

The Effects of Side Branch Predilation During Provisional Stenting of Coronary Bifurcation Lesions: A Double-Blind Randomized Controlled Trial

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Received 2015 July 9; Revised 2015 August 18; Accepted 2015 September 1.

Abstract

Background: There is a paucity of data regarding the role of side branch (SB) predilation during the provisional stenting of bifurcation lesions.

Objectives: The present study aimed to assess the effects of SB predilation on the outcomes of true bifurcation interventions.

Patients and Methods: Sixty patients with true bifurcation lesions according to the Medina classification were included in the study and randomly assigned to receive SB predilation before stenting the main branch (n = 30) or no predilation as the control group (n = 30).

Results: There was a trend toward the higher occurrence of dissection in the predilated ostial lesions of the SB compared to the non-predilated group (16.7% vs. 0, P = 0.07). Performance of the SB predilation was not associated with improved flow of the SB or fewer degrees of ostial stenosis after stenting the main branch, the need to rewire, rewiring time, or the rate of use of the final kissing balloon dilation and double stents procedures.

Conclusions: Routine predilation of the SB in provisional stenting of true bifurcation lesions seems to be ineffective and might be associated with some undesirable consequences. Still, there are some complex ostial lesions of the SB which could benefit from predilation.

Keywords: Coronary Artery Disease, Coronary Artery Stenting, Percutaneous Coronary Intervention

1. Background

Coronary bifurcation atherosclerotic lesions are quite common as a result of anatomical reasons and resultant flow-dependent alternations leading to pro-atherogenous low wall shear stress (1). The presence of a bifurcation lesion increases the complexity of percutaneous coronary intervention (PCI) and affects the results of the procedure, including lower rates of success, higher cost, and higher rates of periprocedural myocardial infarction (MI), restenosis and stent thrombosis (2). The primary cause of lower success rates in these lesions is side branch (SB) failure which could be due to dissection, flow disturbance, occlusion or significant residual stenosis (3-10). There are many stenting techniques which have been reported for the treatment of these lesions, with provisional stenting being the preferred and most widely used approach. This technique constitutes stent implantation in the main branch (MB) across the SB and stent implantation in the SB only if it is necessary. Although many operators have adopted this technique as their default strategy, certain anatomical considerations might suggest systematic double stenting as an initial approach (11, 12). SB predilation is a

controversial topic during provisional stenting because it could be associated with impairment of the SB flow and difficulty of access; however, its performance may be necessary for maintaining SB patency in some cases (13). Pan et al. reported that SB predilation in true bifurcation lesions was associated with improved Thrombolysis in Myocardial Infarction (TIMI) flow after MB stenting and less need to subsequently treat the SB. In addition, if SB rewiring was needed, predilation did not hinder this maneuver (14).

2. Objectives

The present study aimed to assess the effect of SB predilation during provisional stenting in patients with true bifurcation lesions.

3. Patients and Methods

3.1. Study Design

This randomized controlled trial was a single-center study on patients with true bifurcation lesions. They were

randomly assigned provisional stenting with and without SB predilation, with a parallel design and allocation ratio of 1:1. The local ethics committee approved the trial design.

3.2. Patient Population and Randomization

Five hundred and fifty patients were initially evaluated between September, 2013, and October, 2014. Patients were considered eligible if they met the following criteria: were older than 18 years of age; had chronic stable angina or acute coronary syndrome and an indication for coronary angiography and PCI; had a true bifurcation lesion according to the Medina classification ([1,1,1], [1,0,1], [0,1,1]); had undergone single vessel PCI; and the diameter of the main MB ≥ 2.5 mm, diameter of the SB ≥ 2 mm, and the length of stenosis in the SB < 5 mm. Patients were excluded due to the following criteria: inability to receive dual antiplatelet therapy; acute ST elevation MI and primary PCI; hemodynamic instability or cardiogenic shock at the time of presentation or during the hospital stay; left main lesion; multivessel PCI; inability to access the SB; the length of stenosis in the SB more than 5 mm beyond the ostium; untreated major complications during the procedure; and being pregnant. Randomization was performed based on the computerized balanced block randomization method in blocks of 4: 30 patients received SB predilation before the MB stenting and 30 had MB stenting without SB predilation. The sealed envelope technique was used to conceal the randomization.

3.3. Procedural Protocol and Follow-Up

The study patients in both groups received the same routine preparation protocol for coronary angiography and PCI, including Aspirin and a 600 mg loading dose of Clopidogrel. Coronary angiography and PCI were performed according to standard routine. After wiring both the main and side branches, balloon angioplasty of the SB was performed in the predilation group using non-compliant balloons with sizes similar to the SB reference size at moderately high inflation pressures (14 - 18 atm). Predilation of the MB was performed if required. The diameter of the MB stent was chosen according to the diameter of the distal segment after the origin of the SB and the majority of the patients received a drug-eluting stent. Final kissing balloon dilation (FKB) dilation was considered in the presence of impaired SB flow (TIMI flow < 3) or SB ostial stenosis $> 80\%$. In the case of continued impaired flow in the SB despite using FKB dilation, a double stenting technique was selected dependent on the anatomy of the bifurcation lesion.

3.4. Primary and Secondary Endpoints

The primary endpoints of the study were the severity of stenosis, the occurrence of dissection in the ostial portion of the SB, and the TIMI flow of the SB after the MB stenting. Secondary endpoints were post-procedural cardiac Troponin-I (cTnI) rise, need for SB rewiring, time of

rewiring, and need for final kissing balloon dilation and double stenting.

3.5. Statistical Analysis

Results were presented as the mean \pm standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using the t test or the non-parametric Mann-Whitney U test whenever the data did not appear to have a normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were compared using the chi-square test. For the statistical analysis, the statistical software SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL) was used. A P value ≤ 0.05 was considered statistically significant.

4. Results

4.1. Baseline Characteristics

Of the 550 patients who were initially evaluated, 60 patients were subjected to random assignment of 30 to each group (Figure 1). The patients were fairly comparable in terms of baseline demographic and clinical characteristics except for hypertension, which was more prevalent in the control group (Table 1). The mean age of the patients was 57.3 years (range: 35 - 79 years) and 73% were male. There was no significant difference in the levels of pre-procedural cardiac Troponin-I between the two groups ($P = 0.44$). The patients were also homogenous regarding angiographic characteristics (Table 2). The most common site of treated bifurcation lesions in both groups was the junction of the left anterior descending artery and the diagonal branches followed by bifurcation lesions of the left circumflex artery and obtuse marginal branches. Based on the Medina classification, the lesion type of 1, 1, 1 was the most common type seen in both groups ($P = 0.94$). The MB stents were comparable in length and diameter in both groups. The mean cTnI level was 0.19 ± 0.56 in the predilation group and 0.43 ± 1.62 in the control group before the procedure without a significant statistical difference ($P = 0.44$). The procedural characteristics of the patients are shown in Table 3.

4.2. Primary and Secondary Outcomes

There was a trend toward higher rates of dissection in the ostium of the SB after predilation (16.7% vs. 0, $P = 0.07$). Impaired flow of the SB was seen in 10% of patients who received MB stenting after SB predilation; it occurred in 6.7% of patients who did not receive predilation ($P = 0.34$). The need for the SB rewiring and mean wiring time was not affected by the SB predilation. FKB dilation and the double stenting procedure were more common in the predilation group although the associations were not significantly important. The mean cTnI level was 0.75 ± 2.51 in the predilation group and 0.55 ± 1.12 in the control group after the procedure without a significant statistical difference ($P = 0.69$). Multivariable linear regression analysis (Table 4) showed

no difference between the predilation and non-predilation groups in mean percent of stenosis in the SB (beta = -2.673, SE = 3.222, P = 0.411). Also, the similar multivariable model

(Table 5) showed no difference between the two groups in the frequency of complications of final kissing balloon inflation (beta = 0.073, SE = 0.079, P = 0.363).

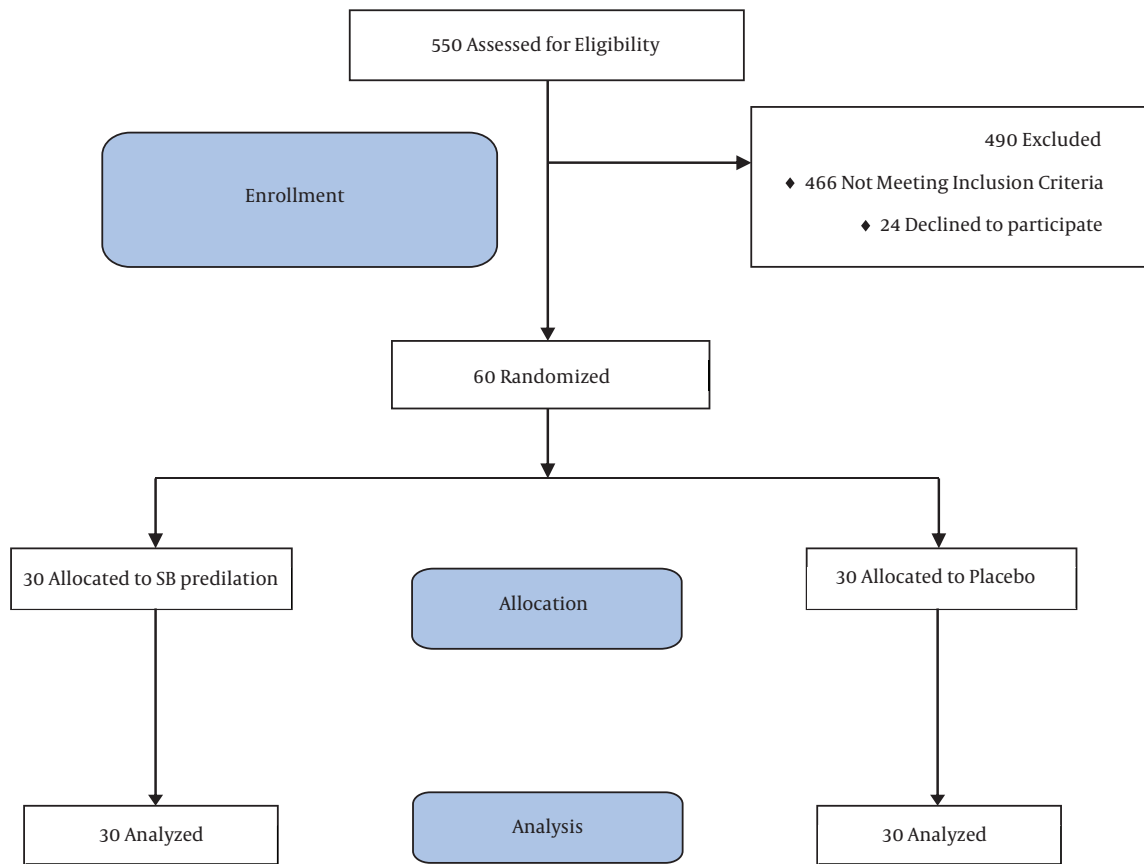


Figure 1. Flow of Study Patients

Table 1. Baseline Demographic and Clinical Data of the Study Participants^{a,b}

Baseline Data	Predilation	Non-Predilation	P Value
Age (Mean), y	58.9 ± 12.7	56.6 ± 9.4	0.42
Gender			0.55
Male	23 (76.7)	21 (70)	
Female	7 (23.3)	9 (30)	
Risk factors			
Smoking	7 (23.3)	7 (23.3)	0.9
Hypertension	8 (26.7)	17 (56.7)	0.01
Dyslipidemia	12 (40)	11 (36.7)	0.31
Diabetes	7 (23.3)	11 (36.7)	0.26
Family history	3 (10.3)	2 (6.7)	0.6
Left ventricular function Mean (%)	44.5 ± 9.41	45.19 ± 8.82	0.77
Clinical presentation			
Stable angina	17 (56.6)	22 (73.3)	0.22
NSTEMI	2 (6.7)	3 (10.3)	0.77
UA	11 (36.7)	5 (17.2)	0.12
Pre-procedural cTnI (µg/L)	0.19 ± 0.56	0.43 ± 1.62	0.44

Abbreviations: cTnI, cardiac Troponin-I; NSTEMI, non-ST-segment elevation MI; UA, unstable angina.

^a(n = 30).

^bValues are presented as No. (%) or Mean ± SD.

Table 2. Angiographic Data of the Study Participants^{a,b}

Angiographic data	Predilation	Non-Predilation	P Value
Lesion location			0.48
LAD-D	24 (80)	27 (90)	
LCX-OM	5 (16.7)	2 (6.7)	
Distal RCA	1 (3.3)	1 (3.3)	
Medina type			0.94
1,1,1	22 (73.3)	21 (70)	
1,0,1	3 (10)	3 (10)	
0,1,1	5 (16.7)	6 (20)	
Main branch			
Lesion length, mm	24.60 ± 6.98	24.33 ± 7.80	0.88
Diameter, mm	3.95 ± 1.23	3.27 ± 1.16	0.29(.99)
Side branch			
Lesion length, mm	4.43 ± 1.74	3.67 ± 1.06	0.06
Diameter, mm	2.33 ± 0.09	2.27 ± 0.13	0.93

Abbreviations: LAD-D, left anterior descending artery-diagonal branch; LCX-OM, left circumflex artery-obtuse marginal branch; RCA, right coronary artery.

^a(n=30).

^bValues are presented as No. (%) or Mean ± SD.

Table 3. Procedural Characteristics of the Patients^{a,b}

Procedural data	Predilation	Non-Predilation	P Value
Type of stent			0.77
Drug-eluting	30 (100)	29 (96.6)	
Bare-metal	0	1 (3.3)	
Main branch stent			
Length	28.53 ± 7.25	26.87 ± 7.86	0.32
Diameter	3.02 ± 0.33	2.96 ± 0.34	0.69
Inflation pressure	11.87 ± 1.41	12.13 ± 1.48	0.66
Side branch			
Dissection	(16.7)	0	0.07
TIMI < 3	3 (10)	1 (6.7)	0.34
Ostial stenosis > 80%	4 (13.3)	8 (26.6)	0.17
Need to rewire	15 (50)	12 (40)	0.43
Rewiring time (mean), min	2.87 ± 1.69	3.08 ± 1.38	0.72
Final kissing inflation	14 (46.7)	11 (36.7)	0.43
Double stent strategy	4 (13.3)	0	0.11
cTnI level, µg/L	0.75 ± 2.51	0.55 ± 1.12	0.69

Abbreviations: cTnI, cardiac troponin-I; TIMI, thrombolysis in myocardial infarction.

^a(n = 30).

^bValues are presented as No. (%) or Mean ± SD.

Table 4. Multivariable Linear Regression Analysis to Assess the Difference Between the Predilation and Non-Predilation Groups in Mean Percent of Stenosis in the Side Branch

Item	B	Std. Error	P Value	Lower Bound	Upper Bound
Constant	70.478	20.912	0.002	28.332	112.624
Predilation	-2.673	3.222	0.411	-9.168	3.821
Gender	0.368	3.423	0.915	-6.530	7.266
Age	0.094	0.144	0.515	-.195	0.384
Diabetes	0.859	3.718	0.818	-6.635	8.353
Hypertension	4.796	3.565	0.185	-2.389	11.982
Dyslipidemia	0.229	4.154	0.956	-8.143	8.601
Smoking	1.001	3.911	0.799	-6.881	8.883
Family history	-9.991	5.081	0.056	-20.232	0.250
Ejection fraction	0.055	0.174	0.753	-0.296	0.407

Table 5. Multivariable Linear Regression Analysis to Assess the Difference Between the Predilation and Non-Predilation Groups in the Frequency of the Complications of Final Kissing Balloon Inflation

Item	B	Std. Error	P Value	Lower Bound	Upper Bound
Constant	1.852	0.510	0.001	0.820	2.883
Predilation	0.073	0.079	0.363	-0.087	0.233
Gender	-0.022	0.082	0.792	-0.188	0.144
Age	7.950	0.003	0.998	-0.007	0.007
Diabetes	0.058	0.090	0.523	-0.123	0.239
Hypertension	-0.111	0.088	0.216	-0.288	0.067
Dyslipidemia	0.029	0.104	0.782	-0.182	0.240
Smoking	-0.105	0.094	0.274	-0.295	0.086
Family history	0.220	0.133	0.105	-0.048	0.488
Ejection fraction	-0.004	0.004	0.285	-0.013	0.004

5. Discussion

In the present clinical trial, the procedural consequences of SB predilation in provisional stenting of true bifurcation lesions were assessed. This study showed that the strategy of SB predilation has no significant effect on the outcome of the procedure including SB dissection, ostial stenosis after MB stenting, impairment of flow, rise in cardiac enzymes, need for rewiring, time of rewiring, and the rate of FKB inflation and double stenting. Instead, it seems there is a trend toward unfavorable results from predilation such as more common dissections in the SB ostium and impairment of flow, as well as a need for more complicated procedures. Even though it numerically reduced the severity of ostial stenosis of the SB after MB stenting and the time for rewiring of the SB, this was not associated with significant improvement of the final outcome. Although this study was not substantive due to the small number of participants, the results were similar to those of other studies. To date, there are not many studies comparing the effects of SB predilation on the outcome of PCI in true bifurcation lesions. The ma-

jority of studies have investigated the results of different types of stenting procedures without looking at initial treatment of the SB. There are three related studies currently available. In a study on provisional stenting of the left main bifurcation, SB predilation was associated with higher rates of FKB dilation and the double stent technique. The rates of long-term target vessel failure and revascularization were also higher in this group (15). The results of this study seem to be affected by various factors, such as being non-randomized and the performance of predilation on more complex SB anatomies. The only other randomized trial on this topic was performed by Pan et al. (14). It showed improved TIMI flow of the predilated SBs and less need to treat the SB after MB stenting. However, SB predilation had no significant effect on the final outcomes of the patients. In this study, post-dilation of the SBs was performed in the case of SB TIMI flow < 3 and SB ostial stenosis > 50%. Given the performance of this study on true bifurcation lesions which is defined as the presence of ostial stenosis > 50%, one can assume that all

the lesions needed post-dilation. As a result, the final outcomes might be affected by SB post-dilation even in the non-predilatation group (14). In our study, further interventions were required with stricter criteria: the occurrence of TIMI flow < 3 and the presence of ostial stenosis > 80% after MB stenting, a practice which is more in accord with real-world practice. It offers the opportunity to best compare the consequences of SB predilatation against non-predilatation. In addition, different techniques of SB predilatation are used by different operators and could result in different consequences. Although there is scarcity of data regarding the effects of SB predilatation in the treatment of bifurcation lesions, our results were in accordance with available data, and have led us to the consensus that this procedure should be avoided in routine practice.

5.1. Limitations

The first and foremost limitation of this study was that it did not involve a significant population due to the small number of the participants. Also, visual estimation of the stenoses was used in this study, rather than quantitative coronary measurements. In addition, we did not use fractional flow reserve for evaluating the significance of SB ostial lesions before and after the procedure.

5.2. Conclusions

Though limited due to the low number of participants, this study gave results that were similar to those of other studies on this issue. It seems that routine SB predilatation is not necessarily associated with better angiographic results or ease of the procedure. Instead, it might result in the occurrence of more dissection and need for more complex procedures. Still, there are some complex ostial lesions of the SB which could benefit from predilatation.

Acknowledgments

The authors would like to thank Dr. Hooman Bakhshandeh for his critical review of the manuscript.

Footnotes

Authors' Contribution: Hamidreza Sanati, Majid Hajikarimi, Ali zahedmehd and Mohammadmehdi Peighambari developed the study concept and designed the study. Majid Hajikarimi and Parham Sadeghipour were in charge of acquisition of data. Hamidreza Sanati, Majid Hajikarimi and Mohammadmehdi Peighambari analyzed and interpreted data. Ata Firouzi and Reza Kiani were in charge of drafting the manuscript. Siamak kazemi Asl revised the article. Hamidreza Sanati was in charge of statistical analysis. The study was technically supported by Mohammadmehdi Peighambari. The study was supervised by Mohammadmehdi Peighambari and

Farshad Shakerian.

Funding/Support: This study did not receive any funding or support.

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