**Predictors and Outcomes of Side Branch Occlusion After Main Vessel Stenting in Coronary Bifurcation Lesions**

Results From the COBIS II Registry (COrony BIfurcation Stenting)

Joo-Yong Hahn, MD, PhD,* Woo Jung Chun, MD, PhD,† Ji-Hwan Kim, MD,* Young Bin Song, MD, PhD,* Ju Hyeon Oh, MD, PhD,† Bon-Kwon Koo, MD, PhD,‡ Seung Woon Rha, MD, PhD,§ Cheol Woong Yu, MD, PhD,,∥ Jong-Sun Park, MD, PhD,¶ Jin-Ok Jeong, MD, PhD,# Seung-Hyuk Choi, MD, PhD,* Jin-Ho Choi, MD, PhD,* Myung-Ho Jeong, MD, PhD,** Jung Han Yoon, MD, PhD,†† Yangsoo Jang, MD, PhD,†† Seung-Jea Tahk, MD, PhD, §§ Hyeo-Soo Kim, MD, PhD,∥∥ Hyeon-Cheol Gwon, MD, PhD* Seoul, Changwon, Bucheon, Daegu, Daejeon, Gwangju, Wonju, and Suwon, Republic of Korea

**Objectives**

This study sought to investigate the predictors and outcomes of side branch (SB) occlusion after main vessel (MV) stenting in coronary bifurcation lesions.

**Background**

SB occlusion is a serious complication that occurs during percutaneous coronary intervention (PCI) for bifurcation lesions.

**Methods**

Consecutive patients undergoing PCI using drug-eluting stents for bifurcation lesions with SB/C21 \( \geq 2.3 \) mm were enrolled. We selected patients treated with the 1-stent technique or MV stenting first strategy. SB occlusion after MV stenting was defined as Thrombolysis in Myocardial Infarction flow grade \(<3\).

**Results**

SB occlusion occurred in 187 (8.4%) of 2,227 bifurcation lesions. In multivariate analysis, independent predictors of SB occlusion were pre-procedural percent diameter stenosis of the SB/C21 \( \geq 50\%\) (odds ratio [OR]: 2.34; 95% confidence interval [CI]: 1.59 to 3.43; \( p < 0.001\)) and the proximal MV/C21 \( \geq 50\%\) (OR: 2.34; 95% CI: 1.57 to 3.50; \( p < 0.001\)), SB lesion length (OR: 1.03; 95% CI: 1.003 to 1.06; \( p = 0.03\)), and acute coronary syndrome (OR: 1.53; 95% CI: 1.06 to 2.19; \( p = 0.02\)). Of 187 occluded SBs, flow was restored spontaneously in 26 (13.9%) and by SB intervention in 103 (55.1%) but not in 58 (31.0%). Jailed wire in the SB was associated with flow recovery (74.8% vs. 57.8%, \( p = 0.02\)). Cardiac death or myocardial infarction occurred more frequently in patients with SB occlusion than in those without SB occlusion (adjusted hazard ratio: 2.34; 95% CI: 1.15 to 4.77; \( p = 0.02\)).

**Conclusions**

Angiographic findings of SB, proximal MV stenosis, and clinical presentation are predictive of SB occlusion after MV stenting. Occlusion of sizable SB is associated with adverse clinical outcomes. (Korean Coronary Bifurcation Stenting Registry II [COBIS]; NCT03642992) (J Am Coll Cardiol 2013;62:1654–9) © 2013 by the American College of Cardiology Foundation
procedural factors such as jailed wire or pre-dilation in the SB are not known. Moreover, impact of sizable SB occlusion on clinical outcomes has not been well studied. Therefore, we investigated predictors and outcomes of SB occlusion after MV stenting in bifurcation lesions, using a large bifurcation registry.

Methods

A detailed description of the study methods is presented in the Online Appendix.

Study population. The COBIS (COronary BIfurcation Stenting) II registry is a retrospective multicenter registry of patients with coronary bifurcation lesions undergoing PCI with drug-eluting stents (DES). From January 2003 through December 2009, 2,897 consecutive patients were enrolled from 18 major coronary intervention centers in Korea. Inclusion criteria were: 1) coronary bifurcation lesions treated with DES only; and 2) MV diameter of ≥2.5 mm and SB diameter of ≥2.3 mm confirmed by core laboratory quantitative coronary analysis. Exclusion criteria were: 1) cardiogenic shock or experience of cardiopulmonary resuscitation; and 2) protected left main disease. The local institutional review board at each hospital approved this study.

To investigate predictors of SB occlusion immediately after MV stenting, we excluded patients undergoing elective SB stenting before MV stenting and selected patients treated with the 1-stent technique or MV stenting first strategy (n = 2,365). Patients with restenotic bifurcation lesions (n = 107) or bifurcation lesions in which the SB had decreased pre-procedural Thrombolysis In Myocardial Infarction (TIMI) flow (n = 31) were excluded. Finally, 2,227 patients who met the selection criteria were included in the analysis.

Data collection and analysis. Data were collected using a Web-based reporting system. Coronary angiograms were reviewed and analyzed quantitatively by an independent core laboratory at Samsung Medical Center (detailed in the Online Appendix). Bifurcation lesions were divided into 3 segments for quantitative coronary angiographic analysis: proximal MV, distal MV, and SB ostium (Fig. 1).

Study outcomes and definitions. SB occlusion was defined as TIMI flow grade <3 immediately after MV stenting. We also performed further analysis using the definition of SB occlusion as TIMI flow grade 0 or 1. Clinical events were defined based on recommendations from the Academic Research Consortium (detailed in the Online Appendix) (6). Major adverse cardiac events (MACE) were defined as a composite of cardiac death, myocardial infarction (MI), or target lesion revascularization (TLR). All events were reported by the principal investigator of each hospital and confirmed by source documentation.

Statistical analysis. Multivariate logistic regression analysis was performed to identify independent predictors of SB occlusion (detailed in the Online Appendix). The Cox proportional hazards method was used to test whether SB occlusion is an independent predictor of clinical outcomes (detailed in the Online Appendix). All p values were 2-tailed, and a p value of <0.05 was considered statistically significant.

Results

Patient characteristics. Of 2,227 bifurcation lesions treated with the 1-stent technique or MV stenting first strategy, SB occlusion occurred in 187 (8.4%) patients. Baseline characteristics of patients are shown in Table 1. Bifurcation location and a prevalence of true bifurcation were significantly different between the 2 groups (Table 2). SB pre-dilation was performed more frequently, but intravascular ultrasound (IVUS) was used less frequently in patients with SB occlusion than in those without SB occlusion. Quantitative coronary angiographic data are presented in Table 3. The angle between the MV and SB was not significantly different between the 2 groups.

Multivariate analysis. Independent predictors of SB occlusion are presented in Table 4. Neither pre-procedural percent diameter stenosis of the distal MV ≥50% nor SB pre-dilation was predictive of SB occlusion. The area under the receiver-operating characteristic (ROC) curve was

---

**Abbreviations and Acronyms**

- **DES** = drug-eluting stent(s)
- **IVUS** = intravascular ultrasound
- **MACE** = major adverse cardiac event(s)
- **MI** = myocardial infarction
- **MV** = main vessel
- **PCI** = percutaneous coronary intervention
- **SB** = side branch
- **TIMI** = Thrombolysis In Myocardial Infarction
- **TLR** = target lesion revascularization

---

**Figure 1 Schematic Diagram of Quantitative Coronary Angiographic Analysis**

Bifurcation lesions were analyzed as follows: (1) main vessel (MV) proximal reference diameter (RD); (2) MV distal RD; (3) side branch (SB) distal RD; (4) MV proximal (proximal to SB take off) minimum luminal diameter (MLD); (5) MV distal (<5 mm distal to takeoff) MLD; (6) SB ostial MLD; (7) MV lesion length; and (8) SB lesion length.
0.75 (95% CI: 0.72 to 0.78) and the Brier score was 0.073. The degree of optimism was 0.024 for the area under the ROC curve, which was acceptable.

**Fate of occluded SB after MV stenting.** SB flow was restored spontaneously in 26 lesions (13.9%) and by SB intervention in 103 (55.1%) lesions but not in 58 (31.0%) of 187 occluded SB. For SB interventions, balloon angioplasty was performed in 88 lesions, and stenting was performed in the SB in 29 lesions. SB was permanently occluded despite ballooning in 11 patients and stenting in 3 patients. Patients with recovery of the occluded SB had jailed wire in the SB more frequently than those without recovery of the occluded SB (74.8% vs. 57.8%, p = 0.02). No other clinical, angiographic, or procedural variables were associated with flow recovery (Online Tables 1 to 3).

**Clinical outcomes.** During follow-up (median: 36 months; interquartile range: 25 to 51 months), SB occlusion was significantly associated with clinical outcomes (Table 5, Fig. 2). In an explanatory 1-month landmark analysis, stent thrombosis occurred more frequently in patients with SB occlusion than in those without SB occlusion, whereas there were no significant differences in other outcomes between the 2 groups after 1 month (Online Fig. 1). Clinical outcomes were more favorable with recovered SB than with persistently occluded SB (see Online Results section and Online Table 4). Among 129 patients with recovered SB, the rate of MACE was significantly higher in the 2-stent group than in the 1-stent group (23.1% vs. 7.8%, p = 0.03). Stent thrombosis occurred in 2 patients (7.7%) of the 2-stent group and in 2 patients (1.9%) of the 1-stent group (p = 0.18).

**Additional analysis using definition of SB occlusion as TIMI flow grade 0 or 1.** SB occlusion after MV stenting occurred in 108 (4.8%) of 2,227 bifurcation lesions. Similar results were found even if SB occlusion was defined as TIMI flow grades 0 to 1 (see Online Results section and Online Table 5).

**Discussion**

Currently, most bifurcation lesions are treated with a provisional strategy (7). However, SB occlusion after MV stenting is one of the most serious complications during the procedure and may be the major reason why operators prefer the systematic 2-stent technique in the complex bifurcation lesions. Predicting the risk of SB occlusion could improve...
stenosis, was independently predictive of SB occlusion. Plaque estingly, the proximal MV stenosis, but not the distal MV plaque than with focal stenosis in the SB ostium (9). In t - occlusion occurred more frequently with diffuse atherosclerotic associated with SB occlusion. An IVUS study reported that SB decrease in the distal MV segment by volumetric IVUS in the proximal MV segment but not with plaque volume

Table 4 Independent Predictors of SB Occlusion

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI) (range)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-procedural %DS of the SB ≥50%</td>
<td>2.34 (1.59–3.43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pre-procedural %DS of the proximal MV ≥50%</td>
<td>2.34 (1.57–3.50)</td>
<td>0.03</td>
</tr>
<tr>
<td>SB lesion length</td>
<td>1.03 (1.00–1.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>1.53 (1.06–2.19)</td>
<td>0.02</td>
</tr>
<tr>
<td>Left main lesions (vs. non-left main lesions)</td>
<td>0.34 (0.16–0.72)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Values are median (interquartile range). *Available in 181 patients with SB occlusion and 1,935 patients without SB occlusion. MLD = minimum luminal diameter; RD = reference diameter.

outcomes. However, no large-scale study has investigated this issue to date. Although several previous studies reported that SB ostial disease was an independent predictor of SB occlusion, those studies had several major limitations (3–5,8). The size of the SB was small (<1.5 mm), and left main bifurcation lesions were not included. Sample sizes were too small to draw definite conclusions. Moreover, bare-metal stents were used in earlier studies, which do not reflect contemporary real-world practice. Therefore, we sought to identify predictors of SB occlusion using data from the COBIS II registry.

SB ostial stenosis was one of the independent predictors of SB occlusion, concordant with the results of previous studies (3–5). In addition, SB lesion length was also significantly associated with SB occlusion. An IVUS study reported that SB occlusion occurred more frequently with diffuse atherosclerotic plaque than with focal stenosis in the SB ostium (9). Interestingly, the proximal MV stenosis, but not the distal MV stenosis, was independently predictive of SB occlusion. Plaque shift was significantly correlated with plaque volume decrease in the proximal MV segment but not with plaque volume decrease in the distal MV by volumetric IVUS analysis (10). These data suggest that plaque in the proximal MV segment is more important for SB occlusion than plaque in the distal MV segment. Acute coronary syndromes were significantly associated with SB occlusion after MV stenting. IVUS imaging in patients with acute coronary syndromes demonstrated that culprit lesions were characterized by thrombus and greater plaque burden, which supports our findings (11). Unexpectedly, SB occlusion occurred less frequently in left main lesions than in non-left main lesions. Operators might adopt an elective 2-stent strategy more aggressively in left main lesions to avoid occlusion of the left circumflex artery. The angle between the MV and SB was not an independent predictor of SB occlusion. Although bifurcation angle has been regarded as one of the important factors for bifurcation PCI, there is a paucity of data regarding its impact on SB occlusion or clinical outcomes. Recently, our group reported that bifurcation angle did not influence final TIMI flow grade in the SB and long-term clinical outcomes, which is concordant to the results of the present study (12). Among procedural factors, pre-dilation or wiring in the SB did not prevent SB occlusion. However, jailed wire in the SB was associated with recovery of the occluded SB. Therefore, we encourage routine wiring in the SB when bifurcation lesions are treated with the provisional approach.

Previous studies reported that SB occlusion was not associated with adverse outcomes (3–5). However, in our study, patients with SB occlusion had worse clinical outcomes than patients without SB occlusion. This discrepancy can be attributable to larger SB and inclusion of left main bifurcation lesions in our study. Whereas worse outcome related to SB occlusion was caused mainly by cardiac death occurring during the very early period, landmark analysis showed that the risk of stent thrombosis was consistently
higher in patients with SB occlusion than in those without SB occlusion. Although we cannot provide the exact mechanism, SB occlusion may impact short-term as well as long-term clinical outcomes.

**Study limitations.** Our large sample size made multivariate analyses for SB occlusion and clinical outcomes possible. However, the discriminative ability of our multivariate model evaluated by ROC curves was reasonable but not excellent. According to our model, unpredictable SB occlusion after MV stenting can occur in substantial numbers of patients. The overfitting problems of Cox hazard model for clinical outcomes are another limitation of our analysis. Because it is not practical to make a separate multivariate survival model for each outcome, we constructed a single

---

**Table 5 Clinical Outcomes at 12-Month Follow-Up**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SB Occlusion (n = 187)</th>
<th>No SB Occlusion (n = 2,040)</th>
<th>Unadjusted HR (95% CI)</th>
<th>p Value</th>
<th>Adjusted HR* (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>10 (5.3)</td>
<td>74 (3.6)</td>
<td>1.55 (0.80–2.99)</td>
<td>0.20</td>
<td>1.50 (0.76–2.97)</td>
<td>0.24</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>7 (3.7)</td>
<td>20 (1.0)</td>
<td>3.95 (1.67–9.35)</td>
<td>0.002</td>
<td>4.19 (1.66–10.59)</td>
<td>0.002</td>
</tr>
<tr>
<td>MI</td>
<td>4 (2.1)</td>
<td>32 (1.6)</td>
<td>1.44 (0.59–4.07)</td>
<td>0.49</td>
<td>1.50 (0.51–4.41)</td>
<td>0.46</td>
</tr>
<tr>
<td>Cardiac death or MI</td>
<td>10 (5.3)</td>
<td>50 (2.5)</td>
<td>2.29 (1.16–4.52)</td>
<td>0.02</td>
<td>2.34 (1.15–4.77)</td>
<td>0.02</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>6 (3.2)</td>
<td>9 (0.4)</td>
<td>7.68 (2.73–21.59)</td>
<td>&lt;0.001</td>
<td>6.19 (2.00–19.13)</td>
<td>0.002</td>
</tr>
<tr>
<td>TLR</td>
<td>14 (7.5)</td>
<td>129 (6.3)</td>
<td>1.26 (0.73–2.19)</td>
<td>0.41</td>
<td>1.31 (0.74–2.30)</td>
<td>0.36</td>
</tr>
<tr>
<td>MACE</td>
<td>23 (12.3)</td>
<td>164 (8.0)</td>
<td>1.63 (1.06–2.53)</td>
<td>0.03</td>
<td>1.64 (1.05–2.58)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Values are n (%). *Adjusted covariates included diabetes, acute coronary syndromes, true bifurcation, left main lesion, use of intravascular ultrasound, SB pre-dilation, MV stent diameter, and MV stent maximal pressure. \( \text{CI} \) = confidence interval; HR = hazard ratio; MACE = major adverse cardiac events; MI = myocardial infarction; TLR = target lesion revascularization.

---

**Figure 2 Kaplan-Meier Curves for Clinical Outcomes**

(A) Kaplan-Meier curves for cardiac death (c-death) or myocardial infarction (MI) in patients with SB occlusion after MV stenting versus those without SB occlusion after MV stenting. (B) Kaplan-Meier curves for target lesion revascularization (TLR). (C) Kaplan-Meier curves for major adverse cardiac events (MACE). (D) Kaplan-Meier curves for definite or probable stent thrombosis (ST).
model for all outcomes. As a result, overfitting could not be avoided regarding the outcomes with few events such as stent thrombosis.

The strength of our study over previous studies is that we included only bifurcation lesions with SB $\geq 2.3$ mm and left main bifurcation lesions. Therefore, SBs that we studied were more clinically important than SBs examined in previous studies. However, there are several limitations to our study. First, although procedural factors were not associated with SB occlusion in our study, we cannot completely exclude the protective effects of pre-dilation or wiring in the SB which might be performed in SBs with greater jeopardy of occlusion. Second, data on clinical outcomes at 3 years were available in only half of all patients. However, the follow-up rate was similar in both groups.

Conclusions

Using data from a large bifurcation registry, pre-procedural stenosis and lesion length of the SB, proximal MV stenosis, and clinical presentation were found to be predictive of SB occlusion after MV stenting. Jailed wire in the SB might be helpful for recovery of the occluded SBs. Occlusion of sizable SB was associated with adverse outcomes.

Reprint requests and correspondence: Dr. Hyeon-Cheol Gwon, Cardiac and Vascular Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea. E-mail: hcgwon@skku.edu.

REFERENCES


Key Words: angioplasty $\bullet$ bifurcation lesion $\bullet$ side branch.

APPENDIX

For supplemental tables and a figure and an expanded Methods section, please see the online version of this article.