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Title: **Very long-term outcome of ABSORB bioresorbable vascular scaffold vs. everolimus-eluting metallic stent in ST-segment elevation myocardial infarction: 5-year results of the BVS-EXAMINATION study.**

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Very long-term outcome of ABSORB bioresorbable vascular scaffold vs. everolimus-eluting metallic stent in ST-segment elevation myocardial infarction: 5-year results of the BVS-EXAMINATION study.

Short title: BRS vs. EES in STEMI

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ABSTRACT

Aim: to compare 5-year clinical outcomes between everolimus-eluting bioresorbable scaffold (BRS) vs. everolimus-eluting metallic stent (EES) in STEMI patients.

Methods and results: This observational and retrospective study included 235 consecutive STEMI patients treated by BRS, compared with 235 STEMI patients treated with EES from the EXAMINATION trial, by applying propensity score matching. Primary endpoint was a device-oriented endpoint (DOCE), including cardiac death, target vessel myocardial infarction and target lesion revascularization at 5-year follow-up.Device thrombosis, according to the ARC criteria, was also evaluated.Optical coherence tomography (OCT) analysis was also performed at 5-year in event-free BRS patients. The cumulative incidence of 5-year DOCE was higher in BRS as compared to EES group (13.2% vs. 7.6%, HR [95%CI] 1.87 [0.94 – 3.44], p=0.071), mainly driven by higher rate of TLR (7.6% vs. 1.7%, HR [95%CI] 1.15 [0.44 – 2.30], p=0.004). Five-year definite BRS thrombosis rate was also higher as compared to EES (4.2% vs. 1.2%, HR [95%CI] 3.49 [0.95 – 12.82], p=0.054. Optical coherence tomography analysis showed high incidence of neo-atherosclerosis in BRS group.

Conclusions: Five-year event risk was higher with BRS vs EES in STEMI. This suggests that the probability of obtaining favorable results at very long-term follow-up is low. Whether better results will be obtained with new generation BVS remains to be determined.

Key words: STEMI; Bioresorbable scaffolds; drug-eluting stent.

Condensed abstract

Data on BRS long-term safety and efficacy in ST-segment elevation myocardial infarction (STEMI) patients are still missing. We aimed to compare 5-year outcomes between BRS and EES in STEMI patients. Two-hundred five STEMI patients treated by BRS, compared with 235 STEMI patients treated with EES from the EXAMINATION trial, by applying propensity score matching. The cumulative incidence of 5-year DOCE was higher in BRS as compared to EES group (13.2% vs. 7.6%, p=0.071), mainly driven by higher rate of TLR (7.6% vs. 1.7%, p=0.004). Five-year definite BRS thrombosis rate was also higher as compared to EES (4.2% vs. 1.2%, p=0.054).

ABBREVIATION LIST

BRS: bioresorbable vascular scaffold

DOCE: device-oriented composite endpoint

EES: everolimus-eluting stent

MI: myocardial infarction

STEMI: ST-elevation myocardial infarction

TLR: target lesion revascularization

INTRODUCTION

Everolimus-eluting bioresorbable vascular scaffolds (BRS, ABSORB BVS, Abbott Vascular, Santa Clara, CA, USA) were designed to provide temporary mechanical support with antiproliferative responses to vascular injury similar to those of metallic drug-eluting stents but with complete resorption within several years, thereby restoring normal vascular function and potentially improving late outcomes. [1]

Analysis of data from four major randomised trials using poly-lactide based BRS (ABSORB BVS) have shown non-inferior outcomes to contemporary metallic drug-eluting stents in patients with stable coronary artery disease at short-term follow-up. However, they raised concerns about increased rates of target vessel-related myocardial infarction and device thrombosis at long-term. [2, 3] Of note, a number of BRS-related events in these trials were reported between 1 and 3 years - the period of active scaffold bioresorption. [4, 5] Because of these concerns, the manufacturer withdrew ABSORB BVS from the market.

Nevertheless, other BRS with differing designs and drugs are still available on the market for use in clinical studies and one of these – a magnesium-based BRS - is being currently tested in ST-segment elevation myocardial infarction (STEMI), where their physiological advantages, such as late lumen enlargement and vasomotion, appear particularly appealing. [6, 7] Previous studies on BRS in STEMI have shown contrasting results with either no-inferior vascular healing response with low rate of event or higher rate of early device thrombosis at 1-year follow-up. [8, 9] However, all these studies are limited by short-term follow-up and lack of data beyond 3-year where the scaffold bioresorption may have a role in scaffold collapse with subsequent thrombosis. [10]

We therefore conducted a 5-year follow-up of the BVS-EXAMINATION study, which match consecutive STEMI patients receiving BRS with a cohort of STEMI

patients receiving everolimus-eluting stent (EES, Xience V, Abbott Vascular, Santa Clara, CA) from the EXAMINATION randomized trial.

METHODS

Study population

The EXAMINATION trial is an all-comer STEMI, multi-center, controlled and randomized trial, which randomized 1:1 a total of 1498 STEMI patients to everolimus-eluting stent (n=751) (EES; Xience; Abbott Vascular, Santa Clara, CA) or Multilink Vision BMS (n= 747) (Abbott Vascular, Santa Clara, CA). [11, 12] Those patients randomized to EES were used for propensity score matching with an observational and retrospective cohort of consecutive STEMI patients treated by BRS in various institutions. The BVS EXAMINATION study was performed according to the privacy policy of the various participating institutions 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.

All consecutive STEMI patients already included in the 1-year follow-up of the BVS EXAMINATION study were included in this analysis. [8] The investigators of each institution who already participated into the study, were invited to perform a 5-year follow-up of their STEMI patients treated by BRS already included in the 1-year study and, if agreed, they were asked to complete a structured patient-level database with clinical outcome data, similar to the EXAMINATION database. Such individual patient data have been sent to the study coordinator (S.B.), who was responsible for data consistency checking and for final pooling in a single database. All STEMI patients included in the BVS EXAMINATION study were already matched with patients of the EXAMINATION randomized trial. [8] Five-year follow-up was performed in the EXAMINATION patients by clinical visits and in the BRS patients either by clinical visit or telephone calls.

Details about primary PCI procedure, definition of clinical outcomes and optical coherence tomography analysis are reported in the supplementary material.

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 (%). Details about propensity score matching analysis are reported in the supplementary material.

Time-to-event variables are presented as Kaplan-Meier curves. Hazard ratios (HRs) of all events at 30 days, 1-year and 5-year were calculated with Cox proportional hazards models.

A 2-side p-value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS (version 25.0, SPSS Inc., Chicago, IL).

RESULTS

Study population

All the participating institutions, but one, agreed to perform 5-year clinical follow-up and to provide follow-up data. For these reasons out of the 290 consecutive STEMI patients, treated by BRS implantation, originally included in the 1-year follow-up of the BVS EXAMINATION study, 235 patients were finally included for 5-year follow-up. By applying the aforementioned methodology of the propensity score matching, all the 235 BVS patients were matched with 235 EES patients from the EXAMINATION trial, as previously shown. [8] Distribution of patient demographics and procedural characteristics between the two matched group was similar to the one previously reported. [8] (Supplementary table A)

Five-year follow-up was available in 100% of EES patients and in 98% of BRS patients, due to 4 patients lost at follow-up. (**Figure 1**)

Clinical outcomes between BRS and EES

At 5-year, DOCE was numerically higher, but not statistically significant in BRS as compared to EES group (13.2% vs. 7.6%; HR 1.87, 95% CI [0.94 – 3.44], p = 0.071). (Table 1) This difference was mainly driven by higher rate of TV-MI (6.0% vs. 2.5%, p=0.086) and TLR (7.6% vs. 1.7%, p=0.004). (**Figure 2**)

Definite device thrombosis rate was also higher in BRS as compared to EES group at 5-year (4.2% vs. 1.2%, HR 3.49, 95% CI 0.95 – 12.82, p=0.054). (**Figure 3**)

At landmark analysis from 1 to 5 years, no differences were found between BRS and EES groups in terms of DOCE (7.8 % vs. 4.3 %, p=0.122) or cardiac death (6.0 % vs. 4.3 %, p=0.574). A numerically higher rate of target vessel myocardial infarction (3.4 % vs. 1.7 %, p = 0.258) and definite device thrombosis (2.2% vs. 0.9%, p=0.283)

were found between 1 and 5 years in BRS vs. EES group with a statistically significant higher incidence of TLR (5.2% vs. 0.9%, p=0.006). No differences were found in terms of dual antiplatelet therapy between the BRS and EES at 5-year (3.4 % vs. 5.0%, p=0.647)

OCT data

A total of 88 patients were screened to participate in the OCT study. A total of 48 patients were excluded (4 patients died, 5 patients had a TLR, 4 patients had a target-vessel MI, 15 patients because of severe comorbidities, 2 patients because of oral anticoagulation, 18 patients refused to participate). Out of the 40 patients who agreed to participate, one patient had target lesion occlusion so eventually 39 patients were included in the analysis. Baseline clinical and angiographic characteristics are reported in table A (**supplementary table B**).

OCT data, as well the combinations of lipid, calcification, and neovascularization, as major atherosclerotic findings in this study, are shown in Table 2.

Overall, 31 patients (79%) exhibited at least one major finding of neoatherosclerosis. In particular, 8 (20%) patients had one 1 major findings of atherosclerosis in the intima at 5-year. Two major findings were present in 9 (22%) patients and all the three major findings of atherosclerosis were present in 13 (33%) patients. (**Figure 4)**

DISCUSSION

This is the first study comparing 5-year long-term follow-up of BRS vs. EES in STEMI patients. The main findings can be summarized as follows: 1) 5-year device-oriented endpoint rate is higher in BRS vs. EES group, mainly driven by higher rate of TLR, which are especially concentrated between 1 and 5 years; 2) rate of long-term definite device thrombosis is also higher in BRS vs. EES group; 3) in event-free patients, incidence of neo atherosclerosis is remarkably high.

After initial enthusiasm around bioresorbable scaffolds, long-term data together with BRS use in more complex lesions have shown not only lack of superiority but even inferiority in terms of hard clinical endpoints as compared to drug-eluting metallic stent. [13, 14] For these reasons, ABSORB BRS has been withdrawn from the market and use of the other BRS have been restricted to clinical studies. [15]

Despite this background, BRS usefulness in STEMI is still controversial. From the clinical point of view, previous STEMI studies on BRS have shown comparable angiographic and OCT performance to everolimus-eluting metallic stent without a clear inferiority of BRS vs. EES, with only higher device thrombosis especially in the early phase and without data beyond 3-year follow-up, when scaffold bioresorption is complete. [8, 9] The TROFI-II trial, which is the only randomized STEMI trial of BRS vs. EES, showed for example at 3-year low rates of DOCE and device thrombosis, in line with the favourable vascular healing process observed at 6-month. [16, 17]

The MAGSTEMI trial, which randomized STEMI patients to magnesium-based BRS (Magmaris, Biotronik, Switzerland) vs. metallic-DES (Orsiro, Biotronik, Switzerland), recently showed a higher 1-year vasodilation of the treated coronary segment after intracoronary nitro-glycerine administration with Magmaris vs. Orsiro. [18]

In this 5-year follow-up of the BVS EXAMINATION trial, we found a higher rate of device-oriented endpoint (DOCE) in BRS vs. EES arm, mainly driven by a higher rate of TLR. Difference in terms of TLR between groups became more important between 1 and 5 years. Incidence of device thrombosis was also higher in BRS vs. EES group; this difference was already evident in the early phase and continues to increase up to 5-year. No differences were found between groups in terms of dual antiplatelet therapy at 5-year with a very low rate in both groups.

It is noteworthy that device-related clinical events continue to accrue yearly and that whereas almost 90 % of the 5-year EES-TLR were due to device thrombosis, only 55 % of the BRS-TLR were caused by device thrombosis. This means that different mechanisms may play a role in determining these events between metallic and bioresorbable devices. Mechanical causes, such as scaffold dismantling, but also neoatherosclerosis should be considered. Whereas scaffold dismantling is known to be important for device thrombosis, neoatherosclerosis may have a role either in thrombosis or in restenosis. [10, 19] (**Figure 5**) In case of metallic stent neo-atherosclerosis was known to contribute to the so-called late catch-up phenomenon. Although BRS was created to reduce this phenomenon, neo-atherosclerosis following BRS implantation not only is qualitatively similar to that of DES, mainly composed of lipid, calcification and neo-vascularization, but it seems to have a higher incidence. [19, 20] Whereas in the RE-EXAMINATION study, incidence of neo-atherosclerosis in STEMI patients who received EES was 22.6% at 5-year, in the present study we found, for example, a higher incidence of 79% in STEMI patients treated by BRS. [21] This high incidence confirms previous observation in a group of stable angina patients enrolled in the ABSORB EXTEND study with OCT analysis at 5-year. [19] Data coming from other BRS platform

would be interesting to understand if this phenomenon is related only to a specific BRS or it is a class-effect.

Last, but not least, a previous study suggests that, despite the increased risk of early events, BRS may still provide a theoretical net clinical benefit to patients in very long-term, but only if the risk of BRS failure beyond 3 years is substantially reduced as compared with EES. [22] However our study shows that this event risk of BRS vs EES is maintained beyond 4 years, despite being performed in STEMI, a setting which is theoretically favorable to BRS. [17] Given this small degree of benefit that clinicians and decision-makers may expect from the first-generation BRS at the current risk not only of device thrombosis but overall of target lesion failure, we guess very long-term follow-up of the first-generation BRS has a very low probability to give positive results. Whether different results will be obtained with generation BRS remains to be determined.

Limitations

Several limitations of the study should be acknowledged. Due to limited number of patients and events and because the study is not randomized, but based on a propensity core analysis, caution should be made in reaching firm conclusions. Dual antiplatelet therapy in STEMI patients with ABSORB BVS implantation did not include guideline-oriented prasugrel or ticagrelor, and the duration was not according to recommendations for the EAPCI taskforce. Of note post-dilatation was performed in a relatively low rate of patients. Nature of clinical follow-up (clinical visit or phone call), such as event adjudication differ in both clinical arms. Nevertheless, this study currently represents the largest cohort of STEMI treated by BVS compared with a controlled arm.

CONCLUSION

At 5-year follow-up, STEMI patients treated with BRS showed higher rate of DOCE, compared with STEMI patients treated with EES, mainly driven by a higher rate of TLR, especially concentrated between 1 and 5 years. Incidence of BRS thrombosis was also higher as compared to EES. In event-free BRS patients, a high incidence of neo-atherosclerosis, composed of lipid, including TCFA, calcification and neovascularization, was found at 5-year. Our 5-year event risk of BRS vs EES suggests that the probability of obtaining positive results at very long-term follow-up is low. Whether better results will be obtained with new generation BVS remains to be determined.

Impact on daily practice

This is the first study to investigate 5-year outcomes in STEMI between BRS and best-in-class second-generation drug-eluting stent. STEMI patients treated with BRS have higher incidence of device-oriented endpoint, mainly driven by TLR clustered between 1 and 5 years. Device thrombosis is higher in BRS. OCT analysis showed also high rate of neo-atherosclerosis in BRS patients. This 5-year event-risk of BRS vs. EES gives a very low probability of positive results at a very long-term follow-up. Effort should be concentrated on data from new generation BRS.

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FIGURES LEGEND

Figure 1. Study flow-chart

Figure 2. Kaplan-Meier curves

Panel A: Kaplan-Meier event curves comparing BRS and EES for the composite device-oriented endpoint (DOCE) of cardiac death, target-vessel myocardial infarction and target lesion revascularization. **Panel B**: Kaplan-Meier events curves comparing BRS and EES for cardiac death. **Panel C**: Kaplan-Meier event curves comparing BRS and EES for target-vessel myocardial infarction (TV-MI). **Panel D**: Kaplan-Meier events curves comparing BRS and EES for target lesion revascularization (TLR).

Figure 3. Kaplan-Meier event curves comparing BRS and EES for definite device thrombosis.

Figure 4. Five-year OCT findings in STEMI patients treated with BRS.

(A) Lipid-laden intima (bidirectional white arc). (B) Macrophage infiltration (white arrow). (C) Deep calcium deposition (white arrow) >200 mm from the end-luminal border. (D) Neointimal calcification (white arrow) <200 mm from the end-luminal border. (E) Neovascularization (white box). (F) TCFA containing lipidic neointima. (G) Intimal rupture (white arrow). (H) Plaque rupture (white arrow) and empty cavity (asterisk). OCT = optical coherence tomography; TCFA: Thin-cap Fibroatheroma.

Figure 5. Examples of events caused by neo-atherosclerosis following BRS implantation in STEMI.

Panel A on the top shows a case of BRS-VLST at 1550 days (4.25 years) after the index procedure. The main OCT finding related to the thrombosis was neo-atherosclerosis with plaque rupture (white arrow and asterisk), visible also in the OCT longitudinal view. Near to the proximal and distal references, scaffold remnants were still observed.

Panel B on the bottom shows a case scaffold restenosis due to neoatherosclerosis. A TCFA with cap rupture (white arrow and asterisk) was identified without thrombus. A FFR of 0.74 was measured.

For both panels, in the longitudinal view the dotted lines correspond to the cross-section images. Minimum lumen area is shown per each cross-section. BRS = bioresorbable scaffold; FFR = fractional flow reserve; OCT = Optical coherence tomography; TCFA = thin-cap fibroatheroma; VLST = very-late scaffold thrombosis.

TABLES

Table 1. Clinical outcome at 30 days, 1-year and 5-year follow-up

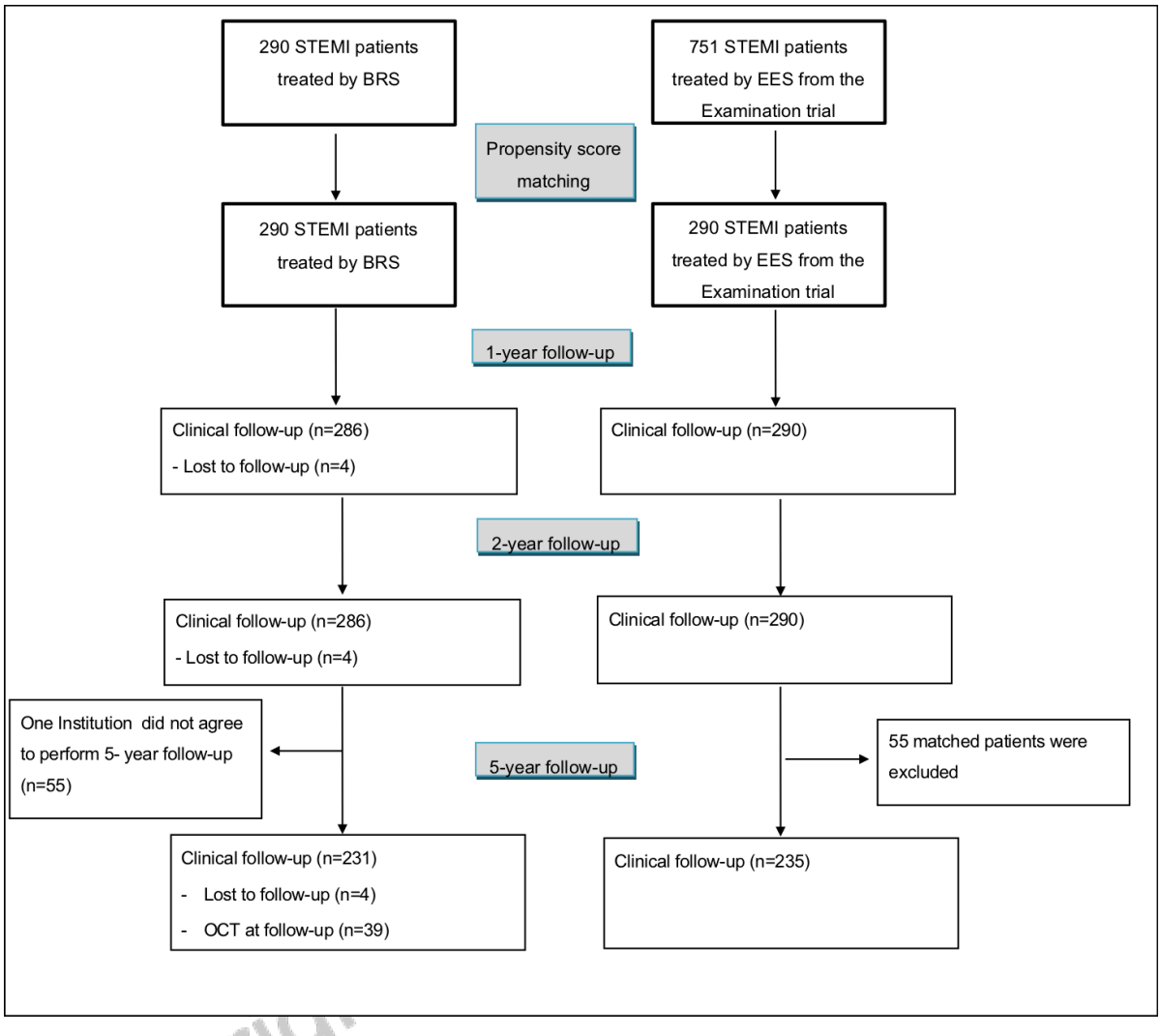
Clinical outcome at 30 days	**BRS group (n=235)**	**EES group (n=235)**	**HR [95%CI]**	**p-value**
DOCE	8 (3.4)	5 (2.1)	0.61 [0.20 - 1.86]	0.381
Cardiac death	5 (2.2)	4 (1.7)	1.27 [0.34 – 4.74]	0.717
TV MI	4 (1.7)	0 (0)	0.15 [0.00 – 46.51]	0.060
TLR	4 (1.7)	0 (0)	0.15 [0.00 – 46.51]	0.060
Definite/probable device thrombosis	4 (1.7)	2 (0.9)	2.05 [0.37 – 11.20]	0.406
Definite device thrombosis	4 (1.7)	0 (0)	0.15 [0.00 – 46.51]	0.060
Clinical outcome at 1-year	**BRS group (n=235)**	**EES group (n=235)**	**HR [95%CI]**	**p-value**
DOCE	10 (4.3)	8 (3.4)	1.86 [0.75 – 4.28]	0.186
Cardiac death	7 (3.0)	5 (2.1)	1.42 [0.45 – 4.50]	0.543
TV MI	6 (2.6)	2 (0.9)	3.10 [0.63 – 15.38]	0.165
TLR	6 (2.6)	2 (0.9)	3.13 [0.63 – 15.53]	0.162
Definite/probable device thrombosis	6 (2.6)	4 (1.7)	1.80 [0.52 – 6.16]	0.346
Definite device thrombosis	5 (1.7)	1 (0.7)	5.16 [0.63 – 44.19]	0.092
Clinical outcome at 5-year	**BRS group (n=235)**	**EES group (n=235)**	**HR [95%CI]**	**p-value**
DOCE	31 (13.2)	18 (7.6)	1.87 [0.94 – 3.44]	0.071
Cardiac death	14 (5.9)	10 (4.2)	1.44 [0.63 – 3.32]	0.366
TV MI	14 (6.0)	6 (2.5)	2.33 [0.88 – 6.14]	0.086
TLR	18 (7.6)	4 (1.7)	4.86 [1.62 – 14.58]	0.004
Definite/probable device thrombosis	13 (5.5)	10 (4.2)	1.34 [0.57 – 3.11]	0.437
Definite device thrombosis	10 (4.2)	3 (1.2)	3.49 [0.95 – 12.82]	0.054

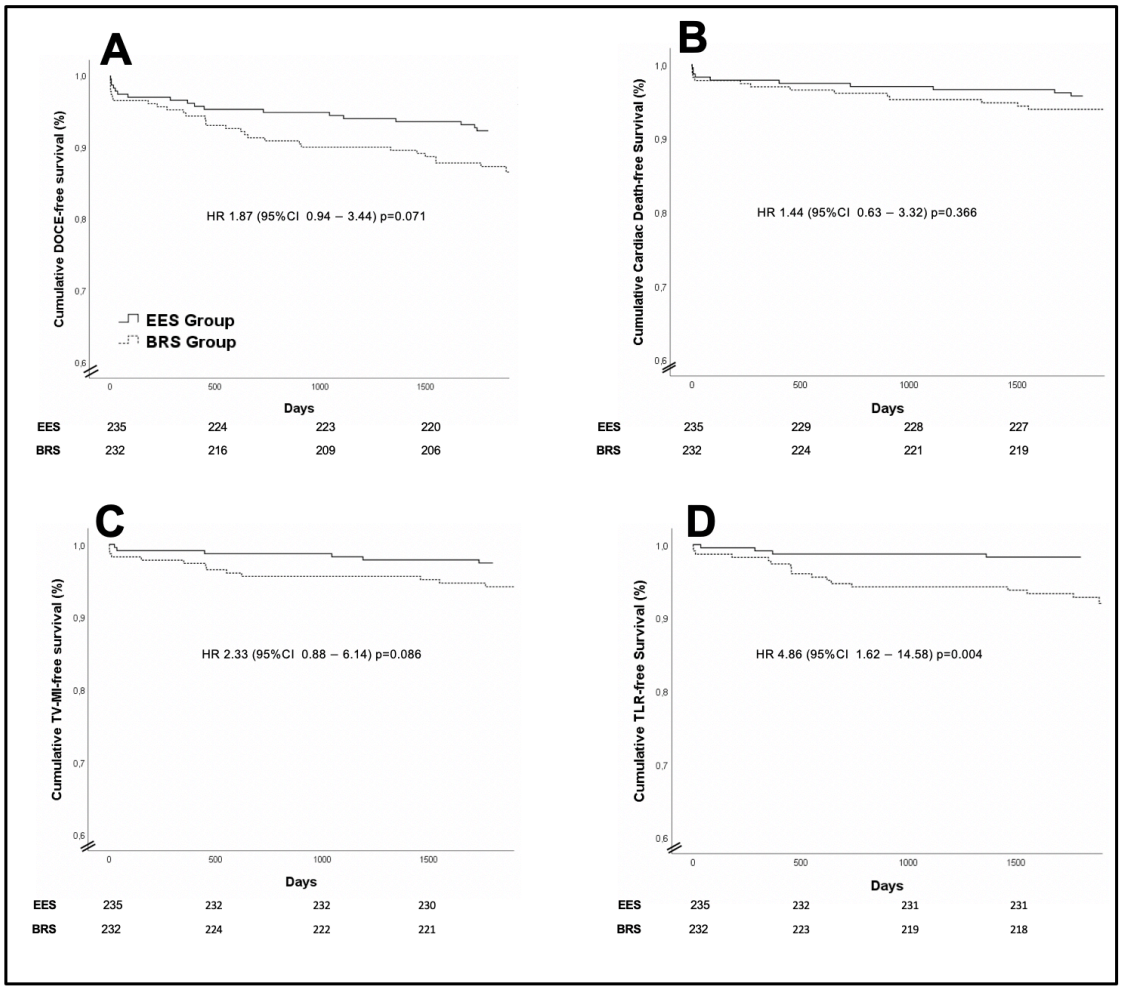
DOCE = Device oriented endpoint; TV = target vessel; MI = myocardial infarction; TLR = target lesion revascularization

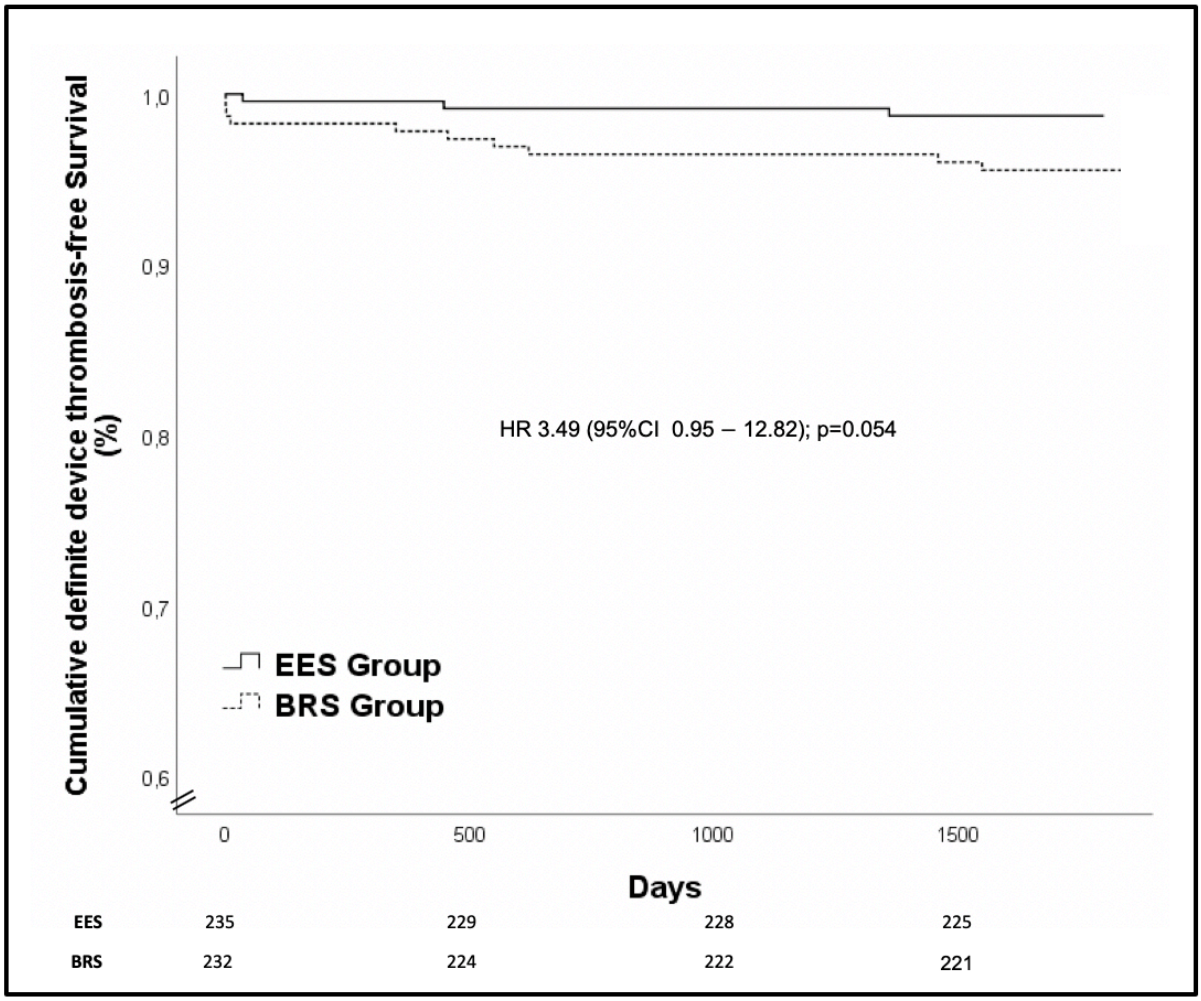
Table 2. OCT data of the BRS patients included in OCT substudy.

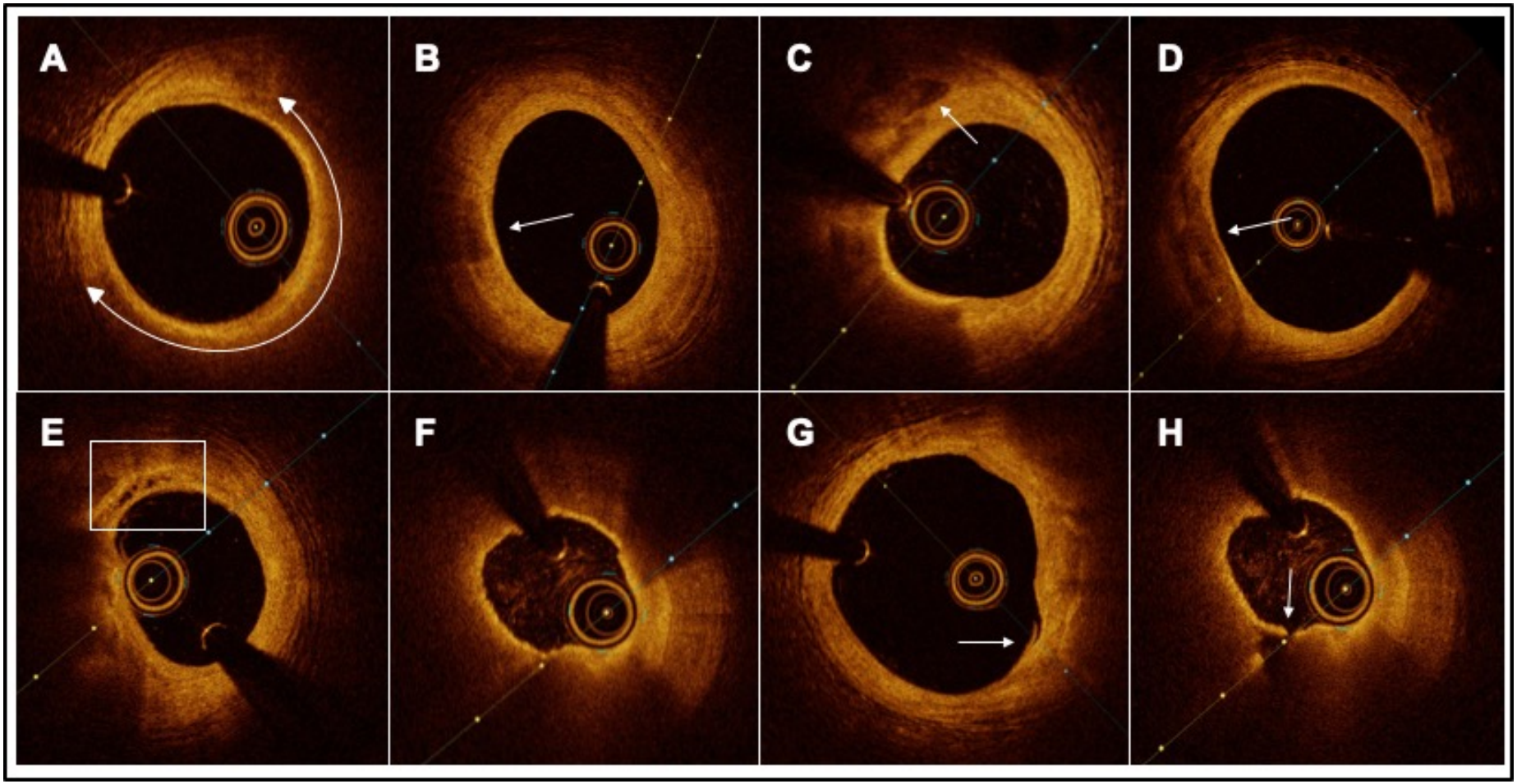
	BRS group (n=39)
Mean lumen area, mm^2	4.97±1.96
Proximal reference lumen area, mm^2	7.38±2.43
Distal reference lumen area, mm^2	6.54±3.04
Lipid, n (%)	27 (69)
Calcification, n (%)	19 (48)
Thrombi, n (%)	2 (0.5)
Internal rupture, n (%)	6 (15)
Neovascularization, n (%)	19 (48)
TCFA, n (%)	6 (15)
Macrophage, n (%)	15 (38)
None of the 3 major findings, n (%)	8 (20)
One finding, n (%) Lipid only Calcification only Neovascularization only	 7 (18) 0 (0) 1 (2.5)
Two findings, n (%) Lipid + calcification Lipid + neovascularization Calcification + neovascularization	 4 (10) 3 (7) 2 (5)
All 3 findings, n (%)	13 (33)

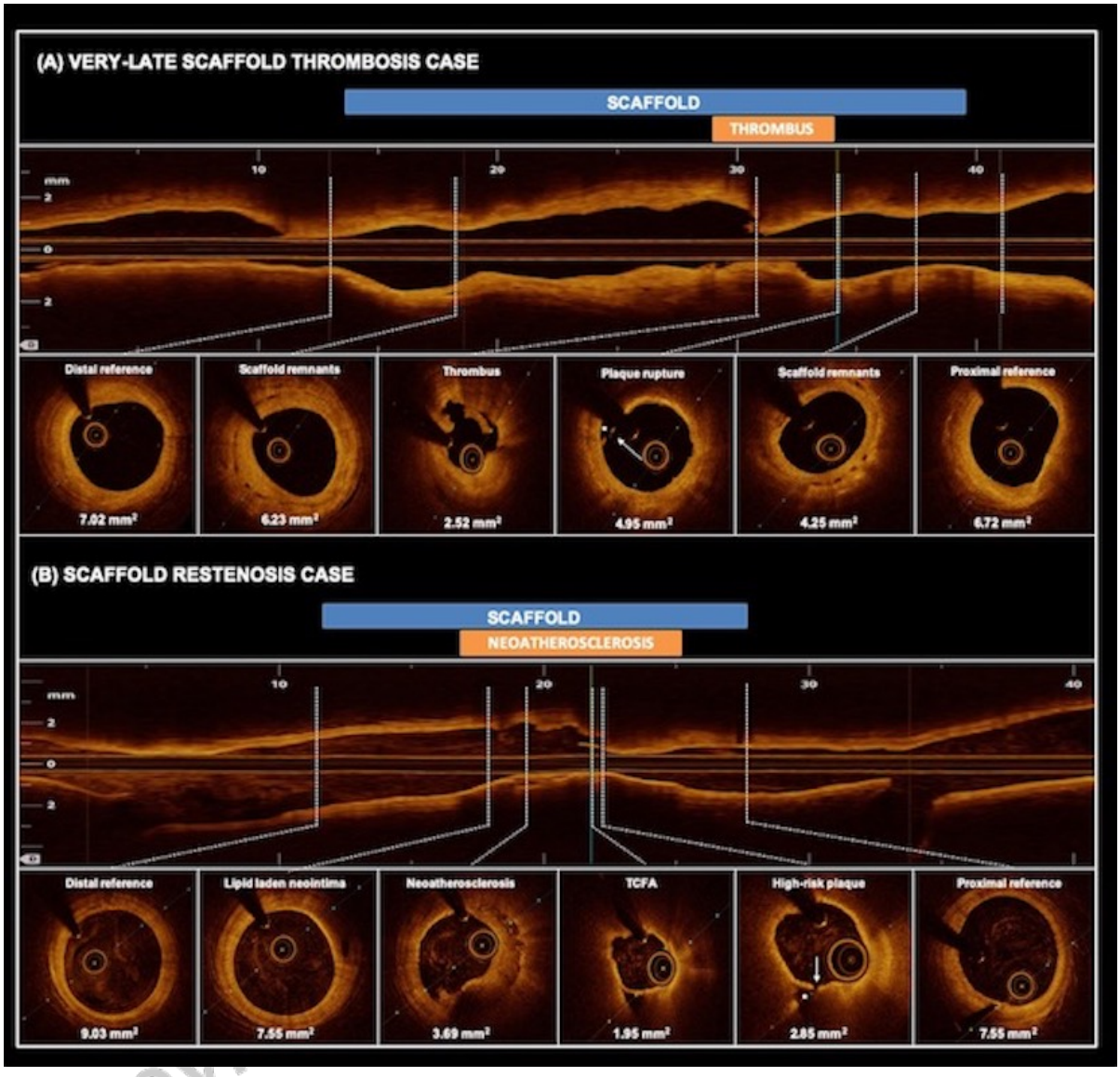
BRS = bioresorbable scaffold; OCT =optical coherence tomography; TCFA = thin-cap fibroatheroma.











Primary PCI procedure

Primary 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-dilatation was not mandatory, but recommended for BRS implantation, according to BRS 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.

Definition of clinical outcomes

The primary endpoint of this analysis was defined as the combined device-oriented composite endpoint (DOCE), including cardiac death, target vessel-myocardial re-infarction (TV-MI) and target lesion revascularization (TLR). All the individual components and device thrombosis (stent/scaffold), defined by the Academic Research Consortium (ARC) criteria, were also analysed. Whereas all the events in the EXAMINATION trial were adjudicated by an independent clinical events committee, blinded to stent assignment after review of original source documentation, all the events in the BRS 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.

Optical coherence tomography analysis

Three participating institutions (n= 88 patients) agreed to participate in a specific optical coherence tomography (OCT) sub-study, which consists of a 5-year angiographic and OCT follow-up. Those event-free patients included in the BRS arm of the BVS-EXAMINATION study in these institutions were screened to participate in the OCT analysis. The exclusion criteria were death, target lesion myocardial infarction or target lesion revascularization during the 5 years following stent implantation. Patients with creatinine clearance < 45 ml/min/m^2, known hyper-sensibility or allergic reaction to contrast, chronic oral anticoagulation, left ventricular ejection fraction ≤30%, platelet count <75000/mm^3 or >700000/mm^3, life-threatening disease, inability to provide informed consent, pregnant or breast feeding were also excluded.

All suitable patients were contacted by phone and were invited to participate in the study. Patients accepting the protocol were cited to the outpatient clinic and signed written informed consent. This study was approved by the local ethics committee of all participating institutions and was conducted in accordance with the Declaration of Helsinki.

OCT analysis was performed by a dedicated core laboratory (BARCICORE-lab, Barcelona, Spain), using specific software for analysis (LightLab Imaging, Westford, Massachusetts). The following analyses were performed:

- identification of the previously treated segment by identifying the radiopaque markers of the BRS;
- quantitative OCT analysis of the mean lumen area of the scaffolded segment, according to standard core-laboratory procedures with analysis each 1-mm cross-section;

- qualitative OCT analysis at scaffold level. As previously reported, we defined lipid-laden intima as a diffusely bordered, signal-poor region with overlying signal-rich bands in the intima. Calcification was defined as a well-delineated, signal-poor region with sharp borders. Calcium deposition at a superficial position (<200 mm from the end-luminal border) showing a sharply delineated region was calculated as neointimal calcification. Thrombi were described as masses protruding into the lumen and discontinuous from the surface of the vessel wall. Intimal rupture was defined as discontinuity of the fibrous cap connecting the lumen. Neovascularization was defined as the presence of signal-poor holes or tubular structures with a diameter of 50 to 300 mm that are not connected to the vessel lumen. Thin-cap fibroatheroma (TCFA)-containing intima was defined as fibrous cap thickness <=65 mm at the thinnest segment and an angle of lipid tissue >=180°. Macrophage infiltration was described as a bright spot with a high signal variance from the surrounding tissue.

  Neoatherosclerosis was defined as lipid-laden plaque including TCFA with or without intimal rupture and/or thrombi, and/or calcific plaque with or without neovascularization and/or macrophage.

Propensity score match analysis

Propensity score matching was applied to compare 5-year device-oriented primary endpoint of STEMI patients treated with BRS and those treated with EES. In the previous 1-year comparison, a propensity score matching was performed using a proprietary macro developed and tested for SPSS 20.0 (www.unc.edu/~painter), as previously shown. First, the program performed a logistic regression to score all patients according to the treatment (BRS vs. EES), using as covariates clinical and

procedural parameters that were clinically relevant for the endpoint: age (years), sex (male/female), diabetes mellitus (yes/no), culprit vessel and stent/scaffold length and diameter (mm). Secondly, the macro searched and selected the best match case of the EES group for every BRS case according to the absolute value of the difference between the propensity score of EES and BRS cases under consideration. Patients in the two groups were matched through a greedy algorithm based on local optimization. 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 two matched groups (EES vs. BRS), stratified by pairs to account for propensity score matching; as one institution did not agree to participate in this long-term follow-up, the EES patients matched with those BRS patients of that institution were excluded.

Table A. Baseline clinical and procedural characteristics

	BVS group (n=235)	EES group (n=235)	p-value
Age, years	56.0±12.9	57.5±12.0	0.624
Male sex	185 (78.7)	194 (82.6)	0.293
Smoking history	150 (63.8)	181 (77.0)	0.002
Hypertension	120 (51.1)	106 (45.1)	0.196
Diabetes	30 (12.8)	30 (12.8)	1.000
Dyslipidemia	83 (35.3)	115 (48.9)	0.003
Previous MI	5 (2.1)	9 (3.8)	0.281
Previous PCI	7 (3.0)	10 (4.3)	0.459
Previous CABG	2 (0.9)	1 (0.4)	0.557
Previous Stroke	5 (2.1)	4 (1.7)	0.736
Infarct-related artery			0.106
LAD	94 (40.0)	105 (44.7)	
RCA	116 (49.4)	92 (39.1)	
LCx	24 (10.2)	36 (15.3)	
SVG	0	0	
Left main	1 (0.2)	2 (0.9)	
Thrombectomy device use	163 (69.4)	162 (68.9)	0.920
Pre-dilatation	181(77.0)	67 (28.9)	<0.001
IIb/IIIa Inhibitor	161 (68.5)	124 (52.8)	<0.001
Bivalirudin	0 (0)	18 (7.7)	<0.001
Unfractionated heparin	235 (100)	182 (77.4)	<0.001
Number of stent/scaffold	1.1±0.4	1.1±0.3	0.911
Stent/scaffold diameter, mm	3.3±0.4	3.2±0.4	0.475
Stent/scaffold length, mm	21.9±8.4	22.0±9.0	0.672
Post-dilatation	54 (23.1)	30 (12.8)	0.004
TIMI pre			0.007
- 0	165 (70.2)	128 (54.9)	
- 1	9 (3.8)	17 (7.3)	
- 2	25 (10.6)	36 (15.5)	
- 3	36 (15.3)	52 (22.3)	

	BVS group (n=235)	EES group (n=235)	p-value
TIMI post			0.353
- 0	1 (0.4)	4 (1.7)	
- 1	1 (0.4)	1 (0.4)	
- 2	11 (4.7)	6 (2.6)	
- 3	222 (94.5)	222 (94.5)	

Data are expressed as mean ± SD or number (%). The p values are from paired *t* test for continuous data and conditional logistic regression for dichotomous and ordinal data. LAD = left anterior descending artery; RCA = right coronary artery; LCx = left circumflex artery; SVG = saphenous vein graft; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery by-pass graft; SD = standard deviation

Table B. Baseline clinical and procedural characteristics of BRS patients included in the OCT sub-study.

	Overall BRS group (n=235)	OCT BRS group (n=39)	p-value
Age, years	56.0±12.9	57.1±11.0	0.921
Male sex	185 (78.7)	26 (70.3)	0.289
Smoking history	150 (63.8)	26 (66.6)	0.579
Hypertension	120 (51.1)	14 (37.8)	0.158
Diabetes	30 (12.8)	4 (10.8)	1.000
Dyslipidemia	83 (35.3)	11 (29.7)	0.580
Previous MI	5 (2.1)	2 (5.4)	0.245
Previous PCI	7 (3.0)	1 (2.7)	1.000
Previous CABG	2 (0.9)	0 (0)	1.000
Previous Stroke	5 (2.1)	0 (0)	1.000
Infarct-related artery			0.489
LAD	94 (40.0)	12 (32.4)	
RCA	116 (49.4)	23 (62.2)	
LCx	24 (10.2)	2 (5.4)	
Left main	1 (0.2)	0 (0)	
Thrombectomy device use	163 (69.4)	20 (54.1)	0.089
Pre-dilatation	181 (77.0)	18 (48.6)	<0.001
Number of scaffold implanted	1.1±0.4	1.1±0.5	0.822
Scaffold diameter, mm	3.3±0.4	3.4±0.4	0.842
Scaffold length, mm	21.9±8.4	22.4±8.1	0.752
Post-dilatation	54 (23.1)	12 (33.3)	0.211