Turk Kardiyol Dern Ars 2021;49(1):40-50 doi: 10.5543/tkda.2020.99249

ORIGINAL ARTICLE

Long-term outcomes of Absorb bioresorbable vascular scaffold using predilation, sizing, and postdilation protocol in a real-world patient population

Predilatasyon, uygun stent çapı, postdilatasyon protokolü ile takılan Absorb eriyebilen vasküler çatının uzun dönem gerçek yaşam takip sonuçları

Sinem Çakal, M.D., Beytullah Çakal, M.D., Oğuz Karaca, M.D., Bilal Boztosun, M.D.

Department of Cardiology, İstanbul Medipol University Faculty of Medicine, İstanbul, Turkey

ABSTRACT

Objective: Bioresorbable vascular scaffolds (BVSs) have been a disappointment in the evolution of drug-eluting stents used in percutaneous coronary intervention because an excessive number of thrombotic complications have been reported. The aim of this study was to evaluate long-term clinical outcomes of the Absorb BVS in patients treated using a predilation, proper sizing, and post-dilation implantation technique.

Methods: The records of 110 patients who had a total of 150 Absorb BVSs implanted were retrospectively analyzed. The rate of major adverse cardiovascular events (MACEs), defined as the composite of cardiac death, target vessel myocardial infarction (MI), and target-lesion revascularization were studied using quantitative coronary angiography.

Results: Of the study population, 80% were male and the mean age was 60±11.3 years. The most common diagnosis was stable angina (84%). The median length of follow-up was 53 months (range: 46–59 months). The rate of predilation and postdilation was 100%, and 95%, respectively. The 4-year rate of MACEs was 20%: cardiac death in 3 patients (2.7%), target vessel MI in 9 (8.2%), and target lesion revascularization in 20 (18.2%). Definite device thrombosis occurred in 6 of 110 patients (5.5%). One case of very late scaffold thrombosis was observed at 47 months. A small BVS diameter (2.5 mm) was found to be the most powerful independent predictor of a MACE (p=0.05).

Conclusion: The Absorb BVS was associated with an increased risk of adverse events, including late and very late device thrombosis, despite the use of a good implementation protocol.

ÖZET

Amaç: Eriyebilen vasküler çatı (EVÇ), ilaç kaplı stent teknolojisinde en heyecan verici gelişme olarak son yıllarda ön plana çıkmış fakat artmış tromboz komplikasyonları nedeniyle hayal kırıklığı yaşatmıştır. Bu çalışmada, çok büyük oranda predilatasyon-uygun çap postdilatasyon protokolü'ne uyarak Absorb EVÇ yerleştirilen hasta grubunda uzun dönem klinik sonuçlar araştırılmıştır.

Yöntemler: Bu geriye dönük çalışmaya 150 Absorb EVÇ yerleştirilen toplam 110 hasta dahil edildi. Uzun dönem takipte kardiyak ölüm, hedef damar miyokart enfarktüsü (ME), hedef lezyon revaskülarizasyonu olarak tanımlanan majör kardiyovasküler olaylar (MKO) değerlendirildi.

Bulgular: Çalışmaya katılan hastaların %80'i erkek, ortalama yaş 60±11.3 yıldı. En sık tanı %84 kararlı anjinaydı. Ortanca takip süresi 53 aydı (aralık 46–59 ay). Hastaların predilatasyon, postdilatasyon oranları sırasıyla %100, %95'ti. Dört yıllık takipte MKO oranı %20 bulundu. Hastaların 3'ünde (%2.7) kardiyak ölüm, 9'unda (%8.2) hedef damar ME ve 20'sinde (%18.2) hedef lezyon revaskülarizasyonu mevcuttu. Kesin çatı trombozu 6/110 (%5.5) hastada gözlemlendi. Bir hastada 47. ayda çok geç dönem çatı trombozu izlendi. Küçük BVS çapı (2.5 mm) MKO'ların en güçlü öngördürücüsü saptandı (p=0.05).

Sonuç: Absorb EVÇ, uygun yerleştirme protokolüne rağmen, artmış geç ve çok geç dönem çatı trombozunu da içeren olumsuz olaylarla ilişkilidir.

Received: June 01, 2020 *Accepted:* August 14, 2020

Correspondence: Dr. Sinem Çakal. İstanbul Medipol Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, İstanbul, Turkey.
Tel: +90 212 - 460 77 77 e-mail: sinemdnz@gmail.com

A bioresorbable vascular scaffold (BVS) represented a revolutionary alternative option to overcome the shortcomings of drug-eluting stents (DESs) in percutaneous coronary intervention (PCI).[1,2]

The initial analyses of the first commercially available everolimus-eluting BVS (Absorb; Abbott Vascular Inc., Santa Clara, CA, USA) used in de novo simple lesions showed non-inferior outcomes to metallic DESs in patients with stable coronary artery disease in short-term follow-up.[3] However, 3-year data from the Absorb II cohort raised questions regarding the long-term safety of an Absorb BVS due to a high rate of device-related thrombosis compared with DESs.[4] The mid- and long-term data of the AIDA (Amsterdam Investigator-initiateD Absorb Strategy All-comers Trial) were also disappointing, reporting a higher rate of late scaffold thrombosis compared with the XIENCE everolimus-eluting stent (EES) (Abbott Vascular, Inc., Santa Clara, CA, USA) (3.5% vs 0.9%; hazard risk [HR]: 3.87; 95% confidence interval [CI]: 1.78–8.42; p<.001).[5,6] A European medical device advisory task force recommended additional testing and study,[7] and in September 2017, the manufacturer halted sales of the first-generation Absorb BVS.

The aim of the present study was to analyze long-term clinical outcomes of Absorb BVS implantation performed with the predilation, sizing, and postdilation (PSP) implantation technique in a single high-volume PCI center.[8]

METHODS

Study design and population

This was an observational, retrospective, single-center study of consecutive patients treated for coronary artery disease at Istanbul Medipol University hospital, Turkey, between May 2014 and December 2016 with the Absorb BVS. The use of an Absorb BVS was at the discretion of the operator in charge. Clinical and procedural characteristics were assembled retrospectively from hospital medical records and follow-up data was collected through hospital visits and telephone consultations. This study was approved by the İstanbul Medipol University Faculty of Medicine Ethics Committee (Approval Date: 08/11/2019 Number: 10840098-604.01.01-E.60925). A total of 110 patients treated with 150 Absorb BVSs were included in the analysis.

Abbreviations:

BVS	*Bioresorbable vascular scaffold*
CI	*Confidence interval*
DAPT	*Dual anti-platelet therapy*
DES	*Drug-eluting stent*
EES	*Everolimus-eluting stent*
HR	*Hazard risk*
IQR	*Interquartile range*
IVUS	*Intravascular imaging*
MACE	*Major adverse cardiovascular event*
MI	*Myocardial infarction*
MLD	*Minimal lumen diameter*
P2Y12	*Adenosine diphosphate chemoreceptor*
PCI	*Percutaneous coronary intervention*
PSP	*Predilation, sizing, and postdilation*
QCA	*Quantitative coronary angiography*
RVD	*Reference vessel diameter*
TLF	*Target lesion failure*
TLR	*Target lesion revascularization*
TVR	*Target vessel revascularization*

Patients who were >18 years of age with evidence of myocardial ischemia, including those with stable coronary artery disease and acute coronary syndrome, with a reference vessel diameter (RVD) ≥2.50 mm were enrolled in the study. Stenosis of >50% was evident in the native coronary arteries of all of the treated lesions. The exclusion criteria were a left main coronary artery lesion, a saphenous vein graft lesion, or the presence of a lesion requiring stents >4.0 mm or <2.5 mm. No restrictions were applied for the number of lesions and vessels treated, lesion length, or the number of implanted stents.

Absorb bioresorbable vascular scaffold implantation

The implantation of an Absorb BVS according the principles of the PSP technique was not mandatory, but was highly recommended given the circumstances at the time. Angiographic assessments of BVS size and position were based on visual assessment using a guiding catheter as a reference for calibration, the length of opaque wire sections, and balloon length. Predilation was performed with compliant or non-compliant balloons. Generally, for more calcified lesions, a Scoreflex balloon (OrbusNeich Medical Co. Ltd., Hong Kong, China) or an AngioSculpt PTA scoring balloon (AngioScore Inc., Fremont, CA, USA) was preferred. The implantation of a scaffold was performed with a gradual increase of 1 atm of pressure every 5 seconds, without exceeding the rated burst pressure. The balloon was then rapidly deflated, reinflated, and kept at nominal pressure for 15–30 seconds. Finally, another angiogram was performed to evaluate BVS expansion. Postdilation was performed with non-compliant balloons with the same size BVS or 0.25–0.5 mm larger. Long-segment lesions (>28 mm) that could not be covered with a single BVS therefore

required a BVS-BVS or DES-BVS combination. An overlapping BVS-BVS was used in prognostically significant segments and vessels, such as the left atrial descending artery, to enable future surgical vessel grafting options. Overlapping DES-BVS was typically preferred if a BVS longer than 28 mm was not available or there were special lesion characteristics of calcification, tortuosity, or bifurcation. In some cases, easier insurance reimbursement was also a factor. All of the patients were anticoagulated with unfractionated heparin to achieve an activated clotting time of 250 seconds. All of the patients were treated with dual anti-platelet therapy (DAPT) for at least 12 months after the procedure. The need for specific treatment strategies, such as additional stent implantation after postdilation were left to the operator's discretion.

Quantitative coronary angiography (QCA) was performed offline using standard techniques with automated edge detection algorithms (CAAS 5.7.1, Pie Medical Imaging BV, Masstricht, The Netherlands) in the hospital's angiographic analysis center. RVD, minimal lumen diameter (MLD), stenosis percentage, MLD after stent implantation, and acute gain (defined as the difference between MLD postprocedure and MLD preprocedure) were measured. Binary angiographic restenosis was defined as stenosis of >50% of the luminal diameter in the target segment. A bend of >45° proximal to the lesion was defined as tortuosity. A single bend of 45–90° proximal to the lesion was defined as mild tortuosity, while 3 or more of 45–90° or one or more >90° was defined as severe tortuosity. Bends not meeting these criteria (mild and severe tortuosity) were defined as moderate tortuosity.[9] Calcification was defined as overt radiopacity of the vessel wall across the lesion site. It was classified as moderate (radiopacity noted only during the cardiac cycle before contrast injection) or severe (radiopacity noted across both sides of the vessel wall before contrast injection and independent of cardiac motion).[10]

Angiographic success was defined as <30% residual diameter stenosis as determined by QCA with a Thrombolysis In Myocardial Infarction grade 3 flow in the treated target vessel. Procedural success was defined as angiographic success in the absence of in-hospital death, myocardial infarction (MI), or revascularization.

Outcomes and definitons

The primary outcomes of the study were a major adverse cardiovascular event (MACE), which was a composite of cardiac death, target vessel MI, and clinically-driven target lesion revascularization (TLR). TLR was defined as any revascularization within 5 mm of the scaffold. Target vessel revascularization (TVR) was defined as repeat PCI or coronary artery bypass graft in the target vessel. Deaths were considered cardiac-related unless a non-cardiac cause was identified. All components of the composite endpoint, and definite stent thrombosis was determined according to the Academic Research Consortium.[11]

Statistical analysis

Continuous variables were expressed as mean±SD or median and interquartile range (IQR), as appropriate. Categorical variables were expressed as number and percentage. The Kolmogorov-Smirnov test was used to test the normality of distribution of continuous variables. A chi-squared test or Fisher's exact test was used to compare binary variables, and Student's t-test or a non-parametric test was used to compare continuous variables. Cumulative event rates were estimated using the Kaplan-Meier method. Cox regression analysis was used to identify the factors affecting the occurrence of a MACE. IBM SPSS Statistics for Windows, Version 23.0 software (IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis.

RESULTS

Baseline characteristics

The demographic characteristics of the overall cohort and the groups with overlapping stents are presented in Table 1. A total of 110 patients with 150 scaffolds were enrolled in the study. Overlapping techniques with a DES or BVS were used in 49 patients (BVS-BVS: 19 patients, DES-BVS: 30 patients). The patients were predominantly male (80%), with a mean age of 60±11.3 years, and there was a high prevalence of stable angina (84%). Diabetes mellitus was present in 38% of the patients, while hypertension, hyperlipidemia, and a current smoking history were recorded in 62%, 65%, and 42%, respectively.

Procedural and angiographic characteristics of the bioresorbable vascular scaffold implantation

Table 2 illustrates the procedural and angiographic

Table 1. Patient characteristics

Variable	BVS (n=110)			Overlap (n=49)		
	n	%	Mean±SD	n	%	Mean±SD
Age (years)			60±11.3			60±10.5
Gender (male)	88	80		41	89	
Hypertension	68	62		27	59	
Diabetes	42	38		21	46	
Hyperlipidemia	71	65		30	64	
Smoking	47	42		18	39	
Family history of coronary artery disease	39	35		18	28	
Myocardial infarction history	23	21		12	26	
Clinical presentation						
Stable angina	92	84		39	85	
Acute coronary syndrome	18	16		7	15	
Heart failure	12	11		5	11	
Ejection fraction			55.5±9.1			55.3±9.6
Hemoglobin (g/dL)			13.4±1.6			13.2±1.7
Platelet count (cells/mm^3)			231±58			227±51
Creatinine (mg/dL)			1.08±0.88			1.13±1.15
Chronic kidney disease	13	12		7	15	
Prior coronary artery by-pass grafting	7	6.4		3	7	
Potent P2Y12 inhibitors	62	56		25	54	

BVS: Bioresorbable vascular scaffold; P2Y12: Adenosine diphosphate receptor; SD: Standard deviation.

characteristics of the lesions treated. Most were in the anterior descending coronary artery (51%), followed by the right coronary (30%) and circumflex (19%) arteries. The mean number of Absorb BVSs implanted per patient was 1.4±0.6. Predilation was performed in all lesions and postdilatation in 95% of the treated lesions. The clinical success of the device was 98%, as well as the procedural clinical success (n=108/110, 98%). Offline QCA indicated that the mean grade of stenosis was 80.3±12.4%, the lesions had a RVD of 3.13±0.44 mm and that the median length of the scaffold per patient was 28 mm (IQR: 17 mm). Most of the lesions (58%) treated with an Absorb BVS were classified as type A or B1 (American Heart Association/American College of Cardiology classification).

Approximately half (51%) of the patients had at least 2 scaffolds implanted. Two BVSs were overlapped in 19 lesions, and an overlapping of BVS and a DES was performed in 31 lesions (Table 3). The overlap patients had more complex lesion morphologies compared with the non-overlap group in terms of tortuosity, lesion calcification, and C-type lesions. Bifurcation lesions were more frequent in the DES-BVS group (Table 3). The implanted stent/scaffold length did not differ significantly between the DES-BVS group (55.2 mm±11 mm) and the BVS-BVS group (49.3 mm±9.6 mm). One patient had a periprocedural MI, and another patient suffered scaffold rupture, which was managed with prolonged balloon inflatation. More than half (57%) of the patients used potent adenosine diphosphate chemoreceptor (P2Y12) inhibitor treatment during first year (Table 1).

Clinical outcomes

Outcomes of the overall cohort and the overlap groups are provided in Table 4. The BVS-BVS overlap and DES-BVS overlap groups had similar clinical outcomes. The median length of follow-up was 53 months (IQR: 46–59 months). The MACE rate was 10% at the 12-month follow-up, 20% at the 4-year

Table 2. Angiographic and procedural characteristics

	BVS (n=150)		BVS (n=150)
Vessels diseased per patient	1.6±0.6	Angiographic features	
Vessels treated, n (%)		Total scaffold length per patient, mm, n (%)	28 (17)
Left anterior descending	77 (51)	Stenosis percentage (%)	80.3±12.4
Circumflex	28 (19)	Minimum lumen diameter, mm	0.6±0.40
Right coronary artery	45 (30)	Reference vessel diameter, mm	3.13±0.44
Number of scaffolds per patient, n (%)		Final minimum lumen diameter, mm	2.91±0.41
1	76 (49)	Acute gain, mm	1.49±0.61
2	27 (36)	Stent diameter, mm	3.1±0.41
3	5 (10)	Predilation balloon size, mm	2.87±0.46
4	2 (5)	Postdilation balloon size, mm	3.25±0.47
Number of scaffolds per patient, mean±SD	1.4 ±0.6	Calcification moderate/severe	26 (17)/13 (8)
Number of BVSs per lesion, mean±SD	1.18±0.4	CTO, n (%)	10 (6.7)
Overlap with BVS, n (%)	19 (13)	In-stent restenosis, n (%)	6 (4.6)
Overlap with DES, n (%)	31 (21)	Bifurcation, n (%)	36 (24)
Femoral access, n (%)	90 (82)	Moderate-severe tortuosity, n (%)	21 (14)/14 (9.3)
Radial access, n (%)	20 (18)	Location, n (%)	
Procedural technique, n (%)		Ostial	4 (2.5)
Pre-dilatation	150 (100)	Proximal	22 (14.6)
Compliant balloon	64 (43)	Mid	94 (62.6)
Scoring balloon	80 (53)	Distal	30 (19.3)
Post-dilatation	142 (95)	Lesion type, n (%)	
Device success	149 (99)	A	34 (23)
Procedural sucess	108 (98)	B1	53 (35)
Procedural complication, n (%)		B2	47 (31)
Slow-flow	1 (1)	C	16 (11)
Scaffold rupture	1 (1)		

DES: Drug-eluting stent; BVS: Bioresorbable vascular scaffold; CTO: Chronic total occlusion; SD: Standard deviation.

follow-up, and 23.6% at the end of the study follow-up period. The 4-year Kaplan-Meier estimate of MACE was 20% (Fig. 1). There were 3 (2.7%) cases of cardiac death, 20 (18.2%) cases of target lesion revascularization, and 9 (8.2%) cases of target vessel MI. Two non-cardiac deaths were due to prostate cancer at 23 and 56 months, and a third patient died of gastric cancer. The rate of early and late device thrombosis was 1.8% and 2.7%, respectively, and very late events continued to accrue beyond 1 year (5.5%). Table 5 provides a detailed description of the cases with definite stent thrombosis. Univariate Cox regression analysis indicated that only a small BVS diameter (2.5 mm) was a risk factor for the development of a MACE during follow-up (HR: 2.23; 95% CI: 0.97–2.23; p=0.05) (Table 6).

DISCUSSION

To the best of our knowledge, this is the largest long-term analysis of Absorb BVS real-world outcomes from a single high-volume center in Turkey. We found that the long-term incidence of MACE was primarily driven by a higher rate of TLR and MI, as well as early, late, and very late scaffold thrombosis events. A higher rate of a MACE was observed despite the greater use of a PSP implantation strategy and more frequent use of P2Y12 inhibitors compared with other Absorb BVS studies.[12]

After initial enthusiasm for the use of a BVS, poor clinical outcomes in terms of TLR and scaffold thrombosis of the Absorb BVS, the most comprehen-

Table 3. Angiographic and lesion features of overlap and non-overlap groups

	No overlap (81 BVSs)	BVS-DES overlap (31 BVSs)	BVS-BVS overlap (38 BVSs)	*p*
Number of BVSs/patient	1.28±0.57	1.04±0.2	2.33±0.59	<0.001*
Vessels treated, n (%)				
LAD	38 (47)	21 (68)	18 (47)	0.12
CX	19 (24)	1 (3)	8 (22)	0.044**
RCA	24 (29)	9 (29)	12 (31)	0.96
ACC/AHA lesion complexity, n (%)				
A	37 (46)	4 (13)	4 (10)	<0.001***
B1	27 (33)	6 (19)	14 (37)	0.19
B2	16 (20)	12 (39)	14 (37)	0.05
C	1 (1)	9 (29)	6 (16)	<0.001***
Total lesion length, mm	19.9±6.1	46.2±7.7	42.8±8.4	<0.001***
Total BVS/DES length/patient, (mm)	25.3±7.6	55.2±11	49.3±9.63	<0.001***
BVS/DES diameter (mm)	3.05±0.41	3.03±0.37	3.09±0.37	0.82
Predilatation balloon size, mm	2.86±0.45	2.98±0.47	2.81±0.44	0.29
Postdilatation baloon size, mm	3.29±0.49	3.26±0.46	3.15±0.45	0.31
Tortuosity, n (%)				
Moderate	6 (8)	7 (23)	8 (21)	<0.001***
Severe	0	7 (23)	7 (18)	<0.001***
Calcification, n (%)				
Moderate	8 (10)	10 (32)	8 (21)	<0.001***
Severe	0	7 (23)	6 (17)	<0.001***
QCA Analysis				
Stenosis percentage (%)	80±12.3	83.9±11.3	78.1±13.3	0.14
MLD, mm	0.63±0.4	0.49±0.35	0.66±0.43	0.17
RVD, mm	3.16±0.42	3.1±0.44	3.1±0.44	0.63
FminLD, mm	2.94±0.4	2.90±0.37	2.87±0.44	0.68
Acute gain, mm	1.48±0.57	0.45±0.68	1.55±0.63	0.77
Bifurcation, n (%)	7 (9)	19 (61)	10 (26)	<0.001*
CTO, n (%)	1 (1)	3 (10)	6 (16)	0.007***
In-stent restenosis, n (%)	3 (4.7)	3 (9.6)	0	0.31

ACC/AHA: American College of Cardiology/American Heart Association; BVS: Bioresorbable vascular scaffold; CTO: Chronic total occlusion; CX: Circumflex; DES: Drug-eluting stent; FminLD: Final minimum lumen diameter; LAD: Left anterior descending; MLD: Minimum lumen diameter; QCA: Quantitative coronary angiography; RCA: Right coronary artery; RVD: Reference vessel diameter.
*Post-hoc analysis showed significant differences between all of the subgroups.
**Post-hoc analysis showed significant differences between the BVS-DES group and the other 2 subgroups in CX vessels.
*** Post-hoc analysis showed significant differences between the no-overlap group and the other 2 subgroups.

sively studied BVS, have hampered the clinical use of BVSs.[13] A meta-analysis of 4 randomized BVS trials assigning patients to an Absorb BVS (n=2164) or a DES (n=1225) resulted in higher 3-year rates of target lesion failure (TLF) in the Absorb BVS group (11.7% versus 8.1%; p=0.006).[14] The manufacturer withdrew the Absorb BVS from the market, and the implementation of BVS was given a class III indication in clinical practice outside of studies in the current European Society of Cardiology guidelines.[15,16] Scaffold discontinuities as a result of intraluminal scaffold dismantling can precipitate thrombosis

Table 4. Clinical outcomes

	Total cohort (n=110)	DES-BVS (n=30)	BVS-BVS (n=19)	*p*
One year, n (%)				
All-cause death	2 (1.8)	0	1 (5.2)	NA
Cardiac death	2 (1.8)	0	1 (5.2)	NA
TV-MI	5 (4.5)	1 (3.3)	3 (15.7)	1
Definite scaffold thrombosis	3 (2.7)	1 (3.3)	1 (5.2)	NA
TVR	9 (8.2)	3 (10)	2 (10.5)	0.95
TLR	8 (7.3)	2 (6.7)	2 (10.5)	0.64
MACE	11 (10)	3 (10)	3 (15.7)	0.67
Four years, n (%)				
All-cause death	5 (4.5)	1 (3.3)	1 (5.2)	NA
Cardiac death	3 (2.7)	1 (3.3)	1 (5.2)	NA
TV-MI	9 (8.2)	4 (13.3)	3 (15.7)	0.81
Definite scaffold thrombosis	6 (5.5)	3 (10)	2 (10.5)	0.36
TVR	20 (18.2)	8 (26.6)	4 (21)	0.74
TLR	20 (18.2)	8 (26.6)	4 (21)	0.74
MACE	6 (5.5)	8 (26.6)	5 (16.7)	0.97
Complete follow-up, n (%)				
All-cause death	5 (4.5)	1 (3.3)	1 (5.2)	NA
Cardiac death	3 (2.7)	1 (3.3)	1 (5.2)	NA
TV-MI	9 (8.2)	4 (13.3)	3 (15.7)	0.81
Definite scaffold thrombosis	6 (5.5)	2 (6.7)	3 (5.2)	0.3
TVR	24 (21.8)	9 (30)	4 (21)	0.48
TLR	24 (21.8)	9 (30)	4 (21)	0.48
MACE	26 (23.6)	9 (30)	5 (16.7)	0.78

BVS: Bioresorbable vascular scaffold; DES: Drug-eluting stent; MACE: Major adverse cardiac event; TLR: Target lesion revascularization; TV-MI: Target vessel myocardial infarction; TVR: Target vessel revascularization.

and/or restenosis more than a year after implantation. An appropriate implantation technique with careful device sizing, appropriate expansion through long periods of balloon inflation, extensive use of post-dilation, and intracoronary imaging guidance in order to accurately assess the dimensions of the vessel and detect the presence of possible calcification were considered to be particularly important during BVS implantation in contrast to current-generation DESs because of the larger strut thickness and less radial strength. Special attention to intravascular imaging (IVUS) is called for when a BVS is implanted, especially in long, complex lesions requiring overlapping, since the stacked struts of BVSs can reach a thickness of ~300 μm in overlap areas. One of the major factors hypothesized to be a determining factor in adverse outcomes is a suboptimal implantation technique. Though a precise optimal definition of PSP implantation remains unknown, the importance of adherence to PSP is frequently emphasized.[8,17] Postdilatation rates of <50% and varying PSP protocols have been reported in previous large-scale, randomized clinical trials and cohort studies.[18] Puricel et al.[13] noted that in a multicenter registry of 1305 patients implanted with an Absorb BVS, the rate of scaffold thrombosis declined significantly in patients when a strategy optimized for BVS was applied rather than a DES-oriented implantation strategy. However, despite optimal implantation practice, in the COMPARE-ABSORB trial, a substantially increased risk of TLF was found in complex de novo target lesions, defined as at least 28 mm in length, located in a small vessel, and with

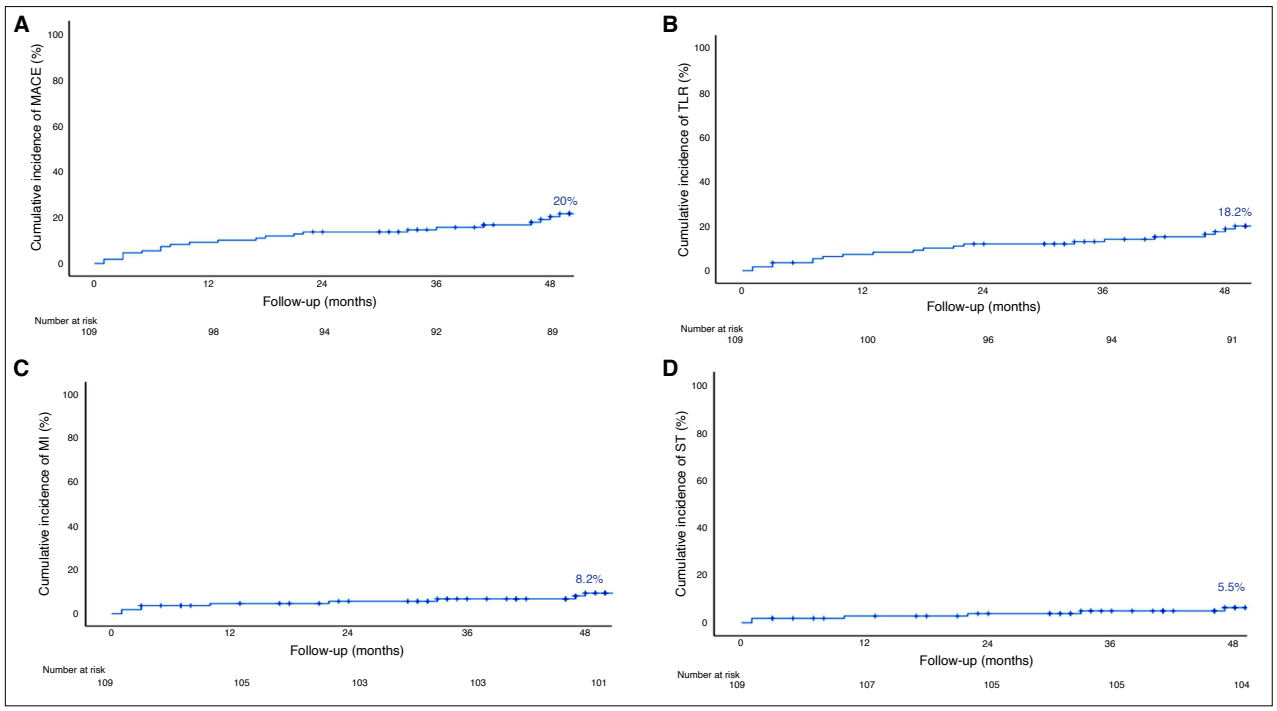

Figure 1. (A-D) Cumulative event curves for major adverse cardiac events calculated using the Kaplan-Meier method. TLR: Target lesion revascularization; MACE: Major adverse coronary event; MI: Myocardial infarction; ST: Stent thrombosis.

a pre-existing total occlusion or bifurcation.[19] In our study, a small BVS diameter (2.5 mm) was the only predictor of a MACE, which is consistent with the results of previous studies.[13,20] In the prospective AIDA trial, scaffold implantation according to an optimised PSP protocol did not result in lower stent thrombosis or TLR rates. The estimated 2-year event rate for TLF (a composite of cardiac death, MI and TVR) was 11.0% for the Absorb BVS and 9.9% for the cobalt-chromium EES (p=0.003 for non-inferiority).[17,21] The careful attention paid to the implantation technique in our study (predilatation: 100%,

Table 5. Detailed description of the cases of scaffold thrombosis

Case	Initial PCI indication	Treated vessel	Lesion type	Calcification	Postdilation	Scaffold size	New P2Y12	Thrombosis (months)	Treatment
1	SAP	LAD	C	No	Yes	2.5x28	No	1	Thrombus aspiration
2	SAP	RCA	C	Yes	Yes	2.5x18, 3.5x18 overlapped with 3x33 Xience	Yes	1	Thrombus aspiration
3	SAP	LAD	B1	No	Yes	2.5x28	No	10	Multiple balloon inflations GIIbIIIa inhibitor
4	SAP	RCA	A	No	Yes	3.0x28	Yes	22	3x28 Xience GIIbIIIa inhibitor
5	ACS	RCA	B2	Yes	Yes	3.5x18 overlapped with 3.5x18 Resolute Integrity	Yes	33	3.0x38 Resolute Integrity
6	SAP	RCA	B2	Yes	Yes	3.0x28 overlapped with 3.5x38 Xience	No	47	Thrombus aspiration 3.0x38 Ultimaster Tansei

ACS: Acute coronary syndrome; LAD: Left anterior descending; P2Y12: Adenosine diphosphate receptor; PCI: Percutaneous coronary intervention; RCA: Right coronary artery; SAP: Stable angina pectoris.

Table 6. Factors associated with major adverse cardiac events at 4 years

	Univariate	
	HR (95% CI)	p
Age	0.98 (0.95–1.02)	
Gender	1.15 (0.43–3.14)	0.77
Hypertension	1.34 (0.55–3.4)	0.52
Diabetes	1.09 (0.47–2.57)	0.83
Hyperlipidemia	1.17 (0.47–2.86)	0.74
Smoker	0.75 (0.31–1.78)	0.52
Acute coronary syndrome	1.73 (0.63–4.7)	0.28
Heart failure	2.03 (0.68–6.01)	0.2
Overlapping	1.94 (0.83–4.55)	0.13
Total DES/BVS length	1.01 (0.99–1.03)	0.27
B2 or C lesion	1.14 (0.49–2.63)	0.76
Small BVS diameter (2.5 mm)	2.23 (0.97–5.16)	0.06

BVS: Biovascular scaffold; DES: Drug-eluting stent; HR: Hazard risk; CI: Confidence interval.

postdilatation: 95%) is consistent with this concept. Nonetheless, while optimization of the implantation technique appears to be of great importance, we still detected a higher MACE rate in our study. Therefore, the effect of an optimal implantation technique on BVS outcomes remains controversial.

Conflicting results from clinical studies have challenged the expectation that complete scaffold degradation occurred within 3–4 years after BVS implantation. Sotomi et al.[22] evaluated the causes of acute and subacute scaffold thrombosis and determined that the most frequent causes of thrombosis were malapposition (23.5%), uncovered struts (17.6%), strut under-deployment (11.8%), acute scaffold disruption (5.9%), overlapping stents (5.9%), and acute scaffold recoil (5.9%). Malapposition and late scaffold discontinuity (34.6% and 30.8%, respectively) were the most common mechanism of thrombosis in late and very late phases. Scaffold thrombosis could be prevented with an appropriate PSP protocol, however, even when optimal PSP technique was applied, extensive scaffold discontinuity with struts protruding into the lumen might cause late scaffold thrombosis. The AIDA and ABSORB III trials and subsequent meta-analyses clearly showed that very late scaffold thrombosis was significantly more frequent after 1 year of implantation with the ABSORB BVS than with the cobalt-chromium EES.[15,23] Whether these events are linked to interruption of dual antiplatelet therapy remains uncertain. Data from the INVEST registry showed that at the time of very late scaffold thrombosis, the majority of patients (83%) were receiving aspirin monotherapy and that a minority were still receiving DAPT.[24] Corroborating previous results, we also observed early, late, and very late scaffold thrombosis events. In our series, there were 3 cases of late thrombosis, 1 of which occurred 47 months after device implantation with ongoing aspirin therapy. We had a higher rate of potent P2Y12 inhibitor use (57%) compared with randomized Absorb BVS trials (Absorb Japan, Absorb China, Absorb III, which had rates of 21–24%).[25] Prolonged use of P2Y12 antagonists, which have been associated with more potent antiplatelet activity than clopidogrel, has been advocated, however, whether this strategy leads to a reduction of very late scaffold thrombosis remains unproven. Moreover, prolongation of dual antiplatelet therapy increases the risk of bleeding events.

Limitations

A small sample size and the lack of randomization or blinding constitute significant limitations in the design of this study. The decision to implant an Absorb BVS was left to the operator; therefore, selection bias cannot be ruled out, and the lack of IVUS guidance is an additional limitation. The absence of IVUS could have, at least in part, had an impact on the adverse events observed in the overlap groups. IVUS was used in only some cases in published BVS trials.[8] Further studies are required to determine whether improved outcomes can be achieved with routine IVUS. Some of the adverse events seen in the current study could be related to DES-BVS overlapping. Since routine angiography and imaging modalities during follow-up were not performed, we may have missed non-clinical BVS stenosis.

Conclusion

Despite greater use of P2Y12 inhibitors and very strict adherence to PSP protocol, we found that the MACE rate was high and that cases of very late stent thrombosis continued to accrue during long-term follow-up after Absorb BVS implantation in a patient population reflecting routine clinical practice.

Funding: This research did not receive any specific grant from any funding agency.

Ethical statement: This study was approved by the

İstanbul Medipol University Faculty of Medicine Ethics Committee (Approval Date: 08/11/2019 Number: 10840098-604.01.01-E.60925).

Peer-review: Externally peer-reviewed.

Conflict-of-interest: None.

Funding: No funding to declare.

Authors' Contribution: All authors provided critical feedback and helped shape the research, analysis and manuscript.

Authorship contributions: Concept: B.Ç., S.Ç.; Design: B.B., O.K.; Supervision: B.B., B.Ç.; Materials: B.Ç., S.Ç.; Data: B.Ç.; Analysis: B.B., O.K.; Literature search: S.Ç., B.Ç.; Writing: B.Ç., O.K.; Critical revision: B.B., O.K.

REFERENCES

1. Serruys PW, Garcia-Garcia HM, Onuma Y. From metallic cages to transient bioresorbable scaffolds: change in paradigm of coronary revascularization in the upcoming decade? Eur Heart J 2012;33:16–25b.
2. Caiazzo G, Kilic ID, Fabris E, Serdoz R, Mattesini A, Foin N, et al. Absorb bioresorbable vascular scaffold: What have we learned after 5 years of clinical experience? Int J Cardiol 2015;201:129–36.
3. Ellis SG, Kereiakes DJ, Metzger DC, Caputo RP, Rizik DG, Teirstein PS, et al. Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease. N Engl J Med 2015;373:1905–15.
4. Serruys PW, Chevalier B, Sotomi Y, Cequier A, Carrie D, Piek JJ, 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 2016;388:2479–91.
5. Kerkmeijer LSM, Tijssen RYG, Hofma SH, van der Schaaf RJ, Arkenbout KE, Kraak RP, et al. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent in routine PCI: three-year clinical outcomes from the AIDA trial. EuroIntervention 2019;15:603–6.
6. Wykrzykowska JJ, Kraak RP, Hofma SH, van der Schaaf RJ, Arkenbout EK, AJ IJ, et al. Bioresorbable Scaffolds versus Metallic Stents in Routine PCI. N Engl J Med 2017;376:2319–28.
7. Byrne RA, Stefanini GG, Capodanno D, Onuma Y, Baumbach A, Escaned J, et al. Report of an ESC-EAPCI Task Force on the evaluation and use of bioresorbable scaffolds for percutaneous coronary intervention: executive summary. Eur Heart J 2018;39:1591–601.
8. Ortega-Paz L, Capodanno D, Gori T, Nef H, Latib A, Caramanno G, et al. Predilation, sizing and post-dilation scoring in patients undergoing everolimus-eluting bioresorbable scaffold implantation for prediction of cardiac adverse events: development and internal validation of the PSP score. EuroIntervention 2017;12:2110–7.
9. Ho HH, Jafary FH, Loh KK, Tan JK, Ooi YW, Ong PJ. Deliverability of integrity coronary stents in severely tortuous coronary arteries: a preliminary experience. J Invasive Cardiol 2012;24:650–4.
10. Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Chuang YC, et al. Patterns of calcification in coronary artery disease. A statistical analysis of intravascular ultrasound and coronary angiography in 1155 lesions. Circulation 1995;91:1959–65.
11. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344–51.
12. Stone GW, Abizaid A, Onuma Y, Seth A, Gao R, Ormiston J, et al. Effect of Technique on Outcomes Following Bioresorbable Vascular Scaffold Implantation: Analysis From the ABSORB Trials. J Am Coll Cardiol 2017;70:2863–74.
13. Puricel S, Cuculi F, Weissner M, Schmermund A, Jamshidi P, Nyffenegger T, et al. Bioresorbable Coronary Scaffold Thrombosis: Multicenter Comprehensive Analysis of Clinical Presentation, Mechanisms, and Predictors. J Am Coll Cardiol 2016;67:921–31.
14. Ali ZA, Gao R, Kimura T, Onuma Y, Kereiakes DJ, Ellis SG, et al. Three-Year Outcomes With the Absorb Bioresorbable Scaffold: Individual-Patient-Data Meta-Analysis From the ABSORB Randomized Trials. Circulation 2018;137:464–79.
15. Ali ZA, Serruys PW, Kimura T, Gao R, Ellis SG, Kereiakes DJ, et al. 2-year outcomes with the Absorb bioresorbable scaffold for treatment of coronary artery disease: a systematic review and meta-analysis of seven randomised trials with an individual patient data substudy. Lancet 2017;390:760–72.
16. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87–165.
17. Tijssen RYG, Kraak RP, Elias J, van Dongen IM, Kalkman DN, Nassif M, et al. Implantation techniques (predilatation, sizing, and post-dilatation) and the incidence of scaffold thrombosis and revascularisation in lesions treated with an everolimus-eluting bioresorbable vascular scaffold: insights from the AIDA trial. EuroIntervention 2018;14:e434–e42.
18. Gori T, Weissner M, Gonner S, Wendling F, Ullrich H, Ellis S, et al. Characteristics, Predictors, and Mechanisms of Thrombosis in Coronary Bioresorbable Scaffolds: Differences Between Early and Late Events. JACC Cardiovasc Interv 2017;10:2363–71.
19. Danzi GB, Bernelli C, Cerrato E. Outcomes of Optimised Implantation Technique with Bioresorbable scaffolds: A Pooled Analysis of ABSORB-IV and COMPARE-ABSORB Trials. Cardiovasc Revasc Med 2020;21:559–61.
20. Ishibashi Y, Nakatani S, Sotomi Y, Suwannasom P, Grundeken MJ, Garcia-Garcia HM, et al. Relation Between Bioresorbable Scaffold Sizing Using QCA-Dmax and Clinical

Outcomes at 1 Year in 1,232 Patients From 3 Study Cohorts (ABSORB Cohort B, ABSORB EXTEND, and ABSORB II). JACC Cardiovasc Interv 2015;8:1715–26.

21. Tijssen RYG, Kerkmeijer LSM, Takahashi K, Kogame N, Katagiri Y, Kraak RP, et al. The influence of implantation techniques on lesion oriented-outcomes in Absorb BVS and Xience EES lesions treated in routine clinical practice at complete three year follow-up: AIDA trial QCA substudy. Int J Cardiovasc Imaging 2020;36:565–75.
22. Sotomi Y, Suwannasom P, Serruys PW, Onuma Y. Possible mechanical causes of scaffold thrombosis: insights from case reports with intracoronary imaging. EuroIntervention 2017;12:1747–56.
23. Montone RA, Niccoli G, De Marco F, Minelli S, D'Ascenzo F, Testa L, et al. Temporal Trends in Adverse Events After Everolimus-Eluting Bioresorbable Vascular Scaffold Versus Everolimus-Eluting Metallic Stent Implantation: A Meta-Analysis of Randomized Controlled Trials. Circulation 2017;135:2145–54.
24. Yamaji K, Raber L, Windecker S. What determines long-term outcomes using fully bioresorbable scaffolds - the device, the operator or the lesion? EuroIntervention 2017;12:1684–7.
25. Kereiakes DJ, Ellis SG, Metzger C, Caputo RP, Rizik DG, Teirstein PS, et al. 3-Year Clinical Outcomes With Everolimus-Eluting Bioresorbable Coronary Scaffolds: The ABSORB III Trial. J Am Coll Cardiol 2017;70:2852–62.

Keywords: Absorb bioresorbable vascular scaffold; coronary artery disease; percutaneous coronary intervention.

Anahtar sözcükler: Absorb eriyebilen vasküler çatı; koroner arter hastalığı; perküten koroner girişim.