

EDITORIAL COMMENT

The Complexity of Stenting in Bifurcation Coronary Lesions*

Ran Kornowski, MD

Petach Tikva, Israel

The treatment of bifurcation lesions remain a technical challenge. Bifurcation lesions represent up to 20% of coronary stenosis that demands percutaneous coronary intervention (1). They are associated with augmented long-term risk for reintervention and stent thrombosis compared with nonbranching lesions (2). Drug-eluting stents (DES) have demonstrated a marked reduction in restenosis, resulting in improved clinical outcomes when compared with bare-metal stents (3,4). Nonetheless, uncertainty remains regarding the long-term safety of DES implantation in bifurcation lesions. In particular, increased incidence of stent thrombosis and/or ischemic coronary events has been reported (5).

[See page 687](#)

The treatment of bifurcation lesions often pose a dilemma to the operator. The dilemma is whether to use 1 or 2 stents (6). This is a strategic decision rather than a technical one, as it may alter the course of the intervention and could affect the patient's long-term prognosis. Current practice in bifurcation lesions involves, if possible, a stenting procedure of the main branch with an option for balloon dilation or a bailout stenting of the side branch in case of a threatened need (e.g., "provisional" technique). However, in lesions with a large side branch and with severe obstructive ostial atherosclerotic involvement, there is a tendency to use a 2-stent strategy up front (7).

It should be appreciated that any comparison between a single- versus double-stent approach might be subjected to inherent bias, as the 2-stent technique is aimed at solving a more complex bifurcation milieu (8). Thus, a sophisticated procedure should be designed to treat more complex bifurcation disease. This is why the comparison between the 2 strategies is somewhat tricky, especially when derived from nonrandomized registries or using case-selective randomized studies.

In this volume, Zimarino et al. (9) have presented their important cross-design meta-analysis of 5 randomized controlled trials and 7 observational studies of bifurcation stenting. The analysis involves 6,961 patients and tests the hypothesis that increased myocardial infarction (MI) after the routine placement of double DES (n = 1,868) compared with single DES (n = 5,093) is caused by DES thrombosis. The investigators observed that, compared with single DES, double DES was associated with increased risks of stent thrombosis (risk ratio [RR]: 2.31, 95% confidence interval [CI]: 1.33 to 4.03) and MI (RR: 1.86, 95% CI: 1.34 to 2.60); however, mortality (RR: 1.18, 95% CI: 0.85 to 1.65) and target vessel revascularization (RR: 1.02, 95% CI: 0.80 to 1.30) were similar between the 2 strategies. The risk of MI and DES thrombosis were associated (p = 0.040). In this report, the investigators confirmed the hypothesis that was tested by the analysis.

For such a meta-analysis to be reliable and conclusive, it must fulfill certain key methods criteria that involve well-defined objectives, precise definitions of clinical variables and outcomes, and a well-documented study identification and selection strategy (10). It must also evaluate potential bias and contain a description and evaluation of heterogeneity and sensitivity analysis. I think that the current work by Zimarino et al. (9) meets most of the key methods standards required for a conclusive meta-analysis. My main concern is that the selection of the trials was heterogeneous, and the data seems somewhat difficult to pool. For example, the ARTS II (Arterial Revascularization Therapies Study Part II) (11) had very little to do with bifurcation lesion techniques, as it involved the treatment of patients with multivessel disease. In addition, most trials quoted by Zimarino et al. (9) were actually retrospective registries, and the potential for selection bias in the treatment approach could not be ruled out. Also, the mentioned studies included the use of the first-generation DES, which is associated with greater long-term thrombogenicity than are contemporary DES platforms (12). Finally, the background pathology does not involve only the stent technique. It also relates to the individual patient characteristics and the bifurcation lesion involved. In other words, one might assume that there are unidentifiable reasons why some patients were treated using >1 stent. The use of >1 stent could be a surrogate marker for more complex atherosclerotic disease or for more advanced bifurcation involvement that may lead to increased thrombotic complications.

Despite these limitations, I share the investigators' view and conclusions regarding the topic at hand. It is probably the clinical experiences and impression obtained by multiple interventional cardiology centers and operators. It is reassuring that whenever needed, long-term mortality has not been augmented by using the double- versus single-stenting technique, despite a significant trend toward more target vessel-related ischemic events. What is the take-home

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

From the Department of Cardiology, Cardiac Catheterization Laboratories, Rabin Medical Center, Petach Tikva, The Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. Dr. Kornowski has reported that he has no relationships relevant to the contents of this paper to disclose.

message for the interventional cardiologist who is confronted with bifurcation lesions in daily practice? And how could this message alter the treatment strategy? I presume that the answer is somewhat unclear. Optimal treatment is about obtaining the best results using the least amount of unnecessary complexity. However, when managing bifurcation lesions, the treatment strategy is often dictated by lesion complexity rather than the operator's desired preferences. Perhaps the most relevant part of the story relates to the role of antithrombotic treatment after intervention. Because there are no available data regarding the potential implications of a single- versus double-stent selection on the mode and/or duration of antiplatelet pharmacotherapy, future studies should assess whether more potent and/or prolonged antiplatelet therapies might reduce the risk of DES thrombosis in the setting of complex bifurcation lesions. Finally, contemporary treatments of complex bifurcations are still evolving. Novel stents and dedicated devices are already in use in many parts of the world. Thus, the current meta-analysis by Zimarino et al. (9) reflects a clinical reality that may change over time.

Reprint requests and correspondence: Dr. Ran Kornowski, Department of Cardiology, Rabin Medical Center, Petach Tikva, 49100 Israel. E-mail: lrn.kornowski@gmail.com.

REFERENCES

1. Hildick-Smith D, Lassen JF, Koo BK. One or two stents for coronary bifurcation lesions? *EuroIntervention* 2010;6 Suppl J:J61-4.
2. Chen SL, Louvard Y, Runlin G. Perspective on bifurcation PCI. *J Interv Cardiol* 2009;22:99-109.
3. Ferenc M, Gick M, Kienzle RP, et al. Long-term outcome of percutaneous catheter intervention for de novo coronary bifurcation lesions with drug-eluting stents or bare-metal stents. *Am Heart J* 2010;159:454-61.
4. Zamani P, Kinlay S. Long-term risk of clinical events from stenting side branches of coronary bifurcation lesions with drug-eluting and bare-metal stents: an observational meta-analysis. *Catheter Cardiovasc Interv* 2011;77:202-12.
5. Latib A, Colombo A. Bifurcation disease: what do we know, what should we do? *J Am Coll Cardiol Intv* 2008;1:218-26.
6. Assali AR, Assa HV, Ben-Dor I, et al. Drug-eluting stents in bifurcation lesions: to stent one branch or both? *Catheter Cardiovasc Interv* 2006;68:891-6.
7. Katritsis DG, Siontis GC, Ioannidis JP. Double versus single stenting for coronary bifurcation lesions: a meta-analysis. *Circ Cardiovasc Interv* 2009;2:409-15.
8. Louvard Y, Medina A, Stankovic G. Definition and classification of bifurcation lesions and treatments. *EuroIntervention* 2010;6 Suppl J:J31-5.
9. Zimarino M, Corazzini A, Ricci F, Di Nicola M, De Caterina R. Late thrombosis after double versus single drug-eluting stent in the treatment of coronary bifurcations: a meta-analysis of randomized and observational studies. *J Am Coll Cardiol Intv* 2013;6:687-95.
10. Walker E, Hernandez AV, Kattan MW. Meta-analysis: its strengths and limitations. *Cleve Clin J Med* 2008;75:431-9.
11. Tsuchida K, Colombo A, Lefèvre T, et al. The clinical outcome of percutaneous treatment of bifurcation lesions in multivessel coronary artery disease with the sirolimus-eluting stent: insights from the Arterial Revascularization Therapies Study part II (ARTS II). *Eur Heart J* 2007;28:433-42.
12. Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *Lancet* 2012;379:1393-402.

Key Words: bifurcation lesion ■ drug-eluting stent ■ stent thrombosis.