




## ORIGINAL STUDIES

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# Predictors of scaffold failure and impact of optimized scaffold implantation technique on outcome: Results from the German-Austrian ABSORB RegIstRy

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## Abstract

**Aims:** We aimed to investigate predictors of scaffold failure and the potential impact of an optimized scaffold implantation technique by means of a learning curve on long-term clinical outcome after bioresorbable scaffold (BRS) implantation and to evaluate predictors of scaffold failure.

**Methods and results:** A total of 3326 patients were included in this prospective, observational, multi-center study (ClinicalTrials.gov NCT02066623) of consecutive patients undergoing BRS implantation between November 2013 and January 2016. The 3144 patients completed follow-up after 24 months, 3265 patients were eligible for time-to-event analysis. Clinical endpoints were major adverse cardiac events—a composite endpoint of death, target vessel revascularization and myocardial infarction, and scaffold thrombosis (ScT). Patients were grouped according to treatment before or since 2015. During follow-up MACE rate improved from 2.52% after 30 days, 5.45% after 6 months and 12.67% after 24 months to 1.52%, 3.44%, and 10.52%, respectively. A total of 75 ScT occurred. In multiple regression analysis, treatment of bifurcations, long lesions, and procedures performed earlier than 2014 were identified as predictors for the occurrence of ScT.

**Conclusion:** Treatment of bifurcation lesions is the strongest predictor of ScT following BRS implantation. A significantly lower incidence of ScT and 24-month target lesion revascularization in patients recruited after 2014 into our observational registry suggests the influence of a learning curve.

## KEYWORDS

bioresorbable scaffold, learning curve, scaffold thrombosis

**Abbreviations:** BRS, bioresorbable scaffold; DES, metallic drug-eluting stent; MACE, major adverse cardiac event; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; ScT, scaffold thrombosis; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.

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## 1 | INTRODUCTION

Bioresorbable scaffolds (BRS) have been developed for interventional treatment of coronary artery disease. Offering transient vessel support and full resorption within 2–3 years, BRS are intended to avoid late adverse events and other limitations of metallic drug-eluting stents (DES) through the absence of permanent caging of the treated coronary arteries, the restoration of vasomotoric function<sup>1</sup> and positive remodeling.<sup>2</sup> Ultimately, they were developed for the mitigation of the long-term risk of device related adverse events including restenosis and stent thrombosis.<sup>3</sup>

Among the several BRS being developed, the BRS with by far the most clinical experience is the Absorb BRS (Abbott Vascular, Santa Clara, CA, USA).<sup>4</sup> Though, despite the initial enthusiasm, the device showed an unexpectedly high incidence of scaffold thrombosis (ScT) early and late after implantation in single- and multi-center observational studies.<sup>5–8</sup> Hence, the device has ultimately been removed from the market due to low commercial sales. Incomplete expansion of the BRS is believed to be the strongest predictor of early ScT.<sup>9</sup> The implantation technique used for BRS is different from metallic stenting, since predilatation is mandatory and postdilatation is often required. This new technique and its particularities had to be adopted by the implanting physician. Hence, we thought to investigate predictors of scaffold failure and the potential impact of an optimized scaffold implantation technique by means of a learning curve on long-term clinical outcome after BRS implantation.

## 2 | METHODS

### 2.1 | Objectives and design

GABI-R is a prospective, observational and multi-center study (ClinicalTrials.gov NCT02066623) of patients undergoing BRS implantation. A total of 92 sites in Germany and Austria consecutively enrolled patients between 2013 and 2016. The study was approved by the responsible ethics board respectively. All patients gave written consent. The informed consent was checked in every case. Data sets were collected via an electronic case report form, which was provided by the IHF (Institut für Herzinfarktforschung, Ludwigshafen, Germany). This ensured an independent source verification quality control. Monitoring was performed in 30 participating sites, which enrolled at least 10 patients each. Follow-up via questionnaire or telephone interview was predefined by protocol after 30 days, 6 months and 2 years. Additional details have been published previously.<sup>10</sup> Patients were divided into two groups to investigate the potential impact of a learning curve by comparing implantations before and after 2015. Patients were included if they completed the 2 years follow-up, or died within the follow-up period.

### 2.2 | Definitions and target parameters

#### 2.2.1 | Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) was performed in accordance with standard clinical practice using the radial approach when technically feasible. Unfractionated heparin at 70 U/kg body weight was administered prior to the procedure. Pre and postdilatation were strongly recommended, albeit not mandatory. The additional use of intravascular imaging, for example, optical coherence tomography, was left to the operator's discretion. Procedural success was defined as a visually estimated residual stenosis <30% within the treated segment.

#### 2.2.2 | Scaffold thrombosis

ScT was classified as definite, probable and possible based on the Academic Research Consortium criteria.<sup>11</sup> Timing of ScT was categorized as early when occurring during the first 30 days, late between 1 month and 1 year, and very late beyond 1 year after BRS implantation. Definite ScT required angiographic or autopsy confirmation with thrombus originating in the BRS or in the segment 5 mm proximal or distal to the BRS. Probable ScT was considered to have occurred after intracoronary stenting in the following cases: any unexplained death within the first 30 days or any MI—irrespective of the time after the index procedure—that is related to documented acute ischemia in the territory of the implanted BRS without angiographic confirmation in the absence of any other obvious cause. Possible stent thrombosis was considered to have occurred with any unexplained death from 30 days after intracoronary stenting until end of trial follow-up.

Target parameters included major adverse cardiac events (MACE) that involved cardiac death, target vessel revascularization (TVR), or myocardial infarction (MI), and target lesion failure, including cardiac death, clinically driven target lesion revascularization (TLR), or target vessel MI. The composite endpoint of target vessel failure (TVF) comprises death, target vessel MI, and TLR. Clinically driven TLR was defined as  $\geq 50\%$  diameter stenosis and recurrent angina, objective signs of ischemia, abnormal results of invasive functional testing or  $\geq 70\%$  diameter stenosis even in the absence of the previously noted criteria.<sup>11</sup> Cardiac death was defined as death from an immediate cardiac cause or complications related to the procedure and those cases in which a cardiac cause could not be excluded. MI was defined according to the World Health Organization extended definition.<sup>12</sup>

All events were adjudicated by an independent events committee based on review of the angiograms. There was no quantitative core laboratory involved for adjudication. The events committee was not involved in the study.

### 2.3 | Statistical analysis

Statistical analysis was performed using SAS<sup>®</sup> software, version 9.4 for Windows. Copyright© 2002–2012 SAS Institute Inc. Categorical

data are presented as absolute numbers and percentages. Metric data are given as mean (*SD*) or median (lower, upper quartile). The frequencies of categorical variables were compared by the Pearson chi-square test, and the distribution of metrical variables by the Mann-Whitney-Wilcoxon test. Descriptive statistics were calculated from the available cases. Time-to-event data were visualized using cumulative incidence functions, regarding all-cause death as concurrent risk. A multiple Cox (i.e., proportional hazard) regression model was performed to evaluate the predictors of ScT. The threshold for statistical significance was  $p < 0.05$ .

### 3 | RESULTS

#### 3.1 | Baseline characteristics

Follow-up data until 2 years after index procedure was available in 3144 patients and therefore represented the basis for descriptive statistics. Until the end of 2014 overall 1430 patients (Group Early) were treated with a BRS and 1714 patients (Group Late) since 2015 respectively. Patients were slightly, but significantly younger in the Group Late (Early  $61.4 \pm 10.9$  vs. Late  $60.4 \pm 11.1$  years;  $p < 0.05$ ). This might have contributed to the difference of other baseline characteristics: patients treated later than 2015 (Group Late) showed less frequent hyperlipoproteinemia (Early 60.5% vs. Late 53.3%;  $p < 0.001$ ), arterial hypertension (Early 76.2% vs. Late 71.0%;  $p < 0.01$ ), prior percutaneous intervention (Early 29.5% vs. Late 26.3%;  $p < 0.05$ ), and chronic kidney disease (Early 9.2% vs. Late 6.8%;  $p < 0.05$ ). On the other hand, more current smokers were found in this group (Early 33.0% vs. Late 36.5%;  $p < 0.05$ ). There were no further significant differences concerning the patients' clinical presentation including the indication for coronary angiography (see Table 1). Medication at discharge can be found in Table S2 and S6.

#### 3.2 | Procedural findings

Procedural characteristics of patients undergoing BRS implantation prior to or later than 2015 did not differ significantly (see Table S1) by means of total scaffold length (Early 18.0 (18.0, 30.0) vs. Late 23.0 (18.0, 30.0);  $p = 0.19$ ), treated segments per patient (Early  $1.36 \pm 0.68$  vs. Late  $1.36 \pm 0.65$ ;  $p = 0.85$ ), average scaffold diameter (Early 3.0 (2.8, 3.5) vs. Late 3.0 (3.0, 3.5);  $p = 0.07$ ), and predilatation (Early 93.8% vs. Late 94.0%;  $p = 0.79$ ). Performance of predilatation itself did differ significantly: in patients in group Late there was a higher usage of high-pressure balloons (Early 37.4% vs. Late 47.5%;  $p < 0.0001$ ), larger balloons (Early  $2.73 \pm 0.42$  mm vs. Late  $2.8 \pm 0.50$  mm;  $p < 0.0001$ ), and most interestingly higher pressure (Early 13.39 bar vs. Late 13.79 bar;  $p < 0.001$ ) was applied. Operators made more use of debulking devices (Early 4.8% vs. Late 14.1%;  $p < 0.0001$ ) if the procedure was performed later. On the other hand, there was a trend towards less intravascular imaging in the later procedures, for example, IVUS (Early 4.1% vs. Late 2.1%;  $p < 0.01$ ). With respect to postdilatation (Early 70.4% vs. Late 81.2%;

$p = < 0.0001$ ), likewise to predilatation, there was a significant increase in those patients treated later than 2015. In addition, postdilatation maximum balloon pressure was slightly higher (Early 16.55 bar vs. Late 16.82 bar;  $p < 0.05$ ) (see Table 2).

Morphologically, in the "Group Late" the treated segments were predominantly classified as type A1/B1 (Early 59.1% vs. Late 67.2%;  $p < 0.0001$ ) rather than B2/C (Early 40.9% vs. Late 32.8%;  $p < 0.0001$ ) (see Table 2). While most lesions were of de-novo type in both groups, patients treated until 2014 showed a de novo lesion less frequently (Early 92.5% vs. Late 95.7%;  $p < 0.0001$ ). On the other hand, patients in Group Late involved less bifurcations (Early 3.6% vs. Late 2.2%;  $p < 0.01$ ).

Medication at discharge of patients undergoing the procedure until 2014 and after 2015 was not different (see Table S2).

Baseline and procedural characteristics divided by the occurrence of ScT during follow-up are shown in Table S3-S6.

#### 3.3 | Clinical outcome

At 30 days follow up the rate of major adverse events (MACE) computed to be 2.52% in Group Early and 1.52% in Group Late, which was statistically significant ( $p < 0.05$ ). This difference was driven by lower rates of TVR (Early 1.96% vs. Late 0.99%;  $p < 0.05$ ) and TLR (Early 1.54% vs. Late 0.70%;  $p < 0.05$ ). On the other hand, rates of definite ScT (Early 1.12% vs. Late 0.64%;  $p = 0.15$ ), TVF (Early 2.10% vs. Late 1.40%;  $p = 0.13$ ) and cardiovascular mortality (Early 0.21% vs. Late 0.41%;  $p = 0.32$ ) were comparable between the two groups (see Table 3).

The reduction in MACE rates was consistently present at 6 months follow up (Early 5.45% vs. Late 3.44%;  $p < 0.01$ ). In addition, patients that have been treated until 2014 showed a higher incidence of TVF (Early 4.83% vs. Late 3.33%;  $p < 0.05$ ), TVR (Early 4.69% vs. Late 2.74%;  $p < 0.01$ ), and TLR (Early 2.94% vs. Late 1.46%;  $p < 0.01$ ) compared to those patients that were treated since 2015. There was no statistical difference in cardiovascular mortality (Early 0.35% vs. Late 0.58%;  $p = 0.34$ ). Patients treated since 2015 suffered less definite ScT (Early 1.61% vs. Late 0.70%;  $p < 0.05$ ) as assessed at 6 months follow up.

Twenty-four months after the initial implantation of the BRS, MACE rates did not differ significantly between the two groups, however, there was still a trend towards a lower rate in the group of patients that were treated later (Early 12.67% vs. Late 10.52%;  $p = 0.08$ ). For TLR there was a statistical difference (Early 7.02% vs. Late 5.12%;  $p < 0.05$ ). Furthermore, there was no statistical difference with respect to TVR (Early 10.65% vs. Late 8.51%;  $p = 0.06$ ), TVF (Early 11.18% vs. Late 9.36%,  $p = 0.12$ ), and definite ScT (Early 2.56% vs. Late 1.52%;  $p = 0.06$ ). Mortality due to cardiovascular reasons was similar (Early 0.98% vs. Late 0.94%;  $p = 0.90$ ), though all-cause mortality was significantly reduced in patients treated since 2015 (Early 3.85 vs. Late 2.4%;  $p < 0.05$ ) 24 months after index procedure. There was no difference in the usage of optical coherence tomography (OCT) before PCI between the two groups (Early 5.0% vs. 4.0%;  $p = 0.18$ ).

**TABLE 1** Baseline characteristics of patients undergoing procedure before 2014 or after 2015 (n = 3144)

	Procedure since 2015 (n = 1714)	Procedure until 2014 (n = 1430)	p
Age (years)	60.4 ± 11.1 (1714)	61.4 ± 10.9 (1430)	<0.05*
Female sex (%)	22.8 (390/1714)	23.1 (331/1430)	0.79
Current or previous smoker (%)	58.3 (931/1596)	57.5 (794/1382)	0.63
Current smoker (%)	36.5 (583/1596)	33.0 (456/1382)	<0.05*
Previous smoker (%)	21.8 (348/1596)	24.5 (338/1382)	0.09
Diabetes mellitus (%)	20.0 (341/1701)	21.9 (310/1416)	0.21
Diabetes therapy diet (%)	61.2 (145/237)	55.8 (126/226)	0.24
Noninsulin-dependent diabetes mellitus (%)	66.4 (215/324)	67.3 (198/294)	0.79
Insulin-dependent diabetes mellitus (%)	35.4 (113/319)	32.4 (95/293)	0.43
Hyperlipoproteinemia (%)	53.3 (874/1641)	60.5 (828/1369)	<0.0001*
Family history for coronary heart disease (%)	39.7 (591/1488)	42.7 (546/1280)	0.12
Arterial hypertension (%)	71.0 (1201/1691)	76.2 (1073/1409)	<0.01*
History of myocardial infarction (%)	22.8 (384/1682)	21.5 (303/1412)	0.36
Prior percutaneous intervention (%)	26.3 (442/1680)	29.5 (417/1412)	<0.05*
Prior bypass surgery (%)	1.9 (32/1705)	3.3 (47/1426)	<0.05*
Chronic kidney disease (%)	6.8 (116/1697)	9.2 (131/1424)	<0.05*
Prior stroke (%)	2.7 (46/1713)	2.7 (39/1430)	0.94
Peripheral arterial disease (%)	4.4 (75/1713)	4.7 (67/1430)	0.68
Cancer	4.4 (75/1713)	5.8 (83/1430)	0.07
Number of diseases vessels			
1-vessel coronary artery disease (%)	43.6 (748/1714)	39.8 (569/1430)	<0.05*
2-vessel coronary artery disease (%)	29.7 (509/1714)	32.5 (465/1430)	0.09
3-vessel coronary artery disease (%)	26.6 (456/1714)	27.7 (396/1430)	0.49
Acute coronary syndrome (%)	52.7 (903/1713)	49.9 (714/1430)	0.12
Clinical indication			
Stable angina (%)	32.2 (552/1713)	35 (501/1430)	0.10
ST-elevation myocardial infarction (%)	18.4 (315/1713)	15.9 (228/1430)	0.07
NonST-elevation myocardial infarction (%)	22.7 (388/1713)	22.3 (319/1430)	0.82
Unstable angina (%)	11.7 (200/1713)	11.7 (167/1430)	1.00
eGFR (ml/min)	79.0 ± 23.2	79.8 ± 24.2	0.63
LVEF (%)	55.6 ± 10.7 (1027)	56.6 ± 10.2 (903)	<0.05

\*Denotes that the significance level is <0.05.

Abbreviations: eGFR, calculated glomerular filtration rate; LVEF, left ventricular ejection fraction.

### 3.4 | Predictors of ScT

The 3265 patients were eligible for time-to-event-analysis. A total of 2658 patients were eligible for descriptive analysis of predictors of ScT. During the follow up of 24 months 75 patients suffered a ScT. One of these patients was lost to follow-up after the event with not information regarding vital status or follow-up at 24 months. Baseline characteristics did not differ significantly (see Table S3). However, patients in which a ScT occurred were more likely to show a positive history of MI (ScT 35.6%vs. No ScT 21%; p < 0.01) and cancer (ScT 18.9% vs. No ScT 4.6%; p < 0.001). They also were more likely to have suffered a stroke previously (ScT 12.2% vs. No ScT 2.2%; p < 0.0001). Procedural characteristics can be found in Table S4-S5. A

multiple Cox regression analysis that included 3265 patients identified higher age (HR 1.14), scaffold diameter smaller than 3 mm (HR 1.17), a lesion length > 28 mm (HR 1.48), a procedure before 2014 (HR 1.57), no dual antiplatelet therapy (HR 2.09) and treatment of bifurcations (HR 3.86) to increase the risk for the occurrence of a ScT (see Figure 1). Cumulative incidences of ScT in dependency of their timing after BVS implantation can be seen in Figure 2.

## 4 | DISCUSSION

In the present study we investigate the procedural results and long-term clinical follow-up data of patients in a real-world population that

**TABLE 2** Procedural characteristics based on treated segments of patients undergoing procedure before 2014 or after 2015 (patients  $n = 3144$ , segments  $n = 4278$ )

	Procedure since 2015 ( $n = 2327$ )	Procedure until 2014 ( $n = 1430$ )	p
<b>Morphology of treated segments</b>			
Type A (%)	30.3 (704/2323)	22.0 (429/1947)	<0.0001*
Type B1 (%)	36.9 (858/2323)	37.0 (721/1947)	0.95
Type B2 (%)	16.7 (389/2323)	23.0 (447/1947)	<0.0001*
Type C1 (%)	12.7 (295/2323)	12.5 (244/1947)	0.87
Type C2 (%)	3.3 (77/2323)	5.4 (106/1947)	<0.0001*
Type A/B1 (%)	67.2 (1562/2323)	59.1 (1150/1947)	<0.0001*
Type B2/C (%)	32.8 (761/2323)	40.9 (797/1947)	<0.0001*
<b>Type of lesion</b>			
De novo (%)	95.7 (2223/2323)	92.5 (1802/1949)	<0.0001*
Re-stenosis (%)	0.6 (13/2323)	0.5 (9/1949)	0.66
In-stent re-stenosis (%)	0.9 (20/2323)	1.1 (21/1949)	0.47
Bifurcation (%)	2.2 (52/2323)	3.6 (71/1949)	<0.01*
<b>Pretreatment</b>			
Predilatation (%)	94.0 (1934/2058)	93.8 (1626/1734)	0.79
with high-pressure balloon (%)	47.5 (916/1928)	37.4 (606/1622)	<0.0001*
with semi-compliant balloon (%)	25.8 (233/904)	32.2 (194/603)	<0.01*
with noncompliant balloon (%)	74.2 (671/904)	67.8 (409/603)	<0.01*
Maximum balloon diameter (mm)	2.80 ± 0.50 (1931)	2.73 ± 0.42 (1626)	<0.0001*
Maximum balloon length (mm)	15.75 ± 4.47 (1931)	16.12 ± 4.51 (1626)	0.06*
Maximum balloon pressure (bar)	13.79 ± 3.31 (1923)	13.39 ± 3.20 (1607)	<0.001*
<b>Scaffold characteristics</b>			
Average scaffold diameter (mm [Quartile])	3.0 (3.0, 3.5)	3.0 (2.8, 3.5)	0.07
Average scaffold length (mm [Quartile])	18.0 (18.0, 23.0)	18.0 (18.0, 23.0)	0.33
<b>Posttreatment</b>			
Postdilatation (%)	81.2 (1671/2058)	70.4 (1220/1732)	<0.0001*
with high-pressure balloon (%)	92.3 (1541/1669)	87.2 (1064/1220)	<0.0001*
with semi-compliant balloon (%)	6.1 (93/1532)	7.8 (83/1061)	0.08
with noncompliant balloon (%)	93.9 (1439/1532)	92.2 (978/1061)	0.08
Maximum balloon diameter (mm)	3.26 ± 0.44 (1667)	3.27 ± 0.46 (1219)	0.62
Maximum balloon length (mm)	15.33 ± 4.26 (1667)	15.15 ± 4.23 (1219)	0.19
Maximum balloon pressure (bar)	16.82 ± 3.95 (1663)	16.55 ± 4.12 (1216)	<0.05*
Procedure successful	98.7 (2292/2323)	99.3 (1937/1950)	<0.05*

\*Denotes that the Significance level is <0.05.

underwent BRS implantation taking timing of PCI into account. We furthermore investigated predictors of ScT in our cohort. The principal findings are:

1. An optimized scaffold implantation technique as assessed by means of implantation period indicates the influence of a learning curve because early procedures (until 2014) show higher adverse event rates and a higher TLR after 24 months compared to procedures since 2015.
2. Treatment of bifurcations, long lesions, and procedures performed earlier than 2014 are predictors for the occurrence of ScT during follow-up.

Various new techniques in cardiology have shown learning curves<sup>13-15</sup> that is being described by an optimized implantation technique. Even for BRS, we find evidence for a learning curve in previously published data. While the ABSORB Cohort B study demonstrated a MACE rate of 9.0%, the following ABSORB Extend study revealed a rate of only 4.3%.<sup>15,16</sup> This finding is not limited to the BRS with by far the most clinical experience, the Absorb BRS (Abbott Vascular, Santa Clara, CA, USA), but can also be derived from two separate studies that investigate the DESolve scaffold (Elixir Medical Corporation, Sunnyvale, California). Here, MACE rate dropped from 13% to 5.7%, and TLR from 6.7% to 3.2% respectively.<sup>17,18</sup> The principal findings of these studies—that, however, were originally designed to

**TABLE 3** Clinical outcome of patients undergoing procedure before 2014 or after 2015 (n = 3144)

	Follow-up after 30 days			Follow-up after 6 months			Follow-up after 24 months		
	Procedure since 2015	Procedure until 2014	p	Procedure since 2015	Procedure until 2014	p	Procedure since 2015	Procedure until 2014	p
All-cause mortality (%)	0.58 (10/1714)	0.42 (6/1430)	0.52	1.28 (22/1714)	1.19 (17/1430)	0.81	2.40 (41/1708)	3.85 (55/1427)	<0.05*
MACE (%)	1.52 (26/1714)	2.52 (36/1430)	<0.05*	3.44 (59/1714)	5.45 (78/1430)	<0.01*	10.52 (153/1454)	12.67 (160/1263)	0.08
TVF (%)	1.40 (24/1714)	2.10 (30/1430)	0.13	3.33 (57/1714)	4.83 (69/1430)	<0.05*	9.36 (136/1453)	11.18 (141/1261)	0.12
TVR (%)	0.99 (17/1714)	1.96 (28/1430)	<0.05*	2.74 (47/1714)	4.69 (67/1430)	<0.01*	8.51 (123/1446)	10.65 (134/1258)	0.06
TLR (%)	0.70 (12/1714)	1.54 (22/1430)	<0.05*	1.46 (25/1714)	2.94 (42/1430)	<0.01*	5.12 (74/1444)	7.02 (88/1254)	<0.05*
Definite ScT (%)	0.64 (1/1714)	1.12 (16/1430)	0.15	0.70 (12/1714)	1.61 (23/1430)	<0.05*	1.52 (22/1443)	2.56 (32/1251)	0.06
Myocardial infarction (%)	1.05 (18/1714)	1.89 (27/1430)	<0.05*	1.34 (23/1714)	3.01 (43/1430)	<0.01*	4.01 (58/1446)	6.28 (79/1257)	<0.01*
Cardiovascular mortality (%)	0.41 (7/1714)	0.21 (3/1430)	0.32	0.58 (10/1714)	0.35 (5/1430)	0.34	0.94 (16/1708)	0.98 (14/1427)	0.90

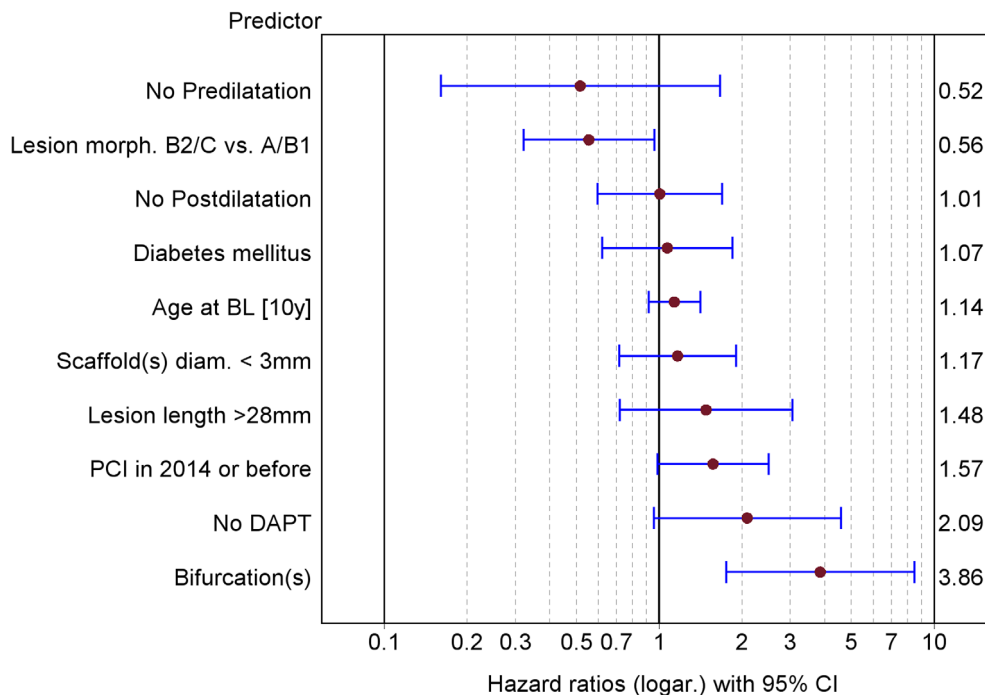
\*Denotes that the Significance level is &lt;0.05.

Abbreviations: MACE, major adverse cardiac event; TVF, target vessel failure; TVR, target vessel revascularization; TLR, target lesion revascularization; ScT, scaffold thrombosis.

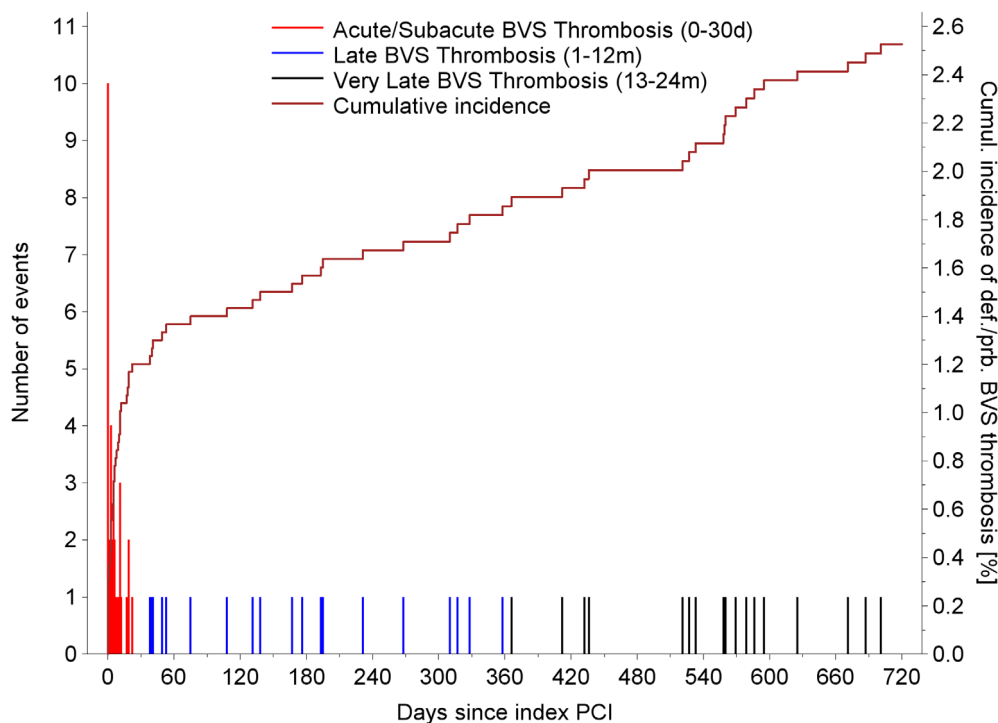
evaluate clinical outcome of the particular study cohort rather than evaluating a learning curve—go well along with the finding of this study. In our population, patients that were treated until 2014 showed significantly higher major adverse event rates than in patients that were treated from 2015 on; this finding was consistently present 30 days and 6 months after the initial implantation of the BRS. These findings are in agreement with reports of Nef et al.<sup>19</sup> and Wiebe et al.<sup>20</sup> Our real-world data show this as a trend even at 24 months follow-up. Furthermore, TLR at follow-up 24 months after the BRS implantation was as high as 7.02% in Group Early and only 5.12% in Group Late (p < 0.05). The most reasonable explanation for this beneficial result in the patients that have been treated later is the effect of the learning curve in the implantation technique. Thus, procedural data clearly showed a more thoughtful lesion preparation. This included the use of high-pressure balloons with larger diameters for predilatation and usage of debulking devices. Following BRS deployment, higher rates of postdilatation (Early 67.2% vs. Late 76.8%; p < 0.0001) with even higher pressure was performed. The expansion of BRS can be improved by aggressive plaque modification with 1:1 predilatation.<sup>21</sup> Postdilatation, on the other hand, does not seem to improve the expansion as reported by Brown et al.<sup>21</sup>; however, no randomized data supporting this are available. The retrospective GHOST-EU registry also showed that systematic predilatation, adequate sizing and systematic postdilatation, the so-called PSP-technique, is associated with improved outcome. However, the authors were not able to demonstrate a learning curve in their cohort.<sup>22</sup> Stone et al.<sup>23</sup> were able to show that vessel sizing and operator technique were strongly associated with BVS-related outcomes during 3-year follow-up, though, included patients of ABSORB studies that partly made inherit major exclusions, for example, left ventricular ejection fraction of <30%, CABG at any time in the past, cancer, previous stroke or an acute coronary syndrome. Moreover, it must be noted that not only implantation technique might have positively influenced the results, but that patient selection did also change over time. Less complex lesion and less bifurcations have been treated with increasing experience. Ultimately, our data show that the learning process and experience gathered with the number of implantations contribute to a reduction in all-cause mortality but also TLR 24 months after initial implantation.

ScT occurred in 74 of the studied patients. The timing of initial implantation did not affect the incidence throughout the whole follow-up in the analysis. One of the reasons may be the vanishingly small usage of intravascular imaging. Intravascular ultrasound (IVUS) was used in 4.1% in Group Early and 2.1% in Group Late (p < 0.01). Optical coherence tomography (OCT) was only used in 5.0% versus 4.0% (p = 0.18). Intravascular imaging can help the operator during implantation process by means of strategical decisions but also to assess the final mechanical outcome. It was shown that a final minimum cross-sectional area < 5 mm<sup>2</sup> increases the risk of stent thrombosis.<sup>24</sup> In addition, it is known that malapposition can lead to stent-related effects and increase the rate of MACE.<sup>25</sup> Malapposed struts may disrupt the laminar flow and activate platelets due to high shear stress and ultimately promote thrombotic events. It has lately been shown that the

**FIGURE 1** Predictors of scaffold thrombosis (ScT) during follow-up



**FIGURE 2** Cumulative incidence and number of events in dependence of timing after initial implantation of bioresorbable scaffold (BRS)



incidental finding of strut malapposition is a predictor of late and very late thrombosis in BRS.<sup>26</sup> Similar data are also available for metallic stents; malapposition was the leading finding in the Bern and PESTO registries of stent thrombosis and among the three leading mechanisms in the PRESTIGE registry.<sup>27,28</sup> Previous IVUS and OCT studies using DES were able to show a reduction of adverse events if the procedure was guided by either OCT or IVUS.<sup>29,30</sup> Therefore, it is highly advisable to include an invasive imaging modality to optimize the deployment when treating patients with BRS.<sup>31</sup>

We performed a multiple Cox regression analysis to identify predictors for ScT. Analysis of our patients showed that the strongest predictors are a lesion length > 28 mm (HR 1.48), a procedure before 2014 (HR 1.57), no dual antiplatelet therapy (HR 2.09), and treatment of bifurcations (HR 3.86). This goes well along with findings of Gori et al.<sup>32</sup> who retrospectively investigated the outcome of patients with complex lesions that involve the ostium. They found a significantly higher rate of ScT and a device-oriented composite endpoint. Furthermore, Bennett et al. note that distorted neo-carinal struts with

adherent strands of chronic thrombus increase the risk for exposed polymeric breakdown products that may be thrombogenic.<sup>33</sup> Hence, the use of BRS in interventions with the chance of suboptimal results should be considered with care.

## 5 | LIMITATIONS

There are several limitations inherent to this study. The protocols used for lesion preparation, scaffold deployment, and postdilatation were the same for all operators contributing to the study; however, potential discrepancies in operator decisions that may have affected the final acute mechanical result cannot be excluded. There were no protocol-mandated criteria predefined regarding the selection of either a BRS or a metallic stent. The decision was left to the implanting physician's discretion. Another limitation is that there was no specific sizing modality required to support optimal BRS selection. In most cases a visual estimation of the vessel size was performed and usage of intravascular imaging modalities (e.g., IVUS or OCT) was rather low in both groups. Its broader and more liberate usage may further improve the acute mechanical performance of BRS. Routine angiographic follow-up was not scheduled for patients in this registry and the analysis does not include any angiographic outcome measurements.

## 6 | CONCLUSIONS

This is the first study to investigate predictors of scaffold failure and the potential impact of an optimized scaffold implantation technique by means of a learning curve on long-term clinical outcome after BRS implantation. We were able to show that the learning curve that is described by an adaptation of implantation technique results in reduced major adverse event rates and ultimately leads to a reduced TLR rates. Using a multiple regression analysis, we were able to identify lesion length > 28 mm, a procedure before 2014, no dual antiplatelet therapy and most notably treatment of bifurcations as predictors of S<sub>CT</sub>.

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### CONFLICT OF INTEREST

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### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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