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Scaffold underexpansion and late lumen loss after bioresorbable scaffold implantation: Insights from ABSORB JAPAN trial

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ABSTRACT

Background: Device underexpansion is associated with late adverse outcomes after bioresorbable vascular scaffold (BVS) implantation. This study, representing official IVUS results of the ABSORB Japan trial, aimed to characterize IVUS findings, focusing specifically on acute device expansion, and to investigate its impact on late lumen loss (LLL) with Absorb-BVS compared with cobalt-chromium everolimus-eluting stents (CoCr-EES).

Methods: ABSORB Japan enrolled 148 patients (2:1 randomization) in the IVUS cohort. Serial IVUS was prescheduled at post-procedure and 3 years. Acute device expansion was evaluated with respect to the degree and uniformity of the implanted device.

Results: Overall, Absorb-BVS showed smaller and more nonuniform device expansion at post-procedure, compared with CoCr-EES, which was particularly prominent in small-vessel lesions. In serial analysis, Absorb-BVS showed unique associations of smaller device expansion ($r = 0.40$, $p = 0.001$) and more nonuniformity ($r = 0.29$, $p = 0.007$) at post-procedure with greater LLL at 3 years, primarily attributable to greater negative remodeling ($r = 0.39$, $p = 0.006$). In contrast, acute device expansion showed no relation with subsequent lumen change in CoCr-EES. In Absorb-BVS, ischemic-driven target lesion or vessel revascularization (ID-TLR or ID-TVR) at 3 years occurred more frequently in small- versus large-vessel lesions (12.5% vs. 0%, $p = 0.04$ for ID-TLR and 15.6% vs. 2.3%, $p = 0.08$ for ID-TVR). Conversely, Absorb BVS had no target lesion nor vessel failure, even in small-vessel lesions, when adequate device expansion was achieved at post-procedure.

Conclusions: Unlike CoCr-EES, underexpansion was associated with greater negative remodeling and LLL in Absorb-BVS. This may in part account for the poorer outcomes of Absorb-BVS than CoCr-EES when under-expanded.

1. Introduction

Pooled individual data from the ABSORB clinical trials support the concept of transient vessel scaffolding of bioresorbable vascular scaffold (BVS) and showed equivalent safety and efficacy outcomes at one year between everolimus-eluting BVS (Absorb BVS) and cobalt-chromium everolimus-eluting stent (CoCr-EES) [1–4]. Conversely, subsequent data from the randomized controlled trials and meta-analyses with long-term follow-up revealed continued higher rates of target lesion failure, including scaffold thrombosis, with Absorb BVS compared with CoCr-EES [5–10]. Although the

Abbreviations: BVS, bioresorbable vascular scaffolds; CV, coefficient of variation; CoCr-EES, cobalt-chromium everolimus-eluting stents; DS, diameter stenosis; ID-TLR, ischemic-driven target lesion revascularization; ID-TVR, ischemic-driven target vessel revascularization; ISA, incomplete strut apposition; LISA, late-acquired incomplete strut apposition; LLL, late lumen loss; IVUS, intravascular ultrasound; MI, myocardial infarction; MLD, minimum lumen diameter; QCA, quantitative coronary angiography; RLD, reference lumen diameter; RVD, reference vessel diameter; ScT, scaffold thrombosis; ST, stent thrombosis; TLF, target lesion failure; TVF, target vessel failure.

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concept of full scaffold resorption remains extremely attractive, these safety concerns eventually led to the market withdrawal of Absorb BVS in 2017.

In general, it is hard to make improvements in anything without first understanding in detail its shortcomings [11]. Also, the development of polymeric scaffold is still at an early stage, and further studies are required for a control of its unique mechanical performance, especially the resorption process. To date, suboptimal device expansion appears to be a key target to improve clinical outcomes after BVS implantation [12,13]. However, little is known about the possible mechanisms of the association between acute device expansion and the additional complications of BVS. This article describes the official serial intravascular ultrasound (IVUS) report of the ABSORB Japan trial [1] and aimed to characterize IVUS findings, focusing specifically on acute device expansion, and to investigate its impact on long-term arterial responses after Absorb-BVS versus CoCr-EES implantation.

2. Methods

2.1. Study design and population

The design of the ABSORB Japan trial has been described previously [1]. In brief, the ABSORB Japan trial was a prospective, multicenter, randomized, single-blind, active-controlled clinical trial where 400 patients undergoing percutaneous coronary intervention from 38 investigational sites in Japan were randomized in a 2:1 ratio to treatment with Absorb BVS or the XIENCE CoCr-EES (both Abbott Vascular, Santa Clara, CA). Among the study cohorts, 150 patients were scheduled in the IVUS subgroup.

Patients were eligible for enrollment if they were ≥20 years old and had evidence of myocardial ischemia (stable angina, unstable angina, or silent ischemia). Patients with left ventricular ejection fraction <30%, estimated glomerular filtration rate <30 mL/min/1.73 m^2, recent myocardial infarction, and those at high bleeding risk were excluded. Key angiographic inclusion criteria were lesions with no more than 24 mm in length, reference lumen diameter (RLD) of ≥2.5 to ≤3.75 mm, and diameter stenosis (DS) of ≥50 to <100% on visual assessment. Key angiographic exclusion criteria were left main or ostial location; excessive vessel tortuosity and/or heavy calcification proximal to or within the target lesion on visual estimation on sites; restenotic lesion; and bifurcation lesion with side branch ≥2 mm in diameter, requiring protection guidewire or dilation.

The details of study procedure were previously described [1]. Pre-dilation of the target lesion was mandatory. The target lesion had to be treated with a single study device and planned overlapping was not allowed. Post-dilatation of Absorb BVS was not mandatory but was allowed, using a low-profile, high-pressure, noncompliant balloon with diameter ≤0.5 mm larger than the nominal size. Post-dilatation of CoCr-EES was per standard of care.

The Institutional Review Board at each investigational site approved the clinical trial protocol. All patients provided written informed consent before enrollment.

2.2. Quantitative coronary angiography

Quantitative coronary angiography (QCA) was performed at an independent angiographic core laboratory (Beth Israel Deaconess Medical Center, Boston, USA). Standard QCA variables were obtained with QAngio XA 7.3 (Medis medical imaging systems, Leiden, the Netherlands); the current analysis used in-segment minimum lumen diameter (MLD), DS, and late lumen loss (LLL) defined as absolute changes in MLD from post-procedure to 3 years. To represent more detailed lesion characteristics, calcification, tortuosity and eccentricity were also assessed. Moderate and severe calcification were defined as "densities noted only during the cardiac cycle prior to contrast injection" and "radio-opacities noted without cardiac motion prior to contrast injection generally involving both sides of the arterial wall", respectively. Moderate and severe tortuosity were defined as "2 bends with >75 degrees or one bend with >90 degrees to reach the target lesion" and "2 bends with >90 degrees to reach target lesion". Eccentric lesion was defined as a stenosis that had one of its luminal edges in the outer one-quarter of the apparent normal lumen.

2.3. Intravascular ultrasound

IVUS was performed in a standard manner using automated transducer pullback at 0.5 mm/sec with a commercially available imaging system. IVUS-guided PCI was not recommended by the study protocol, but operators were allowed to use IVUS information to optimize device deployment. Final IVUS images obtained at the end of procedure were submitted for independent IVUS analysis at Stanford Cardiovascular Core Analysis Laboratory, blinded to clinical and angiographic information. Using a validated quantitative IVUS analysis system (echoPlaque 4. Indec Systems, Santa Clara, CA), vessel, lumen, device (scaffold/stent), plaque (vessel minus lumen) and neointima (device minus lumen) areas were manually traced at 1-mm intervals from proximal to distal 5-mm reference-segments throughout the target segment with automated interpolated measurements of the remaining frames. Each volume calculated using Simpson's method was standardized as volume index (volume / analyzed length, mm^3/mm). As previously described [14], 1) Percent device expansion [a ratio of device volume index (percent volume expansion) or minimum device area (percent area expansion) to reference lumen volume index (average of proximal and distal references)]; 2) Uniformity index of device expansion (minimum / maximum device areas) and coefficient of variation (CV) of device cross-sectional areas (standard deviation of device area/mean device area); 3) Device sizing (nominal device diameter minus mean RLD); and 4) Small-vessel lesions (mean RLD <2.75 mm) and tapered-type lesions [tapering index (proximal/distal RLD) ≥1.2] were evaluated. As long-term arterial response analysis, LLL was defined as a decrease in lumen volume index from post-procedure to 3-year follow-up; vessel remodeling and plaque/neointimal proliferation were assessed as a change in vessel and plaque volume indexes, respectively. Neointimal volume at 3 years after Absorb BVS implantation could not be measured precisely due to the resorption of bioresorbable scaffolds; therefore, the present study used plaque volume (i.e., peri-device plaque plus in-device neointimal volume) for comparative analysis of tissue proliferation between the 2 devices. Incomplete strut apposition (ISA) was defined as separation of at least one strut from the intimal surface, with evidence of blood flow behind the strut(s) in a vessel segment not associated with any side branches. ISA was classified as persistent, resolved, or late-acquired ISA [6]. Strut fracture was evaluated as longitudinal strut discontinuity. Any residual scaffold/stent edge dissection detected as a fissure or separation within intima or plaque was also counted [15].

2.4. Clinical endpoints

Patients were followed for up to 3 years post-procedure. Cardiac death, target-vessel myocardial infarction (MI), ischemic-driven target lesion revascularization (ID-TLR), ischemic-driven target vessel revascularization (ID-TVR), stent thrombosis (ST) and scaffold thrombosis (ScT), and binary restenosis (DS ≥ 50% on angiogram) were adjudicated by an independent blinded clinical events committee (Harvard Clinical Research Institute, Boston). Independent study monitors verified all case report forms on-site. A Data Safety Monitoring Board monitored patient safety.

Definitions of ST/ScT and other endpoints were based on the Academic Research Consortium criteria [1]. Primary clinical endpoint was target lesion failure (TLF: a composite of cardiac death, target-vessel MI, or ID-TLR) as reported in previous study [1]. Target vessel failure (TVF: a composite of cardiac death, target-vessel MI, ID-TLR or ID-TVR), ST/ScT and binary restenosis were also evaluated as secondary clinical endpoints.

2.5. Statistical analysis

Sample size calculation for the IVUS cohort of ABSORB Japan was performed to assess the in-device mean lumen area change from post-procedure to 3 years as the secondary powered endpoint of the trial. Statistical calculations were performed with JMP Pro® 12 software (SAS Institute Inc., Cary, NC). Data are expressed as frequencies and percentages for categorical variables and as mean ± SD for continuous variables. Categorical comparisons were performed using chi-square test or Fisher's exact test. Continuous values were compared using unpaired or paired Student *t* test, Wilcoxon rank-sum test, nonparametric Mann-Whitney *U* test, or one-way analysis of variance, as appropriate. A two-way repeated measures analysis of variance was used to test for group and time effects and their interactions. Correlations between continuous variables were investigated using linear regression analysis. Logistic regression analysis was performed to find the relationship of the presence of ISA to IVUS indexes. Clinical outcomes between the 2 device arms were compared using the log-rank test. A p-value <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

Between April 2013 and January 2014, 153 lesions from 148 patients were enrolled in this analysis of the IVUS cohort of the ABSORB Japan trial (detailed patient flow is shown in Fig. 1). Patient, lesion and procedural characteristics with post-procedural IVUS were comparable between the 2 device arms, except for a lower prevalence of prior MI in the Absorb BVS arm (Table 1). Pre-dilation was performed using slightly undersized balloons with moderate pressure in both arms. Total device length was similar between the arms. Post-dilation was performed in a similar proportion.

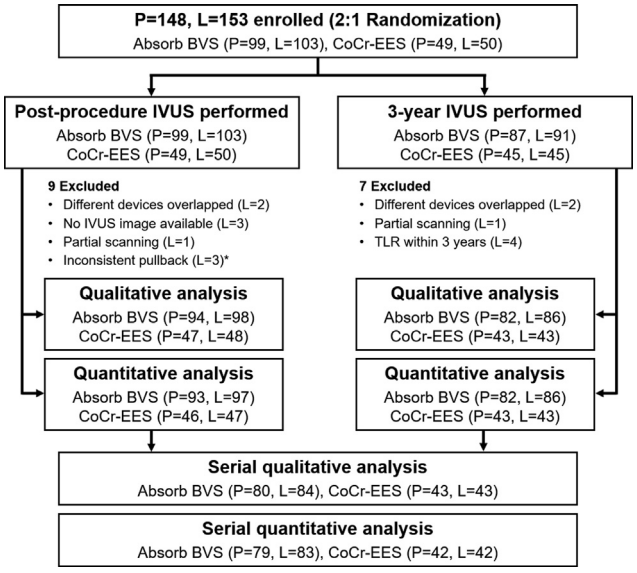

Fig. 1. Patient disposition. P is for patient number, and L is for lesion number. IVUS = intravascular ultrasound. Other abbreviations as in Table 1.

Table 1
Patient, lesion and procedural characteristics.

Variables	Absorb BVS arm	CoCr-EES arm	p value
Patient characteristics			
Number of patients	94	47	
Age (years)	68 ± 9	66 ± 9	0.08
Male	74 (78.7)	36 (76.6)	0.77
Body mass index (kg/mm^2)	23.5 ± 3.0	24.2 ± 2.9	0.21
Current smoker	18 (19.2)	10 (21.3)	0.77
Hypertension	72 (76.6)	36 (76.6)	1.00
Dyslipidemia	76 (80.9)	40 (85.1)	0.53
Diabetes mellitus	27 (28.7)	13 (27.7)	0.89
Treated with insulin	13 (13.8)	5 (10.6)	0.59
Prior intervention to target vessel	3 (3.2)	2 (4.3)	0.75
Prior myocardial infarction	13 (14.0)	12 (25.5)	0.10
Family history of premature CAD	5 (5.3)	4 (8.5)	0.47
Current evidence of ischemia	94 (100)	47 (100)	–
Stable angina	54 (57.4)	32 (68.1)	
Unstable angina	11 (11.7)	7 (14.9)	0.19
Silent ischemia	29 (30.9)	8 (17.0)	
Number of target lesions			
One	90 (95.7)	46 (97.9)	0.50
Two	4 (4.3)	1 (2.1)	
Lesion characteristics			
Total number of target lesions	98	48	
Target vessel			
Left anterior descending artery	45 (45.9)	18 (37.5)	0.52
Left circumflex/ramus artery	23 (23.5)	11 (22.9)	
Right coronary artery	30 (30.6)	19 (39.6)	
Lesion location			
Proximal	33 (33.7)	14 (29.2)	0.35
Mid	52 (53.1)	23 (47.9)	
Distal	13 (13.3)	11 (22.9)	
Calcification (moderate/severe)	33 (33.7)	15 (31.3)	0.77
Tortuosity (moderate/severe)	10 (10.2)	5 (10.4)	0.97
Eccentric lesion	77 (78.6)	41 (85.4)	0.31
ACC/AHA lesion classification			
A/B1	28 (28.6)	13 (27.1)	0.85
B2/C	70 (71.4)	35 (72.9)	
Procedural characteristics			
Pre-dilation (per lesion)			
Pre-dilation performed	98 (100)	48 (100)	–
Nominal balloon diameter (mm)	2.83 ± 0.40	2.82 ± 0.37	0.85
Pre-dilation balloon pressure (atm)	11.3 ± 3.7	11.1 ± 3.2	0.97
Pre-dilation balloon type			
Semi-compliant balloon	49 (50.0)	25 (52.1)	0.74
Scoring or cutting balloon	17 (17.3)	6 (12.5)	
Non-compliant balloon	32 (32.7)	17 (35.4)	
Device deployment (per device)			
Nominal device diameter (mm)	3.06 ± 0.38	3.16 ± 0.41	0.13
Total device length (mm)	20.0 ± 6.0	19.0 ± 5.8	0.25
Post-dilation (per lesion)			
Post-dilation performed	85 (86.7)	38 (79.2)	0.25
Nominal balloon diameter (mm)	3.21 ± 0.45	3.31 ± 0.57	0.47
Balloon pressure (atm)	15.2 ± 4.3	16.1 ± 3.9	0.21
Post-dilation balloon type			
Semi-compliant balloon	1 (1.2)	1 (2.6)	
Balloon of device delivery system	16 (18.8)	13 (34.2)	0.15
Non-compliant balloon	68 (80.0)	24 (63.2)	

Values are number (%) or mean ± SD. p values for Absorb BVS arm vs. CoCr-EES arm. ACC/AHA = American College of Cardiology/American Heart Association, BVS = bioresorbable vascular scaffold, CAD = coronary artery disease, CoCr-EES = cobalt-chromium everolimus-eluting stent. p values for Absorb BVS arm vs. CoCr-EES arm. Categorical comparisons were performed using chi-square test. Continuous values were compared using unpaired Student *t* test for body mass index and Wilcoxon rank-sum test for age.

3.2. Primary IVUS results

Quantitative and qualitative IVUS results are summarized in Tables 2 and 3. At reference segments, mean vessel, lumen and pla-

Table 2
IVUS results at reference segments.

Variables	Absorb BVS arm	CoCr-EES arm	p value
Distal reference segment			
Number of segments analyzed			
Post-procedure	89	46	
3 years	76	42	
Mean lumen diameter (mm)			
Post-procedure	2.79 ± 0.53	2.90 ± 0.63	0.41
3 years	2.70 ± 0.57	2.77 ± 0.52	0.44
Vessel volume index (mm^3/mm)			
Post-procedure	11.2 ± 4.8	12.4 ± 5.0	0.18
3 years	10.8 ± 4.6	12.4 ± 4.6	0.04
Lumen volume index (mm^3/mm)			
Post-procedure	6.3 ± 2.6	6.9 ± 3.1	0.40
3 years	6.0 ± 2.6	6.2 ± 2.4	0.44
Plaque volume index (mm^3/mm)			
Post-procedure	4.9 ± 3.0	5.5 ± 2.8	0.21
3 years	4.9 ± 2.5	6.2 ± 2.9	0.02
Percent plaque volume (%)			
Post-procedure	41.7 ± 12.6	43.2 ± 13.2	0.51
3 years	44.4 ± 11.1	48.5 ± 11.7	0.07
Dissection			
Post-procedure	0 (0)	0 (0)	–
3 years	0 (0)	0 (0)	–
Proximal reference segment			
Number of segments analyzed			
Post-procedure	82	42	
3 years	73	38	
Mean lumen diameter (mm)			
Post-procedure	3.09 ± 0.51	3.19 ± 0.60	0.46
3 years	3.02 ± 0.56	3.08 ± 0.59	0.70
Vessel volume index (mm^3/mm)			
Post-procedure	15.0 ± 5.0	15.8 ± 6.0	0.63
3 years	14.6 ± 5.2	15.8 ± 5.9	0.28
Lumen volume index (mm^3/mm)			
Post-procedure	7.7 ± 2.6	8.2 ± 3.1	0.47
3 years	7.4 ± 2.8	7.7 ± 3.0	0.71
Plaque volume index (mm^3/mm)			
Post-procedure	7.3 ± 3.3	7.6 ± 3.4	0.73
3 years	7.2 ± 3.1	8.1 ± 3.6	0.22
Percent plaque volume (%)			
Post-procedure	47.9 ± 10.8	47.1 ± 9.1	0.72
3 years	49.1 ± 9.8	50.5 ± 9.4	0.46
Dissection			
Post-procedure	0 (0)	0 (0)	–
3 years	0 (0)	0 (0)	–
Average of both reference segments			
Number of segments analyzed			
Post-procedure	75	42	
3 years	64	38	
Mean lumen diameter (mm)			
Post-procedure	2.94 ± 0.50	3.05 ± 0.55	0.25
3 years	2.87 ± 0.57	2.94 ± 0.50	0.52
Vessel volume index (mm^3/mm)			
Post-procedure	13.3 ± 4.7	14.2 ± 5.2	0.40
3 years	12.8 ± 4.8	14.3 ± 4.9	0.14
Lumen volume index (mm^3/mm)			
Post-procedure	7.0 ± 2.5	7.6 ± 2.8	0.26
3 years	6.7 ± 2.7	7.0 ± 2.4	0.49
Plaque volume index (mm^3/mm)			
Post-procedure	6.3 ± 2.9	6.6 ± 2.9	0.54
3 years	6.2 ± 2.5	7.3 ± 3.0	0.09
Lesion classification at post-procedure			
Number of segments analyzed	75	42	
Small vessel lesions	32 (42.7)	14 (33.3)	0.32
Tapering index	1.12 ± 0.15	1.12 ± 0.19	0.90
Tapered-type lesions	19 (25.3)	10 (23.8)	0.85

Values are number (%) or mean ± SD. *p value for Absorb BVS arm vs. CoCr-EES arm, †p value for post-procedure vs. 3 years. Categorical comparisons were performed using chi-square test. Continuous values were compared using unpaired Student *t* test for percent plaque volume at 3 years at the distal reference segment, mean lumen diameter at post-procedure and percent plaque volume both at post-procedure and at 3 years at the proximal reference segment, and mean vessel diameter of average of both proximal and distal references and tapering index at post-procedure and Wilcoxon rank-sum test for the other variables.

que volumes were comparable between the 2 device arms at both post-procedure and 3 years. At in-device segments, each device arm showed identical values between lumen and device volume indexes due to similar rates of prolapse and ISA at post-

Table 3
QCA and IVUS results at in-device segments.

Variables	Absorb BVS arm	CoCr-EES arm	p value
QCA analysis			
Number of segments analyzed			
Post-procedure	98	48	
3 years	88	45	
Mean RLD (mm)			
Post-procedure	2.75 ± 0.45	2.86 ± 0.42	0.13
3 years	2.73 ± 0.46	2.84 ± 0.43	0.17
In-segment MLD (mm)			
Post-procedure	2.18 ± 0.39	2.31 ± 0.40	0.07
3 years	2.03 ± 0.49	2.12 ± 0.46	0.31
In-segment DS (%)			
Post-procedure	20.7 ± 6.8	19.4 ± 6.4	0.31
3 years	25.8 ± 11.7	25.0 ± 12.9	0.31
Quantitative IVUS analysis			
Number of segments analyzed			
Post-procedure	97	47	
3 years	86	43	
Device length analyzed (mm)	20.3 ± 5.9	19.6 ± 6.0	0.89
Post-procedure	20.0 ± 5.7	19.2 ± 5.8	0.98
3 years	20.0 ± 5.9	19.7 ± 6.1	0.50
Vessel volume index (mm^3/mm)			
Post-procedure	13.7 ± 4.5	14.6 ± 5.0	0.36
3 years	13.4 ± 4.5	14.9 ± 5.0	0.09
Lumen volume index (mm^3/mm)			
Post-procedure	6.5 ± 2.0	7.3 ± 2.1	0.02
3 years	6.1 ± 2.4	6.8 ± 2.3	0.08
Device volume index (mm^3/mm)			
Post-procedure	6.5 ± 2.0	7.3 ± 2.1	0.02
3 years	–	7.7 ± 2.4	–
Plaque volume index (mm^3/mm)			
Post-procedure	7.3 ± 2.7	7.3 ± 3.1	0.91
3 years	7.5 ± 2.3	8.1 ± 3.1	0.35
Neointimal volume index (mm^3/mm)			
Post-procedure	–	–	–
3 years	–	0.9 ± 0.9	–
Percent neointimal area (%)			
Post-procedure	–	–	–
3 years	–	11.5 ± 9.0	–
MLA (mm^2)			
Post-procedure	5.4 ± 1.8	6.3 ± 2.0	0.009
3 years	4.6 ± 2.1	5.2 ± 2.1	0.05
Minimum device area (mm^2)			
Post-procedure	5.4 ± 1.8	6.3 ± 2.0	0.009
3 years	–	6.5 ± 2.2	–
Uniform expansion at post-procedure			
Number of segments analyzed	97	47	
Uniformity index of device expansion	0.70 ± 0.10	0.76 ± 0.12	0.0003
CV of device cross-sectional areas	0.10 ± 0.05	0.08 ± 0.05	0.0005
Device expansion at post-procedure			
Number of segments analyzed	75	42	
%volume expansion (×100)	0.96 ± 0.14	1.01 ± 0.16	0.08
%area expansion (×100)	0.79 ± 0.15	0.87 ± 0.16	0.02
%area expansion (×100) < 0.80	39 (52.0)	12 (28.6)	0.01
Device sizing at post-procedure			
Number of segments analyzed	75	42	
Oversized	30 (40.0)	18 (42.9)	0.34
Properly sized	37 (49.3)	16 (38.1)	
Undersized	8 (10.7)	8 (19.0)	
Qualitative IVUS analysis			
Number of segments analyzed			
Post-procedure	98	48	
3 years	86	43	
Prolapse			
Post-procedure	12 (12.2)	13 (27.1)	0.03
3 years	0 (0)	0 (0)	–
ISA			
Post-procedure	9 (9.2)	9 (18.8)	0.11
3 years	6 (7.0)	3 (7.0)	1.00
Strut discontinuity			
Post-procedure	0 (0)	0 (0)	–

(*continued on next page*)

Table 3 (*continued*)

Variables	Absorb BVS arm	CoCr-EES arm	p value
3 years	2 (2.3)	0 (0)	0.55
ISA changes during 3 years			
Number of segments analyzed	84	43	
Resolved ISA	3 (3.6)	6 (14.0)	
Persistent ISA	2 (2.4)	3 (7.0)	0.04
Late acquired ISA	4 (4.8)	0 (0)	

Values are number (%) or mean ± SD. *p value for Absorb BVS arm vs. CoCr-EES arm, †p value for post-procedure vs. 3 years. Device sizing was classified by Δdiameter (nominal device - mean reference lumen): oversized (>0.25 mm), properly sized (−0.25 to 0.25 mm) and undersized (<-0.25 mm). CV = coefficient of variation (standard deviation of device area / mean device area), ISA = incomplete strut apposition, MLA = minimum lumen area. Other abbreviations as in Table 1. Categorical comparisons were performed using Fisher's exact test for ISA and strut discontinuity at 3 years and ISA changes during 3 years, and chi-square test for the other variables. Continuous values were compared using unpaired Student *t* test for percent volume and area expansion at post-procedure and Wilcoxon rank-sum test for the other variables.

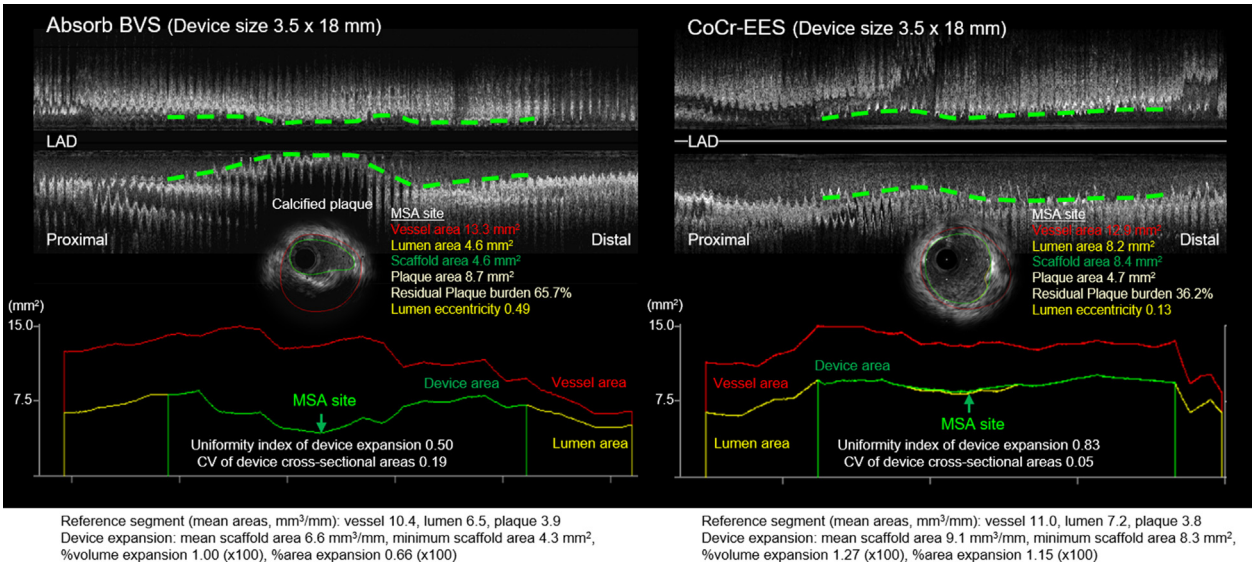

Fig. 2. Representative cases of non-uniform expansion. Longitudinal IVUS images with the corresponding figures of volumetric analyses. X-axis represents the pullback length; Y-axis represents area. Despite the comparable profile of the reference segments, Absorb BVS showed more nonuniform expansion (i.e. smaller uniformity index, and greater CV of device areas and lumen eccentricity*), as well as smaller mean and minimum device areas, compared with CoCr-EES. *calculated as (maximum device area – minimum device area)/maximum device area.

procedure. On the other hand, significantly smaller lumen and device volumes, as well as smaller minimum lumen and device areas, and more nonuniform expansion (i.e. smaller uniformity index and greater CV of device areas) were seen in the Absorb BVS arm than in the CoCr-EES arm at post-procedure (Table 3 and Fig. 2). At 3 years, the initial difference in lumen volume between the 2 device arms became non-significant, although a trend towards smaller lumen volume in the Absorb BVS arm persisted.

Percent device expansion in relation to the reference segment dimension at post-procedure was analyzed in 117 lesions because neither proximal nor distal reference was available due to the involvement of major branches in 27 lesions. As previously reported [14], percent device expansion tended to be smaller in the Absorb BVS arm compared with the CoCr-EES arm, which was particularly prominent in small-vessel lesions (Fig. 3) as well as tapered-type lesions. With respect to procedure techniques, small-vessel lesions were treated more frequently with noncompliant balloons at post-dilatation (83.3% vs. 53.8%, p = 0.06) but using significantly lower pressure (16.3 ± 3.6 vs. 19.7 ± 2.1 mmHg, p = 0.02) in the Absorb BVS arm compared with the CoCr-EES arm. In contrast, tapered-type lesions were post-dilated at equivalent pressure (17.1 ± 4.1 vs. 17.9 ± 2.4 mm, p = 0.57), but with significantly smaller balloons (3.03 ± 0.36 vs. 3.50 ± 0.65 mm, p = 0.047) in the Absorb BVS arm than in the CoCr-EES arm, partially contributing to smaller device expansion at post-procedure in the Absorb BVS arm in these complex lesions [14].

3.3. Serial changes of IVUS variables

Overall, both device arms showed no significant vessel volume change during 3 years, while plaque volume increased significantly from post-procedure to 3-year follow-up: as a result, lumen volume decreased significantly in both device arms (with no interaction) (Fig. 4). In the Absorb BVS arm, while LLL significantly correlated with both negative vessel remodeling and plaque progression, correlation coefficient was higher with negative vessel remodeling (r = 0.76, p < 0.0001) than with plaque progression (r = −0.34, p = 0.005). In the CoCr-EES arm, LLL strongly correlated with neointimal area at 3 years (r = −0.87, p < 0.0001) as expected.

At 3-year, all lesions treated with Absorb BVS showed partial struts remaining unresorbed within vessel wall and/or lumen, although the strut visibility was insufficient for quantitative device analysis (Fig. 5). In the CoCr-EES arm, there was no significant chronic stent recoil (device volume decrease ≥10%).

3.4. Acute device expansion and long-term arterial responses

In the Absorb BVS arm, both smaller device expansion and more nonuniform expansion at post-procedure significantly correlated

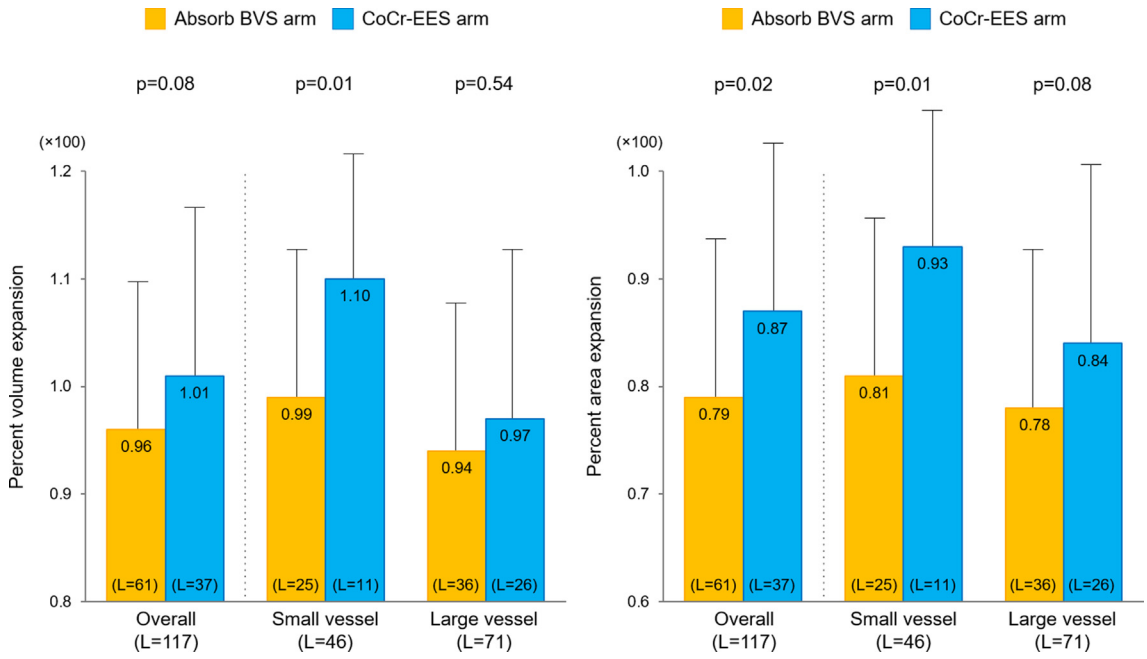

Fig. 3. Acute device expansion. Abbreviations as in Table 1. Smaller device expansion seen in the Absorb BVS arm compared with the CoCr-EES arm was more prominent in small-vessel lesions.

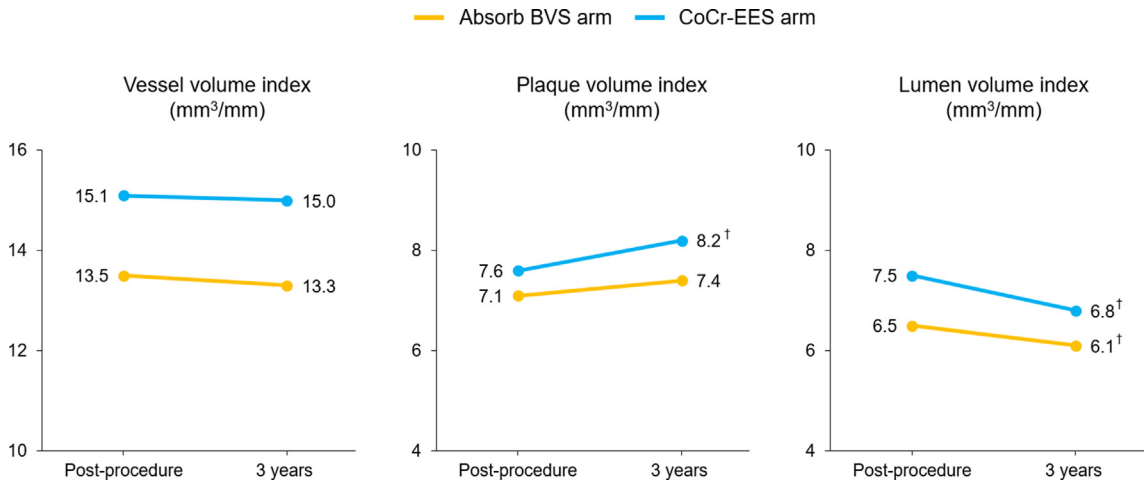

Fig. 4. Serial changes in volumetric IVUS indexes at in-device segment. Analysis includes only lesions which had both post-procedure and 3-year quantitative IVUS measurements (n = 125). *p value is for Absorb BVS arm vs. CoCr-EES arm. †p < 0.001 for post-procedure vs. 3 years. Abbreviations as in Table 1. In both arms, there was no significant vessel volume change during 3 years, whereas significant plaque increase and lumen decrease during the follow-up were observed. Initial difference in lumen volume between the arms became non-significant at 3 years.

with greater decrease in lumen volume during 3 years. While no relationship was observed between the acute device expansion and plaque volume change, both the degree and uniformity of initial device expansion significantly correlated with vessel volume change (Figs. 6 and 7, and Table 4), indicating negative vessel remodeling as the predominant mechanism of the larger lumen loss in lesions with suboptimal scaffold expansion. In contrast, the CoCr-EES arm showed no significant correlations between the acute device expansion and any arterial responses assessed as IVUS volume changes. These results were confirmed by analyzing correlation between the acute device expansion and LLL by QCA (Fig. 8) in a larger population. Minimum device area at post-procedure did not correlate with any arterial responses in the Absorb BVS nor CoCr-EES arm (Table 4).

3.5. Incomplete strut apposition

Post-procedural ISA tended to be less frequent in the Absorb BVS arm compared with the CoCr-EES arm (Table 3). In both arms, about two-thirds of acute ISA had been resolved during 3 years, while there were 4 cases of late-acquired ISA (LISA) (including 2 late strut discontinuity), all of which were seen in the Absorb BVS arm: 2 within scaffold body and 2 at scaffold distal edge. Accordingly, the incidence of ISA at 3 years was comparable between the 2 device arms.

Representative ISA cases of Absorb BVS are shown in Fig. 5. All resolved ISA struts were accompanied by complete strut resorption, neointimal tissue coverage or their combination at 3 years, whereas persistent ISA struts were associated with inadequate

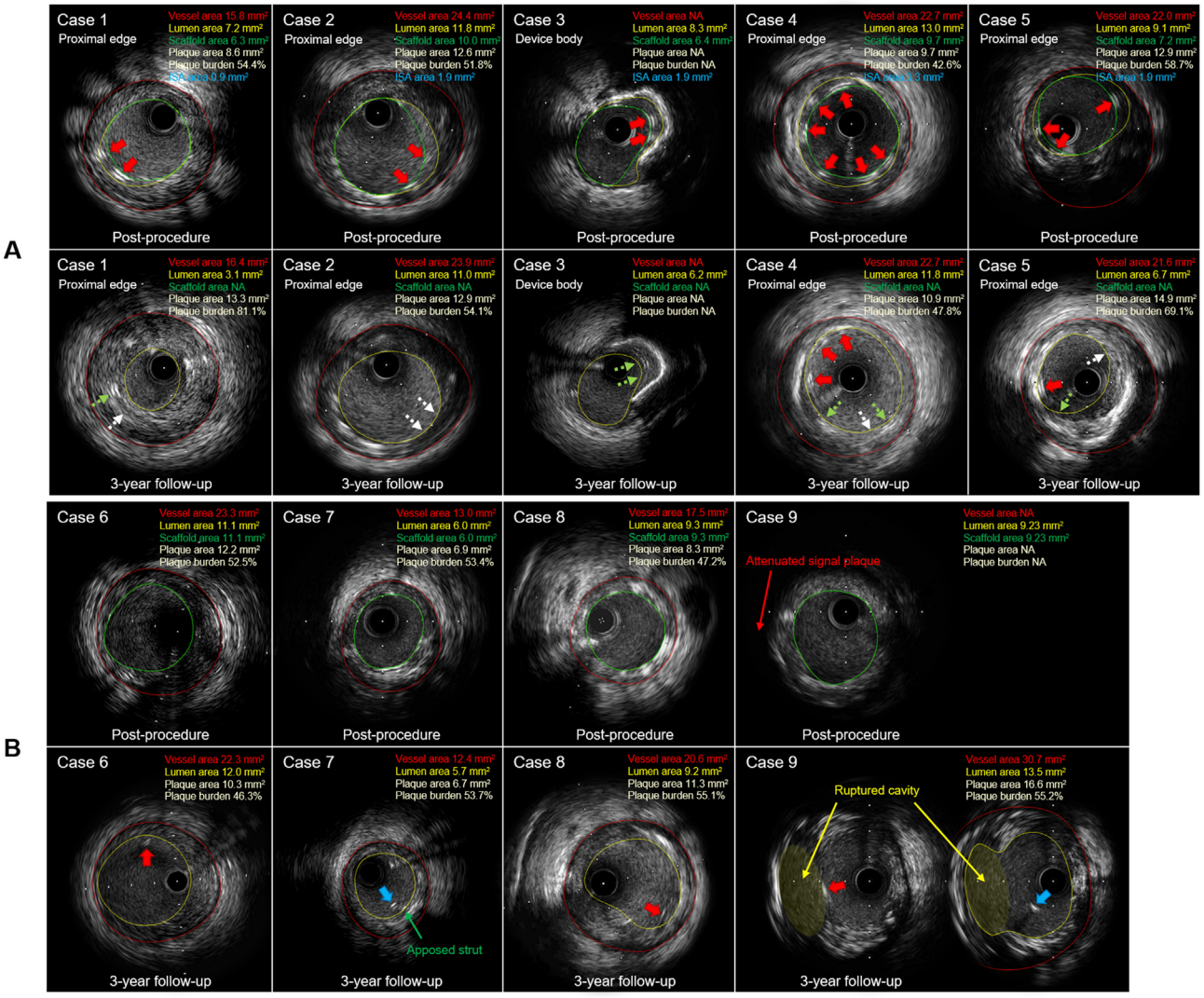

Fig. 5. Representative ISA cases of Absorb BVS. **A.** Resolved and persistent ISA Cases 1–5. Red arrows represent ISA struts. White dashed arrows represent absorbed ISA struts; green dashed arrows represent covered ISA struts. All resolved ISA struts were accompanied by strut resorption, neointimal tissue coverage, or their combination, whereas persistent ISA cases showed no or inadequate resorption and neointimal coverage, and appeared to have greater ISA areas, compared with resolved ISA cases. **B.** late-acquired ISA and late strut discontinuity Cases 6–9. Red arrows represent LISA struts; blue arrows represent strut discontinuity. Various arterial responses during 3-year follow-up were observed in the sites with late scaffold ISA and discontinuity. Case 9 showed LISA and strut discontinuity at the site with plaque rupture at 3 years, which corresponds to the site with attenuated-signal plaque at post-procedure.

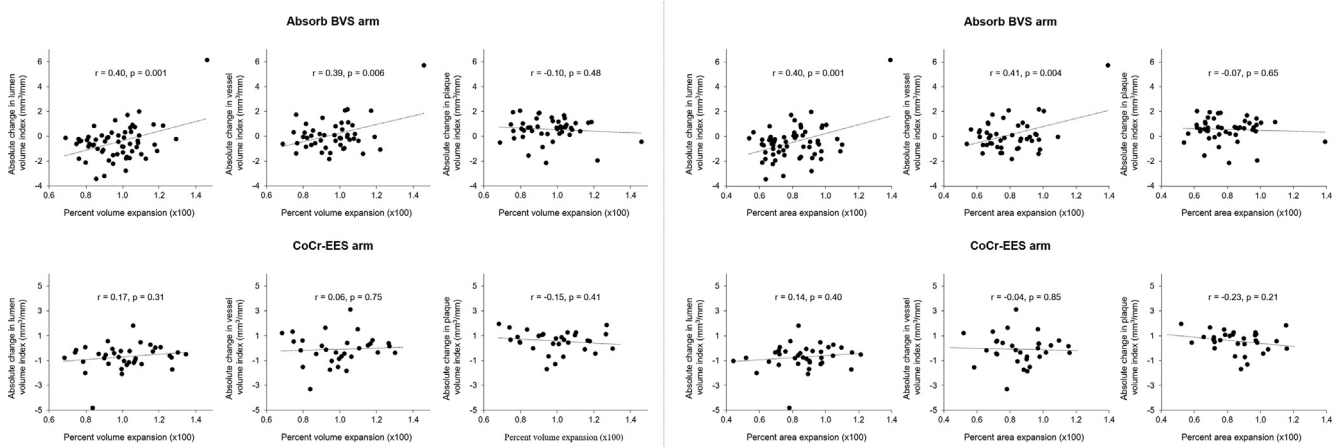

Fig. 6. Correlations between acute device expansion and long-term arterial responses. Abbreviations as in Table 1. In the Absorb BVS arm, smaller percent volume and area expansion at post-procedure were significantly associated with greater lumen and vessel volume decreases during 3 years, while no relationship was observed between acute device expansion and plaque volume change. The CoCr-EES arm showed no correlation between acute device expansion and any IVUS volume change.

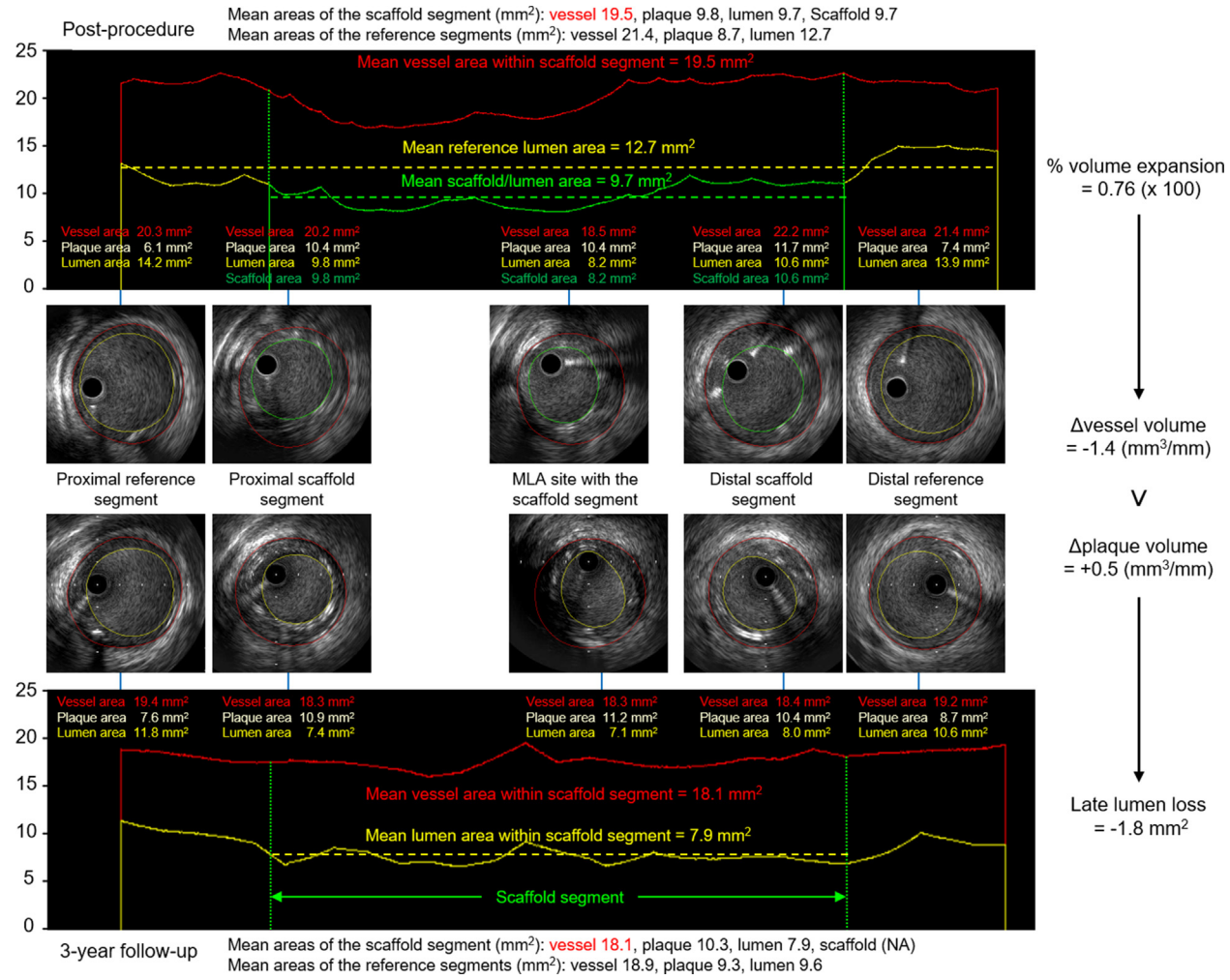

Fig. 7. Representative case of scaffold underexpansion with late lumen loss at 3 years. Late lumen loss at the scaffold segment was predominantly due to negative remodeling (−1.4 mm^3/mm), rather than plaque/neointimal proliferation (+0.5 mm^3/mm).

Table 4
Correlations with long-term arterial responses.

Variables	Absorb BRS arm (L = 83)		CoCr-EES arm (L = 42)	
Uniformity index of device expansion	r	p	r	p
Absolute change in lumen volume (mm)	0.29	0.007	−0.02	0.92
Absolute change in vessel volume (mm)	0.32	0.01	−0.25	0.15
Absolute change in plaque volume (mm)	0.02	0.87	−0.30	0.08
CV of device cross-sectional areas	r	p	r	p
Absolute change in lumen volume (mm)	−0.29	0.009	0.01	0.96
Absolute change in vessel volume (mm)	−0.29	0.02	0.23	0.18
Absolute change in plaque volume (mm)	−0.04	0.74	0.29	0.09
Minimum device area				
Absolute change in lumen volume (mm)	0.11	0.34	−0.11	0.48
Absolute change in vessel volume (mm)	0.10	0.42	−0.14	0.42
Absolute change in plaque volume (mm)	−0.17	0.18	−0.09	0.62

Abbreviations as in Table 1.

strut resorption or lack of IVUS-detectable gross tissue coverage at 3 years. With respect to LISA, various arterial responses, including negative or positive vessel remodeling with plaque proliferation or reduction, were observed at 3 years. Plaque rupture (suggestive of neoatherosclerosis) was also found at 3 years in one case of LISA with strut discontinuity, where significant attenuated-signal plaque (ASP) was observed at post-procedure, suggesting possible interaction between underlying plaque and bioresorption process (Fig. 5).

Higher tapering index (p = 0.01) was significantly associated with post-procedural ISA as previously reported [14], while device sizing (p = 0.009) and large-vessels (p = 0.02) were associated with ISA at 3 years after Absorb BVS implantation in the multivariate analysis. Of note, in the Absorb BVS arm, no ISA was seen at

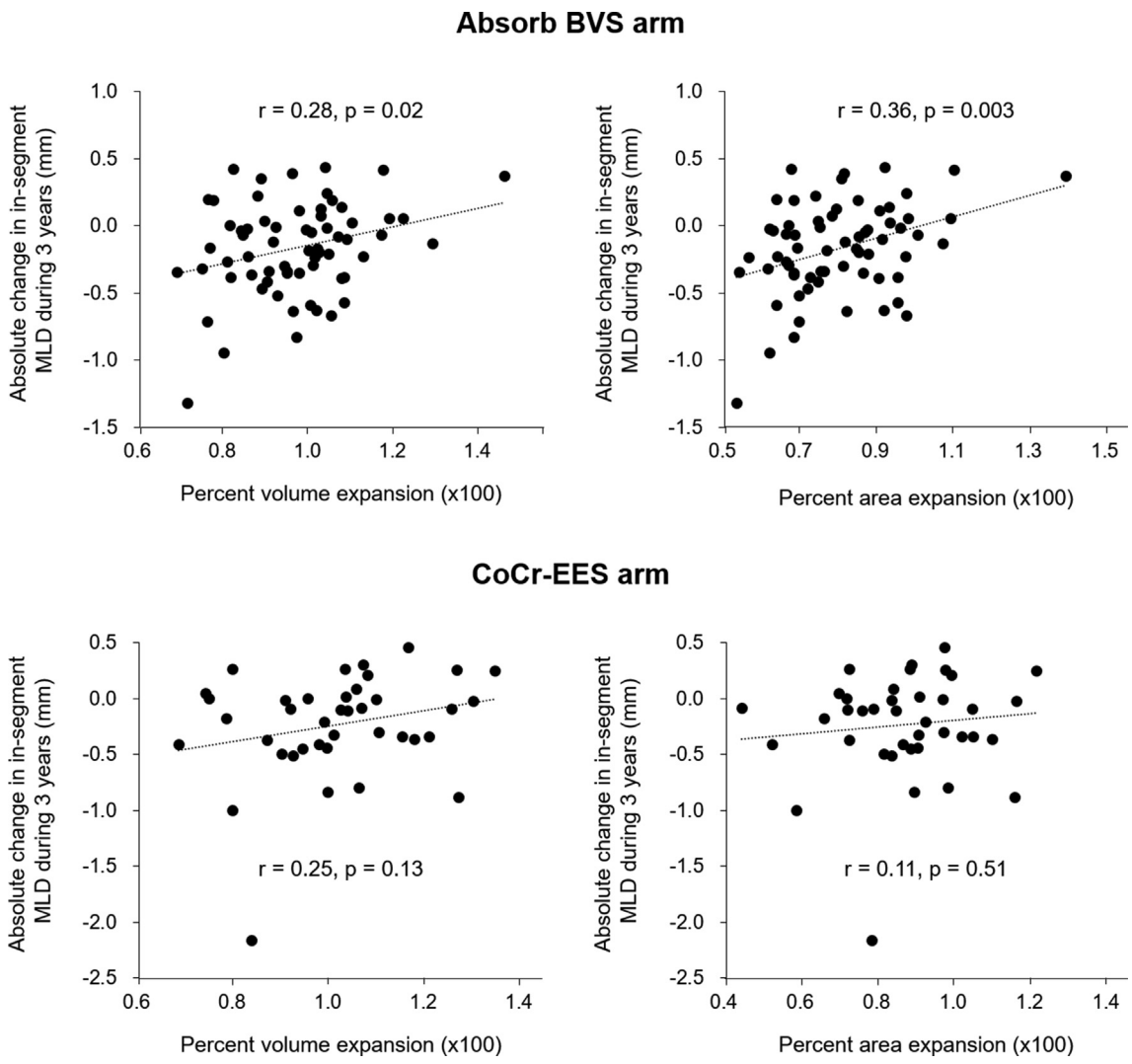

Fig. 8. Correlations of acute device expansion with late lumen loss as assessed by QCA. Only Absorb BVS showed significant associations between smaller percent volume and area expansion at post-procedure and late lumen loss during 3 years as assessed by QCA.

post-procedure nor at 3 years in lesions with use of over-sized device (>0.25 mm than mean RLD) or adequate device expansion (volume expansion $\geq$1.1).

3.6. Clinical outcomes

During 3-year follow-up period, the IVUS cohort had 12 (8.2%) TLF, 15 (10.3%) TVF and 2 (1.4%) ScT (Table 5). The cumulative incidence of TLF or TVF was numerically higher without statistical significance in the Absorb BVS arm compared with the CoCr-EES arm: this difference appeared to be primarily due to higher event rates (especially, ID-TLR or ID-TVR) in small-vessel or tapered-type lesions treated with Absorb BVS. Indeed, ID-TLR (12.5% vs. 0%, p = 0.04) and ID-TVR (15.6% vs. 2.3%, p = 0.08) were or tended to be more frequently seen in small- versus large-vessel lesions (both for Log-rank) in the Absorb BVS arm. ID-TVR also tended to be more frequent in tapered- versus non-tapered-type lesions (21.1% vs. 3.6%, p = 0.056 for Log-rank) in the Absorb BVS arm. When the analyses were limited to small-vessel lesions, a tendency toward smaller scaffold expansion (% area expansion) was seen in TLF versus non-TLF lesions (0.72 ± 0.14 vs. 0.82 ± 0.15, p = 0.16) as well as in TVF versus non-TVF lesions (0.72 ± 0.13 vs. 0.83 ± 0.15, p = 0.12) in the Absorb BVS arm (Table 6). Conversely, Absorb BVS had no TLF nor TVF, even in small-vessel lesions, when adequate device expansion (volume expansion $\geq$1.1) was achieved.

A tendency toward higher TLF rates during 3 years was also seen in lesions with versus without post-procedural ISA (22.2% vs. 7.9%, p = 0.097 for Log-rank) in the Absorb BVS arm, but not in the CoCr-EES arm (p = 0.26). There were 2 ScT only in the Absorb BVS arm, both of which occurred in lesions without post-procedural ISA. In both ScT cases, scaffold expansion in relation to reference lumen area appeared to be acceptable, while significant residual plaque burden with ASP, and nonuniform scaffold expansion were seen within target segments (Fig. 9).

4. Discussion

4.1. Inadequate scaffold expansion and late lumen loss

LLL after metallic stent implantation is primarily attributable to neointimal proliferation [16]. The present study expands this and demonstrated that negative vessel remodeling, in addition to plaque/neointimal proliferation, was another important and stronger determinant of LLL after polymeric scaffold implantation. The present study also revealed the significant association between suboptimal (i.e., smaller and more nonuniform) device expansion

Table 5
Clinical outcomes during 3 years.

	Absorb BRS arm	CoCr-EES arm	p value
Overall	L = 98	L = 48	
TLF	9 (9.2)	3 (6.3)	0.58
TVF	11 (11.2)	4 (8.3)	0.29
Cardiac death	0 (0)	0 (0)	–
Target vessel MI	5 (5.1)	0 (0)	0.11
ID-TLR	4 (4.1)	3 (6.3)	0.50
ID-TVR	6 (6.1)	4 (8.3)	0.61
Scaffold/stent thrombosis	2 (2.0)	0 (0)	0.31
Binary restenosis	1 (1.0)	0 (0)	0.47
Small-vessel lesions*	**L = 32**	**L = 14**	
TLF	5 (15.6)	1 (7.1)	0.59
TVF	6 (18.8)	1 (7.1)	0.43
Cardiac death	0 (0)	0 (0)	–
Target vessel MI	1 (3.1)	0 (0)	0.51
ID-TLR	4 (12.5)	1 (7.1)	0.78
ID-TVR	5 (15.6)	1 (7.1)	0.56
Scaffold/stent thrombosis	0 (0)	0 (0)	–
Binary restenosis	1 (3.1)	0 (0)	0.48
Tapered-type lesions*	**L = 19**	**L = 10**	
TLF	3 (15.8)	1 (10.0)	0.92
TVF	5 (26.3)	1 (10.0)	0.42
Cardiac death	0 (0)	0 (0)	–
Target vessel MI	1 (3.1)	0 (0)	0.47
ID-TLR	2 (10.5)	1 (10.0)	0.71
ID-TVR	4 (21.1)	1 (10.0)	0.59
Scaffold/stent thrombosis	0 (0)	0 (0)	–
Binary restenosis	1 (5.3)	0 (0)	0.45

Values are number (%). Abbreviations as in Table 1. p value for Log-rank test. TLF was defined as a composite of cardiac death, target-vessel MI or ischemic-driven target lesion revascularization (ID-TLR) within 3 years. TVF was defined as a composite of cardiac death, target-vessel MI, ID-TLR or ischemic-driven target vessel revascularization (ID-TVR). *Subgroup analysis was performed only in lesions with both proximal and distal reference measurements at post-procedure because of the definitions of small-/large-vessel lesions and tapered-/non-tapered-type lesions.

Table 6
Acute device performance in small-vessel lesions: TLF versus non-TLF and TVF versus non-TVF.

Variables	TLF (L = 5)	Non-TLF (L = 27)	p value
Device volume index (mm^3/mm)	4.8 ± 1.2	4.9 ± 0.8	0.84
Minimum device area (mm^2)	3.6 ± 1.2	4.1 ± 0.8	0.38
%area expansion	0.72 ± 0.14	0.82 ± 0.15	0.16
%volume expansion	0.96 ± 0.10	0.99 ± 0.15	0.68
%area expansion ≥0.8	2 (40.0)	16 (59.3)	0.43
%volume expansion ≥1.1	0 (0)	6 (22.2)	0.13
Variables	TVF (L = 6)	Non-TVF (L = 26)	p value
Device volume index (mm^3/mm)	4.7 ± 1.1	4.9 ± 0.8	0.79
Minimum device area (mm^2)	3.6 ± 1.1	4.1 ± 0.8	0.32
%area expansion	0.72 ± 0.13	0.83 ± 0.15	0.12
%volume expansion	0.94 ± 0.11	1.00 ± 0.15	0.34
%area expansion ≥0.8	2 (33.3)	16 (61.5)	0.21
%volume expansion ≥1.1	0 (0)	6 (23.1)	0.09

Values are mean ± SD and number (%). Abbreviations as in Tables 1 and 5. Categorical comparisons were performed using chi-square test. Continuous values were compared using unpaired Student *t* test for percent volume and area expansion at post-procedure and Wilcoxon rank-sum test for the other variables.

at post-procedure and greater LLL at 3 years, which was uniquely observed in the Absorb BVS arm alone. In metallic stents, although suboptimal expansion has been consistently reported as the strong risk factor for instent restenosis, it is essentially because initial stent underexpansion can result in clinically significant lumen compromise even with minimal neointimal proliferation. To the best of our knowledge, no stent study has shown that initial underexpansion could directly increase LLL or affect arterial response after device implantation.

Although exact mechanisms for this observation would need further studies, the difference in the primary cause of LLL between metallic stents and bioresorbable scaffolds appears to play a key role. Indeed, the detailed serial IVUS analysis in the current study demonstrated that the larger lumen loss in lesions with suboptimal scaffold expansion was predominantly attributable to greater negative vessel remodeling, rather than neointimal proliferation seen as the primary mechanism for LLL in metallic stents. Several possible explanations could be hypothesized for this finding, based on material and design differences as well as unique long-term behavior of polymeric struts. First of all, the Absorb BVS is made of a lactic acid-based polymer with intrinsic differences in mechanical properties from metallic stents, which may possibly be augmented in a state of underexpansion. Technically, stents/scaffolds are designed to achieve the nominal radial strength in a fully expanded state measured in bench models. Indeed, despite the similar radial strength reported in bench testing, several *in vivo* studies have demonstrated that the Absorb BVS can show greater acute recoil than metallic stents, particularly in complex lesions where smaller device expansion was prominent in the Absorb BVS than in the CoCr-EES [14,17,18]. Another investigation of polymeric scaffold demonstrated the inverse trend between acute recoil and scaffold expansion, supporting the results of previous and current studies [19].

Relatively thick and wide struts of the first-generation BVS may also contribute to acute and chronic recoil by inducing constrictive vessel remodeling, especially at the segments with underexpansion. Scaffold underexpansion leads to the crowding of multiple thick struts with the larger footprint relative to vessel surface, potentially resulting in laminar-flow disturbance with low wall shear stress (WSS) between the struts [9,11,20,21]. The flow disturbance with low WSS attenuates the endothelial release of vasodilators, such as nitric oxide, prostacyclin I_2, and tissue plasminogen activator, and in turn increases release of vasoconstrictors (particularly, endhotelin-1), thereby favoring constrictive vessel remodeling with LLL [22–24].

Other potentially relevant factors may include non-uniform biodegradation process that could occur in a setting of suboptimal scaffold expansion. A study using bench test and *in vivo* implantation models demonstrated that strut degradation speed and location were closely related to the stress concentration on the scaffold after the implantation [25]. The non-uniform strut degradation may lead to chronic scaffold deformation and abnormal strut disintegration, which may further accentuate insufficient radial force and/or laminar-flow disturbance with resultant constrictive remodeling as mentioned earlier. At this point, it remains to be elucidated whether this unique association between initial device expansion and subsequent lumen loss is specific to the first-generation Absorb BVS or inherently seen in other bioresorbable scaffolds as well.

4.2. Incomplete strut apposition

Multiple studies of Absorb BVS have repeatedly identified that ISA was associated with an increased risk of scaffold thrombosis [12,20,26,27]. The present study was not powered to investigate the direct association of ISA with this infrequent event. However, despite no significant relationship between scaffold underexpansion and ISA at post-procedure, higher TLF rates tended to be seen in lesions with versus without post-procedural ISA in the Absorb BVS arm, suggesting that, unlike metallic platforms, isolated post-procedural ISA itself may have an impact on clinical outcomes after BVS implantation. One plausible explanation is that significantly thicker struts of Absorb BVS may disrupt the lamina flow and create eddies with areas of reversal of the flow behind the non-apposed struts, resulting in an heterogeneous WSS pattern

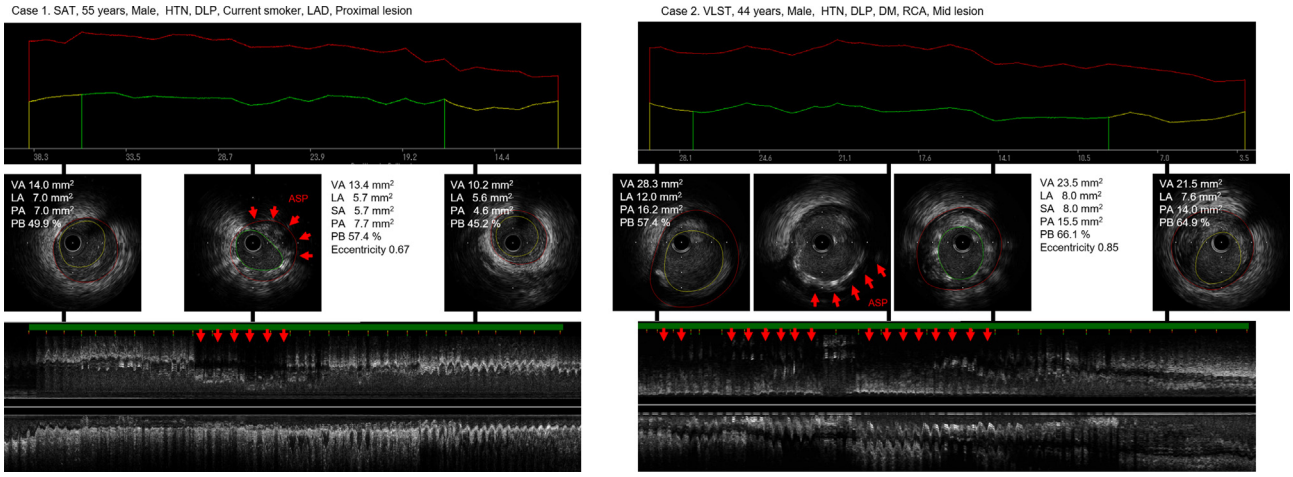

Fig. 9. Post-procedural images of scaffold thrombosis cases. In both cases, percent volume and area expansion were relatively preserved; however, non-uniform scaffold expansion and residual plaque burden with signal-attenuation within the target segment were observed at post-procedure.

and leading to the increased risks of both thrombosis and plaque/-neointimal proliferation [20,21].

Recent investigations suggest late scaffold discontinuity, followed by late scaffold ISA and neoatherosclerosis, as the leading cause of very late scaffold thrombosis (VLST) [11,20]. Theoretically, late scaffold discontinuity is a programmed (benign) phenomenon in bioresorption process of BVS. Indeed, previous and current studies have repeatedly reported discontinuous struts embedded in neointima without any clinical repercussion [11,20]. Conversely, uncovered struts not immobilized by neointima can protrude into the lumen, thus exposing the highly thrombogeneic remnant scaffold material to the blood flow (i.e., intraluminal scaffold dismantling), with subsequent activation of the coagulation cascade [20]. Especially, due to the larger strut thickness/width and abluminal surface area, BVS exert a lower penetrating pressure at the time of implantation, which might result in less embedment of struts in the vessel wall, leading to impaired neointimal encapsulation. The present study supports this and suggests that complete and functional neointimal coverage may be particularly important for avoiding the abnormal findings of resorption-related ISA and discontinuity, and ultimately preventing subsequent device-related thrombosis [11,20]. The present study also suggested that adequate device sizing (oversized device selection) with uniform expansion appeared to be important in reducing the occurrence of late ISA as a possible precursor of VLST.

5. Limitations

First, the sample size of the IVUS cohort of the ABSORB Japan trial was predetermined to test the secondary powered endpoint of the original trial (i.e. serial lumen area change from post-procedure to 3 years); therefore, the IVUS cohort was underpowered to perform detailed analyses of specific lesion subsets; clinical impact of our findings needs to be determined in larger studies with predefined endpoints. Second, since the ABSORB Japan trial enrolled a selected patient population with primarily stable coronary artery disease and single, *de novo,* relatively simple target lesions, the study results may not be generalized. Third, because pre-interventional IVUS was not mandated by the protocol, influence of underlying plaque types on scaffold expansion and arterial remodeling following Absorb BVS could not be evaluated in detail. Fourth, exact pathological mechanism for the association between suboptimal device expansion and negative vessel remodeling and its impact on long-term clinical outcomes remain to be investigated. Fifth, the resolution of IVUS is limited to evaluate ISA and residual edge dissection in detail, although our results were in line with those in the optical coherence tomography cohort [6]. Lastly, detailed analyses for the possible impacts of procedural techniques on post-procedural device under-expansion and subsequent long-term arterial responses require further studies.

6. Conclusions

Unlike CoCr-EES, under- and nonuniform device expansion were associated with greater negative remodeling and late lumen loss in Absorb BVS; this may in part account for the poorer outcomes after Absorb BVS implantation compared with CoCr-EES implantation in the lesions with suboptimal device expansion. Further studies are warranted to investigate appropriate deployment and optimization strategies, possibly different between polymer and metallic devices, and possible benefits of intravascular imaging guidance to improve long-term outcomes of scaffold implantation.

Clinical Registration

ClinicalTrials.gov, number NCT01844284.

CRediT authorship contribution statement

Hajime Kusano, Wai-Fung Cheong, and Krishnankutty Sudhir contributed to data curation and writing -review & editing -. Hideki Kitahara, Masayasu Ikutomi, Ryo Kameda, M. Brooke Hollak, Paul G. Yock and Peter J. Fitzgerald contributed to formal analysis and Writing -review & editing- as members of the intravascular ultrasound team of Stanford Medical Center. Jeffrey J. Popma contributed with formal analysis as the director of angiographic core laboratory of Beth Israel Deaconess Medical Center. Takeshi Kimura contributed to conceptualization, ddata curation, project administration, supervision, and Writing -review & editing-. Yasuhiro Honda also contributed with formal analysis and Writing -review & editing- as the corresponding author. Kozo Okada contributed to formal analysis, Writing -original draft- and Witing -review & editing- as the first author.

Declaration of Competing Interest

T.K., and J.J.P. are members of Advisory Board of Abbott Vascular; T.K. is a member of Advisory Board of Abbott Vascular Japan; K.S., H.

K., and W-F.C. are employees of Abbott Vascular; P.G.Y., and P.J.F received institutional research grant from Abbott Vascular; the other authors report no conflicts of interest with regards to this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100623.

References

[1] T. Kimura, K. Kozuma, K. Tanabe, S. Nakamura, M. Yamane, T. Muramatsu, et al., A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan, Eur. Heart J. 36 (2015) 3332–3342, https://doi.org/10.1093/eurheartj/ehv435.

[2] S.G. Ellis, D.J. Kereiakes, D.C. Metzger, R.P. Caputo, D.G. Rizik, P.S. Teirstein, et al., Everolimus-eluting bioresorbable scaffolds for coronary artery disease, N. Engl. J. Med. 373 (2015) 1905–1915, https://doi.org/10.1056/NEJMoa1509038.

[3] P.W. Serruys, B. Chevalier, D. Dudek, A. Cequier, D. Carrié, A. Iniguez, et al., A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial, Lancet 385 (2015) 43–54, https://doi.org/10.1016/S0140-6736(14)61455-0.

[4] R. Gao, Y. Yang, Y. Han, Y. Huo, J. Chen, B. Yu, et al., Bioresorbable vascular scaffolds versus metallic stents in patients with coronary artery disease: ABSORB China Trial, J. Am. Coll. Cardiol. 66 (2015) 2298–2309, https://doi.org/10.1016/j.jacc.2015.09.054.

[5] P.W. Serruys, B. Chevalier, Y. Sotomi, A. Cequier, D. Carrié, J.J. Piek, et al., Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial, Lancet 388 (2016) 2479–2491, https://doi.org/10.1016/S0140-6736(16)32050-5.

[6] Y. Onuma, Y. Sotomi, H. Shiomi, Y. Ozaki, A. Namiki, S. Yasuda, et al., Two-year clinical, angiographic, and serial optical coherence tomographic follow-up after implantation of an everolimus-eluting bioresorbable scaffold and an everolimus-eluting metallic stent: insights from the randomised ABSORB Japan trial, EuroIntervention 12 (2016) 1090–1101, https://doi.org/10.4244/EIJY16M09_01.

[7] D.J. Kereiakes, S.G. Ellis, C. Metzger, R.P. Caputo, D.G. Rizik, P.S. Teirstein, et al., 3-Year clinical outcomes with everolimus-eluting bioresorbable coronary Scaffolds: the ABSORB III trial, J. Am. Coll. Cardiol. 70 (2017) 2852–2862, https://doi.org/10.1016/j.jacc.2017.10.010.

[8] B. Xu, Y. Yang, Y. Han, Y. Huo, L. Wang, X. Qi, et al., Comparison of everolimus-eluting bioresorbable vascular scaffolds and metallic stents: three-year clinical outcomes from the ABSORB China randomised trial, EuroIntervention 14 (2018) e554–e561, https://doi.org/10.4244/EIJ-D-17-00796.

[9] J.J. Wykrzykowska, R.P. Kraak, S.H. Hofma, R.J. van der Schaaf, E.K. Arkenbout, A.J. IJsselmuiden, et al., Bioresorbable Scaffolds versus Metallic Stents in Routine PCI, N. Engl. J. Med. 376 (2017) 2319–2328. 10.1056/nejmoa1614954.

[10] C.M. Felix, V.J. van den Berg, S.E. Hoeks, J.-M. Fam, M. Lenzen, E. Boersma, et al., Mid-term outcomes of the Absorb BVS versus second-generation DES: a systematic review and meta-analysis, PLoS ONE. 13 (2018) e0197119, https://doi.org/10.1371/journal.pone.0197119.

[11] R. Virmani, H. Jinnouchi, A.V. Finn, Discontinuity: is it a major cause of scaffold thrombosis?, J. Am. Coll. Cardiol. 70 (2017) 2345–2348, https://doi.org/10.1016/j.jacc.2017.09.029.

[12] S. Puricel, F. Cuculi, M. Weissner, A. Schmermund, P. Jamshidi, T. Nyffenegger, et al., Bioresorbable coronary Scaffold thrombosis: multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors, J. Am. Coll. Cardiol. 67 (2016) 921–931, https://doi.org/10.1016/j.jacc.2015.12.019.

[13] P. Suwannasom, Y. Sotomi, Y. Ishibashi, R. Cavalcante, F.N. Albuquerque, C. Macaya, et al., The impact of post-procedural asymmetry, expansion, and eccentricity of bioresorbable everolimus-eluting scaffold and metallic everolimus-eluting stent on clinical outcomes in the ABSORB II trial, JACC Cardiovasc Interv. 9 (2016) 1231–1242, https://doi.org/10.1016/j.jcin.2016.03.027.

[14] K. Okada, Y. Honda, H. Kitahara, K. Otagiri, S. Tanaka, M.B. Hollak, et al., Bioresorbable scaffold for treatment of coronary artery lesions: intravascular ultrasound results from the ABSORB Japan trial, JACC Cardiovasc. Interv. 11 (2018) 648–661, https://doi.org/10.1016/j.jcin.2017.11.034.

[15] H. Kitahara, K. OKADA, T. Kimura, P.G. Yock, A.J. Lansky, J.J. Popma, et al., Impact of Stent Size Selection on Acute and Long-Term Outcomes After Drug-Eluting Stent Implantation in De Novo Coronary Lesions, Circ Cardiovasc Interv. 10 (2017) 103. 10.1161/CIRCINTERVENTIONS.116.004795.

[16] R. Moreno, C. Fernández, A. Sánchez-Recalde, G. Galeote, L. Calvo, F. Alfonso, et al., Clinical impact of in-stent late loss after drug-eluting coronary stent implantation, Eur. Heart J. 28 (2007) 1583–1591, https://doi.org/10.1093/eurheartj/ehl423.

[17] S. Puricel, D. Arroyo, N. Corpataux, G. Baeriswyl, S. Lehmann, Z. Kallinikou, et al., Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds, J. Am. Coll. Cardiol. 65 (2015) 791–801, https://doi.org/10.1016/j.jacc.2014.12.017.

[18] Y. Onuma, P.W. Serruys, J. Gomez, B. De Bruyne, D. Dudek, L. Thuesen, et al., Comparison of in vivo acute stent recoil between the bioresorbable everolimus-eluting coronary scaffolds (revision 1.0 and 1.1) and the metallic everolimus-eluting stent, Catheter Cardiovasc Interv. 78 (2011) 3–12, https://doi.org/10.1002/ccd.22864.

[19] Q. Wang, G. Fang, Y. Zhao, G. Wang, T. Cai, Computational and experimental investigation into mechanical performances of Poly-L-Lactide Acid (PLLA) coronary stents, J. Mech. Behav. Biomed. Mater. 65 (2017) 415–427, https://doi.org/10.1016/j.jmbbm.2016.08.033.

[20] K. Yamaji, Y. Ueki, G. Souteyrand, J. Daemen, J. Wiebe, H. Nef, et al., Mechanisms of very late bioresorbable Scaffold thrombosis: the INVEST registry, J. Am. Coll. Cardiol. 70 (2017) 2330–2344, https://doi.org/10.1016/j.jacc.2017.09.014.

[21] E. Tenekecioglu, R. Torii, C. Bourantas, Y. Sotomi, R. Cavalcante, Y. Zeng, et al., Difference in haemodynamic microenvironment in vessels scaffolded with Absorb BVS and Mirage BRMS: insights from a preclinical endothelial shear stress study, EuroIntervention 13 (2017) 1327–1335, https://doi.org/10.4244/EIJ-D-17-00283.

[22] Y.S. Chatzizisis, A.U. Coskun, M. Jonas, E.R. Edelman, C.L. Feldman, P.H. Stone, Role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling: molecular, cellular, and vascular behavior, J. Am. Coll. Cardiol. 49 (2007) 2379–2393, https://doi.org/10.1016/j.jacc.2007.02.059.

[23] C. Collet, Y. Sotomi, R. Cavalcante, P. Suwannasom, E. Tenekecioglu, Y. Onuma, et al., Coronary stent thrombosis: what have we learned?, J. Thorac. Dis. 8 (2016) 1398–1405, https://doi.org/10.21037/jtd.2016.05.69.

[24] B.D. Gogas, P.W. Serruys, R. Diletti, V. Farooq, S. Brugaletta, M.D. Radu, et al., Vascular response of the segments adjacent to the proximal and distal edges of the ABSORB everolimus-eluting bioresorbable vascular scaffold: 6-month and 1-year follow-up assessment: a virtual histology intravascular ultrasound study from the first-in-man ABSORB cohort B trial, JACC Cardiovasc. Interv. 5 (2012) 656–665, https://doi.org/10.1016/j.jcin.2012.02.017.

[25] Q. Luo, X. Liu, Z. Li, C. Huang, W. Zhang, J. Meng, et al., Degradation model of bioabsorbable cardiovascular stents, PLoS ONE 9 (2014) e110278–e110279, https://doi.org/10.1371/journal.pone.0110278.

[26] A. Karanasos, N. van Mieghem, N. van Ditzhuijzen, C. Felix, J. Daemen, A. Autar, et al., Angiographic and optical coherence tomography insights into bioresorbable scaffold thrombosis: single-center experience, Circ Cardiovasc Interv. 8 (2015) e002369–e002369. 10.1161/CIRCINTERVENTIONS.114.002369.

[27] S.G. Ellis, G. Steffenino, D.J. Kereiakes, G.W. Stone, R.J. van Geuns, A. Abizaid, et al., Clinical, angiographic, and procedural correlates of acute, subacute, and late absorb scaffold thrombosis, JACC Cardiovasc. Interv. 10 (2017) 1809–1815, https://doi.org/10.1016/j.jcin.2017.06.067.