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# Absorb Bioresorbable Vascular Scaffold Versus Everolimus-Eluting Metallic Stent in ST-Segment Elevation Myocardial Infarction: 1-Year Results of a Propensity Score Matching Comparison

## The BVS-EXAMINATION Study (Bioresorbable Vascular Scaffold-A Clinical Evaluation of Everolimus Eluting Coronary Stents in the Treatment of Patients With ST-segment Elevation Myocardial Infarction)

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## ABSTRACT

**OBJECTIVES** The purpose of this study was to compare the 1-year outcome between bioresorbable vascular scaffold (BVS) and everolimus-eluting metallic stent (EES) in ST-segment elevation myocardial infarction (STEMI) patients.

**BACKGROUND** The Absorb BVS (Abbott Vascular, Santa Clara, California) is a polymeric scaffold approved for treatment of stable coronary lesions. Limited and not randomized data are available on its use in ST-segment elevation myocardial infarction (STEMI) patients.

**METHODS** This study included 290 consecutive STEMI patients treated by BVS, compared with either 290 STEMI patients treated with EES or 290 STEMI patients treated with bare-metal stents (BMS) from the EXAMINATION (A Clinical Evaluation of Everolimus Eluting Coronary Stents in the Treatment of Patients With ST-segment Elevation Myocardial Infarction) trial, by applying propensity score matching. The primary endpoint was a device-oriented endpoint (DOCE), including cardiac death, target vessel myocardial infarction, and target lesion revascularization, at 1-year follow-up. Device thrombosis, according to the Academic Research Consortium criteria, was also evaluated.

**RESULTS** The cumulative incidence of DOCE did not differ between the BVS and EES or BMS groups either at 30 days (3.1% vs. 2.4%, hazard ratio [HR]: 1.31 [95% confidence interval (CI): 0.48 to 3.52], $p = 0.593$; vs. 2.8%, HR: 1.15 [95% CI: 0.44 to 2.30], $p = 0.776$, respectively) or at 1 year (4.1% vs. 4.1%, HR: 0.99 [95% CI: 0.23 to 4.32], $p = 0.994$; vs. 5.9%, HR: 0.50 [95% CI: 0.13 to 1.88], $p = 0.306$, respectively). Definite/probable BVS thrombosis rate was numerically higher either at 30 days (2.1% vs. 0.3%, $p = 0.059$; vs. 1.0%, $p = 0.324$, respectively) or at 1 year (2.4% vs. 1.4%, $p = 0.948$; vs. 1.7%, $p = 0.825$, respectively), as compared with EES or BMS.

**CONCLUSIONS** At 1-year follow-up, STEMI patients treated with BVS showed similar rates of DOCE compared with STEMI patients treated with EES or BMS, although rate of scaffolds thrombosis, mostly clustered in the early phase, was not negligible. Larger studies with longer follow-up are needed to confirm our findings. (J Am Coll Cardiol Intv 2015;8:189–97) © 2015 by the American College of Cardiology Foundation.

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**ABBREVIATIONS AND ACRONYMS**

**BVS** = bioresorbable vascular scaffold(s)

**CI** = confidence interval

**DOCE** = device-oriented endpoint

**EES** = everolimus-eluting stent(s)

**GP** = glycoprotein

**HR** = hazard ratio

**MI** = myocardial infarction

**PCI** = percutaneous coronary intervention

**RR** = relative risk

**STEMI** = ST-segment elevation myocardial infarction

**TIMI** = Thrombolysis in Myocardial Infarction

The ABSORB trials have shown the safety and feasibility of everolimus-eluting bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California) implantation in patients with stable angina or silent ischemia and with de novo nonthrombotic coronary artery lesions, with many physiological advantages of BVS over metallic prosthesis and a low rate of major adverse cardiovascular events up to 4-year follow-up (1,2).

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The physiological advantages of BVS, such as late lumen enlargement and vasomotion, appear particularly appealing for the treatment of ST-segment elevation myocardial infarction (STEMI) (3). Recent studies have shown short-term safety and feasibility of BVS implantation in STEMI patients (4,5). However, those data are limited by lack of a control group, small sample size, and short-term follow-up. In addition, some reports of scaffold thrombosis have recently raised concerns about actual BVS safety in a thrombotic milieu, such as STEMI, especially in light of the very low incidence of such events with second-generation drug-eluting metallic stents, reported in recent trials and meta-analyses (5–10).

We therefore conducted an analysis by matching consecutive STEMI patients receiving BVS at 6 centers with the cohorts of STEMI patients receiving everolimus-eluting stents (EES) (Xience V, Abbott Vascular) and bare-metal stent (BMS) (Multilink Vision, Abbott Vascular) from the EXAMINATION (A Clinical Evaluation of Everolimus Eluting Coronary Stents in the Treatment of Patients With ST-segment Elevation Myocardial Infarction) trial, with the aim to compare the 1-year device-oriented endpoint (DOCE) between the 2 groups.

## METHODS

**STUDY POPULATION.** All consecutive STEMI patients treated by BVS between December 2012 and June 2013 at 6 different institutions were enrolled for this analysis. All baseline clinical and procedural characteristics were retrospectively collected. We used propensity score to match each STEMI patient treated by BVS to a comparable STEMI patient treated by everolimus-eluting Xience V stent or by BMS (see the Statistical Methods section for further details). Patients from the controlled EXAMINATION trial, randomized to Xience V or BMS, were used for matching with BVS patients (7).

Percutaneous coronary intervention (PCI) was performed according to conventional clinical practice: manual thrombus aspiration, glycoprotein (GP) IIb/IIIa inhibitors, heparin, and bivalirudin administration were performed according to operator's choice. Balloon pre-dilation was not mandatory but was recommended for BVS implantation, according to BVS instructions for use. Dual antiplatelet therapy with aspirin plus clopidogrel, ticagrelor, or prasugrel was prescribed in all patients for 12 months. Of note, neither prasugrel nor ticagrelor were approved during the recruitment period of the EXAMINATION trial.

The investigators of each institution who participated in the study were asked to complete a structured patient-level database including a series of key baseline clinical and procedural data as well as the clinical outcome data, similar to the EXAMINATION database. Such individual patient data were sent to the study coordinator (S.B.), who was responsible for checking data consistency and for final pooling in a single database.

The 1-year follow-up was performed in the EXAMINATION patients by clinical visits and in the BVS patients either by clinical visit or telephone calls. Clinical follow-up in BVS patients was pre-specified in all institutions because of the involvement of these patients in local BVS registries.

This is an observational and retrospective study, performed according to the privacy policy of the various institutions that participate and to their regulations for the appropriate use of data in patient-oriented research, which are based on international regulations, including the Declaration of Helsinki.

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Moreover, as the BVS has the CE (Conformité Européenne) mark for clinical use without any restriction in terms of clinical presentation, it can be routinely used in different settings including STEMI without a specific written informed consent in addition to the standard informed consent to the procedure. Patients from the EXAMINATION trial had signed informed consent to participate in that trial. Because the present analysis is based on propensity matching and no randomization was performed, no additional consent is required.

**DEFINITION OF CLINICAL OUTCOMES.** The primary endpoint of this analysis was defined as the combined DOCE, including cardiac death, target vessel myocardial reinfarction, and target lesion revascularization. All individual components and device thrombosis (stent/scaffold), defined by the Academic Research Consortium criteria, were also analyzed (11). Whereas all events in the EXAMINATION trial were adjudicated by an independent clinical events committee that was blinded to stent assignment after review of original source documentation, all events in the BVS group were adjudicated by investigators collecting any relevant medical records, discharge letters, and documentation of hospital stay from the hospitals providing treatment and physicians in private practice, using the same definitions of events applied in the EXAMINATION trial. (7,12)

**STATISTICAL ANALYSIS.** For the present analyses, individual data were pooled on a patient-level basis. Continuous variables are expressed as mean ± SD, and categorical variables are presented as absolute number and proportion (%). Overall comparisons between nonmatched groups were performed by the *t* test for continuous variables and by chi-square or Fisher exact test when the Cochran rule was not met for categorical variables.

Propensity score matching was applied to compare the 1-year device-oriented primary endpoint of STEMI patients treated with BVS and those treated with EES or BMS. A propensity score matching was performed using a proprietary macro developed and tested for SPSS version 20.0 (SPSS Inc., Chicago, Illinois). First, the program performed a logistic regression to score all patients according to the treatment (BVS vs. EES; BVS vs. BMS), using as covariates clinical and procedural parameters that were clinically relevant for the endpoint: age (years), sex (male/female), diabetes mellitus (yes/no), and culprit vessel and stent/scaffold length and diameter (mm). Second, the macro searched and selected the best match case of the EES group and BMS group for every BVS case according to the absolute value of the difference between the propensity score of EES/BMS and BVS cases under consideration. Patients in the 2 groups were matched through a greedy algorithm based on local optimization (13). The control selected for a particular case was the one closest to the case in terms of distance, whereby the maximum allowed distance for matching was set to 0.10. Analyses were then performed on the 2 matched groups (EES vs. BVS and BMS vs. BVS), stratified by pairs to account for propensity score matching.

Time-to-event variables are presented as Kaplan-Meier curves. Hazard ratios (HRs) of all events at 30 days and 1 year were calculated with Cox proportional hazards models. The validity of the proportionality assumption was verified for all covariates by a visual examination of the log (minus log) curves and a test based on Schoenfeld residuals. Because it was not met for treatment, HRs by Cox regression were estimated separately into the timeframes up to 30 days and from 1 to 12 months.

A Cox regression model was developed to adjust the DOCE between the EES and BVS groups for use of GP IIb/IIIa inhibitors (yes/no) and use of clopidogrel versus other platelet inhibitors (ticagrelor/prasugrel). Two other Cox regression models were also developed to compare definite/probable device thrombosis between the EES and BVS groups, adjusting separately for use of GP IIb/IIIa inhibitors (yes/no) and use of clopidogrel versus others (ticagrelor or prasugrel), to avoid any overfitting due to the small number of events. A 2-sided p value $<0.05$ was considered statistically significant. All statistical analyses were performed using SPSS version 20.0.

## RESULTS

**STUDY POPULATION.** A total of 290 consecutive STEMI patients, treated by BVS implantation, were collected for this analysis among the various institutions. In the EXAMINATION trial, 751 and 747 STEMI patients were randomly assigned to receive EES or BMS, respectively. Of those who received EES, 17 withdrew informed consent, and 14 were missed during follow-up, leaving 734 patients who were used as a control group for matching with BVS. Of those who received BMS, 6 withdrew informed consent, and 15 were missed during follow-up, leaving 726 patients who were used as control group for matching with BVS. Online Table A shows baseline clinical and procedural characteristics in the overall population.

By applying the aforementioned methodology of the propensity score matching, all 290 BVS patients were matched with either 290 EES patients or 290 BMS patients (**Table 1**).

**TABLE 1 Baseline Clinical and Procedural Characteristics**

| | BVS Group (n = 290) | EES Group (n = 290) | BMS Group (n = 290) | p Value* | p Value† |
|---|---|---|---|---|---|
| Age, yrs | 56.01 ± 12.75 | 57.57 ± 12.01 | 56.62 ± 11.83 | 0.090 | 0.363 |
| Male | 236 (81.4) | 231 (79.7) | 245 (84.5) | 0.141 | 0.115 |
| Smoking history | 177 (61.0) | 220 (75.9) | 236 (81.4) | 0.005 | <0.001 |
| Hypertension | 144 (49.7) | 127 (43.8) | 135 (46.6) | 0.835 | 0.560 |
| Diabetes | 37 (12.8) | 37 (12.8) | 33 (11.4) | 0.886 | 0.876 |
| Dyslipidemia | 121 (41.7) | 132 (45.5) | 104 (36.0) | 0.115 | 0.137 |
| Previous MI | 10 (3.5) | 10 (3.5) | 14 (4.8) | 0.838 | 0.927 |
| Previous PCI | 10 (3.4) | 11 (3.8) | 7 (2.4) | 0.287 | 0.350 |
| Previous CABG | 3 (1.0) | 1 (0.3) | 1 (0.3) | 0.234 | 0.573 |
| Previous stroke | 6 (2.1) | 5 (1.7) | 5 (1.7) | 0.828 | 0.622 |
| Infarct-related artery | | | | 0.188 | 0.486 |
| LAD | 145 (50.0) | 117 (40.3) | 124 (42.8) | | |
| RCA | 114 (39.3) | 126 (43.4) | 127 (43.8) | | |
| LCx | 29 (10.0) | 45 (15.5) | 38 (13.1) | | |
| SVG | 1 (0.3) | 0 (0) | 0 (0) | | |
| Left main | 1 (0.3) | 2 (0.7) | 1 (0.3) | | |
| Multivessel disease | 24 (8.2) | 28 (9.7) | 21 (7.2) | 0.768 | 0.872 |
| Thrombectomy device use | 217 (74.8) | 199 (68.6) | 197 (68.0) | 0.513 | 0.144 |
| Pre-dilation | 230 (81.0) | 83 (29.0) | 87 (30.5) | <0.001 | <0.001 |
| GP IIb/IIIa inhibitor | 196 (67.6) | 150 (51.7) | 159 (54.8) | 0.003 | 0.174 |
| Bivalirudin | 0 (0) | 20 (6.9) | 21 (7.2) | 0.957 | 0.957 |
| Unfractionated heparin | 290 (100) | 231 (79.7) | 235 (81.0) | 0.925 | 0.930 |
| Number of stents/ scaffold | 1.14 ± 0.39 | 1.13 ± 0.37 | 1.15 ± 0.40 | 0.587 | 0.790 |
| Stent/scaffold diameter, mm | 3.22 ± 0.33 | 3.19 ± 0.40 | 3.23 ± 0.40 | 0.348 | 0.906 |
| Stent/scaffold length, mm | 22.53 ± 8.80 | 21.78 ± 9.17 | 22.08 ± 8.53 | 0.128 | 0.363 |
| Post-dilation | 105 (36.3) | 44 (15.2) | 33 (11.4) | <0.001 | <0.001 |
| TIMI flow grade pre | | | | <0.001 | 0.178 |
| 0 | 202 (69.7) | 159 (55.2) | 170 (58.8) | | |
| 1 | 15 (5.2) | 18 (6.2) | 28 (9.7) | | |
| 2 | 34 (11.7) | 44 (15.3) | 36 (12.5) | | |
| 3 | 39 (13.4) | 67 (23.3) | 55 (19.0) | | |
| TIMI flow grade post | | | | 0.244 | 0.478 |
| 0 | 1 (0.3) | 5 (1.7) | 2 (0.7) | | |
| 1 | 1 (0.3) | 1 (0.3) | 2 (0.7) | | |
| 2 | 13 (4.5) | 7 (2.4) | 10 (3.4) | | |
| 3 | 275 (94.8) | 275 (95.5) | 276 (95.2) | | |

Values are mean ± SD or n (%). *Comparison between BVS and EES. †Comparison between BVS and BMS. The p values are from paired *t* test for continuous data and conditional logistic regression for dichotomous and ordinal data.

BMS = bare-metal stent; BVS = bioresorbable vascular scaffold; CABG = coronary artery by-pass graft; EES = everolimus-eluting stent; GP = glycoprotein; LAD = left anterior descending artery; LCx = left circumflex artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; SVG = saphenous vein graft; TIMI = Thrombolysis In Myocardial Infarction.

After propensity score matching, patient demographics were comparable between the matched groups, except for history of smoking, which was more prevalent in the BVS group.

With regard to procedural characteristics, the BVS and EES groups differ in the device implantation technique used, with higher use of pre- and post-dilation in the BVS than in the EES group. Whereas pre-PCI Thrombolysis In Myocardial Infarction (TIMI) flow was lower in the BVS than in the EES group, no differences were found in post-PCI TIMI flow. A higher rate of GP IIb/IIIa inhibitor use was found in the BVS group than in the EES group. A higher rate of pre- and post-dilation was also found in the BVS than in the BMS group.

Whereas all EES and BMS patients were on aspirin and clopidogrel, BVS patients were taking clopidogrel (33.3%), ticagrelor (32.9%), or prasugrel (33.8%) in addition to aspirin.

The 1-year follow-up data were available in 100% of BMS and EES patients and in 98% of BVS patients, due to 4 patients lost to follow-up.

**CLINICAL OUTCOMES BETWEEN BVS AND EES.** At 1 year, no differences were found between the 2 groups with regard to the DOCE (HR: 0.94 [95% confidence interval (CI): 0.23 to 4.32], p = 0.994), even after adjustment for GP IIb/IIIa inhibitors and clopidogrel (HR: 1.50 [95% CI: 0.24 to 9.50], p = 0.662) (Table 2). The DOCE was also not different between the BVS and EES groups at 30 days (HR: 1.31 [95% CI: 0.48 to 3.52], p = 0.593) (Figure 1A). No differences were found in its individual components either at 30 days or 1 year (Table 2).

At 1 year, the definite/probable device thrombosis rate was not different between the groups (HR: 1.10 [95% CI: 0.69 to 17.54], p = 0.948), also after adjustment for clopidogrel (HR: 2.94 [95% CI: 0.18 to 47.08], p = 0.445) or GP IIb/IIIa inhibitor use (HR: 1.59 [95% CI: 0.10 to 25.43], p = 0.743) (Figure 1B). Within 30 days after implantation, early definite/probable device thrombosis rate tended to be higher in the BVS than in the EES group (2.1% vs. 0.3%, p = 0.059), whereas no differences were found in terms of early definite device thrombosis (1.4% vs. 0.3%, p = 0.341).

One BVS thrombosis occurred in a patient with 2 BVS overlapped, who stopped the prescribed antiplatelet therapy (aspirin + ticagrelor) 3 days before the event; no other patients with device thrombosis withdrew any antiplatelet agent (Table 3).

**CLINICAL OUTCOMES BETWEEN BVS AND BMS.** Either at 30 days or at 1 year, no differences were found between the 2 groups (Table 2). Figures 1C and 1D show Kaplan-Meier curves for the DOCE and definite/probable device thrombosis.

## DISCUSSION

This is the first study comparing BVS versus EES versus BMS in STEMI patients, based on propensity score matching. The main findings of the present study can be summarized as follows. 1) The 30-day

**TABLE 2 Clinical Outcome at 30 Days and 1 Year**

| | BVS Group (n = 290) | EES Group (n = 290) | BMS Group (n = 290) | HR [95% CI]* | p Value* | HR [95% CI]† | p Value† |
|---|---|---|---|---|---|---|---|
| Clinical outcome at 30 days | | | | | | | |
| DOCE | 9 (3.1) | 7 (2.4) | 8 (2.8) | 1.31 (0.48–3.52) | 0.593 | 1.15 (0.44–2.30) | 0.776 |
| Cardiac death | 5 (1.7) | 4 (1.4) | 5 (1.7) | 1.27 (0.34–4.72) | 0.724 | 1.01 (0.30–3.50) | 0.981 |
| TV MI | 4 (1.4) | 2 (0.7) | 0 (0) | 4.00 (0.45–35.79) | 0.215 | 6.64 (0.02–20.68) | 0.306 |
| TLR | 3 (1.0) | 2 (0.7) | 3 (1.0) | 1.50 (0.25–8.98) | 0.657 | 1.02 (0.20–5.06) | 0.979 |
| Definite/probable device thrombosis | 6 (2.1) | 1 (0.3) | 3 (1.0) | 6.00 (0.72–49.84) | 0.059 | 2.00 (0.50–8.32) | 0.324 |
| Definite device thrombosis | 4 (1.4) | 1 (0.3) | 1 (0.3) | 3.00 (0.31–28.84) | 0.341 | 4.00 (0.45–35.86) | 0.214 |
| Clinical outcome at 1 year‡ | | | | | | | |
| DOCE | 12 (4.1) | 12 (4.1) | 17 (5.9) | 0.94 (0.23–4.32) | 0.994 | 0.50 (0.13–1.88) | 0.306 |
| Cardiac death | 6 (2.1) | 6 (2.1) | 6 (2.1) | 0.87 (0.08–9.90) | 0.908 | 2.46 (0.15–40.43) | 0.528 |
| TV MI | 6 (2.1) | 4 (1.4) | 3 (1.0) | 1.65 (0.28–9.90) | 0.583 | 2.52 (0.62–10.31) | 0.198 |
| TLR | 5 (1.7) | 4 (1.4) | 10 (3.4) | 1.93 (0.25–14.91) | 0.527 | 0.95 (0.15–5.85) | 0.955 |
| Definite/probable device thrombosis | 7 (2.4) | 4 (1.4) | 5 (1.7) | 1.10 (0.69–17.54) | 0.948 | 0.79 (0.07–9.20) | 0.852 |
| Definite device thrombosis | 5 (1.7) | 2 (0.7) | 2 (0.7) | 1.10 (0.70–17.66) | 0.944 | 1.19 (0.74–19.03) | 0.902 |

*Comparison between BVS and EES. †Comparison between BVS and BMS. ‡HRs have been estimated in the timeframe after 30 days up to 1 year.
CI = confidence interval; DOCE = device-oriented endpoint; HR = hazard ratio; TLR = target lesion revascularization; TV = target vessel; other abbreviations as in Table 1.

and 1-year DOCE rates appear to be acceptable among the groups. 2) Some concerns may be raised about BVS thrombosis, especially in the early phase after implantation, compared with the EES group; although no definite conclusions could be drawn given the small sample size, these findings should be interpreted with caution. 3) Despite propensity matching, there were significant differences between groups in the implantation technique, with higher use of balloon pre- and post-dilation associated with BVS compared with other groups.

A lot of attention has been recently focused on BVS use in STEMI, as thrombotic lesions, which are most frequently thin-cap fibroatheromas, rich in necrotic core and covered by a thin fibrous cap (<65 μm), may represent the best scenario for the BVS "vascular restoration therapy" (14). Autopsy studies suggested that metallic struts embedded in necrotic core may remain uncovered even in the long term and thus potentially be a trigger for stent thrombosis (15). Conversely, BVS, which in the long term are completely replaced by connective tissue and smooth muscle cells, may overcome the problem of metal persistence into the coronary vessel wall and may at the same time stabilize a thin-cap fibroatheroma with a neointimal layer (3). In addition, from a physiological perspective, the absence of permanent vessel caging facilitates the restoration of vasomotor function, adaptive shear stress, cyclic strain, and late lumen enlargement (14).

The first few data published on BVS in acute coronary syndrome showed safety and feasibility of its implantation; however, all these reports were limited by lack of a randomized control group, very small sample size, and short-term follow-up (4,16,17). In addition, some concerns have been recently raised on the high thrombogenicity of BVS in a thrombotic milieu, such as STEMI (5,6,18). Given this background, our analysis collected individual data from 6 high-volume centers with large experience in BVS implantation in STEMI, allowing us to have the largest current cohort of STEMI treated by BVS. By using a propensity score matching with STEMI treated by EES or BMS, a comparison of these therapeutic strategies was performed. In this regard, the EXAMINATION trial, which randomized 1,501 all-comer STEMI patients 1:1 to EES versus BMS, provided perfect controlled EES and BMS groups to build a propensity score (7).

We found that at 1 year, DOCE was not different between BVS and EES or BMS. It is noteworthy that, compared with the EXAMINATION trial, our selected EES and BMS population had a DOCE rate slightly lower (4.1% vs. 5.9% and 5.9% vs. 8.4%, respectively), was younger, and had less incidence of diabetes. Of note, taking as reference the DOCE rate of the EES group in the EXAMINATION trial, our analysis would have been 80% powered to demonstrate superiority of BVS over EES (7). Despite a lower DOCE rate, 1-year definite/probable EES thrombosis rate was higher than that of the EXAMINATION trial (1.4% vs. 0.9%); this finding translated to a lack of statistically significant difference compared with definite/probable BVS thrombosis at 1 year, but with a trend toward a higher early device thrombosis in the BVS than in the EES group, without any effect on 30-day

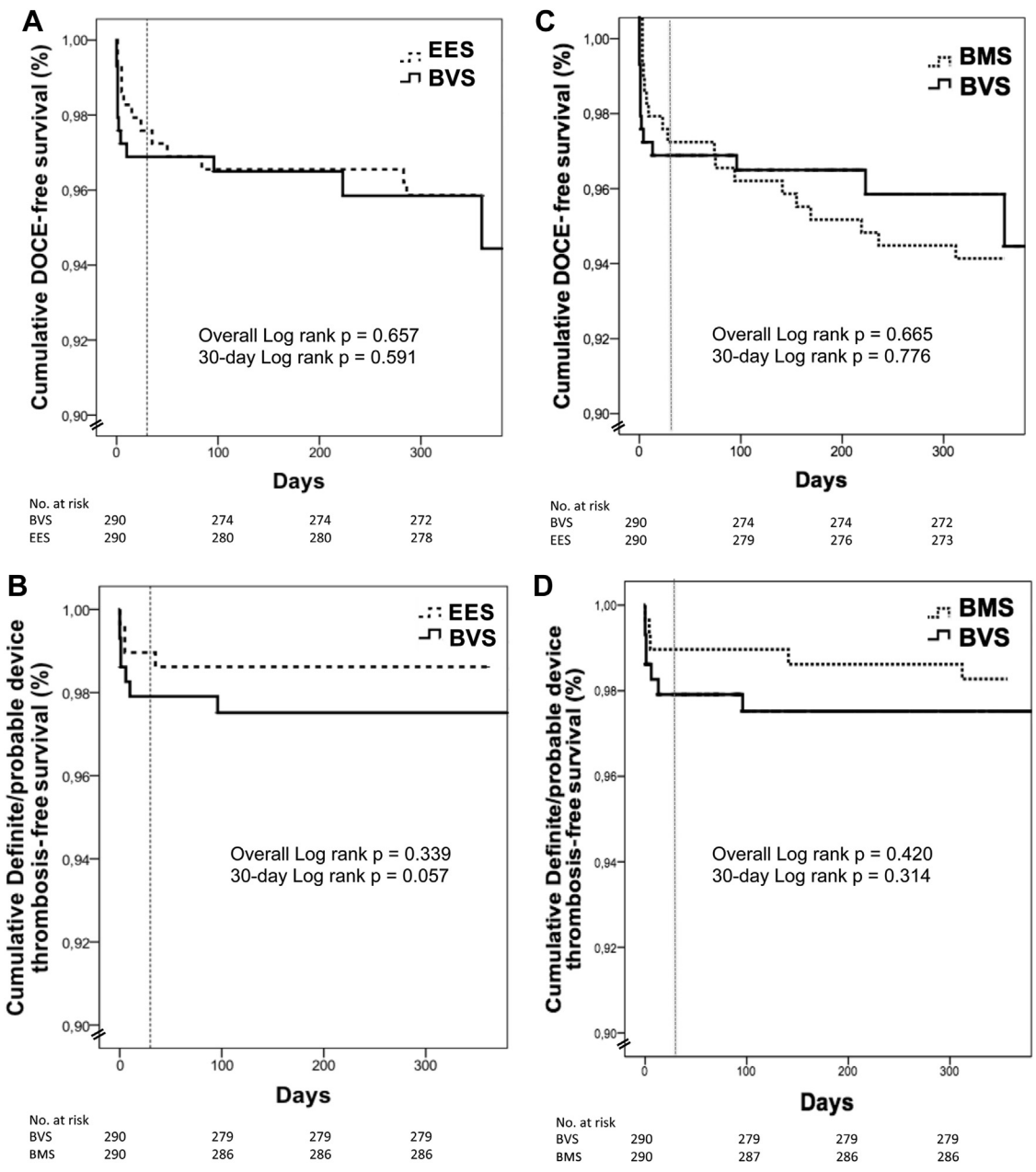


**FIGURE 1** **Kaplan-Meier Curves for the Comparison Between BVS and Either EES or BMS**

**(A)** Kaplan-Meier event curves comparing bioresorbable vascular scaffold (BVS) and everolimus-eluting stents (EES) for the composite device-oriented endpoint (DOCE) of cardiac death, target vessel myocardial infarction, and target lesion revascularization. **(B)** Kaplan-Meier event curves comparing BVS and EES for definite/probable device thrombosis. **(C)** Kaplan-Meier event curves comparing BVS and bare-metal stents (BMS) for the composite DOCE of cardiac death, target vessel myocardial infarction, and target lesion revascularization. **(D)** Kaplan-Meier event curves comparing BVS and BMS for the definite/probable device thrombosis. The **dotted line** on the vertical axis indicates the 30-day time point.

DOCE. In contrast, the 1-year definite/probable BMS thrombosis rate was lower than that of the EXAMINATION trial (1.7% vs. 2.5%), being therefore numerically lower than BVS thrombosis despite the absence of statistically significant difference. A matter of chance or differences in periprocedural variables or in-device material (metal vs. polymer) and in-strut thickness (BVS: 150 μm vs. EES: 90 μm) may

**TABLE 3** Cases of Definite DT in the BVS and EES Groups

| Case # | Type of Device | Device Size (mm) | Location of MI | Timing of DT (Days After the Primary Procedure) | Use of GP IIb/IIIa | Antiplatelet Regimen at the Time of DT |
|---|---|---|---|---|---|---|
| 1 | BVS | 3.0 × 28 | LAD | 96 | No | ASA + clopidogrel |
| 2 | BVS | 3.5 × 18 | RCA | 1 | Yes | ASA + ticagrelor |
| 3 | BVS | Two 3.5 × 12 overlapped | LAD | 13 | No | ASA and ticagrelor stopped 3 days before the event |
| 4 | BVS | 3.0 × 18 | RCA | 0 | No | ASA + prasugrel |
| 5 | BVS | 3.5 × 28 | LCx | 0 | Yes | ASA + clopidogrel |
| 6 | EES | 3.0 × 18 | RCA | 0 | Yes | ASA + clopidogrel |
| 7 | EES | 3.5 × 23 | LCx | 35 | No | ASA + clopidogrel |

ASA = aspirin; DT = device thrombosis; other abbreviations as in Tables 1 and 2.

be advocated to explain these findings, which in any case should be considered as hypothesis-generating and confirmed in future trials powered for this safety endpoint. In particular, a reduction in strut thickness, which will take place in the new BVS generation, will probably represent an important step forward in this regard.

In comparison with a previous large-scale randomized trial, 1-year BVS DOCE rate was found to be comparable to other second-generation DES, based on biodegradable polymer (8), and lower than first-generation DES, mainly driven by lower rate of target lesion revascularization (19,20). Conversely, 1-year definite/probable BVS thrombosis (2.4%) appeared to be higher than that reported in a recent meta-analysis for second-generation DES in STEMI (1.7% for EES and biolimus-eluting stents), almost resembling that of first-generation DES (3.2% for paclitaxel-eluting stents and 3.4% for sirolimus-eluting stents) (9,19,20). Importantly, compared with EES, the increased risk of definite BVS thrombosis appears to be similar to the increased risk with the zotarolimus-eluting Resolute stent (Medtronic, Santa Rosa, California) (relative risk [RR]: 2.47 [95% CI: 1.24 to 4.96]), biodegradable-polymer-based thick-strut stent (RR: 2.04 [95% CI 1.27 to 3.35]), and BMS (RR EES/BMS: 0.32 [95% CI: 0.11 to 0.78]) (10,21). These concerns about BVS thrombosis are in line with the recently published all-comer GHOST (Gauging coronary Healing with biOresorbable Scaffolding plaTforms) registry, which showed 2.1% incidence of definite/probable BVS thrombosis at 6 months, mostly clustered within 30 days after implantation (22). A learning curve of the operators involved in BVS implantation cannot be excluded, although previous reports were not able to demonstrate a significant effect of the learning curve on clinical outcomes of patients treated with the Absorb BVS (22). It is noteworthy that although the Cox model adjusted for new antiplatelet drugs did not show any difference in definite/probable device thrombosis between the groups, any influence of these drugs on such endpoint cannot be excluded, given the small number of patients. It may be hypothesized that a higher use of new antiplatelet agents in the EES arm, potentially reducing incidence of device thrombosis, would make the trend herein toward a higher device thrombosis statistically significant in the BVS versus EES arm. A sensitivity analysis, comparing only those patients taking clopidogrel in both groups (overall 194 patients), showed higher device thrombosis in the BVS than in the EES group (3.1% vs. 1.0%, $p = 0.312$), which was not statistically significant due to the small sample size.

It is important to highlight that variables related to lesion preparation were not used in propensity score matching. This decision was based on the rationale that, in daily clinical practice, balloon pre-dilation is highly recommended in the case of BVS implantation (23). For this reason, in a hypothetical STEMI randomized trial comparing BVS with a metallic DES lesion, preparation by means of thrombectomy or balloon pre-dilation would not be mandatory by protocol but left to the operator's decision, as, for example, in the ABSORB TROFI-II trial (NCT01986803), which is currently randomizing STEMI patients to BVS versus EES. It is also important to note that GP IIb/IIIa inhibitor use, left to operator discretion, could translate to higher usage in BVS than metallic DES, especially in light of recent reports encouraging optimization of antithrombotic/antiplatelet regimen in the case of BVS implantation (5). Nevertheless, after adjusting either for GP IIb/IIIa inhibitor use or for usage of new antiplatelet agents (ticagrelor/prasugrel), which could have favored the BVS arm, our analysis did not show any difference between groups in terms of DOCE.

It is interesting to note that the higher use of balloon pre-dilation in the BVS group did not translate into an increase in distal embolization with

no-reflow phenomenon. In particular, whereas pre-procedure TIMI flow was lower in the BVS than the EES group, in contrast, post-procedure TIMI flow was not different between groups. This finding can be explained either by higher use of GP IIb/IIIa inhibitors or by the so-called snow racket effect of BVS on the thrombus entrapped between the scaffold and the vessel wall, due to the higher scaffold/vessel ratio of BVS compared with EES (26% vs. 12%) (24).

**STUDY LIMITATIONS.** Due to the limited number of patients and events, caution should be made in reaching firm conclusions. Notably, this study currently represents the largest cohort of STEMI treated by BVS compared with a controlled arm. Imbalance in the use of new antiplatelet agents, which were not available at the time of the EXAMINATION trial, should be taken into account in the results interpretation, despite the adjusted Cox model. Quantitative coronary angiography and device implantation maximal pressures data were not collected, as they were unavailable in the EXAMINATION trial. A longer follow-up is needed to fully evaluate the performance of this novel device in STEMI patients, as the physiological advantages of BVS over metallic prosthesis seem to accrue at a follow-up longer than 1 year (23,25,26).

## CONCLUSIONS

The use of BVS in the setting of STEMI showed an acceptable rate of DOCE at 30 days and 1 year, compared with EES and BMS. However, rates of BVS thrombosis, especially within 30 days after implantation, were not negligible, compared with EES and BMS.

Larger studies with longer follow-up are needed to confirm our preliminary findings and to fully evaluate the performance of BVS in STEMI patients.

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**KEY WORDS** ABSORB, everolimus-eluting stent, STEMI

**APPENDIX** For a supplemental table, please see the online version of this article.