

# Mid-term outcomes of bioresorbable vascular scaffolds vs second-generation drug-eluting stents in patients with acute coronary syndromes

## A systematic review and meta-analysis

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### Abstract

**Background:** Everolimus-eluting bioresorbable vascular scaffolds (BVS), which have the characteristics of scaffold absorption and vascular function recovery, are the latest innovation in the treatment of coronary artery disease. This new concept has become a hot topic in the field of interventional cardiology. Data regarding mid-term clinical outcomes of BVS in acute coronary syndromes are currently scarce. The aim of this systematic review and meta-analysis is to compare mid-term outcome data for BVS and second-generation drug-eluting stents (DES) in the treatment of acute coronary syndromes.

**Methods:** We searched PubMed, Embase, the Cochrane Library, Web of Science, and relevant web sites for studies with a follow-up of  $\geq 1$  years that studied percutaneous coronary interventions with BVS vs second-generation DES in acute coronary syndromes. A meta-analysis was performed with the software RevMan following the standards of the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.

**Results:** Five studies, 2 randomized controlled trials, and 3 observational studies, with a total of 1758 patients (BVS  $n=917$ ; DES  $n=841$ ) and a median follow-up duration of 24 months, were included. BVS, when compared with DES, resulted in higher rates of target lesion revascularization (TLR) (OR, 2.20; 95% CI, 1.12–3.64;  $P=.02$ ) and stent/scaffold thrombosis (ST/ScT) (OR=2.35, 95% CI: 1.13–4.89,  $P=.02$ ). When TLR due to device thrombosis were excluded, the difference in risk estimates between the 2 groups was no longer significant (OR: 1.67, 95% CI: 0.73–3.82,  $P=.22$ ). The risk for all-cause death (OR=1.32 95% CI: 0.61–2.88,  $P=.48$ ), cardiac death (OR=1.29, 95% CI: 0.58–2.86  $P=.52$ ), target vessel myocardial infarction (OR=1.50, 95% CI: 0.86–2.61,  $P=.15$ ), and target lesion failure (OR=1.34, 95% CI: 0.76–2.35,  $P=.31$ ) did not differ between BVS and DES groups.

**Conclusion:** At mid-term follow-up, BVS had a higher risk of TLR and ST/ScT than the second-generation DES in patients with acute coronary syndromes. ST/ScT was the key factor indicating the decreased safety and effectiveness of BVS relative to DES.

**Abbreviations:** AMI = acute myocardial infarction, BVS = bioresorbable vascular scaffolds, DES = drug-eluting stents, EES = everolimus-eluting stents, FDA = Food and Drug Administration, GABG = coronary artery bypassgraft, IVUS = intra-vascular ultrasound, LAD = left anterior descending artery, LCx = left circumflex artery, MI = myocardial infarction, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, RCA = right coronary artery, ST/ScT = stent/scaffold thrombosis, TIMI = thrombolysis in myocardial infarction, TLR = target lesion revascularization.

**Keywords:** acute coronary syndromes, bioresorbable vascular scaffolds, drug-eluting stents

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## 1. Introduction

Drug-eluting stents (DES) reduce the rate of in-stent restenosis, myocardial infarction, and target lesion revascularization (TLR) compared with bare-metal stents for patients undergoing coronary intervention.<sup>[1]</sup> However, permanent structures hinder surgical myocardial revascularization and physiological vessel remodeling and exposes patients to increased risk of stent/scaffold thrombosis (ST/ScT) for a long time.<sup>[2]</sup> Everolimus-eluting bioresorbable vascular scaffolds (BVS), however, represent a new technique designed to overcome the long-term limitations of metal stent implantation in percutaneous coronary intervention. They provide support for the vessels over a short period of time and then are completely resorbed, potentially overcoming the long-term adverse events experienced with permanent metallic stents.

Early studies<sup>[3,4]</sup> have shown that the safety and effectiveness of BVS are comparable to second-generation DES. Trials with longer follow-up<sup>[5,6]</sup> and several meta-analyses<sup>[7,8]</sup> have shown that patients receiving BVS had a higher rate of ST/ScT compared with patients receiving second-generation DES during percutaneous coronary intervention. The negative results of the ABSORB II and ABSORB III trials led the Food and Drug Administration (FDA) to restrict the use of BVS to clinical trials/registrations and the facility that was producing BVS is no longer in operation. However, the exploration of BVS has not stopped. The recently published ABSORB IV<sup>[9]</sup> trial showed that the rate of ST/ScT was 0.7% at 1 year, compared with 0.9% for the ABSORB II trial<sup>[3]</sup> and 1.5% for the ABSORB III trial<sup>[4]</sup>.

Currently, data on the effects of BVS applied to acute coronary syndromes and data on mid-term clinical follow-up results are scarce. We performed a meta-analysis of the mid-term clinical outcomes of BVS and second-generation DES in acute coronary syndromes, providing some reference for clinical decisions.

## 2. Methods

### 2.1. Data sources and search strategy

We searched PubMed, <http://links.lww.com/MD/D911>, EMBASE, Cochrane Library, Web of Science, and relevant web sites (<https://www.clinicaltrials.gov>) for studies that compared BVS to second-generation DES in acute coronary syndromes. All relevant combinations of the following keywords were searched: “bioresorbable vascular scaffold(s)”, “bioresorbable scaffold(s)”, “bioresorbable stent(s)”, “Everolimus-eluting stent(s)”, “drug-eluting stent(s)”, “acute coronary syndromes,” and “acute myocardial infarction”. The search was conducted on all articles in these databases published prior to April 1, 2019.

### 2.2. Study selection

Studies were included in the meta-analysis if they met the following criteria:

- (1) randomized controlled trial and observation study;
- (2) compared the outcomes between BVS and second-generation DES;
- (3) reported clinical outcomes with follow-up time  $\geq 12$  months. Case reports, registries, reviews, and editorials were excluded from consideration.

### 2.3. Data extraction

Two reviewers (KJS and ZHY) independently assessed the eligibility of studies. Disagreements were resolved by a third reviewer (LP). For studies reported in multiple publications, we selected the report with the largest number of patients and the longest follow-up.

### 2.4. Study endpoints

The primary efficacy endpoint was TLR, and the primary safety endpoint was definite ST/ScT. Secondary endpoints included all-cause death, cardiac death, target vessel myocardial infarction, and target lesion failure. TLR was described as any repeated revascularization of the target lesion. Definite ST/ScT was classified according to standards of the academic research consortium.<sup>[10]</sup> Target lesion failure was defined as the composite of cardiac death, target vessel myocardial infarction, and ischemia-driven target lesion revascularization.

### 2.5. Risk of bias assessment

Quality and risk of bias in reporting data were assessed according to the Cochrane Handbook of Systematic Reviews<sup>[11]</sup> and using the Newcastle-Ottawa Quality Assessment Scale for observational studies. Publication bias for the primary endpoint was assessed using a funnel plot analysis.

### 2.6. Data analysis

We reported clinical outcomes and their respective effect size using ORs with 95% CIs. Heterogeneity testing was performed using the Cochran Q test and Higgin  $I^2$  tests;  $I^2$  values of  $< 25\%$ ,  $25\%$  to  $50\%$ , and  $> 50\%$  indicated low, moderate, and high heterogeneity, respectively.<sup>[12]</sup> For  $P$  value  $< .10$  or  $I^2 > 50\%$ , the sources of heterogeneity needed to be further analyzed. After excluding the influence of obvious clinical heterogeneity, a random effect model was used. If  $P > .1$  and  $I^2 < 50\%$ , a fixed-effect model was used to analyze the results. Further, sensitivity analysis was carried out by comparing the consistency of the results of the random effect model and fixed-effect model. All data analyses were performed using the RevMan software (version 5.3.5).

### 2.7. Ethical approval and informed consent

This study is a systematic review and meta-analysis of previously approved and published studies and does not require ethical approval and patient consent.

## 3. Results

### 3.1. Search results and study characteristics

Flow diagram illustrates the search strategy. The search strategy identified a total of 1246 records. After removing duplicates, the title and abstract of 678 records were screened, 15 full-text articles were assessed for eligibility, and 5 studies were included in the systematic review and meta-analysis. Two randomized trials<sup>[14,15]</sup> and 3 observational<sup>[15–17]</sup> studies were included. There was a combined total of 1758 patients, including 917 patients in the “BVS” group and 841 patients in the “DES” group. The median follow-up for the studies was 24 months (range 12–36 months). The duration of dual antiplatelet therapy (DAPT) prescribed by each study was at least 12 months. Tables 1–3 show the design of

**Table 1****Main characteristics of the included studies.**

Study	Year	BVS/DES treated		Study type	Clinical presentation	BVS/DES Scaffold type	Follow-up months
		Centers, n	Patients, n				
ISAR-Absorb MI <sup>[14]</sup>	2019	5	173/89	prospective, randomized, non-inferiority, clinical trial	AMI	Everolimus-Eluting BVS /EES	12
TROFI II <sup>[15]</sup>	2018 2016	8	95/96	Randomized controlled trial Prospective	STEMI	Everolimus-Eluting BVS/EES	36
BVS EXAMINATION <sup>[16]</sup>	2016 2015	6	290/290	retrospectively, propensity matched	STEMI	Everolimus-Eluting BVS/EES	24
BVS STEMI FIRST <sup>[17]</sup>	2016	1	145/151	Prospective, propensity matched	STEMI	Everolimus-Eluting BVS/EES	18
Imori et al <sup>[18]</sup>	2016	8	214/215	Propensity matched analysis	ACS	Absorb BVS/EES	24

AMI=acute myocardial infarction, BVS=bioresorbable vascular scaffolds, DES=drug eluting stents, EES=everolimus-eluting stents.

**Table 2****Baseline characteristics of included studies.**

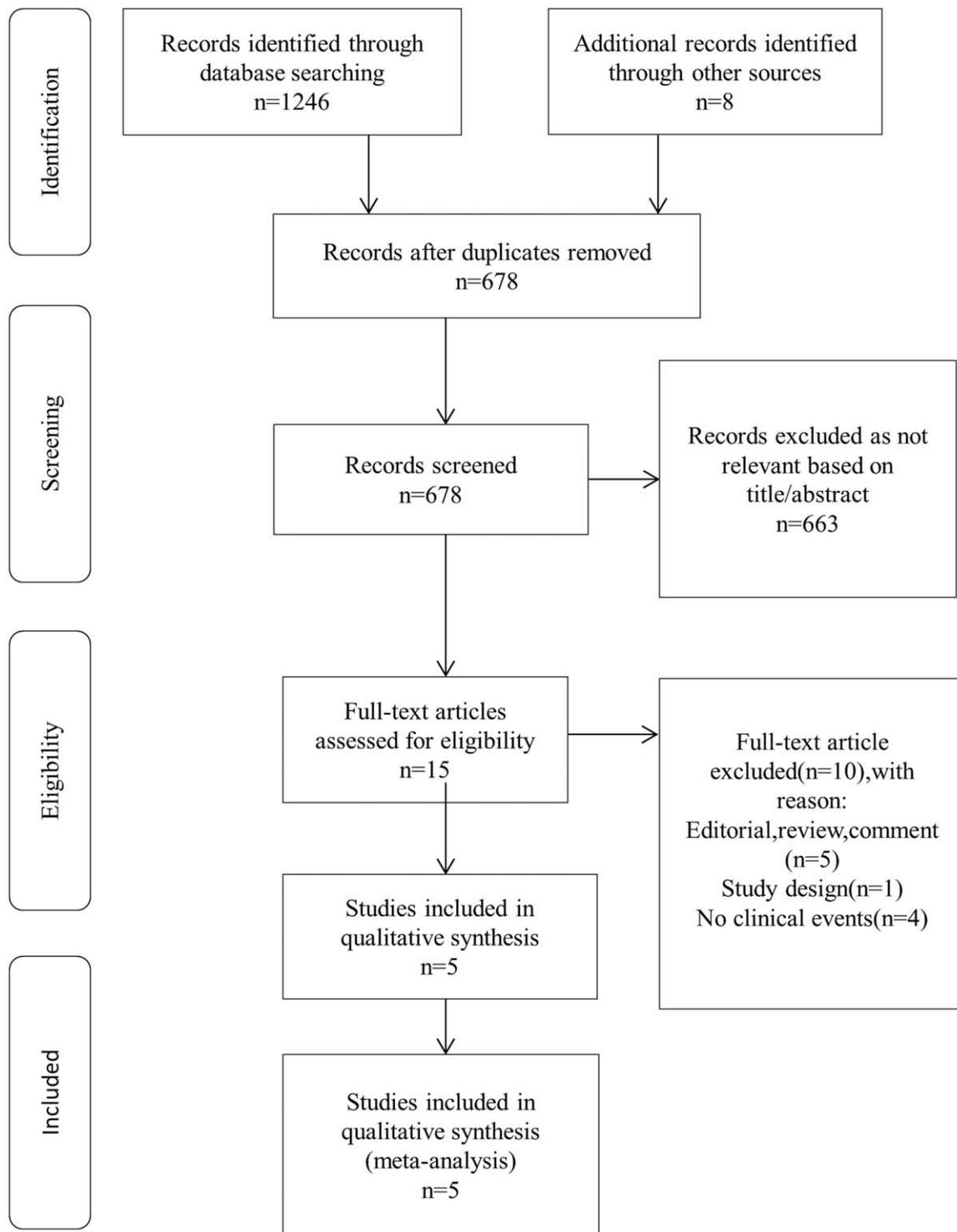
Variable	ISAR-Absorb MI <sup>[14]</sup>		TROFI II <sup>[15]</sup>		BVS EXAMINATION <sup>[16]</sup>		BVS STEMI FIRST <sup>[17]</sup>		Imori et al <sup>[18]</sup>	
	BVS (173)	DES (89)	BVS (95)	DES (96)	BVS (290)	DES (290)	BVS (145)	DES (151)	BVS (214)	DES (215)
Age, years	61.7 ± 11.0	63.3 ± 9.9	59.1 ± 10.7	58.2 ± 9.6	56.0 ± 12.8	57.6 ± 12.0	56.3 ± 10.2	54.9 ± 11.5	59.7 ± 13.0	61.2 ± 11.9
Male	138 (79.8%)	75 (73.0%)	73 (76.8%)	84 (87.5%)	236 (81.4%)	231 (79.7%)	109 (72.2%)	113 (74.8%)	170 (79.4%)	173 (80.5%)
Smoking history	77 (44.5%)	38 (43.2%)	46 (48.4%)	47 (49.0%)	37 (12.8%)	37 (12.8%)	71 (41.0%)	89 (58.9%)	110 (51.4%)	89 (41.4%)
Diabetes	37 (26.6%)	17 (19.3%)	18 (18.9%)	14 (14.6%)	177 (61.0%)	220 (75.9%)	17 (11.3%)	15 (9.9%)	30 (14.0%)	36 (16.7%)
Dyslipidemia	74 (43.5%)	40 (47.6%)	60 (63.8%)	55 (57.3%)	121 (41.7%)	132 (45.5%)	43 (28.4%)	41 (27.1%)	88 (41.1%)	92 (42.8%)
Hypertension	93 (53.5%)	54 (62.1%)	41 (44.1%)	35 (36.5%)	144 (49.7%)	127 (43.8%)	60 (39.7%)	56 (37.1%)	120 (56.1%)	117 (54.4%)
Previous MI	12 (6.9%)	6 (6.7%)	2 (2.1%)	3 (3.1%)	10 (3.5%)	10 (3.5%)	-	-	-	-
Previous PCI	15 (8.8%)	7 (7.9%)	4 (4.2%)	3 (3.1%)	10 (3.5%)	11 (3.8%)	-	-	-	-
Previous GABG	0	0	-	-	3 (1.0)	1 (0.3)	-	-	-	-
Infarct-related artery										
LAD	82 (47.4%)	43 (48.3%)	34 (35.8%)	41 (42.7%)	145 (50.0%)	117 (40.3%)	64 (42.4%)	62 (41.1%)	141 (65.9%)	96 (44.7%)
RCA	61 (35.3%)	36 (40.4%)	44 (46.3%)	44 (45.8%)	114 (39.3%)	126 (43.4%)	51 (33.8%)	46 (30.5%)	67 (31.3%)	65 (30.2%)
LCx	30 (17.3%)	10 (11.2%)	17 (17.9%)	13 (13.5%)	29 (10.0%)	45 (15.5%)	32 (21.2%)	40 (26.5%)	40 (18.7%)	38 (17.6%)
Multivessel disease	70 (40.5%)	37 (41.5%)	-	-	24 (8.2%)	28 (9.7%)	-	-	-	-
Killip class										
I	124 (93.9%)	62 (95.4%)	90 (94.7%)	93 (96.9%)	-	-	-	-	-	-
II	5 (3.8%)	1 (1.5%)	4 (4.2%)	3 (3.1%)	-	-	-	-	-	-
III	1 (0.8%)	1 (1.5%)	1 (1.1%)	0	-	-	-	-	-	-
IV	2 (1.5%)	1 (1.5%)	0	0	-	-	-	-	-	-

GABG=coronary artery bypassgraft, LAD=left anterior descending artery, LCx=left circumflex artery, MI=myocardial infarction, PCI=percutaneous coronary intervention, RCA=right coronary artery.

**Table 3****Procedural characteristics of the included studies.**

Variable	ISAR-Absorb MI <sup>[14]</sup>		TROFI II <sup>[15]</sup>		BVS EXAMINATION <sup>[16]</sup>		BVS STEMI FIRST <sup>[17]</sup>		Imori et al <sup>[18]</sup>	
	BVS (173)	DES (89)	BVS (95)	DES (96)	BVS (290)	DES (290)	BVS (151)	DES (151)	BVS (214)	DES (215)
Numbers of lesionsings	-	-	95	98	-	-	-	-	-	-
Thrombectomy	-	-	89 (93.7%)	84 (85.7%)	217 (74.8%)	199 (68.6%)	115 (76.2%)	115 (76.2%)	-	-
Predilation	164 (95.3%)	72 (81.8%)	53 (55.8%)	50 (51.0%)	230 (79.3%)	83 (28.6%)	80 (54.0%)	42 (28.4%)	-	-
Postdilation	98 (56.6%)	31 (34.8%)	48 (50.5%)	25 (25.5%)	105 (36.2%)	44 (15.2%)	60 (39.7%)	33 (21.8%)	117 (55.2%)	-
Device success	-	-	91 (95.8%)	96 (100.0%)	-	-	149 (98.7%)	150 (99.3%)	-	-
Stent diameter	3.205 ± 0.40	3.20 ± 0.40	3.25 ± 0.30	3.12 ± 0.37	3.22 ± 0.33	3.19 ± 0.40	3.21 ± 0.33	3.20 ± 0.46	3.1 ± 0.4	3.0 ± 0.4
Stent length	25.7 ± 12.3	20.6 ± 6.7	20.6 ± 6.7	20.7 ± 6.7	22.5 ± 8.80	21.7 ± 9.17	26. ± 13.27	27.76 ± 14.81	20.8 ± 5.2	19.7 ± 5.1
OCT/IVUS guidance	-	-	-	-	-	-	-	-	-	-
TIMI flow grade pre										
0	80 (46.2%)	52 (58.4%)	60 (63.2%)	61 (62.9%)	202 (69.7%)	159 (54.8%)	80 (53.0%)	85 (56.3%)	-	-
1	10 (5.8%)	3 (3.2%)	3 (3.2%)	3 (3.1%)	15 (5.2%)	18 (6.2%)	16 (10.6%)	12 (7.9%)	-	-
2	30 (17.3%)	8 (9.0%)	8 (8.4%)	13 (13.4%)	34 (11.7%)	44 (15.2%)	31 (20.5%)	40 (26.5%)	-	-
3	53 (30.6%)	26 (29.3%)	24 (25.3%)	20 (20.6%)	39 (13.4%)	67 (23.1%)	24 (15.9%)	14 (9.3%)	-	-
TIMI flow grade post										
0	0	1 (1.1%)	0	0	1 (0.3%)	5 (1.7%)	0	0	-	-
1	5 (2.9%)	3 (3.4%)	0	0	1 (0.3%)	1 (0.3%)	2 (1.3%)	0	-	-
2	5 (2.9%)	3 (3.4%)	0	2 (2.0%)	13 (4.5%)	7 (2.4%)	17 (11.3%)	21 (13.9%)	-	-
3	168 (97.1%)	85 (95.5%)	95 (100.0%)	96 (98.0%)	275 (94.8%)	275 (94.8%)	132 (87.4%)	130 (86.1%)	-	-

IVUS=intra-vascular ultrasound, OCT=optical coherence tomography, TIMI=thrombolysis in myocardial infarction.



**Figure 1.** Flow diagram. Search strategy and study selection as per Preferred Reporting Items for this meta-analysis.

the individual studies, baseline clinical, angiographic characteristics, and the procedural characteristics.

### 3.2. Quality assessment and sensitivity analysis

Quality assessments for RCT and observational studies are provided in the Table 4. All included studies were found to be

high quality with a low risk of bias. The funnel plots for TLR and definite ST/ScT were quite symmetrical, suggesting that there is little publication bias (Fig. 2). In the sensitivity analysis, compared with the fixed-effect model and the random-effect model, the changes in the study results were statistically significant, suggesting that the study results were relatively stable.

**Table 4**

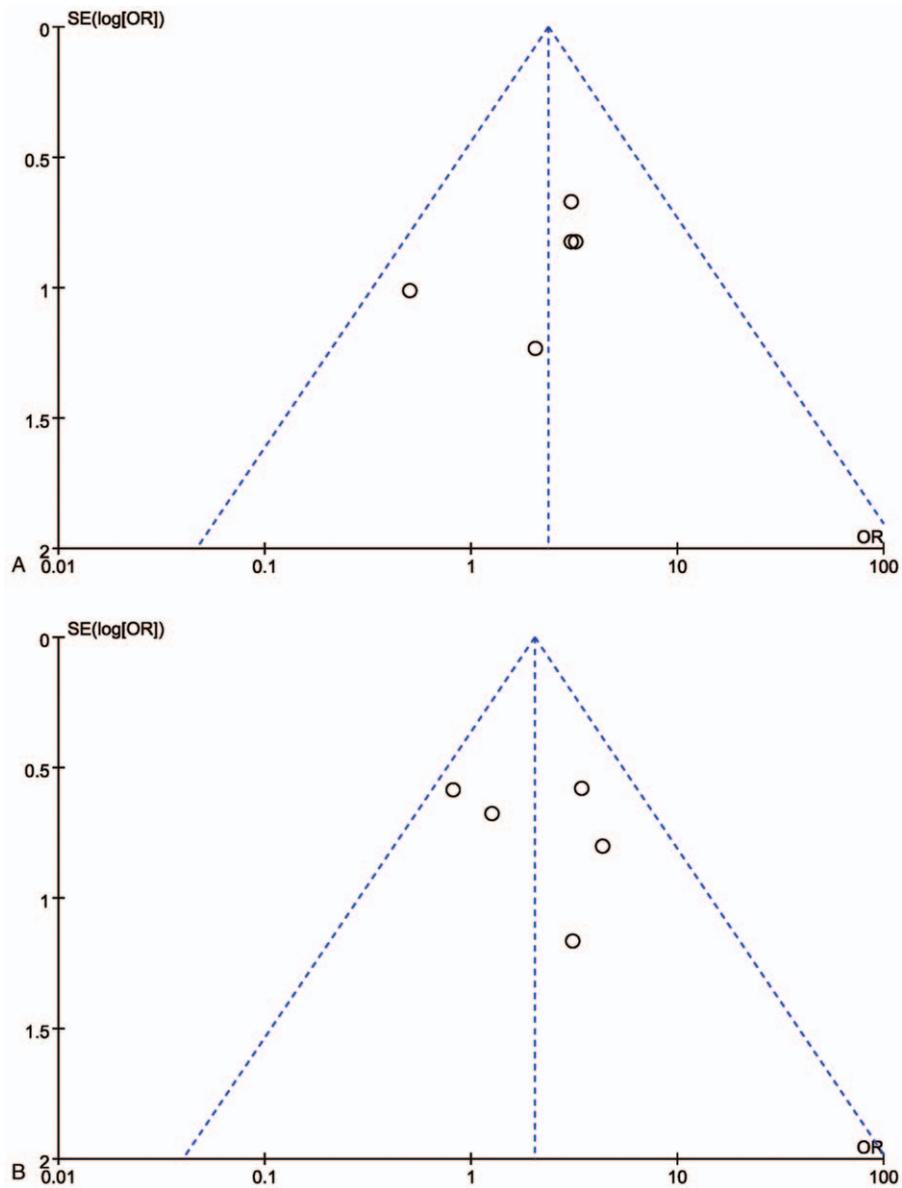
**Quality assessment of included studies for meta-analysis.**

Study	Selection	Comparability	Outcome
BVS EXAMINATION <sup>[16]</sup>	****	*	***
BVS STEMI FIRST <sup>[17]</sup>	****	*	***
Imori et al <sup>[18]</sup>	****	*	***

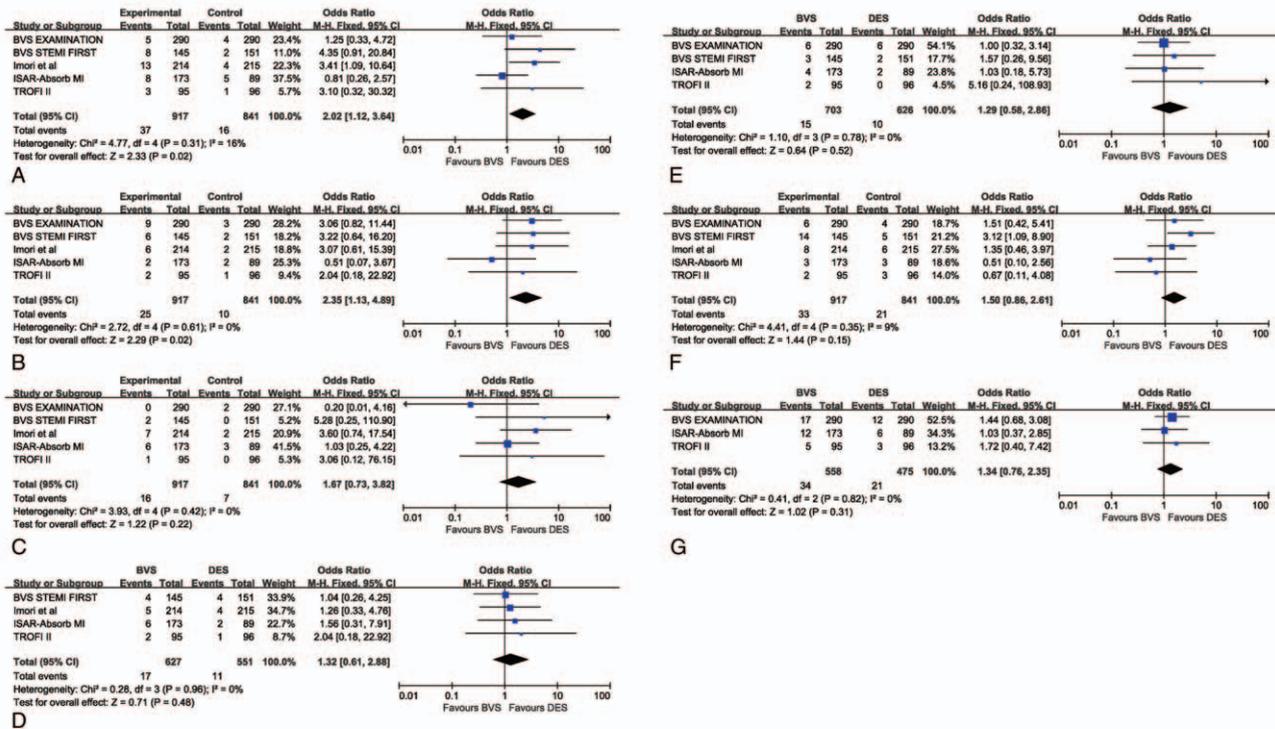
1. Quality assessment of the Observational studies, as per Newcastle Ottawa scale. Score of nine is maximum score (= lowest risk of bias)

Trial	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
ISAR-Absorb MI <sup>[14]</sup>	Low-risk	Low-risk	Low-risk	Low-risk	Low-risk	Low-risk
TROFI II <sup>[15]</sup>	Low-risk	Low-risk	Low-risk	Low-risk	Low-risk	Low-risk

2. Assessment of risk of bias for randomized controlled trials



**Figure 2.** Funnel plot analysis for definite ST/ScT (A), TLR (B). ST/ScT=stent/scaffold thrombosis, TLR=target lesion revascularization.



**Figure 3.** Forest plots for the clinical endpoint. TLR(A), definite ST/ScT(B), TLR after exclusion of events due to ST/ScT(C), all-cause death(D), cardiac death(E), target vessel myocardial infarction(F), target lesion failure(G). BVS=bioresorbable vascular scaffolds, DES=drug-eluting stents, ST/ScT=stent/scaffold thrombosis, TLR=target lesion revascularization.

**3.3. Clinical outcomes**

**3.3.1. TLR.** All studies<sup>[13–17]</sup> reported incidence of TLR. The rates of the TLR were higher with BVS compared with DES (4.0% vs 1.9%; OR = 2.20, 95% CI, 1.12–3.64; *P* = .02, Fig. 3A).

**3.3.2. Definite ST/ScT.** All studies<sup>[13–17]</sup> reported definite ST/ScT. Patients treated with BVS had a significantly higher risk of definite ST/ScT compared with those receiving DES (2.7% vs 1.1%; OR = 2.35, 95% CI: 1.13–4.89, *P* = .02, Fig. 3B).

**3.3.3. TLR after exclusion of events due to ST/ScT.** When TLR due to ST/ScT were excluded, the difference in risk estimates between BVS and DES was not significant (1.7% vs 0.8%; OR = 1.67, 95% CI: 0.73–3.82, *P* = .22, Fig. 3C).

**3.3.4. All-cause death.** Four studies<sup>[13,14,16,17]</sup> reported all-cause death. There was no significant difference between BVS and DES (2.7% vs 2.0% OR = 1.32 95% CI: 0.61–2.88, *P* = .48, Fig. 3D).

**3.3.5. Cardiac death.** Cardiac death was reported by 4 studies<sup>[13–16]</sup> included in the analysis and was similar in BVS and DES (2.1% vs 1.6% OR = 1.29, 95% CI: 0.58–2.86 *P* = .52, Fig. 3E).

**3.3.6. Target vessel myocardial infarction.** Five studies<sup>[13–17]</sup> reported incidence of target vessel myocardial infarction, and there was no difference between BVS and DES (3.6% vs 2.5% OR = 1.50, 95% CI: 0.86–2.61, *P* = .15, Fig. 3F).

**3.3.7. Target lesion failure.** Only 3 studies<sup>[13–15]</sup> reported target lesion failure. The risk of target lesion failure between the 2

groups was not significant (6.1% vs 4.4% OR = 1.34, 95% CI: 0.76–2.35, *P* = .31, Fig. 3G).

**4. Discussion**

Our meta-analysis had several main findings. First, compared with DES, BVS were associated with a higher incidence of TLR and ST/ScT. Second, when TLR due to device thrombosis were excluded, there were no statistically significant differences between the 2 groups, which indicated that ST/ScT was the key factor driving the inferior safety and effectiveness of BVS compared to DES. Third, risks for all-cause death, cardiac death, target vessel myocardial infarction, and target lesion failure were not statistically significantly different between BVS and DES.

**4.1. Causes of very late ST/ScT**

The mechanism of very late ST/ScT (> 1 year after stent implantation) remains unclear and may be related to factors such device characteristics (e.g., strut thickness, mechanical properties), the operator (e.g., the procedure and technique), and the lesion (e.g., vessel characteristics, especially the extent of calcification).<sup>[18]</sup> In addition, ostial lesions and decreased left ventricular ejection fraction may be associated with ST/ScT.<sup>[19]</sup>

The strut thickness of BVS and second-generation DES is about 150 μm and 80 μm respectively. Compared to DES, BVS had lower tensile strength and stiffness, limited elongation, lower mechanical strength, and lower ductility.<sup>[20]</sup> The increased crossing profile and limited mechanical properties of BVS required special technology to ensure their efficacy, namely a

PSP strategy (pre-dilatation, sizing, post-dilatation): proper lesion preparation, accurate vessel sizing, and mandatory high-pressure post-dilatation.<sup>[21]</sup> In a study by Puricel et al, the application of PSP implantation strategy reduced ST/ScT to 70% in 1 year.<sup>[22]</sup> Procedural disintegration of the polymeric scaffold struts may lead to stent discontinuity and subsequent ST/ScT if not adequately constrained by the neointima.<sup>[23]</sup> Also, BVS can cause an inflammatory reaction during polymer degradation which may also be one of the causes of very late ST/ScT.<sup>[24]</sup> BVS can theoretically reduce the time of DAPT, but the higher rate of ST/ScT after BVS implantation suggests the need to prolong DAPT. In the ABSORB II trial, 63 patients with DAPT lasting for 3 years had no late or very late ST/ScT.<sup>[5]</sup> Published reviews recommend that patients with BVS have DAPT for at least 12 months and that prasugrel or ticagrelor is superior to clopidogrel after BVS implantation.<sup>[25]</sup> Ongoing clinical trials, BVS LATE (ClinicalTrials.gov:NCT02939872) and SMART-CHOICE II (ClinicalTrials.gov: NCT03119012) may provide further clarity on the optimal DAPT time.

#### 4.2. Reducing the incidence of very late ST/ScT

The current view is that a combination of improved scaffolds with thinner struts and improved mechanical properties, coupled with a superior implant technique (ideally with intravascular imaging guidance), will be necessary to optimize the mid-term results with a BVS during its biosorption process so that their potential long-term advantages can emerge.<sup>[9]</sup> Improved mid-term results will allow their potential long-term advantages to become evident. The new generation of BVS includes thinner struts, coarse radial strength, shorter resorption time, and easier injection strategies, which can help overcome the shortcomings of first generation BVS.<sup>[26]</sup> The new generation of BVS has shown encouraging results in clinical trials. The 5-year data from DESolve Nx BVS showed 0% ST/ScT and 4.1% TLR, and DREAMS 2G BVS showed 0% ST/ScT and 3.4% TLR at the 24 month follow-up.<sup>[27]</sup>

#### 4.3. Acute coronary syndromes is an ideal scenario for BVS implantation

In acute coronary syndromes patients, some crucial points must be highlighted. First, culprit lesions are often located in the proximal segments of the coronary arterial tree, in which restoration of physiological vasomotion might have a greater effect.<sup>[28]</sup> Second, lesions are mostly soft plaques covered by a thin fibrous cap. After absorption of BVS, a thicker fibrous layer will be formed to cover the plaque surface, thus stabilizing the plaque.<sup>[29]</sup> Last, patients are usually young and have a long life expectancy, which allows them to benefit more from the lack of a permanent, rigid metal cage for the coronary arteries. In theory, strut resorption will help preserve the physiological integrity of coronary arteries, restore reactive vasomotion, and allow long-term positive vessel remodeling and further repeat revascularizations if needed.<sup>[30]</sup>

#### 4.4. The potential of BVS

BVS are an encouraging and revolutionary technology. Although there are still shortcomings at present, their broad applicability and significant clinical potential will likely make them an important topic in stent-related research for years to come.

#### 4.5. Limitations of this study

First, only 2 of the included studies were randomized controlled trials; thus, the partially available data investigating BVS suffer a risk of bias due to their observational nature. Second, the follow-up time of the studies was not uniform, which made the included study possible to select, implement and measure bias. In addition, a subgroup analysis was not performed in detail for different follow-up periods to clarify the comparison of outcomes over different durations. Third, this meta-analysis is based on aggregated data and shared the possible limitations of the original studies. Fourth, BVS was used for the first time by most of the investigators in these studies, and confounding effects of clinicians' learning curve have to be taken into account. Finally, only one type of BVS was evaluated in this study, and the results of this meta-analysis cannot be generalized to all types of BVS.

#### 5. Conclusions

At the mid-term follow-up, BVS had a higher risk of TLR and ST/ScT than the second-generation DES in patients with acute coronary syndromes. ST/ScT was the key differential outcome showing the decreased safety and effectiveness of BVS relative to DES. Larger clinical studies with a longer followup are required to better understand the safety and efficacy of BVS in acute coronary syndromes.

#### Author contributions

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