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Original article

Clinical Outcomes After Implantation of Overlapping Bioresorbable Scaffolds vs New Generation Everolimus Eluting Stents

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ABSTRACT

Introduction and objectives: There is limited evidence on procedural and clinical outcomes in patients treated with overlapping bioresorbable scaffolds vs overlapping everolimus-eluting stents. We evaluated the outcomes of propensity-matched patients treated with overlapping scaffolds vs everolimus-eluting stents.

Methods: After propensity matching, 70 consecutive stable angina patients treated with overlapping bioresorbable scaffolds and 70 patients treated with overlapping new generation everolimus stents were included in this study. The primary outcome was the 1-year rate of major adverse cardiovascular events, defined as the composite of all-cause mortality, nonprocedural myocardial infarction, and target-vessel revascularization.

Results: Patients in the 2 groups had similar age (scaffold vs stent: 64.5 ± 10.3 vs 66 ± 9.7 years; $P = .381$), sex, diabetes, previous cardiovascular history, and SYNTAX score (scaffold vs stent: 18.6 ± 9.2 vs 19.4 ± 10.4; $P = .635$). Postprocedural acute gain was significantly lower in patients treated with scaffolds (1.82 ± 0.66 vs 2.03 ± 0.68 mm; $P = .033$). At 1-year follow up, the estimated major adverse cardiovascular event rate was not significantly different between the 2 groups (scaffold vs stent: 14.5% vs 14.6%; $P_{\text{log-rank}} = .661$). Similarly, no significant differences were seen in 1-year rates of target vessel (scaffold vs stent: 14.5% vs 10%; $P_{\text{log-rank}} = .816$) or target lesion revascularization (scaffold vs stent: 9.7% vs 8.3%; $P_{\text{log-rank}} = .815$).

Conclusions: Treating long lesions with overlapping scaffolds is feasible with acceptable 1-year outcomes.

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Resultados clínicos tras el implante de armazones bioabsorbibles solapados en comparación con *stents* liberadores de everolimus de nueva generación

Palabras clave:
Armazón bioabsorbible
Stent liberador de everolimus
Solapamiento
Strut
Stent farmacoactivo

RESUMEN

Introducción y objetivos: La evidencia sobre los resultados de la intervención y la evolución clínica de los pacientes tratados con armazones bioabsorbibles solapados en comparación con los tratados con *stents* liberadores de everolimus solapados es escasa. Se evalúan los resultados de pacientes tratados con armazones solapados frente a los tratados con *stents* liberadores de everolimus emparejados por puntuación de propensión.

Métodos: Tras aparearlos por puntuación de propensión, se incluyó en este estudio a 70 pacientes consecutivos con angina estable tratados con armazones bioabsorbibles solapados y 70 pacientes tratados con *stents* liberadores de everolimus de nueva generación. El objetivo principal fue la tasa a 1 año de eventos adversos cardiovasculares mayores, definidos como el conjunto de muerte por cualquier causa, infarto de miocardio no asociado a la intervención y revascularización del vaso diana.

Resultados: Los pacientes de los 2 grupos tenían características similares en cuanto a edad (grupo de armazones bioabsorbibles frente a grupo de *stents*, 64,5 ± 10,3 frente a 66 ± 9,7 años; p = 0,381), sexo, diabetes mellitus, antecedentes cardiovasculares y puntuación SYNTAX (armazón frente a *stent*, 18,6 ± 9,2 frente a 19,4 ± 10,4; p = 0,635). La ganancia aguda tras la intervención fue significativamente menor en los pacientes tratados con armazones bioabsorbibles (1,82 ± 0,66 frente a 2,03 ± 0,68 mm; p = 0,033). En el seguimiento a 1 año, la tasa de eventos adversos cardiovasculares mayores estimada no mostró diferencias

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significativas entre los 2 grupos (el 14,5 y el 14,6%; $p_{log\text{-}rank}$ = 0,661). De manera análoga, no se observaron diferencias significativas en las tasas a 1 año de revascularización del vaso diana (el 14,5 y el 10%; $p_{log\text{-}rank}$ = 0,816) o de revascularización de lesión diana (el 9,7 y el 8,3%; $p_{log\text{-}rank}$ = 0,815).

Conclusiones: El tratamiento de lesiones largas con el uso de armazones bioabsorbibles solapados es viable y proporciona unos resultados a 1 año aceptables.

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Abbreviations

BRS: bioresorbable scaffold
EES: everolimus-eluting stent
MACE: major acute cardiovascular events
MI: myocardial infarction
PMI: periprocedural myocardial infarction
TLR: target lesion revascularization

INTRODUCTION

The initial experience with bioresorbable scaffold (BRS) implantation in *de novo* simple lesions has been promising with acceptable long-term outcomes in the ABSORB cohort A.[1] The ABSORB[2] multi-imaging modality study revealed unchanged late lumen loss after the first year of Absorb v1.1 implantation, whereas on intravascular ultrasound (IVUS), mean lumen, scaffold and vessel area showed enlargement up to 2 years.

Even though the emerging randomized data[3-8] suggest similar angiographic and intermediate-term clinical outcomes in patients treated with BRS and those treated with new generation everolimus-eluting stents (EES), real-world studies have revealed some worrying signs of increased rates of scaffold thrombosis in patients treated with BRS. The 6-month 3.0%, 2.2%, 2.1% scaffold thrombosis rates quoted in the AMC, BVS EXPAND and GHOST-EU registries,[9] respectively, cannot be considered negligible and several potential scaffold thrombosis mechanisms have been proposed, one of which involves overlapping segments. Previous studies in porcine models[10] revealed reduced endothelial coverage of stacked BRS struts 28 days post implantation, suggesting a potential substrate for scaffold thrombosis and future target lesion revascularization (TLR).

The current study sought to evaluate procedural (acute gain, angiographic, and procedural success) and mid-term clinical outcomes among stable angina patients treated with percutaneous coronary intervention with overlapping BRS or new generation EES.

METHODS

A total of 590 stable angina patients were treated at the EMO GVM Centro Cuore Columbus, Milan, Italy with BRS (Absorb v1.1, Abbott Vascular; Santa Clara, California, United States) from May 2012 to July 2014 or new generation durable polymer EES (XIENCE Prime, Abbott Vascular or Promus Element, Boston Scientific; Natick, Massachusetts, United States), from May 2011-July 2014. Of these, 219 were treated with BRS and 371 with new generation EES. There were no particular selection criteria for the implantation of BRS vs EES in our population other than patient preference. A vessel reference vessel diameter $>$ 4.2 mm or $<$ 2.5 mm was prohibitive for BRS implantation. Overlapping lesions (Figures 1 and 2) were identified as those requiring implantation of at least 2 overlapping stents/scaffolds, excluding bifurcation lesions treated with a 2-stent/scaffold strategy. Other exclusion criteria included acute coronary syndrome (ACS) presentation and end-stage renal failure (on hemodialysis).

A total of 109 stable angina patients treated with overlapping BRS and 149 patients treated with overlapping new generation EES were included in the analysis. All patients provided written informed consent, according to the Declaration of Helsinki. All clinical data at follow-up were collected from hospital visits or telephone consultations for all patients.

All patients were pretreated with aspirin and clopidogrel, ticagrelor or prasugrel and were instructed to continue with dual antiplatelet therapy for at least 1 year. Quantitative coronary angiographic measurements were performed offline using a validated edge detection system (CMS, version 5.2, Medis Medical Imaging Systems BV; Leiden, The Netherlands) by an expert operator; pre- and postprocedural minimal lumen diameter and the percentage of diameter stenosis were measured at baseline. The in-stent/scaffold acute gain was defined as the difference between pre- and postprocedural minimal lumen diameter. Stent overlap was defined as the presence of $\geq$ 2 stents within a single treated lesion, as determined by quantitative coronary angiography.[11] For patients presenting with TLR, overlapping stent zones were identified based on the position of the stent balloon markers of the second stent relative to the first stent. In particular, the overlapping segments were characterized as adjacent scaffolds/stents (overlap $<$ 1 mm), minimal (1-2 mm) and complete ($>$2 mm overlap). Intravascular ultrasound was used in the majority of BRS cases to ensure optimal expansion and apposition of the scaffold. The fairly high use of IVUS among patients with EES reflects the complexity of the lesions treated (calcified, in-stent restenosis, bifurcations etc).

Furthermore, lesions with TLR were categorised using the Mehran classification.[12] Angiographically moderate/severe calcification was defined as radiopacities noted with or without cardiac motion before contrast injection, generally compromising both sides of the arterial lumen.[13,14] The SYNTAX score was prospectively calculated for all patients.[13] Angiographic success was defined as a minimum diameter stenosis of $<$ 20%, with TIMI flow grade 3 without occlusion of a significant side branch, flow-limiting dissection, distal embolization, or angiographic evidence of thrombus. Procedural success was defined as the composite endpoint of angiographic success without associated in-hospital major clinical complications (ie, death, myocardial infarction [MI], stroke, or emergency coronary artery bypass [CABG]).[15] Periprocedural myocardial infarction (PMI) definition was similar to that used in the study by Vranckx et al.[16]

The primary endpoint was the 1-year rate of major acute cardiovascular events (MACE), defined as the composite of all-cause mortality, nonprocedural MI, and target vessel revascularization (TVR). Secondary endpoints included procedural outcomes (acute gain, angiographic and procedural success), TLR and TVR. TVR was defined as repeat revascularization of the target vessel,

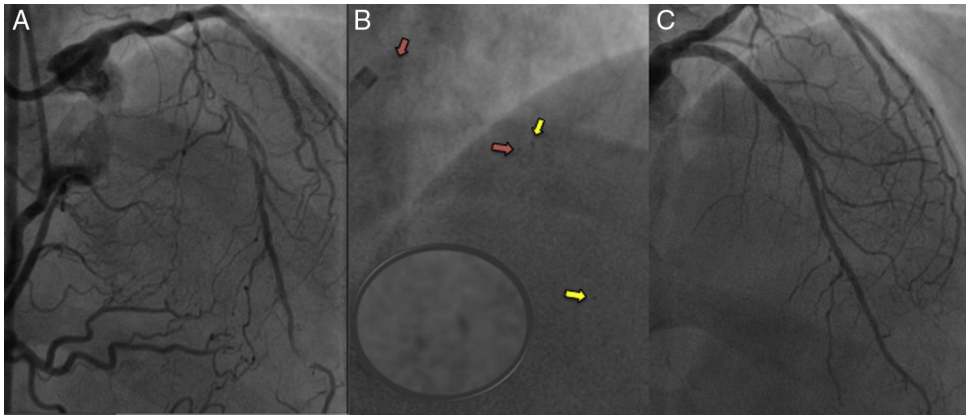


Figure 1. Overlapping proximal and mid segment bioresorbable scaffolds (BRS) in a young patient with a chronic total occlusion of the left anterior descending. A: left anterior descending backfilling from collaterals from the distal right. Long segment of chronic total occlusion seen in ostial-proximal segment. B: after aggressive lesion preparation, 2 BRS (3.5 × 18 mm Absorb) were implanted at the ostial-proximal and mid segments with minimal overlap. The platinum markers of the proximal BRS are shown with the red arrows, while the platinum markers of the mid segment BRS are shown with the yellow arrows. At the overlap segment, the distal platinum marker of the proximal BRS and the proximal platinum marker of the distal BRS (enlarged circle) can be seen side by side. C: final result after postdilatation of the proximal-mid segment BRS and drug eluting balloon at the distal segment.

and TLR was defined as repeat revascularization of the stented segment, or within 5 mm from the stent edges. Nonprocedural follow-up acute MI was defined as per current guidelines.[17] Stent thrombosis was classified according to the Academic Research Consortium definition.[18]

Statistical Analysis

All continuous variables were tested for normality using the Kolmogorov-Smirnov test. Continuous variables are presented as mean ± standard deviation or median [interquartile range] for normally and not normally distributed variables, respectively. Differences in continuous variables between overall cohort groups were analysed using the Student *t*-test or Mann-Whitney U test.

To reduce the effect of selection bias and other baseline confounding in this retrospective study, we performed propensity score matching (BRS:EES, 1:1). The propensity scores were estimated with the use of a nonparsimonious multivariable logistic regression model, with percutaneous intervention with BRS or EES as the dependent variable, and the following patient and angiographic characteristics as covariates (considered clinically important predictors of MACE): age, sex, diabetes mellitus, prior MI, prior percutaneous coronary intervention, prior CABG, SYNTAX score, and total stent length. Matching was performed with the use of a 1:1 matching protocol without replacement (greedy matching algorithm), with caliper width equal to 0.2 of the standard deviation of the logit of the propensity score. After propensity score matching, all of the standardized differences for each of the baseline variables were < 0.10 (10%). After propensity matching, differences in continuous variables were analyzed using the paired *t*-test. Categorical variables are expressed as numeric values and percentages. Categorical data were compared using the chi-square or Fisher exact tests (overall cohort) or McNemar test (propensity-matched cohort). The cumulative incidences were generated using Kaplan-Meier analysis, and the significance of observed differences was assessed with the log-rank test (overall cohort) or with the use of a Cox proportional-hazards regression model that was stratified on the matched pair to preserve the benefit of matching (propensity matched cohort).

All reported *P* values were 2-sided, and values of $P < .05$ were regarded as statistically significant. Analyses were performed using SPSS (version 21.0, IBM Corp.; Armonk, New York, United States).

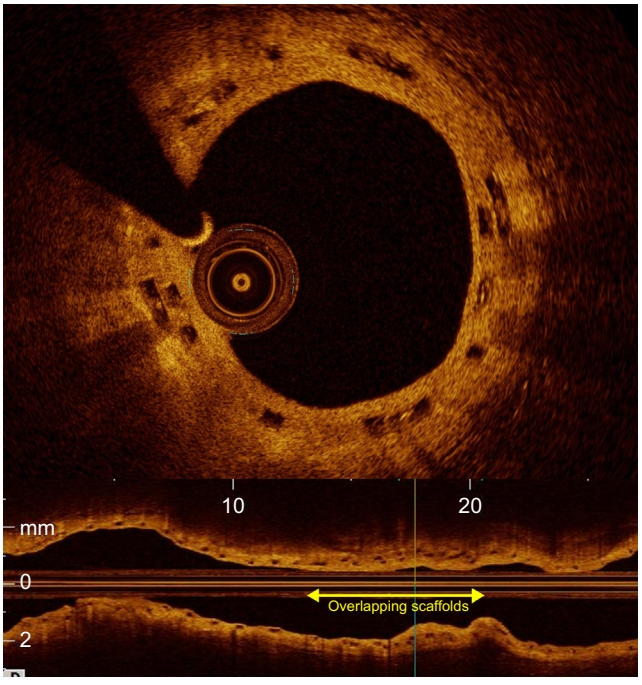


Figure 2. Optical coherence tomography (cross-section and longitudinal images) of a patient treated with overlapping bioresorbable scaffolds (~15 mm overlap) at the 2-year follow-up. Scaffold struts can been seen stacked on each other (black boxes) and fully covered by neointima. In the longitudinal cross-section, the length of the overlap is shown with the yellow arrow.

RESULTS

Baseline Characteristics

Patient Demographics

Baseline characteristics of the overall overlap cohort are presented in Table 1. Of these, 70 patients treated with BRS

were matched 1:1 with 70 EES patients. Baseline characteristics of the propensity matched cohort are presented in Table 2. None of the propensity-matched variables showed any statistically significant differences between the 2 groups. Patients treated with BRS were more often ex-smokers, while patients treated with EES had a significantly lower estimated glomerular filtration rate (Table 2). Single-vessel disease was present in 60% of the patients in both groups. Intravascular ultrasound was more commonly used among patients treated with BRS.

Lesion and Procedural Characteristics in the Propensity Matched Cohorts

Rates of type B2/C lesions were similar in the 2 groups (Table 3). The left anterior descending artery was more frequently treated in the BRS group than in the EES group, whereas the right coronary artery was more frequently treated in the EES group. There was a significantly higher rate of calcific and bifurcation lesions among patients treated with BRS whereas there was a trend for higher rates of chronic total occlusions and in-stent restenosis in the EES group (Table 3). SYNTAX scores were similar between the 2 groups (Table 2). Predilatation (with both conventional and scoring balloons) and postdilatation were more frequently performed in patients treated with BRS (Table 3). Out of 101 lesions treated in the BRS group, 78 involved overlapping segments, whereas out of 120 lesions in the EES group, 79 involved overlapping segments (Table 3).

Table 1
Baseline Characteristics in the Overall Cohort

	BRS (n = 109)	EES (n = 149)	*P*
Age, y	63.4 ± 9.8	68.1 ± 10.2	< .001
Male sex	98 (89.9)	141 (94.6)	.151
Risk factors			
Diabetes mellitus	35 (32.1)	40 (26.8)	.358
Hypertension	68 (62.4)	77 (53.5)	.156
Smoking status			.026
Curent	14 (12.8)	24 (16.6)	
Ex-smoker	52 (47.7)	45 (31.0)	
Never smoked	43 (39.4)	76 (52.4)	
Dyslipidemia	77 (70.6)	72 (48.3)	< .001
Family history	40 (36.7)	61 (40.9)	.490
Cardiovascular history			
Previous MI	29 (31.5)	62 (41.6)	.117
Previous PCI	54 (49.5)	83 (55.7)	.327
Previous CABG	7 (6.4)	33 (22.3)	.001
LEVF, %	54.9 ± 6.7	53.4 ± 10.8	.336
eGFR (mL/min/1.73 m^2)	75.3 ± 18.9	58.2 ± 20.4	< .001
Angiographic parameters			
SYNTAX Score	19.7 ± 9.0	22.7 ± 12.9	.043
Total stent length, mm	70.5 ± 23.8	91.3 ± 47.7	< .001
IVUS use (%)	89 (81.7)	98 (65.8)	.005
Procedural/In-hospital outcomes			
Intraprocedural death	0 (0.0)	2 (1.3)	.136
Angiographic success	104 (95.4)	140 (97.2)	.442
Periprocedural MI	10 (9.2)	19 (12.8)	.369
Procedural success	96 (88.1)	121 (84.0)	.362

BRS, bioresorbable scaffold; CABG, coronary artery bypass surgery; EES, everolimus-eluting stents; eGFR, estimated glomerular filtration rate; IVUS, intravascular ultrasound; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 2
Baseline Characteristics in the Propensity Matched Groups

	BRS (n = 70)	EES (n = 70)	*P*
Age, y	64.5 ± 10.3	66.0 ± 9.7	.381
Male sex	64 (91.4)	67 (95.7)	.301
Risk factors			
Diabetes mellitus	22 (31.4)	22 (31.4)	1.000
Hypertension	46 (65.7)	34 (50.7)	.076
Smoking status			.034
Current	6 (8.6)	13 (18.8)	
Ex-smoker	34 (48.6)	20 (29.0)	
Never smoked	30 (42.9)	36 (52.2)	
Dyslipidemia	49 (70.0)	38 (54.3)	.055
Family history	29 (41.4)	28 (40.0)	.863
Cardiovascular history			
Previous MI	17 (28.3)	29 (41.4)	.120
Previous PCI	34 (48.6)	35 (50.0)	.866
Previous CABG	5 (7.1)	8 (11.6)	.367
LVEF, %	54.3 ± 7.2	53.1 ± 9.7	.312
eGFR (mL/min/1.73 m^2)	76.0 ± 18.6	58.2 ± 20.1	< .001
Angiographic parameters			
Isolated LMS disease	0	0	.261
LMS + single vessel disease	1 (1.4)	4 (5.7)	
LMS + double vessel disease	4 (5.7)	2 (2.9)	
LMS and triple vessel disease	1 (1.4)	0 (0.0)	
Single vessel	42 (60)	42 (60)	
Double vessel	21 (30.0)	17 (24.3)	
Triple vessel disease	1 (1.4)	5 (7.1)	
SYNTAX score	18.6 ± 9.2	19.4 ± 10.4	.635
Total stent length, mm	67.4 ± 24.0	71.7 ± 36.1	.410
IVUS use	56 (80.0)	45 (64.3)	.038
Procedural/In-hospital outcomes			
Intraprocedural death	0 (0.0)	1 (1.4)	1.000
Angiographic success	66 (94.3)	64 (95.5)	.742
Periprocedural MI	5 (7.1)	4 (5.7)	.730
Procedural success	62 (88.6)	60 (89.6)	.854

BRS, bioresorbable scaffold; CABG, coronary artery bypass surgery; EES, everolimus-eluting stents; eGFR, estimated glomerular filtration rate; IVUS, intravascular ultrasound; LMS, left main stem; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.
Data are expressed as No. (%) or mean ± standard deviation.

Outcomes

Procedural Outcomes

Postprocedural acute gain was significantly lower in patients treated with BRS (1.82 ± 0.66 vs 2.03 ± 0.68; *P* = .033). Angiographic success rates were similar in the 2 groups (BRS vs EES: 94.3% vs 95.5%; *P* = .742). The prevalence of PMI was also similar (BRS vs EES: 7.1% vs 5.7%; *P* = .73) as were the rates of procedural success (BRS vs EES: 88.6% vs 89.9%; *P* = .854).

Clinical Outcomes in the Propensity Matched Cohort

Clinical outcomes in the overall overlap cohort are presented in Table 4. Mean follow-up time for patients implanted with BRS was 14.6 ± 6.3 months and 25.3 ± 18 months for EES-treated patients (*P* < .001). In the propensity matched cohort, at 1-year follow up, the

Table 3
Lesion and Procedural Characteristics in the Propensity Matched Groups

	BRS	EES	*P*
Number of lesions in each group, no.	101	120	
Lesion characteristics			
Lesion type B2/C	93 (92.1)	106 (90.6)	.699
Vessel diseased			.020
Left anterior descending	65 (64.4)	57 (47.5)	
Left circumflex	22 (21.8)	24 (20.0)	
Right coronary artery	13 (12.9)	32 (26.7)	
Left main stem	1 (1)	6 (5)	
Venous graft	0 (0.0)	1 (0.8)	
In-stent/BRS restenosis	6 (5.9)	12 (10.0)	.272
Chronic total occlusion	9 (8.9)	20 (16.7)	.089
Mod-severe calcification	35 (34.7)	23 (19.2)	.009
Bifurcation	46 (45.5)	36 (30.0)	.017
Procedural characteristics			
Predilatation	101 (100)	78 (65)	<.001
Angiosculpt balloon	10 (9.9)	0 (0.0)	<.001
Rotablator	4 (4.0)	7 (5.8)	.524
Number of stents/BRS per lesion			
1*	23 (22.8)	41 (34.2)	.197
2	51 (50.5)	58 (48.3)	
3	21 (20.8)	16 (13.3)	
4	6 (5.9)	5 (4.2)	
Total stent/BRS length per lesion, mm	46.1 ± 19.7	40.6 ± 24.0	.066
Minimum stent/BRS diameter, mm	2.85 ± 0.35	2.83 ± 0.41	.769
Postdilatation	101 (100.0)	75 (62.5)	<.001
Postdilatation balloon size, mm	3.3 ± 0.4	3.2 ± 0.6	.177
Postdilatation max pressure, atm	21.1 ± 4.5	17.6 ± 5.0	<.001
IVUS use	80 (79.2)	75 (62.5)	.007
QCA data			
Reference vessel diameter, mm	3.09 ± 0.47	3.20 ± 0.51	.101
Pre MLD, mm	0.87 ± 0.50	0.73 ± 0.48	.044
Post MLD, mm	2.69 ± 0.50	2.81 ± 0.55	.177
Acute gain, mm	1.82 ± 0.66	2.03 ± 0.68	.033
Post diameter stenosis, %	12.84 ± 6.76	12.25 ± 8.56	.590

BRS, bioresorbable scaffold; EES, everolimus-eluting stent; MLD, minimal lumen diameter; QCA, quantitative coronary angiography.
* These single stent lesions belong to patients with at least 1 or more lesions treated with ≥ 2 stents, hence they were included in the analysis.

estimated MACE rate (Figure 3) was not significantly different between the 2 groups (BRS vs EES: 14.5% vs 14.6%; $P_{\text{log-rank}}$ = .661). Similarly, no significant differences were seen in 1-year rates of TVR (BRS vs EES: 14.5% vs 10%, $P_{\text{log-rank}}$ = .816), TLR (BRS vs EES: 9.7% vs 8.3%; $P_{\text{log-rank}}$ = .815), follow-up MI (BRS vs EES: 0% vs 0%; $P_{\text{log-rank}}$ = .144) or all-cause mortality (BRS vs EES: 0% vs 3.2%; $P_{\text{log-rank}}$ = .137). No cases of definite stent thrombosis were observed whereas 1 case of probable stent thrombosis occurred in the EES group 40 days after stent implantation (sudden death). Analysis of 1-year TLR for the overlapping lesions in the propensity matched cohort showed no significant differences (BRS: 7.4% vs 7.6%; $P_{\text{log-rank}}$ = .935).

Characteristics of Restenotic Lesions

The Mehran classification[12] of each restenotic lesion in the 2 groups is presented in Table 5. In patients with angiographic follow-up (BRS group: 6 of 70, EES group: 9 of 70), the overlap was involved in 2 BRS in-stent restenosis patients (Figure 4) but in none of the EES patients (BRS 33.3% vs EES 0%; *P* = .063), despite the much higher prevalence of complete overlap amongst EES TLR patients (55.5% vs 0%; *P* = .025).

DISCUSSION

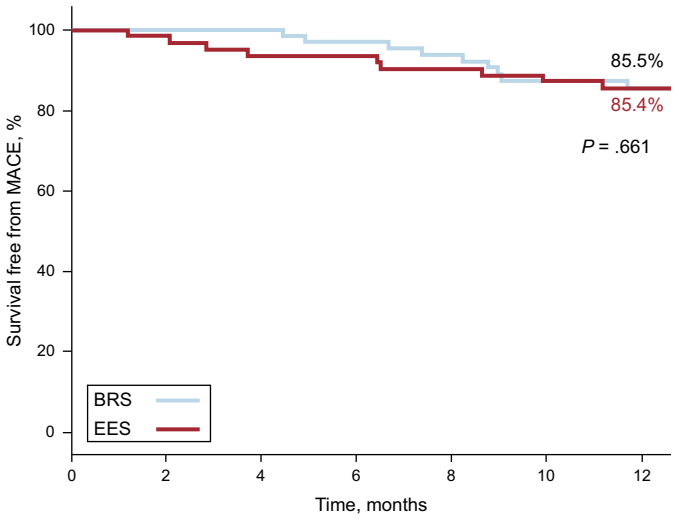
The current propensity matched study demonstrated that stable angina patients with overlapping BRS have comparable outcomes to patients with overlapping EES. Of interest, a third of total TLR occurred at the overlapping site in lesions treated with BRS compared to none for lesions treated with EES, despite the longer overlap segments in the latter. Future, large, purposefully powered randomized controlled studies are required to confirm these findings.

Our results suggest that despite lower acute gain, treatment of coronary lesions with overlapping BRS is feasible with acceptable angiographic and procedural success. A small study from 2 Australian centers[19] in 23 patients also suggested that

Table 4
Kaplan Meier Estimated 1-year Outcomes in the Total and the Propensity-matched Cohort

	BRS	EES	$P_{logrank}$
Total cohort, no.	109	149	
MACE, %	11.7	12.5	.513
TLR, %	7.5	6.5	.917
TVR, %	11.7	8.1	.800
All-cause mortality, %	0.0	3.1	.068
Follow-up MI, %	0	0	.098
Definite stent thrombosis, %	0	0	NA
Propensity matched cohort, no.	70	70	
MACE, %	14.5	14.6	.661
TLR, %	9.7	8.3	.815
TVR, %	14.5	10	.816
All-cause mortality, %	0.0	3.2	.137
Follow-up MI, %	0	0	.144
Definite stent thrombosis, %	0	0	NA

BRS, bioresorbable scaffold; EES, everolimus-eluting stent; MACE, major adverse cardiovascular events (death, MI, TVR); MI, myocardial infarction; NA, not available; TLR, target lesion revascularization; TVR, target vessel revascularization.



Time, months	0	6	12
Number at risk			
BRS	70	63	46
EES	70	58	51

Figure 3. Kaplan-Meier curves showing the percentage (%) of survival, free from major adverse cardiovascular events (MACE) up to 1 year. BRS, bioresorbable scaffold; EES, everolimus-eluting stent.

implantation of overlapping BRS was "feasible and safe", despite the presence of 2 PMI in the overlapping group (8.7%). The very small patient numbers and absence of a control group did not allow the authors of that study to draw any conclusions on the safety and efficacy of overlapping BRS compared with new generation EES. In a larger study (n = 1627 patients) from the European multicenter GHOST-EU registry,[20] 287 (17.6%) patients had lesions treated with overlapping BRS. The patient-oriented clinical endpoint at 1 year was very similar to that reported in the current study (13.6%). Of interest, in the same study, 1-year rates of scaffold thrombosis were similar, yet not negligible, in the overlap vs no overlap group (2.1 vs 2.2%; $P = 1.000$). The 1-year follow-up of the ABSORB-EXTEND study[21] (n = 812) reported a significantly higher rate of MI amongst patients with overlap vs those without (8.7% vs 2.4%; $P = .002$), likely reflecting a more complex subset of patients. In our cohort, even though we observed no follow-up MIs, there was a similarly high rate of PMI ~7.1%, a noteworthy complication. Importantly, the ABSORB-EXTEND also reported a 1.8% rate of scaffold thrombosis in the overlapping BRS group at 1-year, resembling the figure from GHOST-EU. In both GHOST-EU and ABSORB-EXTEND, however, no comparison was made with a new generation EES cohort to provide insights on comparative safety/efficacy.

Even though more than 180 000 Absorb BRS have been implanted worldwide, only 6, relatively small, randomized studies have so far been published suggesting comparable outcomes between ABSORB and new generation EES in patients with simple lesions.[3–8] The ABSORB II randomized controlled trial,[3] despite the lower post implantation acute lumen gain in the BRS group, revealed similar 1-year target lesion failure rates in the 2 groups

Table 5
Characteristics of In-stent/Scaffold Restenosis Involved in Target Lesion Revascularization and Type of Overlap

Type of stents/scaffolds	Time from implantation, months	In-stent restenosis Mehran classificaton	Overlap type	Overlap involved in in-stent restenosis
BRS	24.6	IC	Adjacent scaffolds	No
BRS	8.7	IA	Adjacent scaffolds	Yes
BRS	4.4	III	Minimum strut overlap	Yes
BRS	9.0	ID	Minimum strut overlap	No
BRS	8.3	IB	Minimum strut overlap	No
BRS	9.0	III	Minimum strut overlap	No
EES	8.6	ID	Minimum strut overlap	No
EES	18.9	IC	Adjacent stents	No
EES	54.1	IC	Adjacent stents	No
EES	11.2	II	Complete strut overlap	No
EES	2.1	IB	Complete strut overlap	No
EES	31.3	IB	Complete strut overlap	No
EES	2.8	IV	Complete strut overlap	No
EES	6.5	IB	Minimum strut overlap	No
EES	13.3	IB	Complete strut overlap	No

BRS, bioresorbable scaffold; EES, everolimus-eluting stent.

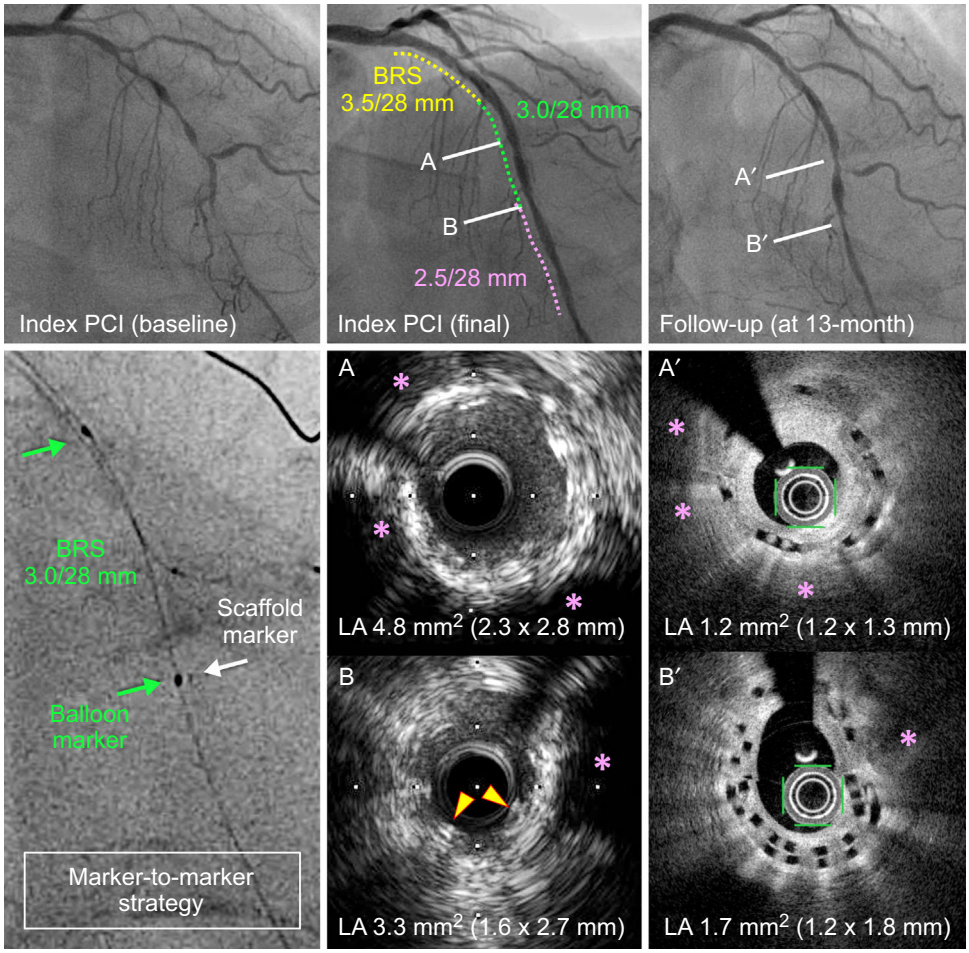


Figure 4. Restenosis at the overlap site shown with optical coherence tomography at the 13-month follow-up angiography of a patient treated with 3 overlapping bioresorbable scaffold (BRS). At 13 months' follow-up, optical coherence tomography images revealed neointimal proliferation at the site of the overlap leading to a minimum lumen area of 1.7 mm^2 (B'). Panels A and B show intravascular ultrasound images (IVUS) at the end of the index procedure. Panels A' and B' show optical coherence tomography images at the same level at 13 months' follow-up. Panels A and A' show an area of scaffold underexpansion at the index procedure (A), which was characterized by excessive neointimal hyperplasia at follow up (A'). Panels B and B' show an area of scaffold overlap, which was also underexpanded at the index procedure (B). As a result, at 13-months' follow-up, neointimal hyperplasia led to in-scaffold restenosis. Pink asterisk: calcified lesions. Yellow arrows show overlapping scaffold struts on initial IVUS (B). LA, lumen area; PCI, percutaneous coronary intervention.

(BRS vs EES; 5% vs 3%; $P = .35$). However, since that study was not powered for clinical outcomes, it was followed by the larger ABSORB III[4] trial, which included 1322 patients treated with BRS and 686 treated with EES. The occurrence of target lesion failure in the BRS group (7.8%) was noninferior to that in the EES group (6.1%); $P_{\text{non-inferiority}} = .007$; $P_{\text{superiority}} = .16$. The smaller ABSORB China[7] and the ABSORB Japan[8] randomized trials similarly revealed no significant differences in 1-year outcomes. The "all-comers" randomized EVERBIO II[5] trial (BRS vs EES vs biolimus-eluting stents) and the ABSORB China[7] (n = 480 patients randomized 1:1 to BRS vs EES) additionally showed no difference in angiographic late lumen loss, at 9 and 12 months, respectively, post stent/scaffold implantation. Furthermore, in the ST-segment elevation myocardial infarction (STEMI) setting, the TROFI II[6] trial demonstrated a similar healing response between BRS and EES at 6 months post implantation.

Real-world BRS registries[22] have demonstrated overall acceptable mid-term outcomes, albeit with some worrying signs of increased stent thrombosis. Ishibashi et al[9] summarized the stent thrombosis experience with BRS in various settings (stable angina, ACS, STEMI). In a total population of 4309 patients implanted with BRS (Absorb v1.1), followed-up for 10.3 months, definite/probable stent thrombosis was seen in 1.22% of patients, of which 0.16% were acute and 0.76% subacute. Stent thrombosis occurred in 0.94% of patients presenting with stable angina, 2.16% in those with ACS, and 1.22% in patients with STEMI. As mentioned above, the 1-year rates of probable/definite scaffold thrombosis in patients treated with overlapping BRS hover around 2%.[20,21] These figures raised some concerns when compared with the very low annual definite/probable stent thrombosis rates of 0.89% reported in studies using new generation EES.[23,24] These concerns were recently confirmed in a meta-analysis of the 6 randomized trials available to date (n = 3738 patients),[25] which showed a significantly higher risk of subacute definite/probable stent thrombosis in BRS patients.

The main current drawback of everolimus BRS (Absorb v1.1) relates to its strut thickness and width (157 × 190.5 μm for the 2.5 mm and 3.0 mm scaffolds and 157 × 216 μm for the 3.5 mm scaffold), which may render it more thrombogenic, particularly when underexpanded or malapposed. In areas of overlap, stacked struts could reach a thickness of ∼300 μm. In a porcine model implanted with BRS, in coronary artery segments with complete overlap (ie, with multiple stacked struts) delayed endotheliazation (BRS: 80.1% vs EES 98.2%; $P < .001$) was observed at 28 days[10] compared with the EES group, whereas increased neointimal thickness was seen in the BRS group at 90 days. In real life intervention, adjacent positioning of BRS struts (by careful positioning of the platinum markers so that they are side by side (Figure 1) without overlap can be a very challenging task.

Geographical miss (gap between BRS) or complete overlap (either with reduced numbers or multiple numbers of stacked struts) often occurs (Figure 2), potentially predisposing to future TLR. In the current study, a third of in-stent restenosis occurred at the overlap site in patients treated with BRS (BRS 33.3% vs EES 0%; $P = .063$), concurring with the results of the porcine model mentioned above. Of interest, no overlap in-stent restenosis was observed among EES patients despite the longer overlap segments (Table 5).

Limitations

The limitations of the current study include the small sample size, the nonrandomized design, and the lack of: *a)* routine angiographic and intracoronary imaging (IVUS, optical coherence tomography) follow-up, and *b)* independent core-lab analysis of angiographic findings. Furthermore, despite propensity matching for patient characteristics, there still remained significant differences in baseline lesion characteristics (such as calcific lesions, IVUS use, bifurcation lesions) that could have biased the results.

CONCLUSIONS

This small propensity matched study demonstrated that treating long lesions with overlapping BRS is feasible with acceptable procedural and clinical outcomes. Future, large randomized trials are needed to assess the clinical performance of BRS compared with new generation EES in patients implanted with overlapping BRS.

CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- Randomized trials have shown noninferior clinical outcomes in patients with simple lesions treated with bioresorbable eluting scaffolds compared with everolimus eluting stents.
- Some concerns, however, have been raised in recent meta-analyses and real-world registries regarding higher rates of scaffold thrombosis with bioresorbable scaffolds.
- No study to date has investigated the impact of overlapping scaffolds on angiographic or clinical outcomes.

WHAT DOES THIS STUDY ADD?

- The current study demonstrated that implantation of overlapping bioresorbable scaffolds is feasible and safe as long as optimal implantation techniques and intracoronary imaging, are used.
- Large randomized studies are required to assess in detail the performance and clinical outcomes of overlapping bioresorbable scaffolds when compared with new generation everolimus eluting metallic platforms.

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