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Coronary evaginations and peri-scaffold aneurysms following implantation of bioresorbable scaffolds: incidence, outcome, and optical coherence tomography analysis of possible mechanisms

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Background Peri-stent coronary evaginations may disturb flow and have been proposed as possible risk factor for late stent thrombosis. We describe incidence, predictors, and possible mechanisms of coronary evaginations 12 months after implantation of bioresorbable vascular scaffolds (BVS).

Methods and results One hundred and two BVS implanted in 90 patients (age 63 ± 13 years, 71 males, 14 diabetics) were analysed with angiography and optical coherence tomography (OCT) 12 months after implantation. Evaginations were identified as any hollow in the luminal vessel contour between well-apposed struts and were classified as major when extending ≥3 mm with a depth ≥10% of the BVS diameter. Fifty-five (54%) of the BVS (50(56%) of the patients) had at least one evagination (6.1 ± 6.2 evaginations per BVS), with a mean volume of 1.9 ± 1.9 mm^3. Major evaginations were only found in one patient, and in-BVS aneurysms in three patients (4BVS). The presence of evaginations was strongly associated with that of malapposition ($P = 0.003$) and strut fractures ($P = 0.01$). No association could be shown between the presence and volume of the evaginations and any clinical variable or the presence of uncovered struts ($P > 0.5$). Peri-strut low-intensity areas (PSLIA) were present in 29 (53%) of the BVS with evaginations and 12 (26%) of those without ($P = 0.0049$); their presence was independently associated with the presence, the number ($P < 0.003$) and volume of the evaginations ($P = 0.004$) and with that of strut fracture.

Conclusions Optical coherence tomography-detected evaginations are relatively common after BVS implantation, but, as for modern drug-eluting metallic stents, major evaginations are very rare. Optical coherence tomography evidence of immature neointima and strut fractures were associated with more severe development of evaginations.

Keywords Coronary artery disease • Bioresorbable scaffolds • Immature neointima

Introduction

Late acquired coronary evaginations—also termed parasailing phenomenon or cauliflower's effect—are optical coherence tomography (OCT) findings frequently described following implantation of first-generation drug-eluting stents (DES). In this setting, evaginations have been proposed to represent the manifestation of pathological vessel healing and have been associated with the presence of uncovered or fractured struts.[1–4] Together with the resulting flow disturbances, they have been hypothesized as possible risk factors

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for stent thrombosis.[5–9] Notably, the incidence of coronary evaginations appears to be significantly lower after implantation of newer-generation stents,[1] an observation that fits well with the lower incidence of in-stent thrombosis reported following implantation of these devices.[10–12]

The everolimus-eluting bioresorbable vascular scaffold (BVS) has been introduced into clinical practice in May 2012 with the hope of overcoming late-occurring complications of DES. While early studies are promising,[13–15] some concerns of an unexpectedly high incidence of scaffold thrombosis were recently raised.[13,16] Accordingly, recent publications reported cases of inadequate vessel healing after BVS implantation, with possible evagination development.[16,17]

We set out to explore the presence, size, predictors, and possible mechanisms of coronary evagination formation 12 months after BVS implantation.

Methods

Study design and population

Absorb BVS (Abbott Vascular, USA) are balloon-expandable scaffolds made with semicrystalline polylactide and eluting the newer-generation drug everolimus. Their strut thickness is 150 μm, similar to the first-generation DES.[18] The present report includes all consecutive patients who received at least one BVS and underwent coronary angiogram with OCT study at 12-month follow-up (an invasive follow-up was recommended in the first 150 patients given the novelty of this therapy and scarcity of data available in real-life settings). Implantation was performed using standard techniques and following instructions for use, dual antiplatelet therapy was recommended for 12 months. Baseline clinical characteristics, angiographic and OCT data were collected in anonymised way. Patients gave written informed consent for the collection of data within the framework of the MICAT Registry (EC 837.123.13;8808-F;NCT02180178). There was no industry involvement in the design, conduct, or analysis of the study. No patient was included in any industry-sponsored trial.

Optical coherence tomography

See also Supplementary material online, Methods.

'Evaginations' were defined as any outwards protrusion in the luminal vessel contour between well-apposed stent struts (*Figure 1A*). Evaginations were considered major when extending >3 mm with a depth>10% of the stent diameter.

'Coronary aneurysms' were defined as an in-scaffold diameter >1.5-times the reference vessel diameter at follow-up (*Figure 2A*).

'Peri-strut low-intensity areas (PSLIA)' were defined as homogenous areas with low-signal attenuation around struts characterized by an intensity 30% lower than that of the surrounding tissue (*Figure 3A* and *B*).

'Strut fracture' was classified in grades as described in Supplementary material online.

Peri-stent staining and quantitative coronary analysis

'Peri-stent contrast staining (PSS)' was defined as evidence of contrast staining outside of the vessel contour (*Figure 3C*). Bioresorbable vascular scaffolds *undersizing* and *oversizing* were defined as (respectively): proximal reference diameter/BVS nominal size >1.2 or <0.8. Definitions are described in more detail in Supplementary material online, Methods.

Vasomotor function

Quantitative coronary analysis was performed in the scaffold segment in random order by staff not aware of the temporal sequence of the images. Endothelium-dependent and -independent vasomotion were studied as previously published.[19]

Follow-up

Clinical follow-up data focused on the incidence of thrombosis were collected from all patients during clinical visits or per telephone using standardized questionnaires. Events were adjudicated by one investigator and monitored by another one.

Statistical analysis

See Supplementary material online, Methods.

Results

The study enrolled 90 patients who underwent BVS implantation and elective 12 months control angiography with OCT. Of the first 150 patients who received BVS in our institution, 23 underwent

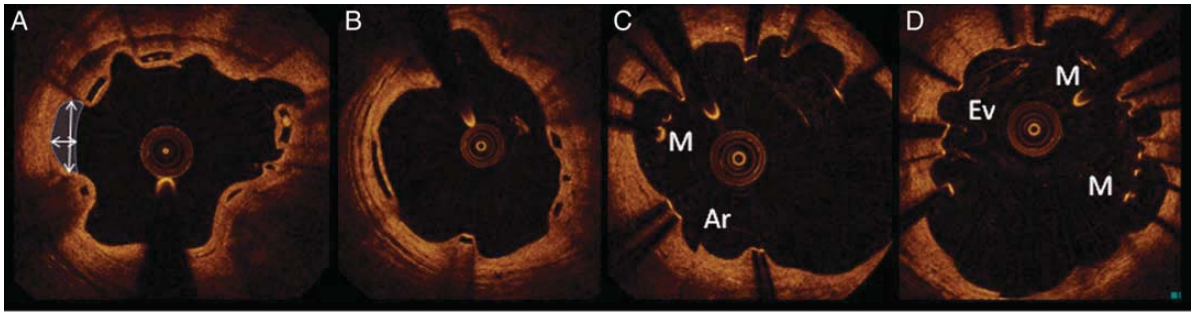

Figure 1 (*A*) Example of optical coherence tomography cross section with evagination. Measures included the area (taken from the abluminal margin of the line connecting the middle points of the most continuous struts), depth, and transversal length. An example of measures is reported in white. Interestingly (*B–D*), this patient also developed evaginations and malapposition (M) at the level of an everolimus-eluting metal stent. Ar marks a typical optical coherence tomography artefact.

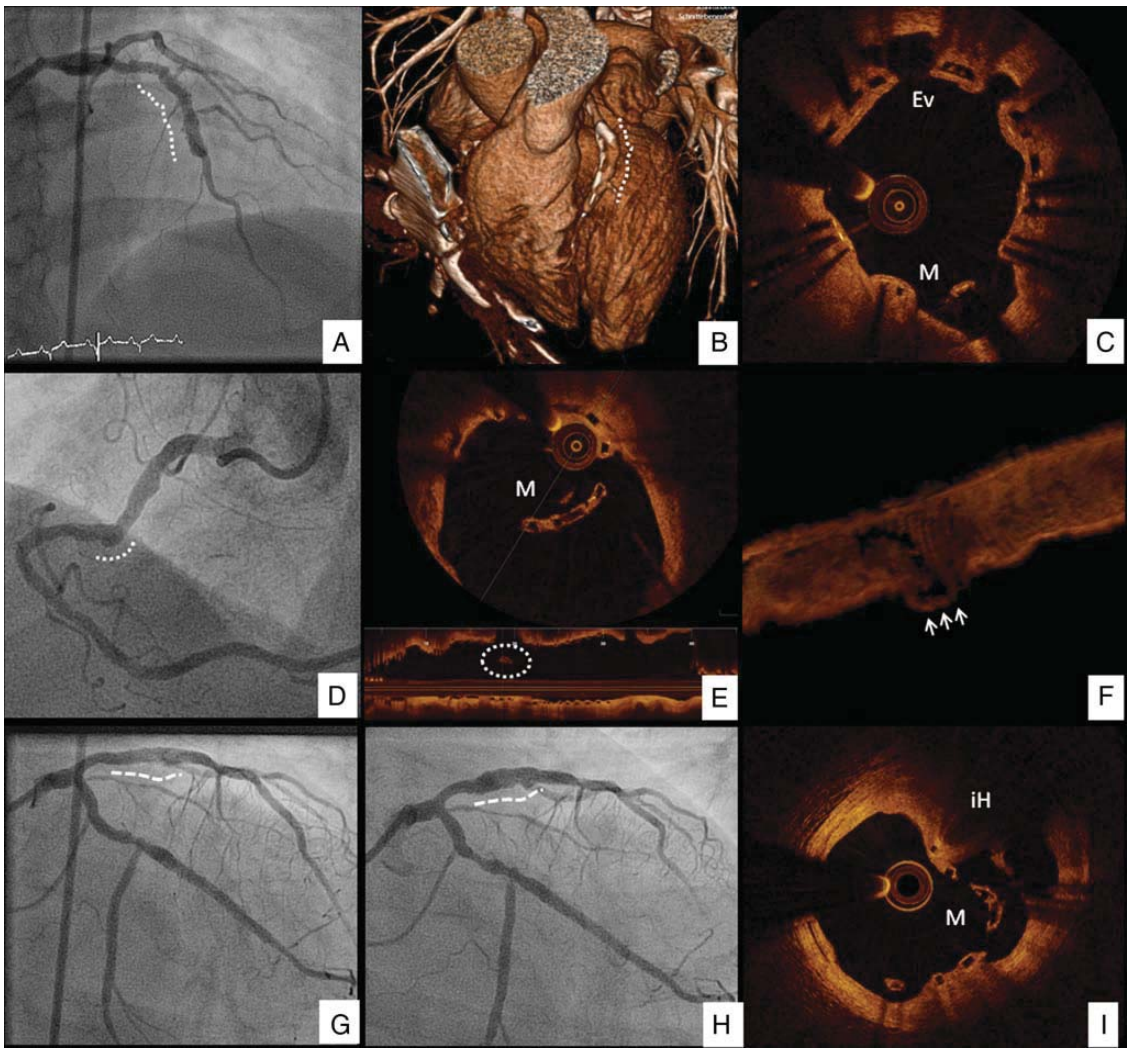

Figure 2 (*A*–*C*) A case of coronary artery aneurysm at the level of the proximal left anterior descending in a 44-year-old woman who presented with ST-elevation myocardial infarction and received a 3 × 18 mm bioresorbable vascular scaffolds in the proximal left anterior descending. Of note, the aneurysm was not present 1-month after implantation, and a similar aneurysmatic reaction was present in another bioresorbable vascular scaffolds implanted in the same patient in the right coronary artery. (*B*) Computed tomography scan of the proximal left anterior descending revealing an ∼6 mm aneurysm 18 months after implantation. (*C*) Evidence of evaginations (Ev) and malapposition (M) in the same patient. This case is described in detail in Ref. [31] (*D*–*F*) late acquired small saccular aneurysm in the mid right coronary artery in a 75-year-old patient who received a 3 × 18 mm in the setting of unstable angina. 12-months optical coherence tomography at this level demonstrated (*E*) collapse of the struts, which were otherwise well apposed in the proximal and distal segments (longitudinal view, white circle). 3D reconstruction confirmed the aneurysm and the collapse of the struts (arrows and dashed circle). (*G*–*I*) the last case of aneurysm was observed in a 69-year-old man who received a 3 × 18 mm bioresorbable vascular scaffolds in the proximal left anterior descending. It is possible that a trauma caused by high-pressure post-dilation with a 3.5 mm balloon might have triggered the aneurysmatic process in this case. (*G*) Immediate result showing overexpansion of the bioresorbable vascular scaffolds (dashed line); (*H*) 12-month angiography showing aneurysmatic evolution of the lesion. (*I*) Optical coherence tomography demonstrating a fibrolipidic plaque protrusion (1 o'clock) which prevented the deployment of the scaffold and required high-pressure dilation, ultimately leading to vascular injury and malapposition. ih, intramural hemoatoma.

coronary angiography at earlier time points (without systematic OCT). Five patients died before 12 months (among these one sudden death on Day 18 after PCI in a patient with severe three-vessel disease, cardiogenic shock, and a history of drug addiction). Finally, four patients underwent elective angiography without OCT at 12 months patient and lesion characteristics are detailed in *Table 1*.

Mean age was 63 ± 13 years, 79% were male, 16% diabetics, 44% smokers, 74% had arterial hypertension, and 30% hypercholesterolaemia. The indication at index procedure was an acute coronary syndrome in 66% of the cases. At the time of the invasive control, angina(-like) symptoms were present in 45 patients (39%). In total, 102 BVS underwent OCT control (1.1 ± 0.5 BVS per patient).

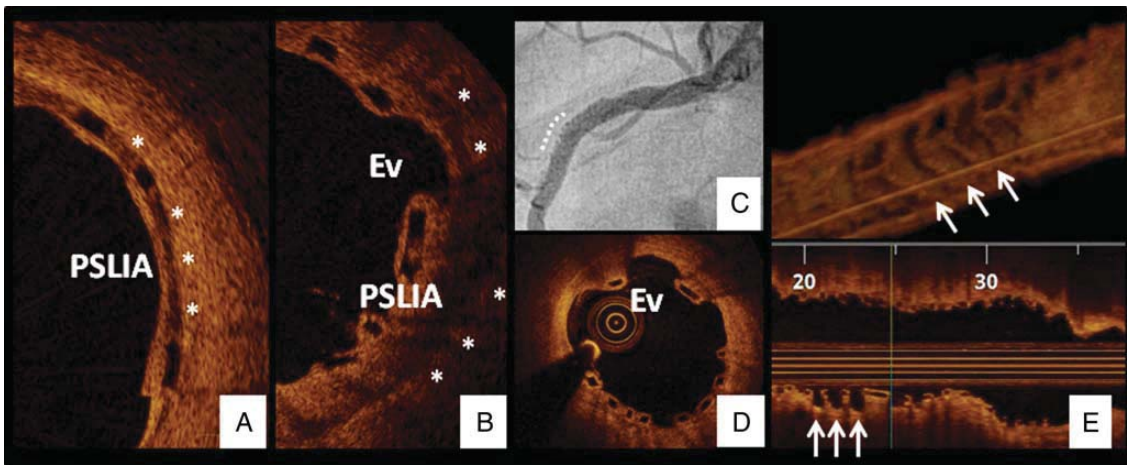

Figure 3 Peri-strut low-intensity area (marked with asterisk) was defined as a region of low intensity and low attenuation in the proximity of bioresorbable vascular scaffolds struts. The presence of peri-strut low-intensity area (*A*) and that of peri-strut low-intensity area at the level of the evaginations (*B*) was recorded. (*C*) Evidence of peri-stent staining in the proximal right coronary artery in a 47-year-old female treated for inferior STEMI. Optical coherence tomography (*D* and *E*) revealed the presence of evaginations which were also visible in 3D and longitudinal reconstructions (white arrows).

Incidence and characteristics of the evaginations

From a total of 102 BVS studied, 55 BVS (54%) in 50 patients (56%) had ≥1 evagination. These patients represent the 'evagination group'. Major evaginations were found in only one BVS. Four (4%) BVS in three patients (3%) showed aneurysms (*Figure 2*), in one case likely provoked by mechanical trauma at implantation. The mean number of evaginations was 6.1 ± 6.2 per BVS and 6.7 ± 8.7 per patient, with a mean total volume of 1.9 ± 1.9 mm^3 per BVS and 2.1 ± 2.6 mm^3 per patient. The volume of the evaginations is presented in Supplementary material online, *Figure S2* as % of the total volume of the corresponding BVS. In 56% of the BVS, the total volume of the evaginations was lower than 1% of the BVS volume. In 2 (4%) BVS, the total evaginations volume exceeded 5% of the BVS volume.

Angiographic and optical coherence tomography findings at follow-up

Peri-stent contrast staining was found in nine BVS segments (18%) (all in the evagination group). Peri-stent contrast staining was associated with an increased number and volume of evaginations ($P = 0.002$ and $P = 0.0001$, respectively).

The RVD values of the segments which presented evaginations were consistently larger when compared with those of the segments that did not show evaginations (Supplementary material online, *Table S1*). In contrast, there was no difference in MLD and late lumen loss. Vascular diameter changes at QCA were different between the evagination group (+0.03 ± 0.48 mm) and the non-evagination group (−0.13 ± 0.39 mm, $P = 0.06$). A larger RVD at 12 months than at index was present in 24 (48%) of the evagination group and 16 (40%) of the non-evagination group ($P = 0.43$). The presence of PSLIA was not associated with changes in RVD ($P = 0.22$).

The OCT characteristics of the BVS are presented in Supplementary material online, *Table S2*. At 12-months, all lumen and BVS measures were significantly larger in the evaginations group. Measures of malapposition were also larger in this group. Peri-strut low-intensity areas was more frequent in BVS with evaginations. In contrast, eccentricity and uncovered struts were not associated with evaginations.

Evaginations, strut fractures, and peri-strut low-intensity areas

Table 2 describes the characteristics of the evaginations based on the presence of PSLIA. Peri-strut low-intensity areas was present in 29(53%) of the BVS with evaginations and 12 (26%) of those without ($P = 0.005$). Peri-strut low-intensity areas was present at the level of the evagination in 13(24%) BVS. Shortly, PSLIA was systematically associated with all measures expressing the severity of the evaginations. As well, PSLIA was associated with the presence ($P = 0.005$) of malapposition. The presence of PSLIA at the trough of the evagination (*Figure 3B*) further identified a subset of patients with more (10.2 ± 7.1 vs. 4.8 ± 5.4, $P = 0.005$) and larger ($P =$ 3.2 ± 2.2 vs. 1.5 ± 1.6 mm^3, $P = 0.0004$) evaginations. Conversely, PSLIA was not associated with neointima thickness ($P = 0.70$) or uncovered struts ($P = 0.85$).

The incidence and distribution of the fractures is described in Supplementary material online, *Table S3*. Strut fracture/misalignments were present in 30% of the BVS, and their rate and complexity were higher in the evaginations group (55% of the BVS with evaginations and 17% of the BVS without evaginations, $P =$ 0.013). Fractures/misalignments were also associated with PSLIA ($P = 0.021$).

Table 1 Clinical and procedural characteristics

	All patients ($n = 90$)	Evaginations present ($n = 50$)	No evagination ($n = 40$)	*P*-value
Patient characteristics (per patient analysis)				
Male sex, *n* (%)	71 (79%)	39 (78%)	32 (80%)	0.053
Age	63 ± 13	64 ± 24	61 ± 12	0.176
Hypertension	67 (74%)	38 (76%)	29 (73%)	0.574
Hyperlipidaemia	27 (30%)	14 (29%)	15 (33%)	0.616
Diabetes	14 (16%)	6 (12%)	8 (20%)	0.414
Smoking	40 (44%)	24 (48%)	16 (40%)	0.461
Previous revascularization	22 (24%)	13 (26%)	9 (23%)	0.514
Clinical presentation				
Stable angina	16 (18%)	9 (18%)	7 (18%)	0.80
Unstable angina	13 (14%)	7 (14%)	6 (15%)	
NSTEMI	27 (30%)	16 (32%)	11 (28%)	
STEMI	32 (35%)	16 (32%)	16 (40%)	
Glomerular filtration rate (mL/min)	87 ± 22	86 ± 39	88 ± 16	0.591
LVEF (%)	52 ± 8	52 ± 15	52 ± 9	0.214
Multi-vessel disease	10 (11%)	7 (14%)	3 (8%)	0.401
DAPT type				0.407
Clopidogrel	30 (33%)	17 (31%)	13 (34%)	
Prasugrel	43 (48%)	23 (48%)	20 (50%)	
Ticagrelor	17 (19%)	10 (19%)	7 (16%)	
Number of implanted BVS	1.1 ± 0.5	1.1 ± 0.5	1.2 ± 0.5	0.617
Total BVS length (mm)	20.64 ± 9.6	21.1 ± 10.5	20.1 ± 8.3	0.631
Total BVS surface (cm^2)	2.23 ± 1.16	2.25 ± 1.19	2.20 ± 1.14	0.839
	$n = 102$	$n = 55$	$n = 47$	
Procedural and scaffold characteristics (per scaffold analysis)				
Vessel treated				
LAD	39 (38%)	19 (35%)	20 (43%)	0.582
RCX	26 (25%)	14 (25%)	12 (26%)	
RCA	38 (37%)	23 (42%)	15 (32%)	
ACC/AHA type B2/C	43 (42%)	30 (55%)	13 (28%)	0.714
BVS diameter	3.07 ± 0.34	3.1 ± 0.4	3.0 ± 0.3	0.398
BVS length	18.9 ± 7.44	19.8 ± 4.9	17.9 ± 3.4	0.024
BVS outer surface (cm^2)	0.57 ± 0.13	0.60 ± 0.15	0.53 ± 0.08	0.008
Implantation pressure	13.7 ± 1.8	13.7 ± 2.0	13.7 ± 1.6	0.888
Post-dilation	17 (17%)	13 (28%)	4 (9%)	0.061
Ballon/artery ratio	1.1 ± 0.3	1.0 ± 02	1.1 ± 0.3	0.128
Undersizing (at index)	19 (19%)	15 (27%)	4 (9%)	0.021
Undersizing (at 12-months)	13 (13%)	11 (20%)	2 (4%)	0.019
Oversizing (at index)	13 (13%)	7 (13%)	6 (13%)	1.000
Oversizing (at 12 months)	11 (11%)	4 (7%)	7 (15%)	0.338
Maximum footprint	36 ± 7	35 ± 10	36 ± 6	0.475
PSLIA at 12-months	37 (36%)	26 (47%)	11 (23%)	0.022

Patients are divided based on the optical coherence tomography finding of evaginations at the 12 months control.
BVS, bioresorbable vascular scaffold; (N)STEMI, (non)ST-elevation myocardial infarction; DAPT, dual antiplatelet therapy; LAD, left anterior descending; RCX, circumflex; RCA, right coronary artery; PSLIA, peri-stent low-intensity area; ACC/AHA, American College of Cardiology/American Heart Association.

Associations with patient and procedural characteristics

Longer BVS and undersizing, as well as PSLIA, were more frequent in the evaginations group (*Table 1*). In univariate analysis, none of the traditional risk factors were associated with the presence of evaginations (*Table 3*). Of the procedural characteristics, the use of post-dilation at the time of BVS implantation, the use of longer stents, undersizing, and PSLIA were all associated with evaginations. In

Table 2 Optical coherence tomography characteristics of the evaginations classified based on the presence of PSLIA at the level of the evagination

	PSLIA ($n = 13$)	No PSLIA ($n = 42$)	P
Total number of evaginations	9 [6.8–11.8]	3 [2–5]	0.003
Total volume	2.3 ± 2.4	1.4 ± 1.1	0.004
% of frames with evaginations	16.7 ± 11.4	6.9 ± 7.5	<0.001
Number of evaginations with depth >10% of BVS diameter	9.4 ± 6.3	4.1 ± 3.9	0.001
Maximum length in mm	0.8 ± 0.6	0.4 ± 0.2	0.009
% of lumen volume	2.1 ± 1.3	1.1 ± 1.2	0.007

PSLIA, peri-strut low-intensity area.

multivariable analysis, the presence of PSLIA remained associated with evaginations; BVS outer surface, undersizing, and post-dilation showed a trend in this direction.

Endothelium-dependent and -independent responses

Acetylcholine and nitroglycerin responses were studied in 21 (38%) of the BVS with evaginations and 29 (62%, $P = 0.02$) of those without evaginations. A vasodilation was observed in 10 (48%) of the BVS with evaginations and 13 (46%) of those without ($P = 1.0$). A vasoconstriction was observed in, respectively, 10(48%) and 7 (25%), $P = 0.13$. A vasodilation in response to intracoronary nitroglycerin was more frequent in the evaginations group (61 vs. 29%, $P = 0.03$).

Follow-up

Data on the incidence of in-BVS thrombosis were available from all patients at a mean follow-up of 780 ± 122 days after index implantation. During this period, two patients included in the present database developed in-BVS thrombosis. In one case (late thrombosis 349 days after implantation), evidence of evaginations, malapposition, and uncovered struts associated with PSLIA was present at OCT (*Figure 3*). In the other case, in which thrombosis occurred at 562 days, there was evidence of severe malapposition without PSLIA or evaginations at 12 months.

Discussion

In-stent coronary evaginations and late malapposition are occasionally found after percutaneous coronary interventions. While from a merely mechanical perspective undersizing or vascular injury at the time of implantation may play a role,[20] an association with localized hypersensitivity reactions and chronic inflammation has also been proposed,[21] even though the specific stent component (metal, polymer, eluted drug) responsible for these reactions has not been identified. Importantly, the incidence of evaginations appears to be lower with newer-generation DES, which are characterized by different polymers, different drugs, and thinner struts.[1] Whatever the mechanism, evaginations, malapposition, and aneurysms may disrupt the laminarity of flow, and their presence, particularly when associated with that of uncovered or fractured struts, or with evidence of vascular inflammation, has been associated with late in-stent thrombosis.[20,22]

Summary of the present findings

Incidence and clinical predictors of evaginations

Although the presence of small evaginations was very frequent, findings of major evaginations were, in line with previous reports on modern generation DES,[1] rare. Evaginations appear to be in a continuum with malapposition (*Figure 4*). None of the clinical and procedural characteristics was formally associated with the presence of evaginations at 12 months, but vessels in which evaginations were present were consistently larger at QCA at index and even more so 12 months after implantation. Coupled with the absence of differences in the size of the BVS implanted between the two groups, this finding suggests that undersizing at the time of implantation and/or vessel dilation thereafter may play a mechanistic role *Figure 5*).

Association with optical coherence tomography evidence suggestive of immature neointima

The intensity of the OCT signal has been previously shown to correlate with the histologic nature of the tissues studied.[23,24] Optical coherence tomography has been demonstrated to be able to OCT-findings of PSLIA have been associated with histology sections richer in elastic fibres and inflammatory cells and macrophages as well as spotty fibrin deposition and relatively poorer in smooth muscle cells and proteoglycans/collagen.[25] In the present cohort, this OCT finding correlated positively with the size and number of the evaginations. Importantly, PSLIA at 12 months was the only predictor that remained associated with the presence of evaginations in multivariable analysis. As well, the presence of PSLIA at the level of the evaginations further identified a subgroup of BVS in which these lesions were more pronounced. Although vasomotor function data were incomplete, in line with the histological correlates of PSLIA, a trend towards more frequent paradoxical vasoconstriction in response to acetylcholine, compatible with the presence of endothelial dysfunction, was shown. As well, the more effective vasodilation in response to nitroglycerin might reflect an impaired resting production of endothelial nitric oxide associated with the presence of evaginations.[26] Finally, the presence of strut fractures was strongly associated with PSLIA and evaginations/malapposed struts. Although a cross-sectional approach does not allow conclusions regarding causality, one might hypothesize that this finding might be involved in the pathogenesis of PSLIA and evaginations.

Table 3 Univariate and multivariable analysis of the associations of evaginations

	HR (5–95% CI)	*P*-value	HR (5–95% CI)	*P*-value
Patient characteristics (per patient analysis)				
Male sex, *n*	0.98 (0.34–2.76)	0.962		
Age	1.02 (0.99–1.06)	0.176		
Hypertension	1.31 (0.5–3.44)	0.583		
Hyperlipidaemia	0.83 (0.34–2.06)	0.689		
Diabetes	0.56 (0.18–1.77)	0.322		
Smoking	1.44 (0.62–3.35)	0.398		
Previous revascularization	1.24 (0.47–3.3)	0.661		
Clinical presentation				
Stable angina	1.06 (0.356–3.16)	0.916		
Unstable angina	0.97 (0.3–3.15)	0.956		
NSTEMI	1.23 (0.51– 3.19)	0.599		
STEMI	0.73 (0.31–1.73)	0.473		
Glomerular filtration rate	0.99 (0.99–1.01)	0.587		
LVEF	0.96 (0.89–1.03)	0.216		
Multi-vessel disease	2.06 (0.55–8.53)	0.321		
DAPT type, *n*	1.21 (0.67–2.19)	0.523		
Clopidogrel				
Prasugrel				
Ticagrelor				
Procedural characteristics (per patient analysis)				
Number of implanted BVS	0.80 (0.34–1.90)	0.616		
Total BVS length	1.01 (0.97–1.06)	0.631		
Total BVS surface	1.04 (0.72–1.50)	0.841		
Vessel treated				
LAD	0.71 (0.32–1.59)	0.412		
RCX	1.0 (0.41–2.45)	0.991		
RCA	1.53 (0.68–3.46)	0.302		
ACC/AHA type B2/C	0.8 (0.36–1.74)	0.574		
Procedural and scaffold characteristics (per scaffold analysis)				
BVS diameter	1.65 (0.52–5.26)	0.394		
BVS length	1.12 (1.01–1.24)	0.029		
BVS outer surface	120.91 (2.66–5503.55)	0.014	58.48 (0.94–3628.85)	0.053
Implantation pressure	0.98 (0.79–1.22)	0.891		
Post-dilation	3.33 (1.00–11.03)	0.049	3.63 (0.99–13.26)	0.051
Ballon/artery ratio	0.18 (0.03–1.04)	0.055		
Undersizing (at index)	4.13 (1.26–13.52)	0.019	4.59 (0.90–23.37)	0.067
Undersizing (at 12 months)	5.75 (1.21–27.48)	0.028		
Oversizing (at index)	0.85 (0.26–2.85)	0.801		
Oversizing (at 12 months)	0.4482 (0.12–1.64)	0.225		
Maximum footprint	0.93 (0.87–1.0)	0.472		
PSLIA at 12 months	2.85 (1.21–6.74)	0.017	3.39 (1.33–8.62)	0.01

Limitations

The following shortcomings have to be taken in consideration when interpreting the results of the present study. First, it is a single-centre, observational trial with limited size; all analysis was performed on-site and not in an independent core laboratory. Second, the analysis was limited to BVS with no direct comparator. Further, the inclusion criterium (OCT at 12 months) might have resulted in an inclusion bias. The elective nature of the 12-months controls, however, partially addresses this bias. It also needs to be acknowledged that there is no histopathological analysis; however, a number of lines of evidence support the concept that PSLIA truly reflects immature neointima and/or oedema as well as deposition of fibrin and extracellular matrix, as demonstrated by findings from animal and

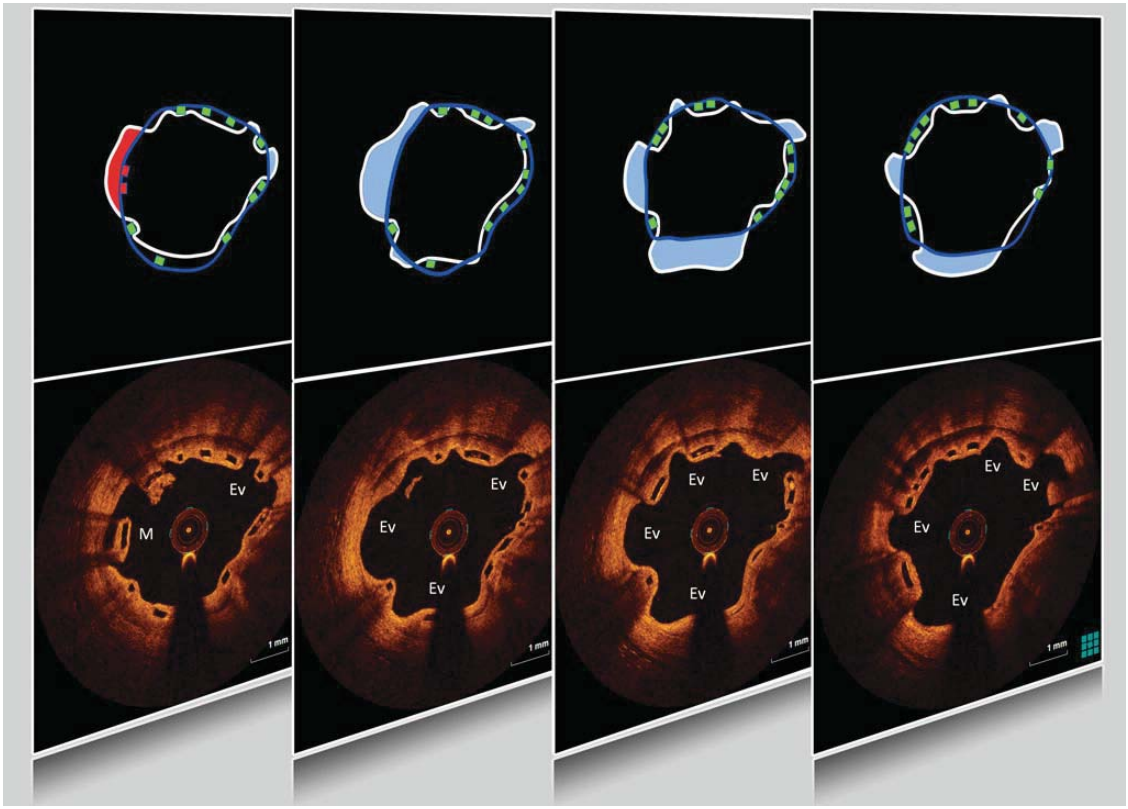

Figure 4 Sequential optical coherence tomography frames showing the continuum between evaginations and malpposition. Evaginations are marked in light blue and the malapposition (left) in red. From proximal to distal, the first three slides from right show the evolution of an evagination. In the fourth section, two malapposed scaffold struts appear, which reclassify this lesion to malapposition. In contrast, the lesion at 6 o'clock does not contain malapposed struts. This sequence emphasized the importance of frame-by-frame analysis.

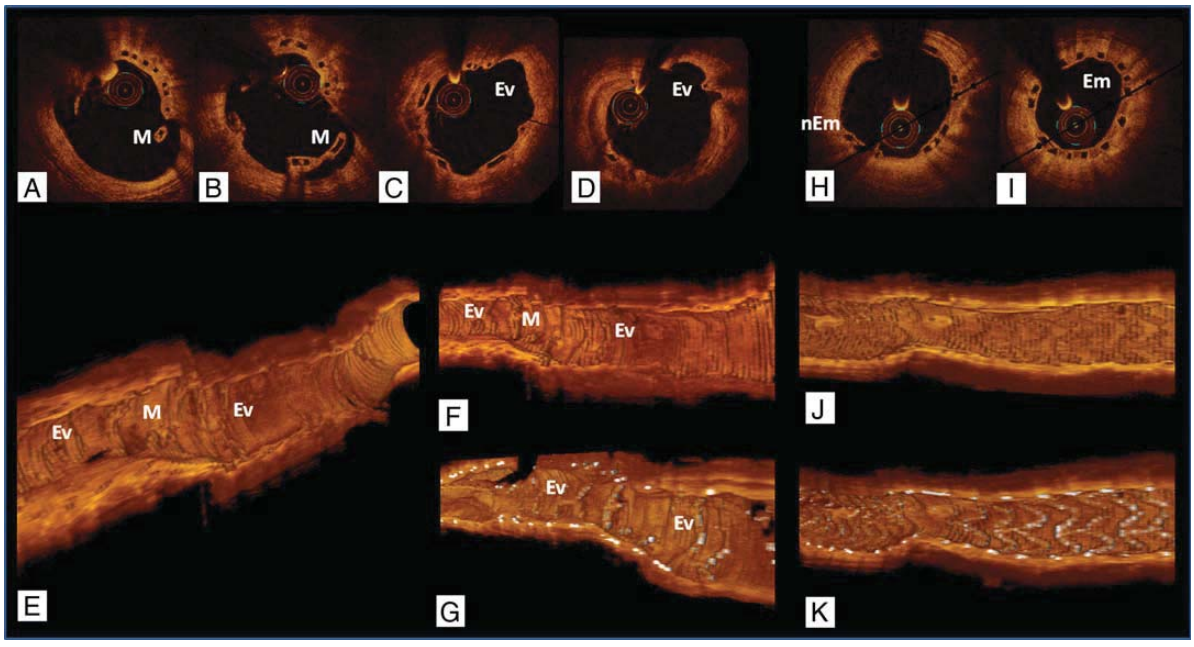

Figure 5 (*A–G*) and Video 1: 2D and 3D images of evaginations (Ev) and malappositions (M). (*H–K*): 2D and 3D images of a patient with well-apposed, covered, embedded (Em), and non-embedded (nEm) struts and no evidence of strut discontinuity (Supplementary material online, *Video S2*).

human autopsy studies.[25,27] Vasomotor function studies were only performed in a limited number of subjects; in particular, acetylcholine was not administered in subjects with more severe evidence of atherosclerosis and/or evaginations/aneurysms, therefore causing a bias that would have reduced the differences (if any) between groups. The impact of severe evaginations/aneurysms/malappositions remains unclear. Prospective studies would however require very large cohorts of patients in whom no action (e.g. prolongation of antiplatelet therapy) is taken. Finally, OCT was performed only once, and we cannot conclude regarding the progression of evaginations/malapposition areas over time and the time of their appearance. In a recent case report, evidence of formation and subsequent receding of a peri-scaffold aneurysm has also been reported.[28] The effect of pulsatile stretch and flow-dependent dilation at the time of scaffold resorption remains to be tested.

Conclusions

Anatomical abnormalities such as aneurysms, malappositions, and evaginations may disturb the laminarity of flow and have been proposed as a possible mechanisms of late stent thrombosis.[20,29,30] In our cohort, incidence and severity of coronary evaginations following BVS implantation were similar to those previously reported for second-generation DES. Undersizing at the time of implantation was a possible mechanism of evaginations; further, strut fracture and immature neointima might be associated with the presence and severity of evaginations (and malapposition) in a small but relevant subgroup of patients. The implications of these abnormalities, and possible interventions, will need further investigation.

Supplementary material

Supplementary Material is available at *European Heart Journal* online.

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