

# Coronary bifurcation lesions: is less more?

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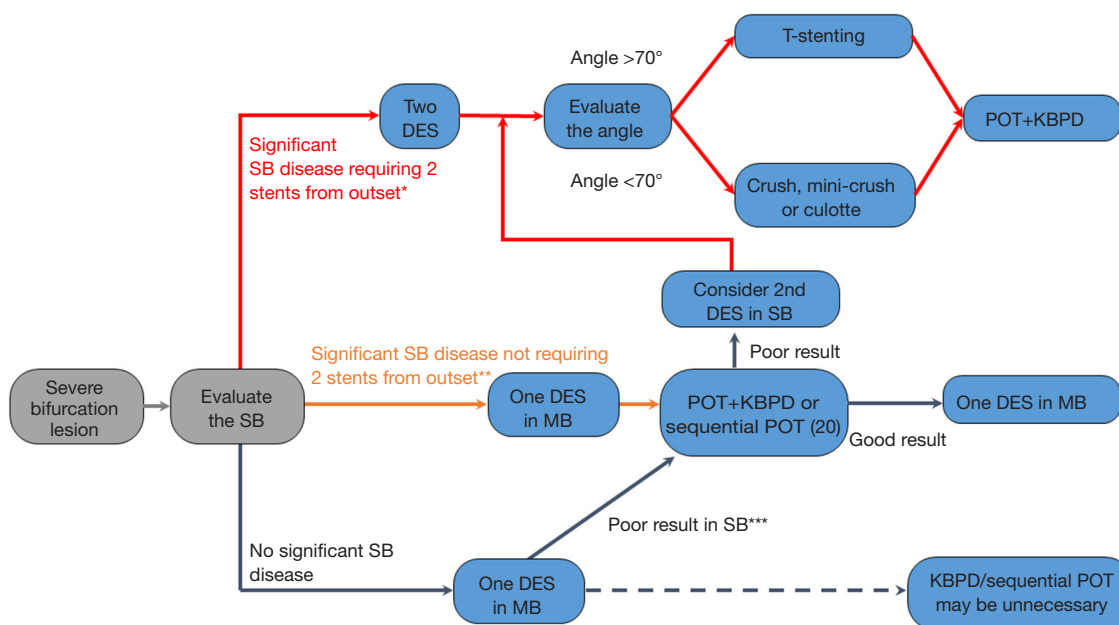
Coronary bifurcation lesions are frequent in everyday practise and account for up to 20% of all percutaneous coronary interventions (PCI) (1). The treatment of bifurcation lesions with drug-eluting stents (DES), especially when a double stent technique is used, remains challenging and is associated with a lower procedural success rate and a higher rate of long-term adverse cardiac events such as stent restenosis and thrombosis compared to non-bifurcation PCI (2). The question relating to a one or two stent strategy for bifurcation lesions has been a subject of many debates over recent years and numerous observational and randomized studies (3-6) have supplied data to this important though at times controversial subject.

Recently, Behan *et al.* (7) presented the 5-year outcome data from a patient-level pooled analysis of coronary bifurcation lesions treated with simple or complex stenting in two pivotal studies (7): more specifically, pooled 5-year results of the NORDIC 1 (8) and the British Bifurcation Coronary Study: Old, New, and Evolving Strategies (BBC ONE) (4), both of similar magnitude and methodology (N=413 and 500, respectively), that compared all-cause mortality and other clinical endpoints after simple single-stent (provisional T stenting) versus complex two-stent (culotte, crush and T-stenting) techniques, using DES.

Before looking at the results in more detail it is important to note that differences in bifurcation anatomy and disease severity are major determinants of treatment approach and remain at the discretion and judgement of the single operator. Several valuable bifurcation classifications have been proposed (9-11), none of them fully encompassing variations in anatomy, including vessel size, bifurcation angle and extent of disease in the side branch. From a practical point of view, the operator is generally speaking

faced with one of two situations: in the first scenario, due to the severity of the disease at the bifurcation and extending in to large calibre branches, two stents are required from the outset. This type has typically not been represented (thus giving rise to selection bias) in the randomized studies to date comparing different strategies as operators are not willing to risk randomising these patients to a single-stent strategy. The second type of bifurcation lesion is where one or two stents can be used. For these bifurcation lesions, multiple randomized studies comparing a routine two-stent strategy with a provisional strategy (single stent in the main vessel with additional side branch stent only if indicated) have shown comparable efficacy outcomes (target vessel/target lesion revascularization rates) between the two treatment strategies, although the provisional strategy resulted in lower rates of peri-procedural myocardial infarction (MI), less contrast use, lower X-ray doses and shorter procedural times (3,4,6). There is therefore, for this second type of lesion, a general consensus that it is better to Keep It as Simple and Safe as possible and implant one stent (KISS provisional strategy) and crossover to two stents only if required (12). Further evidence supporting this consensus statement is provided by the recent analysis by Behan *et al.* of the 5-year clinical outcomes up of the NORDIC 1 and BBC ONE bifurcation studies.

Both these multicenter randomized trials compared simple single-stent (provisional T stenting) versus complex two-stent (culotte, crush and T-stenting) techniques, using DESs. Although there were several differences in terms of trial design, mainly in the criteria for crossover from one-stent to two stent strategy and planned angiographic follow up, overall there were many similarities between the two studies with similar complex bifurcation techniques



**Figure 1** Proposed contemporary approach to treatment of severe bifurcation lesion (20). \*, typically a large SB (>2.5 mm) supplying a large territory of myocardium with significant ostial disease extending over a long segment into the SB; \*\*, typically a smaller SB (<2.5 mm) with focal involvement of the ostium; \*\*\*, presence of important dissection or < TIMI 3 flow in SB. SB, side branch; DES, drug-eluting stent; MB, main branch; POT, proximal optimization technique; KBPD, kissing balloon post-dilatation.

and similar endpoints being assessed. There are several limitations to the studies as pointed out by the authors and by Colombo and Jabbour (13): (I) both studies were performed with 1<sup>st</sup> generation DES which have been shown to be inferior to current generation DES, either with regard to the risk for death, MI or repeat revascularization, and/or with regard to stent thrombosis (14-16). Especially the usage of the paclitaxel-eluting stent (Taxus, Boston Scientific Corp, Natick, MA, USA) in the BBC ONE study is a major limitation given the higher rate of stent thrombosis compared with other 1<sup>st</sup> generation DES (17,18); (II) the techniques employed in the complex bifurcation techniques were suboptimal with the recommended kissing balloon post-dilatation only being performed in  $\pm 75\%$  of cases; whilst there is no data regarding the performance of the proximal optimization technique; (III) approximately 28% of lesions were not true bifurcation lesions and therefore not appropriate for a two-stent strategy according to current practice; (IV) dual antiplatelet therapy (DAPT) was only mandated for a minimum of 6 months in the NORDIC patients and 9 months in the BBC ONE patients though there is no data on actual length of DAPT. Furthermore, newer antiplatelet agents would now be

considered, especially in the 1/3 of patients who presented with an acute coronary syndrome or not responding to clopidogrel; (V) finally, all-cause mortality was presented rather than cardiac death which only allows one to postulate that the excess deaths in one of the groups were due to associated cardiac events.

The authors of the current analysis were able to collect 5-year follow-up data in 97% of patients. Both simple and complex groups were similar in terms of patient and lesion characteristics. The rate of side branch stenting in the provisional group was similarly low in the Nordic 1 and BBC ONE studies (4.3% *vs.* 3%,  $P=0.33$ ). The 5-year mortality rates were reassuringly low in both the simple and complex groups. Interestingly, the overall mortality rate appears to be almost twice as high in the NORDIC I study compared to the BBC ONE study despite the fact that the NORDIC I study employed the superior sirolimus-eluting stent (Cypher, Cordis, Johnson and Johnson, Bridgewater, NJ, USA). The main finding of this analysis is that 5-year mortality was lower among patients who underwent a simple strategy rather than a complex strategy [17 patients (3.8%) *vs.* 31 patients (7.0%);  $P=0.04$ ]. Interestingly, the Kaplan-Meier curves appear to separate after 2 years

suggesting that the complex strategy yields elevated risk of events beyond the time at which technical procedure-related factors play a role. The authors suggest that the higher mortality rates following complex strategies may be due to a higher incidence of very late stent thrombosis. Although there is data supporting the theory that a double stent strategy may increase the risk of stent thrombosis (2), this study can only postulate that there may be excess death in the complex group given the important limitation that the investigators only reported all-cause mortality and not cardiovascular death. Furthermore, as Colombo and Jabbour rightly point out, a “play of chance” cannot be ruled out.

Nevertheless, this study adds further weight to the case that a provisional stent strategy should be used as the default approach for the treatment of coronary bifurcation lesions when there is a possibility of using one stent from the outset. It of course remains a challenge to distinguish the more complex bifurcation lesions which are likely to require complex stenting procedures with multiple stents or dedicated bifurcation stents (19) from the more “simple” bifurcation lesions which are likely to be adequately treated with the provisional strategy. A proposed contemporary approach to the treatment of severe bifurcation lesion is summarized in *Figure 1*. Use of contemporary DES, optimal stenting techniques, and newer antiplatelet agents will further improve the clinical outcomes by reducing the incidence of long-term adverse cardiac events such as stent restenosis and thrombosis.

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