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Clinical Trial

A Pilot Study on Culottes versus Crossover Single Stenting for True Coronary Bifurcation Lesions

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Background: The purpose of our study was to compare clinical and angiographic outcomes of planned culottes technique with that of provisional crossover single stenting in the treatment of true coronary bifurcation lesions (CBL) with drug-eluting stent (DES).

Methods: True CBL patients (n = 104) were randomly assigned to either the provisional stenting of the side branch (crossover group) or the culottes group. Additional side branch (SB) stenting in the crossover group was required if there was thrombolysis in myocardial infarction flow ≤ 1 flow). The primary end point was the occurrence of major adverse cardiac events (MACE) at nine months, including cardiac death, myocardial infarction, target lesion/vessel revascularization and in-stent thrombosis. The secondary end point was angiographic in-segment restenosis at nine months.

Results: The rate of MACE at nine months was similar between the crossover and culottes groups (7.7% vs. 7.7%, p = 1.000). Additional SB stenting in the crossover group was required in 3.8% of patients. There was one procedural occlusion of SB in the crossover group. At nine months, the rate of in-segment restenosis was similar in the parent main vessel (0% vs. 1.9%, p = 1.000), main branch (1.9% vs. 7.7%, p = 0.363) and SB (17.3% vs. 9.6%, p = 0.250) between the crossover and culottes groups, respectively.

Conclusions: This study demonstrated that there is no significant difference in cumulative MACE or in-segment restenosis between crossover and culottes groups. Larger randomized clinical trials are warranted to re-evaluate the outcomes of the provisional crossover stenting versus the culottes stenting techniques utilizing DES for true CBL.

Key Words: Angioplasty • Bifurcation lesion • Clinical trial • Coronary stenting • Drug-eluting stent • Restenosis

INTRODUCTION

Coronary bifurcation lesions (CBL) account for 15-20% of all percutaneous coronary interventions (PCI), and remain amongst the most challenging lesions to treat both due to difficulty in the techniques used and an increased risk of restenosis and stent thrombosis.[1,2] Although several stenting approaches for CBL have been proposed, recent randomized studies revealed that planned dual-stenting techniques do not demonstrate clinical or angiographic superiority compared to a planned single stenting strategy,[3-5] even in the era of the drug-eluting stent (DES). Based on these studies, crossover provisional single stenting has been generally accepted as a favored strategy for CBL. Nevertheless, there are limitations to these trials which should be taken into account when interpreting the data. First, not all lesions in these studies were true bifurcations, with true bifurcation rates varying between 71% (Nordic) and 92% (CACTUS).[3,4] Second, dual-stenting techniques are more com-

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plex to perform than single-stenting techniques, and thus the success of dual-stenting techniques are highly operator-dependent. Third, most studies compared a single-stenting strategy with dual-stenting strategy, but allowed several different stenting techniques in the dual-stenting arm.[3-5] In particular, the rate of crush technique used in these trials was quite high. However, crush stenting carries potential risks of restenosis and stent thrombosis due to incomplete coverage of the side-branch ostium, or inadequate opening at the ostium of the side branch (SB) because of crushed stent layers.[6] Amongst the various dual-stenting strategies performed in the DES era, there has been renewed interest in the culottes technique, because it provides optimal bifurcation coverage, less residual stenosis, and less stent distortion compared with other techniques.[6,7] This was supported by the NORDIC II trial,[8] which demonstrated an in-stent SB binary restenosis rate of 9.8% after crush stenting compared with 3.8% after culottes stenting ($p = 0.04$), although the difference between techniques was insignificant when assessing restenosis in the entire in-segment bifurcation [crush 12.1% vs. culottes 6.6% ($p = 0.1$)]. Of note, final kissing balloon inflation (FKBI) could be performed in more cases in the culottes group, which might be explained by the greater difficulty in re-wiring the SB and advancing a balloon through the two crushed stent layers that jail the SB. Thus, whether to choose a provisional single stent strategy or a dual-stent culottes strategy in bifurcations remains an open question that warrants additional studies.

To address this question, we prospectively compared two different approaches for the treatment of true CBL in a randomized fashion that included the: (1) crossover provisional single stenting with DES placement in the main branch (MB) with SB stenting only if final results were found to be suboptimal (TIMI $\leq$ 1 flow), and (2) culottes technique with DES in both branches of the CBL.

METHODS

Patient selection

Recruitment of patients for this pilot study was conducted in our hospital from January 2010 to December 2013. A total of 104 consecutive patients were eligible for enrollment and included in our study. Patients were assigned to receive crossover single stenting or culottes stenting with DES for CBL. All patients gave written informed consent for participation in this study, which was approved by the Ethics Committee of our hospital. Patients were deemed eligible for this study who were 18 years of age or older, with a *de novo* true CBL. A true CBL was defined according to Medina classifications (1,1,1; 0,1,1; 1,0,1)[9,10] and could be located either in the (i) left main stem (LM), the anterior descending artery (LAD) and the left circumflex artery (LCX); (ii) LAD and a diagonal branch (DB); (iii) LCX and an obtuse marginal branch (OM); or the (iv) right coronary artery (RCA), posterior descending artery (PDA) and postero-lateral artery (PLA). The diameter of the MB and the SB by visual estimate was to be $\geq$ 2.5 mm and $\geq$ 2.0 mm, respectively. Patients were excluded if they presented with ST-segment elevation acute myocardial infarction (STEMI) within 24 hours, a life expectancy of < 1 year and allergies to any of the drugs (aspirin, clopidogrel, sirolimus, zotarolimus, everolimus and paclitaxel) used in the study.

Procedures

Permuted block randomization was performed using a computer-generated randomization procedure where sealed numbered envelopes were provided to patients that were assigned to one of two different treatment groups. After baseline angiography was performed, patients were randomly assigned in a 1:1 manner to either (1) DES implantation in the MB with balloon angioplasty and provisional stenting for the SB (crossover group), or (2) elective dual-stenting with DES with the culottes technique (culottes group). Pre-dilation was determined at the discretion of the operator. In the crossover group, the procedure included: (1) stenting of MB; (2) SB dilation if there was TIMI flow < 3 in the SB and FKBI after SB dilation at the discretion of the operator (Figure 1); and (3) SB stenting was allowed by the T-stenting technique only when the TIMI flow was $\leq$ 1 in the SB after dilation. FKBI was required if SB stenting was performed. In the culottes group, stenting was performed by a technique described previously (Figure 2).[9-11] First, a stent was deployed into the more angulated branch, usually the SB. The non-stented branch was then rewired through the struts of the stent and dilated. A second stent was advanced and expanded into the non-stented branch,

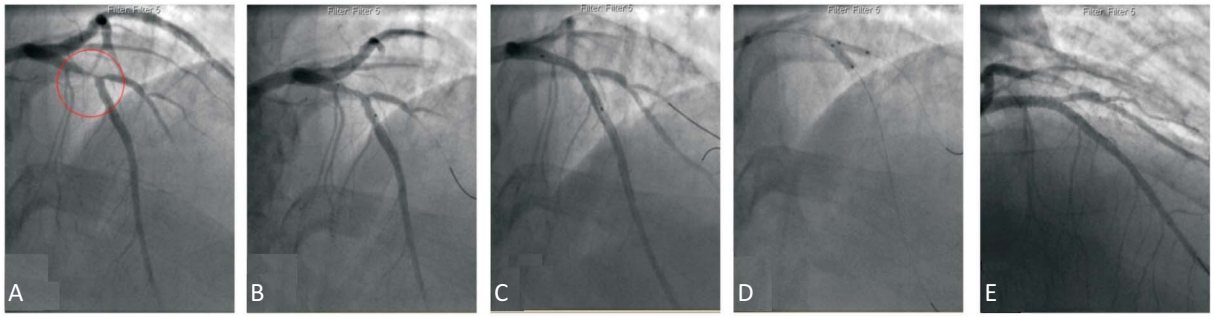

Figure 1. *Angiography of provisional stenting with SB dilation of a patient with a true CBL. (A) A patient with a typical (1,0,1) CBL (red circle) according to Medina's classification, located at the left anterior descending artery (MB) and the first diagonal branch (SB); which underwent (B) wiring of the SB and MB; (C) stenting of the first MB and (D) re-wiring of the SB and performing a FKBI. (E) Final outcome of the stenting is presented. CBL, coronary bifurcation lesions; MB, main branch; SB, side branch.*

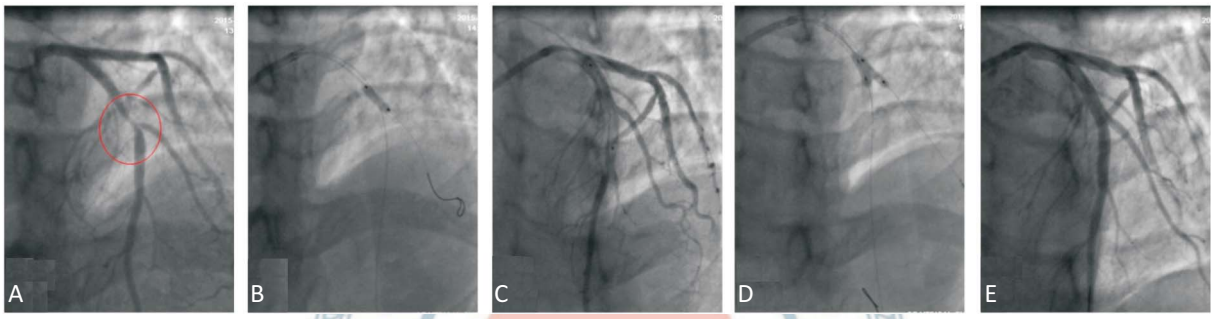

Figure 2. *Angiography of the culottes stenting technique on a patient with a true CBL. (A) A patient with a typical (1,1,1) CBL (red circle) according to Medina's classification, located at the left anterior descending artery (MB) and the first diagonal branch (SB), underwent (B) wiring of the SB and MB and stenting of the first SB with a relatively long protrusion of the SB stent into the PMV and then (C) ballooning of the side-hole of the SB stent and stenting of the MB and (D) advancing of the deflated balloon in the MB, followed by rewiring of the SB at a point close to the carina and then performing a FKBI. (E) Final outcome of the stenting is indicated. CBL, coronary bifurcation lesions; MB, main branch; SB, side branch.*

which was usually the MB, with the stent extending proximal to the SB ostium. FKBI was a necessary final step of the procedure. When FKBI was performed, two noncompliant balloons of diameters equal to the distal MB and SB, respectively, were simultaneously inflated at a low pressure of 10 to 12 atm at the bifurcation after separate high pressure dilation of SB and MB.

All patients received appropriate pretreatment with aspirin and clopidogrel, including a clopidogrel-loading dose. After PCI, lifelong aspirin (75 mg/d) and clopidogrel (75 mg/d) was recommended for 12 months. Procedural heparin administration was done according to standard hospital procedures, and activated clotting time control was not guided by this study. Glycoprotein receptor antagonists were used at the discretion of the operator. The DES used included Excel (JW Medical Co. Inc., China); Resolute (Medtronic Inc., Fridley, MN, USA); Xience V (Abbott Vascular Co., Abbott Park, IL, USA); and Taxus (Boston Scientific Co., Marlborough, MA, USA), with a preference for open-cell design stents. Radial access was used routinely with 6/7F guiding catheters and the femoral approach utilizing the 7/8F guiding catheters was only used when delivery of larger profile stents was needed, or at the discretion of the operator. Selection of the access site, stent type and size, balloon size and inflation pressure were based on the operator's preference. Implantation of additional stents to cover the whole lesion or to cover a dissection was allowed. Different types of DESs in the same vessel were not allowed.

A 12-lead ECG was obtained before and 12-18 hours post-procedurally. Creatine kinase-myocardial band (CK-MB) and cardiac troponin T/cardiac troponin I (cTnT/cTnI) were measured at the time of the procedure and after 12-18 hours. CK-MB was used as the primary marker and cTnT/cTnI only if CK-MB was unavailable. To

avoid confounding non-procedure-related marker elevation, patients with unstable angina pectoris were included in biomarker analysis only if pre-procedure markers were normal. Marker elevation of three times the upper limit of normal was considered significant.

Clinical follow-up

Clinical follow-up was performed with visits or telephone contact at one, three, six and nine months post-procedure. Adverse events were monitored throughout the entire study period. Follow-up coronary angiography was performed at nine months after the index procedure unless clinical reasons indicated earlier. No patients were lost upon clinical and angiographic follow-up.

Quantitative coronary angiographic measurements

Angiography was performed at (i) baseline, (ii) completion of the procedure, and at (iii) the nine-month follow-up period. Quantitative coronary angiographic measurements (QCA) were obtained using dedicated software (Qangio XA, version 7.0, Medis, Leiden, the Netherlands). QCA measurements of CBL were obtained in three segments: the proximal parent main vessel (PMV) segment, the MB and the SB. In-segment restenosis was defined as restenosis at any of the following sites: (1) inside the stent; (2) within 5 mm proximal or distal to the stent, and (3) within the 5 mm proximal of the non-stented SB.

Study end points and definitions

The primary clinical end point was the occurrence of major adverse cardiac events (MACE) at nine months, including cardiac death, Q-wave myocardial infarction (QWMI)/Non-Q-wave myocardial infarction (NQWMI), target lesion/vessel revascularization (TLR/TVR) and in-stent thrombosis (IST). A secondary angiographic end point was in-segment restenosis in the MB or SB at nine months. NQWMI was defined as a CK-MB or cTnT/cTnI that had increased to $\geq$ 3 times the upper limit of the normal range combined with clinical signs of myocardial infarction (MI), without new onset of pathological Q waves. QWMI was defined as new development of pathological Q waves in two contiguous leads, together with clinical signs of MI (chest pain or increase in myocardial injury markers). TLR/TVR was the repeat target lesion/vessel therapy either by PCI or by surgery. IST was diagnosed according to the Academic Research Consortium definition. Acute, subacute, or late thrombosis were defined as occurring within 24 hours, within 1 month, or during the succeeding 5 months after stent implantation, respectively. Percent diameter stenosis (PDS) was calculated as (reference diameter – minimal luminal diameter)/reference diameter $\times$ 100. Defined binary stenosis of > 50% was considered significant. Minimal lumen diameter (MLD) was assessed on a projection best suited to evaluate the lesion. Late lumen loss was defined as post-procedure MLD minus MLD at nine-month follow-up.

Angiographic success was defined as a minimal stenosis diameter reduction to < 20% together with grade 3 TIMI flow in the MB, plus grade 3 TIMI flow in the SB. Procedural success was defined as angiographic success without an in-hospital MACE, such as death, MI or emergency revascularization.

All events were classified and adjudicated by two observers in the Core Laboratory of the Fujian Institute of Coronary Artery Disease who were not involved in the stent implantations and the follow-up process. Clinical data entry and quantitative coronary angiography were double-checked by a trained study member.

Statistical analysis

Based on our clinical experience, we expected a primary end-point event rate of 35% in the culottes group. A power calculation assuming α = 5%, and power = 80%, and a two-sided $\chi 2$ test was completed. To detect a reduction in the primary end-point rate by 15%, 40 patients were necessary in each group. To allow for patients lost to follow-up, 104 patients were recruited in the study. Discrete and categorical variables are presented as numbers (percentages), and continuous variables as mean $\pm$ standard deviation (SD). To compare differences in the variables between each group, the chi-square test or Fisher's exact test was employed for discrete variables and an analysis of variance (ANOVA) for the continuous variables. Time-to-event data were analyzed with the Kaplan-Meier method and the log-rank test. All probability values were two-sided, and the level of significance was 5%. Analyses were performed with SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline characteristics

From January 2010 to December 2013, 104 patients with true CBL were enrolled and randomly assigned to either crossover single stenting (crossover group, n = 52) or culottes stenting (culottes group, n = 52). Baseline characteristics are listed in Table 1. The two groups were well-matched for all demographic and clinical characteristics. There were no differences between the indications for treatment between the crossover and culottes groups, respectively: stable angina, 15 (28.8%) versus 20 (38.5%); unstable angina, 25 (48.1%) versus 28 (53.8%); NSTEMI, 7 (13.5%) versus 1 (1.9%); STEMI, 5 (9.6%) versus 3 (5.8%).

Table 1. Baseline clinical characteristics of CBL patients

Variables	Crossover (n = 52)	Culottes (n = 52)	p
Age(y)	64.52 ± 10.67	64.19 ± 7.27	0.856
Gender, male/female	48/4	43/9	0.138
Diabetes mellitus	10 (19.2)	11 (21.2)	0.807
Hypercholesterolemia	6 (11.5)	6 (11.5)	1.000
Hypertension	35 (67.3)	33 (63.5)	0.578
Current smokers	31 (59.6)	27 (51.9)	0.430
LVEF < 40%	7 (13.5)	6 (11.5)	0.767
Prior MI	12 (23.1)	10 (19.2)	0.631
Prior PCI	13 (25.0)	12 (23.1)	0.819
Prior CABG	0 (0)	0 (0)	1.000
Stable angina	15 (28.8)	20 (38.5)	0.299
Unstable angina	25 (48.1)	28 (53.8)	0.556
NSTEMI	7 (13.5)	1 (1.9)	0.060
STEMI	5 (9.6)	3 (5.8)	0.715
Single-vessel disease	19 (36.5)	14 (26.9)	0.746
Multi-vessel disease	33 (63.5)	38 (73.1)	0.746
Simultaneous treated multi-vessel disease	5 (9.6)	8 (15.4)	0.374

CABG, coronary artery bypass grafting; CBL, coronary bifurcation lesions; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non ST-segment elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation acute myocardial infarction.

Angiographic and procedural data

Procedural data are shown in Table 2. The target bifurcation lesions were located similarly in LM/LAD/LCX, LAD/DB, LCX/OM and RCA/PDA/PLA, with no differences between the two groups. There was also no significant difference between the two groups with respect to type of bifurcation, vessel size, or severity of stenosis as assessed by the operator. Angulation of the side branch < 70° was seen in 80.8%, Type B2/C lesions in 95.2%, chronic total occlusions in 11.5%, calcification in 7.7%, and proximal tortuosity in 19.2% of the lesions, with no difference between the two groups. FKBI was performed after MB stenting in 82.7% of the crossover group and 92.3% of the culottes group (p = 0.138). In the crossover group, dissection of type A without TIMI flow grade < 3 in the SB after FKBI was observed in 6 patients (14.0%). An additional stent in the SB was implanted in 2 (3.8%) of 52 patients. The reason for additional stenting was dissection of type B with TIMI flow grade ≤ 1 in the SB. Angiographic success was attained in 49 cases (94.2%) in the crossover group and 51 (98.1%) in the culottes group (p = 0.610), and procedural success was attained in 92.3% and 98.1% of cases, respectively (p = 0.359). In the crossover group, 2 cases were not able to achieve a residual stenosis < 20% in the MB after the procedure. In addition, 1 patient in the crossover group developed complete SB occlusion during the procedure. In the culottes group, only 1 patient presented without angiographic success because of residual stenosis < 20% in the MB. The two cases of in-hospital MACE included QWMI in 1 case and NQWMI in 1 in the crossover group. Additionally, procedure duration and contrast media volume were significantly lower in the crossover group.

Quantitative coronary angiographic measurements

The results of the QCA analysis are shown in Table 3. There were no significant differences in pre-procedure baseline characteristics between the two groups. However, in the SB, culottes stenting was associated with significantly larger MLD post-PCI (2.40 ± 0.35 versus 2.01 ± 0.61 mm, p < 0.001) and at follow-up (2.03 ± 0.51 versus 1.62 ± 0.65 mm, p = 0.001). This resulted in a significant lower PDS in the SB relative to the crossover group at follow-up (24.90 ± 16.54% versus 34.03 ± 19.49%, p = 0.011). In the entire lesion (PMV, MB and SB), the rate of in-segment restenosis was 17.3% in the crossover group and 15.4% in the culottes group (p = 0.791). The rate of in-segment restenosis was similar in the PMV (0% vs. 1.9%, p = 1.000), MB (1.9% vs. 7.7%, p = 0.363) and SB (17.3% vs. 9.6%, p = 0.250) for the crossover and culottes groups, respectively.

Table 2. Angiographic and procedural data of techniques deployed on CBL patients

Variables	Crossover (n = 52)	Culottes (n = 52)	p
Target vessel			0.503
LM/LAD/LCX	16 (30.8)	14 (26.9)	
LAD/DB	33 (63.5)	34 (65.4)	
LCX/OM	3 (5.8)	2 (3.8)	
RCA/PDA/PLA	0 (0)	2 (3.8)	
Medina classification			0.534
1,1,1	30 (57.7)	34 (65.4)	
1,0,1	6 (11.5)	7 (13.5)	
0,1,1	16 (30.8)	11 (21.2)	
Angulation			0.320
Y type (< 70°)	40 (76.9)	44 (84.6)	
T type (> 70°)	12 (23.1)	8 (15.4)	
Lesion characteristics			
Type B2/C lesions	48 (92.3)	51 (98.1)	0.363
Chronic total occlusions	4 (7.7)	8 (15.4)	0.220
Calcification	5 (9.6)	3 (5.8)	0.462
Tortuous lesions	11 (21.2)	9 (17.3)	0.619
Reference diameter (mm)			
PMV	3.38 ± 0.56	3.29 ± 0.49	0.404
MB	3.06 ± 0.49	3.01 ± 0.42	0.592
SB	2.44 ± 0.40	2.56 ± 0.30	0.095
Mean lesion length (mm)			
PMV	7.64 ± 4.86	8.13 ± 4.54	0.593
MB	14.73 ± 7.70	15.78 ± 8.59	0.515
SB	12.80 ± 4.92	14.10 ± 7.12	0.279
No. of implanted stents per CBL			
MB			0.150
1 stent	44 (84.6)	38 (73.1)	
2 stents	8 (15.4)	14 (26.9)	
SB			< 0.001
0 stent	50 (96.2)	0 (0)	
1 stent	2 (3.8)	50 (96.2)	
2 stents	0 (0)	2 (3.8)	
Type of DES implanted			0.167
SES	32 (61.5)	41 (78.8)	
PES	2 (3.8)	0 (0)	
ZES	8 (15.4)	6 (11.5)	
EES	10 (19.2)	5 (9.6)	
Maximal inflation pressure (atm)			
MB	12.76 ± 3.21	12.62 ± 3.48	0.847
SB	12.76 ± 3.21	12.67 ± 3.46	0.893
Final kissing balloon inflation	43 (82.7)	48 (92.3)	0.138
Angiographic success	49 (94.2)	51 (98.1)	0.610
Procedural success	48 (92.3)	51 (98.1)	0.359
Procedure time (min)	57.06 ± 24.99	88.25 ± 20.19	< 0.001
Contrast volume (ml)	236.15 ± 76.08	336.54 ± 106.75	< 0.001

CBL, coronary bifurcation lesions; DB, diagonal branch; DES, drug eluting stent; EES, everolimus-eluting stent; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main stem; MB, main branch; OM, obtuse marginal branch; PDA, posterior descending artery; PES, paclitaxel eluting stent; PLA, postero-lateral artery; PMV, parent main vessel; RCA, right coronary artery; SB, side branch; SES, sirolimus-eluting stent; ZES, zotarolimus-eluting stent.

Table 3. Quantitative coronary angiography measurements of CBL in patients after crossover and culottes techniques

Variable	PMV			MB			SB		
	Crossover n = 52	Culottes n = 52	p	Crossover n = 52	Culottes n = 52	p	Crossover n = 52	Culottes n = 52	p
Lesion length, (mm)	7.64 ± 4.86	8.13 ± 4.54	0.593	14.73 ± 7.70	15.78 ± 8.59	0.515	12.80 ± 4.92	14.10 ± 7.12	0.279
Reference diameter, (mm)									
Baseline	3.38 ± 0.56	3.29 ± 0.49	0.404	3.06 ± 0.49	3.01 ± 0.42	0.592	2.44 ± 0.40	2.56 ± 0.30	0.095
Post-PCI	3.48 ± 0.62	3.33 ± 0.50	0.188	3.19 ± 0.53	3.04 ± 0.42	0.109	2.45 ± 0.40	2.74 ± 0.35	< 0.001
Follow-up	3.45 ± 0.58	3.34 ± 0.48	0.269	3.18 ± 0.48	3.05 ± 0.43	0.148	2.42 ± 0.39	2.70 ± 0.36	< 0.001
Minimal lumen diameter, (mm)									
Baseline	1.29 ± 0.88	1.16 ± 0.81	0.431	0.76 ± 0.62	0.85 ± 0.62	0.439	0.59 ± 0.30	0.56 ± 0.33	0.666
Post-PCI	3.24 ± 0.59	3.13 ± 0.48	0.326	2.88 ± 0.53	2.74 ± 0.43	0.159	2.01 ± 0.61	2.40 ± 0.35	< 0.001
Follow-up	3.11 ± 0.63	3.02 ± 0.57	0.414	2.59 ± 0.49	2.45 ± 0.67	0.230	1.62 ± 0.65	2.03 ± 0.51	0.001
PDS %									
Baseline	61.42 ± 26.99	64.93 ± 24.54	0.490	75.21 ± 20.62	71.69 ± 19.87	0.379	76.22 ± 11.60	77.79 ± 12.61	0.512
Post-PCI	7.02 ± 5.66	6.11 ± 4.86	0.384	9.97 ± 5.71	9.87 ± 6.01	0.929	18.73 ± 16.52	12.30 ± 7.43	0.012
Follow-up	9.62 ± 12.42	9.73 ± 8.86	0.959	18.38 ± 13.23	19.99 ± 16.88	0.589	34.03 ± 19.49	24.90 ± 16.54	0.011
In-stent late lumen loss, (mm)	0.12 ± 0.42	0.11 ± 0.41	0.926	0.29 ± 0.42	0.29 ± 0.49	0.966	0.39 ± 0.31	0.37 ± 0.50	0.812
Restenosis (in-segment)	0 (0)	1 (1.9)	1.000	1(1.9)	4 (7.7)	0.363	9 (17.3)	5 (9.6)	0.250

CBL, coronary bifurcation lesions; MB, main branch; PCI, percutaneous coronary intervention; PDS, percent diameter stenosis; PMV, parent main vessel; SB, side branch.

Clinical outcome

The cumulative event rate for the primary end point of MACE (cardiac death, MI, TLR/TVR and IST) in-hospital and after nine months of follow-up is shown in Table 4 and Figure 3. There were no significant differences in MACE rate between the two groups (p = 1.000). The cumulative MACE in the crossover group included NQWMI in 2 patients (3.8%), QWMI in 1 (1.9%) and TLR/TVR in 1 (1.9%); whereas in the culottes group, MACE consisted of TLR/TVR in 4 patients (7.7%) and cardiac death in 1 (1.9%) occurring during target-lesion revascularization by surgery. There were no acute, subacute or late IST in the two groups.

DISCUSSION

The present study was the first study in which the culottes technique was used as the primary dual-stenting technique in the dual-stenting arm that was then compared with the crossover provisional single stenting technique. The main findings included that: (1) good clinical and angiographic outcomes can be achieved by both crossover single stenting and culottes stenting for the treatment of true CBL; (2) SB stenting following MB stent implantation is permitted only for severely impaired blood flow (Thrombolysis in Myocardial Infarction flow ≤ 1), with the rate of crossover with SB stenting being only 3.8%; and (3) regardless of the stenting strategy used, DES implantation in true bifurcation lesions provides good clinical and angiographic results with an acceptable midterm safety profile.

The current consensus for treatment of bifurcation lesions is to use the crossover single stent approach as the default strategy.[11] This consensus is based on the results of large randomized trials comparing single stenting with dual-stenting techniques, such as the Nordic,[3] CACTUS[4] and BBC-1 trials.[5] From these trials, it appears that the single stent technique is less expensive and more simple compared with dual-stent techniques. This justifies the current preference for the single-stent approach. However, our current study has demonstrated that there is no significant difference between the cumulative MACE or in-segment restenosis between the crossover and culottes groups in the treatment of true CBL. Additionally, compared with crossover stenting, cu-

Table 4. In-hospital and nine month follow-up MACE in CBL patients after crossover and culottes techniques

Variables	Crossover n = 52	Culottes n = 52	p
Periprocedural MACEs	2 (3.8)	0 (0)	0.495
Cardiac death	0 (0)	0 (0)	1.000
MI	2 (3.8)	0 (0)	0.495
TLR/TVR	0 (0)	0 (0)	1.000
IST	0 (0)	0 (0)	1.000
MACE at nine-month	2 (3.8)	4 (7.7)	0.678
Cardiac death	0 (0)	1 (1.9)	1.000
MI	1 (1.9)	0 (0)	1.000
TLR/TVR	1 (1.9)	4 (7.7)	0.363
IST	0 (0)	0 (0)	1.000
Cumulative MACE at 9-month	4 (7.7)	4 (7.7)	1.000
Cardiac death	0 (0)	1 (1.9)	1.000
MI	3 (5.8)	0 (0)	0.243
TLR/TVR	1 (1.9)	4 (7.7)	0.363
IST	0 (0)	0 (0)	1.000

CBL, coronary bifurcation lesions; IST, in-stent thrombosis; MACE, major adverse cardiac events; MI, myocardial infarction; TLR/TVR, target lesion/vessel revascularization.

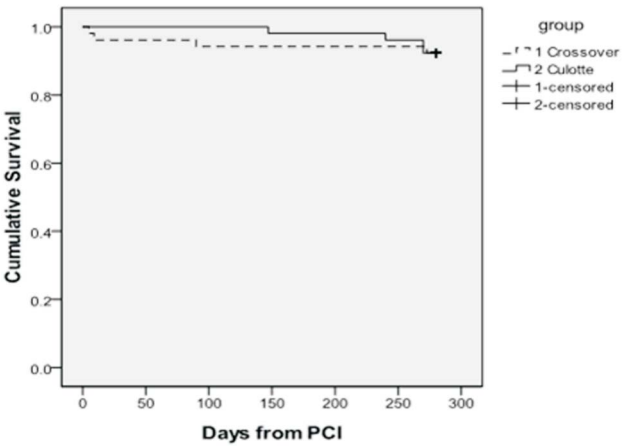

Figure 3. *Kaplan-Meier survival curve of MACE in CBL patients following crossover and culottes techniques.*

lottes stenting was associated with improved MLD and PDS angiographically both post-PCI and at follow-up, which indicated that stenting of the SB with this dual-stenting technique might be more effective in attaining better anatomic and hemodynamic parameters. These findings may justify the choice of culottes stenting in selected cases with true CBL or CBL with large vessel disease.

Over the past several years, the importance of FKBI has become increasingly clear. In 2006, Hoye et al.[12] reported good outcomes in the group undergoing FKBI, with restenosis of 6.4% in the MB and 9.6% in the SB. Ge et al.[13] found restenosis rates of 13.8% in the MB and 8.6% in the SB in patients undergoing FKBI. The authors stated that the SB restenosis rate was influenced by whether FKBI was performed. The Nordic-Baltic Bifurcation Study III[14] also demonstrated that FKBI reduced angiographic SB restenosis, particularly in patients with true bifurcation lesions. The interventionist desires bifurcation techniques that are safe, easy to perform, and have a low repeat intervention rate. The major safety challenge is to ensure that the SB is protected and has a satisfactory final result with or without stenting. Properly performed FKBI may result in relocation of the flow divider and restoration of the anatomy and function of the bifurcation without stent distortion.[15,16] In our study, the FKBI technique was refined. First, two non-compliant balloons of diameters equal to the distal MB and SB were used in FKBI. Compliant balloons expanded beyond their nominal diameter and increased the risk of SB dissection. Second, the kissing balloons were simultaneously inflated at a low pressure of 10 to 12 atm at the bifurcation after separate high pressure dilation of the SB and MB. This inflation approach might provide strut apposition and avoid the detrimental distortion and higher wall stress in the bifurcation. In the present study, the low rates of SB dissection and further stenting (3.8%) might be attributed to the refined FKBI technique, although FKBI was performed in 82.7% of the crossover group. Moreover, no significant differences in the rates of angiographic in-segment restenosis were found in all of the segments assessed, which included the: PMV (0% vs. 1.9%, p = 1.000), MB (1.9% vs. 7.7%, p = 0.363) and SB (17.3% vs. 9.6%, p = 0.250) for both crossover and culottes groups, respectively. Largely, the low rates of restenosis achieved by both crossover single stenting and culottes stenting may be due to FKBI being properly performed.

The culottes stenting technique, which was largely abandoned in the BMS era,[2] has experienced a resurgence with the use of DES because the culottes technique can provide full side-branch scaffolding and drug application with patency of the MB and SB. From a technical point of view, culottes stenting has several major advantages. First, it allows the operator to start the in-

tervention using a provisional SB stenting approach, if desired. Second, it provides the assurance of completely covering the bifurcation carina. Third, final re-wiring into the SB, with the aim of performing FBKI, is easier after culottes than after crush stenting. The results after properly performed culottes stenting and FBKI lead to optimal bifurcation coverage, less recoil at the ostial site, less residual stenosis, and less stent distortion compared with other techniques. These considerations are supported by the work of Ormiston et al.[7] in a bench testing model of coronary bifurcation interventions. Despite these advantages, interventionalists should note that culottes stenting was associated with increased procedure time and greater contrast volume, that related to the greater complexity of the procedure compared to single stent deployment.

Previous studies revealed that the rate of crossover with SB stenting in the single stenting group varied mainly depending on the criteria used for treatment. When residual stenosis of < 50% was considered as one of the criteria, stenting the SB was required for between 22%[17] and 31.3%[4] of the cases. However, if stenting of the SB was limited to cases with severely impaired blood flow, this rate was significantly reduced (around 2-4%),[3,18] similar to our results (3.8%) without the increased occurrence of MACE or ISR. The clinical implication of this finding is that hemodynamic parameters such as TIMI flow or fractional flow reserve (FFR) are an increasingly important part of the decision making process for stenting the SB in CBL.

The overall outcomes of the present study indicate a good safety profile for DES implantation in CBL. Regardless of the DES deployment method adopted, the incidence of MACE (7.7%) was lower than that reported in studies from the BMS era.[1,3,5] This finding further indicates that DES implantation can be considered a viable treatment in most CBL.

Study limitations

This study was limited by the small study population which occurred at a single center. It also had an open design, and operators and patients that were aware of the technique used. These limitations might introduce bias in the interpretation of symptoms upon follow-up. Rates of MACE and in-segment restenosis were low after nine months; however, the durability of these results on long-term outcomes is not known. Both clinical and histological studies of DES have demonstrated evidence of continuous neo-intimal growth during long-term follow-up, which is designated as the "late catch-up" phenomenon.[19,20] The "late catch-up" phenomenon in patients with DES placement was indicated by the higher rate of late TLR/TVR. Thus, extended clinical and angiographic follow-up is necessary in these types of studies.[21]

CONCLUSIONS

This small study demonstrated that there are no significant differences in cumulative MACE and in-segment restenosis between the crossover and culottes groups in the treatment of true bifurcation lesions. Both crossover stenting and culottes stenting provided promising clinical and angiographic outcomes. Larger randomized trials are warranted to further re-evaluate these two techniques utilizing DES for treatment of true CBL.

CONFLICTS OF INTEREST

None declared.

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REFERENCES

1. Yamashita T, Nishida T, Adamian MG, et al. Bifurcation lesions: two stents versus one stent--immediate and follow-up results. *J Am Coll Cardiol* 2000;35:1145-51.
2. Al Suwaidi J, Berger PB, Rihal CS, et al. Immediate and long-term outcome of intracoronary stent implantation for true bifurcation lesions. *J Am Coll Cardiol* 2000;35:929-36.
3. Steigen TK, Maeng M, Wiseth R, et al. Randomized study on simple versus complex stenting of coronary artery bifurcation le-

sions: the Nordic bifurcation study. *Circulation* 2006;114:1955-61.
4. Colombo A, Bramucci E, Saccà S, et al. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: the CACTUS (Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting Stents) Study. *Circulation* 2009;119:71-8.
5. Hildick-Smith D, de Belder AJ, Cooter N, et al. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British Bifurcation Coronary Study: old, new, and evolving strategies. *Circulation* 2010;121:1235-43.
6. Murasato Y. Impact of three-dimensional characteristics of the left main coronary artery bifurcation on outcome of crush stenting. *Catheter Cardiovasc Interv* 2007;69:248-56.
7. Ormiston JA, Webster MW, El Jack S, et al. Drug-eluting stents for coronary bifurcations: bench testing of provisional side-branch strategies. *Catheter Cardiovasc Interv* 2006;67:49-55.
8. Erglis A, Kumsars I, Niemela M, et al. Randomized comparison of coronary bifurcation stenting with the crush versus the culottes technique using sirolimus eluting stents: the Nordic stent technique study. *Circ Cardiovasc Interv* 2009;2:27-34.
9. Lefevre T, Louvard Y, Morice MC, et al. Stenting of bifurcation lesions: classification, treatments, and results. *Catheter Cardiovasc Interv* 2000;49:274-83.
10. Medina A, Suarez de Lezo J, Pan M. A new classification of coronary bifurcation lesions. *Rev Esp Cardiol* 2006;59:183.
11. Hildick-Smith D, Lassen JF, Albiero R, et al. Consensus from the 5th European Bifurcation Club meeting. *EuroIntervention* 2010; 6:34-8.
12. Hoye A, Iakovou I, Ge L, et al. Long-term outcomes after stenting of bifurcation lesions with the "crush" technique: predictors of an adverse outcome. *J Am Coll Cardiol* 2006;47:1949-58.
13. Ge L, Airoldi F, Iakovou I, et al. Clinical and angiographic outcome after implantation of drug-eluting stents in bifurcation lesions with the crush stent technique: importance of final kissing balloon post-dilation. *J Am Coll Cardiol* 2005;46:613-20.
14. Niemelä M1, Kervinen K, Erglis A, et al. Randomized comparison of final kissing balloon dilatation versus no final kissing balloon dilatation in patients with coronary bifurcation lesions treated with main vessel stenting: the Nordic-Baltic Bifurcation Study III. *Circulation* 2011;123:79-86.
15. Hariki H, Shinke T, Otake H, et al. Potential benefit of final kissing balloon inflation after single stenting for the treatment of bifurcation lesions--insights from optical coherence tomography observations. *Circ J* 2013;77:1193-201.
16. Mylotte D, Hovasse T, Ziani A, et al. Non-compliant balloons for final kissing inflation in coronary bifurcation lesions treated with provisional side branch stenting: a pilot study. *Eurointervention* 2012;7:1162-9
17. Tsuchida K, Colombo A, Lefèvre T, et al. The clinical outcome of percutaneous treatment of bifurcation lesions in multivessel coronary artery disease with the sirolimus-eluting stent: insights from the Arterial Revascularization Therapies Study part II (ARTS II). *Eur Heart J* 2007;28:433-42.
18. Pan M, de Lezo JS, Medina A, et al. Rapamycin-eluting stents for the treatment of bifurcated coronary lesions: a randomized comparison of a simple versus complex strategy. *Am Heart J* 2004; 148:857-64.
19. Grube E, Dawkins K, Guagliumi G, et al. TAXUS VI final 5-year results: a multicentre, randomised trial comparing polymer-based moderate-release paclitaxel-eluting stent with a bare metal stent for treatment of long, complex coronary artery lesions. *EuroIntervention* 2009;4:572-7.
20. Nakazawa G, Finn AV, Vorpahl M, et al. Coronary responses and differential mechanisms of late stent thrombosis attributed to first-generation sirolimus- and paclitaxel-eluting stents. *J Am Coll Cardiol* 2011;57:390-8.
21. Nakagawa Y, Kimura T, Morimoto T, et al. Incidence and risk factors of late target lesion revascularization after sirolimus-eluting stent implantation (3-year follow-up of the j-Cypher Registry). *Am J Cardiol* 2010;106:329-36.