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Clinical outcomes of bioresorbable vascular scaffold to treat all-comer patients. Are patients with acute coronary syndrome better candidates for bioresorbable vascular scaffold?☆

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ABSTRACT

Background: Scaffold thromboses (ST) and adverse events and have been associated with bioresorbable vascular scaffolds (BVS) at long-term, but their mechanism remains unclear. We sought to evaluate patient and lesion characteristics associated with mid- to long-term outcomes in patients treated with BVS.
Methods: This is an observational single-center, single-arm, retrospective study evaluating the performance of BVS in an all-comer population, including complex lesions (chronic total occlusions, long lesions), small vessels, and acute coronary syndromes (ACS).
Results: From May 2013 to June 2015, we included 482 patients (580 lesions) that were treated with BVS implantation including 71.2% treated for ACS in the present analysis. Mean follow-up period was 816.2 ± 242.6 days. The primary endpoint was device oriented cardiac events (DOCE), defined as a composite of target-lesion revascularization (TLR), ST, target vessel myocardial infarction (TVMI) and cardiac death. Using Kaplan-Meier methods, the DOCE and ST rates at 36 months were 9.4% and 2.3%, respectively. No ST occurred between 2 and 3 years and ST occurred after 3 years, in one patient. Using multivariate analysis, ACS was the only significant predictor of lower rates of DOCE ($p = 0.04$, HR: 0.47, 95% CI: 0.23–0.96).
Conclusions: In this large all-comers real-world cohort, lesions treated with BVS had non-negligible rates of DOCE and ST, in line with previous published randomized trials. The occurrence of very late event was very low after 24 months. ACS patients had lower rates of DOCE.

1. Introduction

Despite the fact that latest-generation drug-eluting metal stents (DES) are considered to be the gold standard in percutaneous coronary interventions (PCI) [1], permanent stent implantation may have some drawbacks such as endothelial dysfunction, a reduction in the potential for vessel remodeling, interference with the normal arterial healing process, the risk of occlusion of covered side branches by neointima hyperplasia, hypersensitivity reactions, late stent thrombosis, as well as preclusion of future surgical revascularization [2, 3]. Bioresorbable vascular scaffolds (BVS) were developed to allow the restoration of anatomical and vascular function and to reduce the long-term risk of stent-related complications, including very late (>1 year) stent thrombosis (ST) and neoatherosclerosis that is associated with the presence of permanent metallic stents [3]. Despite these potentials advantages, BVS have faced recent drawbacks, where randomized controlled trials suggested that the risk of target lesion failure, including ST was increased with BVS, as compared with latest generation DES [4–6].

These worrisome outcomes could be related to suboptimal device expansion and insufficient intracoronary imaging guidance, as well as patients and lesions subsets [7]. Nevertheless, the underlying mechanism for increased target lesion failure after BVS implantation remains unclear and data is scarce on lesion patterns that could lead to worse long-term outcomes.

Abbreviations: ACS, acute coronary syndrome; BMS, bare-metal stent; BVS, bioresorbable vascular scaffolds; DES, drug-eluting stent; DOCE, device oriented composite endpoint; IVUS, intravascular ultrasound; KM, Kaplan-Meier; MI, myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; POCE, patient oriented composite endpoint; RVD, reference vessel diameter; ST, scaffold/stent thrombosis; TLR, target lesion revascularization; TVMI, target vessel myocardial infarction.

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In the present study, we report mid to long-term follow-up of consecutive patients treated with BVS and sought to evaluate the clinical outcomes after BVS implantation in a more complex real-world population.

2. Methods

2.1. Study design and population

This was an observational, single-center, single arm, retrospective study of consecutive patients treated with the Absorb™ BVS (Abbott Vascular, Santa Clara, California) in an all-comer population between May 2013 and June 2015 that was conducted at the Montreal Heart Institute, an academic quaternary center. In this analysis, all consecutive patients presenting with stable angina, silent ischemia or acute coronary syndrome (ACS) caused by a stenotic lesion with BVS implantation during the study period were included. The study was conducted according to the Declaration of Helsinki. As this was a retrospective analysis conducted per institutional guidelines for data security and privacy, a waiver of consent was granted. Data were anonymized by authors prior to analysis.

2.2. Procedural details

During this period, the decision to treat the lesion with an Absorb™ BVS rather than a new generation DES or a bare-metal stent (BMS) was left to the operator's discretion, but conditioned by the presence of suitable anatomy (absence of tortuosity or severe calcification proximal to the target lesion), the lesion (reference vessel diameter (RVD) visually assessed at the target lesion site ≥2.5 mm and < 4 mm) and the clinical characteristics (absence of severe comorbid conditions, contraindications to drug-eluting stents). Available BVS lengths during the study period were 12, 18, and 28 mm. BVS were implanted to cover 2 to 5 mm of non-diseased endothelium on either side of the target lesion. Pre-dilation, post-dilation and the use of optical coherence tomography (OCT) or intravascular ultrasound (IVUS), the BVS overlap strategy (marker-to-marker vs marker over marker) and arterial access (radial vs femoral) were left at the operator's discretion.

2.3. Medical therapy

The use of peri-procedural antithrombotics (i.e., glycoprotein IIb/IIIa inhibitors and heparin or bivalirudin) and the use of a second antiplatelet agent before PCI was left at the operator's discretion. All patients received a daily dose of 81 mg of aspirin daily in association with either clopidogrel (75 mg daily), ticagrelor (90 mg twice a day) or prasugrel (10 mg daily) for a minimum of 12 months after PCI. Statins use was encouraged.

2.4. Data collection and follow-up

Baseline demographics, medical history, cardiac catheterization data and cardiac outcomes were abstracted from medical charts and by reviewing the coronary angiography by three independent interventionists that did not participate in the procedure. Additional follow-up and outcome data was collected via systematic telephone calls or clinical visits. Routine angiographic follow-up was not scheduled but performed only in case of symptom recurrence or non-invasive demonstration of inducible myocardial ischemia.

2.5. Clinical endpoints and definitions

The primary endpoints were two composite endpoints, one that was device-oriented (DOCE) and one patient-oriented (POCE) defined according to the Academic Research Consortium definition for trials involving stents [8]. The DOCE includes cardiac death, myocardial infarction (MI) attributed to the target vessel, ST and target lesion revascularization (TLR). The POCE includes all-cause mortality (cardiovascular and non-cardiovascular deaths), any MI (target-vessel or non-target-vessel MI or ST) or any revascularization (target-vessel or non-target-vessel revascularization). As a secondary outcome, we also defined the rate of stent thrombosis yearly, during the first three years. Procedural success was defined as a final residual stenosis at the stenotic site <30% without in-hospital event. ACS was defined as unstable angina, NSTEMI or STEMI. In a same patient, two non-overlapping BVS implantations during the same procedure were considered as two distinct lesions in the analysis.

2.6. Statistics

Continuous variables were described using means ± standard deviation (SD) or medians ± interquartile range as appropriate. Categorical variables were presented as number (percentages). Proportions were compared using the Chi-square-test. Statistical significance was determined at the two-sided $\alpha = 0.05$ level. Survival curves for our two primary outcomes (POCE and DOCE) and for ST were obtained using Kaplan-Meier estimates. Univariate cox proportional-hazards models were developed to assess the association between the occurrences of POCE, DOCE and scaffold thrombosis with pre-specified patient, lesion and procedural variables. Candidate covariates that showed marginal

Table 1
Baseline clinical characteristics.

	$N = 482$
Age, y	60.9 (±10.5)
Sex	
Male	367 (76.1%)
Female	115 (23.9%)
Risk factor	
Current or former smoking	159 (33.0%)
Hypertension	271 (56.2%)
Dyslipidemia	322 (66.8%)
Diabetes mellitus	110 (22.8%)
Family history of CAD	205 (42.5%)
Obesity	159 (33.0%)
Previous MI	98 (20.3%)
Previous PCI	130 (27.0%)
Previous CABG	30 (6.2%)
Previous stroke/TIA	15 (3.1%)
Peripheral artery disease	28 (5.8%)
COPD	28 (5.8%)
Renal insufficiency	32 (6.6%)
Creatinine, mmol/L	86.6 (±31.1)
Anticoagulation for arrhythmia	6 (1.2%)
Multivessel disease	190 (39.4%)
LVEF	54.1 (±11.5)
Indications for PCI	
Stable angina	109 (22.6%)
Unstable angina	121 (25.1%)
STEMI	86 (17.8%)
NSTEMI	136 (28.2%)
Silent ischemia	30 (6.2%)
Aspirin pre PCI	482 (100%)
DAPT before PCI	430 (89.2%)
Clopidogrel	222 (46.1%)
Prasugrel	53 (11.0%)
Ticagrelor	155 (32.2%)
Discharge DAPT post PCI	
Clopidogrel	179 (37.1%)
Prasugrel	105 (21.8%)
Ticagrelor	198 (41.1%)

Values are n (%) or mean (SD).
Abbreviations: SD: Standard deviation; y: years; CAD: Coronary artery disease; MI: Myocardial Infarction; PCI: Percutaneous coronary intervention; CABG: Coronary-artery bypass graft; TIA: Transient ischemic attack; COPD: Chronic obstructive pulmonary disease; LVEF: Left ventricular ejection fraction; STEMI: ST-segment elevation MI; NSTEMI: Non-ST segment elevation MI; DAPT: dual antiplatelet therapy

associations to outcome on univariate testing ($p \leq 0.20$), up to a maximum of a tenth of the number of POCE and DOCE, in order to prevent overfitting, were included in our multivariate analysis. Proportional hazards assumptions were assessed graphically with the use of methods of Grambsch and Therneau, and covariates were adjusted with the use of a cubic regression spline where this assumption was not met. No imputation of data was made for missing variables. Data analyses were performed with the SPSS software package (version 24.0) and R Studio software package (version 1.0.136).

3. Results

3.1. Population baseline characteristics

From May 2013 to June 2015, a total of 482 patients (580 lesions) underwent BVS implantation and were included in the present analysis. Baseline clinical and demographic characteristics of the population are reported in Table 1. Briefly, the mean age was 60.9±10.5 years, 76.1% of the patients were male, 22.8% had diabetes, and 27.0% had prior PCI. 22.6% presented with stable angina, 25.1% with unstable angina, 28.2% for non-ST elevation myocardial infarction, 17.8% for ST-segment elevation myocardial infarction and 6.2% for silent ischemia. At discharge, all patients were treated with aspirin and 37.1% had additional clopidogrel, 21.8% prasugrel and 41.1% ticagrelor.

3.2. Angiographic and procedural details

Angiographic and procedural characteristics of the lesions are shown in Tables 2 and 3. A third of lesions (29.3%) were American College of Cardiology/American Heart Association classification type B2/C lesions and 3.8% were chronic total occlusion lesions. Predilatation was performed in 95.2% of the lesions. A mean of 1.26 ± 0.59 scaffolds per lesion were implanted with a mean diameter of 3.01 ± 0.39 mm and a mean length of 26.3 ± 14.9 mm. Mean deployment pressure was 11.6 ± 2.8 atm. Post-dilatation was performed in 84.5% of lesions and the mean post-dilatation pressure was 17.8 ± 3.5 atm. Post-dilation balloon over scaffold diameter ratio was 1.06 ± 0.07. Image guidance with IVUS or OCT was used in only 32 lesions (5.5%).

Table 2
Vessel characteristics.

	$N = 580$ lesions
Target vessel	
LAD/diagonal branch	294 (50.7%)
LCx/marginal branch	118 (20.3%)
RCA/PDA/PLB	155 (26.7%)
SVG	13 (2.2%)
Lesion AHA A1/B1/B2/C	198(34.1%)/212(36.6%)/ 100(17.2%)/70(12.1%)
CTO	22 (3.8%)
Bifurcation lesion	99 (17.1%)
Long lesion (>32 mm)	93 (16.0%)
Small vessel diameter (<2.75 mm)	125 (21.6%)
Presence of in-stent restenosis, during index procedure	42 (7.2%)
Multivessel disease	190 (32.8)
Multivessel PCI	152 (26.2)
Ostial lesion	16 (2.8)
Device type	
BVS only	551 (95%)
BVS + DES	28 (4.8%)
BVS + BMS	1 (0.2%)
TIMI grade flow pre-procedure	
0	79 (13.6%)
1	25 (4.3%)
2	35 (6%)
3	441 (76.0%)
TIMI grade flow post-procedure	
0	2 (0.3%)
1	1 (0.2%)
2	0 (0)
3	577 (98.5%)

Values are n (%) or mean (SD).
Abbreviations: LAD: Left anterior descending artery; LCx: Left circumflex artery; RCA: Right coronary artery; PDA: posterior descending artery; PLB: postero-lateral branch; SVG: Saphenous vein graft; CTO: Chronic total occlusion; BVS: Bioresorbable scaffold; DES: Drug-eluding stent; BMS: Bare-metal stent; TIMI: Thrombolysis In Myocardial Infarction.

Table 3
Procedural characteristics.

	$N = 580$ lesions
Treated lesions per procedure	1.13 (±0.36)
Aspiration thrombectomy	88 (15.2%)
Intracoronary imaging	32 (5.5%)
IVUS	13 (2.2%)
OCT	19 (3.3%)
Pre-dilation	552 (95.2%)
Reference vessel diameter, mm	3.05 (±0.44)
Max pre-dilation diameter, mm	2.74 (±1.05)
Numbers of scaffolds/lesion	1.26 (±0.59)
Number of scaffolds 1/2/3/4/5	466(80.3%)/83(14.3%)/ 26(4.5%)/4(0.7%)/1(0.2%)
Scaffold diameter, mm	3.01 (±0.39)
Scaffold length implanted, mm	26.3 (±14.9)
Overlapping stents	116 (20.0%)
Scaffold implantation pressure, atm	11.6 (±2.8)
Post-dilation	490 (84.5%)
Maximum post-dilation balloon, mm	3.15 (±0.58)
Maximum post-dilation inflation pressure, atm	17.8 (±3.5)
Post-dilation balloon over scaffold diameter ratio	1.06 (±0.07)
Pharmacotherapy	
Use of GPIIB/IIIA antagonists	62 (10.7%)
Heparin	576 (99.3%)
Bivalirudin	4 (0.7%)
Procedural complications	
Dissection	20 (3.4%)
Slow flow	7 (1.2%)
No reflow	2 (0.3%)
SB occlusion	11 (1.9%)
Distal embolization	9 (1.6%)
Perforation	1 (0.2%)
In-hospital outcomes	
Cardiac death	2 (0.4%)
ST	1 (0.2%)
TVMI	1 (0.2%)
TLR	2 (0.4%)

Values are n (%) or mean (SD).
Abbreviations: IVUS: Intra-vascular ultrasound; OCT: Optical coherence tomography; SB: Side branch; ST: Scaffold thrombosis; TVMI: Target vessel myocardial infarction; TLR: Target lesion revascularization.

Table 4
Major adverse cardiac events.

Follow-up time, days	816.2 (±242.6)
POCE	63 (13.1%)
All-cause death	9 (1.9%)
Myocardial ischemia	25 (5.2%)
Any revascularization	54 (11.2%)
DOCE	36 (6.2%)
Cardiac death	1 (0.2%)
TLR	31 (5.3%)
Target vessel MI	21 (3.6%)
Stent/scaffold thrombosis	11 (1.9%)
Early (<30 days)	3 (0.5%)
Late (30 days–1 year)	2 (0.3%)
Very late (>1 year)	6 (1.0%)
Other endpoints	
Non-target vessel MI	6 (1.2%)
Non-target vessel revascularization	25 (5.2%)
Non-cardiac death	8 (1.7%)

Values are n (%) or mean (SD).
Abbreviations: POCE: Patient-oriented composite endpoint; DOCE: Device-oriented composite endpoint; TLR: Target-lesion revascularization; MI: Myocardial infarction; TVR: Target-vessel revascularization.

3.3. Periprocedural outcomes

Periprocedural and in-hospital outcomes are shown in Table 3. Briefly, dissection occurred in 3.4% of the cases, side-branch occlusion occurred in 1.9% of the cases and distal embolization occurred in 1.6% of the cases. In-hospital cardiac death occurred in 2 patients (0.4%) and definite ST leading to TVMI occurred in 1 patient (0.2%).

3.4. Long-term outcomes

The long-term outcomes are summarized in Table 4. Follow-up was available for 87.2% patients. Mean follow-up period was 816.2 ± 242.6 days. The composite endpoint of POCE occurred in 63 patients (13.7%) where 9 patients experienced all-cause death (1 cardiovascular death; 4 unknown cause of death and 4 non-cardiovascular deaths), 25 patients experienced myocardial ischemia (5.2%) and 54 (11.2%) patients required subsequent revascularization. The composite endpoint of DOCE occurred in 34 patients (9.4%), where 1 patient experienced cardiovascular death (0.2%), 21 patients experienced target vessel MI (3.6%), 31 patients experienced target lesion revascularization (5.3%), and 11 patients experienced ST (2.3%). Regarding the timing of scaffold thrombosis, 5 (1.1%) occurred before 1 year (3 were early scaffold thrombosis within 30 days and 2 occurred between 1 month and 1 year), 5 (1.2%) occurred between year 1 and year 2, none (0%) occurred between year 2 and year 3. Only 1 ST occurred after 3 years. Using KM estimates at 36-months, the POCE, DOCE and ST rates were 17.0%, 9.4% and 2.3% respectively. Rates of ST at 12, 24 and 36 months were 1.1%, 2.3% and 2.3%, respectively (Fig. 1 and Supplemental Table 1). The rate of POCE & ST diminished over time and was lower between year 2 and 3, than at 1 year or than during year 1 and 2 (Supplemental Table 1). The rate of DOCE remained stable over time (Supplemental Table 1).

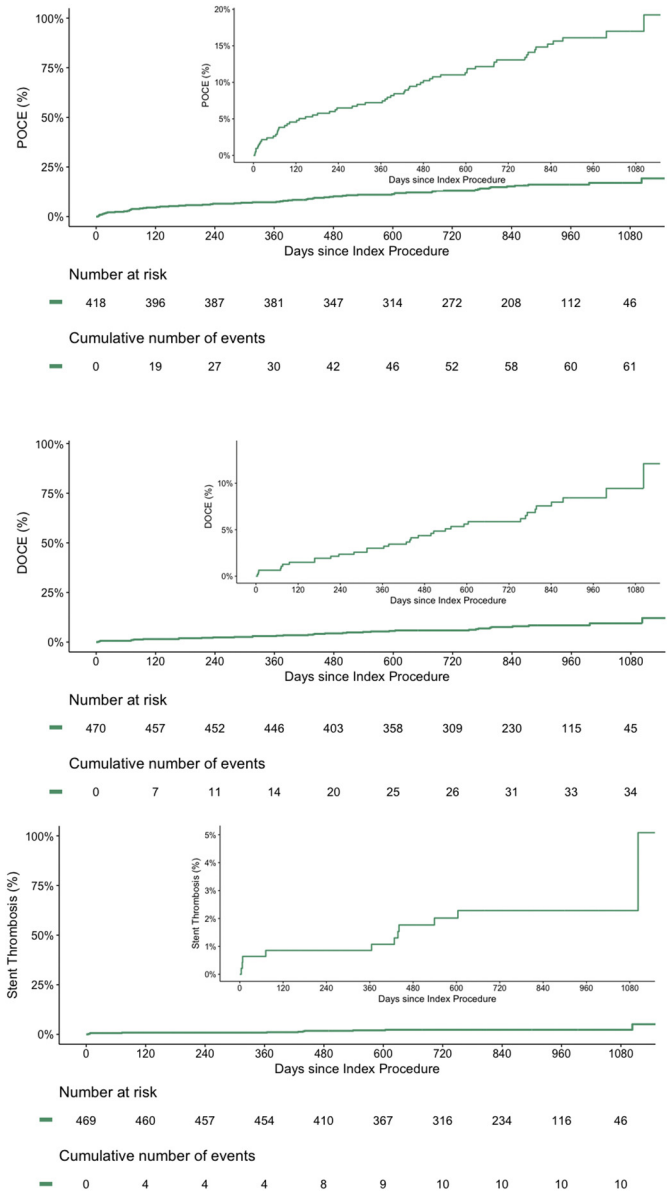

Fig. 1. Cumulative Kaplan-Meier estimates of survival for DOCE, POCE, and definite/probable ST up to 3 years. POCE: Patient-oriented composite endpoint; DOCE: Device-oriented composite endpoint; ST: Scaffold thrombosis.

3.5. Outcomes predictors

Univariate and multivariate cox proportional-hazards models were used to identify predictors of the occurrence of POCE, DOCE and ST, and are shown in Table 4 and Supplemental Tables 2 and 3. For POCE multivessel disease, age, ticagrelor or prasugrel use, scaffold diameter and males were found to have a marginal association with POCE and were subsequently included in our multivariate analysis (Supplemental Table 2). After multivariate adjustment, only the presence of multivessel disease ($p = 0.01$, HR: 1.99, 95% CI: 1.16–3.39) was found to be increase the risk of POCE. For DOCE, the presence of in-stent restenosis in the BVS treated lesion as the reason of revascularization at index procedure, ACS at presentation, diabetes, multivessel disease, long lesions (>32 mm), males, age, scaffold diameter, post-dilation, small vessel diameter (<2.75 mm) and number of BVS implantation were univariate predictors that have shown marginal association with the occurrence of DOCE. (Table 5). After multivariate analysis, only ACS remained a predictor of fewer DOCE ($p = 0.04$, HR:0.47, 95% CI: 0.23–0.96). The use of post-dilation was not associated with better DOCE using univariate or multivariate analysis. The use of a more powerful anti-platelet agent such as Prasugrel or Ticagrelor was also not associated with a protective effect on the occurrence of DOCE. Regarding ST, and due to lack

Table 5
Cox proportional-hazards regression model for the predictors of DOCE.

	X^2	Hazard ratio	95% CI	*p*-value	ß
Univariate predictors					
Presence of in-stent restenosis[a]	8.03	3.32	1.45–7.61	0.01	1.2
ACS[a]	5.12	0.45	0.22–0.90	0.02	−0.81
Diabetes[a]	4.01	2.02	1.02–4.00	0.05	0.70
Multivessel disease[a]	3.24	1.89	0.95–3.78	0.07	0.64
Long lesion (>32 mm)[a]	3.17	1.99	0.93–4.25	0.08	0.69
Males[a]	2.94	2.50	0.88–7.05	0.09	0.91
Age[a]	2.72	1.03	1.00–1.06	0.10	0.03
Scaffold diameter[a]	2.25	0.52	0.22–1.22	0.13	−0.65
Post-dilatation[a]	2.07	2.40	0.73–7.92	0.15	0.88
Small vessel diameter (<2.75 mm)[a]	1.90	1.68	0.80–3.5	0.17	0.52
Number of BVS implanted[a]	1.88	1.38	0.87–2.20	0.17	0.32
Ostial lesion	0.77	0.03	0.00–65.72	0.38	−3.39
Ticagrelor or Prasugrel use post PCI (vs Clopidogrel)	0.18	1.16	0.58–2.35	0.67	0.15
Use of imaging	0.17	0.73	0.17–3.24	0.68	−0.31
Pre-PCI DAPT use	0.08	0.86	0.30–2.46	0.78	−0.15
Implantation inflation pressure	0.06	0.99	0.88–1.11	0.8	−0.02
Bifurcation	0.01	1.04	0.43–2.51	0.93	0.04
Multivariate predictors					
ACS	4.41	0.47	0.23–0.96	0.04	−0.75
Mutivessel disease	2.38	1.76	0.86–3.62	0.12	0.57
In-stent restenosis	1.93	2.00	0.75–5.30	0.17	0.69
Diabetes	1.56	1.56	0.73–3.34	0.25	0.45

Abbreviations: ACS: Acute coronary syndrome; BVS: Biovascular scaffolds; PCI: Percutaneous coronary intervention.

[a] These variables had an association with the occurrence of DOCE and were included in our multivariate analysis.

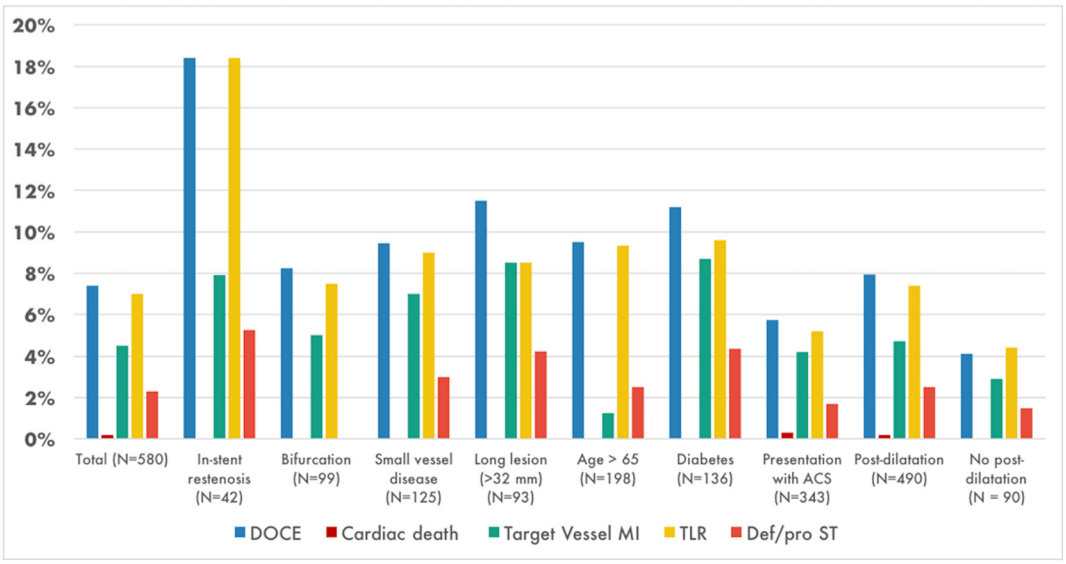

Fig. 2. Rate of DOCE and Definite/Probable ST, Divided by Subgroups. DOCE: Device-oriented composite endpoint; ST: Scaffold thrombosis; ACS: acute coronary syndrome; MI: myocardial infarction; TLR: Target-lesion revascularization.

of power, none of the factors was a significant predictor (Supplemental Table 3). In Fig. 2 we present DOCE, its components, and definite/probable ST rates in various subgroups. Patients treated for previous metallic stent restenosis had a 2-fold increased number of DOCE and scaffold thrombosis. Interestingly, when comparing patients presenting with ACS compared to the non-ACS population, there was a significant reduction in the rate of DOCE (5.7% vs 12.5%, $p = 0.03$). This was driven by a lower rate of TLR (4.0% in ACS vs 11.7% in non-ACS), TVMI (1.7% in ACS vs 5.8% in non-ACS) and ST (1.7% in ACS vs 4.2% in non-ACS) in the ACS population. Moreover, there was a numerical decrease of POCE (13.0% vs 18.5%, $p = 0.24$) and ST without reaching statistical significance (1.7% vs 4.2%, $p = 0.15$) (Fig. 3).

4. Discussion

This retrospective study of 482 patients (580 lesions) reports extended follow-up beyond 2 years, with a mean follow-up duration of 816.2 ± 242.6 days. The main findings of our study are that rate of POCE, DOCE and definite/probable ST is higher when compared to a historical second-generation DES cohort [9], as well as metallic stents [10]. Additionally, the rate of POCE, DOCE and ST decreases over time and patients presenting with ACS have a reduced risk of DOCE. Supporting these findings, we found that the rate of scaffold thrombosis declines over time with only one scaffold thrombosis after 2 years.

To the best of our knowledge, our study is one of the largest real-world study that reports long follow-up in an all-comer population. Our study depicts the medium to long-term outcomes in a population including complex lesions such as long lesions, small vessels, chronic total occlusion, saphenous vein grafts, in-stent restenosis, American College of Cardiology/American Heart Association type B2/C and patients with ACS (either unstable angina, non-ST elevation myocardial infarction or ST elevation myocardial infarction), which reflects daily practice.

Taking in account the complexity of treated lesions and the inclusion of ACS population, the DOCE rate of 5.9% and the ST rate of 2.3% at two-

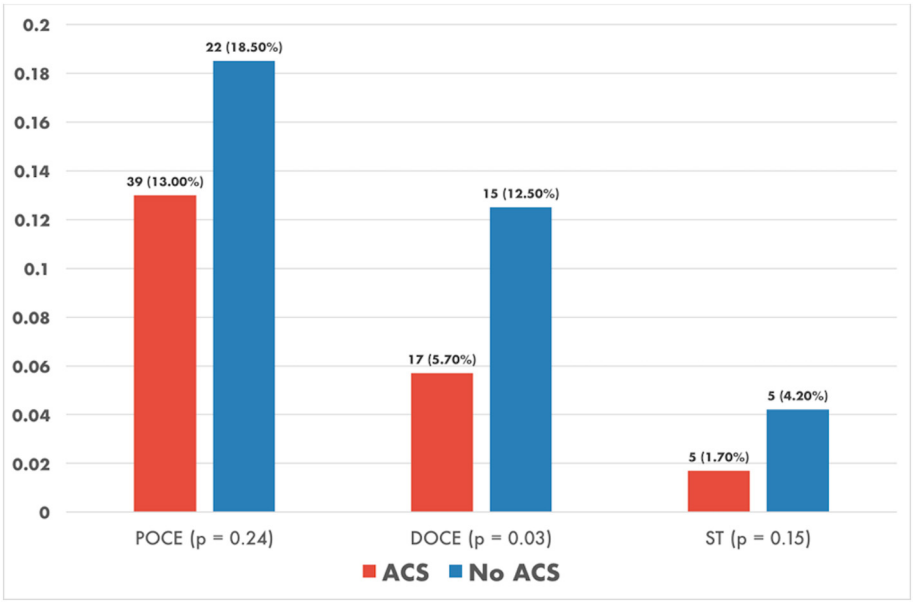

Fig. 3. Rate of DOCE and Definite/Probable ST, according to ACS vs non-ACS patients. DOCE: Device-oriented composite endpoint; ST: Scaffold thrombosis; ACS: acute coronary syndrome.

years observed in the current study are in line with reported data in relatively more simple lesions [4, 11]. Additionally, we found lower rates of DOCE [5.9% vs 8.7% respectively] and ST [2.3% vs 3.5%] at 2-years than the AIDA trial [4]. This is an all-comers trial that included an equal proportion of ACS patients (46% STEMI/NSTEMI in AIDA vs 46% STEMI/NSTEMI in our cohort), however these patients had also more complex lesions treated (55% ACC-AHA type B2/C lesions in AIDA vs 29.3% in our cohort) [4].

Recently, some concerns were raised regarding a potentially increased rate of ST after BVS implantation at long-term follow-up [5, 6, 9, 10, 12, 13]. Patient selection, lesion preparation, pre- and post-dilation, and the consideration of invasive imaging for optimal device deployment have been emphasized, and dual antiplatelet therapy continuation for at least 1 year and use of more potent antiplatelet therapy has been suggested [3, 7, 14]. Nevertheless, in our study, the high rate of pre (95.2%) and post-dilation (84.5%) was not predictive of better outcomes. Conversely, there was a trend for higher DOCE rates, even though non-significant, when post-dilation was performed. This may reflect the high percentage of post-dilatation in our cohort. Furthermore, the patients that did not have post-dilatation might have suffered a selection bias, where they had less resistant or calcified lesions which led to a reduction in the occurrence of DOCE and subsequently might have hidden the protective effect of post-dilatation. Furthermore, because of the low rate of intracoronary imaging performed (5.5%), we cannot ensure perfect scaffold apposition was obtained. However, the post-dilatation rate at 17.6 ATM using a balloon to artery ratio of 1.06 should have led to appropriate expansion [14].

Interestingly, ACS patients had half the DOCE rate, including less ST, compared to our non-ACS patients. Whether this is due to anti-platelet therapy regimen or the potential of vessel remodeling warrants further investigations. The fact that ACS patients have more often soft, with a relatively small plaque burden might be one of the potential explanation, in regard of the careful lesion preparation that is now advised for BVS [15]. In addition, among ACS, the vulnerable plaque of a STEMI lesion is often characterized by a large necrotic core covered by a thin fibrous cap. This could be an ideal scenario for the BVS implantation [16]. Indeed, large necrotic cores may interfere with vascular healing after metallic stent implantation, leading to potential coronary invagination or late-acquired malapposition that can trigger ST [15].

Our study included a large proportion of patients discharged with a 12-month prescription of new P2Y12 inhibitors (37.1% were under clopidogrel whereas 21.9% were under prasugrel and 41% under ticagrelor) but the most potent P2Y12 were not protective against POCE, DOCE or ST. A potential explanation for such early DOCE and POCE rates could be the increased thickness of the BVS struts, potentially triggering platelet deposition and subsequent thrombosis, especially in settings with suboptimal flow conditions [17]. For this reason, BVS with thinner struts are currently being developed.

Interestingly, the rate of scaffold thrombosis decreased over time with only one scaffold thrombosis after three years and none between 2 and 3 years. This could be potentially explained by the fact that some BVS have been reabsorbed by that time [18]. Nevertheless, the fact that one ST occurred after 3 years warrants further investigations and could be due to different reabsorption durations among patients.

The present study has several limitations. First, our manuscript provides real world data; however the fact that BRS are no longer currently commercially available could be a limitation. Despite this, our findings will come of value as new generation BRS-devices will undergo development and clinical testing [19]. Despite this, our findings will come of value as new generation BRS-devices will undergo development and clinical testing [20]. Additionally, due to observational nature of the study, unknown confounders may have influenced event rates. However, by including all consecutive patients, we have minimized the risk of selection bias and our findings are similar to the numerous published registries available [10]. Despite this, we cannot exclude that there was a selection bias when the operator decided to implant a BVS instead of a conventional stent. Furthermore, some data was not collected as part of our follow-up, such as presence of extended DAPT (>1 year), which could've provided further insight into the event rates observed. Moreover, comparisons to other registries are difficult, given the differences in patient and lesion characteristics, implantation procedure, and follow-up duration. Third, while the follow-up was achieved in a high percentage of patients, uncertainty remains with the long-term results in the 13% of patients that we were not able to reach. Nevertheless, the majority of our study population is followed at our institution, which increases the probability of detecting outcomes. Forth, while the angiograms were analyzed by independent interventionists, we cannot present quantitative measurements because quantitative coronary angiography (QCA) use was not systemically used.

5. Conclusion

In a large real-world cohort treated with BVS, the rate of POCE, DOCE and ST was in line with previous published randomized trials and registries. ST rates declined over time and only one scaffold thrombosis occurred after 2-year follow-up. Moreover, ACS patients had twice as low DOCE as compared with non-ACS patients and could represent an indication for optimal BVS implantation. However, our findings should be confirmed in a larger, randomized controlled study and presently, are only hypothesis generating.

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References

[1] Bønaa KH, Mannsverk J, Wiseth R, et al. Drug-eluting or bare-metal stents for coronary artery disease. N Engl J Med 2016;375:1242–52. https://doi.org/10.1056/NEJMoa1607991.
[2] Katz G, Harchandani B, Shah B. Drug-eluting stents: the past, present, and future. Curr Atheroscler Rep 2015;17:485. https://doi.org/10.1007/s11883-014-0485-2.
[3] Indolfi C, De Rosa S, Colombo A. Bioresorbable vascular scaffolds — basic concepts and clinical outcome. Nat Publ Group 2016;13:719–29. https://doi.org/10.1038/nrcardio.2016.151.
[4] Wykrzykowska JJ, Kraak RP, Hofma SH, et al. Bioresorbable scaffolds versus metallic stents in routine PCI. N Engl J Med 2017;376:2319–28. https://doi.org/10.1056/NEJMoa1614954.
[5] Ali ZA, Serruys PW, Kimura T, 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. https://doi.org/10.1016/S0140-6736(17)31470-8.
[6] Nairooz R, Saad M, Sardar P, Aronow WS. Two-year outcomes of bioresorbable vascular scaffold versus drug-eluting stents in coronary artery disease: a meta-analysis. Heart 2017;103:1096–103. https://doi.org/10.1136/heartjnl-2016-310886.
[7] Puricel S, Cuculi F, Weissner M, et al. Bioresorbable coronary scaffold thrombosis: multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors. JACC 2016;67:921–31. https://doi.org/10.1016/j.jacc.2015.12.019.
[8] Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation. American Heart Association, Inc.; 2007. p. 2344–51.
[9] Serruys PW, Chevalier B, Sotomi Y, 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. https://doi.org/10.1016/S0140-6736(16)32050-5.
[10] Moscarella E, Ielasi A, Varricchio A, et al. Clinical findings after bioresorbable vascular scaffold implantation in an unrestricted cohort of patients with ST-segment elevation myocardial infarction (from the RAI registry). Int J Cardiol 2018;258:50–4. https://doi.org/10.1016/j.ijcard.2018.01.135.
[11] (null), (null), (null), et al. Mid- to long-term clinical outcomes of patients treated with the everolimus-eluting bioresorbable vascular scaffold. J Am Coll Cardiol Intv 2016;9:1652–63. https://doi.org/10.1016/j.jcin.2016.04.035.
[12] Kereiakes DJ, Ellis SG, Metzger C, et al. 3-year clinical outcomes with everolimus-eluting bioresorbable coronary scaffolds: The ABSORB III Trial. JACC 2017;70:2852–62. https://doi.org/10.1016/j.jacc.2017.10.010.
[13] Sorrentino S, Giustino G, Mehran R, et al. Everolimus-eluting Bioresorbable scaffolds versus everolimus-eluting metallic stents. JACC 2017;69:3055–66. https://doi.org/10.1016/j.jacc.2017.04.011.
[14] Tanaka A, Jabbour RJ, Latib A, Colombo A. Bioresorbable vascular scaffolds: from patient selection to optimal scaffold implantation; tips and tricks to minimize device failure. Catheter Cardiovasc Interv 2016;88:10–20. https://doi.org/10.1002/ccd.26812.
[15] Joner M, Finn AV, Farb A, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. JACC 2006;48:193–202. https://doi.org/10.1016/j.jacc.2006.03.042.

[16] Picard F, de Hemptinne Q, Avram R, et al. Bioresorbable vascular scaffold during ST-elevation myocardial infarction: a systematic review. Can J Cardiol 2017;33:515–24. https://doi.org/10.1016/j.cjca.2016.11.022.
[17] Abizaid A, Ribamar Costa JJ. The unmet needs: how future technologies will address current limitations of bioresorbable scaffold technology. Catheter Cardiovasc Interv 2016;88:54–9. https://doi.org/10.1002/ccd.26813.
[18] Onuma Y, Serruys PW, Perkins LEL, et al. Intracoronary optical coherence tomography and histology at 1 month and 2, 3, and 4 years after implantation of everolimus-eluting bioresorbable vascular scaffolds in a porcine coronary artery model: an attempt to decipher the human optical coherence tomography images in the ABSORB trial. Circulation 2010;122:2288–300. https://doi.org/10.1161/CIRCULATIONAHA.109.921528.
[19] Byrne RA, Stefanini GG, Capodanno D, 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. https://doi.org/10.1093/eurheartj/ehx488.
[20] Tenekecioglu E, Torii R, Bourantas CV, et al. Hemodynamic analysis of a novel bioresorbable scaffold in porcine coronary artery model. Catheter Cardiovasc Interv 2018;91:1084–91. https://doi.org/10.1002/ccd.27253.