

## Comparison of Sequential POT-Side-POT and Kissing Balloon Techniques in Patients with Coronary Bifurcation Lesions Treated with Single-Stent Strategy; Which One is Simple and Safe? Propensity Score Analysis

ORIGINAL INVESTIGATION

### ABSTRACT

**Background:** It is unknown whether the novel POT-side-POT technique is more useful than the commonly preferred kissing balloon inflation in patients with non-complex coronary bifurcation lesions treated with a single-stent strategy. The aim of this study was to compare the efficacy of POT-side-POT and kissing balloon inflation techniques in one-stent strategy for non-complex coronary bifurcation lesions.

**Methods:** In this study, 283 patients were retrospectively analyzed (POT-side-POT group, n=149; KBI group, n=134). Primary endpoints of the study were defined as follows: in-hospital and 30-day mortality, contrast-induced acute kidney injury, stent thrombosis, side branch dissection, and need for side-branch stenting. Characteristics of patients at baseline were balanced by using propensity score inverse probability weighting.

**Results:** Procedure time (minute,  $30.6 \pm 8.5$  vs.  $34.3 \pm 11.6$ ;  $P=.003$ ) and contrast volume (milliliter,  $153.7 \pm 42.4$  vs.  $171.1 \pm 58.2$ ;  $P=.004$ ) were significantly lower in POT-side-POT group. Besides, side branch residual stenosis and number of patients with >50% side branch residual stenosis remained significantly higher in POT-side-POT group both in general and true bifurcation subgroup analysis ( $20.3 \pm 19.8\%$  vs.  $16.5 \pm 16.4\%$ ,  $P=.022$ ;  $11.9\%$  vs.  $5.7\%$ ,  $P=.013$  and  $24.1 \pm 23.2\%$  vs.  $18.8 \pm 18.7\%$ ,  $P=.033$ ;  $17.6\%$  vs.  $6.6\%$ ,  $P=.005$ ; respectively). Combined clinical adverse outcomes were similar between groups. Side branch dissection ( $10.2\%$  vs.  $20.1\%$ ,  $P=.001$ ) and need for side branch stenting ( $12.6\%$  vs.  $19\%$ ,  $P=.040$ ) reached statistically significance in kissing balloon inflation group after adjustment.

**Conclusion:** POT-side-POT may be a simple and safe technique with a shorter procedure time and lower incidence of adverse clinical events in non-complex coronary bifurcation lesions treated with single-stent strategy.

**Keywords:** Coronary bifurcation lesions, POT-side-POT, kissing balloon inflation, single-stent strategy

### INTRODUCTION

Coronary bifurcations are the primary sites of atherosclerosis and constitute approximately 15%-20% of percutaneous coronary interventions (PCIs).<sup>1</sup> Coronary bifurcation lesions (CBL) are commonly related to complex revascularization procedures and are associated with high complication rates and procedural costs compared to PCI of simple coronary lesions.<sup>2</sup>

The effectiveness of proposed strategies for bifurcation stenting remains controversial. According to the 15<sup>th</sup> Consensus Document from the European Bifurcation Club,<sup>3</sup> "keep it simple and safe" approach has emerged as the recommended bifurcation treatment strategy. In many recent data, provisional stenting had strongly been recommended as first-line therapy for CBL, because simultaneous deployment of stents in both the main vessel (MV) and a side branch (SB) had clearly demonstrated no additional clinical benefit over stenting of the MV only.<sup>4-7</sup> Thus, it may be reasonable to prefer 2-stent techniques only for

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**Received:** October 6, 2021

**Accepted:** March 11, 2022

**Available Online Date:** May 13, 2022

**Cite this article as:** Çetinkal G, Balaban Koçaş B, Keskin K, Kilci H, Ser ÖS, Kılıçkesmez K. Comparison of sequential POT-side-POT and kissing balloon techniques in patients with coronary bifurcation lesions treated with single-stent strategy; Which one is simple and safe? propensity score analysis. *Anatol J Cardiol.* 2022;26(7):559-566.



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DOI:10.5152/AnatolJCardiol.2022.1136

patients with complex CBL before starting the procedure. As most of the bifurcation lesions that we encounter do not involve complex anatomy, the single-stent strategy is more frequently used in daily practice.

Since the early 2000s, kissing balloon inflation (KBI) has been the most widely used technique in provisional single stenting, but its validation has not been demonstrated clinically or by bench tests.<sup>9</sup> In several studies, the weaknesses of the KBI technique have been listed as follows: inducing a major oval distortion in the proximal part of the MV, longer procedure time, increased use of contrast media, and higher incidence of procedure-related myocardial infarction.<sup>5,6</sup> The novel 3-step technique, called POT-side-POT, has superior results from bench testing to randomized, controlled trials by preserving the ellipticity of the proximal part of the MV stent and restoring ideal bifurcation anatomy.<sup>9,10</sup> Besides its simplicity and efficacy, shorter procedure time and low cost have made it a more preferred technique in simple CBL.

Over the years, it has clearly emerged that KBI is the most widely preferred and routinely applied approach during single stenting. However, it is unknown whether the new sequential strategy called POT-side-POT is much more effective and reliable than KBI in patients with CBL treated with single-stent strategy. Due to the lack of data regarding direct comparison of the 2 techniques, we aimed to compare the clinical and angiographic properties of 2 strategies in single-stent provisional stenting.

## METHODS

The present single-center clinical study was based on a retrospective design and aimed to compare the POT-side-POT technique with KBI in terms of safety and efficacy in provisional stenting of CBL. A total of 283 patients with bifurcation lesions admitted for PCI between October 2018 and October 2020 were enrolled in our study. The MV diameter had to be  $\geq 2.5$  mm and the SB diameter had to be  $\geq 2$  mm by visual evaluation for inclusion. Revascularization strategies other than provisional stenting, provisional stenting without SB intervention, SB lesion length  $> 5$  mm, indications for coronary or valvular surgery, contraindications to use dual antiplatelet therapy, and poor life expectancy ( $< 1$  year) were defined as exclusion criteria. Also, patients who

were pregnant or under 18 years of age were not eligible for our study. This study complied with the edicts of the 1975 Declaration of Helsinki and was approved by the Local Ethics Committee.

Provisional stenting was the initial strategy for all CBL. Decision to perform SB intervention was held in the case of a critical lesion ( $> 70\%$  stenosis) or flow impairment in the SB following the stent implantation to MV. All patients undergone provisional stenting with SB intervention, and the preference between KBI or POT-side-POT techniques was performed according to the operator's discretion. Side branch was treated with the T and small protrusion (TAP) or T-stent techniques in case of a critical SB stenosis or thrombolysis in myocardial infarction (TIMI)-flow  $< \text{grade } 3$  after final proximal optimization technique (POT) and/or SB dissection.

The 3-step novel technique, POT-side-POT, was fully performed by initial POT, SB opening, and final POT. Initial POT was performed via positioning the balloon with the distal marker at the carina point under fluoroscopy, and both compliant and non-compliant (NC) balloons were sized according to the diameter of the MV. In the second (SB opening) step, NC balloons adopted to the SB diameter were used. Lastly, final POT was implemented the same as the initial POT.

Kissing balloon inflation technique was started with initial POT in order to facilitate SB rewiring, following simultaneously dilatation of 2 juxtapositioned NC balloons sized to the SB and distal MV at nominal pressure. Final POT was done the same as mentioned above.

All patients were given 300 mg of aspirin before the procedure if they were not received previously. Also, patients received a loading dose of 300-600 mg clopidogrel for stable coronary artery disease (CAD) and 180 mg of ticagrelor for acute coronary syndromes (ACS) unless they were on long-term treatment. This resulted in 125 patients (44.2%) treated with clopidogrel and 158 patients (55.8%) treated with ticagrelor, respectively. In the catheterization laboratory, heparin was administered and glycoprotein receptor inhibitors were used according to the operators' preference. Lifelong aspirin (81-100 mg/day) and clopidogrel (75 mg/day) or ticagrelor (90 mg twice a day) for 12 months were recommended after the procedure. The high percentage of stents used in our study group is everolimus-eluting (Xience Pro-X, Abbott Vascular, Santa Clara, Calif, USA) stents at a percentage of 71 ( $n = 201$ ), whereas zotarolimus-eluting (Resolute Integrity, Medtronic, Santa Rosa, Calif, USA) stents were used at a percentage of 29 ( $n = 82$ ).

The primary endpoints of the study were defined as the combined clinical adverse events, in-hospital and 30-day mortality, contrast-induced acute kidney injury (CI-AKI), acute stent thrombosis (ST), SB dissection, and need for SB stenting. Stent thrombosis was defined according to Academic Research Consortium classification.<sup>11</sup> Only patients with early (within 1 month after index procedure) definite ST during follow-up were enrolled in our study. Definite ST was defined as angiographic confirmation of a thrombus in the

## HIGHLIGHTS

- The effectiveness of the novel POT-side-POT technique in patients with non-complex coronary bifurcation lesions (CBL) treated with single-stent strategy is unclear.
- POT-side-POT is a simple and safe technique providing shorter procedure time and lower incidence of adverse clinical outcomes compared to kissing balloon inflation in patients with non-complex CBL.
- The use of this easily applicable technique should be encouraged in non-complex CBL treated with single-stent strategy.

stent or in the segment 5 mm proximal or distal to the stent, with or without vessel occlusion. Contrast-induced acute kidney injury was defined as  $\geq 0.5$  mg/dL or  $\geq 25\%$  increase in creatinine level between 48 and 72 hours after contrast media exposure. True bifurcation (complex bifurcation) lesion was defined according to Medina classification (1-1-1; 0-1-1; 1-0-1).

### Statistical Analysis

Continuous variables were reported as mean  $\pm$  standard deviation (SD) or median with interquartile ranges, while categorical variables were presented as percentages. The Kolmogorov–Smirnov test was performed to test the normality of distributions. The Student's *t* test or Mann–Whitney *U* test for continuous variables and the chi-square test for categorical variables were used for comparison between the study groups. The logistic regression analysis was used to determine independent predictors of combined clinical adverse events. Values of  $P < .05$  were considered statistically significant. Statistical Package for the Social Sciences 22 software (SPSS Inc, Chicago, Ill, USA) was used to carry out all statistical analyses. Inverse probability weighting (IPW) using propensity scores was used to adjust the differences and to reduce the bias associated with the retrospective data collection. The propensity score was calculated using a logistic model with baseline characteristics that may

influence the adverse clinical events, including patients' age, sex, ACS, diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HPL), chronic kidney disease (CKD), ejection fraction (EF), true bifurcation lesion, previous CAD, number of diseased vessel, and smoking status. The propensity score was calculated by  $1/\text{probability}$  for POT-side-POT group and by  $1/1-\text{probability}$  for KBI group.

### RESULTS

Table 1 demonstrated both weighted and unweighted demographic, clinical features, and laboratory parameters of the study group. History of DM, HTN, HPL, CAD, cerebrovascular disease, and CKD was similar between groups. Besides, age, EF, smoking status, and rate of ACS on admission did not differ between groups. Serum levels of blood glucose, HbA1c, creatinine, alanine aminotransferase, lipid, and complete blood count parameters were similar between groups, except serum aspartate aminotransferase.

Both weighted and unweighted angiographic properties and procedural characteristics of the study group were demonstrated in Table 2. Procedure time and contrast volume were significantly higher in KBI group compared to POT-side-POT group. Although the ratio of true bifurcation lesion was significantly higher in POT-side-POT group, it was equalized between groups after adjustment with IPW.

**Table 1. Demographic, Clinical Features, and Laboratory Parameters of the Study Group**

	Unweighted			Weighted		
	POT-side-POT (n=149)	KBI (n=134)	P	POT-side-POT (n=149)	KBI (n=134)	P
Age (years)	58.1 $\pm$ 11.9	58.5 $\pm$ 11.7	.771	58.2 $\pm$ 11.6	58 $\pm$ 11.2	.861
Men	115 (77.2%)	115 (85.8%)	.063	120 (80.6%)	108 (81%)	.922
DM	56 (37.6%)	44 (32.8%)	.423	51 (34.2%)	46 (34.1%)	.993
HTN	77 (51.7%)	55 (41%)	.074	68 (45.4%)	59 (44.2%)	.783
HPL	97 (65.1%)	68 (50.7%)	.014	88 (59.2%)	77 (57.7%)	.732
Previous CAD	59 (39.6%)	56 (41.8%)	.711	59 (39.8%)	53 (39.9%)	.972
Previous CVD	7 (4.7%)	3 (2.2%)	.264	7 (4.9%)	3 (2.2%)	.083
CKD	9 (6%)	11 (8.2%)	.483	10 (6.7%)	9 (6.8%)	.971
ACS on admission	90 (60.4%)	68 (50.7%)	.112	83 (55.6%)	72 (53.6%)	.633
Smoking status	61 (40.9%)	46 (34.3%)	.253	57 (38%)	50 (37.6%)	.920
EF (%)	53.2 $\pm$ 9.6	52.8 $\pm$ 9.4	.764	53 $\pm$ 9.9	53 $\pm$ 8.9	.942
Glucose (mg/dL)	132.7 $\pm$ 51.3	128.4 $\pm$ 52	.482	128.8 $\pm$ 47.1	129.2 $\pm$ 50.4	.923
HbA1c (%)	6.4 $\pm$ 1.4	6.4 $\pm$ 1.6	.981	6.3 $\pm$ 1.3	6.4 $\pm$ 1.6	.420
Creatinine (mg/dL)	1.18 $\pm$ 1.1	1.2 $\pm$ 1.02	.893	1.17 $\pm$ 1.03	1.14 $\pm$ 0.9	.731
Total cholesterol (mg/dL)	193.7 $\pm$ 66.1	186.7 $\pm$ 48.6	.324	186.7 $\pm$ 65.3	188.9 $\pm$ 48.7	.651
HDL (mg/dL)	40.6 $\pm$ 9.9	39.2 $\pm$ 9	.212	39.8 $\pm$ 9.8	38.8 $\pm$ 8.6	.192
LDL (mg/dL)	125.6 $\pm$ 56.1	118.5 $\pm$ 40.9	.224	120.5 $\pm$ 55.2	120.8 $\pm$ 41.8	.944
Triglyceride (mg/dL)	143.9 $\pm$ 86.2	147.4 $\pm$ 79.9	.723	141.7 $\pm$ 81.4	149.5 $\pm$ 79.6	.252
ALT (U/L)	35 $\pm$ 45.1	26.4 $\pm$ 22.8	.074*	35.7 $\pm$ 51.1	26.5 $\pm$ 22.6	.061*
AST (U/L)	65.6 $\pm$ 100.5	45 $\pm$ 69	.011*	61.7 $\pm$ 95.5	44.8 $\pm$ 71.2	.049*
WBC (/mm <sup>3</sup> )	10051 $\pm$ 3530	10230 $\pm$ 3490	.672	10000 $\pm$ 3580	10200 $\pm$ 3450	.511
Hemoglobin (g/dL)	13.5 $\pm$ 2.1	13.3 $\pm$ 2	.464	13.5 $\pm$ 2.1	13.3 $\pm$ 2.1	.251

\*Mann–Whitney *U* test.

POT, proximal optimization; KBI, kissing balloon inflation; DM, diabetes mellitus; HTN, hypertension; HPL, hyperlipidemia; CAD, coronary artery disease; CVD, cerebrovascular disease; CKD, chronic kidney disease; ACS, acute coronary syndrome; EF, ejection fraction; HDL, high density lipoprotein; LDL, low density lipoprotein; ALT, alanine transaminase; AST, aspartate transaminase; WBC, white blood cell.

**Table 2. Angiographic Properties and Procedural Characteristics of the Study Group**

	Unweighted			Weighted		
	POT-side-POT (n=149)	KBI (n=134)	P	POT-side-POT (n=149)	KBI (n=134)	P
Lesion location (%)			.061			.001
LAD	110 (73.8)	88 (65.7)		111 (74.3)	87 (65.2)	
CX	27 (18.1)	25 (18.7)		26 (17.3)	25 (18.6)	
RCA	8 (5.4)	7 (5.2)		9 (6)	7 (5)	
LMCA	4 (2.7)	14 (10.4)		3 (2.5)	15 (11.1)	
Number of diseased vessels (%)			.321			.974
One-vessel disease	45 (30.2)	52 (38.8)		53 (35.6)	49 (36.3)	
Two-vessel disease	58 (38.9)	46 (34.3)		55 (36.6)	48 (35.6)	
Three-vessel disease	46 (30.9)	36 (26.9)		41 (27.8)	37 (28.1)	
Medina classification (%)			.001			.521
1,0,0	9 (6)	16 (11.9)		13 (8.8)	13 (9.7)	
1,1,0	24 (16.1)	32 (23.9)		31 (21.1)	25 (18.7)	
0,1,0	20 (13.4)	37 (27.6)		30 (19.4)	29 (21.6)	
0,0,1	1 (0.7)	1 (0.7)		1 (0.7)	1 (0.7)	
1,1,1	39 (26.2)	24 (17.9)		31 (21.1)	34 (25.5)	
0,1,1	38 (25.5)	18 (13.4)		28 (19)	24 (18)	
1,0,1	18 (12.1)	6 (4.5)		15 (9.9)	8 (5.8)	
True bifurcation lesion (Medina 1,1,1; 1,0,1; 0,1,1), n (%)*	95 (63.8)	48 (35.8)	<.001	(75) 50	66 (49.1)	.830
Procedure time (minute)	30.6 ± 8.5	34.3 ± 11.6	.003	30.2 ± 8.3	34.9 ± 12.1	<.001
Contrast volume (mL)	153.7 ± 42.4	171.1 ± 58.2	.004	152.4 ± 41.2	174.1 ± 60.4	<.001
MV stent diameter (mm)	2.97 ± 0.17	3.01 ± 0.3	.184	2.98 ± 0.16	3.02 ± 0.31	.041
MV stent length (mm)	33.2 ± 14.3	29.7 ± 11.8	.032	32.9 ± 14.1	29.5 ± 11.3	.002
Number of stents (%)			.610			.142
One stent usage	113 (75.8)	99 (74)		115 (76.8)	96 (71)	
Two stents usage	31 (20.8)	33 (24.6)		30 (20.4)	36 (27.2)	
Three stents usage	5 (3.4)	2 (1.5)		4 (2.8)	2 (1.8)	
Final MV stent diameter (mm)	3.58 ± 0.29	3.68 ± 0.49	.034	3.6 ± 0.3	3.7 ± 0.5	.002
Proximal MV reference diameter (mm)	3.43 ± 0.33	3.53 ± 0.52	.048	3.44 ± 0.33	3.56 ± 0.53	.001
SB reference diameter (mm)	2.47 ± 0.29	2.60 ± 0.28	<.001	2.47 ± 0.31	2.58 ± 0.3	<.001
SB residual stenosis (%)	21.1 ± 20.9	15.7 ± 15.8	.011	20.3 ± 19.8	16.5 ± 16.4	.022
Number of pts with >50% SB residual stenosis (%)	20 (13.4)	8 (6)	.042	18 (11.9)	8 (5.7)	.013
SB balloon type (%)			.230			.532
Compliant	24 (16.1)	15 (11.2)		23 (15.5)	18 (13.6)	
Non-compliant	125 (83.9)	119 (88.8)		126 (84.5)	116 (86.4)	
Initial TIMI-3 flow of MV and SB	123 (82.6)	115 (85.8)	.551	124 (83.5)	111 (82.8)	.321
Final TIMI-3 flow of MV and SB	146 (98)	132 (98.5)	.402	147 (98.6)	132 (98.2)	.112
Aspiration	5 (3.4)	2 (1.5)	.322	5 (3.2)	2 (1.4)	.173
Tirofiban usage	8 (5.4)	4 (3)	.324	8 (5.3)	5 (3.6)	.333

\*Visual estimation.

POT, proximal optimization; KBI, kissing balloon inflation; LAD, left anterior descending artery; CX, circumflex artery; RCA, right coronary artery; LMCA, left main coronary artery; MV, main vessel; SB, side branch; Pts, patients; TIMI, thrombolysis in myocardial infarction.

Also, the higher number of left anterior descending artery lesions in POT-side-POT group and left main coronary artery (LMCA) lesions in KBI groups reached statistical significance after adjustment. Additionally, proximal MV and SB reference diameters and final MV stent diameter tended to be higher in KBI group compared to POT-side-POT group. Side

branch residual stenosis and number of patients with >50% SB residual stenosis remained significantly higher in POT-side-POT group than KBI group, both baseline and after adjustment. Number of diseased vessels and stents used, initial and final TIMI-3 flow, and tirofiban usage were similar between groups.

The rate of adverse clinical outcomes such as in-hospital and 30-day mortality, CI-AKI, acute ST, SB dissection, and need for SB stenting between groups was shown in Figures 1 and 2. Mortality rates were numerically higher in POT-side-POT group than KBI, but there was no statistically significance between the groups in terms of mortality; only 6 patients died and all of them suffered from ACS. They were ST-elevation myocardial infarction patients complicated with cardiogenic shock. Three of them had true bifurcation lesions and 4 of them underwent POT-side-POT procedure. Combined clinical adverse outcomes were similar between groups both at baseline and after adjustment. In addition to the need for SB stenting, the number of SB dissection and CI-AKI tended to be higher in KBI group. Only a small number of patients experienced acute ST or in-hospital and 30-day mortality. Side branch dissection and need for SB stenting reached statistical significance in KBI group after adjustment with IPW. Furthermore, we performed another analysis by excluding 18 patients with LMCA lesions. It showed similar results to previous analysis performed on whole study population in terms of both individual adverse clinical endpoints and combined adverse outcomes.

Tables 3 and 4 demonstrated the true and non-true bifurcation subgroups of the study population. In true bifurcation subgroup analysis, procedure time and contrast volume were

significantly higher in KBI group compared to POT-side-POT group. Side branch residual stenosis and number of patients with >50% SB residual stenosis were significantly higher in POT-side-POT group than KBI group after adjustment with IPW. Side branch dissection and ST were significantly higher in both baseline and after adjustment in KBI group. In non-true bifurcation subgroup analysis, procedure time and contrast volume remained significantly lower in POT-side-POT group, whereas other outcomes and endpoints remained similar between groups.

Univariate and multiple logistic regression analysis results were demonstrated in Table 5. POT-side-POT technique was not related to an increase in combined adverse outcomes both baseline [odds ratio(OR)=1.01; P=.982, 95% CI: 0.59-1.69] and after adjustment with IPW (OR=1.28; P=.193, 95% CI: 0.88-1.86). Ejection fraction was determined as an independent predictor of combined adverse clinical events both at baseline and after adjustment with IPW. However, hemoglobin level was found as an independent predictor of combined adverse clinical events only after adjustment with IPW.

**DISCUSSION**

To our knowledge, this is the first study that compares POT-side-POT and KBI techniques in single-stenting of non-complex CBL, highlighting real-life circumstances. The results

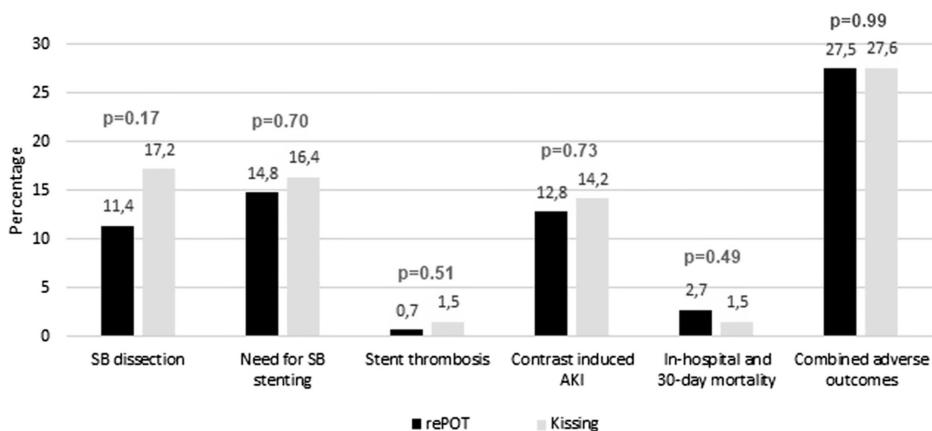


Figure 1. The rate of adverse clinical outcomes; unweighted.

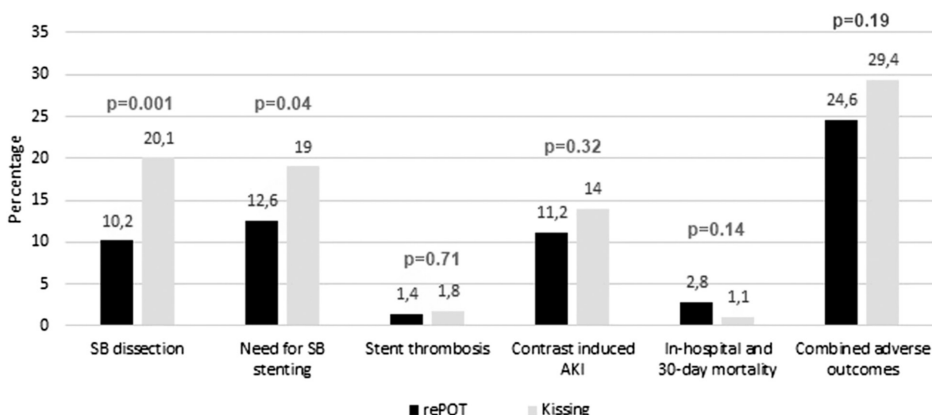


Figure 2. The rate of adverse clinical outcomes; weighted.

**Table 3. True Bifurcation Subgroup of the Study Population**

	Unweighted			Weighted		
	POT-side-POT (n=95)	KBI (n=48)	P	POT-side-POT (n=95)	KBI (n=48)	P
Procedure time (minute)	32.3 ± 8.9	36.6 ± 13.3	.022	32.5 ± 8.9	36.8 ± 13.2	.001
Contrast volume (mL)	161.6 ± 44.1	182.4 ± 66.3	.031	162.4 ± 43.9	183.9 ± 66.2	.002
SB residual stenosis (%)	24.1 ± 23.1	18.9 ± 17.9	.112	24.1 ± 23.2	18.8 ± 18.7	.033
Number of pts with >50% SB residual stenosis (%)	17 (17.9)	3 (6.2)	.064	16 (17.6)	4 (6.6)	.005
CI-AKI (%)	15 (15.8)	9 (18.8)	.651	14 (14.8)	8 (17.5)	.541
In hospital and 30-day mortality (%)	3 (3.2)	0	.210	3 (3.5)	0	.064
SB dissection (%)	14 (14.7)	16 (33.3)	.011	14 (14.8)	17 (33.6)	<.001
Need for SB stenting (%)	19 (20)	14 (29.2)	.224	19 (20.3)	13 (28.7)	.111
Stent thrombosis (%)	0	2 (4.2)	.042	0	1 (3.7)	.022
Combined adverse outcomes (%)	33 (34.7)	20 (41.7)	.421	32 (34.3)	19 (40.1)	.321

POT, proximal optimization; KBI, kissing balloon inflation; Pts, patients; SB, side branch; CI-AKI, contrast-induced acute kidney injury.

**Table 4. Non-true Bifurcation Subgroup of the Study Population**

	Unweighted			Weighted		
	POT-side-POT (n=54)	KBI (n=86)	P	POT-side-POT (n=54)	KBI (n=86)	P
Procedure time (minute)	27.6 ± 6.9	33 ± 10.5	.001	27.9 ± 6.9	33 ± 10.6	<.001
Contrast volume (mL)	140 ± 35.6	164.5 ± 52.4	.003	142.4 ± 35.8	164.7 ± 52.8	<.001
SB residual stenosis (%)	15.9 ± 15.1	14.4 ± 13.8	.551	16.4 ± 15	14.4 ± 13.3	.241
Number of pts with >50% SB residual stenosis (%)	3 (5.6)	5 (5.8)	.952	3 (5.6)	4 (4.9)	.792
CI-AKI	4 (7.4)	10 (11.6)	.421	4 (7)	9 (10.6)	.291
In hospital and 30-day mortality	1 (1.9)	2 (2.3)	.854	2 (2.8)	2 (2.1)	.703
SB dissection	3 (5.6)	7 (8.1)	.562	2 (4.9)	7 (7.7)	.334
Need for SB stenting	3 (5.6)	8 (9.3)	.423	2 (4.9)	8 (9.2)	.161
Stent thrombosis	1 (1.9)	0	.211	2 (2.8)	0	.112
Combined adverse outcomes	8 (14.8)	17 (19.8)	.463	8 (14.8)	16 (19)	.344

POT, proximal optimization; KBI, kissing balloon inflation; Pts, patients; SB, side branch; CI-AKI, contrast-induced acute kidney injury.

**Table 5. Predictors of Combined Clinical Adverse Events According to Multiple Logistic Regression Analysis**

	Unweighted				Weighted			
	Univariate		Multiple		Univariate		Multiple	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
POT-side-POT	1.01 (0.59-1.69)	.982			1.28 (0.88-1.86)	.193		
ACS on admission	1.49 (0.87-2.54)	.145			1.49 (1.02-2.18)	.039		
Ejection fraction	0.95 (0.93-0.98)	.001	0.96 (0.93-0.99)	.002	0.94 (0.92-0.97)	<.001	0.95 (0.93-0.97)	<.001
Age	1.01 (0.99-1.04)	.241			1.01 (0.99-1.02)	.376		
Male gender	1.38 (0.86-1.64)	.136			1.63 (1.04-2.55)	.033		
Hypertension	1.12 (0.67-1.89)	.666			1.18 (0.82-1.73)	.364		
Diabetes mellitus	1.11 (0.66-1.92)	.689			1.11 (0.75-1.64)	.597		
Hyperlipidemia	1.20 (0.71-2.05)	.496			1.05 (0.72-1.54)	.786		
Three vessel disease	1.24 (0.55-1.61)	.405			1.02 (0.65-1.62)	.920		
Hemoglobin	0.90 (0.79-1.01)	.085			0.86 (0.78-0.94)	.001	0.83 (0.73-0.93)	.001
Chronic renal disease	1.46 (0.56-3.79)	.442			1.36 (0.67-2.74)	.391		
Smoking	1.16 (0.58-1.52)	.495			1.21 (0.82-1.55)	.275		

ACS, acute coronary syndrome; OR, odds ratio.

of our study suggest that POT-side-POT technique is more rapid, easily applicable, and reliable in non-complex CBL treated with single-stent strategy compared to KBI. Based on our entire study population results, SB dissection and need for SB stenting were higher in KBI group. Meanwhile, in true bifurcation subgroup analysis, POT-side-POT remained simpler and faster technique in comparison to KBI. Also, lower incidence of SB dissection and ST, whereas similar incidence of CI-AKI, need for stenting, in-hospital and 1-month mortality was detected.

In complex CBL, a two-stent bifurcation technique provides better results than provisional stenting,<sup>12</sup> while a single-stent approach should remain the preferred technique in the setting of simple bifurcations.<sup>13,14</sup> However, it is still controversial which technique should be preferred during single-stenting. The POT-side-POT sequence respects fractal geometry by reducing SB ostium stent-strut obstruction, providing perfect proximal stent apposition with almost perfect circularity, reducing ellipticity index, proximal area overstretch, and global strut malapposition. Also, the experimental fractal bifurcation bench model studies confirm that the optimization of provisional stenting is more effectively performed by using POT-side-POT technique.<sup>15</sup> Accordingly, a simple POT-side-POT sequence that can be applied with a single balloon provided shorter procedure time and lesser contrast media usage even in true bifurcation lesions in our study. Although the reduction in CI-AKI was not detected, results may change when large-scale studies are conducted. With a shorter procedure time and lesser contrast volume, POT-side-POT procedure may be a useful technique for the protection of kidneys, especially in patients with CKD. Although there was no statistically significant difference between the groups in terms of CI-AKI in our study, the number of patients with CI-AKI is numerically lower in the POT-side POT group. It may be a procedure of choice in patients with non complex bifurcation lesions who have worse clinical status. Operators may prefer this technique when they have to perform a faster and safer procedure in this group of patients. Based on the results of our study, the lower final SB opening observed in POT-side-POT group may be explained by the following mechanisms: (1) POT-side-POT technique was much more preferred in true bifurcation lesions by the operators, supporting the philosophy of "making complex matters simple" and (2) simultaneous dilatation of the juxtapositioned balloons enlarged the luminal opening, at the expense of dissection. Moreover, in non-true bifurcation subgroup analysis, final SB opening was found to be similar between groups that support our hypothesis mentioned above. Inflating a single balloon in the POT-side-POT sequence instead of simultaneously inflating 2 balloons in the coronary artery may provide lesser shear stress and radial force to the SB ostium. This may reduce the rates of SB dissection at the expense of reduced SB opening. Inversely, KBI provides better lumen diameter, but flow-limiting dissections may occur more easily due to increased shear stress and arterial overstretch. Therefore, the need for SB stenting is more frequently seen in the KBI group compared to POT-side-POT group.

Prior studies indicated a positive relation between ST and stent strut malapposition.<sup>16-18</sup> Finet et al<sup>10</sup> demonstrated that POT-side-POT technique provides the restoration of circular geometry and improves strut apposition opposite the SB ostium. This may be the possible explanation for lower number of ST detected in POT-side-POT group compared to KBI group. Arterial overstretch occurred by inflating 2 juxtapositioned balloons while performing KBI may cause minimal stent edge dissections, higher rates of SB dissections, fracture of proximal stent struts, and asymmetric stent expansion with elliptical stent deformation. These are the possible mechanisms that may explain the higher ST rates in the KBI group.

Based on a prospective multicenter registry,<sup>19</sup> the efficiency of KBI was reported in provisional stenting of bifurcation lesions not involving the left main coronary artery, under intravascular ultrasound (IVUS) guidance. Maintaining larger mean luminal diameter with less symmetry in the proximal MV and reducing angiographic SB restenosis with similar major adverse cardiac events rate favor KBI technique in single-stent strategies. Since our results reflect the results of this registry, the number of patients with >50% SB stenosis is lesser, whereas SB opening is greater in KBI group. Likewise, greater final lumen diameter observed in KBI group may also be due to the adjacent balloon inflation and arterial overstretch.

Nevertheless, KBI may lead to asymmetric stent expansion that results in elliptical stent deformation, neointimal hyperplasia, or a low shear stress region in the over dilated part which promotes neoatherosclerosis. Improvements to reduce this proximal deformation were described, such as completing KBI procedure with final POT. Even though POT preserves the proximal ellipticity index, it can not prevent overstretching. Thus, this proximal deformation induced by the juxtapositioned balloons and arterial overstretch might be the principle mechanism for the increased incidence of SB dissection observed in our entire patient group, more prominently in true bifurcation subgroup.

Whatever the provisional stenting technique, final POT provides benefits and appears to be mandatory. It fails in complete correction of the proximal elliptic deformation, but it improves global malapposition and ellipticity ratio, with no effect on final SB obstruction.<sup>20,21</sup> Hence, including both the initial and final POT may be considered to increase the effectiveness of POT-side-POT technique. Since our results reflect the results of the lesions frequently encountered in daily practice and concluded in favor of POT-side-POT arm, it may be reasonable to use POT-side-POT technique more commonly, especially in non-complex CBL.

### Study Limitations

There were some limitations to be noted in our study. First of all, our results were based on retrospective single-center study, and therefore, a relatively small number of patients were analyzed. Propensity score analysis was performed to adjust for confounding factors, but we were not able to check all variables. Second, imaging exams such as optical coherence tomography and IVUS could not be performed because they are not covered by insurance in our country,

thereby our results reflect more daily routine practice. Third, the decision of which provisional stenting technique to perform for each patient was made by the operators. Fourth, our results represent results of simple CBL, therefore they cannot be generalized to complex CBL and distal LMCA lesions. Finally, investigating the mechanisms for the differences between the 2 strategies were precluded due to the lack of angiographic follow-up.

## CONCLUSION

Our study demonstrates that POT-side-POT may be a simple and safe technique that provides shorter procedure time and lower rate of adverse outcomes in comparison with KBI. Wider usage of this easily applicable technique may be preferred in non-complex CBL treated with single-stent strategy in daily clinical practice. Nevertheless, further prospective randomized studies are needed to confirm our findings in a larger cohort of patients.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital (approval no: 2817/2020).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** B.B.K., G.C., O.S.S., H.K., conception and design; H.K., O.S.S. collected the data; K.K. and K.K., supervision; K.K. literature review; K.K. and K.K. made critical revision of article, G.C. and K.K. performed the analysis, B.B.K. and G.C. wrote the paper.

**Acknowledgments:** The authors deeply thanks Murat Kocas and Suleyman Atas for their help in this study.

**Declaration of Interests:** The authors declare that they have no competing interest.

**Funding:** This study received no funding.

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