# Safety and Efficacy of Bioresorbable Scaffolds in Daily Practice: Experience from a Single Center in Taiwan

Tse-Hsuan Yang[1,2*], Guang-Yuan Mar[2*], Chin-Chang Cheng[1,2,3], Cheng-Chung Hung[2], Cheng-Hung Chiang[1,2,3], Feng-You Kuo[2], Tung-Chen Yeh[2], Hsiang-Chiang Hsiao[2], Tao-Yu Lee[2], Hsin-Li Liang[1], Wei-Chun Huang[1,2,3,4,5#], Chun-Peng Liu[1,2,3#]

[1]*Department of Critical Care Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan*
[2]*Cardiovascular Center, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan*
[3]*School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[4]*Department of Physical Therapy, Fooyin University, Kaohsiung, Taiwan*
[5]*Graduate Institute of Clinical Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*
[#]*Both corresponding authors contributed equally to this work*

## Abstract

**Introduction:** The bioresorbable material of the stent frame, capable of providing mechanical support and drug-delivery functions, has been developed in an attempt to improve long-term outcomes. However, publications about long-term outcomes of bioresorbable scaffolds (BRS) in Asia are still limited. This study is to investigate the long-term outcomes of bioresorbable scaffolds in a single tertiary medical center.

**Method:** Data regarding BRS placement in consecutive patients receiving percutaneous coronary intervention was collected from the cardiovascular center ofa single tertiary medical center from 2014 to 2017.

**Result:** A total of 138 cases were included during 3.5 years follow up. The mortality rate was 2.2%, whereby the cause of mortality in these 3 patients was not derived from coronary artery disease. One patient suffered acute myocardial infarction (0.7%). The rate of target lesion restenosis was 3.6% and that of target vessel restenosis was 2.9%.

**Conclusion:** This study demonstrated that BRS placement had low cardiac cause mortality and acute myocardial infarction at long-term follow up in a single tertiary medical center.

**Keywords:** acute myocardial infarction, bioresorbable scaffolds, coronary artery disease, percutaneous coronary intervention

## INTRODUCTION

Cardiovascular disease, especially ischemic heart disease, is one of the leading causes of mortality and morbidity worldwide. Catheterization intervention with metallic drug-eluting stent

**Address for correspondence:** Wei-Chun Huang, MD, Ph.D.; E-mail: wchuanglulu@gmail.com
Chun-Peng Liu, MD; E-mail: cpliu@vghks.gov.tw
Department of Critical Care Medicine Kaohsiung Veterans General Hospital; No. 386, Dazhong 1st Rd., Zuoying Dist., Kaohsiung City 813, Taiwan
Tel: +886-7-3468278; Fax: +886-7-3455045

placement for coronary artery stenosis is the mainstream treatment option in the modern era. Moreover, the second generation of metallic drug-eluting stent has already been proven safe and effective for coronary artery disease treatment.[1,2] However, the development of late adverse events with permanent metallic stents may be caused by persistent inflammation, loss of normal vessel curvature, impaired vasomotion, strut fracture, ongoing tissue growth within the stent frame, and neoatherosclerosis.[3] Consequently, fully bioresorbable material has been developed for the stent frame, capable of providing both mechanical support and drug-delivery functions, in an attempt to improve long-term outcomes.

The clinical randomized trial revealed everolimus-eluting bioresorbable scaffolds (BRS), as compared with everolimus-eluting cobalt-chromium stents (EES), were within the pre-specified margin for non-inferiority with respect to target-lesion failure at one year in patients with noncomplex obstructive coronary artery disease.[4] However, the following trial revealed a higher rate of device-oriented composite endpoint due to target vessel myocardial infarction, including peri-procedural myocardial infarction in the BRS group.[5] The ABSORB III study showed a 2.3 percent rate of thrombosis within BRS versus 0.7 percent within the EES at 3 years.[6] Furthermore, the meta-analysis study and other long-term follow-up clinical results revealed that compared with metallic EES, the currently approved BRS is associated with higher rates of major adverse cardiac events and BRS thrombosis, from the non-US ABSORB II, ABSORB Japan, ABSORB China studies and US-based ABSORB III study.[7] Those results have ledthe U.S. Food and Drug Administration (FDA) to issue a safety alert for the Absorb BRS due to an increased rate of major adverse cardiac events observed in patients receiving the device, and they have recommended the reference vessel diameter $\geq$ 2.5 mm and $\leq$ 3.75 mm, with longer dual antiplatelet therapy to be considered in small heart vessels patients.

In Taiwan, BRS has been approved since 2014. Currently, there has been no long-term follow-up trial providing information about the safety and efficacy of BRS practice in Taiwan. This study is to investigate the long-term safety and efficacy of BRS in daily practice in Taiwan.

## METHODS

### Data Source

A totalof 138 consecutive patients, who had received BRS placements, were enrolled from the cardiovascular center of a tertiary medical center in Taiwan from 2014 to 2017, and analyzed. All patients met the diagnosis criteria of coronary artery disease with more than 70% stenosis compared with the reference vessel on coronary angiography. This study, approved by the Human Research Committee, contains comprehensive medical records of patients, offering researchers detailed data.

### Study Population

Those who were admitted for coronary artery disease received complete basic laboratory, chest X-ray, and electrocardiography survey prior to percutaneous catheterization intervention. All patients were monitored at the hospitalfor at least 24 hours after the procedure.

### Outcome Analysis

All enrolled patients were followed until death or 28th February 2018. To measure the outcome, both out patient department and hospital admission medical records were checked. The medical charts of patients were reviewed by two independent physicians. Patients lost to follow-up, as recognized from medical chart reviews, were contacted by telephone. Furthermore, follow-up questionnaire, including medication compliance, complications, and mortalities, was performed.

### Statistical Analyses

Categorical data were reported as percentages and evaluated by the Chi-square test. Continuous variables were reported as the mean

and standard deviation (SD) and compared by paired t-test. The Kaplan–Meier method was used to estimate cumulative survival. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC).

## RESULT

### Descriptive Characteristics

A total of 138 patients with coronary artery disease receiving BRS were enrolled in this study. The clinical characteristics are displayed in Table 1. Most patients were male (N = 127; 92.%) and the average age was 58.7 ± 12.1 years old. Average body height and body weight was 167.4 ± 7.1 cm and 73.2 ± 10.5 kg, and body mass index was 26.1 ± 3.3 kg/m$^2$. Of the patients, 60.1% had hypertension (N = 83), 35.5% had diabetes mellitus (N = 49), 39.1% had dyslipidemia (N = 54), 11.6% had previous myocardial infarction (N = 16) and 55.8% had a family history of coronary artery disease (N = 77). Fifty patients (36.2%) were cigarette smokers (Table 1).

Laboratory data showed hemoglobin at 14.0 ± 1.5 g/dL, glycated hemoglobin (HbA1c) at 6.6 ± 1.5%, blood sugar at 138.4 ± 64.2 mg/dL, creatinine at 1.1 ± 0.4 mg/dL, low-density lipoprotein-cholesterol (LDL-C) at 94.7 ± 28.9 mg/dL and high-density lipoprotein (HDL-C) at 41.7 ± 12.0 mg/dL (Table 1). The percentage of antiplatelet therapy is shown in Table 1, including aspirin (97.8%), clopidogrel (55.0%) and ticagrelor (43.4%). In these patients, the average duration of antiplatelet therapy use was 566.6 ± 370.4 days for aspirin, 351.96 ± 311.78 days for clopidogrel and 513 ± 330.16 days for ticagrelor (Table 1).

### Angiographic and Procedure Characteristics

Regarding lesion characteristics on coronary angiography, there were 20.3% type A lesions (N = 28), 32.6% type B1 lesions (N = 45), 26.1% type B2 lesionsand 21.0% type C lesions (N = 29). The Syntax score was 13.0 ± 7.8. Furthermore, chronic total occlusion lesions accounted for 10.9% of

**Table 1.** Baseline Characteristicsof Patients Who Received Bioresorbable Scaffolds

| Characteristics | N = 138 |
|---|---|
| Gender (Male ratio) | N = 127 (92.0%) |
| Age (years) | 58.7 ± 12.1 |
| Body mass index; BMI (kg/m$^2$) | 26.1 ± 3.3 |
| Height (cm) | 167.4 ± 7.2 |
| Weight (kg) | 73.2 ± 10.5 |
| Comorbidities | |
| Hypertension | N = 83 (60.1%) |
| Diabetes Mellitus | N = 49 (35.5%) |
| Dyslipidemia | N = 54 (39.1%) |
| Family History of coronary artery disease | N = 77 (55.8%) |
| Previous myocardial infarction | N = 16 (11.6%) |
| Previous ischemia stroke | N = 0 (0.0%) |
| Peripheral artery disease | N = 1 (0.7%) |
| Coronary artery bypass grafting | N = 3 (2.2%) |
| End stage renal disease | N = 0 (0.0%) |
| Heart failure | N = 1 (0.7%) |
| Cigarette smoking | N = 50 (36.2%) |
| Lab Data | |
| Hemoglobin (g/dL) | 14.0 ± 1.5 |
| Creatinine (mg/dL) | 1.1 ± 0.4 |
| Hemoglobin A1c; HbA1C (%) | 6.6 ± 1.5 |
| Blood sugar (mg/dL) | 138.4 ± 64.2 |
| Glutamate pyruvate transaminase (U/L) | 35.2 ± 26.7 |
| Cholesterol (mg/dL) | 165.0 ± 41.5 |
| High-density lipoprotein; HDL (mg/dL) | 41.7 ± 12.0 |
| Low-density lipoprotein; LDL (mg/dL) | 94.7 ± 28.9 |
| Triglyceride (mg/dL) | 140.1 ± 96.9 |
| Antiplatelet therapy | |
| Aspirin (Percentage) | N = 135 (97.8%) |
| Average duration (days) | 566.57 ± 370.43 |
| Clopidgrel (Percentage) | N = 76 (55.0%) |
| Average duration (days) | 351.96 ± 311.78 |
| Ticagrelor (Percentage) | N = 60 (43.4%) |
| Average duration (days) | 513.00 ± 330.16 |

lesions; 12.3% of patients had ostial lesions (N = 17), 25.4% had bifurcation lesions (N = 35) and only 2 lesions were left main bifurcation lesions (Table 2).

In the study, a total of 209 bioresorbable scaffolds were deployed. The frequency of BRS sizes was 18.2% for 2.5 mm (N = 72), 47.4% for 3.00 mm (N = 72) and 34.4% for 3.5 mm (N = 72). The frequency of BRS lengths was 3.8% for 12 mm (N = 8), 20.1% for 18 mm (N = 42), 29.7% for 23 mm (N = 62) and 46.4% for 28 mm (N = 97) (Table 2). During the percutaneous catheter intervention procedure, 94.7% of patients received balloon post-dilatation after BRS implantation and 60.1% of patients received intravascular image guide, including optical coherence tomography (N = 55, 39.9%) and intravascular ultrasound (N = 28, 20.3%) (Table 2).

**Table 2.** Angiographic and Procedure Characteristics

| Coronary Angiography Findings (N=138) | |
|---|---|
| Lesion type | |
| A | N= 28 (20.3%) |
| B1 | N= 45 (32.6%) |
| B2 | N= 36 (26.1%) |
| C | N= 29 (21.0%) |
| Left mainbifurcation lesion | N= 2 (1.4%) |
| Ostial lesion | N= 17 (12.3%) |
| Bifurcation lesion | N= 35 (25.4%) |
| Chronic total occlusion | N= 15 (10.9%) |
| Syntax score | 13.0 ± 7.8 |
| **Bioresorbable Scaffolds (N=209)** | |
| BRS size (mm) | |
| 2.50 | N= 38 (18.2%) |
| 3.00 | N= 99 (47.4%) |
| 3.50 | N= 72 (34.4%) |
| BRS length (mm) | |
| 12 | N= 8 (3.8%) |
| 18 | N= 42 (20.1%) |
| 23 | N= 62 (29.7%) |
| 28 | N= 97 (46.4%) |
| Post-BRS balloon dilatation | N=198 (94.7%) |
| Intravascular image guide | N=83 (60.1%) |
| Optical Coherence Tomography (OCT) | N=55 (39.9%) |
| Intravascular ultrasound (IVUS) | N=28 (20.3%) |

BRS = bioresorbable scaffolds

### OutcomeAnalysis

A total of 138 cases were included during the 3.5 years follow-up. The mortality rate was 2.2% (N = 3) (Figure 1), whereby the cause of mortality in these 3 patients was not derived from coronary artery disease. One patient suffered acute myocardial infarction (0.7%) (Figure 2). The rate of target lesion restenosis was 3.6% (N = 5) (Figure 3) and the rate of target vessel restenosis was 2.9% (N = 4) (Figure 4).

## DISCUSSION

This study is the first study to show the long-term safety and efficacy of BRS in daily practice in Taiwan. In 3.5 years follow-up, there were few major adverse cardiac events, including cardiovascular death, myocardial infarction, target lesion restenosis, and target vessel restenosis.

BRS was developed to dissolve fully within patients' vessels, and within three years of implantation, with the intent of bypassing any negative side effects sustained from a metal stent. In the ABSORB III randomized trial, the Absorb BRS proved noninferior to the Xience device with regard to the occurrence of target lesion failure (TLF), target vessel myocardial infarction (TVMI) and ischemia-driven target lesion revascularization (TLR). The U.S. Food and Drug Administration approved Abbott's BRS device upon the release of these positive results, but recent reports from the Absorb III trials[6] have suggested increased instances of thrombosis and MI directly related to the dismantling process of the bioresorbable vascular scaffold. Around 2,000 cardiac patients took part in the ABSORB III study, all of whom were undergoing PCI. The Absorb BRS was deemed noninferior to the Xience stent for the study's primary endpoint of

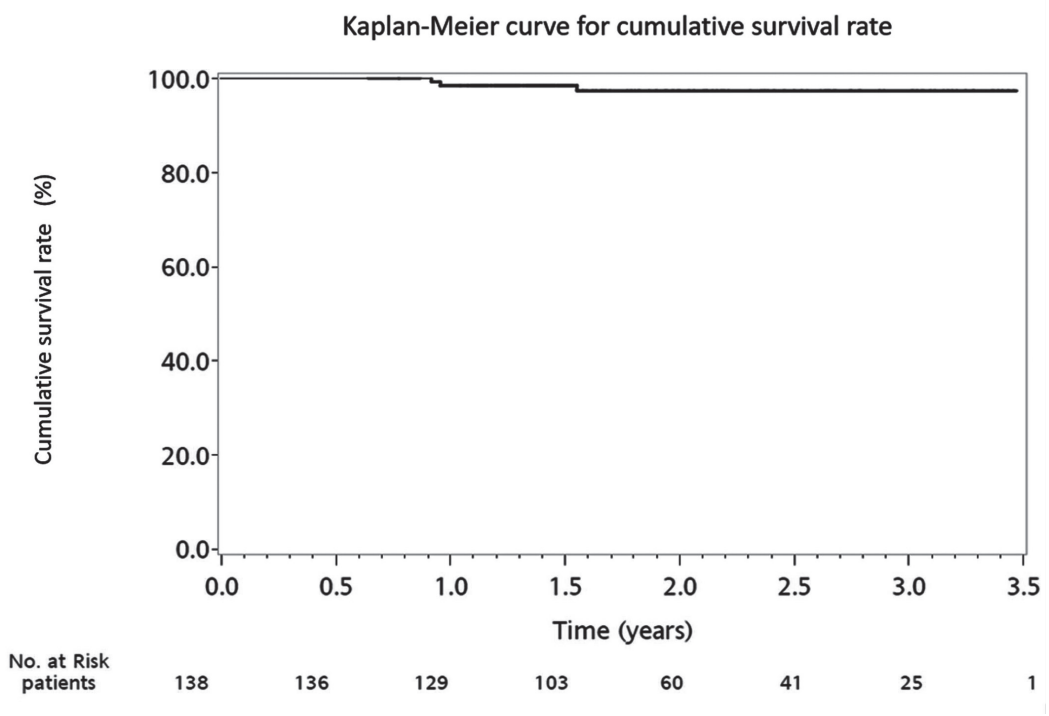


**Figure 1.** Kaplan-Meier curve forcumulative survival rate for patients after bioresorbable scaffolds (BRS) implantation.

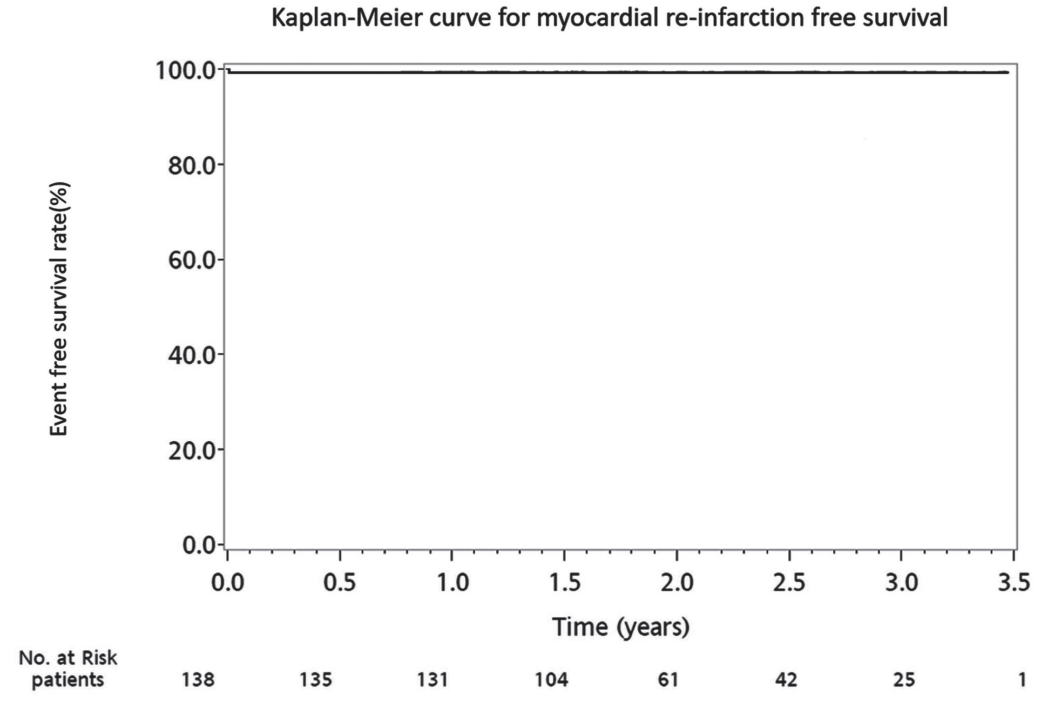


**Figure 2.** Kaplan-Meier curve for myocardial re-infarction free survival rate for patients after bioresorbable scaffolds (BRS) implantation.

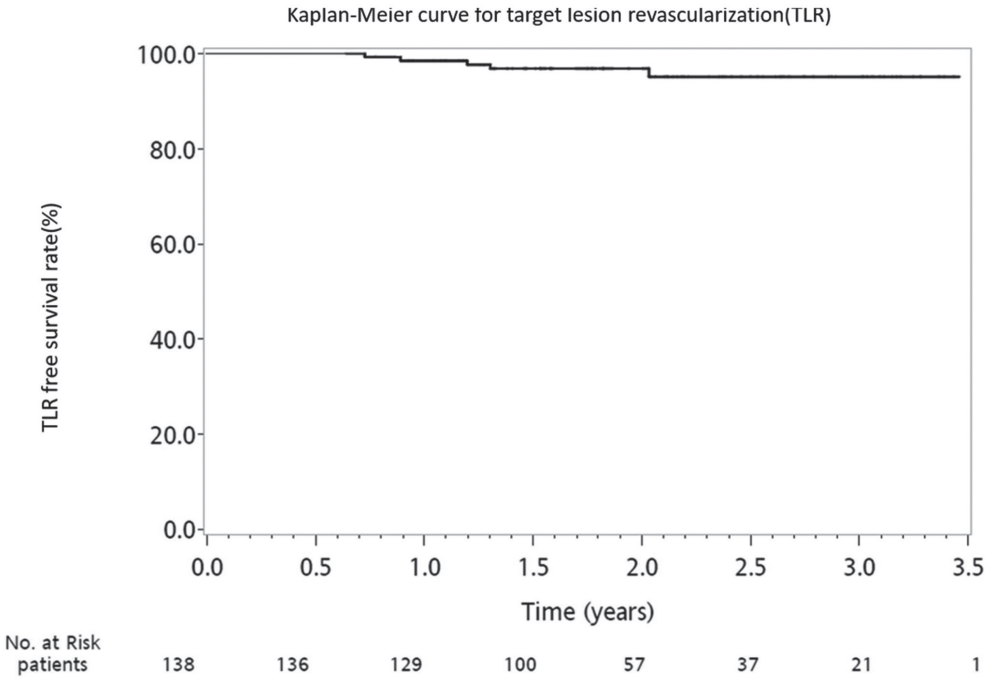


**Figure 3.** Kaplan-Meier curve for target lesion revascularization (TLR) free survival rate for patients after bioresorbable scaffolds (BRS) implantation.

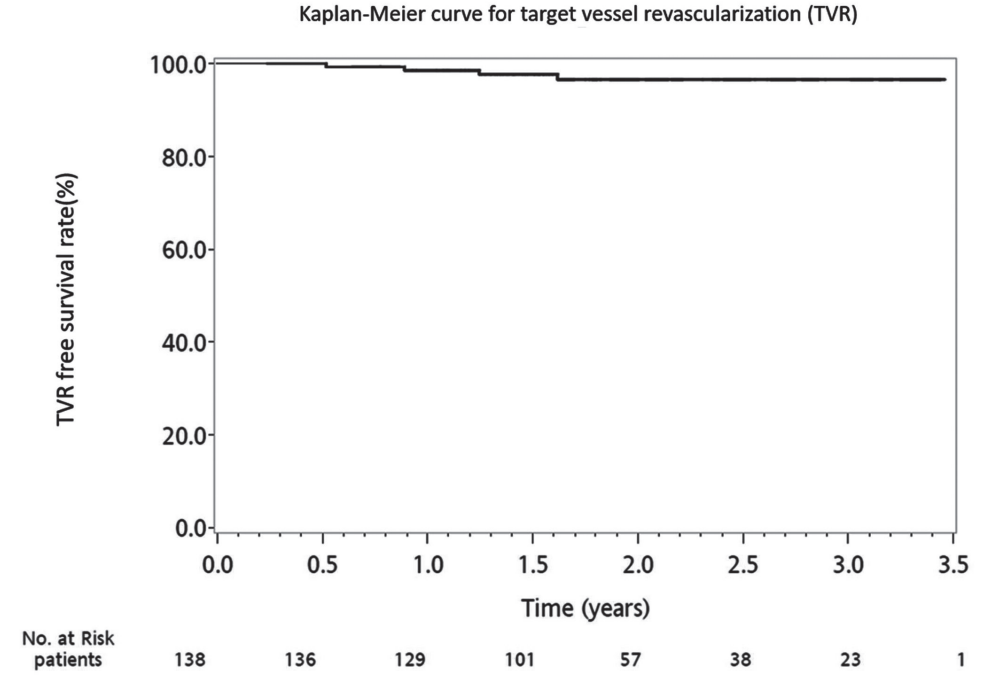


**Figure 4.** Kaplan-Meier curve for target vessel revascularization (TVR) free survival rate for patients after bioresorbable scaffolds (BRS) implantation.

one-year target lesion failure (TLF), recording a risk difference of just 1.7 percent between the two devices. Device thrombosis was recorded in 1.5 percent of BRS patients and 0.7 percent of EES patients after those first 12 months. Three years into the study results varied more widely—the device-oriented primary endpoint was observed in 13.4 percent of BRS subjects compared to 10.4 percent of EES patients. Between one and three years after treatment, TLF occurred in 7 percent and 6 percent of all BRS and EES patients, respectively. BRS patients also recorded higher rates of target vessel failure, death, myocardial infarction, TVMI, and revascularization. Factors like a prior cardiovascular intervention, diabetes, and vessel size were all found to be independent predictors of adverse outcomes in BRS-treated patients. Scaffold thrombosis events seemed to be clustered in very small vessels prior to the one-year treatment mark, the researchers wrote, while between one and three years thrombosis presented itself mainly invessels more appropriately sized for the scaffold device.

To our knowledge, late thromboembolism events were most related to multifactorial origins, including the patient, antithrombotics, procedural issues, the lesion and the device.[9,10] Attention to technical details may also improve results when percutaneous catheter intervention (PCI) is performed with BRS. Because both the number of stents and the stent length enhance the risk of thromboembolism events, refraining from excessive overall stent length and from stent overlap is judicious. Moreover, proper deployment of the BRS should be ensured, with care taken to fully expand it over its entire length, particularly incalcified lesions, and residual dissections should be avoided as when deploying drug-eluting stents (DES). Among patients with these larger vessels, the TLF rate was 9.4% among the Absorb-treated patients and 7.0% among the Xience-treated patients, a difference that was not statistically significant (HR 1.35; 95% CI 0.93-1.96).[6] Similarly, in those with an RVD ≥ 2.25 mm, the 2-year rate of definite/probable ST was 1.3% and 0.6% in the Absorb- and Xience-treated patients, respectively. Again, this difference was not statistically significant. An additional analysis of the data showed that when physicians followed the PSP protocol (predilatation, appropriate sizing, and post-dilatation), the rates of TLF and ST in the Absorb BRS arm were much closer to rates observed with the Xience stent.

In this study, we did not notice any remarkable recurrent stent thromboembolism events during 3.5 years follow-up. The main reasons for the lack of major cardiac events in this study might be that most BRS used i more than 3.00 mm in size with optimal technique by post-stent balloon dilatation. Moreover, intravascular images were used in more than half the cases to assess the proper reference lumen size, lesion type, and length. Appropriate use of intravascular images increases the accuracy of chosenstent size and length. Dual antiplatelet therapy (DAPT) in all cases continued for at least one year after the procedure. All of the above might explain why there were relatively few major cardiac eventsin this study.

However, there are some limitations to this study. First, the sample size is small, and second, there is no control group in this study. Further comprehensive, prospective, randomized control trials should be under taken in Taiwan.

## CONCLUSION

This study demonstrates that BRS implantation has low cardiac-cause mortality and acute myocardial infarction at long-term follow-up in a single tertiary medical center, which might be explained by relatively larger size of BRS, optimization of post-stent balloon dilatation, use of intravascular image and at least one-year dual-antiplatelet therapy.

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## LIST OF ABBREVIATIONS

ACS = Acute coronary syndrome
AMI = Acute myocardial infarction
BRS = Bioresorbable vascular scaffold
CABG = Coronary artery bypass grafting
CAD = Coronary artery disease
CTO = Chronic total occlusion
DM = Diabetes mellitus
ESRD = End-stage renal disease
HF = Heart failure
IVUS = Intravascular ultrasound
OCT = Optical Coherence Tomography
PCI = Percutaneous coronary intervention.
PAD = Peripheral artery disease
SD = Standard deviation
TLR = Target lesion revascularization
TVR = Target vessel revascularization

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