Bifurcation Intervention

Is it Crush Time Yet?*

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Bifurcation lesions remain an unresolved problem for percutaneous coronary intervention (PCI). Broadly defined as stenoses that involve the origin of an arterial side branch exceeding 2.0 mm in diameter, bifurcation lesions present a challenge to achieve relief of arterial narrowing, deliver interventional devices including balloon catheters and stents, avoid arterial occlusion, and sustain initially successful results.

Part of the complexity in treating bifurcation lesions relates to the number of different anatomic patterns of bifurcation stenosis. Given the potential involvement of the proximal main branch, the distal main branch, and the side branch, one classification system identifies at least six different possible stenosis configurations (1). Furthermore, there may be major variations in the diameter of each of the branches and of the angle at which the side branch originates from the main branch. Independent of the bifurcation type and vessel characteristics, the degree of ostial side branch stenosis is the main determinant of the need for side branch protection during PCI with a low risk of acute side branch occlusion with minimal disease (<4%) but a much higher rate (up to 27%) for significant stenosis (2).

Bifurcation lesions were attempted during the era of balloon angioplasty. However, inability to achieve consistently a <50% stenosis of both the main branch (e.g., the left anterior descending artery) and the side branch (e.g., diagonal artery) was obvious a shortcoming. Alternating shift of plaque or the “isthmus” between the two branches was one explanation for this failing. Attempts at plaque volume reduction, with debulking devices such as extraction or rotational atherectomy, subsequently gained popularity as adjuncts to balloon angioplasty. Such “new device” strategies, however, were technically demanding, occasionally resulted in serious complications, and were never thoroughly evaluated by comparative randomized trials (3,4). These considerations plus the introduction of intracoronary stents resulted in the discontinuation of their routine use.

Bare metal stents have been implanted singly or in combination in an attempt to improve outcomes. Multiple combinations of balloons and stents have been explored (5–9). Strategies have ranged from a single stent in the main branch with or without balloon angioplasty of the side branch to two or more stents placed in both the main and side branches. In an attempt to ensure complete stent apposition to the entire surface of the bifurcation plaque, a special concern for drug-eluting stents (DES), stents have been deployed in an overlapping fashion with one stent inside or adjacent to the other (5,10). Such approaches typically require large guide catheters, simultaneous use of more than one balloon catheter, and advanced operator skill and experience. Obviously the procedure time and radiation exposure are longer than otherwise in these instances. On the positive side, use of stents has clearly improved the immediate results of bifurcation angioplasty (8,11). These benefits even apply to such very complex lesions as those involving the left main, left anterior descending, and circumflex arteries. Almost uniformly the acute angiographic results are excellent. Similar benefits have not been observed, however, during late follow-up, as rates of major adverse events, in particular restenosis, have been relatively high. These mixed results have prompted some to recommend a strategy of routine stenting of the main branch with discretionary (i.e., only if needed) stenting of the side branch (12).

Many expected that the effectiveness of DES for preventing restenosis in uncomplicated lesions would extend to bifurcation disease. Although a relative improvement was observed, the benefits for bifurcation lesions have not been as pronounced. In one small observational study of bifurcation DES use, the restenosis rate was 25.7% with recurrence seen primarily at the origin of the side branch (13).

The inclusion of four original reports in this issue of the Journal provides us with an opportunity to learn more about the treatment of bifurcation lesions by PCI. One of these is a database analysis of a broad multicenter experience, two focus on the two stent “crush” technique, and one discusses a new investigational stent specifically designed for bifurcation lesions (Table 1).

In this issue of the Journal, Garot et al. (14) describe the in-hospital and nine-month outcomes of 1,412 patients having PCI for a bifurcation lesion and compare these findings to those of 10,068 patients who had PCI for other types of lesions. This analysis is derived from the database of the Prevention of Restenosis with Tranilast and its Outcomes (PRESTO) trial, a randomized clinical trial that

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evaluated tranilast, a pharmacologic agent with the potential to reduce restenosis; PRESTO trial investigators compared various dosages of tranilast to placebo and found no effect of tranilast on outcome (15). In the database comparison between bifurcation and other lesions, Garot et al. (14) found differences in the prevalence of a few baseline features, but in general these differences were small in magnitude. Of note, stents were used in only 71% of bifurcation lesions, a rate lower than that for nonbifurcation lesions. At nine months, incidences of death or myocardial infarction (MI) were similar between the two groups although target vessel revascularization (TVR) for the entire group was 14.9%, higher than 9.5% lower rate of restenosis of both the main and side branches (8.9% and 11.1%, respectively). We are not provided with a more contemporary adaptation) was associated with a lower rate of restenosis of both the main and side branches (8.9% and 11.1%, respectively). We are not provided with the entire cohort rate for any restenosis, but it was at least 21.6%. At nine months target lesion revascularization (TLR) for the entire group was 14.9%, higher than 9.5% with final kissing balloon. Importantly, stent thrombosis was observed in 4.4% of patients. This rate is considerably higher than the 1% to 2% usually observed with DES (17). No technical features were associated with stent thrombosis, while premature discontinuation of dual antiplatelet therapy was.

Additional insight into the results of the crush technique is provided by Costa et al. (18) in their intravascular ultrasound analysis of 40 patients presented in this issue of the Journal. They observed that the area of the crush (i.e., the segment of stent overlap with three adjacent layers of stent) was most often the narrowest segment within the main vessel segment. Incomplete expansion of the crushed area was present in the majority of patients, even if the final kissing balloon technique was used. Importantly, although the number of patients in this study was small, one developed stent thrombosis and that patient demonstrated “incomplete crushing.” Coronary angiography failed to detect incomplete stent expansion, and the correlation between intravascular ultrasound (IVUS) and quantitative coronary angiography was significant, but considerable variability was observed.

In this issue of the Journal, Lefèvre et al. (19) describe the performance and safety of a new investigational stent, the
Multi-Link Frontier, designed specifically for use in bifurcation lesions. This stent system features two balloon catheters, two guidewires, and a stent that has a portal ensuring access to the side branch. The stent was successfully implanted in 96 of 108 (91%) patients. During the initial hospitalization, two patients experienced an MI (one Q-wave) and one patient required CABG. By six months, there were no deaths, 3.8% experienced MI, and 13.3% TLR. The authors concluded that the rates of major adverse events for this stent were low.

What are the implications of these reports? Specifically do they change our perceptions of the effectiveness or safety of PCI for bifurcation lesions or the manner in which PCI should be performed? In terms of effectiveness, these studies support prior observations that acute success rates for achieving excellent relief of bifurcation narrowing as judged by angiography are high. A less than optimal result, however, may be experienced with the crush technique.

The durability of this very favorable initial outcome remains a concern. A comparison of the rates for TVR between the reports of Garot et al. (14) (favoring bare metal stent, provisional side branch stenting) and Ge et al. (16) using DES and the crush technique shows no difference, and the rates are higher (17% and 17.1%, respectively) than with DES for nonbifurcation lesions. Of note, when the final kissing balloon technique was added to the DES-crush approach, the TVR was reduced to 10.3%. Whether this difference represents a true superiority of the DES-crush approach over a more conventional approach is unclear. Also since the Garot et al. (14) experience was limited to bare-metal stents, we have no comparative data about the outcomes of the main vessel stent-discretionary side branch strategy using a DES. Additionally, all patients in the study by Ge et al. (16) had routine angiographic follow-up that may have increased the rate of TVR.

Should we expect less restenosis and fewer repeat revascularization procedures when using the new Frontier stent described by Lefèvre et al. (19)? Not necessarily, as the TVR rate observed after implantation of this side branch access stent with 43% of patients receiving a side branch stent actually appeared to be higher than that of the Garot et al. (14) historical bare-stent group (19.0% vs. 17.0%, respectively). Clearly we must be cautious in direct comparisons of these reports, but these observational studies are representative of the types of information we have available.

The profile of safety, assessed as the occurrence of death, MI, or the need to perform emergency CABG, was favorable in the conventional experience of Garot et al. (14) and with the use of the new side branch access stent. Stent thrombosis, however, was observed in 4.4% of the patients treated by the crush technique. Intraprocedural thrombosis, which is exceedingly rare apart from the setting of preexisting thrombus (e.g., acute ST-segment elevation MI), was noted in 1.7%. An additional 2.8% of patients experienced stent thrombosis by nine months. Importantly, the consequences of stent thrombosis such as MI or death are of much greater concern than those of restenosis that typically presents as recurrent ischemia. The report of Costa et al. (18) is particularly relevant to this issue. They identified an association between incomplete apposition of stent struts against the main vessel wall in the area of the crush to the development of stent thrombosis. Moreover, they observed that incomplete crushing was observed in the majority of patients and that the most narrowed area of the main vessel stent was also at the site of the crush despite 75% of these patients having had final kissing balloon inflations. Taken together, these observations suggest that the crush technique inherently creates a structural substrate that increases the chance for stent thrombosis and that the increase in rate of stent thrombosis reported by Ge et al. (16) may accurately reflect a safety concern for this technique.

In the final analysis, we have not yet identified an appropriate solution to the problems associated with PCI for bifurcation lesions. If the crush technique is used, final kissing balloon angioplasty appears essential to optimize sustained patency, and safety may be enhanced by IVUS-guided stent deployment. Selecting the crush approach to reduce the incidence of restenosis, however, may incur the expense of an increased risk for stent thrombosis. New stent designs will be developed for bifurcation lesion intervention but must incorporate the benefits of drug elution and ensure drug availability to all diseased surfaces. Until these objectives are achieved, the simple approach of drug-eluting stenting of the main branch with provisional stenting of the side branch remains a reasonable option with a very acceptable profile of safety and effectiveness.

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