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Are BVS suitable for ACS patients? Support from a large single center real live registry

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ABSTRACT

Objectives: To investigate one-year outcomes after implantation of a bioresorbable vascular scaffold (BVS) in patients presenting with acute coronary syndrome (ACS) compared to stable angina patients.
Background: Robust data on the outcome of BVS in the setting of ACS is still scarce.
Methods: Two investigator initiated, single-center, single-arm BVS registries have been pooled for the purpose of this study, namely the BVS Expand and BVS STEMI registries.
Results: From September 2012–October 2014, 351 patients with a total of 428 lesions were enrolled. 255 (72.6%) were ACS patients and 99 (27.4%) presented with stable angina/silent ischemia. Mean number of scaffold/patient was 1.55 ± 0.91 in ACS group versus 1.91 ± 1.11 in non-ACS group (P = 0.11). Pre- and post-dilatation were performed less frequent in ACS patients, 75.7% and 41.3% versus 89.0% and 62.0% respectively (P = 0.05 and P = 0.001). Interestingly, post-procedural acute lumen gain and percentage diameter stenosis were superior in ACS patients, 1.62 ± 0.65 mm (versus 1.22 ± 0.49 mm, P < 0.001) and 15.51 ± 8.47% (versus 18.46 ± 9.54%, P = 0.04). Major adverse cardiac events (MACE) rate at 12 months was 5.5% in the ACS group (versus 5.3% in stable group, P = 0.90). One-year definite scaffold thrombosis rate was comparable: 2.0% for ACS population versus 2.1% for stable population (P = 0.94), however, early scaffold thromboses occurred only in ACS patients.
Conclusions: One-year clinical outcomes in ACS patients treated with BVS were similar to non-ACS patients. Acute angiographic outcomes were better in ACS than in non-ACS, yet the early thrombotic events require attention and further research.

1. Introduction

Drug-eluting stents (DES) are the first choice devices in percutaneous coronary interventions (PCI). Despite recent advantages, shortcomings related to the use of DES still are present such as delayed arterial healing, late stent thrombosis (ST), neo-atherosclerosis and hypersensitivity reactions to the polymer [1,2].

To overcome these limitations, coronary devices made of fully bioresorbable material were developed to provide mechanical support and drug-delivery within the first year, followed by complete resorption. The first bioresorbable vascular scaffold (BVS) was commercially introduced in September 2012 as the Absorb BVS (Abbott Vascular, Santa Clara, CA). The BVS provides transient vessel support and gradually elutes the anti-proliferative drug everolimus. After degradation of the polymer (after approximately two to three years) no foreign material remains and need for late reintervention triggered by foreign material should thus be reduced [3].

First-in-man trials have proven the safety of the BVS up to five years [4,5] with a fully completed bioresorption process, a late luminal enlargement due to plaque reduction and a persistent restoration of vasomotion [6–8]. The 1-year results of the larger ABSORB II, ABSORB Japan, ABSORB China and ABSORB III randomized controlled trials comparing BVS with DES (Xience V), confirmed the safety in relatively simple coronary lesions with similar clinical event rates for both devices [9–12].

In all these early studies, ACS patients were largely excluded while BVS would comprise a more attractive choice in this setting as ACS patients are in general younger with a longer life expectancy, less previous

Abbreviations: ACS, acute coronary syndrome; BMS, bare metal stent; BVS, bioresorbable vascular scaffold; BRS, bioresorbable scaffold; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CEC, clinical events committee; DES, drug-eluting stent; ITT, intention-to-treat; IVUS, intravascular ultrasound; LM, left main; MACE, major adverse cardiac events; MI, myocardial infarction; MLD, minimal lumen area; Non-TVR, non-target vessel revascularization; NSTEMI, non-ST elevation myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; PT, per-treatment; QCA, quantitative coronary angiography; RVD, reference vessel diameter; ST, scaffold thrombosis; STEMI, ST elevation myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization; UA, unstable angina pectoris; %DS, percentage diameter stenosis.

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MI and revascularizations with implantation of metallic stents, that would conflict with a therapy aiming at maximal recovery and restoration of normal anatomy of both the coronary artery and myocardium. Furthermore, lesions primarily consisting of soft plaque would be conceptually easy to expand thus facilitating BVS implantation in ACS population. On the other hand, ACS patients are in a much higher prothrombotic state which might accelerate thrombus formation on the larger struts of the BVS impacting much more on shear stress compared to the thinner struts of current metallic DES.

Few registries focused on the performance of the BVS in patients presenting with ACS, mainly ST-elevation myocardial infarction (STEMI). BVS STEMI First examined the procedural and short-term clinical outcomes of 49 STEMI patients, revealing excellent results: procedural success was 97.9% and only 1 patient suffered an event (non-target vessel MI) [13]. Kočka et al. reported similar results in the Prague-19 study [14]. Extending the initial Prague-19 study, the BVS Examination is currently the largest registry on BVS in STEMI with encouraging MACE rates (Device oriented clinical endpoint: 4.1% at one year for both the BVS and the DES), although with a not negligible definite/probable scaffold thrombosis rate (2.4% at one year for the BVS) [15].

The recently published TROFI II randomized trial investigated arterial healing in 90 STEMI patients treated with a BVS compared to those treated with an everolimus-eluting stent (EES). Based on OCT, arterial healing at 6 months after BVS implantation was non-inferior to that after EES implantation [16].

In general, the previous studies on BVS in ACS are limited in size and procedural details and there is a need for more data on the efficacy of BVS in the setting of PCI for ACS. The aim of this study was to compare the angiographic and clinical outcomes of BVS in ACS patients with stable patients.

2. Material and methods

2.1. Population

Two investigator-initiated, prospective, single-center, single-arm studies performed in an experienced, tertiary PCI center have been pooled for the purpose of this investigation. Patients presenting with NSTEMI, stable or unstable angina (UA), or silent ischemia caused by a *de novo* stenotic lesion in a native previously untreated coronary artery with intention to treat with a BVS were included in BVS Expand registry. Angiographic inclusion criteria were lesions with a Dmax (proximal and distal maximal lumen diameter) within the upper limit of 3.8 mm and the lower limit of 2.0 mm by online quantitative coronary angiography (QCA). Complex lesions such as bifurcation, calcified (as assessed by angiography), long and thrombotic lesions were not excluded. Exclusion criteria were patients with a history of coronary bypass grafting (CABG), presentation with cardiogenic shock, bifurcation lesions requiring kissing balloon post-dilatation, ST-elevation myocardial infarction (STEMI) patients, allergy or contra-indications to antiplatelet therapy, fertile female patients not taking adequate contraceptives or currently breastfeeding and patients with expected survival of less than one year. As per hospital policy patients with a previously implanted metal DES in the intended target vessel were also excluded. Also, although old age was not an exclusion criterion, BVS were in general reserved for younger patients, and left to operator's interpretation of biological age.

Patients presenting with STEMI, were approached to participate in the BVS STEMI Registry, which started two months after the BVS Expand registry. The study design has been described elsewhere [13]. The most important inclusion criteria were presentation with STEMI and complaints <12 h. The remaining inclusion criteria were similar to the BVS-EXPAND registry.

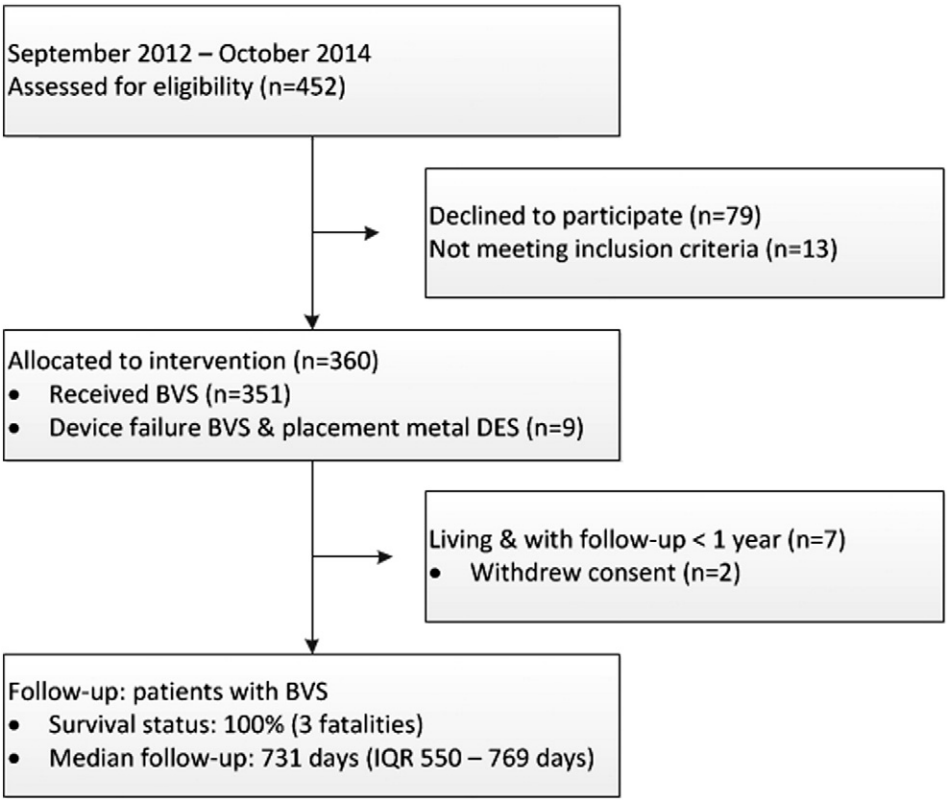

Fig. 1. Flowchart study.

2.2. Ethics

This is an observational study, performed based on international regulations, including the declaration of Helsinki. Approval of the ethical board of the Erasmus MC was obtained. All patients undergoing clinical follow-up provided written informed consent to be contacted regularly during the follow-up period of the study.

2.3. Procedure

PCI was performed according to current clinical practice standards. The radial or femoral approach using 6 or 7 French catheters were the principal route of vascular access. Pre-dilatation was recommended with a balloon shorter than the planned study device length. Advanced lesion preparation was left to the operator's discretion. Post-dilatation was recommended with a non-compliant balloon without overexpanding the scaffold beyond its limits of expansion (by >0.5 mm larger than nominal diameter). Intravascular imaging with the use of Intravascular Ultrasound (IVUS) or Optical Coherence Tomography (OCT) was used for pre-procedural sizing and optimization of scaffold deployment on the discretion of the operator. All patients were treated with unfractionated heparin (at a dose of 70–100 UI/kg). Patients with stable angina were preloaded with 300 mg of aspirin and 600 mg of clopidogrel. Patients presenting with ACS were preloaded with 300 mg of aspirin and 60 mg of prasugrel or 180 mg of ticagrelor.

2.4. Angiographic analysis

The angiographic analysis was performed by three independent investigators (YI, JF and YO). Coronary angiograms were analyzed with the CAAS 5.10 QCA software (Pie Medical BV, Maastricht, the Netherlands). The QCA measurements provided reference vessel diameter (RVD), percentage diameter stenosis (%DS), minimal lumen diameter (MLD), and maximal lumen diameter (Dmax). Acute gain was defined as post-procedural MLD minus pre-procedural MLD (in an occluded vessel MLD value was zero by default).

2.5. Follow-up

Survival status of all patients was obtained from municipal civil registries. Follow-up information specific for hospitalization and cardiovascular events was obtained through questionnaires. If needed, medical records or discharge letters from other hospitals were collected. Events were adjudicated by an independent clinical events committee (CEC).

2.6. Definitions

The primary endpoint was MACE, defined as the composite endpoint of cardiac death, myocardial infarction (MI) and target lesion revascularization (TLR). Deaths were considered cardiac unless a non-cardiac cause was definitely identified. TLR was described as any repeated revascularization of the target lesion. Target vessel revascularization (TVR) was defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. Non-target vessel revascularization was described as any revascularization in a vessel other than the vessel(s) of the target lesion(s). Target lesion failure (TLF) was defined as a composite endpoint of cardiac death, target vessel MI and TLR. Scaffold thrombosis (ST) and MI were classified according to the Academic Research Consortium (ARC) [17]. Clinical device success was defined as successful delivery and deployment of the first study scaffold/stent at the intended target lesion and successful withdrawal of the delivery system with attainment of final in-scaffold/stent residual stenosis of <30% as evaluated by QCA. Clinical procedure success was described as device success without major peri-procedural complications or in-hospital MACE (maximum of 7 days).

Table 1
Patient characteristics.

	ACS patients	Non-ACS patients	P value
Number of patients (%)	255 (72.6)	96 (27.4)	
Mean age in years (±SD)	57.9 ± 10.7	63.4 ± 8.9	<0.001
Gender (%)			
Male	191/255 (74.9)	73/96 (76.0)	0.84
Female	64/255 (25.1)	23/96 (24.0)	0.84
Smoking (%)	149/255 (58.4)	44/96 (45.8)	0.03
Hypertension (%)	130/253 (51.0)	55/95 (57.3)	0.29
Dyslipidemia (%)	92/251 (36.1)	49/95 (51.0)	0.01
All diabetes mellitus (%)	33/255 (12.9)	18/98 (18.8)	0.16
Insulin dependent	7/255 (2.7)	3/96 (3.1)	1.00
Family history of CAD (%)	104/252 (40.8)	39/94 (41.5)	0.94
History of MI (%)	25/255 (9.8)	21/96 (21.9)	0.003
History of PCI (%)	12/255 (4.7)	12/96 (12.5)	0.01
Cardiogenic shock (%)	5/255 (2.0)	0/96 (0.0)	0.33
Renal insufficiency (%)	8/255 (3.1)	8/88 (8.3)	0.046
Presentation (%)			<0.001
Stable angina	0/255 (0.0)	95/96 (99.0)	
Unstable angina	40/255 (15.6)	0/96 (0.0)	
STEMI	120/255 (46.9)	0/96 (0.0)	
NSTEMI	95/255 (37.3)	0/96 (0.0)	
Silent ischemia	0/255 (0.0)	1/96 (1.0)	
Single vessel disease (%)	183/255 (71.5)	52/96 (54.2)	0.02
P2Y12 inhibition use			<0.001
Clopidogrel	60/255 (23.5)	86/96 (89.6)	
Prasugrel	164/255 (64.3)	9/96 (9.4)	
Ticagrelor	30/255(11.8)	1/96 (1.0)	

Values are expressed as percentages or mean ± standard deviation when appropriate. P values are based on Chi square test or Fishers' exact test for categorical variables and Student's *t* test for continuous variables. ACS: acute coronary syndrome, CAD: coronary artery disease, MI: myocardial infarction, NSTEMI: non-ST elevation myocardial infarction, PCI: percutaneous coronary intervention, STEMI: ST elevation myocardial infarction.

The intention-to-treat (ITT) group includes all the patients regardless of whether or not the scaffold was successfully implanted. The per-treatment (PT) group consists of all patients in whom the

Table 2
Lesion characteristics.

	ACS patients N = 255, L = 300	**Non-ACS patients N = 96, L = 128**	**P value**
Number of lesions per patient	1.18 ± 0.49	1.33 ± 0.56	
Left anterior descending artery (%)	48.0	54.4	0.23
Left circumflex artery (%)	24.3	20.0	0.38
Right coronary artery (%)	27.7	25.6	0.61
Bifurcation (%)	20.3	30.7	0.009
Calcification (moderate or severe) (%)	31.8	50.4	<0.001
(Chronic) total occlusion(%)	26.2	8.7	<0.001
CTO (%)	1.7	7.0	0.007
ACC/AHA lesion classification (%)			
A	14.1	15.0	0.75
B1	53.4	41.7	0.02
B2	24.2	22.0	0.66
C	7.2	19.7	<0.001
TIMI (%)			
Pre-procedure			<0.001
TIMI 0	25.2	9.4	
TIMI I	4.6	0.8	
TIMI II	16.1	6.3	
TIMI III	52.1	81.9	
Post-procedure			0.61
TIMI 0	0.0	0.0	
TIMI I	0.3	0.0	
TIMI II	4.6	3.1	
TIMI III	93.4	95.3	

Values are expressed as percentages or mean ± standard deviation when appropriate. P values are based on Chi square test or Fishers' exact test for categorical variables and Student's *t* test for continuous variables. ACS: acute coronary syndrome (ST-elevation myocardial infarction, non-ST myocardial infarction and unstable angina), non-ACS: non acute coronary syndrome (stable angina and silent ischemia).

BVS was successfully implanted. All analyses were performed in the PT group.

As a measure of scaffold expansion, the expansion index was calculated as post-procedural MLD divided by nominal device diameter. A cut-off value of <0.70 below was used to define underexpansion.

2.7. Statistical analysis

Categorical variables are reported as counts and percentages, continuous variables as mean ± standard deviation. The Student's *t* test and the chi square test (or Fishers' exact test) were used for comparison of means and percentages. The cumulative incidence of adverse events was estimated according to the Kaplan–Meier method. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. Kaplan–Meier estimates were compared by means of the log-rank test. For the endpoint MACE, a landmark survival analysis was performed with the landmark time point of 30 days. All statistical tests were two-sided and the P value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS, version 21 (IL, US).

A univariate logistic regression analysis was performed to look for predictors of TLF and probable/definite ST.

3. Results

From September 2012 up to October 2014, 452 patients were intended to be treated with one or more BVS. Thirteen patients were excluded based on protocol related exclusion criteria of the BVS Expand registry and the BVS STEMI registry and 79 patients declined to participate in one of the two follow-up registries. Thus 360 patients (intention-to-treat group) remained for the purpose of this study. There were 9 cases of device failure in which a metallic stent was implanted and the per-treatment group consisted of 351 patients. A flowchart of the study is given in Fig. 1.

3.1. Baseline characteristics

Baseline characteristics are presented in Table 1. Presentation with ACS was present in 72.6% of the patients and 27.4% were stable patients. Mean age was significantly different between the two groups: 57.9 ± 10.7 years for ACS patients and 63.4 ± 8.9 years for non-ACS patients (P < 0.001). Dyslipidemia, history of MI, history of PCI and renal insufficiency were factors that occurred significantly more frequent in stable patients. ACS patients had more single vessel disease (71.5% versus 54.2%, P = 0.02).

Table 3
Procedural and angiographical characteristics.

	ACS N = 255, L = 300	Non-ACS N = 96, L = 128	P value
Procedural characteristics			
Aspiration (%)	34.4	0.0	<0.001
Rotablation (%)	1.0	5.6	0.02
Scoring balloon (%)	1.3	3.9	0.14
Invasive imaging at baseline (%)			
OCT	25.2	36.2	0.10
IVUS	9.9	24.8	<0.001
Pre-dilatation (%)	75.7	89.0	0.05
Pre-dilatation balloon: artery ratio	1.01 ± 0.21	1.05 ± 0.25	0.11
Maximum pre-dilatation balloon diameter (mm)	2.57 ± 0.42	2.60 ± 0.34	0.49
Maximum pre-dilatation inflation pressure (atm)	13.96 ± 3.02	14.01 ± 3.41	0.91
Buddy wire (%)	9.8	10.2	0.74
Daughter catheter (%)	3.6	4.0	0.80
Total number of scaffolds implanted	394	183	
Mean number of scaffolds/patient	1.55 ± 0.91	1.91 ± 1.11	0.11
Mean number of lesions/patient	1.18 ± 0.49	1.33 ± 0.56	0.015
Mean scaffold diameter (mm)	3.14 ± 0.37	3.02 ± 0.38	0.003
Mean scaffold length (mm)	20.35 ± 5.67	20.75 ± 5.99	
Overlap (%)	20.7	31.5	0.04
Post-dilatation (%)	41.3	62.2	0.001
Post-dilation balloon: mean scaffold diameter ratio	1.23 ± 0.21	1.31 ± 0.23	0.11
Maximum post-dilatation balloon diameter (mm)	3.38 ± 0.42	3.19 ± 0.42	0.003
Maximum post-dilatation inflation pressure (atm)	15.40 ± 3.00	16.10 ± 3.31	0.17
Clinical device success (%)	98.0	97.7	0.82
Clinical procedural success (%)	95.4	96.9	0.49
Angiographical characteristics			
Mean lesion length (mm)	22.41 ± 12.24	24.58 ± 14.58	0.35
Pre-procedure, overall			
RVD (mm ± SD)	2.65 ± 0.54	2.57 ± 0.45	0.22
MLD (mm ± SD)	0.69 ± 0.51	1.04 ± 0.40	<0.001
DS (%)	64.82 ± 42.0	47.94 ± 43.48	<0.001
Pre-procedure, non-total occlusion			
RVD (mm ± SD)	2.60 ± 0.48	2.58 ± 0.44	0.72
MLD (mm ± SD)	0.89 ± 0.39	1.06 ± 0.37	0.002
In-scaffold DS (%)	65.45 ± 20.91	58.62 ± 13.84	0.002
Pre-procedure, total occlusion (L = 80 for ACS and L = 11 for non-ACS)			
RVD (mm ± SD)	2.81 ± 0.69	1.78 ± 1.34	<0.001
Post-procedure, overall			
RVD (mm ± SD)	2.79 ± 0.48	2.77 ± 0.43	0.66
MLD (mm ± SD)	2.35 ± 0.42	2.26 ± 0.38	0.05
In-scaffold DS (%)	15.57 ± 8.47	18.46 ± 9.54	0.04
Acute gain (mm ± SD)	1.62 ± 0.65	1.22 ± 0.49	<0.001

Values are expressed as percentages or mean ± standard deviation when appropriate. P values are based on Chi square test or Fishers' exact test for categorical variables and Student's *t* test for continuous variables. ACS: acute coronary syndrome (ST-elevation myocardial infarction, non-ST myocardial infarction and unstable angina), non-ACS: non acute coronary syndrome (stable angina and silent ischemia), %DS: percentage diameter stenosis, IVUS: intravascular imaging, OCT: optical coherence tomography, MLD: minimal lumen diameter, RVD: reference vessel diameter.

Table 4
Clinical outcomes at one year.

	ACS (N = 255)	Non-ACS (N = 96)	P value
All-cause death (%)	0.0 (0)	3.2 (3)	0.05
Cardiac	0.0 (0)	3.2 (3)	0.05
Non-Cardiac	0.0 (0)	0.0 (3)	–
MACE (%)	5.5 (14)	5.3 (5)	0.90
Myocardial infarction (%)	5.1 (13)	2.1 (2)	0.22
Target lesion revascularization (%)	3.1 (8)	3.2 (3)	0.99
Target vessel revascularization (%)	3.5 (9)	3.2 (3)	0.86
Non-target vessel revascularization (%)	3.2 (8)	5.5 (5)	0.35
Overall scaffold thrombosis[a] (%)	2.4 (6)	4.2 (4)	0.37
Definite scaffold thrombosis (%)	2.0 (5)	2.1 (2)	0.94
Acute	1.2 (3)	0.0 (0)	0.29
Subacute	0.4 (1)	0.0 (0)	0.54
Late	0.4 (1)	2.1 (2)	0.12
Definite/probable scaffold thrombosis (%)	2.4 (6)	2.1 (2)	0.88
Acute	1.2 (3)	0.0 (0)	0.29
Subacute	0.4 (1)	0.0 (0)	0.54
Late	0.8 (2)	2.1 (2)	0.30

Event rates are summarized as %. P values are based on log rank test for comparing Kaplan Meier. MACE: major adverse cardiac events (composite endpoint consisting of cardiac death, myocardial infarction and target lesion revascularization).
[a] Includes definite, probable and possible ST.

Lesion characteristics are presented in Table 2. In both groups, the left anterior descending coronary artery (LAD) was most commonly treated (48.0% in ACS group and 54.4% in non-ACS group, P = 0.23). Lesions in stable patients were more complex, with a higher percentage of AHA/ACC type B2/C lesions. Pre-procedural TIMI flow was significantly different (P < 0.001). The mean lesion length was comparable in both groups (24.58 ± 14.58 mm for non-ACS versus 22.41 ± 12.24 mm for ACS, P = 0.35) (Table 3). Pre-procedural QCA analysis revealed significant differences between the groups in MLD: 0.69 ± 0.51 mm for ACS patients versus 1.04 ± 0.40 in stable patients (P < 0.001). After excluding the thrombotic total occlusions, this statistical difference remained (0.89 ± 0.39 mm for ACS versus 1.06 ± 0.37 mm for non-ACS, P = 0.002). Pre-procedural %DS was 65.45 ± 20.91% in the ACS group versus 58.62 ± 13.84% in non-ACS group (P < 0.001). Post-procedural QCA measurements revealed a superior acute performance in the ACS population: remaining %DS was significant lower (15.57 ± 8.47% versus 18.46 ± 9.54%, P = 0.04). Final MLD was larger (2.35 ± 0.42 mm versus 2.26 ± 0.38 mm, P = 0.05) and also acute lumen gain was higher (1.62 ± 0.65 mm versus 1.22 ± 0.49 mm, P < 0.001).

3.2. Procedural details

Procedural and angiographic details are summarized in Table 3. In ACS patients, pre-dilatation was performed in 75.7% of the lesions, compared to 89.0% in stable patients (P = 0.05). Pre-dilatation balloon to artery ratio was comparable (1.01 ± 0.21 versus 1.05 ± 0.25, P = 0.11). Post-dilatation was significantly less frequently performed in the ACS group (41.3% versus 62.2%, P = 0.001). Advanced lesion preparation was less often performed in ACS patients than in stable patients (rotational atherectomy: 1.0% versus 5.6%, P = 0.02; scoring balloon 1.3% versus 3.9%, P = 0.14). A total of 582 BVS were implanted: 399 in the ACS group (with a mean of 1.55 ± 0.91 scaffolds per patient) and 183 in stable patients (with a mean of 1.91 ± 1.11 per patient in stable patients).

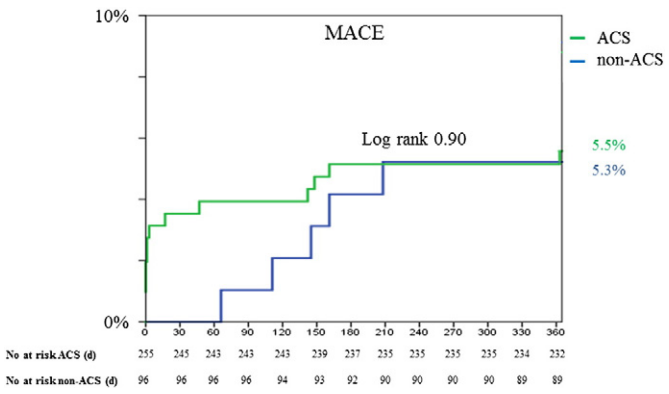

Fig. 2. Kaplan–Meier curve for MACE.

In the ACS population 6 cases of device failure occurred, all due to delivery failure. Main causes of these delivery failures were calcification and angulation (see Table 6 for details). Eight in-hospital MACE were reported. Whereas in the stable population 3 device failures (placement metal DES due to dissection after BVS implantation and delivery failures due to severe calcification and tortuosity) and no in-hospital MACE were documented in stable patients. Clinical device and procedural success were 98.0% and 95.4% for the ACS population and 97.7 and 96.9% respectively for stable patients.

3.3. Clinical outcomes

Data on survival status was available in 100% with a median follow-up period of 731 days (interquartile range [IQR]: 550–769 days). A total of 340 (96.9%) patients had a follow-up duration of at least 365 (±2) days.

Cumulative clinical events rates are summarized in Table 4. Clinical outcomes appeared to be comparable with no significant difference between patients presenting with ACS as compared to stable patients. Rate of death was 0.0% in the ACS group versus 3.1% in the non-ACS group (P = 0.06). Three patients died within the first year. One patient, with extensive cardiovascular disease died at day 166, 4 days after he went through a definite ST and MI, most probably due to a brief interruption of his antithrombotic medication during an elective surgery. The second patient died a few days after his prostate was surgically removed. In this case, dual antiplatelet inhibition therapy (DAPT) was also shortly interrupted causing a MI (probable ST). The last patient died of a sudden cardiac death 66 days after baseline PCI (possible ST).

MACE rate in the ACS population was comparable to the non-ACS population (5.5% versus 5.3%, P = 0.90, Fig. 2). MACE was mainly driven by MI and TLR. TLR rate was comparable in both groups. Rate of TVR was in 3.2% in ACS patients versus 3.5% in stable patients (P = 0.86). Non-TVR rate was 3.2% and 5.5% in respectively ACS and non-ACS patients (P = 0.350). Rate of definite ST was similar in both groups: 2.0% in the ACS group versus 2.1% in stable patients (P = 0.94). Of note, early ST only occurred in the ACS group, late thrombosis was more prevalent in stable patients (Table 4 and Fig. 3B).

A landmark survival analysis of MACE, definite/probable ST, MI and TLR indicated a trend for higher event rates of the ACS population in the short-term (<30 days). Conversely, mid-term event rates were higher in stable patients, although log rank test failed to prove significance (Fig. 3A–D).

In an univariate analysis of TLF the following characteristics tended to be related by at least a twofold increase in odds ratio (OR): renal insufficiency, bifurcation, male gender and age above 65 years (Table 5). The use of intravascular imaging at baseline might be protective for TLF (OR 0.49, P = 0.22).

4. Discussion

The present study reports on the comparative procedural and the one-year clinical outcomes of ACS patients versus non-ACS patients treated with an Absorb bioresorbable scaffold. The main findings of this study are summarized as follows: 1) angiographic outcomes were better in ACS patients despite the fact that less aggressive lesion preparation and less frequent post-dilatation were performed; 2) overall one-year ST rate in ACS patients was similar to the non-ACS patients.

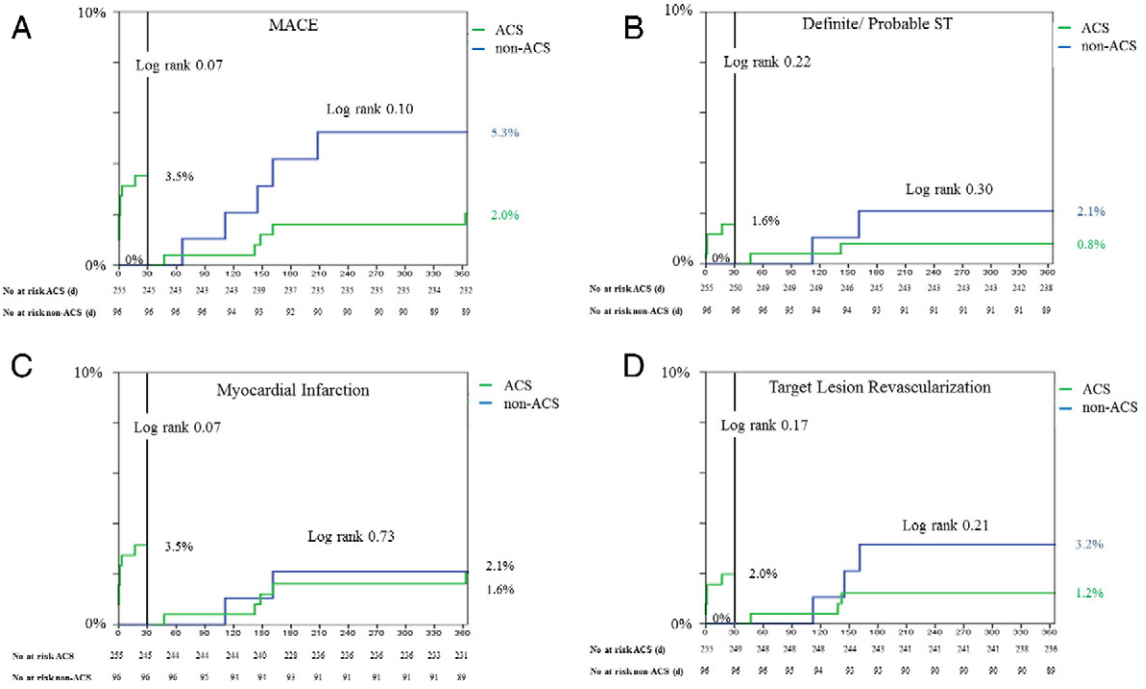

Fig. 3. A–D Landmark survival analysis for MACE, probable/definite ST, MI and TLR.

Interestingly, early definite ST occurred only in the ACS population while late ST seemed more frequent in stable patients; 3) despite the higher rate of early complications in the ACS group, landmark analyses after one month demonstrated that event rates were lower in this group than the stable patient group; and 4) clinical outcomes at one year were comparable among ACS and stable patients.

Differences between ACS patients and stable patients exist at multiple levels. On a patient level, patients presenting with ACS often are younger and thus have a longer life expectancy. Cardiovascular disease in this group is less extensive when compared to stable patients. Additionally, a different plaque composition is present, featured by a lipid-rich necrotic core with a thin fibrous cap. All these factors make ACS patients very attractive for bioresorbable technologies where full expansion is important and acute recoil a concern. Moreover, in ACS patients DAPT pretreatment is usually short (especially in STEMI patients) and frequently not yet resulting in active platelet function inhibition, while the thrombus burden is greater with high platelet activation and a systemic inflammatory response. These factors might amplify the risk of acute thromboses and cause a higher risk of MACE. For these reasons studies like ours are important to investigate the suitability of BVS in ACS patients. To the best of our knowledge, no data is available comparing the performance of BVS in ACS with stable patients compared to stable patients.

Table 5
Univariate analysis of TLF.

	Odds ratio ACS vs. non ACS (95% confidence interval)	P value
Renal insufficiency	3.28 (0.68–15.83)	0.14
Bifurcation	2.68 (0.98–7.36)	0.06
Male gender	2.38 (0.53–10.69)	0.26
Age above 65 years	2.10 (0.77–5.75)	0.15
History of MI	1.57 (0.43–5.73)	0.50
Small vessel (<2.5 mm)	1.54 (0.56–4.20)	0.40
Post-procedural TIMI 0/1	1.45 (0.53–3.99)	0.47
Underexpansion	1.30 (0.46–3.66)	0.62
Calcification	1.26 (0.46–3.46)	0.66
Long lesion (>32 mm)	1.20 (0.33–4.36)	0.78
Smoking	1.07 (0.74–1.54)	0.72
Diabetes mellitus	0.83 (0.18–3.78)	0.81
Presentation with ACS	0.82 (0.28–2.43)	0.72
Intravascular imaging at baseline	0.49 (0.15–1.54)	0.22

ACS: acute coronary syndrome, MI: myocardial infarction, TLF: target lesion failure (cardiac death, target vessel MI, ischemia driven TLR).

The BVS Expand registry and the BVS STEMI registry are two single-center, single-arm registries describing procedural clinical outcomes of patients treated with BVS. At variance of previous studies investigating the Absorb bioresorbable scaffold, all events were adjudicated by an independent clinical event committee (CEC). Also, all angiograms were analyzed using QCA. Lastly, combining the results of the two registries, both handling less restrictive inclusion criteria, we were able to create a study population reflecting a real-world population with a considerable amount of ACS patients.

The superior acute angiographic outcome in ACS patients compared to stable patients is an important observation. In previous studies it was demonstrated that the acute performance of the Absorb scaffold is somewhat inferior to metallic stents for stable angina patients. For example, in-device acute lumen gain in the ABSORB II trial was 1.15 ± 0.38 mm in BVS group versus 1.46 ± 0.38 mm in the EES group ($P < 0.001$). In the ABSORB III trial reported lumen gain was 1.45 ± 0.45 mm versus 1.59 ± 0.44 mm ($P < 0.001$). Finally, in the ABSORB Japan and ABSORB China trials acute lumen gain numbers were as follows: 1.46 ± 0.40 mm versus 1.65 ± 0.40 mm ($P < 0.0001$) and 1.51 ± 0.03 versus 1.59 ± 0.03 ($P = 0.04$) respectively. Remarkably, in STEMI patients no difference in acute gain was observed between BVS and DES (2.16 ± 0.52 mm versus 2.21 ± 0.56 mm, $P = 0.57$). This finding also suggests that the somewhat inferior angiographic results only imply for stable angina patients while the current semi-compliant balloon and wide strut BVS design are sufficient for the general softer plaque composition of ACS patients. In the current study, post-dilatation was significantly less frequently performed in ACS patients, however angiographic outcomes were better. Post-procedural MLD, RVD, %DS and in-scaffold acute lumen gain were all superior compared to post-procedural QCA measurements in stable patients. These promising angiographic results in ACS patients support the use BVS in this setting as they are predictive for clinical events.

Overall, one-year ST rate in ACS patients was similar to the non-ACS patients. The observed rate of early ST in the ACS population might raise some concerns. Previous studies have stated that presentation with ACS is an independent risk factor for the development of (metal) stent

Table 6
Details device failures in ACS population.

	Age (yr.)	Gender	Presentation	Culprit	Location	AHA/ACC	Calc.	Bif.	Ang.	Tort.	Additional device	Treatment
1	71	M	NSTEMI	RCA	RCA	B2	Severe	No	No	No	PT Graphix Super Support	3.0 × 28, 3.0 × 28 Xience
2	37	M	UAP	RCA	LCx	B1	No	No	Yes	No	None	2.5 × 12 Xience
3	60	M	UAP	LCx	LCx	B2	Moderate	No	Yes	No	None	2.5 × 18, 2.25 × 12 Xience
4	47	M	STEMI	LAD	LAD	B2	No	Yes	No	Yes	STO1 Heartrail	3.5 × 23 Xience
5	71	F	UAP	RCA	RCA	B2	Severe	No	No	No	Rotablator	4 Promus stents
6	59	M	UAP	LCx	LCx	B2	Severe	Yes	Yes	No	STO1 Heartrail	3.5 × 8 Xience

Ang = angulation, Bif = bifurcation, Calc = calcification, NSTEMI = non-ST elevation myocardial infarction, STEMI = ST elevation myocardial infarction, Tort = tortuositas, UAP = unstable angina pectoris.

thrombosis [18–20]. Using metal devices, multiple studies have documented that stenting of lesions with appeared plaque rupture are prone to delayed healing, characterized by higher percentages of uncovered, malapposed and protruding stent struts with a subsequent risk of stent thrombosis [21–24]. Furthermore, underexpansion appeared to be an important predictor [25–27]. This is also the case for ST in BVS patients [28,29]. In ACS patients, high thrombus burden, increased platelet activation and vasospasm are mechanisms that trouble optimal sizing resulting in higher rates of malapposition. In the acute setting, lesion preparation using pre-dilatation and intravascular imaging are less frequently performed than in stable patients. Although the acute scaffold expansion is on average better in the ACS population than in the stable population, it is very important to properly size the vessel and to optimize the final scaffold expansion in order to avoid early ST.

The landmark analysis beyond one month up to 12 months showed favorable results with regard to ST and TLR for the ACS patients (0.8% and 1.2% respectively). The somewhat higher event rates in the non-ACS group are a representation of a more complex non-study real world patient population. Therefore, the one-year MACE (composite of cardiac death, MI and TLR) rates of 5.5% (ACS) and 5.3% (non-ACS) are acceptable and comparable to trials using BVS in relatively simple lesions: 5.0% in the ABSORB II trial and 3.8% in the ABSORB China trial [9,12]. A comparable endpoint, target lesion failure (TLF: composite endpoint consisting of cardiac death, target vessel MI and ischemia driven TLR), in the ABSORB III and ABSORB Japan trials were 7.8% and 4.2% respectively [10,11]. In these studies, STEMI patients were excluded. Compared to studies investigating clinical outcomes of metal DES in STEMI patients, event rates in our report are higher than for EES but for lower compared to first-generation DES [30,31].

Recently, few concerns were raised concerning a potentially increased incidence of ST after implantation of a BVS [27,32–34]. Also, in our registry rate of definite ST (2.0% for ACS patients and 2.1% for stable patients) was higher compared to that of currently available metallic DES [35,36]. The importance of patient selection, lesion preparation, pre- and post-dilatation and also the consideration of intra-vascular imaging have to be underlined [37,38]. A pilot imaging study suggested suboptimal implantation as an important cause for BVS ST [28]. Use of intravascular imaging could improve pre-procedural vessel sizing, optimize lesion coverage and eventually reduce adverse events.

Next generation BVS with smaller scaffold struts may reduce the early event rates in ACS patients. For the current design, using more potent P2Y12 inhibitors such as ticagrelor, a direct-acting platelet inhibitor or cangrelor, an intravenous antiplatelet drug, could be valuable. In the ATLANTIC trial, ticagrelor was administered prehospital in the ambulance to STEMI patients, leading to a reduction in ST rate [39]. The CHAMPION PHOENIX trial assessed ischemic complications of PCI after administration of cangrelor and showed a decrease in these complications, with no significant increase in severe bleeding [40]. The upcoming HORIZONS-ABSORB AMI will compare the performance of BVS to DES when cangelor is used on top of heparin or bivalirudin in STEMI patients [41].

Rate of mortality in ACS patients is worse compared with patients who present with stable CAD [42–45]. In our patient cohort, mortality was 0% in the ACS population probably reflecting our exclusion criteria for the STEMI population (exclusion of patients presenting with cardiogenic shock). As shown by our landmark survival analyses, events in the ACS group are especially clustered in the early phase after BVS implantation. On the other hand, one-year Kaplan Meier curves for events are lower in ACS patients. This is probably due to patient selection, where ACS patients present with different patient and lesion factors (younger age, less extensive cardiovascular disease and more often simple lesions), and the higher intake of prasugrel and ticagrelor in these patients (76.1% versus 10.4%).

In summary, our results warrant further confirmation in a large-scale trial with a high number of ACS patients and an optimal implantation strategy tailored at the limitation of this first generation fully bioresorbable scaffolds. Ongoing and upcoming trials such as the AIDA, Compare Absorb (NCT02486068) and HORIZON-ABSORB AMI, will provide data derived from larger patient cohorts and in direct comparison to metallic DES [41,46].

5. Limitations

These results are derived from two single-center, single-arm registries with no direct comparison with metallic DES. The total number of patients in this study was limited.

Baseline differences in patient and lesion characteristics could have led to biased outcome in clinical event rates.

Furthermore, deciding which patient or lesion was suitable for BVS implantation could have led to selection bias. However, there was a fair amount of patients presenting with ACS and with B2/C lesions were included, indicating the complexity of the present study population.

6. Conclusion

Despite the higher rate of early complications due to early ST in the ACS population, the one-year clinical outcomes for BVS implantations in ACS patients versus non-ACS patients are comparable. The early ST rate observed in ACS needs further attention and optimized antiplatelet therapy may play a role. Angiographic outcomes for BVS in ACS patients are at least as good as non-ACS patients. Therefore, ACS patients may be suitable candidates for the treatment with the BVS if early procedural related complications can be avoided.

Conflict of interest

This study was supported by an unrestricted grant from Abbott Vascular. Robert-Jan van Geuns, Nicolas van Mieghem and Yoshinobu Onuma received speaker's fee from Abbott Vascular. The other authors have no conflicts of interest to declare. All authors have approved the final article.

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