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Original article

Drug-Coated Balloon versus Provisional Percutaneous Transluminal Coronary Angioplasty to Side Branch in Bifurcation Lesions

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Abstract:

Background: Interventions involving coronary artery bifurcation lesions are technically demanding and have been historically linked with lower procedural success rates and poorer clinical outcomes compared to non-bifurcation lesions, necessitating specialized preparation and distinct expertise. This study aimed to contrast the application of drug-coated balloons with that of conventional balloons in the provisional stenting of coronary artery bifurcation lesions. **Methods:** The study is an interventional clinical trial . sixty participants who fulfilled the inclusion criteria were recruited into our study and divided into two categories: Group A: Patients who underwent provisional stenting using the traditional method with plain balloon angioplasty. Group B: Patients who underwent provisional stenting using a drug-coated balloon. Immediate patient outcomes were evaluated, and a clinical follow-up was conducted after six months to monitor for major adverse cardiac events. **Results:** Our study indicates that Drug-coated balloons (DCBs) have surfaced as a compelling therapeutic strategy in managing coronary bifurcation lesions. A substantial difference was noted between group A and group B to MACE after 6 months. The incidence of MACE was 28.6% (8 out of 30 patients) in group A, compared to 3.3% (1 patient) in group B, with a p-value of 0.02. However, no significant difference was observed between the two groups regarding in-hospital MACE in this study. The secondary endpoint of the study was defined as lesion success, and procedure success. **Conclusion:** our study highlighted the promising results of drug-coated balloons and their potential utilization in managing coronary artery bifurcation lesions.

Keywords: Drug-coated balloons; coronary bifurcation lesions; PCI .

Introduction

Cardiovascular Disease (CVD) has become the primary cause of death on a global scale, imposing a substantial burden on global health [(1)]. In Egypt, the World Health Organization (WHO) documented that in 2014, coronary artery disease (CAD) was responsible for 107,232 fatalities, which accounted for 23.14% of the total deaths in the country [(2)]. Percutaneous coronary intervention (PCI) is a minimally invasive surgical procedure commonly employed to treat atherosclerotic arteries. Specifically, a coronary bifurcation lesion is a lesion occurring at or near a significant division of a major epicardial vessel [(3)]**.** These lesions, involving a bifurcation with a mid-large size side-branch, constitute approximately 15-20% of all PCI cases and present a challenge for interventional cardiologists [(4)]**.** Although the introduction of the latest generation drug-eluting stents (DES) has improved outcomes for this complex lesion subset, certain issues such as stent thrombosis (ST) and loss of side branch (SB) continue to pose challenges [(5)]**.**

Provisional stenting is typically the preferred approach for managing these lesions; however, a considerable number of cases still experience side branch (SB) stenosis or occlusion, even with the utilization of a final kissing balloon inflation technique [(6)]**.** Drug-coated balloons (DCBs) have demonstrated promising potential as a technique for effectively addressing the challenges associated with treating bifurcation lesions [(7)]**.** PCI procedures are challenging in bifurcation lesions due to lower procedural success and poor outcomes.

Drug coated balloon (DCB) plays roles in not only preventing side branch (SB) from occlusion but also delivering anti-proliferative drug on the vessel wall so we investigated the visibility and efficiency of this strategy. This study aimed to compare the use of drug-coated balloons versus ordinary balloons in provisional stenting of coronary artery bifurcation lesions and its impact on the procedural success rate & short-term MACE. [(8)]

Patients and Methods

This is a randomized controlled trial conducted in the cardiology department - the Faculty of Medicine, Banha University, and National Heart Institute (NHI) 60 Patients were indicated for percutaneous coronary intervention either urgent or on an elective basis based on 2018 Myocardial revascularization guidelines of the European Society of Cardiology (ESC).

This study was done admitted at the Cardiology departments in Benha University, throughout the period from July 2022 till January 2024.

The inclusion criteria were patients with age above 18 years indicated for elective coronary angiography according to ESC 2018 guidelines with a bifurcation lesion affected Side branch (SB), who planned for provisional stenting technique from the start or shifted to 2-stent strategy as a bailout to the Side branch and Bifurcation lesion with medina classification (1,1,1), (1,0,1) and (0,1,1). **The angiographical exclusion criteria as** Medina classification (1,1,0),(0,1,0) or (1,0,0); Side branch less than 2 mm in diameter; Lesions with provisional stenting in which the side branch is not affected and does not need dilation; Patients who have multiple lesions with high syntax scores and clinical characteristics favouring coronary artery bypass grafting according to the latest ESC guidelines 2018 and Need for concomitant valvular surgery. **The clinical exclusion criteria were** Left ventricular ejection fraction of less than 30%; Intolerance to anti-platelet or anticoagulant drugs; Acute renal failure or severe kidney disease with creatinine clearance less than 30 ml /mins and Patient with severe concomitant systemic illness whose life expectancy is less than 1 year due to non-cardiac cause. Subjects were classified into 2 groups: Group A: 30 patients who

underwent provisional stenting using a standard technique with plain balloon angioplasty and Group B: 30 patients who underwent provisional stenting using Drug- coated balloon. The patients were randomly assigned for each group using a computer randomizing software application. All studied cases were subjected to Pre-procedural to the following: Detailed history taking, General &Physical examination, laboratory investigations and Echocardiography were done routinely for all patients.

The second phase was the interventional procedure including Angiographic analysis. Serial coronary angiography was performed at baseline (before and after intervention) and angiograms were obtained in multiple views after intracoronary nitrate if the coronary spasm was suspected. coronary angiograms were digitally recorded and analyzed by experienced personnel using a validated offline quantitative angiographic system and Medina classification was used for coronary bifurcation lesions (9).

- **Intervention:** Wire both branches, MV and SB, with two coronary guide wires, main branch pre-dilation, side branch dilation using (ordinary balloon in group "**A"** and Drug coated balloon in group "**B"** for the side branch), main vessel stenting and proximal optimization technique (POT) of the main vessel stent. **Figure 1.**

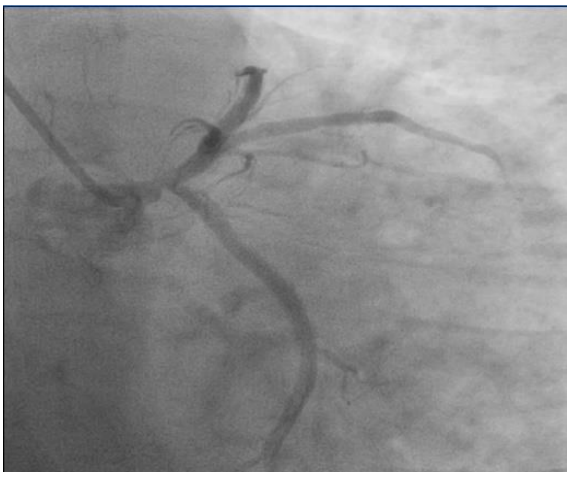

Figure (1): An image illustrating a bifurcation lesion that is affecting the left main artery (LM), the left anterior descending artery (LAD), and the left circumflex artery (LC).

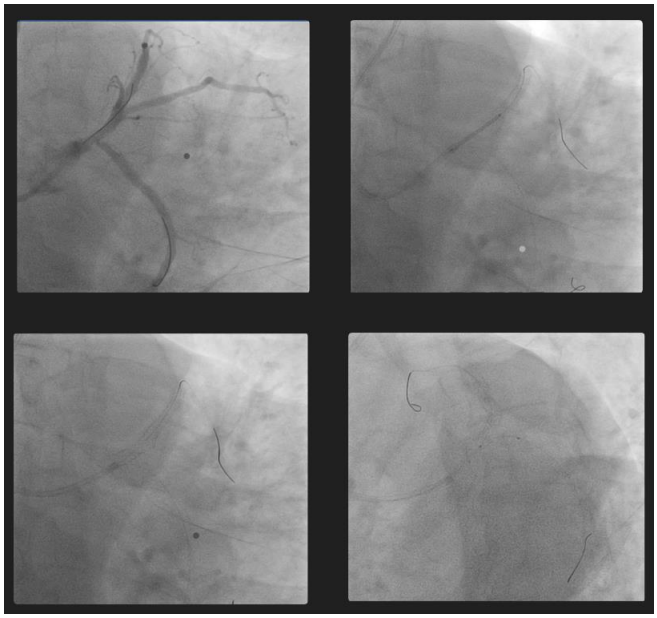

Figure (2): A picture depicting phases of provisional stenting using drug-coated balloons in a side branch. these images were obtained from one of the patients participating in the study.

After Intervention: reference luminal diameter (mm), minimal luminal diameter in-stent (mm), minimal luminal diameter in the lesion (mm), lesion success (Achievement of >50% residual stenosis of the target lesion, as measured by quantitative coronary angiographic analysis) and procedure success (Achievement of a final lesion success and no major angiographic complications such as dissection or perforation). Post-procedural, medications were prescribed according to 2018 ESC myocardial revascularisation guidelines according to bleeding and ischemic risk assessed by DAPT and precise- DAPT scores for the duration and types of dual antiplatelet therapy, and minor modifications in regimen and duration will be applied for some patients according to standard practice guided by the latest ESC 2018 guidelines. (10). Patients were assessed and monitored for 24 hours after the procedure and in the outpatient clinic after 6 months (single visit), followed up clinically after 6 months for MACEs. The primary target is a 6-month follow-up for MACEs (major adverse cardiac events). The secondary endpoints included lesion success and procedure success. occurrence of any complication to the side branch aborting the procedure and shifting to standard 2-stent techniques. **Figure 2.**

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Statistical analysis

Statistical analysis was done by SPSS v28 (IBM©, Armonk, NY, USA). Quantitative parametric data were presented as mean and standard deviation (SD) and were analysed by unpaired student t-test. Qualitative variables were presented as frequency (%) and analysed using the Chi-square test. A two-tailed P value < 0.05 was considered statistically significant

Results

The study groups were comparable as regards socio-demographic and clinical data (P>0.05), table (1). Most of the patients had sinus rhythm while 53.3% were presenting with CCS in group (A) compared to 60.0% in group (B). Also, most of them had two vessels affection and were 1,1,1 Medina classification 53.3% versus 70.0% in group (A) versus group (B) and LAD was the vessel stented first in 80.0% compared to 66.7% in the group (A) versus group (B) the difference between the studied groups were not statistically significant (p>0.05) and showed that there was no statistical significance between studied groups as regard the laboratory findings (p>0.05). table (2)

The angiographic characteristics of group (A) and group (B) showed no statistical significance in terms of the main branch maximum balloon size used for pre-dilation, inflation pressure, or type of drug-eluting stent (DES) used in bifurcation lesions shown in table (2)

Table (1): Baseline sociodemographic and clinical characteristics.

	Group (A) N=30	Group (B) N=30	Test of significant	P
Age (years)	60.5 ±7.2	61.1±7.6	0.29	0.77
Male, n(%)	23 (76.7%)	22(73.3%)	0.09	0.76
Current smoker, n (%)	14 (46.7%)	12 (40.0%)	0.27	0.60
Dyslipidemia, n (%)	22 (73.3%)	24(80.0%)	0.37	0.54
Hypertension, n (%)	18 (60.0%)	19 (63.3%)	0.07	0.79
Diabetes mellitus, n(%)	13 (43.3%)	12(40.0%)	0.07	0.79
Family history, n(%)	14(46.7%)	16(53.3%)	0.27	0.60
Prior MI , n(%)	9 (30.0%)	8(26.7%)	0.08	0.77
Prior CABG, n(%)	1(3.3%)	1(3.3%)	0.00	1.00
CKD , n (%)	2(6.7%)	3(10.0%)	0.00	1.00
PAD , n (%)	2(6.7%)	1(3.3%)	0.00	1.00

Table (2): ECG rhythm, presentation, number of vessels effected, Medina classification and laboratory data and Comparison between the studied groups regarding main branch balloon and stent data.

	Group (A) n=30	**Group (B) n=30**	$x2$	**P**
-ECG rhythm				
Sinus	27 (90.0%)	25 (83.3%)	0.14	0.7
AF	3 (10.0%)	5 (16.7)		
-Presentation				
CCS	16 (53.3%)	18 (60.0%)		
NSTEMI	10 (33.3%)	7 (23.3%)	3.45	0.32
STEMI	3 (10.0%)	1 (3.3%)		
Unstable Angina	1 (3.3%)	4 (13.3%)		
-Number of vessel affected				
Two	20 (66.7%)	19 (63.3%)	0.07	0.78
Three	10 (33.3%)	11 (36.7%)		
-Medina				
1,1,1	16 (53.3%)	21 (70.0%)		
1,0,1	7 (23.3%)	3 (10.0%)	2.35	0.3
0,1,1	7 (23.3%)	6 (20.0%)		
-Vessel stented first				
LAD	24 (80.0%)	20 (66.7%)		
LCX	2 (6.7%)	5 (16.7%)	2.65	0.44
RCA	2 (6.7%)	4 (13.3%)		
OM	2 (6.7%)	1 (3.3%)		
HB	11.8 ± 1.45	11.4 ± 1.3	1.4	0.14
HbA1c	7.5 ± 1.9	7.4 ± 1.6	0.1	0.9
Creatinine	1.5 ± 0.4	1.3 ± 0.75	1.85	0.06
Troponin	0.094 ± 0.38	0.012 ± 0.026	1.16	0.24
LDL	104.6 ± 31.5	107.1 ± 38.8	0.25	0.79

		Group(A) No. = 30	**Group(B) No. = 30**	**Test value**	**P-value**	**Sig.**
Main branch maximum balloon size	**Mean ± SD**	2.96 ± 0.67	3.01 ± 0.46	0.59	0.55	NS
	Range	2 – 5	2.5 – 4.5			
Main branch balloon length (mm)	**Mean ± SD**	16.4 ± 4.8	16 ± 4.5	0.62	0.53	NS
	Range	2 – 20	10 – 25			
Maximum inflation pressure	**Mean ± SD**	16.2 ±2.50	15.36±2.57	1.4	0.16	NS
	Range	12 – 22	12 – 18			
Main branch -Type of drug-eluting stent	**Ultimaster**	6 (20.0%)	8 (26.7%)	0.6	0.87	NS
	Resolute onynx	10 (33.3%)	9 (30.0%)			
	Xinece alpine	11 (36.7%)	9 (30.0%)			
	Promus	3 (10.0%)	4 (13.3%)			
Number of stents used main branch	**1**	24 (80.0%)	25 (83.3%)	0.11	0.73	NS
	2	6 (20.0%)	5 (16.7%)			

The comparison between group (A) and group (B) showed no statistical significance in the size of the drug-eluting stent (DES) involved in bifurcation lesions. Additionally, there were no statistically significant differences in the term of inflation time, DES size or length. Also, there was no statistical significance between the two groups in terms of TIMI flow in the side branch after the main branch stent, the need for GPIIb/IIIa inhibitor or minimal lumen diameter in a stent in both groups demonstrated in Table (3)

There was a statistically significant difference between group (B) and group (A) in terms of the need for a stent in the side branch using the TAP technique, either because of compromised flow in the side branch less than TIMI III flow or compromised ostium more than 70% stenosis. Specifically, 6 patients from the studied 30 patients in group (A) needed a stent for the side branch, while no patients in group (B) required a stent shown in Figure (3)

Table 4 presents a statistically significant difference between group (A) and group (B) in terms of the fluoroscopy time needed for all interventions, including target lesions and other vascularized vessels. There was no statistical significance between the studied groups in terms of in-hospital MACE. After 6 months, The results indicate that there was a statistical significance between group (A) and group (B) in terms of the late lumen gain, specifically, the mean late lumen gain in group (B) was 0.9 mm with a standard deviation of 0.2, while the mean late lumen gain in the group (A) was -0.13 mm with a standard deviation of 0.3. All measurements were done and analyzed by expert personnel using offline Quantitative Coronary Analysis (QCA) as shown in Table 4.

Table (3): Comparison between the studied groups regarding main and side branch results after intervention and the fluoroscopy time.

		Group (A)	Group (B)	Test value	P-value	Sig.
		No. = 30	**No. = 30**			
Size of DES used in main branch bifurcation	**Mean±SD**	3.5 ± 0.4	3.6 ± 0.65	1.01	0.31	NS
	Range	2.5 – 4	2.5 – 5			
DES length	**Mean±SD**	30.6± 8.77	27.8 ± 8.9	1.2	0.22	NS
	Range	18 – 48	12 – 48			
Inflation time (sec.)	**Mean±SD**	33.1 ± 5.6	33 ± 6.2	0.1	0.9	NS
	Range	25 – 45	20 – 45			
Diameter of stent after inflation	**Mean±SD**	3.6 ± 0.37	3.70 ± 0.7	0.74	0.45	NS
	Range	2.75 – 4.2	2.5 – 6			
TIMI flow in side vessel after 1st stent	**TIMI I**	2 (6.7%)	0 (0.0%)	3.16	0.2	NS
	TIMI II	1 (3.3%)	0 (0%)			
	TIMI III	27 (90%)	30(100.0%)			
GPbII/aIII inhibitor.	**Not used**	28 (93.3%)	29 (96.7%)	0.0	1.0	NS
	Used (bailout)	2 (6.7%)	1 (3.3%)			
Need of stent in side branch	**No**	24(80.0%)	30(100.0%)	4.63	0.03	S
	Yes	6 (20.0%)	0 (0.0%)			
After intervention minimal luminal diameter in stent	**Mean ± SD**	3.54±0.36	3.59 ± 0.74	0.26	0.79	NS
	Range	2.55 – 4.4	2.5 – 5.58			
Fluoroscopy time (min).	**Mean±SD**	69.26±28.10	54.00±26.7	2.15	0.03	S
	Range	27 – 133	18 – 110			

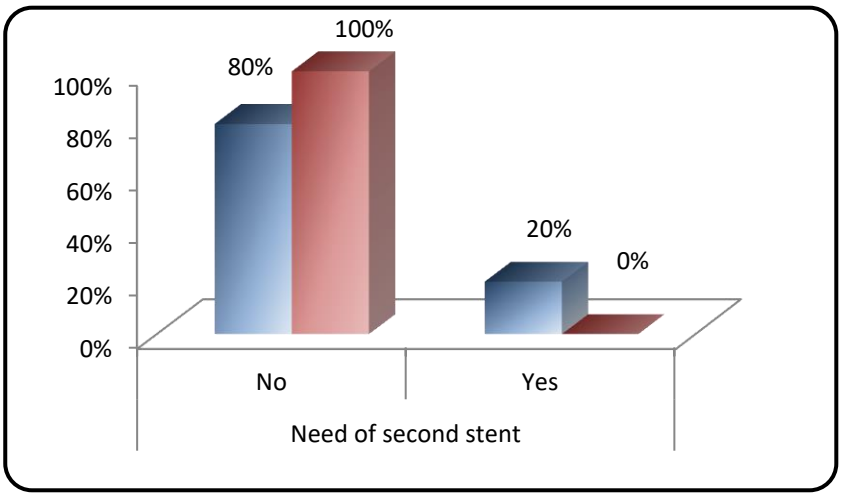

Figure (3): Comparison between group (A) and group (B) regarding need of second stent of the studied patients.

Table (4): Comparison between the studied groups regarding in-hospital MI, stent thrombosis, EF and in-hospital MACE among the studied patients and Comparison between the studied groups regarding outcome after 6 months and complications.

		Group(A) No. = 30	Group(B) No. = 30	Test value	P-value	Sig.
In-hospital death	**No**	29 (96.7%)	30 (100.0%)	0.0	1.0	NS
	Yes	1 (3.3%)	0 (0.0%)			
CV mortality	**No**	29 (96.7%)	30 (100.0%)	0.0	1.0	NS
	Yes	1 (3.3%)	0 (0.0%)			
Stroke(type)	**No**	30 (100.0%)	30 (100.0%)	–	–	–
	Yes	0 (0.0%)	0 (0.0%)			
In-hospital MI	**No**	28 (93.3%)	30 (100.0%)	0.52	0.47	NS
	Yes	2 (6.7%)	0 (0.0%)			
Stent thrombosis (occlusion more than 50%)	**No**	29 (96.7%)	30 (100.0%)	0.0	1.0	NS
	Yes	1 (3.3%)	0 (0.0%)			
EF	**Mean± SD**	52.90±9.30	52.69±9.72	0.087•	0.931	NS
	Range	35 – 68	35 – 68			
In-hospital MACE	**No**	28 (93.3%)	30 (100.0%)	0.52	0.47	NS
	Yes	2 (6.7%)	0 (0.0%)			
		Group(A) No. = 28	**Group(B) No. = 30**	**Test value**	**P-value**	**Sig.**
MPI after 6 months	**No ischemia**	18(64.3%)	19(63.3%)	1.25	0.74	NS
	No MPI	6 (21.4%)	8 (26.7%)			
	Ischemia not related to target vessel	3 (10.7%)	3 (10.0%)			
	Ischemia related to target vessel	1 (3.6%)	0 (0.0%)			
Need for CA	**No**	20 (71.4%)	23(76.7%)	0.21	0.64	NS
	Yes	8 (28.6%)	7 (23.3%)			
After 6 month- Death	**No**	27 (96.4%)	30 (100.0%)	0.001	0.97	NS
	Yes	1 (3.6%)	0 (0.0%)			
After 6 month - nonfatal MI	**No**	26 (94.7%)	29(96.7%)	0.069*	0.792	NS
	Yes	2 (5.3%)	1 (3.3%)			
After 6 month-Stroke(type)	**No**	25 (89.3%)	30(100.0%)	1.56	0.21	NS
	Yes	3 (10.7%)	0 (0.0%)			
MACE after 6 months	**No**	20 (71.4%)	29(96.7%)	5.2	0.02	S
	Yes	8 (28.6%)	1 (3.3%)			

Discussion

Bifurcation lesions account for up to 20% of total percutaneous coronary intervention (PCI) procedures, which is challenging due to its lower procedural success and poor outcomes. Recently drug coated balloon (DCB) improving SB outcomes attracts striking attention in bifurcation lesions. [10] . Drug-coated balloons have led to an overall improvement in outcomes. However, the loss of side branches and major adverse cardiac events (MACE) remain a significant concern. Therefore, it is necessary to develop appropriate cardioprotective strategies to limit the side effects of bifurcation lesions revascularization and establish the best revascularization strategy [3]. DCBs significantly reduce target lesion revascularization (TLR), major adverse cardiac events (MACE), and stent thrombosis compared to conventional balloon angioplasty. However, further randomized controlled trials are warranted to define better the optimal use, patient selection, and long-term outcomes associated with DCB deployment. Through ongoing research and technological advancements, DCBs have the potential to revolutionize the field of interventional cardiology and improve patient outcomes [11].

The PEPCAD V pilot study, a preliminary investigation conducted in 2011, demonstrated that the use of drug-coated balloons (DCBs) in treating severe bifurcation disease was entirely successful at the 9-month mark, particularly when employed as standalone procedures, thereby avoiding the need for side branch stenting [12]. However, the results of a subsequent randomized trial by Stella et al., [13] were less positive, potentially due to the use of a matrix-free DCB. Matrix-free DCBs are inferior to DCBs that include an excipient in addition to the drug, which facilitates the rapid absorption of paclitaxel into the vascular wall.

Other researchers have studied DCB angioplasty in bifurcations following provisional stenting of the MB with a subsequent kissing balloon or provisional T-stenting. For instance, Sgueglia et al., [14] assessed the feasibility of using second-generation DCB following provisional bare-metal stent (BMS) in the treatment of coronary bifurcation lesions in 14 patients who had contraindications to drug-eluting stents. All patients achieved angiographic and procedural success, and at a mean follow-up of 234±81 days, all patients were asymptomatic and free from major adverse cardiac events (MACE).

In the BABILON trial, [15] proposed that paclitaxel drug-eluting balloons could be a viable option to reduce side-branch restenosis in bifurcation lesions. They compared angiographic and clinical outcomes with DCB plus BMS versus drug-eluting stents (DES) in de novo bifurcated lesions. While the in-segment LLL in the MB was higher in the DCB group compared to the DES group, the difference was not statistically significant. However, significant differences were found in the MB in-segment restenosis, with better results in the DES group. No differences were found between groups in the case of the side branch, and positive remodelling in the side branch ostium was observed in both groups.

In a single-armed pilot study by Schulz et al., [16] a total of 39 patients were treated with DCB-only in de novo bifurcation lesions, including left main (LM) bifurcations. They concluded that the DCB-only strategy in selected patients was associated with a low 4-month MACE rate (7.7%).

The current study included a total of 60 patients who were indicated for elective coronary angiography according to ESC 2018 guidelines with a bifurcation lesion and affected Side branch (SB)size of more than 2 mm, patients were randomly assigned into two groups, group (A) (30 patients) patient Who underwent provisional stenting using standard technique with plain balloon angioplasty Interventional group (30 patients) Who

underwent provisional stenting using Drug coated balloon in the side branch.

Both group (A) and group (B) were similar in age (60.5 ± 7.2 years and 61.1 ± 7.6 years, respectively). There was no statistically significant difference between the two groups regarding the prevalence of diabetes mellitus, hypertension, chronic kidney disease, dyslipidaemia, and family history. No differences were observed between the two groups in terms of baseline HB levels or baseline LDL levels.

The distribution of bifurcation as Medina classification was not significantly different between group (A) and group (B). The group (A) had 53.3% of bifurcations represented as (1,1,1), 23.3% as (1,0,1), and 23,3% as (0,1,1). Group (B) had 70% of bifurcations represented as (1,1,1), 10% as (1,0,1), and 20% as (0,1,1).

A significant difference was observed between group (A) and group (B) in terms of the minimal luminal diameter in the side branch lesion after intervention. despite the lack of a substantial difference between the two groups in the reference diameter.

A meta-analysis was performed by *Jiang and Liu* [17] to assess the results of using a drug-coated balloon (DCB) as opposed to an uncoated balloon (UCB) for side branch (SB) protection during a procedure. The analysis encompassed 803 patients from seven studies who underwent provisional stenting using DES, with a follow-up period of 6 to 12 months. The findings indicated that SB protection with DCB resulted in a reduced degree of postoperative diameter stenosis compared to those with UCB.

A significant disparity was observed between the studied groups in terms of Fluoroscopy time, this discrepancy could be attributed to the necessity of transitioning to a two-stent strategy (TAP technique) in approximately 20% of the group (A).

The study's primary endpoint was the occurrence of major adverse cardiac events (MACEs), including death, non-fatal myocardial infarction, target lesion revascularization (TLR), and stroke, at a 6-month follow-up. A significant difference was observed between group (B) and group (A) in terms of MACE after 6 months. The incidence of MACE was 28.6% (8 out of 30 patients) in the group (A), compared to only 3.3% (1 patient) in the group (B), with a p-value of 0.039. However, no significant difference was found between the two groups concerning in-hospital MACE in this study.

Our study results are concordant with the study conducted by Zheng et al., [7] study examined the effect of a drug-coated balloon (DCB) in side branch protection for de novo coronary bifurcated lesions (CBL). The study included 10 studies with 934 patients. The meta-analysis results of angiographic outcomes suggested that DCB group had less side branch late lumen loss (LLL), diameter stenosis (DS) and binary restenosis (BR) and the higher minimum lumen diameter (MLD) compared with a non-drug-coated balloon (NDCB) group at follow-up ($P < 0.05$).

A discrepancy was observed in the incidence of Major Adverse Cardiovascular Events (MACE) between the present study and the research by Megaly et al., [18]. The authors searched for studies that compared drug-coated balloon (DCB) and non-drug-coated balloon angioplasty (BA) in the treatment of the side branch (SB) in coronary bifurcation lesions. They evaluated the outcomes of SB late lumen loss, SB binary restenosis, and target-lesion revascularization.

They found no significant difference between DCB and BA in terms of major adverse cardiac events (MACE) or other outcomes.

Furthermore, as demonstrated in the study by Megaly et al., [19], a meta-analysis of five RCTs with 1459 patients (734 treated with DCB and 725 with DES) was conducted to evaluate the outcomes of DCB and DES in de-novo small vessel coronary artery disease. After a median follow-up period of 12 months, both treatment methods showed comparable risks of MACE, all-cause mortality, TLR,

and TVR. However, the use of DCBs was associated with a reduced risk of MI compared to DES. In a sub-study of the HYPER trial by Pellegrini et al., [20], a prospective, single-arm, multi-centre pilot study was conducted to assess the feasibility, safety, and efficacy of a hybrid approach. This approach combined a drug-coated balloon (DCB) and a new generation drug-eluting stent (DES) for treating coronary bifurcation lesions. The hybrid strategy involved implanting a new generation DES in the main branch and inflating a DCB for treating the side branch lesion. The procedure was successful in 96% of cases. This partially aligns with the findings of the study conducted by Li et al., [21]. The study's objective was to compare the effects of paclitaxel-coated balloons (PCBs) and conventional balloons (CBs) on side branch (SB) lesions and major adverse cardiovascular outcomes in patients presenting with de novo true bifurcation lesions. The study found no significant differences in the diameter, minimum lumen diameter (MLD), and stenosis for bifurcation lesions between the two groups before and immediately after percutaneous coronary intervention (PCI). However, after 12 months, the PCB group demonstrated a higher SB-Minimal lumen diameter (MLD) and lower SB-LLL compared to the CB group. Moreover, the group treated with paclitaxel-coated balloons exhibited a lower risk of MACE than the CB group. The study by Yamamoto et al., [22] provides valuable insights into the mechanisms and predictive factors associated with late lumen gain, a clinical advantage observed in patients with de novo coronary artery disease undergoing treatment with drug-coated balloons (DCB). A clinical expert consensus document from the Japanese Association of Cardiovascular Intervention and Therapeutics provided practical guidelines on the indications, techniques, and management of DCBs for coronary artery disease (CAD), inclusive of bifurcation lesions. The document endorsed DCBs as a viable option for side branch (SB) treatment in bifurcations, particularly when provisional stenting is planned or when the SB diameter is less than 2.5 mm. The document also proposed that DCBs could be employed for main branch (MB) treatment in bifurcations, either alone or in conjunction with a drug-eluting stent (DES) or a bioresorbable scaffold, contingent on lesion characteristics and operator preference. The document recommended that DCBs should be inflated for a minimum of 30 seconds to ensure sufficient drug transfer and that post-dilation with a non-drug-coated balloon should be performed if residual stenosis exceeds 30% or if dissection is present [23].

Despite the promising potential of DCBs, several limitations persist. The optimal drug, dosage, and coating formulation are still subjects of ongoing research. Furthermore, the long-term safety and efficacy of DCBs in comparison to newer-generation DES require further investigation. Additionally, the cost-effectiveness of this technology in routine clinical practice remains a consideration. Other important considerations include the heterogeneity of study designs, patient populations, and the variety of DCB types used, which may influence the generalizability and comparability of study outcomes.

Future research should strive to clarify the ideal patient and bifurcation characteristics for DCB therapy, as well as incorporate them into current guidelines. The effectiveness of DCBs in CAD management could be enhanced by refined coating technologies, innovative drug combinations, and personalized medicine approaches.

Conclusion

The application of drug-coated balloons in provisional stenting for coronary artery bifurcation lesions is feasible and acceptable in short-term follow-up. DCB

demonstrated superiority over conventional balloons in terms of short-term major adverse cardiac events (MACE). It could decrease SB-LLL and MACE risk and DCB exhibited non-inferiority concerning lesion or procedural success.

References

1. Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SKBM, AlKatheeri R, et al. Global epidemiology of ischemic heart disease: results from the global burden of disease study. Cureus. 2020;12(7).
2. World Health Organization (WHO). Country statistics and global health estimates. Geneva Switzerland: World Health Organization; 2015.
3. Yang H, Song Y, Cao J, Chen J, Zhang F, Huang Z, et al. A novel hybrid strategy of drug coated balloon and stent for coronary bifurcation lesions. Scand Cardiovasc J. 2023;57(1):2161620. https://doi.org/10.1080/14017431.2022.2161620
4. Wassef AWA, Liu S, Yanagawa B, Verma S, Cheema AN. Percutaneous management of coronary bifurcation lesions: Current perspective. Curr Opin Cardiol. 2020;35(5):574–582. doi:10.1097/hco.0000000000000775
5. Zilio F, Verdoia M, De Angelis MC, Zucchelli F, Borghesi M, Rognoni A, et al. Drug Coated Balloon in the Treatment of De Novo Coronary Artery Disease: A Narrative Review. J Clin Med. 2023;12(11):3662.
6. 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(16):1307–1317. doi:10.4244/eij-d-20-00169
7. Zheng Y, Li J, Wang L, Yu P, Shi H, Wu L, et al. Effect of drug-coated balloon in side branch protection for de novo coronary bifurcation lesions: a systematic review and meta-analysis. Front Cardiovasc Med. 2021;8:758560.
8. Megaly M, Buda KG, Xenogiannis I, Vemmou E, Nikolakopoulos I, Saad M, et al. Systematic review and meta-analysis of short-term outcomes with drug-coated balloons vs. stenting in acute myocardial infarction. Cardiovasc Interv Ther. 2020;1-9.
9. Medina A, de Lezo JS, Pan M. A new classification of coronary bifurcation lesions. Rev Esp Cardiol. 2006;59(2):183.
10. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39(2):119–177. https://doi.org/10.1093/eurheartj/ehx393
11. Aedma SK, Naik A, Kanmanthareddy A. Coronary Bifurcation Stenting: Review of Current Techniques and Evidence. Curr Cardiol Rev. 2023;19(1). https://doi.org/10.2174/1573403X18666220406113517
12. Mathey DG, Wendig I, Boxberger M, Bonaventura K, Kleber FX. Treatment of bifurcation lesions with a drug-eluting balloon: the PEPCAD V (Paclitaxel Eluting PTCA Balloon in Coronary Artery Disease) trial. EuroIntervention. 2011;7(Suppl K)–K65. https://doi.org/10.4244/EIJV7SKA11
13. Stella PR, Belkacemi A, Dubois C, Nathoe H, Dens J, Naber C, et al. A multicenter randomized comparison of drug-eluting balloon plus bare-metal stent versus bare-metal stent versus drug-eluting stent in bifurcation lesions treated with a single-stenting technique: Six-month angiographic and 12-month clinical results of the drug-eluting balloon in bifurcations trial. Catheter Cardiovasc Interv. 2012;80(7):1138-1146.
14. Sgueglia GA, Todaro D, Bisciglia A, Conte M, Stipo A, Pucci E. Kissing inflation is feasible with all second-generation drug-eluting balloons. Cardiovasc Revasc Med. 2011;12(5):280-285.
15. Alfonso F, Byrne RA. Limus-coated balloons in “de novo” coronary lesions. JACC Cardiovasc Interv. 2022;15(12):1227–1230. doi:10.1016/j.jcin.2022.04.011
16. Schulz A, Hauschild T, Kleber FX. Treatment of coronary de novo bifurcation lesions with DCB only strategy. Clin Res Cardiol. 2014;103:451-456.
17. Jiang ZM, Liu L. Drug-Coated versus Uncoated Balloon for Side Branch Protection in Coronary Bifurcation Lesions Treated with Provisional Stenting Using Drug-Eluting Stents: A Meta-analysis. Int J Clin Pract. 2022;2022:1–10. doi:10.1155/2022/5892589.
18. Megaly M, Michael Rofael MD, Saad M, Shishehbor M, Brilakis ES. Outcomes with drug-coated balloons for treating the side branch of coronary bifurcation lesions. J Invasive Cardiol. 2018;30(11).
19. Megaly M, Buda K, Saad M, Tawadros M, Elbadawi A, Basir M, et al. Outcomes with

drug-coated balloons vs. drug-eluting stents in small-vessel coronary artery disease. Cardiovasc Revasc Med. 2022;35:76-82.
20. Pellegrini D, Donahue M, Regazzoli D, Tedeschi D, Loffi M, Pellicano M, et al. Drug-coated balloon combined with drug-eluting stent for the treatment of coronary bifurcation lesions: insights from the HYPER study. Eur Heart J Suppl. 2023;25(Supplement_C)
21. Li Y, Mao Q, Liu H, Zhou D, Zhao J. Effect of paclitaxel-coated balloon angioplasty on side branch lesion and cardiovascular outcomes in patients with de novo true coronary bifurcation lesions undergoing percutaneous coronary intervention. Cardiovasc Drugs Ther. 2021;1-8.
22. Yamamoto T, Sawada T, Uzu K, Takaya T, Kawai H, Yasaka Y. Possible mechanism of late lumen enlargement after treatment for de novo coronary lesions with drug-coated balloon. Int J Cardiol. 2020;321:30-37.
23. Jeger RV, Eccleshall S, Ahmad WAW, Ge J, Poerner TC, Shin ES, et al. Drug-coated balloons for coronary artery disease: third report of the International DCB Consensus Group. JACC Cardiovasc Interv. 2020;13(12):1391-1402.

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