Clinical and Angiographic Predictors of Major Side Branch Occlusion after Main Vessel Stenting in Coronary Bifurcation Lesions

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Abstract

Background: Major side branch (SB) occlusion is one of the most serious complications during percutaneous coronary intervention (PCI) for bifurcation lesions. We aimed to characterize the incidence and predictors of major SB occlusion during coronary bifurcation intervention.

Methods: We selected consecutive patients undergoing PCI (using one stent or provisional two stent strategy) for bifurcation lesions with major SB. All clinical characteristics, coronary angiography findings, PCI procedural factors and quantitative coronary angiographic analysis data were collected. Multivariate logistic regression analysis was performed to identify independent predictors of SB occlusion. SB occlusion after main vessel (MV) stenting was defined as no blood flow or any thrombolysis in myocardial infarction (TIMI) flow grade decrease in SB after MV stenting.

Results: Among all 652 bifurcation lesions, 32 (4.91%) SBs occluded. No blood flow occurred in 18 lesions and TIMI flow grade decreasing occurred in 14 lesions. In multivariate analysis, diameter ratio between MV/SB (odds ratio [OR]: 7.71, 95% confidence interval [CI]: 1.53–38.85, P = 0.01), bifurcation angle (OR: 1.03, 95% CI: 1.02–1.05, P < 0.01), diameter stenosis of SB before MV stenting (OR: 1.05, 95% CI: 1.03–1.07, P < 0.01), TIMI flow grade of SB before MV stenting (OR: 3.59, 95% CI: 1.48–8.72, P < 0.01) and left ventricular ejection fraction (LVEF) (OR: 1.06, 95% CI: 1.02–1.11, P < 0.01) were independent predictors of SB occlusion.

Conclusions: Among clinical and angiographic findings, diameter ratio between MV/SB, bifurcation angle, diameter stenosis of SB before MV stenting, TIMI flow grade of SB before MV stenting and LVEF were predictive of major SB occlusion after MV stenting.

Key words: Coronary Bifurcation Lesions; Major Side Branch Occlusion; Percutaneous Coronary Intervention

INTRODUCTION

Approximately 15–20% of percutaneous coronary intervention (PCI) are performed to treat coronary bifurcation lesions.[1-2] Coronary bifurcation lesions are one of the most challenging subsets in interventional cardiology, and the treatment is still the subject of substantial debate. Several randomized clinical trials have recommended a provisional technique of stenting as the routine bifurcation stenting technique.[3-6] However, side branch (SB) occlusion after main vessel (MV) stenting is a serious procedural complication for the provisional approach. Previous studies have reported that the reference vessel diameter (RVD) of the SB and the prevalence of a stenosis at SB ostium were independent predictors of SB occlusion,[7-9] but numerous factors such as clinical and angiographic characteristics could impact the risk of SB occlusion. Accordingly, this study was designed to characterize the incidence and predictors of major SB occlusion during coronary bifurcation intervention in a cohort of consecutive patients who underwent PCI in a single center for cardiovascular disease.

METHODS

Study population
All the patients enrolled in our study population were patients with coronary bifurcation lesions, which were defined as a coronary artery narrowing occurring adjacent to or involving the origin of a significant SB.[10] From January 2012 to July 2012, a cohort of 7007 consecutive patients with 9421 lesions underwent PCI at Fuwai Hospital in Beijing, China. In our study, inclusion criteria were: (1) Patients with coronary bifurcation lesions undergoing PCI; and (2) the bifurcation...
Lesion consists at least one major SB. The definition of major SB was consistent with previous studies: RVD measured by quantitative coronary angiography (QCA) ≥2.0 mm. To investigate predictors of SB occlusion after MV stenting, exclusion criteria was: Patients undergoing elective SB stenting before MV stenting. Among the 7007 patients, 5172 patients without bifurcation lesions and 290 patients with bifurcation lesions undergoing elective SB stenting were excluded. 908 coronary bifurcation patients with SB baseline reference diameter <2.0mm were also excluded. Finally, 637 patients with 652 bifurcation lesions which met all the inclusion criteria and had no exclusion criteria were included in this study. Primary endpoint of the study was SB occlusion, which was defined as no blood flow or any thrombolysis in myocardial infarction (TIMI) flow grade decrease in SB after MV stenting. The Ethics Committee of the Cardiovascular Institute and Fuwai Hospital approved this study.

Procedure and periprocedural practices
Coronary angioplasty was performed in the conventional manner and coronary stents or other procedures/devices were used only when required. In all cases, the interventional strategy and instrumentation used were at the discretion of the interventional cardiologists. Decisions on treatment strategy for bifurcation lesions were made by individual operators. The administration of periprocedural antiplatelet and antithrombotic medications was based on the operator’s discretion and current guidelines. Administration of 300 mg clopidogrel and 300 mg aspirin as loading doses within the 24 h before the procedure was mandatory. Lifelong aspirin (100 mg/d) was prescribed to all patients. At least 12 months of clopidogrel (75 mg/d) was recommended to all patients.

Data collection and quantitative coronary angiography
Clinical data were obtained through a review of the medical records. All baseline and procedural coronary angiography were reviewed and analyzed by an independent core laboratory at Fuwai Hospital. Coronary angiography findings including bifurcation location, Medina classification, baseline and post-procedural TIMI flow grade in MV and SB as well as plaque distribution were recorded. Procedural characteristics such as SB predilation and jailed wire in the SB were also observed. Quantitative coronary angiography was performed using standard quantitative analyses and definitions. A main principle of our QCA approach was to ensure as little observer interference as possible. Angiograms obtained at baseline and before MV stenting were analyzed with the use of a computer-based system dedicated to bifurcation analysis (Qangio XA, version 7.3, Medis, Leiden, the Netherlands). We obtained quantitative angiographic measurements of the four segments of the bifurcation lesion: The proximal MV segment, the distal MV segment, the SB segment and the bifurcation core segment [Figure 2]. Bifurcation core is defined as the central part of the bifurcation which begins where the common vessel starts to split into two branches and ends at the carinal point, which area was calculated by the Qangio XA software. We also obtained the bifurcation angle (the angle between the distal MV and the SB) from the analysis system.

In addition to the inherent data from the QCA analysis, another innovative variable was calculated based on the QCA data: Diameter ratio between MV/SB (formula = [reference diameter of proximal MV + reference diameter of distal MV]/2 [reference diameter of SB]), which is a parameter reflects the relative plaque burden of SB.

Statistical analysis
Continuous data are presented as mean ± standard deviation (SD) and were compared using the Student’s t-test. Categorical variables were summarized as counts and percentages and were compared by Chi-square test or Fisher’s exact test as appropriate.

Multivariate logistic regression analysis was performed to identify independent predictors of SB occlusion. The covariates that were either statistically significant on univariate analysis (P < 0.25) or considered important were included in the multivariate model. Totally, 28 covariates were employed in the multivariate model, including diabetes, previous PCI, medina classification, plaque location,
reference diameter of the proximal and distal MV, reference
diameter of the SB, preprocedural percent diameter stenosis
of the proximal MV, preprocedural percent diameter stenosis
of the distal MV, true bifurcation lesions, lesion length of
the MV and SB, bifurcation angle, predilation of the SB and
jailed wire in SB. Estimates of the adjusted differences in
risks are presented with 95% confidence intervals (CIs) of
the difference. All P values were two-tailed, and a P < 0.05
was considered as statistically significant. All analyses were
performed with SAS 9.4 system (SAS Institute, Cary, NC,
USA).

RESULTS

Patient, lesion and procedural characteristics

Side branch occlusion occurred in 32 (4.9%) of 652
bifurcation lesions treated with one stent technique or MV
stenting first strategy. Patients and lesions were divided into
two groups according to SB occlusion or not.

Patient characteristics are shown in Table 1. All the baseline
characteristics were balanced between the two groups.
Lesion characteristics are presented in Table 2. Medina
classification and plaque distribution differ significantly
between the two study groups. Procedure data are shown in
Table 3. All the data except the rate of jailed wire in SB are
significantly different between the two groups. QCA data
are presented in Table 4. There are significant differences
between the two groups in diameter stenosis of proximal
MV, bifurcation core and SB. However, regarding the lesion
length, there were no significantly different between the two
groups of all four parts. Lesions in SB occlusion group have
higher bifurcation angle, diameter ratio between MV/SB and
diameter stenosis of SB before MV stenting.

Fate of occluded side branch after main vessel stenting

No blood flow occurred in 18 (56.3%) lesions and TIMI flow
grade decreasing occurred in 14 (43.7%) lesions. Blood flow
in SB was restored spontaneously in 2 (6.3%) lesions and
by SB intervention in 3 (9.4%) lesions of 32 occluded SB.
A total of 27 (84.4%) lesions were occluded permanently.
For SB interventions, rewiring and balloon angioplasty was
performed in 4 SBs, among them, 1 SB was permanently
occluded despite rewiring and ballooning.

Predictors of side branch occlusion

Independent predictors of SB occlusion are presented in
Table 5. After adjustment using a multiple logistic regression
model, diameter ratio between MV/SB and TIMI flow grade
of SB before stenting is two important predictors. Bifurcation
angle, diameter stenosis of SB before MV stenting and
left ventricular ejection fraction (LVEF) are also predictive
of SB occlusion. Preprocedural diameter stenosis of the
proximal MV, distal MV was not independent predictors of
major SB occlusion. Also, the lesion length of proximal MV,

| Table 1: Characteristics of patients undergoing PCI |
|---------------------------------------------------|
| Characteristics | SB occlusion (n = 31) | No SB occlusion (n = 606) | P |
| Age, years | 57.5 ± 12.2 | 57.7 ± 10.2 | 0.93 |
| Male | 26/31 (83.9) | 494/606 (81.5) | 0.74 |
| BMI, kg/m² | 26.4 ± 3.2 | 26.1 ± 3.3 | 0.70 |
| Diabetes | 10/31 (32.3) | 152/606 (25.1) | 0.37 |
| Hypertension | 18/31 (58.1) | 356/606 (58.9) | 0.92 |
| Hyperlipemia | 24/31 (77.4) | 477/606 (79.0) | 0.84 |
| Myocardial infarction in 1-month | 8/31 (25.8) | 109/606 (18.0) | 0.27 |
| Emergency PCI | 3/31 (9.7) | 14/606 (2.3) | 0.06 |
| Unstable angina | 12/31 (38.7) | 281/606 (46.5) | 0.40 |
| LVEF | 59.5 ± 9.9 | 63.1 ± 7.7 | 0.06 |
| Previous myocardial infarction (>1-month) | 7/31 (22.6) | 99/606 (16.3) | 0.36 |
| Previous PCI | 7/31 (22.6) | 99/606 (16.4) | 0.37 |
| Previous CABG | 0/31 (0) | 2/606 (0.3) | 0.75 |
| Previous stroke | 5/31 (16.1) | 66/606 (10.9) | 0.55 |
| Family history of CAD | 3/31 (9.7) | 104/606 (17.2) | 0.40 |
| Previous peripheral vascular disease | 4/31 (12.9) | 93/606 (15.4) | 0.90 |
| Smoking history | 14/31 (45.2) | 242/606 (40.1) | 0.57 |

Values presented as n/N (%) or mean ± SD. SB: Side branch; BMI: Body mass index; PCI: Percutaneous coronary intervention; LVEF: Left ventricular
ejection fraction; CABG: Coronary artery bypass grafting; CAD: Coronary artery disease; SD: Standard deviation.
Table 2: Lesion characteristics

| Characteristics                          | SB occlusion (n = 32) | No SB occlusion (n = 620) | P     |
|------------------------------------------|-----------------------|---------------------------|-------|
| Coronary distribution                    |                       |                           |       |
| Right dominant coronary                  | 30/32 (93.8)          | 568/620 (91.6)            | 0.69  |
| Left dominant coronary                   | 1/32 (3.1)            | 38/620 (6.1)              |       |
| Codominant coronary                      | 1/32 (3.1)            | 14/620 (2.3)              |       |
| Location of bifurcation                  |                       |                           |       |
| LM                                       | 0/32 (0)              | 30/620 (4.8)              | 0.49  |
| LAD                                      | 16/32 (50.0)          | 336/620 (54.2)            |       |
| LCX                                      | 7/32 (21.9)           | 124/620 (20.0)            |       |
| RCA                                      | 9/32 (28.1)           | 130/620 (21.0)            |       |
| Medina classification                     |                       |                           |       |
| 1,0,0                                    | 5/32 (15.6)           | 182/620 (29.4)            | <0.01 |
| 0,1,0                                    | 3/32 (9.4)            | 204/620 (32.9)            |       |
| 1,1,0                                    | 3/32 (9.4)            | 79/620 (12.7)             |       |
| 1,1,1                                    | 9/32 (28.1)           | 78/620 (12.6)             |       |
| 0,0,1                                    | 1/32 (3.1)            | 2/620 (0.3)               |       |
| 1,0,1                                    | 5/32 (15.6)           | 42/620 (6.8)              |       |
| 0,1,1                                    | 6/32 (18.8)           | 33/620 (5.3)              |       |
| MV Plaque located at the same side of SB | 18/32 (56.3)          | 174/620 (28.1)            | <0.01 |
| Moderate–severe lesion calcification     | 4/32 (12.5)           | 27/593 (4.4)              | 0.09  |
| Moderate–severe angulation               | 15/32 (46.9)          | 347/620 (56.0)            | 0.31  |
| Thrombosis                               | 2/32 (6.3)            | 22/620 (3.5)              | 0.76  |
| Preprocedural TIMI flow grade            |                       |                           |       |
| TIMI 1                                   | 5/32 (15.6)           | 27/620 (4.4)              | 0.12  |
| TIMI 2                                   | 5/32 (15.6)           | 72/620 (11.6)             |       |
| TIMI 3                                   | 22/32 (68.8)          | 521/620 (84.0)            |       |
| Irregular plaque                         | 3/32 (9.4)            | 21/620 (3.4)              | 0.20  |
| SB Moderate–severe lesion calcification  | 0/32 (0)              | 2/620 (0.3)               | 1.00  |
| Moderate–severe angulation               | 2/32 (6.3)            | 26/620 (4.2)              | 0.91  |
| Thrombosis                               | 0/32 (0)              | 1/620 (0.2)               | 1.00  |
| Preprocedural TIMI flow grade            |                       |                           |       |
| TIMI 1                                   | 0/32 (0)              | 4/620 (0.6)               | 0.63  |
| TIMI 2                                   | 3/32 (9.4)            | 8/620 (1.3)               |       |
| TIMI 3                                   | 29/32 (90.6)          | 608/620 (98.1)            |       |
| Irregular plaque                         | 1/32 (3.1)            | 5/600 (0.8)               | 0.70  |

Values presented as n/N (%). SB: Side branch; LM: Left main; LAD: Left anterior descending; LCX: Left circumflex; OM: Obtuse marginal branch; RCA: Right coronary artery; MV: Main vessel; TIMI: Thrombolysis in myocardial infarction.

distal MV, bifurcation core and SB were not predictive of major SB occlusion.

Using SB occlusion after MV stenting as a state variable and these five independent predictors were as test variables, a receiver operating characteristic (ROC) curve was generated [Figure 3]. The area under the ROC curve was 0.84 (95% CI: 0.81–0.87, P < 0.01).

**DISCUSSION**

Nowadays, the provisional strategy has been considered as the preferred stenting technique in the majority of coronary bifurcation lesions. Provisional technique of stenting has been found to be noninferior to elective double stenting with respect to clinical outcome in 5-year follow-up. However, abrupt closure of the SB may occur after MV stent implantation. The complication of SB occlusion in complex bifurcation lesions is

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**Figure 3:** Receiver operating characteristic (ROC) curve. The area under ROC curve was 0.84 (95% confidence interval: 0.81–0.87, P < 0.001).
limits the utilization of provisional stenting. Identifying the predictors of SB occlusion could help to select the optimal intervention strategy during coronary bifurcation PCI. Although previous studies have reported that the RVD of the SB and the SB ostial stenosis are independent predictors of SB occlusion,\[7,8\] SB occlusions are determined by many factors including the clinical and angiographic characteristics. Accordingly, our study sought to characterize the predictors of SB occlusion during coronary bifurcation intervention in a cohort of consecutive patients who underwent PCI in a large single center for cardiovascular disease.
The major findings of this study are that: (1) Angiography characteristics like diameter stenosis of SB before MV stenting, TIMI flow grade of SB before MV stenting and bifurcation angle are independent predictors of SB occlusion; (2) Innovative parameter in this study “diameter ratio between MV/SB” is an important predictor of SB occlusion; (3) LVEF is also predictive for SB occlusion after MV stenting.

Diameter stenosis of SB at baseline has been reported to be a predictive factor of SB occlusion, also, diameter stenosis of SB before MV stenting has been considered as an independent predictor of SB occlusion. Diameter stenosis of SB before MV stenting can reflect the real plaque burden and lesion severity of SB. Both diameter stenosis of SB at baseline and diameter stenosis of SB before MV stenting were enrolled in the present study and only diameter stenosis of SB before MV stenting was selected as an independent predictor. Arteries with lower TIMI flow grade are more likely to have thrombus or other complex lesion features, and, therefore, are more likely to have SB occlusion. Previous study has reported that preprocedural TIMI Grade 2 flow in SB was a predictive factor for SB occlusion. In our study, TIMI flow grade of SB before MV stenting was found to be an independent predictor of SB occlusion after MV stenting. We also found that the risk of SB occlusion increased as the ratio of the diameter between MV/SB increased, which is concordant with the results of previous studies. Diameter ratio between MV/SB reflects the relative plaque volume of MV. Larger diameter ratio between MV/SB indicates relatively larger plaque burden to SB.

One study found that LVEF <50% was a risk factor for periprocedural myocardial infarction (hazard ratio: 2.08, 95% CI: 1.13–3.82, \( P = 0.018 \)). Hahn et al. have reported that LVEF of patients in SB occlusion group (median: 56.0%, interquartile range: 47.0–63.0%) were significantly lower than patients in no SB group (median: 60.0%, interquartile range: 54.0–65.7%) \( (P < 0.01) \). However, Hahn et al. failed to detect LVEF as an independent predictor of SB occlusion in multivariable analysis. LVEF was selected as an independent predictor of SB occlusion after adjustment using a multivariable model in the present study. One potential explanation is that lower LVEF may directly reflect impaired coronary blood flow, which could contribute to SB occlusion.

The effect of bifurcation angle on the rate of SB occlusion during PCI is controversial. Previous studies have reported that smaller angle in coronary bifurcations predicted higher SB compromise, restenosis, and major adverse cardiac events (MACE) rates based on small sample size. However, Yoshitaka Goto et al. reported that bifurcation angle was not associated with SB compromise after MV stenting. On the other hand, Dzavik et al. found that bifurcation angle >50° is an independent predictor of MACE after bifurcation crush stenting. In our study, a wide bifurcation angle predicted SB occlusion after MV stenting. Part of the explanation was that bifurcations with smaller bifurcation angle was easier for flow diversion into SB and too large bifurcation angle might increase the pressure drop and flow resistance, thus increasing the SB occlusion risk. Another potential explanation was that increasing bifurcation angle decreased wall shear stress and increases oscillatory shear index significantly around the carina, which might induce plaque proliferation at the bifurcation region. Higher plaque volume in bifurcation core may contribute to the higher SB occlusion risk.

Both jailed wire in SB and predilatation of SB were considered as potential factors affecting SB occlusion in the present study. After univariate analysis, jailed wire in SB and predilatation of SB were employed in the multivariate model; however, none of them was selected as an independent risk factor for SB occlusion. The results of the present study was consistent with previous studies and differences in technique were not independent predictors of SB occlusion. Although jailed wire in SB and other procedural factors may affect the SB occlusion and SB flow recovery, none of these factors were selected as independent predictors of SB occlusion in the present study. Acute coronary syndrome has reported to be an independent predictor of SB occlusion; nevertheless, there is no significant difference in unstable angina, myocardial infarction within 1 month or emergency PCI between the two groups in the present study. Other factors which may be considered as predictors of SB occlusion like thrombus burden and lesion length of SB were also not selected as independent predictors of SB occlusion. Additional prospective clinical studies may further help to clarify these questions.

Previous studies have reported that the incidence of SB occlusion was 7.37–19.00%. In our study, the rate of SB occlusion was 4.91%. This wide range of SB occlusion rate can be attributable to the difference in RVD of SB in these studies. Smaller RVD was an independent predictor of SB occlusion reported in the previous study, and the rate of SB occlusion do increase as the RVD of SB become smaller. Compared with these previous studies, the mean RVD of SB was larger in the present study (2.3 ± 0.2 mm), which may explain the relative lower incidence of SB occlusion.

In the present study, the mean reference of SB was 2.3 ± 0.2 mm in SB occlusion group, and not all SBs were suitable for stent implantation. Selective two-stent strategy is helpful to prevent SB occlusion for large SB with high risk of occlusion. For these relative small SBs with high occlusion risk, jailed-balloon technique is recommended in consideration of that jailed-balloon technique was associated with a high procedural success rate, lower rates of SB loss and MACE at late follow-up. Compared with previous studies, the strength of our study is that we have included all the clinical, angiographic, procedural factors as well as other innovative parameters like diameter ratio between MV/SB in this large-scale study, which is significantly predictive of SB occlusion. Another
strength of our study was that the study was conducted in a consecutive cohort of bifurcation patients, which could reflect the real-world clinical practice.

There are several limitations of our study. First, we designed our trial as a mechanistic angiographic study that addressed the issue of identifying predictors of SB occlusion after MV stenting. Hence, our study was not powered to address clinical endpoints, but further studies are needed to research the impact on long-term clinical outcomes. Second, selection of treatment strategies, stent types, and other instruments were at the discretion of operators. Our findings are subject to selection bias and compounded with unmeasured variables. Additionally, due to the low incidence of major SB occlusion, only 32 cases of SB occlusion were included in the present study, there is a possibility of statistical overfit which could limit reproducibility of this model in other populations.

In conclusion, among clinical and coronary angiographic findings, diameter ratio between MV/SB, bifurcation angle, diameter stenosis of SB before MV stenting, TIMI flow grade of SB before MV stenting and LVEF were predictive of major SB occlusion after MV stenting.

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Received: 16-12-2014 Edited by: Li-Min Chen
How to cite this article: Zhang D, Xu B, Yin D, Li YP, He Y, You SJ, Qiao SB, Wu YJ, Yan HB, Yang YJ, Gao RL, Dou KF. Clinical and Angiographic Predictors of Major Side Branch Occlusion after Main Vessel Stenting in Coronary Bifurcation Lesions. Chin Med J 2015;128:1471-8.

Source of Support: This research was supported by grants from the Beijing Municipal Science and Technology Commission (No. Z141107002514096) and from PUMC Youth Fund and Fundamental Research Funds for the Central Universities (No. 33320140166). Conflict of Interest: None declared.