Bifurcation Lesions
An Inside View
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Listening to dodecaphonic music requires patience and a willingness to be prepared to study the same piece over and over again. We experienced a similar feeling after reading 2 important studies about bifurcation lesions featured in this issue of Circulation: Cardiovascular Interventions. The first read gives a general impression; however, understanding and appreciation only comes after reading them a few times and devoting an effort to understand them. Bifurcation lesions historically have been associated with high restenosis rates\(^1,2\) and early atherogenesis,\(^3,4\) with the ostium of the side branch (SB) being the most common site of restenosis after stenting.\(^1,5\) Improvements in bifurcation stent techniques, the results from numerous randomized controlled trials,\(^6–9\) and registry data have led to the commonly held belief that provisional stenting should be our first-line strategy in the majority of lesions.\(^9,10\) However, the mechanism of SB neointimal hyperplasia and the implications of our choice of bifurcation stent technique still require further evaluation to ensure that we understand the long-term outcomes after percutaneous coronary intervention (PCI) in this complex lesion subgroup. The featured articles address a few of our ongoing queries with regard to bifurcation disease and provide some further information on the anatomy of these lesions and the relative significance of the SB.

**Articles see pp 105 and 113**

Koo et al\(^11\) evaluated the mechanisms of changes in the geometry of the ostium of the SB after main branch (MB) stenting and investigated the predictors of a functionally significant SB stenosis using intravascular ultrasound (IVUS) and fractional flow reserve (FFR). The authors enrolled patients with a predetermined provisional SB strategy for de novo, proximal, or mid left anterior descending (LAD) artery lesions and went on to perform IVUS of the MB before and after MB stenting to measure the vessel volume index, lumen volume index, and plaque volume index in the proximal and mid-MB, thereby testing the hypothesis that MB stenting was likely to cause worsening of an SB ostial lesion as a result of MB plaque and carina shift. In addition, FFR of the SB was measured after intervention and compared with preintervention angiographic and IVUS parameters to assess the predictors of a functionally significant SB stenosis (defined as FFR <0.75) after PCI to the MB.

The main findings of this study in terms of IVUS evaluation after MB stent implantation were (1) a significant increase in the vessel and lumen volume index in both the proximal and distal segments of the MB, (2) a significant decrease in the plaque volume index in the proximal segment of the MB, and (3) no change in the plaque volume index in the distal segment of the MB after PCI. Furthermore, the preintervention angiographic and IVUS predictors of a functionally significant SB stenosis were (1) SB minimal lumen diameter, (2) plaque volume index of the proximal MB, (3) SB percentage stenosis, and (4) lumen volume index of the distal MB. The investigators concluded that the decrease in plaque volume in the proximal MB, with no associated increase in plaque volume in the distal MB, was indirect evidence of plaque shift from the MB to the SB ostium after stent implantation. Additionally, the increased luminal volume in the distal MB, with no significant decrease in the plaque volume, was believed to be due to vessel enlargement and provided support to the theory that carina shift is likely to contribute to the degree of luminal narrowing of the SB. Furthermore, preintervention factors such as the size of the SB, the degree of SB stenosis, the degree of plaque within the proximal MB, and the size of the lumen in the distal MB may be useful in predicting the likelihood of significant SB stenosis by FFR after PCI.

Interestingly, FFR assessment of the SB after intervention revealed that a hemodynamically significant SB stenosis was present only in 54.5% of lesions classified as severe by angiography and that 29.4% of angiographically nonsignificant SB lesions were associated with an abnormal FFR. These results are not entirely consistent with a previous study by Koo et al\(^12\) in which only 27% of SB with a severe stenosis by angiography had an FFR <0.75, and no SB lesions with an angiographic stenosis of <75% were associated with a hemodynamically significant FFR, a finding that stresses the value of extending observations to larger numbers of lesions before drawing firm conclusions, such as the widespread opinion that a moderate stenosis of the SB is never hemodynamically significant.

The choice of stenting technique and the impact of IVUS-guided PCI is perhaps most important when tackling bifurcation lesions of the left main coronary artery (LMCA).\(^1,13,14\) In the second study, Oviedo et al\(^15\) assessed the distribution and significance of LMCA bifurcation disease by IVUS and proposed a new IVUS-based classification system for describing these lesions in comparison with the Medina angio-
graphic classification system. IVUS evaluation was performed in 140 patients with evidence of LMCA bifurcation lesions on angiography and was used to assess all 3 components of the bifurcation, namely the LMCA, LAD, and circumflex artery. The most important findings of this study were as follows: (1) IVUS assessment revealed that the majority of lesions comprised a continuous distribution of plaque from the LMCA into one or both of the LAD and circumflex branches in 90% of cases; (2) extension of LMCA plaque into the ostial LAD occurred far more frequently than into the circumflex artery; (3) little correlation seemed to exist between the Medina classification system on angiography and the distribution of plaque by IVUS, except in Medina 0 lesions that were associated with less plaque on IVUS; (4) no relationship was found between plaque distribution by IVUS compared with lesion significance as assessed using angiography; (5) the carina was spared in all lesions with the presence of plaque predominantly on the opposite side of the flow divider; and (6) the significance of stenosis was not affected by the length of the LMCA or the size of the angle between the LAD and circumflex arteries (≥90°). However, the results of this study were limited by the fact that all lesions were intermediate in severity; therefore, a direct extrapolation to severe distal LMCA lesions is problematic.

What can we take home from these 2 detailed reports, and how can we further tailor our approach to the treatment of bifurcation lesions? The following is our understanding and practical suggestions based on these studies.

1. When treating a bifurcation lesion, the degree of MB disease may affect the result in the SB. Protection of the SB and the need for SB treatment depends not only on the degree of the SB stenosis, but also on the severity of the disease in the MB. The differential contribution of plaque shift and carina shift on SB stenosis has been debated, with equal numbers of supporters on both sides of the argument. However, although we are unclear about the clinical implications for a distinction between these 2 entities in post-PCI SB stenosis, it is clear that plaque redistribution has a greater impact when the bifurcation plaque burden is large. It is possible that stenting a SB is more effective when the residual stenosis is caused by plaque redistribution, whereas balloon angioplasty is adequate for a significant SB lesion caused only by carina shift.

2. Anatomy is a poor predictor of the clinical impact of a stenosis, a fact particularly true for SB lesions. The need to evaluate the impact of a residual stenosis on the SB by FFR is a question of clinical value and depends on the relative importance of this vessel.12

3. It is difficult to predict the final angiographic result after MB stenting from the baseline coronary anatomy; therefore, we should be prepared for the potential need for greater procedural complexity until the end of every case.

4. When treating a lesion located at the ostium of the LAD, an involvement of the distal LMCA should be expected. Therefore, a strategy to stent from the LMCA into the LAD frequently is the most practical approach. This strategy is less likely to be important when dealing with an ostial circumflex lesion because concurrent involvement of the distal LMCA is far less frequent in this lesion subgroup.

5. Supplementary information often is gained by performing IVUS to evaluate bifurcation disease due to the limitations of angiography in assessing lesions associated with 2 vessels and a carina; this is particularly true when treating the LMCA. Indeed, the main leitmotif of both of these studies is that the IVUS gives additional information when compared with the use of angiography alone.

Despite the knowledge that IVUS often provides valuable supplementary data, efforts in interventional cardiology have been devoted to negating the additional value of IVUS compared with angiography. This approach has been taken by some for the sake of simplicity and ease and, perhaps, because there are no definitive randomized studies that support the use of IVUS in improving clinical outcomes yet. Possibly a pragmatic approach of kissing balloon postdilatation of both branches of a bifurcation, accompanied by a selective use of IVUS to aid selection of optimum technique and final balloon size, is currently the best option available.

Importantly, there are some limitations to these studies that need to be considered. Neither group of investigators addressed the clinical implications of their findings; therefore, their observations may have unproven value in enhancing long-term outcomes after PCI. In addition, an important factor when assessing both studies is that Koo et al.11 evaluated the lesions that had been preselected for a provisional stenting strategy and excluded lesions with severe involvement (>10 mm in length) of the SB, whereas Oviedo et al12 mainly assessed LMCA lesions with moderate stenosis by angiography. Therefore, neither study evaluated the anatomy of severe bifurcation lesions with large plaque burden in the SB.

The recently published British Bifurcation Coronary Study: Old, New, and Evolving Strategies study evaluated the clinical implications of the choice of bifurcation stent technique in a cohort of patients in which the majority (>80%) had true bifurcations by the Medina classification system.10 The results suggest a significantly higher incidence of periprocedural myocardial infarction and major adverse cardiac events at 9-month follow-up after the use of a complex bifurcation technique compared with a simple provisional strategy. However, it is possible that an appropriate use of IVUS after complex bifurcation PCI, and a critical FFR-guided appraisal of the results obtained following a simple strategy, would have given different outcomes.

Perhaps the most pragmatic advice is that each operator should continue to apply his or her most preferred and successful approach to make individual procedures simpler and more streamline. In addition, the optimum strategy should be tailored to each interventional case, and although provisional T-stenting has its technical advantages, it is not ideal for all lesions. With that in mind, we leave with the final thought that the simplest approach is not always the best approach.

Disclosures
Antonio Colombo is a minor share holder in Cappella, Inc, a company manufacturing a self-expanding bare-metal stent for ostial lesions.
References


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