Evaluation of Long-Term Outcomes of Crossover or Focal Ostial Stenting of Left Anterior Descending Artery Ostial Stenosis

ORIGINAL INVESTIGATION

ABSTRACT

Background: Optimal management of patients with ostial left anterior descending artery stenosis remains an unresolved issue.

Methods: Patients with ostial left anterior descending stenosis who underwent stent implantation were included in this study. Coronary records of all patients were monitored, and long-term clinical outcomes were recorded. The patients were divided into 2 groups according to the stenting method: focal left anterior descending stenting [ostial stenting group] and stenting from the left main coronary artery to the left anterior descending [crossover stenting group].

Results: Of the 97 eligible consecutive patients, 56 were treated with ostial stenting and 41 with crossover stenting. At a mean follow-up of 23.6 ± 12.6 months, non-fatal myocardial infarction (3.9% vs. 12.8%, $P = .118$), target lesion revascularization (5.9% vs. 12.8%, $P = .252$), and all-cause death (2.0% vs. 7.7%, $P = .191$) rates were not statistically significant. However, the rate of major adverse cardiovascular events defined as a composite of non-fatal myocardial infarction, target lesion revascularization, or all-cause death was significantly higher in the crossover stenting group (8.2% vs. 28.2%, $P = .013$). In the multiple regression analysis, left main coronary artery diameter (odds ratio = 4.506; 95% CI: 1.225-16.582, $P = .024$) and application of the crossover stenting technique (odds ratio = 5.126; 95% CI: 1.325-19.833, $P = .018$) were found to be the most effective predictors of major adverse cardiovascular events.

Conclusion: In our study, the ostial stenting group was associated with better clinical outcomes in the treatment of ostial left anterior descending stenosis. However, it is not appropriate to apply a single method to all patients with such lesions.

Keywords: Medina, bifurcation, ostial, coronary, stenting

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INTRODUCTION

The optimal strategy for treating ostial left anterior descending artery (LAD) stenosis remains unclear according to the recent consensus document of the European Bifurcation Club.[1] In terms of stent positioning, 2 basic strategies can be mentioned: focal ostial stenting (OS) and crossover stenting (CS) from the left main coronary artery (LM) to the LAD. Intravascular ultrasound (IVUS) studies have shown that ostial LAD plaques mostly extend to the distal LM level. Therefore, it has been suggested that CS is a better implantation technique than focal OS.[2] However, data on the long-term outcomes of these 2 strategies with the current stents are inconclusive. Although mortality and myocardial infarction (MI) rates were similar in a few retrospective analyses, target lesion revascularization (TLR) and target vessel revascularization (TVR) were reported to be lower in favor of CS.[2-4]

Many additional factors such as distal LM stenosis, left circumflex artery (LCx) ostium stenosis, bifurcation angle, IVUS use, and kissing balloon (KB) inflation should be taken into consideration when deciding on the stenting strategy for ostial LAD stenosis. Therefore, it is obvious that more data are needed on this subject. In the present study, we conducted a multicenter

Soylu et al. Left Anterior Descending Ostial Stenting

Anatol J Cardiol 2022; 26: 827-831

retrospective evaluation of patients who underwent percutaneous coronary intervention (PCI) for ostial LAD stenosis.

METHODS

This was a multicenter retrospective study. Patients with ostial LAD stenosis who underwent stent implantation were included in the study (median, 0.1.0).[5] The PCI images of patients screened in all centers were re-watched by at least 2 interventional cardiologists. The exclusion criteria were as follows: presence of angiographic plaque in the distal LM; restenotic lesions; STEMI; use of bare metal stent, bioresorbable scaffold or rotablator; and inappropriate dual antiplatelet therapy.

The patients were divided into 2 groups according to the stenting strategy. Patients who underwent only LAD stenting starting from the ostial LAD were defined as the OS group and stenting from the LM to the LAD were defined as the CS group.

This study was approved by the Institutional Ethics Committee and was conducted in accordance with the ethical principles described in the Declaration of Helsinki.

Definitions

Patients with stenosis located within 3 mm of the LAD ostium in the least-foreshortened angiographic projection were considered to have ostial LAD stenosis.

Target lesion procedure time was defined as the time interval between the first wiring image and the last image of the intervention related to the target lesion. Other coronary intervention times performed in the same session were excluded.

Target lesion revascularization was defined as the new revascularization procedure performed within the stent or 5 mm borders proximal or distal to the stent, including the LM, LAD, or LCx.

Major adverse cardiovascular events (MACE) were defined as a composite of all-cause death, non-fatal MI or TLR.

The follow-up information of the patients was obtained from the hospital databases and the central database of the Ministry of Health.

Statistical Analysis

The research data were analyzed using Statistical Package for Social Sciences version 15.0. Before making comparisons between the groups, the normal distribution of data was

tested using the Kolmogorov–Smirnov test. The logarithmic transformation was applied to non-normally distributed continuous data. The independent samples t-test was used to compare normally distributed transformed continuous data, and the chi-squared test was used to compare categorical data. The relationship between MACE and variables was tested using the univariate and multiple regression analyses. Age, total stent length, maximum post-dilatation (post-D) balloon diameter, diabetes mellitus, side branch (SB) narrowing, KB inflation, previous PCI, non-target lesion intervention, multi-vessel disease, stenting technique, and LM diameter were used as potential confounders. Data were presented as mean $\pm$ standard deviation or percentage. Statistical significance was set at $P < .05$.

RESULTS

Retrospective screening identified 126 consecutive patients who met the inclusion criteria and 29 of these were excluded due to the exclusion criteria. Of the 97 patients included in the study, 56 were treated with OS and 41 with CS. The clinical and diagnostic angiographic parameters of the study groups are presented in Table 1. The groups were similar in terms of age, gender, diabetes frequency, and diagnosis at admission. The rate of previous PCI was higher in the CS group (24.1% vs. 48.8%, $P = .012$). While baseline angiographic features such as LM diameter, proximal LAD diameter, proximal LCx diameter, and percentage of stenosis were similar in both groups, the number of patients with multi-vessel

Table 1. Baseline Clinical and Angiographic Characteristics

	OS Group (n = 56)	CS Group (n = 41)	P
Age, year	59.5 ± 13.7	61.6 ± 14.7	.487
Male, n (%)	42 (75.0)	30 (73.2)	.839
Chronic coronary syndrome, n (%)	25 (44.6)	22 (53.7)	.380
NSTE-ACS, n (%)	21 (37.5)	13 (31.7)	.555
STEMI, n (%)	10 (17.9)	6 (14.6)	.673
Diabetes mellitus, n (%)	24 (42.9)	20 (48.8)	.563
Previous percutaneous coronary intervention, n (%)	13 (24.1)	20 (48.8)	.012
Previous coronary artery bypass grafting, n	0	0	
Left ventricular ejection fraction, %	51.7 ± 9.2	53.5 ± 8.8	.344
Multi-vessel disease, n (%)	27 (48.2)	26 (63.4)	.163
Left main coronary artery diameter, mm	5.1 ± 0.6	5.1 ± 0.4	.665
Proximal left anterior descending artery diameter, mm	3.4 ± 0.4	3.4 ± 0.3	.890
Proximal left circumflex artery diameter, mm	3.1 ± 0.4	3.0 ± 0.2	.116
Percentage of stenosis, %	86.9 ± 15.9	87.2 ± 10.8	.923

CS, crossover stenting; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; OS, ostial stenting; STEMI, ST-segment elevation myocardial infarction.

HIGHLIGHT

- The issue of how ostial left anterior descending stenosis should be stented remains unclear. After reporting non-prognostic results in favor of crossover stenting in only a few retrospective analyses, a perception began to emerge that focal ostial stenting should be abandoned. However, owing to the different dynamics of bifurcations, 1 method cannot be expected to be more successful in all cases.

Anatol J Cardiol 2022; 26: 827-831

Soylu et al. Left Anterior Descending Ostial Stenting

Table 2. Procedural Parameters

	OS Group (n=56)	CS Group (n=41)	P
Intravascular ultrasound use, n (%)	3 (5.4)	6 (14.6)	.120
Non-target lesion intervention, n (%)	13 (23.6)	20 (48.8)	.010
Stent diameter, mm	3.1 ± 0.3	3.3 ± 0.4	<.001
Total stent length, mm	20.3 ± 6.5	23.9 ± 6.7	.008
Maximum post-dilatation balloon diameter, mm	3.5 ± 0.4	4.3 ± 0.7	<.001
Target lesion procedure time, min	26.7 ± 13.8	34.0 ± 17.3	.026
Side branch narrowing >50%, n (%)	4 (7.3)	15 (36.6)	<.001
Side branch occlusion, n (%)	1 (1.8)	1 (2.4)	.823
Kissing balloon inflation, n (%)	5 (8.9)	18 (43.9)	<.001
Side branch stenting, n (%)	2 (3.7)	4 (9.8)	.230

CS, crossover stenting; OS, ostial stenting.

Table 3. Long-term Outcomes

	OS Group (n=56)	CS Group (n=41)	P
Follow-up period, month	23.9 ± 13.0	23.2 ± 12.1	.776
Major adverse cardiovascular events, n (%)	4 (8.2)	11 (28.2)	.013
Non-fatal myocardial infarction, n (%)	2 (3.9)	5 (12.8)	.118
Target lesion revascularization, n (%)	3 (5.9)	5 (12.8)	.252
All-cause death, n (%)	1 (2.0)	3 (7.7)	.191

CS, crossover stenting; OS, ostial stenting.

disease was numerically higher in the CS group (48.2% vs. 63.4%, $P = .137$).

With regard to the procedural parameters, the number of non-target lesion intervention in the same session (23.6% vs. 48.8%, $P = .010$), stent diameter (3.1 ± 0.3 mm vs. 3.3 ± 0.4 mm, $P < .001$), total stent length (19.8 ± 5.6 mm vs. 23.9 ± 6.7 mm, $P = .020$), maximum post-D balloon diameter (3.5 ± 0.4 mm vs. 4.3 ± 0.7 mm, $P < .001$), target lesion procedure time (26.7 ± 13.8 min vs. 34.0 ± 17.3 minutes, $P = .026$), SB narrowing after post-D (7.3% vs. 36.6%, $P < .001$), and KB inflation (8.9% vs. 43.9%, $P < .001$) were significantly higher in the CS group (Table 2). Final proximal optimization technique (POT) was performed on all patients undergoing KB inflation in the CS group. When looking at LM diameter and maximum post-D balloon diameter in the CS group, the ideal diameter of the LM was reached in 51.2% of the patients in this group. Side branch occlusion was detected in only 1 case

in both groups. The use of stent for SB after main branch (MB) intervention was numerically higher in the CS group (3.7% vs. 9.8%, $P = .230$). In addition, in a subgroup analysis, the duration of the procedure was significantly longer in patients with KB inflation compared to those without (41.5 ± 18.5 minutes vs. 26.4 ± 13.1 minutes, $P < .001$).

At a mean follow-up of 23.6 ± 12.6 months (23.9 ± 13.0 in the OS group and 23.2 ± 12.1 in the CS group, $P = .776$), 90 patients were reached. During the follow-up, although the rates of non-fatal MI (3.9% vs. 12.8%, $P = .118$), TLR (5.9% vs. 12.8%, $P = .252$), and all-cause mortality (2.0% vs. 7.7%, $P = .191$) were numerically higher in the CS group, there was no statistical significance. However, the rate of MACE defined as the combination of these parameters was significantly higher in the CS group (8.2% vs. 28.2%, $P = .013$) (Table 3).

When variables that could be determinative for the development of MACE were analyzed using the univariate regression analysis, total stent length, LM diameter, and application of the CS technique showed statistical significance. In the multiple regression analysis, LM diameter [odds ratio (OR) = 4.506; 95% CI: 1.225-16.582, $P = .024$] and application of the CS technique (OR = 5.126; 95% CI: 1.325-19.833, $P = .018$) were determined to be the most effective models for MACE estimation (Table 4).

Table 4. Predictors of Major Adverse Cardiovascular Events by Multiple Regression Analysis

	Univariate Logistic Regression			Multiple Logistic Regression		
Predict	Odds Ratio	95% CI	P	Odds Ratio	95% CI	P
Age (year)	0.994	0.955-1.035	.766			
Total stent length (mm)	1.101	1.019-1.190	.015	1.076	0.985-1.175	.102
Post-D balloon diameter (mm)	0.897	0.386-2.082	.799			
Stent diameter (mm)	0.987	0.202-4.829	.987			
Diabetes mellitus (0/1)	1.464	0.480-4.464	.503			
Side branch narrowing (0/1)	0.875	0.220-3.484	.850			
Kissing balloon inflation (0/1)	0.775	0.195-3.079	.717			
Previous PCI (0/1)	0.792	0.205-2.474	.593			
Non-target lesion intervention (0/1)	2.698	0.699-10.406	.150			
Multi-vessel disease (0/1)	0.700	0.229-2.136	.531			
Crossover stenting (0/1)	4.420	1.282-15.239	.019	5.126	1.325-19.833	.018
LM diameter (mm)	3.319	1.025-10.744	.045	4.506	1.225-16.582	.024

LM, left main coronary artery; PCI, percutaneous coronary intervention; post-D, post-dilatation.

Soylu et al. Left Anterior Descending Ostial Stenting

Anatol J Cardiol 2022; 26: 827-831

DISCUSSION

In our study, the 2 different techniques used to treat ostial LAD stenosis were compared. Target lesion procedure time, SB narrowing, KB inflation, and MACE rates were higher in the CS group than in the OS group. These results differ in some aspects from those of very few similar studies in the literature.

Most procedural parameters differed significantly between the groups in the present study. Since the stent used in the CS technique slightly extends into the LM, it can be expected to be longer compared to the stent used in the OS technique. In previous studies, the stent length was found to be greater or similar in the CS technique.[2-4] This means a greater metal load, despite the advantage of better covering of the ostial plaque. Increased stent length has also been reported to be an independent predictor of restenosis.[6,7]

In our study, approximately 5 times more KB was applied to the CS group. Yamamoto et al[4] (30% vs. 0%) and Seung et al[8] (39.1% vs. 6.7%) also reported significantly higher KB inflation with CS compared to OS for ostial LAD stenosis. Larger stents and post-D balloons used in the CS technique may lead to the shift of plaque and carina to the LCx ostium. According to our study results, SB narrowing was significantly higher, and conversion to double stent strategy with SB stenting was numerically higher in the CS group. These parameters have not been reported in previous studies.[2-4] Only Seung et al[8] reported that the number of stents per lesion was higher in the group using both CS and OS techniques compared to the group using only OS. Another possible reason for the higher KB rate in the CS group may be the concern that floating stent struts in the ostium of the LCx, which is a major epicardial coronary artery, may complicate future LCx interventions. Although these struts are thought to increase the risk of fenestrated restenosis in the SB ostium, recent analyses have failed to demonstrate the clinical benefits of routine KB inflation after a single-stent strategy.[9,10] Moreover, it has been shown that while the incidence of SB restenosis decreases with KB inflation, the risk of MB restenosis increases.[11] Finally, the fact that the stenosis in the SB ostium was evaluated only anatomically, but not physiologically, may have contributed to the high KB rate in the CS group in our study.

Optimal positioning of the stent in the OS technique can prolong the procedure time. In contrast, in our study, target lesion procedure time was longer in the CS group. This result is likely related to the higher KB rate in the CS group. In a subgroup analysis in our study, the long duration of the procedure in patients undergoing KB inflation also supports this view. Yamawaki et al[12] showed that routine KB inflation after CS had a longer fluoroscopy time of approximately 16 minutes (20.1 ± 10.9 minutes vs. 36.1 ± 15.8 minutes, $P < .001$) compared to the provisional KB strategy. Conversely, Rigatelli et al[2] found that the duration of fluoroscopy was longer in OS than in CS. In the aforementioned study, although the patients in the CS group had higher The Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) scores, more use of rotablators, and IVUS, the lower fluoroscopy time could not be explained.

In our study, the rate of MACE defined as a composite of all-cause death, non-fatal MI, or TLR was significantly lower in the OS group. In addition, univariate and multiple regression analyses revealed a significant relationship between the use of CS technique and MACE. In previous studies, the clinical results of these 2 techniques were reported to be similar or in favor of CS. Rigatelli et al[2] reported statistically similar rates of MACE (death or stroke), cardiovascular mortality, stent restenosis, and stent thrombosis but significantly higher TVR rates in the OS group (18.4% vs. 5.6%, $P = .04$) at the 50-month follow-up. Yamamoto et al[4] did not find statistically significant differences in any of the clinical parameters, including TLR and TVR, at a follow-up period of approximately 19 months. Capranzano et al[3] reported similar TLR rates at a 24-month follow-up. The mainstay of clinical results in favor of CS in previous studies is that the ostial LAD plaque mostly extends into the LM in these lesions; therefore, CS may provide better plaque stabilization. However, we believe that this estimation is incomplete to explain the issue. It should be noted that the CS technique includes LM stenting. Thus, in the CS technique, the stent selected in accordance with the distal reference vessel diameter (LAD in the present study) should be capable of expanding to the LM diameter. Although many new-generation stents have an open-cell design, their expansion capacity is not unlimited. In tests where many new-generation stents were included, the maximal expansion capacities of different brands were between 4.0 and 4.4 mm for a 3.0 mm stent, 4.2 and 5.4 mm for a 3.5 mm stent, and 5.7 and 6.0 mm for a 4.0 mm stent.[13,14] Intravascular imaging studies have shown that the cross-sectional area of the LM is 20-27 mm² based on the external elastic membrane in male patients.[15,16] Mathematically, it means that a stent implanted in the LM should be expanded to a diameter of approximately 5 mm. In our study, the angiographic mean LM diameter was measured as 5.1 mm in both groups. Stents with a diameter of 3.0 mm and 3.5 mm may fail to expand properly in patients with a large LM diameter, even when dilated with large-diameter balloons. This may increase the risk of both stent restenosis and thrombosis. The statistical significance of the LM diameter in the MACE-related regression analysis in our study also supports this idea. In our study, although the stent diameter used in the CS group was significantly higher than that in the OS group, it had a mean diameter of 3.3 ± 0.4 mm. In the study by Yamamoto et al,[4] this value was 3.15 ± 0.35 mm. Rigatelli et al[2] did not specify the stent diameter, but they reported the final stent diameter after post-D as 4.8 ± 1.0 mm in the CS group. In our study, although LM diameter was measured as 5.1 ± 0.4 mm in the CS group, mean post-D balloon diameter was 4.3 ± 0.7 mm. The fact that the ideal diameter of the LM reached in only 51.2% of the patients in this group may have caused the higher MACE rates. In other words, the effect of the LM diameter on MACE in our study may be due to the inability to select the appropriate post-D balloon diameter. Given the importance of ideal stent apposition within the LM in patients undergoing CS from the LM to the LAD, the use of IVUS in these cases is pivotal. However, IVUS is not always accessible in clinical practice due to cost.

Anatol J Cardiol 2022; 26: 827-831

Soylu et al. Left Anterior Descending Ostial Stenting

Study Limitations

Similar to the few previous studies on this subject, the most important limitation of our study was that it was a retrospective analysis. Although the baseline clinical and angiographic features of the groups were comparable, parameters that were not taken into account may also have affected the outcomes. The number of patients included in this study is limited to make precise conclusions. Last but not least, the use of IVUS, which is a proven method for better outcomes in LM stenting, was very rare in the present study.

CONCLUSION

The optimal percutaneous treatment strategy for isolated ostial LAD stenosis remains unclear. Although CS has gained popularity in recent years and has several advantages, it is not a completely trouble-free and suitable strategy for every patient. In the CS technique, SB narrowing and the need for KB inflation are more frequent. In addition, the risk of stent malapposition may increase, particularly in patients with a large LM diameter. Therefore, OS should be considered in cases where the distal LM is lesion-free, the LM diameter is large, and the maximal expansion capacity of the selected stent is likely to be insufficient for CS. It is obvious that the debate on OS and CS for ostial LAD stenosis continues, and prospective studies are needed to clarify this issue.

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