25] it is likely that profound vasoconstriction also affects epicardial arteries. The use of intracoronary vasodilators, such as nitroglycerine and adenosine, can probably help alleviating the problem of undersizing BVS in ST-elevation myocardial infarction.

Table 4. OCT Characteristics and Postprocedural Findings

ID No	OCT Runs	Failed or Very Poor Quality OCT Runs (Reason)	Percentage of Good Quality on Analyzed OCT Run(s)	Reason for Poor Quality	OCT at End of Procedure	Percentage of Good Quality OCT After Treatment	Residual Thrombus Burden, mm^3	Final Treatment
1	2	1 (poor flushing)	73%	Backscattering/ attenuation because of thrombus	No			Thrombus aspiration, PTCA with NC 3.0
2	5	0	100%	None	No			PTCA with NC 3.0, implantation of another BVS proximal to the first one
3	2	0	61%	Backscattering/ attenuation because of thrombus	Yes	100%	14.13	PTCA with NC 3.0, implantation of a Xience 3.0
4	3	1 (poor flushing and occlusive thrombus)	71%	Backscattering/ attenuation because of thrombus	No			PTCA with Maverick 1.5 ≤2.5, NC 3.0,
5	3	1 (occlusive thrombus)	60%	Backscattering/ attenuation because of thrombus	Yes	100%	4.93	Thrombectomy, direct stenting with DES
6	2	0	75%	Poor flushing in proximal part of BVS	Yes	100%	2.24	PTCA, DES
7	2	1 (poor flushing)	83%	Backscattering/ attenuation because of thrombus	No			PTCA with 2.75 SC, OCT, 2× implantation Xience 2.75
8	1	0	75%	Backscattering/ attenuation because of thrombus in distal scaffold	No			PTCA, DES
9	4	1 (poor flushing)	100%	None	Yes	90% (poor flushing)	3.51	PTCA, DES
10	2	0	50%	Backscattering/ attenuation because of thrombus	No			PTCA without stent
11	4	0	73%	Backscattering/ attenuation because of thrombus	Yes	95% (poor flushing)	15.53	PTCA, DES
12	3	0	82%	Backscattering/ attenuation because of thrombus	No			Thrombectomy, DES (XIENCE) implantation with pre- and postdialation
13	1	0	50%	Poor flushing and catheter partly in false lumen	No			Thrombus aspiration, PTCA with NC 3.5 and implantation of a BVS 3.5 mm directly proximal to the BVS
14	3	1 (occlusive thrombus)	83%	Backscattering/ attenuation because of thrombus	Yes	90% (poor flushing)	2.57	Thrombus aspiration, PTCA with NC 3.5, Xience 3.5
15	1	0	92%	Backscattering/ attenuation because of thrombus	No			No intervention

BVS indicates bioresorbable vascular scaffold; DES, drug-eluting stent; NC, noncompliant; OCT, optical coherence tomography; and PTCA, percutaneous transluminal coronary angioplasty.

Underexpansion is a well-known risk factor for ST. In the present series, underexpansion was encountered in 2 patients, 1 of whom presented a calcified lesion. This may highlight the importance of lesion selection and optimal lesion preparation before BVS implantation. It moreover raises the question regarding the radial strength of the current version of the Absorb BVS. In a study from 2007, acute recoil was compared between the Absorb BVS (revision 1.0) and the everolimus-eluting cobalt chromium stent. There was a trend toward more acute stent recoil in the Absorb BVS but the difference was not statistically significant.[26] In a later study, acute recoil was similar between Absorb BVS revision 1.0

Table 5. Optical Coherence Tomography Measurements at the Time Point of Scaffold Thrombosis (n=15)

Reference segment	
EEM CSA, mm^2	13.5±4.4
Lumen CSA, mm^2	7.9±4.2
Scaffold segment	
Maximal EEM CSA, mm^2	14.8±4.0
Remodeling index	1.1±0.2
Scaffold CSA, mm^2	6.5±1.9
Minimal scaffold CSA, mm^2	5.2±1.9
Minimal scaffold CSA < 4 mm^2, n (%)	2 (13)
Scaffold expansion index	0.95±0.36
Underexpanded scaffolds, n (%)	9 (60)
In-scaffold lumen CSA, mm^2	5.8±2.3
Neo-intimal hyperplasia, mm^2	1.3±1.0
ISA, n (%)	8 (53)
Maximal ISA CSA, mm^2	1.3±1.3
Maximal ISA depth, mm	0.5±0.4
Maximal ISA length, mm	3.4±4.1

CSA indicates cross-sectional area; EEM, external elastic membrane; and ISA, incomplete scaffold apposition.

and 1.1 and slightly but not significantly lower than metallic everolimus-eluting cobalt chromium stent.[27] Of course, this difference might be even intensified in all-comer series of patients presenting with more complex lesions. Consistently, the acute recoil in the EverBio-2 trial was greater in BVS (9.5±6.5%) than in metallic comparators (6.6±4.7%, $P<0.01$).[12]

Late ScT: BVS Resorption, Peristrut Light Intensity, Neovessels, and Scaffold Rupture

Delayed healing has been identified as a possible mechanism of late/very late ST after implantation of early generation DES. The pathological correlate of this process was thought to be a lack of strut coverage,[28,29] late acquired stent malapposition,[4] and late drug or polymer-related hypersensitivity reactions characterized by neutrophilic or eosinophilic infiltrates.[6,30] A recently published study reported a comparison of vascular responses to the implantation of Absorb BVS versus a metallic everolimus-eluting cobalt chromium stent in nonatherosclerotic swines. Although there was no inflammation at 1 month for both devices, the inflammation scores were greater for the Absorb BVS at 6 to 36 months.[31] Interestingly, the authors described segments with late-occurring strut discontinuities where the scaffold geometry was modified because of a low-grade inflammatory reaction with increasing eosinophils count and secondary integration of arterial tissue. The results of the present OCT study in ScT demonstrate a time-dependent increase in PSLIA together with neovessel formation and in vivo scaffold discontinuities. This phenomenon is illustrated in Figure 2. Although the causes and consequences of PSLIA remain uncertain in BVS, a recently published trial in 26 coronary swine segments treated with everolimus-eluting DES demonstrates a direct correlation between the degree of PSLIA and peristrut inflammation at histology.[32] PSLIA has been associated with malapposition, evaginations, strut fracture, and uncovered struts as possible mechanisms of a late in-stent/ScT.[33,34] An association between PSLIA and the risk of thrombosis has been provided by a study on delayed healing and late thrombotic risk after DES implantation in humans by Joner et al.[30] Alternatively—and as PSLIA is more frequently encountered with bioresorbable polymers—it could be a marker of vascular edema because of the hydrolysis of polylactide. Yet and as edema increases the vascular vulnerability, the association of this PSLIA pattern with the occurrence of late ScT is concerning.

Limitations

Some limitations that are inherent to the analysis of device thrombosis are true for the present study: Even though great care was taken to repeat OCT after sufficient thrombectomy, interpretation of pullbacks may be affected by poor image quality because of backscattering or light attenuation by thrombi. Furthermore, quantification of residual thrombus may be adversely affected (inaccurate measurements) in regions where light attenuation or backscattering because of a thrombus did not allow for delineation of the underlying neointima from the latter. Another limitation of the present study is the lack of a control group without ScT.

Conclusions

Although early BVS thrombosis seems similar to bare-metal stent or DES thrombosis, late and very late BVS thrombosis are associated with a different morphological OCT pattern. This suggests that vascular edema (with or without low-grade

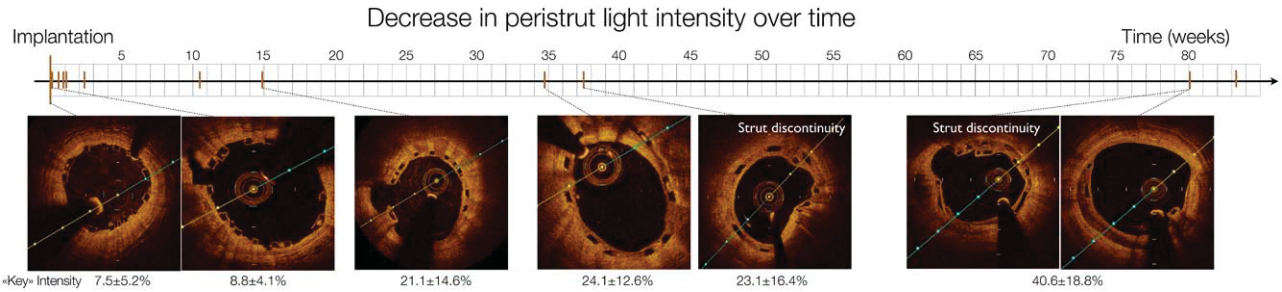

Figure 3. Occurrence of peristrut low-intensity areas increases over time. As illustration, the measurements of the intensity of the key component of the cyan, magenta, yellow, key/black (CYMK) color model are given for each cross-sectional image on bottom. The occurrence of ScT are marked as vertical lines on the time scale.

inflammation) might be the prevailing pathophysiological mechanism of late ScT.

Disclosures

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