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Coronary bifurcation lesion treatment with the BioMime™ Branch sirolimus-eluting coronary side-branch stent system: A single-center experience

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ABSTRACT

Background: Coronary bifurcation lesions (CBL) comprise 15 %–20 % of percutaneous coronary procedures and remain a challenge despite advances in stent and interventional techniques. The BioMime™ Branch sirolimus-eluting coronary side-branch stent (BBSES) is specifically designed for CBL treatment in conjunction with a standard drug-eluting stent (DES). We report the first single-center experience of treating complex CBL with the novel BBSES.

Methods: This is a retrospective, single-center study involving consecutive prospectively identified patients who underwent treatment of true CBL with the BBSES. The protocol included BBSES + DES implantation in the CBL and simultaneous final kissing balloon inflation.

Results: Fifty-eight CBL were treated in 58 consecutive patients (89.6 % men, mean age 69.0 ± 9.5 years) presenting primarily with stable angina (84.4 %) and true (Medina 1,1,1,) CBL. Procedural success was 100 % without major adverse cardiac events (MACE). At a median follow-up of 18 months, one sudden death was reported that was accounted as possible late stent thrombosis. One patient had spontaneous myocardial infarction due to subacute thrombosis of a DES implanted in the main vessel proximally to the BBSES before the index procedure. Another patient was hospitalized for atrial fibrillation.

Conclusions: This is the first clinical experience to date of true CBL treatment with the BBSES demonstrating high procedural success, no in-hospital MACE and sustained clinical results at a median follow-up of 18 months.

1. Introduction

Coronary bifurcation lesions (CBL) comprise 15 %–20 % of all cases of percutaneous coronary intervention (PCI) [1]. A CBL is defined as a stenosis of a major epicardial coronary artery adjacent to and/or including the origin of a significant side branch (SB) [2]. A SB is considered significant if its narrowing or acute occlusion before or during PCI can cause considerable ischemia or acute myocardial infarction (AMI), which can lead to major adverse cardiac events (MACE) [1]. Anatomically, a CBL comprises three different vessel segments, namely, proximal main vessel (PMV), distal main vessel (DMV), and SB [2]. Various angiographic classifications of CBL have been proposed, of which the Medina classification is most commonly followed [3]. The Medina classification describes CBL as "true" and "non-true" CBL. This is based on the presence (graded as "1") or absence (graded as "0") of significant stenosis (diameter stenosis [DS] ≥50 %) in the PMV, DMV, and SB [1]. While true CBL is an independent predictor of SB occlusion during PCI [4], the complexity of performing PCI on a CBL depends on multiple conditions including clinical, angiographic and procedural factors [5]. Treating CBL remains a challenge despite several advances in stents and interventional techniques in recent decades and no strategy has been universally accepted as superior over the others [6]. PCI of a CBL can lead to high rates of periprocedural myocardial injury (PMI), and SB occlusion after main vessel (MV) stenting is one of the most important events causing AMI.

The CBL stenting techniques recommended by the European Bifurcation Club (EBC) are one-stent techniques, including provisional stenting technique (PST) and inverted PST, or two-stent techniques (elective, or bailout in PST). Two-stent techniques could be T or T and protrusion (TAP) stenting, culotte or inverted culotte stenting, and double kissing (DK) crush [1]. The PST consists in implanting a single MV stent only. The wired SB is not treated or is treated with balloon inflation or placing a stent if needed [7]. Despite favorable results of the two-stent techniques in recent studies and meta-analyses, the guidelines continue to recommend PST as the default strategy for complex CBL, while the DK-crush technique has a class IIb recommendation over the PST in true CBL of the left main coronary artery (LMCA) bifurcation [7–10]. Most guideline

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Abbreviations

ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
BBSES	BioMime™ Branch sirolimus-eluting coronary side-branch stent
CBL	Coronary bifurcation lesions
CTA	Computed tomography angiography
DAPT	Dual antiplatelet therapy
DES	Drug-eluting stent
DK	Double kissing
DMV	Distal main vessel
DS	Diameter stenosis
EACTS	European Association for Cardio-Thoracic Surgery
EBC	European Bifurcation Club
ESC	European Society of Cardiology
FKBI	Final kissing balloon inflation
ISR	In-stent restenosis
LMCA	Left main coronary artery
MACE	Major adverse cardiac events
MI	Myocardial infarction
MV	Main vessel
PCI	Percutaneous coronary intervention
PLGA	Poly (lactic-co-glycolic acid)
PLLA	Poly (L-lactide acid)
PMI	Periprocedural myocardial injury
PMV	Proximal main vessel
PST	Provisional stenting technique
QCA	Quantitative coronary angiography
SB	Side branch
SD	Standard deviation
ST	Stent thrombosis
TAP	T and protrusion stenting
TLF	Target lesion failure
TLR	Target lesion revascularization
TVMI	Target vessel myocardial infarction
TVR	Target vessel revascularization
URL	Upper reference limit

recommendations are based on studies in which bare-metal stents or first-generation drug-eluting stents (DES) were used in CBL [11]. However, the EBC 15th consensus statement released in 2021 states that in more complex CBL, especially those involving the LMCA, dedicated two-stent techniques should be considered. Moreover, it declares that CBL with extensive atherosclerosis involving a large and significantly diseased SB might benefit from an elective two-stent technique [12]. The recent DEFINITION II trial showed that a two-stent strategy was superior to PST, with a reduction in target lesion failure (TLF) at 12 months, mainly due to lower rates of target vessel myocardial infarction (TVMI) and target lesion revascularization (TLR) [13]. Further, there was a numerical reduction in definite/probable stent thrombosis (ST) with the two-stent technique compared to PST. Similarly, a recent systematic review and network meta-analysis including 26 randomised controlled trials and a total of 7257 patients demonstrated that the two-stent approach, especially DK crush, improved significantly the clinical outcomes in patients with complex CBL [14].

The new-generation BioMime™ Branch sirolimus-eluting coronary side-branch stent (BBSES) system (Meril Life Sciences Pvt. Ltd, India) is specifically designed for the treatment of CBL with a two-stent approach. It provides optimal MV and SB scaffolding and coverage, limits multiple layering of stent struts at the carina, and may save overall procedural time compared to CBL stenting using multiple DES and complex techniques [15]. We report the first single-center experience of true CBL treatment with the novel BBSES.

2. Materials and methods

2.1. Study design and population

This was a retrospective, single-center study involving consecutive patients who underwent CBL treatment between September 2020 and December 2021. The study was approved by the Institutional Ethics Committee and conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from all patients. The key inclusion criteria were: 1) age > 18 years, 2) maximum of one *de novo* true CBL with >50 % diameter stenosis in the MV and SB (Medina class 1,1,1/1,0,1/0,1,1), as assessed by visual angiography and confirmed by offline quantitative coronary angiography (QCA), 3) successful treatment of other epicardial vessel lesions prior to the index procedure for CBL, 4) diameter of the target lesion reference vessel between 2.5 and 4.0 mm in the MV and > 2.5 mm in the SB, 5) negative pregnancy test within 7 days before the procedure for females. The exclusion criteria were: 1) life expectancy <1 year, 2) AMI within one week before the index procedure 3) target lesion with thrombus, 4) severely calcified lesion 5) need for rotational atherectomy, 6) excessive tortuosity in the vessel not suitable for balloon dilatation and stent delivery, 7) left ventricular ejection fraction <30 %, 8) history of PCI of the target lesion, 9) known hypersensitivity or allergies to everolimus, sirolimus, Poly (L-lactide acid) (PLLA), Poly (lactic-*co*-glycolic acid) (PLGA), cobalt, chromium, nickel, tungsten, acrylic and fluoropolymers or contrast sensitivity that cannot be adequately suppressed with premedication, 10) history of bleeding diathesis or coagulopathy, 11) history of organ transplant or ongoing immunosuppressant therapy, 12) ongoing pregnancy or lactation, 13) planning conception within two years following the index procedure, 14) any other medical illness such as cancer or congestive heart failure, renal insufficiency, cerebrovascular accident or transient ischemic attack within the last 6 months, 15) known history of substance abuse (alcohol, cocaine, heroin etc.), 16) elective surgery planned within 1 year after the index procedure that might require discontinuation of dual antiplatelet therapy (DAPT).

2.2. Study device

The BBSES is a sirolimus-eluting coronary balloon-expandable stent with an ultra-thin (65-μm strut thickness) L605 cobalt-chromium alloy platform (Fig. 1). The BBSES coating consists of a blend of antiproliferative sirolimus drug and biocompatible, biodegradable PLLA and PLGA *co*-polymers, which act as drug reservoirs and drug-releasing platforms [15]. The BBSES has a unique hybrid design featuring a PMV anchoring segment and a distal tapered SB segment. The two segments are joined through an advanced “Flexi Connector Technology” for continuous access and protection of the SB (Fig. 1). The MV and SB segments are crimped on a stepped delivery balloon that has four markers. In addition to standard proximal and distal markers delineating the stent edges, there are two additional markers delineating the L2 zone that are used to precisely position the proximal edge of the SB segment at the SB ostium. The BBSES is available with different lengths and diameters (Fig. 1) to accommodate the mismatch between MV and SB size and the length of the SB lesion. The design offers ease of implantation (no need for rotational orientation, no risk of wire wrapping, no bifurcation angle limitation) and MV integration with a standard DES. The MV and SB segments are deployed in a single step, reducing the overall procedural time and complexity of using multiple hardware. After BBSES deployment, the MV can be stented as in regular stenting procedures.

2.3. Study endpoints

The primary study endpoint was procedural success defined as angiographic success without in-hospital MACE (composite endpoint of cardiac

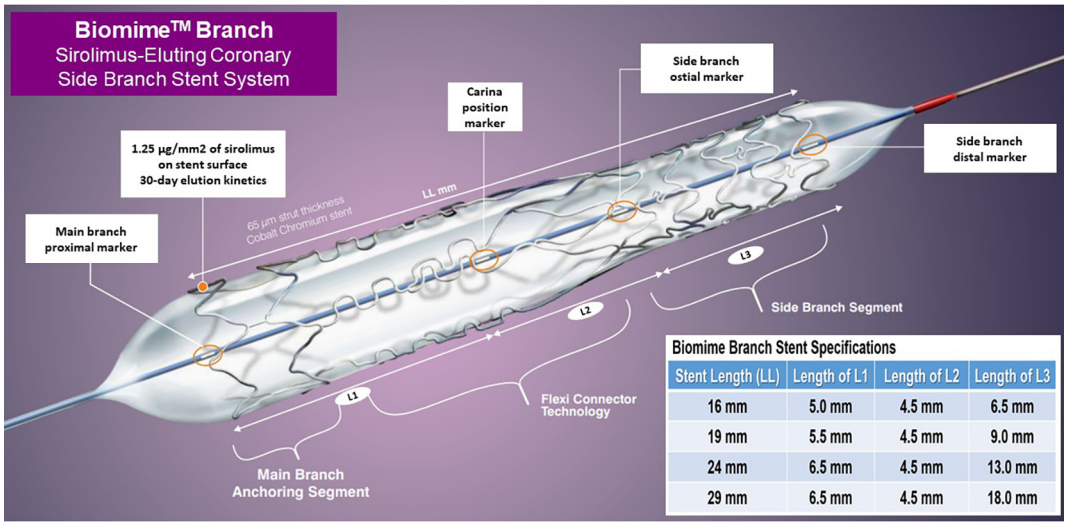

Fig. 1. The BioMime™ Branch sirolimus-eluting coronary side-branch stent (BBSES) system. BBSES is made of cobalt chromium, has ultra-thin (65-µm) strut thickness and is coated with sirolimus-eluting biodegradable and biocompatible (Poly [L-lactide] and Poly [lactic-*co*-glycolic acid]) polymers. The BBSES has a proximal main branch-anchoring segment and a distal tapered side branch segment. The two segments are joined through an advanced "Flexi Connector Technology" for continuous access and protection of the side branch. The main branch and side branch segments are crimped on a stepped balloon that has four markers. In addition to standard proximal and distal markers delineating the stent edges, there are two additional markers delineating the L2 zone that are used to precisely positioning the proximal edge of the side branch segment at the side branch ostium. After BBSES deployment, the main branch segment can be stented with a standard drug-eluting stents using a regular stenting procedure.

death, AMI, coronary artery bypass graft surgery, or TLR). The diagnosis of PMI was made according to the fourth universal definition of myocardial infarction (MI) [16]. The secondary endpoint was event-free survival at a median 18-month clinical follow-up.

2.4. Procedure

All procedures were performed via a 6Fr guiding catheter with a radial approach. The MV and SB were wired (Fig. 2A) and both vessels were predilated. The BBSES, whose diameter and length were chosen according to MV and SB size and SB lesion length, was then positioned in the SB with the central markers of the L2 segment straddling the SB ostium, deployed (Fig. 2B) and post-dilated (Fig. 2C). After BBSES deployment, the stent delivery balloon was retrieved. Unlike standard culotte stenting, at this stage of the procedure proximal optimization technique is not required because the BBSES design facilitates easier wire exchange, offering the advantage of reduced procedural time. Therefore, after BBSES deployment, the SB guidewire was guided through the L2 segment into the DMV (Fig. 2D),

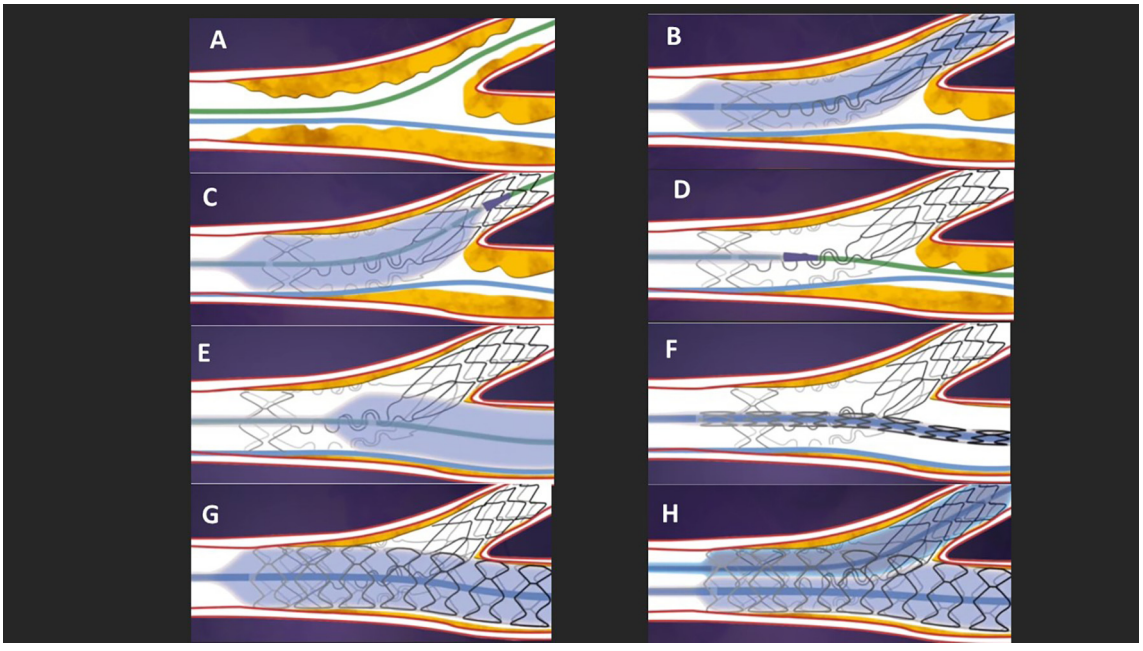

Fig. 2. Deployment technique of the BioMime™ Branch sirolimus-eluting coronary side-branch stent (BBSES). The side branch and main vessel lesions are pre-dilated leaving the guidewires in both vessels (A). The BBSES is then deployed with the two central markers straddling the side branch origin (B), after which the stent delivery system is removed and the distal branch segment is post-dilated (C). The guidewire initially placed in the side branch is repositioned in the distal main vessel (D) and the L2 segment of the BBSES is dilated (E). A standard drug-eluting stent is then tracked through the proximal main branch segment into the distal main vessel (F), the guidewire initially placed in the main vessel is withdrawn, the stent is deployed (G) and the delivery balloon is removed. The side branch is reaccessed, after which a simultaneous kissing balloon inflation is performed (H).

and the L2 segment was dilated (Fig. 2E). A standard DES was then positioned with the proximal end inside the proximal region of the BBSES and the distal segment passing through the L2 segment (Fig. 2F) and deployed (Fig. 2G). After DES deployment in the MV, the SB was recrossed to allow simultaneous final kissing balloon inflation (FKBI) (Fig. 2H) using minimal overlap of a short non-compliant balloon of a size equivalent to the SB diameter and another short non-compliant balloon of a size equivalent to the MV diameter inserted into the MV. The length of the balloons was chosen to prevent inflation outside the PMV stent and the disease-free region of the SB and to kiss in the CBL polygon of confluence to limit the risk of PMV stent distortion. Final proximal optimization technique was finally performed in the MV using a short non-compliant balloon, according to PMV diameter. After the procedure, all patients were prescribed DAPT for 6 months as per standard guidelines [17].

2.5. Follow-up

Follow-up data were collected using hospital records and telephone interviews.

2.6. Statistical analysis

For continuous data, the descriptive statistics are presented as the number of observations, mean, standard deviation (SD), median, minimum, and maximum values. The frequency data are represented as numbers (n) and percentages (%). A P value <0.05 was considered significant. All statistical analyses were performed using SPSS software package version 25. All MACE were reported.

3. Results

After a comprehensive screening process, 58 eligible consecutive patients were included in the study. The mean age was 69.0 ± 9.5 and 89.6 % were males. The baseline characteristics of the patients are shown in Table 1. Nine patients presented with acute coronary syndrome (ACS) while 49 patients had chronic coronary syndrome at presentation. All patients had true CBL (1,1,1 according to Medina classification). The lesions were located in the LMCA-left circumflex coronary artery in one (2 %) case, left anterior descending coronary artery-diagonal branch in 44 (77.5 %) cases, left circumflex coronary artery-obtuse marginal branch in 10 (16.5 %) cases and right coronary artery-posterior descending artery in 3 (4 %) cases. The mean stenosis was 72.3 ± 3.8 % and 75.1 ± 4.1 % in the MV and SB, respectively. In all cases, successful stent implantation and FKBI in the SB and MV were performed with satisfactory stent expansion. Post-implantation, quantitative coronary angiography (QCA) showed that the percentage stenosis in the MV was reduced to 5 % and that in the SB stenosis to 8 %. A stand-alone rise of high-sensitive troponin above the 99th percentile upper reference limit (URL) was noted in 4 (6.8 %) patients qualifying as a PMI without clinical sequelae [16].

Follow-up data were available for all the 58 patients enrolled in the study. At a median follow-up of 18 months, one sudden death occurred at 11 months and was considered as a possible late ST and one patient had a spontaneous MI due to subacute ST of a DES that was implanted before the index procedure in the MV proximally to the BBSES. During an urgent PCI, performed 2 days after the index procedure, the operator used IVUS to assess the cause of ST. This showed a non completely apposed stent that was fully expanded. The patient did well without any additional event. Another patient was re-hospitalized for atrial fibrillation (Table 2).

3.1. Clinical case example

An 80-year-old man presented with recent onset exertional angina (Canadian Cardiovascular Society Angina Grade II). He had no history of cardiovascular disease. Computed tomography angiography (CTA) revealed a true CBL of the left anterior descending coronary artery-first diagonal branch (Medina 1,1,1) (Fig. 3A). A BBSES (24 mm in lenght) was implanted in the SB followed by DES (Xience Sierra 3.0 × 23 mm, Abbott Vascular, CA, USA) delivery and implantation in the MV (Fig. 3) and FKBI was performed. Post-procedure intravascular ultrasound revealed complete coverage of the SB ostium with full stent expansion and a large final area at the carina site (Fig. 4). No in-hospital event was observed, and the patient was discharged in healthy condition on DAPT. At 8 months, CTA showed patent MV and SB stents without any image of significant neointimal proliferation.

Table 1
Baseline characteristics.

Baseline characteristics	Value
No. of patients, n	58
Male, n (%)	52 (89.6)
Age, years (mean ± SD)	69.0 ± 9.5
Risk Factors	
Obesity, n (%)	9 (15.5)
Hypertension, n (%)	43 (74.1)
Hypercholesterolemia, n (%)	44 (75.8)
Smoking, n (%)	29 (50)
Family history of CVD, n (%)	17 (29.3)
Diabetes mellitus, n (%)	16 (27.5)
History of CAD, n (%)	18 (31)
Prior MI, n (%)	9 (15.5)
Prior CABG, n (%)	1 (1.7)
Prior PCI, n (%)	22 (37.9)
LVEF, % (mean ± SD)	57 ± 8
Prior stroke, n (%)	2 (3.4)
Chronic kidney disease, n (%)	15 (25.8)
Creatinine (mean ± SD), mg/dl	1.07 ± 0.43
Peripheral artery disease, n (%)	8 (13.7)
Clinical Presentation	
Chronic coronary syndrome, n (%)	49 (84.4)
Acute coronary syndrome, n (%)	9 (15.6)
Unstable angina, n (%)	2 (3.4)
NSTEMI, n (%)	6 (10.3)
STEMI, n (%)	1 (1.7)

Abbreviations: CVD, cardiovascular diseases; CAD, coronary artery disease; MI, myocardial infarction; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

Table 2
Procedural characteristics and outcomes.

Location of the lesion, n (%)	Value
Left main coronary artery-left circumflex coronary artery	1 (2)
Left anterior descending coronary artery-diagonal branch	44 (77.5)
Left circumflex coronary artery-obtuse marginal branch	10 (16.5)
Right coronary artery-posterior descending artery	3 (4)
Procedural outcomes, n (%)	
BBSES delivered	58 (100)
Pre-PCI stenosis percentage (assessed by QCA)	
Main branch (%)	72.3 ± 3.8
Side Branch (%)	75.1 ± 4.1
Side Branch lesion length (mm)	13.0 ± 3.2 mm
Post-PCI stenosis percentage (assessed by QCA)	
Main Vessel (%)	5
Side Branch (%)	8
Clinical outcomes, n (%)	
Follow-up (median)	18 months (IQR 16–22)
Cardiac death	1 (1.7)
PMI	4 (6.8)
Spontaneous MI	1 (1.7)
Stent thrombosis	1 (1.7)

Abbreviations: BBSES, BioMime Branch sirolimus-eluting coronary side-branch stent; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography; PMI, periprocedural myocardial injury; MI, myocardial infarction.

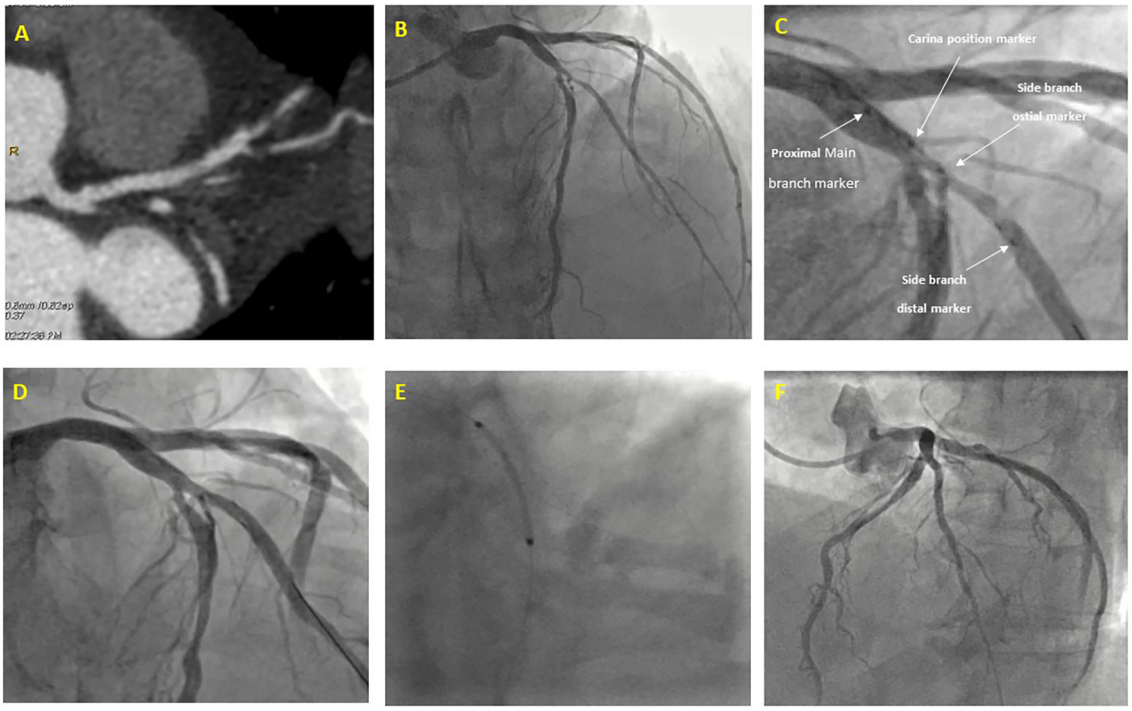

Fig. 3. (A) Computed tomographic coronary angiography showing severe stenosis of the left anterior descending coronary artery and first diagonal branch; (B) At invasive coronary angiography the lesion was classified as Medina 1,1,1 bifurcation lesion; (C) BBSES (3.5 × 2.5 × 24 mm) positioning; (D) Side branch stenting result and wire exchange technique; (E) Main vessel stenting with a Xience Sierra 3.0 × 23 mm drug-eluting stent; (F) Final angiogram after FKBI.

4. Discussion

This is the first clinical experience to date of true CBL treatment with the BBSES demonstrating excellent results (100 % procedural success with a predictable acute result of the SB) with the absence of in-hospital MACE. We observed only a stand-alone 6.8 % ($n = 4$) rate of post-procedural increase of high-sensitive troponin above the 99th percentile URL indicating a diagnosis of PMI but not of 4a MI, as specified by the fourth universal definition of MI [16]. Of note, low TLR and MACE rates (one subacute ST and one sudden death, adjudicated as a late possible ST) were also seen at 18-month median follow-up.

Despite guidelines recommending a provisional single-stent strategy as the preferred method of PCI for CBL, many factors influence interventional cardiologists to adopt a two-stent strategy. The major reasons are the importance of the SB and the risk of SB occlusion during provisional stenting [13]. Indeed, recent guidelines endorse dedicated two-stent techniques for complex CBL. The new recommendations of the 15th consensus document from the EBC include a two-stent strategy according to bifurcation anatomy and the operator's experience. According to EBC recommendations, a two-stent approach seems appropriate when there is a long SB lesion, when a SB >2.5 mm is a vessel that you do not want to lose because of the large subtended territory, when significant difficulties are encountered in wiring the SB and when converting to a two-stent technique may be difficult. The DEFINITION study has suggested certain criteria for classifying CBL as complex. Accordingly, a CBL was defined as complex when one of the major plus any two minor criteria were met. The major criteria included SB lesion length ≥ 10 mm with SB DS ≥70 % for distal LMCA disease or DS of SB ≥90 % for non-LMCA CBL. The minor criteria included moderate-to-severe calcification, multiple vessel lesions, CBL angle <45°, MV reference diameter < 2.5 mm, thrombus-containing lesions, and MV lesion

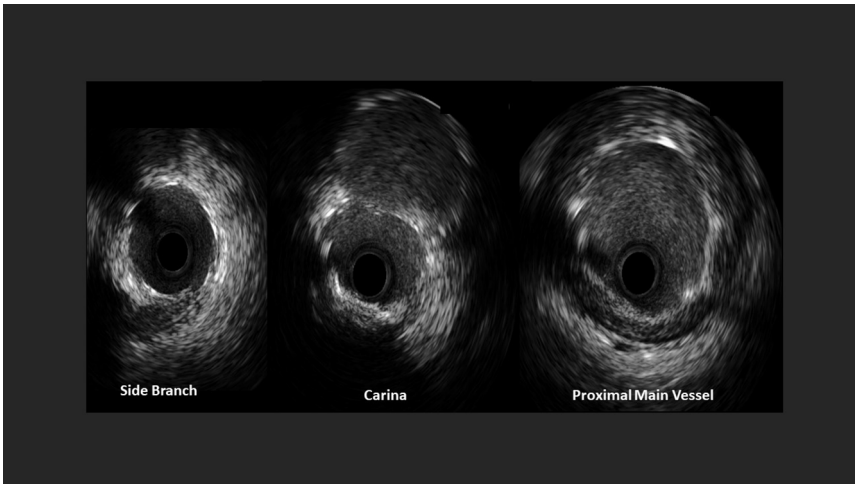

Fig. 4. Post-implantation intravascular ultrasound shows complete coverage of the left anterior descending coronary artery-first diagonal branch with good stent expansion. The "figure-of-eight" is visible at the carina site.

length ≥ 25 mm [18]. In the RESOLVE study, plaque on the same side of the SB, SB stenosis >50 %, bifurcation angle >70 %, MV/SB diameter ratio (diameter of PMV + DMV/2 × diameter of SB) >1 and a low MV thrombolysis in myocardial infarction flow grade were found to be angiographic predictors of SB occlusion after MV stenting [19].

Several recent studies in which newer-generation DES were used for CBL treatment indicate that two-stent techniques result in better clinical outcomes. One of the potential reasons for this improvement could be the enhanced features of newer-generation DES, such as thinner struts, open-cell design, decreased links, and higher conformability. Furthermore, they have more biocompatible polymers and eluting drugs with better pharmacokinetics. Another likely reason is the use of intracoronary imaging for planning the procedural strategy, guiding stent implantation and optimizing acute results in complex CBL, particularly when treated with a two-stent technique [20]. In the DKCRUSH II trial, Chen et al. showed that TLR and target vessel revascularization (TVR) were significantly lower in the DK-crush group than in the PST group [21]. The 8-month angiographic restenosis rates in the DK-crush group of MV and SB were 3.8 % and 4.9 %, respectively, while TVR, MACE, and ST were 6.5 %, 10.3 %, and 2.2 %, respectively. However, there were no significant differences in MACE and definite ST rates. The difference in TLR rate between the two groups was sustained through the 5-year follow-up [22]. Our outcomes at a median follow-up of 18 months compare favorably with those of the DKCRUSH II trial. However, any comparison requires careful consideration due to differences in patient populations and lesion characteristics. Most of our patients underwent elective PCI for stable disease, with only one LMCA lesion treated using BBSES. In contrast, the DKCRUSH II trial included mostly patients with ACS and a high prevalence of LMCA lesions treated. In 2017, the DKCRUSH V study reported a lower rate of TVMI (0.4 %), definite or probable ST (0.4 %), clinically driven TLR (3.8 %) and angiographic restenosis (7.1 %) at 1 year with the DK-crush technique than with the PST in complex CBL of distal LMCA [23]. In a recent meta-analysis, Fujisaki et al. investigated the efficacy of various two-stent techniques compared with PST for CBL with newer-generation DES [11]. The primary endpoint was the MACE rate at the longest reported follow-up time. The study included 13 randomized controlled trials with a total of 4041 patients. Compared to PST, the two-stent techniques significantly decreased the incidence of the primary endpoint (TVMI and TVR) with numerically lower TLR. However, there were no significant differences in all-cause mortality, cardiovascular mortality and ST. In another meta-analysis, Wang et al. analyzed 26 studies including 7257 patients randomly assigned to six different stent techniques for CBL treatment [14]. They found that DK-crush was significantly superior to the other five stent techniques in reducing MACE, cardiac death, TLR, and ST. Further, in patients with complex CBL, DK-crush was notably more efficacious than provisional, culotte, and T-stenting/TAP techniques in reducing MACE and TLR. Di Gioia et al. through a network meta-analysis showed that TLR was significantly lower with the two-stent technique than with the PST [24]. However, there were no differences in cardiac death, MI, or ST rates. In addition, this meta-analysis showed a clinical benefit with elective two-stent techniques over PST in CBL with a SB lesion length ≥ 10 mm. In the DEFINITION II trial, elective two-stent techniques (DK-crush 77.8 %, culotte 17.9 %, and other 4.3 %) provided a significant reduction in TLF (mainly driven by lower TVMI and clinically driven TLR) compared to the PST in complex CBL at one year [13]. The Nordic-Baltic Bifurcation Study IV demonstrated that newer-generation DES decreased MACE, a composite of cardiac death, MI, TLR, and definite ST, by 50 % in the two-stent technique group with complex CBL compared with first-generation DES [25].

The final step after deploying the BBSES in the SB followed by regular stenting of the MV involves performing FKBI in the MV and SB stents using two short non-compliant balloons one in the MV and the other in the SB, whose proximal parts are aligned in the proximal MV [1]. Indeed, FKBI is strongly recommended in all two-stent techniques to secure SB patency, achieve adequate stent expansion and apposition, remove jailing struts, and reduce the risk of in-stent restenosis (ISR) and ST [8,26]. Thus, although the clinical benefit of performing FKBI in PST is still under debate [27,28], there is strong evidence to support the efficacy of FKBI in the two-stent techniques [29,30].

Finally, many interventional cardiologists feel that stents designed specifically for CBL treatment may overcome numerous limitations of conventional DES. The BBSES is a new-generation stent dedicated to CBL treatment with the thinnest (65 μm) struts and is coated with biodegradable polymers, PLGA and PLLA [15]. Its unique design simplifies the procedure and reduces the number of steps in the two-stent technique for CBL treatment. An additional advantage is the fact that the BBSES can be successfully used for treating CBL with different bifurcation angles. Indeed the device provides good results even in very acute angles (i.e. <70°). Moreover, the tapered delivery balloon allows safe treatment of CBL that have a significant diameter discrepancy between MV and SB. These distinctive features may explain the good procedural and clinical results observed in our study.

4.1. Study limitations

Our study has several limitations. Although it represents the first clinical experience with BBSES to date, only a small number of consecutive patients were enrolled in a single academic center. These data lack formal control patients with CBL treated with different stenting techniques. Moreover, only one LMCA lesion was treated in this series, and patients mainly presented with stable disease. Therefore, we caution against generalizing the outcomes reported in our series to other more complex scenarios. Nevertheless, we did not find any concerns in using the BBSES in true CBL. Since the decision to use the BBSES was made by the operator at the time of the procedure, we believe that many operators felt more confident using this novel stent in less challenging clinical and anatomic conditions during their early experience. In this study, we performed clinical follow-up only and no angiographic follow-up was available. Therefore, it is not possible to provide data regarding angiographic ISR in our patients.

5. Conclusions

The BBSES is a new-generation, dedicated DES for treating true CBL. Its unique design, biodegradable sirolimus-eluting polymer coating and ease of use make it a promising treatment option for patients with this type of complex coronary artery lesions.

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CRediT authorship contribution statement

Antonio L. Bartorelli: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Giovanni Monizzi:** Writing – review & editing, Investigation, Data curation. **Luca Grancini:** Writing – review & editing, Investigation. **Emanuele Gallinoro:** Writing – review & editing, Investigation. **Angelo Mastrangelo:** Writing – review & editing, Investigation. **Vincenzo Mallia:** Writing – review & editing, Investigation. **Franco Fabbiocchi:** Writing – review & editing, Investigation.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Antonio L Bartorelli reports a relationship with Abbott Vascular that includes: consulting or advisory and speaking and lecture fees. The other authors declare

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References

[1] Kirat T. Fundamentals of percutaneous coronary bifurcation interventions. World J Cardiol. 2022;14:108–38. https://doi.org/10.4330/wjc.v14.i3.108.

[2] Lassen JF, Holm NR, Banning A, Burzotta F, Lefèvre T, Chieffo A, et al. Percutaneous coronary intervention for coronary bifurcation disease: 11th consensus document from the European bifurcation Club. EuroIntervention. 2016;12:38–46. https://doi.org/10.4244/EIJV12I1A7.

[3] Medina A, Suarez de Lezo J, Pan M. A new classification of coronary artery bifurcation le-sions. Rev Esp Cardiol. 2006;59:183. [PMID: 16540043].

[4] Park TK, Park YH, Song YB, Oh JH, Chun WJ, Kang GH, et al. Long-term clinical outcomes of true and non-true bifurcation lesions according to Medina classification-results from the COBIS (coronary bifurcation stent) II registry. Circ J. 2015;79:1954–62. https://doi.org/10.1253/circj.CJ-15-0264.

[5] Chang CF, Chang KH, Lai CH, Lin TH, Liu TJ, Lee WL, et al. Clinical outcomes of coronary artery bifurcation disease patients underwent Culotte two-stent technique: a single center experience. BMC Cardiovasc Disord. 2019;19:208. https://doi.org/10.1186/s12872-019-1192-2.

[6] Zhang D, Xu B, Yin D, Li Y, He Y, You S, et al. Predictors and Periprocedural myocardial injury rate of small side branches occlusion in coronary bifurcation intervention. Medicine (Baltimore). 2015;94:e992. https://doi.org/10.1097/MD.0000000000000992.

[7] Banning AP, Lassen JF, Burzotta F, Lefèvre T, Darremont O, Hildick-Smith D, et al. Percutaneous coronary intervention for obstructive bifurcation lesions: the 14th consensus document from the European bifurcation Club. EuroIntervention. 2019;15:90–8. https://doi.org/10.4244/EIJ-D-19-00144.

[8] Burzotta F, Lassen JF, Louvard Y, Lefèvre T, Banning AP, Daremont O, et al. European bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. Catheter Cardiovasc Interv. 2020;96:1067–79. https://doi.org/10.1002/ccd.29071.

[9] Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J. 2019;40:87–165. https://doi.org/10.1093/eurheartj/ehy394.

[10] Burzotta F, Lassen JF, Banning AP, Lefèvre T, Hildick-Smith D, Chieffo A, et al. Percutaneous coronary intervention in left main coronary artery disease: the 13th consensus document from the European bifurcation Club. EuroIntervention. 2018;14:112–20. https://doi.org/10.4244/EIJ-D-18-00357.

[11] Fujisaki T, Kuno T, Numasawa Y, Takagi H, Briasoulis A, Kwan T, et al. Provisional or 2-stent technique for bifurcation lesions in the second-generation drug-eluting stent era. J Soc Cardiovasc Angiogr Interv. 2022;1:100410. https://doi.org/10.1016/j.jscai.2022.100410.

[12] Burzotta F, Lassen JF, Lefèvre T, Banning AP, Chatzizisis YS, Johnson TW, et al. Percutaneous coronary intervention for bifurcation coronary lesions: the 15th consensus document from the European bifurcation Club. EuroIntervention. 2021;16:1307–17. https://doi.org/10.4244/EIJ-D-20-00169.

[13] Zhang JJ, Ye F, Xu K, Kan J, Tao L, Santoso T, et al. Multicenter, randomized comparison of two-stent and provisional stenting techniques in patients with complex coronary bifurcation lesions: the DEFINITION II trial. Eur Heart J. 2020;41:2523–36. https://doi.org/10.1093/eurheartj/ehaa543.

[14] Wang R, Ding Y, Yang J, Wang K, Gao W, Fang Z, et al. Stenting techniques for coronary bifurcation disease: a systematic review and network meta-analysis demonstrates superiority of double-kissing crush in complex lesions. Clin Res Cardiol. 2022;111:761–75. https://doi.org/10.1007/s00392-021-01979-9.

[15] Meril Life Sciences, BioMime branch sirolimus-eluting coronary side branch stent system. Available online: . https://www.merillife.com/medical-devices/vascular-intervention/coronary/stents/drug-eluting-stents/biomime-branch (Accessed on 10 May 2023).

[16] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA. Et al; executive group on behalf of the joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/world heart federation (WHF) task force for the universal definition of myocardial infarction. Fourth universal definition of myocardial infarction (2018). Circulation. 2018;138(20). https://doi.org/10.1161/CIR.0000000000000617. e618-e51.

[17] Zimarino M, Angiolillo DJ, Dangas G, Capodanno D, Barbato E, Hahn JY, et al. Antithrombotic therapy after percutaneous coronary intervention of bifurcation lesions. EuroIntervention. 2021;17(17):59–66. https://doi.org/10.4244/EIJ-D-20-00885.

[18] Chen SL, Sheiban I, Xu B, Jepson N, Paiboon C, Zhang JJ, et al. Impact of the complexity of bifurcation lesions treated with drug-eluting stents: the DEFINITION study (defnitions and impact of complex bifurcation lesions on clinical outcomes after percutaneous coronary intervention using drug-eluting stents). JACC Cardiovasc Interv. 2014;7:1266–76. https://doi.org/10.1016/j.jcin.2014.04.026.

[19] Dou K, Zhang D, Xu B, Yang Y, Yin D, Qiao S, et al. An angiographic tool for risk prediction of side branch occlusion in coronary bifurcation intervention: the RESOLVE score system (risk prEdiction of side branch OccLusion in coronary bifurcation interVEntion). JACC Cardiovasc Interv. 2015;8:39–46. https://doi.org/10.1016/j.jcin.2014.08.011.

[20] Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, et al. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. Eur Heart J. 2018;39:3281–300. https://doi.org/10.1093/eurheartj/ehy285.

[21] Chen SL, Santoso T, Zhang JJ, Ye F, Xu YW, Fu Q, et al. A randomized clinical study comparing double kissing crush with provisional stenting for treatment of coronary bifurcation lesions: results from the DKCRUSH-II (double kissing crush versus provisional stenting technique for treatment of coronary bifurcation lesions) trial. J Am Coll Cardiol. 2011;57:914–20. https://doi.org/10.1016/j.jacc.2010.10.023.

[22] Chen SL, Santoso T, Zhang JJ, Ye F, Xu YW, Fu Q, et al. Clinical outcome of double kissing crush versus provisional stenting of coronary artery bifurcation lesions. The 5-year follow-up results from a randomized and multicenter DKCRUSH-II study (randomized study on double kissing crush technique versus provisional stenting technique for coronary artery bifurcation lesions). Circ Cardiovasc Interv. 2017;10:e004497. https://doi.org/10.1161/CIRCINTERVENTIONS.116.004497.

[23] Chen SL, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, et al. Double kissing crush versus provisional stenting for left main distal bifurcation lesions: DKCRUSH-V randomized trial. J Am Coll Cardiol. 2017;70:2605–17. https://doi.org/10.1016/j.jacc.2017.09.1066.

[24] Di Gioia G, Sonck J, Ferenc M, Chen SL, Colaiori I, Gallinoro E, et al. Clinical outcomes following coronary bifurcation pci techniques: a systematic review and network meta-analysis comprising 5,711 patients. JACC Cardiovasc Interv. 2020;13:1432–44. https://doi.org/10.1016/j.jcin.2020.03.054.

[25] Kumsars I, Holm NR, Niemelä M, Erglis A, Kervinen K, Christiansen EH, et al. Randomised comparison of provisional side branch stenting versus a two-stent strategy for treatment of true coronary bifurcation lesions involving a large side branch: the Nordic-Baltic bifurcation study IV. Open Heart. 2020;7:e000947. https://doi.org/10.1136/openhrt-2018-000947.

[26] Murasato Y, Finet G, Foin N. Final kissing balloon inflation: the whole story. EuroIntervention. 2015;11:V81–5. https://doi.org/10.4244/EIJV11SVA18.

[27] Gwon HC, Choi SH, Song YB, Hahn JY, Jeong MH, Seong IW, et al. Long-term clinical results and predictors of adverse outcomes after drug-eluting stent implantation for bifurcation lesions in a real-world practice: the COBIS (coronary bifurcation stenting) registry. Circ J. 2010;74:2322–8. https://doi.org/10.1253/circj.cj-10-0352.

[28] Brueck M, Scheinert D, Flachskampf FA, Daniel WG, Ludwig J. Sequential vs. kissing balloon angioplasty for stenting of bifurcation coronary lesions. Catheter Cardiovasc Interv. 2002;55:461–6. https://doi.org/10.1002/ccd.10100.

[29] Sgueglia GA, Chevalier B. Kissing balloon inflation in percutaneous coronary interventions. JACC Cardiovasc Interv. 2012;5:803–11. https://doi.org/10.1016/j.jcin.2012.06.005.

[30] Lassen JF, Burzotta F, Banning AP, Lefèvre T, Darremont O, Hildick-Smith D, et al. Percutaneous coronary intervention for the left main stem and other bifurcation lesions: 12th consensus document from the European bifurcation Club. EuroIntervention. 2018;13:1540–53. https://doi.org/10.4244/EIJ-D-17-00622.