Impact of Coronary Stent Design in Proximal Balloon Edge Dilation Technique for Bifurcation Percutaneous Coronary Intervention

Teruyoshi Kume, MD, Satoshi Koto, MD, Yoshinobu Murasato, MD, Ryotaro Yamada, MD, Terumasa Koyama, MD, Tomoko Tamada, MD, Koichiro Imai, MD, Hiroshi Okamoto, MD, Yasuyuki Sudo, MD, Ayano Enzan, MD, Yoji Neishi, MD and Shiro Uemura, MD

Summary
The proximal optimizing technique (POT)-proximal balloon edge dilation (PBED) sequence for side branch (SB) dilatation with cross-over single-stent implantation decreases both strut obstruction at the SB ostium and stent deformation at the main branch (MB).

The purpose of this experimental bench test was to assess the impact of stent design on stent deformation, obstruction by stent struts at a jailed SB ostium, and stent strut malapposition in the POT-PBED sequence.

Fractal coronary bifurcation bench models (60- and 80-degree angles) were used, and crossover single-stent implantation (3-link stent: XIENCE Sierra, Abbott Vascular, Santa Clara, CA, \( n = 10 \); 2-link stent: Synergy, Boston Scientific, Marlborough, MA, \( n = 10 \)) was performed from the MB using the POT-PBED sequence. Jail- ing rates at the SB ostium, stent deformation, and stent strut malapposition of the bifurcation segment were assessed using videography and optical coherence tomography.

After SB dilatation using the PBED technique, jailing rates at the SB ostium and stent deformation did not differ significantly between the two types of stents. Conversely, the rate of malposed struts of the bifurcation segment after the PBED procedure was significantly lower with 3-link stents than with 2-link stents for both 60- and 80-degree angles (60-degree angle: \( 4.3\% \pm 4.4\% \) versus \( 22.0\% \pm 11.1\% \), \( P = 0.044 \); 80-degree angle: \( 20.8\% \pm 15.1\% \) versus \( 57.2\% \pm 17.0\% \), \( P < 0.001 \), respectively).

In the POT-PBED sequence, 3-link stents might be a preferable coronary bifurcation stent, maintaining a jailed SB ostium while significantly reducing stent strut malapposition of the bifurcation segment when compared with 2-link stents.

Key words: 3-link stent, 2-link stent, Videography, Optical coherence tomography

Bifurcation percutaneous coronary intervention (PCI) remains an area of ongoing procedural challenge, and simple strategies with a single stent or provisional side branch (SB) stenting has generally been accepted as the default approach in bifurcation PCI.1-4) Informative experimental studies have recently demonstrated that a repetitive proximal optimizing technique (re-POT) sequence, comprising an initial proximal optimizing technique (POT), SB inflation, and a second POT, significantly improved final results for crossover single-stent implantation of bifurcation lesions.5,6) We have previously reported an experimental bifurcation bench model study that showed good effects on obstruction by stent struts at a jailed SB ostium using a proximal balloon edge dilation (PBED) technique in the re-POT sequence compared with conventional SB balloon dilation.7) In this experimental study, SB dilation with the PBED technique prevented stent deformation induced by SB dilation and eliminated the need for the second POT procedure in the re-POT sequence. This new sequence (POT-PBED sequence) might thus, reduce procedure time and the risk of stent deformation following insertion of the second POT balloon. However, whether any kind of coronary stent shows more favorable results with the POT-PBED sequence in bifurcation PCI remains unclear. The purpose of this experimental bench test was thus, to assess the impact of stent design on stent deformation, obstruction by stent struts at a jailed SB ostium, and stent strut malapposition in the POT-PBED sequence.

Methods

Experimental protocols: A fractal coronary bifurcation bench model made of flexible urethane with 1-mm thick-
A flexible urethane coronary bifurcation bench model with a 1-mm thickness was specially designed with lumen diameters of 3.5 mm for the main branch and 3.0 mm for the side branch. Two types of coronary bifurcation bench models were assessed, with carina angles of 60 and 80 degrees.

Two types of coronary bifurcation bench models were assessed, with carina angles of 60° and 80°. An experimental bench test was performed with a series of coronary stents used as the MB stent in the coronary bifurcation model and compared between 3- and 2-link stents (XIENCE Sierra; Abbott Vascular, Santa Clara, CA, n = 10 and Synergy; Boston Scientific, Marlborough, MA, n = 10). The stents were deployed as follows. First, 3.5-mm stents in the MB were implanted in accordance with compliance charts from the manufacturer to reach a diameter of 3.70 mm three times for 10 seconds. Second, a POT was performed using a 4.0-mm non-compliant balloon at the rated burst pressure (compliance chart from the manufacturer to achieve a diameter of 4.13 mm) for 10 seconds. The POT balloon was positioned precisely, with the medial edge of the distal radiopaque marker lying in the cross-sectional plane of the carina. Third, another guidewire was then advanced into the SB with distal cell crossing under direct visual observation using a videoscope (IPLEX TX; Olympus, Tokyo, Japan) because distal cell re-wiring at the SB ostium has been reported to minimize stent deformation and obstruction by stent struts at jailed SB ostium after SB balloon dilation.8,9) SB ostium strut cells were opened using a 3.0-mm non-compliant balloon at the nominal pressure (compliance charts from the manufacturer to achieve a diameter of 2.97 mm) for 10 seconds. During SB balloon dilation, stent deformation, obstruction by stent struts at a jailed SB ostium, and stent strut malapposition were compared between 3- and 2-link stents. To assess the impact of the carina angle on stent deformation after PBED procedure, two types of coronary bifurcation bench model with 60° and 80-degree carina angles were tested (3-link stent in the 60-degree angle group, n = 5; 3-link stent in the 80-degree angle group, n = 5; 2-link stent in the 60-degree angle group, n = 5; 2-link stent in the 80-degree angle group, n = 5, respectively).

**Optical coherence tomography (OCT) and videoscope analyses:** OCT images were obtained using an FD-OCT system (Dragonfly OPTIS and OPTIS stent optimization software; Abbott Vascular, St. Paul, MN). The FD-OCT catheter was placed distal (>10 mm) to the stented lesion and pulled back to the stent proximal edge using a motorized catheter pullback system (18 mm/second). OCT recording was performed before and after the PBED procedures. Ellipticity ratios at the proximal and distal MBs were calculated as maximal diameter/minimal diameter, respectively, with 1.0 corresponding to perfect circularity. OCT analysis was performed millimeter by millimeter. A malapposed strut on OCT was defined as a distance of >150 μm between the center reflection of the strut and the vessel wall on axial-section OCT.10) Overall malapposed struts, except for the SB ostium, were quantified on each slice of the area connected to the SB as the percentage of malapposed struts to the total number of struts analyzed.

The videoscope was inserted into the SB to obtain images of the SB ostium. Obstruction by stent struts at a jailed SB ostium was evaluated as the SB jailing ratio, calculated as \((A1/A2) \times 100\%\), where A1 is the total area jailed by stent struts, and A2 is the area of the ostium. Both A1 and A2 were measured manually on digi-
Ellipticity ratio in both proximal and distal segments before and after the PBED procedures, stent parameters such as ellipticity ratio and rate of malapposed struts were assessed and compared between 3- and 2-link stents using OCT. In addition, the SB jailing ratio was assessed and compared between the two groups using videography.

**Statistical analysis:** All analyses were performed using JMP version 14.2.0 software (SAS Institute, Cary, NC). Continuous variables are presented as mean ± standard deviation. Wilcoxon’s nonparametric statistical test for continuous quantitative variables was used to compare 3- and 2-link stent groups. Dunnett’s multiple comparison test was used to compare changes in the rate of malapposed struts during the PBED procedures. A value of $P < 0.05$ was considered significant.

## Results

Ellipticity ratio in both proximal and distal segments before the PBED procedure did not differ significantly between the 3- and 2-link stent groups with both 60- and 80-degree angles (Table I). On the other hand, the rate of malapposed struts after the PBED procedure was significantly lower in the 3-link stent group than in the 2-link stent group (13.2% ± 12.3% versus 39.0% ± 24.5%, $P = 0.017$). In addition, the rate of malapposed struts after the PBED procedure was significantly lower in the 60-degree angle group than in the 80-degree group (12.5% ± 13.6% versus 39.6% ± 23.0%, $P = 0.007$). The rate of malapposed struts after the PBED procedure in the 2-link stent, 80-degree angle group was significantly higher than in the 3-link stent, 60-degree or 2-link stent, 60-degree angle groups (57.2% ± 17.0% versus 4.3% ± 4.4%, $P < 0.05$ and 57.2% ± 17.0% versus 20.8% ± 15.1%, $P < 0.05$, respectively). The change in the rate of malapposed struts during the PBED procedure in the 3-link stent, 60-degree angle group was minimum and was significantly lower than that in the 2-link stent, 80-degree angle group (Figure 2). Likewise, the change in the rate of malapposed struts during the PBED procedure was significantly lower in the 3-link stent, 80-degree angle group than in the 2-link stent, 80-degree angle group. In the comparisons between the 3-link stent, 60-degree angle group and 2-link stent, 60-degree angle group, differences in the rate of malapposed struts during the PBED procedures did not reach statistical significance but tended to be lower in the 3-link stent, 60-degree angle group (4.3% ± 4.4% versus 22.0% ± 11.1%, $P = 0.124$).

SB jailing rate after the PBED procedure did not differ significantly between the 3- and 2-link stent groups with both 60- and 80-degree angles (Table II). Figures 3, 4 show representative SB ostial videoscope images after the PBED procedure and OCT images before and after the PBED procedure.
Figure 2. Changes in the rate of malapposed struts of the bifurcation segment during the PBED procedure. Changes in the rate of malapposed struts during the PBED procedure in the 3-link stent, 60-degree angle group were minimal and significantly lower than those in the 2-link stent, 80-degree angle group. Likewise, changes in malapposed strut rates during the PBED procedure were significantly lower in the 3-link stent, 80-degree angle group than in the 2-link stent, 80-degree angle group.

Figure 3. Representative videoscope images of the side branch ostium after the PBED procedure and OCT images before and after the PBED procedures with 3-link stents. Jailing ratio is 18% in the 3-link stent, 60-degree angle group (upper left) and 13% in the 3-link stent, 80-degree angle group (lower left). The side branch (SB) jailing area is highlighted in yellow. Malapposed struts of the bifurcation segment before and after the PBED procedure are not observed in the 3-link stent, 60-degree angle group (upper right). Malapposed struts of the bifurcation segment after the PBED procedure are observed in the 3-link stent, 80-degree angle group (lower right, arrowhead).
PBED procedures in the 3- and 2-link stent groups.

Discussion

The present experimental bifurcation bench model study using two different stents showed that the rate of malapposed struts of bifurcation segment after the PBED procedure was significantly lower with 3-link stents compared with 2-link stents. These differences were more significant with the 80-degree angle in comparison with the 60-degree angle.

Distal cell re-wiring at the SB ostium could reportedly minimize stent deformation and obstruction by stent struts at the jailed SB ostium after SB balloon dilation. In the present study, the guidewire for SB dilation was advanced into the SB with distal cell crossing under direct visual observation using a videoscope. In addition, link location at the SB ostium is an important factor for stent deformation in bifurcation PCI. To avoid any influence of link location, we intentionally set the absence (link-free) of stent links in the distal semicircle of the SB ostium under videoscopic observation in the present study. The differences in the rate of malapposed struts identified in our study might thus, be based on stent design, but not the location of wire re-cross or stent link. Two-link stents might be easily deformed toward the SB by SB dilation, explaining the significantly higher rate of malapposed struts of the bifurcation segment after PBED procedure observed in the 2-link stent group compared with the 3-link stent group. On the other hand, 3-link stents, especially the XIENCE stent, comprise a horseshoe-shaped prolonged link connecting each stent strut. Such characteristics might minimize the deformation of stent cells by stretching the horseshoe-shaped prolonged link during the POT-PBED sequence. Considering these points, the XIENCE stent could minimize the risk of strut malapposition during the POT-PBED sequence, indicating the importance of stent selection in bifurcation treatment.

Recently, highly informative experimental studies have demonstrated that the re-POT sequence comprising an initial POT, SB inflation, and a second POT significantly improved the final result of crossover single-stent implantation in bifurcation lesions. However, the second POT procedure might reform the stent back to its original shape and pull well-deployed stent struts at the SB vessel wall toward the MB, thus, increasing obstruction by stent struts at a jailed SB ostium even when the PBED technique is used. In the present study, a wide bifurcation angle would be associated with a higher rate of malapposed struts of the bifurcation segment after the PBED procedure. This negative phenomenon was observed more frequently with 2-link stents. If a second POT procedure was performed to fix residual malapposed struts at the MB with 2-link stents, obstruction by stent struts at a jailed SB ostium might be increased by the second POT procedure, resulting in narrowing of the SB ostial area due to delayed neointimal coverage at follow-up. From these results, 2-link stents might not be suitable for crossover single-stent implantation in bifurcation PCI using the POT-PBED sequence, especially in lesions with wider bifurcation angles.

The present findings may help bifurcation PCI achieve better clinical outcomes. However, the clinical benefit of the POT-PBED sequence remains unclear. The clinical impact of the PBED technique in the POT-PBED sequence should be evaluated in a future clinical study.
Limitations: Several limitations to this study need to be considered. First, the present experimental study used a flexible urethane coronary bifurcation bench model without stenosis. Narrowing of the lumen by coronary plaque might affect the results of stent deformation and the SB jailing ratio in the POT-PBED sequence. Second, the present results are not applicable to non-left main trunk bifurcation lesions because of the small difference in vessel size between the MB and SB. Third, the present experimental study used two types of coronary stents. Bench tests are further needed to compare the effectiveness of the POT-PBED sequence among different types of coronary stents. Fourth, considering the stent strut thickness and OCT image resolution, a malapposed strut on OCT was defined as a distance of > 150 μm between the center reflection of the strut and the vessel wall in the present study. Previous clinical study demonstrated that the malapposed stent struts with a distance of < 355 μm between the center reflection of the strut and the vessel wall immediately after everolimus-eluting stent implantation resolved spontaneously at 8-12-month follow-up. In the present study, the maximum distance between the center reflection of the strut and the vessel wall was < 400 μm in all cases. Therefore, the clinical impact of small malapposed struts of the bifurcation segment observed in the present study after PBED procedure is still unclear, and future clinical studies are needed. Lastly, experimental comparison data between the POT-PBED procedures and kissing balloon technique that is widely used in real practice are not available. Future experimental investigations are necessary to reveal the advantage of PBED technique in comparison to the kissing balloon technique.

Conclusions

In the POT-PBED sequence, 3-link stents might be preferable for coronary bifurcation stenting, maintaining a jailed SB ostium while significantly reducing stent strut malapposition of the bifurcation segment compared with 2-link stents.

Disclosure

Conflicts of interest: Dr. Kume has received personal fees from Abbott Japan Co., Ltd. Dr. Uemura has received academic funding and personal fees from Daiichi Sankyo Company, Astellas Amgen Biopharma, Abbott Japan Co., Ltd., and Terumo Corporation. The other authors report no financial relationships to disclose. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

References

1. Nasir M, Shafique HM, Hussain S, Tuyyah F, Aziz S, Khadim R. Percutaneous coronary intervention for left main coronary artery bifurcation lesions: two-stent versus one-stent strategy for comparison of 6-month mace. J Coll Physicians Surg Pak 2020; 30: 894-9.
2. Hildick-Smith D, Behan MW, Lassen JF, et al. The ebc two study (European bifurcation coronary two): a randomized comparison of provisional t-stenting versus a systematic 2 stent cut-lotte strategy in large caliber true bifurcations. Circ Cardiovasc Interv 2016; 9: e003643.
3. Huang CL, Jen HL, Huang WP, Tsao TP, Shing Young M, Yin WH. The impact of fractional flow reserve-guided coronary re-vascularization in patients with coronary stenoses of intermediate severity. Acta Cardiol Sin 2017; 33: 353-61.
4. Buzzotta F, Lassen JF, Lefèvre T, et al. Percutaneous coronary intervention for bifurcation coronary lesions: the 15th consensus document from the European bifurcation club. EuroIntervention 2021; 16: 1307-17.
5. Derimay F, Souteyrand G, Motreff P, et al. Sequential proximal optimizing technique in provisional bifurcation stenting with everolimus-eluting biolosorbable vascular scaffold: fractal coronary bifurcation bench for comparative test between absorb and xience xpedition. JACC Cardiovasc Interv 2016; 9: 1397-406.
6. Finet G, Derimay F, Motreff P, et al. Comparative analysis of sequential proximal optimizing technique versus kissing balloon inflation technique in provisional bifurcation stenting: fractal coronary bifurcation bench test. JACC Cardiovasc Interv 2015; 8: 1308-17.
7. Kume T, Murasato Y, Yamada R, et al. Effect of proximal balloon edge dilation technique for opening a side branch ostium in repetitive-proximal-optimizing technique sequence. Catheter Cardiovasc Interv 2021; 97: E12-8.
8. Okamura T, Onuma Y, Yamada I, et al. 3d optical coherence tomography: new insights into the process of optimal rewiring of side branches during bifurcational stenting. EuroIntervention 2014; 10: 907-15.
9. Onuma Y, Okamura T, Muramatsu T, Uemura S, Serruys PW. New implication of three-dimensional optical coherence tomography in optimising bifurcation pci. EuroIntervention 2015; 11: V71-4.
10. Sawada T, Shite J, Negi N, et al. Factors that influence measurements and accurate evaluation of stent apposition by optical coherence tomography. Assessment using a phantom model. Circ J 2009; 73: 1841-7.
11. Kume T, Yamada R, Koyama T, et al. Coronary bifurcation bench test using multimodality imaging: impact of stent strut link location on stent deformity and jailed side-branch orifices during re-proximal optimizing technique. Catheter Cardiovasc Interv 2019; 93: E17-23.
12. Kume T, Yamada R, Terumasa K, et al. Neointimal coverage of jailed side branches in coronary bifurcation lesions: an optical coherence tomography analysis. Coron Artery Dis 2018; 29: 114-8.
13. Fujino Y, Attizzani GF, Tahara S, et al. Difference in vascular response between sirolimus-eluting- and everolimus-eluting stents in ostial left circumflex artery after unprotected left main as observed by optical coherence tomography. Int J Cardiol 2017; 230: 284-92.