Original article

Eccentric morphology of jailed side-branch ostium after stent crossover in coronary bifurcation lesions: A three-dimensional optical coherence tomographic analysis

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ABSTRACT

Background: Angiographic stenosis of a jailed side-branch ostium is usually observed after a single-stent crossover at coronary bifurcation lesions. However, the stenosis severity is typically overestimated due to the limited information obtained from two-dimensional morphology by angiography. We evaluated the actual stenosis of jailed side-branch ostium using three-dimensional (3D) optical coherence tomography (OCT).

Methods: Using 3D reconstructions of OCT data, we analyzed minimal lumen area (MLA) and eccentricity of the jailed side-branch ostium in 41 patients who were treated with single stent crossover at coronary bifurcation lesions and subsequently underwent serial OCT follow-up.

Results: The MLA of jailed side-branch ostium calculated from quantitative coronary angiography (QCA) assuming a circular lumen markedly decreased after stent implantation (1.73 ± 1.22 mm2 pre-intervention to 0.84 ± 0.91 mm2 post-intervention, p < 0.001). However, the MLA of jailed side-branch ostium measured at post-intervention by 3D-OCT (2.67 ± 1.75 mm2) was significantly larger than that measured by QCA (p < 0.001). There were no statistically significant changes in MLA of jailed side-branch ostium based on 3D-OCT measurements during the follow-up (2.35 ± 1.50 mm2 at 3–6 months post-intervention; 2.44 ± 1.27 mm2 at 1–2 years post-intervention, p = 0.998). The shapes of the jailed side-branch ostium were nearly elliptical (mean eccentricity index: 2.97 ± 1.27 post-intervention; 2.79 ± 1.17 at 3–6 months post-intervention; 2.59 ± 1.02 at 1–2 years post-intervention).

Conclusions: Compared to 3D-OCT measurements, QCA measurements overestimated the jailed side-branch ostial stenosis because single stent crossover due to eccentric morphology from orthogonal projection in coronary angiography. Significant changes in the MLA of jailed side-branch ostium by 3D-OCT were not observed during the follow-up.

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Introduction

Coronary bifurcation lesions remain a therapeutic challenge to percutaneous coronary intervention due to high complication and restenosis rates, particularly at the side-branch ostium [1,2]. Simple stent implantation across the side-branch has been preferred to treat bifurcation lesions because the double-stenting technique in both the main vessel and side-branch resulted in higher rates of complications and poor clinical outcomes [3–5]. However, in bifurcation lesions treated with single-stent implantation, jailed side-branch ostial stenosis is frequently observed in coronary angiography and compromised side-branches are a serious concern after single-stent implantation across the large-sized side-branch. However, a previous study that used pressure wire reported that jailed side-branch stenosis in angiographic evaluation was not always functionally impaired [6]. Coronary angiography typically overestimates the severity of side-branch ostial stenosis in most lesions treated with single-stent implantation.

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of the main vessel across the side-branch [7], and most jailed side-branch lesions do not have functionally significant stenosis [8,9]. The purpose of this study was to determine the reason for discrepancies between angiographic stenosis and actual stenosis after single crossover stent implantation at coronary bifurcation lesions. Therefore, we evaluated the morphological features and the area of the jailed side-branch ostium using three-dimensional (3D) optical coherence tomography (OCT).

Materials and methods

Study patients

From January 2011 to November 2013, non-consecutive patients who underwent single-stent crossover at coronary bifurcation lesions and three serial OCT examinations (post-intervention, 3–6 month follow-up, and 1–2 year follow-up) were retrospectively enrolled from the OCT registry database of our institute. Additional inclusion criteria were: 1) A side-branch ostium with a minimum lumen diameter ≥2 mm and lesion length <10 mm by visual estimation, and 2) thrombolysis in myocardial infarction flow grade 3 in the side-branch after stent implantation into the main vessel. Patients who had angiographically visible thrombi or a history of any previous intervention at the side-branch before OCT examination were excluded. A total of 50 patients were enrolled during the study period; however, nine patients were excluded due to poor image quality or wire artifacts of the 3D-OCT images. Thus, a total of 41 lesions in 41 patients were available for final analysis. Among 41 lesions, 4 lesions were true bifurcation (medina classification: 1.0.1, 0.1.1). A second guide wire was used for protecting side-branch in 4 lesions, but none of the lesions underwent kissing balloon inflation. This study protocol was approved by the Institutional Review Board of our institution, and adhered to the Declaration of Helsinki. All patients provided written informed consent. Coronary stent implantation of the bifurcation lesions with drug-eluting stents was performed using conventional techniques and a single-stent crossover strategy. Unfractionated heparin was administered at an initial bolus of 100 IU/kg, with additional boluses administered during the procedure to achieve an activated clotting time of 250–300 s. Dual anti-platelet therapy (aspirin and clopidogrel) was recommended to all patients for >12 months after drug-eluting stent implantation.

Quantitative angiography analyses

Quantitative coronary angiography (QCA) analyses were performed by a single expert analyst in an independent core laboratory (Cardiovascular Research Center, Seoul, Korea) using an offline computerized QCA system (CASS system, Pie Medical Imaging, Maastricht, Netherlands). Quantitative angiographic parameters in the side-branch were measured before and after single-stent crossover; reference vessel diameter, minimal lumen diameter (MLD), and percent diameter stenosis were measured. The minimal lumen area (MLA) of side-branch ostium by QCA (MLA-QCA) was calculated using the equation \( \pi \times (\text{MLD}/2)^2 \) based on the assumption that the lumen of the side-branch ostium is circular. The assumption for calculating MLA from QCA is classic but instinctively acceptable and has been employed in previous studies [10–12].

OCT procedure, 3D-OCT reconstruction, and analyses

OCT imaging of the main vessel was serially performed three times (immediately post-intervention, 3–6 months post-intervention, and 1–2 year post-intervention) in all patients using a frequency-domain OCT system (C7-XR OCT Imaging System, LightLab Imaging, Inc., St. Jude Medical, St. Paul, MN, USA). In this study, OCT cross-sectional images were generated at a rate of 100 frames/s while the fiber optic probe was withdrawn at a speed of 20 mm/s within the stationary protective sheath. All OCT images were analyzed at a core laboratory (Cardiovascular Research Center) by analysts who were blinded to patient and procedural information. Because of limitations in understanding and assessing the 3D geometry of the side-branch ostium with direct side-branch imaging after main vessel stent implantation, we evaluated the jailed side-branch ostium from images obtained during OCT imaging of the stented segment of the main vessel rather than directly during OCT imaging of the side-branch through the main vessel stent struts. The cross-sectional OCT images were processed using the free software Image Processing and Analysis in Java (Image J) [13] and then imported into a 3D volume-rendering program (OsiriX 3.9.4, The OsiriX Foundation, Geneva, Switzerland) [14]. Next, 3D images around the bifurcation lesion of the main vessel, including the side-branch ostium, were reconstructed (Fig. 1C,D). The cross-sectional image of side-branch ostium perpendicular to the expected blood flow direction was selected and the MLA (MLA-OCT) was measured. Using the multiplanar reconstruction viewer supported in the OsiriX volume-rendering program (Fig. 1E,F). Minimal and maximal diameters of the side-branch ostium were measured to calculate the eccentricity index (maximal diameter/minimal diameter). The degree of eccentricity indexes of side-branch ostia were defined as group 1 (1.0–1.5), group 2 (1.5–2.5), group 3 (2.5–3.5), group 4 (3.5–4.5), and group 5 (4.5–5.5). Additionally, we analyzed the shape of side-branch ostium.

Statistical analyses

Statistical analyses were performed using the GraphPad Prism for Windows version 5.01 (GraphPad Software, San Diego, CA, USA). Comparisons between groups were analyzed using Student’s t-tests, paired t-tests, or repeated analyses of variance (ANOVA) with Bonferroni’s post hoc tests. Correlations between the post-intervention MLA-OCT and the pre- or post-intervention MLA-QCA were analyzed using Spearman’s correlation coefficient. A p-value of <0.05 was considered statistically significant. All values are expressed as the mean ± standard deviation (SD) for continuous variables or as the number and percentage for categorical variables.

Results

The baseline clinical and angiographic characteristics of 41 patients with 41 bifurcation lesions are summarized in Tables 1 and 2, respectively. There was a significant positive correlation between post-intervention MLA-OCT with post-intervention MLA-QCA (\( r = 0.78, p < 0.001 \); Fig. 2A) and pre-intervention MLA-QCA (\( r = 0.83, p < 0.001 \); Fig. 2B). The MLA-QCA significantly decreased from 1.73 ± 1.22 mm² pre-intervention to 0.84 ± 0.91 mm² post-intervention (average percent change: –54.0%, \( p < 0.001 \); Fig. 3). However, the post-intervention MLA-OCT (2.67 ± 1.75 mm²) was significantly greater than the post- or pre-intervention MLA-QCA (\( p < 0.001 \), respectively). There were no statistically significant changes in MLA-OCT during the follow-up (2.39 ± 1.50 mm² at 3–6 months post-intervention; 2.44 ± 1.27 mm² at 1–2 years post-intervention, \( p = 0.098 \); Fig. 3). Fig. 4 shows the eccentricity index and the shape of the jailed side-branch ostium that were evaluated with 3D-OCT after single-stent implantation in the main vessel. The mean eccentricity indices were 2.97 ± 1.27 post-intervention, 2.79 ± 1.17 at 3–6 months post-intervention, and
The jailed side-branch ostia were approximately elliptical in shape, and only approximately 10% of jailed side-branch ostia had circular shapes (when the eccentricity index was defined as <1.5; 12% post-intervention, 5% at 3–6 months post-intervention, and 10% at 1–2 years post-intervention). In all cases, the long axis of the ellipsoidal jailed side-branch ostium was vertical to the main-branch axis. There were no cases with horizontally ellipsoidal jailed side-branch ostium.

**Discussion**

Angiographic assessments of jailed side-branch ostium in coronary bifurcation lesions are known to be limited. Previous studies have reported that only a small percentage of lesions with jailed side-branches and angiographically significant stenosis have functionally significant stenosis [6–8]. That is, jailed side-branch ostial stenosis that was evaluated by angiography typically overestimates the actual stenosis. Our data indicate that pre- and post-intervention MLA-QCA was much smaller than post-intervention MLA-OCT and also highlighted this limitation of angiographic overestimation of jailed side-branch ostial stenosis.

We hypothesized that morphological changes in the side-branch ostium induced by radially forced stent implantation lead to false interpretations of the decreased jailed side-branch ostial lumen area by QCA assessment. Our hypothesis regarding MLA-QCA and MLA-OCT images is supported by the 3D-angio images.

**Table 1**

Baseline clinical characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (n=41)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>61.1 ± 8.4</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>32 (78%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (59%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13 (32%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>28 (68%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>17 (41%)</td>
</tr>
<tr>
<td>Clinical diagnosis</td>
<td></td>
</tr>
<tr>
<td>Stable angina</td>
<td>32 (80%)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Previous coronary intervention</td>
<td>6 (15%)</td>
</tr>
</tbody>
</table>

*Data are presented as the number (%) or mean ± SD.*
morphological changes of the jailed side-branch ostium is illustrated in Fig. 5. When the stent is implanted at the stenotic bifurcation lesion, the vessel is radially dilated. The radial force of vessel dilatation leads to circumferential stretching of the vessel wall including side-branch ostium. Plaque redistribution or carina shift are suggested mechanisms of side-branch ostial compromise after main vessel stenting and may contribute to circumferential wall stretching [15]. These changes of bifurcation vessel should make the side-branch ostial lumen into an oval shape, which elongates in the vertical direction and shortens in the horizontal direction to the main vessel (Fig. 5A). Our hypothesis regarding morphological changes in the jailed side-branch ostium correlates with the results of this study: the mean eccentricity index of jailed side-branch ostium post-intervention was nearly 3, and only small numbers of jailed side-branch ostia had circular shapes. In addition, because all ellipsoidal vessel-side-branch ostia were vertically directed to the main vessel axis, ostial stenosis cannot be adequately evaluated by two true orthogonal angiographic views due to an overlap with the main vessel (Fig. 5B). Subsequently, angiographic assessments of jailed side-branch ostium necessarily overestimate the actual stenosis.

Previous studies have shown that most side-branch lesions after single-stent crossover implantation do not produce functionally significant stenosis [8,9], and the fate of jailed-looking side-branch ostium is favorable [16,17]. In the present study, post-intervention MLA-OCT was larger than pre-intervention MLA-QCA, and there were no significant decreases in MLA-OCT during the follow-up period. Although we did not perform a functional study, the maintenance of the ostial lumen area over time after stent implantation corresponds with results of previous studies [16,17]. The use of fractional flow reserve that is measured by pressure wire is the standard method to evaluate functional stenosis. However, there are several limitations in using it in a jailed side-branch. Crossing the pressure wire through the stent struts into the side-branch vessel is sometimes difficult to perform. The fractional flow reserve evaluation prolongs the procedure and the procedure itself may lead to complications such as dissections and additional stent implantation [8,18]. Recent studies have suggested that OCT may be superior to intravascular ultrasound or coronary angiography in predicting the functional significance of stenosis [19–21]. Furthermore, 3D-OCT imaging and en face analyses of side-branch ostium obtained from the main vessel also

**Fig. 2.** Correlation between post-intervention MLA by 3D-OCT with post-intervention MLA by QCA (A) or pre-intervention MLA by QCA (B). MLA, minimal lumen area; MLD, minimal lumen diameter; 3D-OCT, three-dimensional optical coherence tomography; QCA, quantitative coronary angiography.

**Fig. 3.** Serial changes in the minimal lumen area of side-branch ostium that was calculated by MLD of QCA and measured by 3D-OCT (*minimal lumen area: mean ± SD, *p = 0.001; **calculated by \( \pi \times (\text{MLD}/2)^2 \)). MLD, minimal lumen diameter; 3D-OCT, three-dimensional optical coherence tomography; QCA, quantitative coronary angiography.

**Fig. 4.** The eccentricity index of side-branch ostium after single-stent implantation in the main vessel. (Vertical to the main vessel axis, *horizontal to the main vessel axis, ***eccentricity index = maximal diameter/minimal diameter, groups on y-axis were categorized based on eccentricity index*).
were modestly able to predict the functional significance of a jailed side-branch ostium [22]. We expect that the eccentricity index of jailed side-branch ostium measured by 3D-OCT will provide additional information for evaluating the functional significance of a jailed side-branch ostium.

Our study has several limitations. First, the study population was relatively small. Second, we did not perform a functional study or fractional flow reserve; thus, we could not evaluate the relationship between the eccentricity index of side-branch ostium and functional stenosis. Third, pre-intervention OCT was not performed and therefore, we did not determine the change in the eccentricity index of the side-branch ostium between pre- and post-intervention. Fourth, poor penetration depth of OCT could have a possibility to generate error for evaluation of blood stream direction of side-branch.

In conclusion, QCA overestimates the jailed side-branch ostial stenosis after single-stent crossover implantation compared to 3D-OCT. The shapes of the side-branch ostium after stent implantation were nearly vertically elliptical. This vertically directed eccentricity of side-branch ostium leads to angiographic overestimation of the jailed side-branch ostial stenosis due to orthogonal X-ray projection in coronary angiography.

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References

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Disclosures
None

Fig. 5. Morphological changes of the side-branch ostium after single-stent implantation in the main vessel. (A) Circumferential wall stretching and plaque redistribution by single-stent implantation across the side-branch should shape the side-branch ostial lumen into an oval shape that elongates in the vertical direction and shortens in the horizontal direction to the main vessel. (B) Because all ellipsoidal side-branch ostia were vertical to the main vessel axis, ostial stenosis cannot be adequately evaluated by true orthogonal angiographic projections (Y and Z-axis directions) due to an overlap with the main vessel. Accurate measurement of the jailed side-branch ostial lumen area can be available in en face projections of side-branch ostium (X-axis direction), which is created by 3-dimensional optical coherence tomography.


