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Two stents, too many?

Should provisional PCI be the default bifurcation strategy?

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What is a bifurcation lesion?

Take Home Messages

- Bifurcation lesions pose added complexity and risk in PCI.
- There are conflicting data regarding when and what type of bifurcation strategy to utilize.
- This article summarises recent trials relating to bifurcation PCI and attempts to distal the key points for the reader.

The European Bifurcation club (EBC) defines a coronary bifurcation lesion as a "coronary artery narrowing occurring adjacent to, and/or involving, the origin of a significant side branch (SB)". A significant SB is a "branch that one does not want to lose in the global context of a particular patient" (1). There are several methods of classification; however, the medina classification (***Figure 1***) is widely accepted with a 'true bifurcation' lesion defined as Medina class (1,0,1), (1,1,1), or (0,1,1) (2).

Why do true bifurcations matter?

Bifurcation lesions pose an additional layer of procedural complexity and are associated with worse clinical outcomes compared to non-bifurcation lesions (3). This is driven, in part, by the risk of losing the side branch during main vessel (MV) intervention. In the bare-metal stent era, bifurcation strategies were originally developed to mitigate this risk; however, when compared to a single stent strategy, outcomes were inferior leading to a historical preference for a provisional approach (***Figure 2***) (4–7).

Why is the treatment strategy contentious*?*

In the era of drug eluting stents (DES), with lower rates of in-stent restenosis (ISR), and the development of new bifurcation techniques such as Culotte and DK crush, old data was questioned, and consensus once again diverged (***Figure 3***) (6,8,9).

NORDIC I and *BBC ONE* were amongst the first to evaluate different stenting techniques in the newer DES era. Both randomised trials compared simple (provisional with option to switch to a

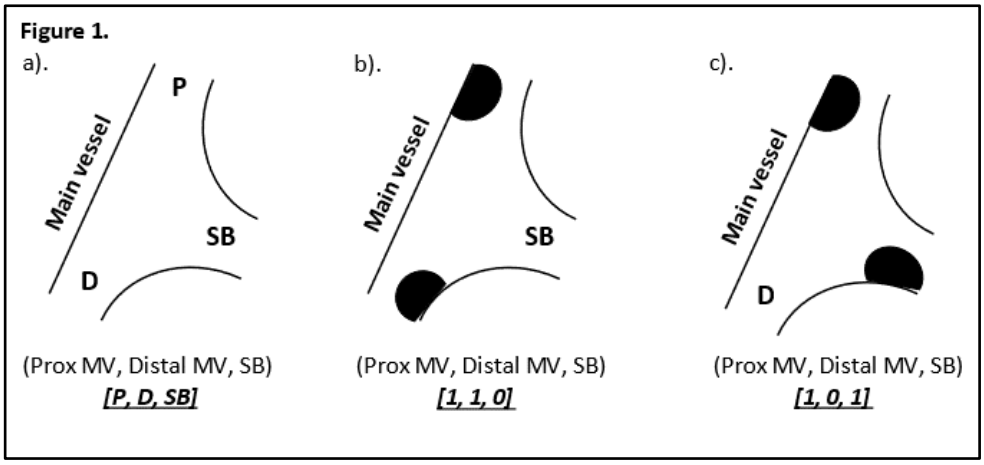

Figure 1: Figurative demonstration of Medina classification with a). Detailing formula for classification b). Example of (1, 1, 0) classification and c). An example of (1, 0, 1) classification.

two-stent strategy) versus complex up-front two stent techniques, with BBC ONE including patients presenting with ACS and NORDIC I including stable angina only. In BBC ONE, at nine months, the composite endpoint of death, myocardial infarction (MI) or target vessel failure (TVF) was noted more frequently in the complex strategy group (15.2% vs. 8.0%, HR 2.0, 95% CI 1.2-3.5, p = 0.01) with higher rates of periprocedural MACE (7.6% vs. 2.0%, RR 3.8, 95% CI 1.5-10.0, p = 0.01) (10). In NORDIC I, there was no difference in the primary composite endpoint (CV death, MI, target vessel revascularisation (TVR) or stent thrombosis) at 6 months (3.4% in the MV+SB group vs. 2.9% in the MV group, p = NS) (11). A combined 5-year follow up of both trials demonstrated no difference in death, non-procedure related MI or TVR (4% vs 7.9%: p=0.09, 13.4% vs 18.3%: p=0.14) (12).

These trials were not without criticism with differing definitions of bifurcation lesions, inclusion of varying SB sizes, methods of stent optimisation and definitions of MI used all points of contention and therefore opinion remained divided. Further conflicting data was introduced by the DK CRUSH trials which evaluated a newly developed bifurcation technique. The DK CRUSH *(Double Kissing Crush versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions*) II trial evaluated the use of a novel two stent DK crush vs provisional strategy for the treatment of non-left main (LM) coronary bifurcation lesions (13). They found lower rates of TVR in the DK group (6.5% vs 14.6%, p=0.02) but a non-significant difference in MACE (10.3% vs 2.2%, p=0.070). DK CRUSH III further demonstrated the

superiority of the DK CRUSH technique to the traditional culotte method in the treatment on LMS bifurcation lesions (14), culminating in *DK CRUSH V* which evaluated the use of a two stent DK crush technique vs provisional strategy in LM bifurcation coronary disease (15). At three years, higher rates of target lesion failure (TLF) (16.9% vs 8.3%, p<0.01) in patients treated provisionally were noted, driven by higher rates of target vessel MI (5.8% vs. 1.7%; p = 0.02) and target lesion revascularization (10.3% vs. 5.0%; p = 0.03). The feeling that bifurcation strategies had a role persisted and led to reflection that conflicting trial data was perhaps due to definitions of complexity and patient selection.

The *DEFINITION II* trial was the first to specifically define a complex bifurcation lesion (***Table 1***) with strict enrolment criteria prior to randomisation to a two-stent technique or provisional stenting strategy (16). The results were promising with 1 year follow-up demonstrating lower rates of TLF in the two-stent group (6.1% vs 11.4%: HR 0.52, 95% CI 0.30-0.90; p=0.02). Interestingly, these results were maintained but not additive at three years (17). Indeed, the majority of TLF seemed to occur within 30-days with a significant difference in TLF rates noted before and after this time point (3.0 % vs. 7.4 %, HR 0.41, 95% CI 0.20-0.85, p = 0.02). Therefore, perhaps suggesting that the choice of strategies became less relevant after one year.

Conversely, *EBC MAIN* (European Bifurcation Club Left Main Coronary Stent) which also randomised patients with true LMS bifurcation lesions to a stepwise provisional strategy or planned 2-stent approach (predominantly culotte), demonstrated no difference between the strategies (MI: 10.0% vs 10.1%,*p* = 0.91; TLR 6.1% vs 9.3%, *p* = 0.16) (18) with results maintained at three years (MI:12% vs 11%; *p* = 0.75) (19). Similarly, *EBC TWO* randomised patients with non-LM bifurcations with side-branch diameter ≥ 2.5 mm and length >5mm, to provisional versus culotte stenting (20). At 5 years, there was no difference in rates of MACE (18.4% vs 23.7%; *P* = 0.36), all-cause death, MI, or TVR (21). Similarly, the *Nordic-Baltic Bifurcation Study IV*, which also randomised patients with true complex bifurcation disease and SB lesion ≤ 15 mm, found no differences in 6-month and 2-year MACE (22).

Unanswered questions

There are still many unanswered questions, including the ubiquity of intravascular imaging in current practice, which is not reflected in previous trials. The recently published *OCTOBER* trial noted lower rates of MACE when bifurcation PCI was OCT-guided vs angiography alone (10.1% vs. 14.1%: HR 0.70, 95% CI 0.50–0.98, p = 0.04) (23). This

highlights that the use of imaging may improve outcomes in two-stent strategies by optimising technical execution. Further trials such as *DK CRUSH VIII* will seek to answer this question with intravascular ultrasound. Moreover, technology continues to evolve with continued iterations of stent and guidewire technology along with new techniques which will inevitably lead to changing opinions and strategies. Additionally, developments in antiplatelet strategies may directly affect outcomes in this patient group. Indeed, current ESC guidance allows for extension of DAPT duration in those with high ischaemic risk, albeit at the clinician's discretion. These strategies, however, often come with the added risk of increased bleeding and are patient specific. New antiplatelet strategies, such as extension of P2Y12 monotherapy or development of novel new aspirin derivatives may help reduce ischaemic events without the associated increased risk of bleeding and may ultimately shift the balance in choice of bifurcation strategy (24).

Whilst in some respects, trial data suggests equipoise, clinical practice invariably introduces nuance and patient-centred decision-making which may not always be teased out of large-randomised trials. Indeed, a default stepwise-provisional strategy may be justified in many cases; however, this may not always be the correct approach, and, in my opinion, one must evaluate the data in the context of the patient they are treating to arrive at the correct strategy.

Fig 2. Provisional technique

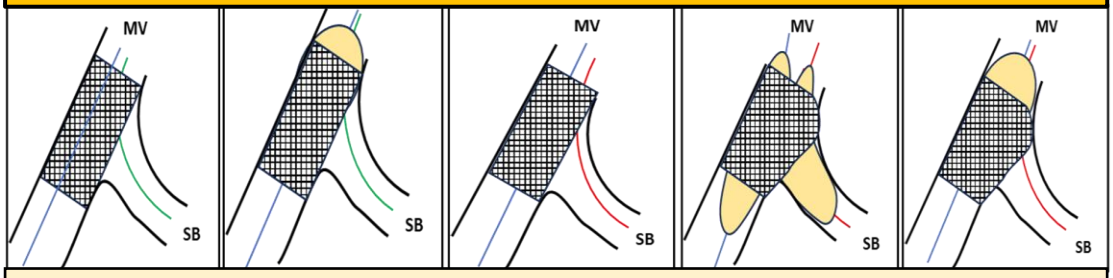

Figure 2: Visual description of provisional stenting technique a). Stent in MV sized in 1:1 fashion according to distal MV diameter and placed across the SB bifurcation b). POT of the MV stent c). the SB is then re-wired through the distal struts into SB ostium d). Followed by kissing balloon inflation simultaneously in both vessels e). A final POT is then performed in the MV (7). MV, main vessel. SB,

Fig 3. Two-stent bifurcation techniques

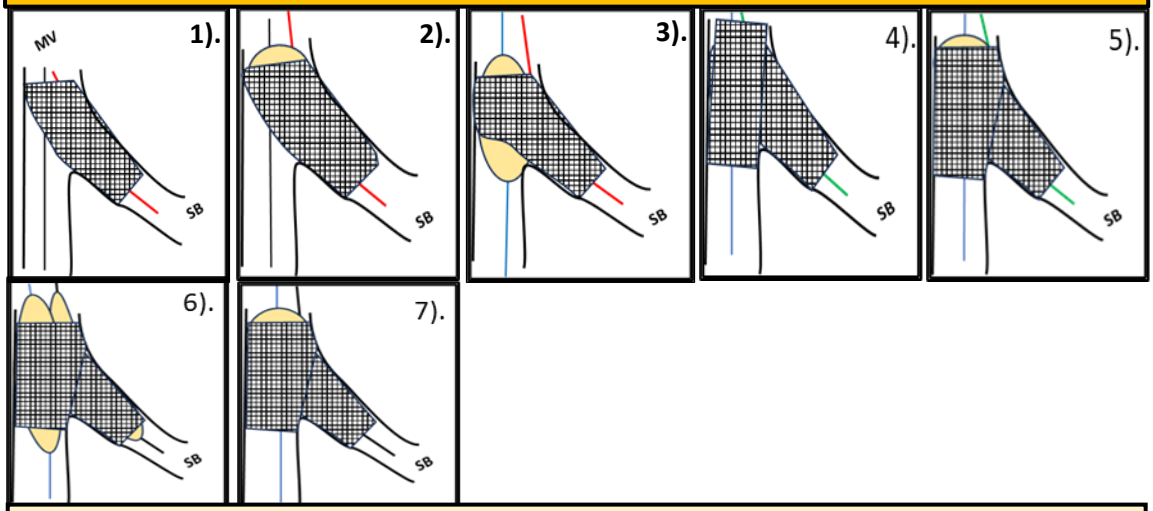

Figure 3*: a).* Diagram demonstrating steps in Culotte bifurcation stenting 1). Stent is deployed across the SB in to the MV sized 1:1 with distal SB. 2). POT is performed with balloon sized 1:1 to distal MV. 3). Distal MV is re-wired using SB wire using pull-back technique the MV stent is dilated using balloon sized 1:1 to distal MV. 4). SB wire is removed and MV is stenting with subsequent re-wiring of SB. 5). POT of MV stent 6). Kissing balloon inflation followed by 7). MV POT (7). MV, main vessel. SB, side branch. POT, proximal optimisation.

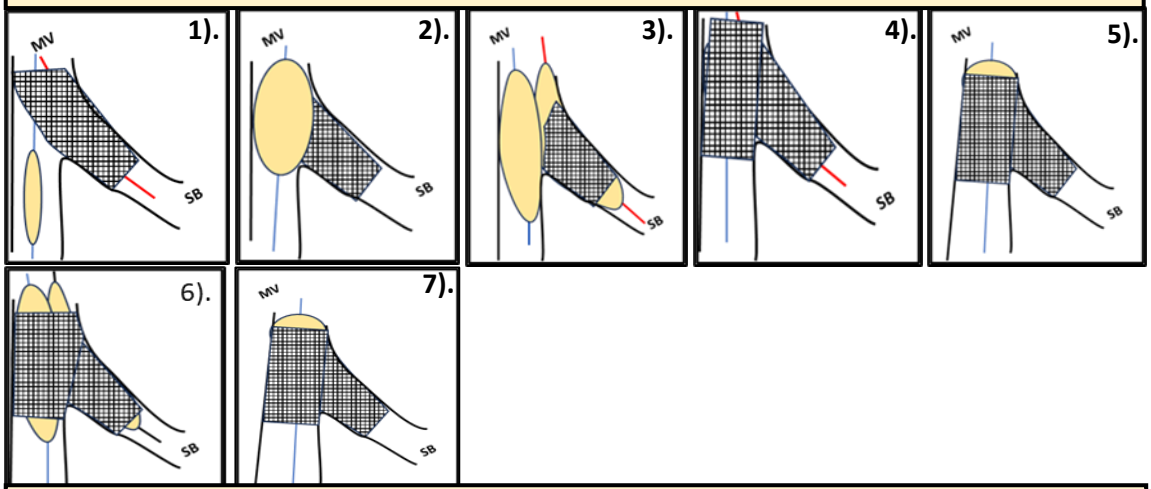

Figure 3*: b).* DK-crush technique 1). SB is stented whilst undilated balloon kept in distal MV 2). SB balloon and wire are removed and MV balloon pulled back and inflated to crush the SB stent with balloon sized 1:1 to distal MV 3). SB is re-wired and alternate followed by simultaneous kissing balloon inflation is performed 4). SB wire removed and MV is stented then 5). POT of MV stent 6). SB is re-wired then final simultaneous kissing inflation followed by 7). Final POT of MV stent (7). DK, double-kiss. MV, main vessel. SB, side branch. POT, proximal optimisation.

Table 1: *DEFINITION* criteria
Major Criteria
1). In left main bifurcation
SB lesion length ≥10mm & stenosis ≥70%
2). In non-left main bifurcation
SB lesion length ≥10mm & stenosis ≥90%
Minor criteria
1). Moderate or severe calcification
2). Multiple lesions
3). Bifurcation angle <45° or > 70°
4). Thrombus containing lesion
5). Main vessel lesion length ≥25mm
6). Main vessel reference vessel diameter <2.5mm

Table 1: *DEFINITION* criteria used to define complex bifurcation lesions in the *DEFINITION II* trial. A complex bifurcation lesion is defined as two major criteria, or one major and two minor criteria.

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