Review

Key words: Coronary bifurcation, stents, angioplasty, percutaneous transluminal coronary, thrombosis

Management of bifurcation lesions

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Dr Antonio Colombo is Director of the Cardiac Catheterisation Laboratory at EM Centro Cuore Columbus SRL in Milan, Italy. He is an interventional cardiologist who has been active in the field of coronary stenting since the early days of this technology and has contributed in several ways to the improvement and refining of various aspects of the procedure. Dr Colombo has been the main author and the co-author of many publications in the area of coronary intervention. Recently, Dr Colombo introduced new approaches to the treatment of bifurcation lesions with drug-eluting stents.

Abstract

Coronary bifurcations are frequently encountered by interventional cardiologists and remain a challenging subset of lesions to treat. Recent advances in percutaneous coronary intervention and the introduction of drug-eluting stents have dramatically improved our ability to successfully treat patients percutaneously, with improved long-term results. However, there has been considerable controversy as to the appropriate management strategy. This review aims to provide a contemporary and practical approach to the percutaneous treatment of coronary bifurcations.

Introduction

Approximately 15% to 20% of percutaneous coronary interventions (PCI) are performed to treat coronary bifurcations.[1,2] Despite recent advances in interventional cardiology and the introduction of drug-eluting stents (DES), PCI for bifurcation remains technically challenging, with lower procedural success rates and worse clinical outcomes than non-bifurcation lesions.

The complexity of treating bifurcations arises not only from the variations in bifurcation anatomy (left main, plaque burden, angle between branches) and dynamic changes in anatomy during treatment (plaque shift, dissection), but also from the fact that the correct management is more time-consuming and technically challenging than is the case with non-bifurcation lesions. Due to the many anatomic variants, there is no single strategy that can be applied to every bifurcation, and an appropriate strategy has to be tailored to each lesion with modification if the need arises.

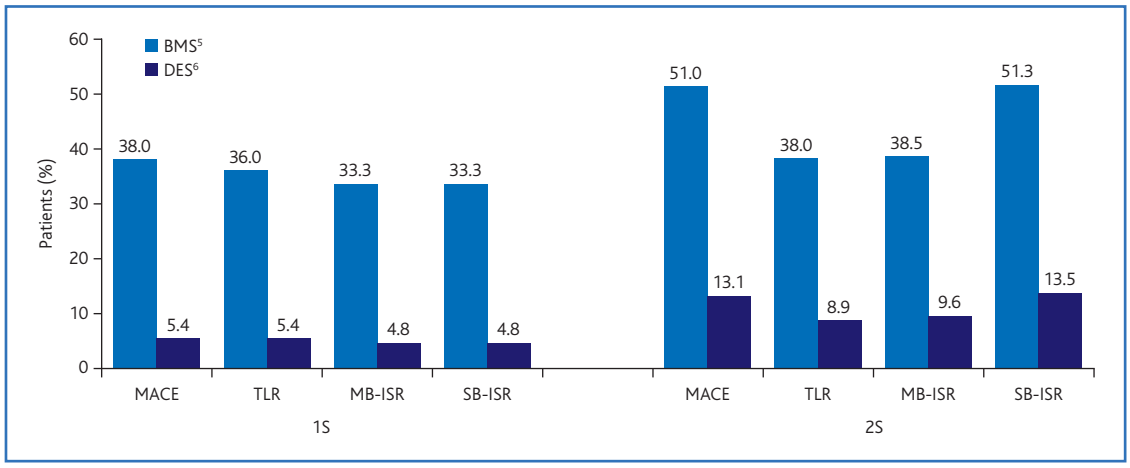
The management of bifurcations is a topic well suited to the title of this journal, as considerable controversy has surrounded the issue and there has been a lack of consensus as to the appropriate treatment strategy. This has predominantly stemmed from a lack of randomised data, which may explain why therapeutic strategies have been largely based on the personal clinical experiences of highly skilled operators practising in high-volume centres.[3] In this review, we attempt to provide a practical approach to the management of bifurcations and to highlight a few current areas of controversy and consensus.

DES *vs.* BMS in bifurcations

The success of DES in reducing restenosis and revascularisation in less complex lesions has been extended to the coronary bifurcation.[4] Although there have been no randomised trials specifically comparing bare metal stents (BMS) to DES in bifurcations, initial registry studies from our centre have shown marked reductions in major adverse cardiac events (MACE) and target lesion revascularisation (TLR) rates, compared with historical BMS controls. These reductions occurred irrespective of whether a one-stent (MACE: 5.4% *vs.* 38%; TLR: 5.4% *vs.* 36%) or two-stent (MACE: 13.3% *vs.* 51%; TLR: 8.9% *vs.* 38%) strategy was used (Figure 1).[5,6] As a result, DES have become the preferred stent platform for the treatment of coronary bifurcations.

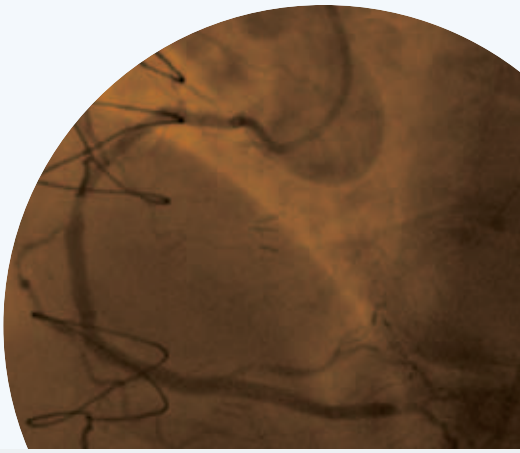
Single *vs.* double stent strategy

Since the advent of stenting and the superior results it has achieved when compared with balloon angioplasty, there has been considerable controversy as to the optimal strategy in bifurcation PCI. In other words, is it better



MACE=major adverse cardiac events; TLR=target lesion revascularisation; MB-ISR=main branch in-stent restenosis; SB-ISR=side branch in-stent restenosis

Figure 1. Clinical and angiographic outcomes in two registry studies performed comparing a one-stent (1S) vs. two-stent (2S) approach with bare metal (BMS) or drug-eluting stents (DES).[5,6]

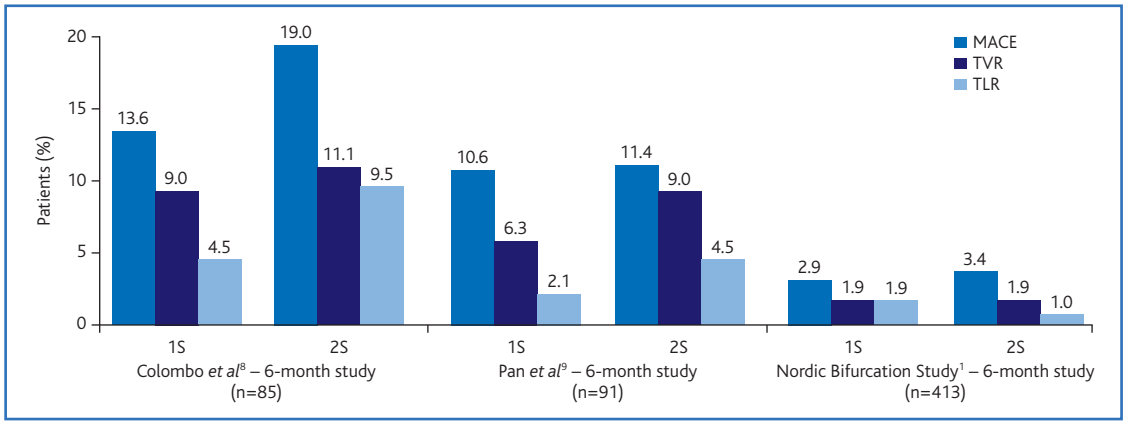


to implant a stent in the main branch only or in both branches of the bifurcation? A practical approach to the above problem can be summarised as follows:

1. Two wires should be placed in most bifurcations and the side branch (SB) wire should be 'jailed' in the majority following deployment of the stent in the main branch (MB). This approach is important in protecting the SB from closure due to plaque shift and/or stent struts during MB stenting. The jailed SB wire also facilitates re-wiring of the SB[7] (if SB post-dilatation/stenting or final kissing balloon inflation [FKI] is needed, or if the SB occludes) by acting as a marker for the SB ostium and by changing the angle of SB take-off. There is no need to remove the jailed wire during high-pressure stent dilatation in the MB. It is preferable to avoid jailing hydrophilic guidewires as there is a risk of removing the polymer coating. Accurate handling of the guiding catheter to prevent migration into the ostium of the coronary vessel will allow removal of the jailed wire.
2. Two stents as 'intention-to-treat' should be the technique when the disease in the SB extends beyond the ostium and when the diameter and territory of distribution are relatively large. There are no solid data to support the supposition that two stents are more thrombogenic than one – that is, provided correct stent placement has been performed and compliance with antiplatelet therapy is maintained.
3. In all other conditions, SB provisional stenting should be the procedure of choice.

Further information on these techniques appears in the *Clinical approach to bifurcation* section, below.

There are currently three published randomised trials comparing a one-DES (1S) *vs*. two-DES (2S) strategy, the results of which are summarised in Figures 2 and 3.[1,8,9]



MACE=major adverse cardiac events; TLR=target lesion revascularisation; TVR=target vessel revacularisation

Figure 2. Clinical outcomes in three randomised trials comparing a 1S vs. 2S approach in the treatment of coronary bifurcations.[1,8,9]

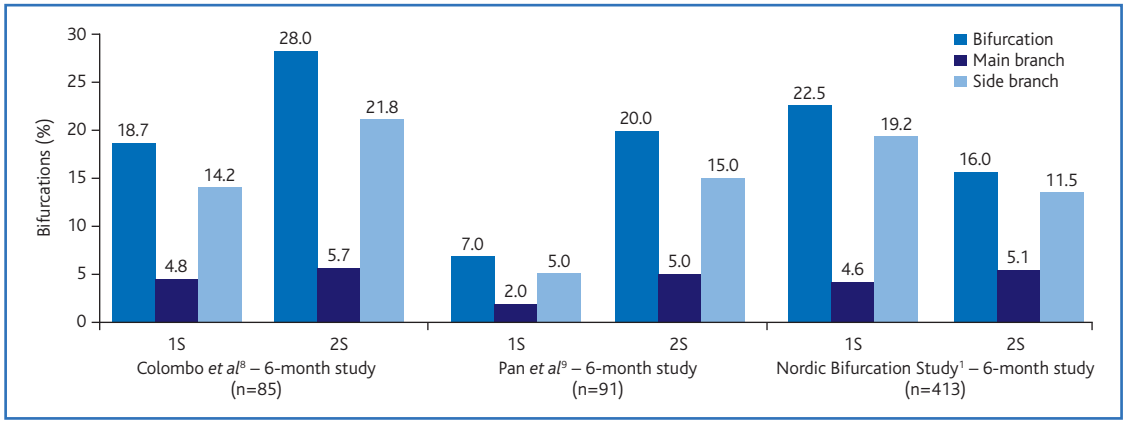


Figure 3. Angiographic restenosis in three randomised trials comparing a 1S vs. 2S approach in the treatment of coronary bifurcations.[1,8,9]

Management of bifurcation lesions *continued*

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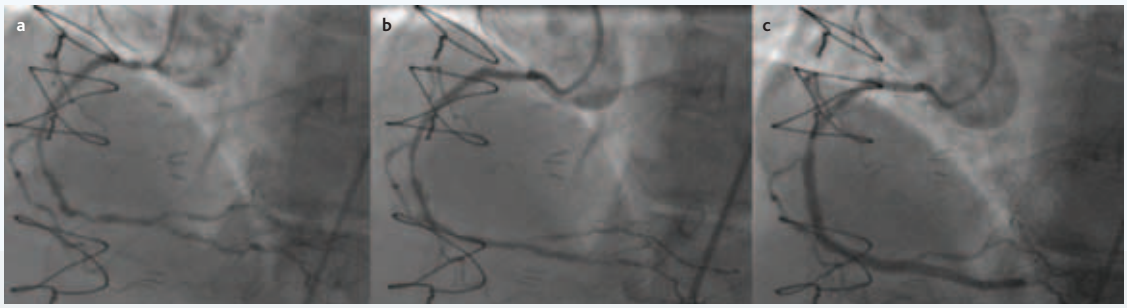


Figure 4. An example of the 'Keep it open' strategy that we use when the SB is small and diffusely diseased. (a) baseline angiogram showing diffusely diseased mid-to-distal right coronary artery with a true bifurcation lesion of posterior descending (PDA) and posterolateral arteries (PL); (b) guidewire placed in MB (i.e. PDA) and SB (i.e. PL). No pre- or post-dilatation of SB after wire placement; (c) final angiographic result, after MB (PDA) successfully stented and jailed wire in SB (PL) removed, confirming patency of SB at end of the procedure.

The Nordic Bifurcation Study,[1] the largest of these (n=413), showed no statistically significant difference in restenosis of the bifurcation (22.5% *vs*. 16%, p=0.15) or SB (19.2% *vs*. 11.5%, p=0.062) between the 1S *vs*. 2S groups. It is interesting that this is the first bifurcation study to show a trend towards fewer episodes of SB restenosis in the 2S group. A strength of the study and an explanation for the low TLR rates was that the clinical event adjudication was performed at 6 months but angiographic follow-up was performed later, at 8 months, thus neutralising the effect of the oculo-stenotic reflex on repeat revascularisation. The 2S approach, not surprisingly, was associated with longer fluoroscopy times and larger contrast doses. However, it must be pointed out that only a small proportion (2%) of the lesions treated were in the left main stem and we do not know what proportion of the lesions treated were true bifurcations.

It is apparent from these data that routine stenting of both branches offers no clear advantage over a provisional strategy of stenting the MB only, with balloon angioplasty of the SB. Thus, there appears to be consensus that a provisional strategy is the preferred approach for the majority of bifurcations, and that the old dictum of 'less metal is better' still applies. The distinction between these strategies is that, in the 1S approach, the operator is willing to accept a suboptimal result in the SB provided TIMI (Thrombolysis in Myocardial Infarction) flow is normal and the SB has limited clinical relevance regarding territory of distribution.

There appears to be increasing evidence that our obsession with trying to get the best cosmetic result in the SB may not be physiologically important. This concept is especially important in smaller SBs, as the majority of angiographically significant SB lesions are not demonstrated to be functionally significant by fractional flow reserve analysis.[10] Further, smaller SBs are less likely to result in angina if a residual stenosis is left untreated or if restenosis occurs.[11,12] However, this should not diminish the importance of protecting SBs with guidewires during the procedure to prevent their closure. It has been shown that SB (≥2 mm) compromise during a provisional approach is not inconsequential and can be associated with a large periprocedural myocardial infarction.[13] The 2S approach becomes important if an optimal result and low restenosis rates are required due to the extent of SB disease and the clinical importance of the SB.

Clinical approach to bifurcation PCI

While the provisional strategy is the default approach for the treatment of the majority of bifurcations, an appropriate decision at the outset will save time and money and reduce the risk of complications. We suggest that there are three questions an operator needs to answer in order to decide the appropriate primary strategy:

1. Is it a true bifurcation – i.e. is there significant (>50% diameter stenosis) disease in SB and MB?
2. Is the SB disease diffuse (>5 mm) and not localised to within 3 mm of the ostium?
3. Is the SB suitable for stenting – i.e.
   a. Is the SB important (does it supply a large territory of myocardium)?
   b. Is the SB ≥2.5 mm in diameter?

All these factors determine the likelihood of success with a provisional approach and whether the operator is willing to accept a suboptimal result in the SB with balloon angioplasty only. If the answers to all of the above questions are **yes**, then the bifurcation may still be treated with 1S but the operator should strongly consider a 2S approach as intention-to-treat. In left main stenosis, a 2S approach should be used almost routinely where the bifurcation has disease in both branches, and the provisional approach could be maintained for one branch of a trifurcation.

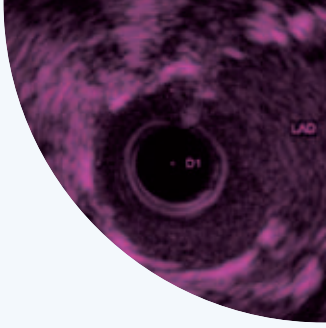
Based on the response to the above three questions, the approach to bifurcation PCI can be divided into three strategies:

- Keep it open
- Provisional approach
- Two-stent approach

Keep it open

This strategy is utilised when the SB has ostial or diffuse disease **and** is not suitable (too small) for stenting or clinically irrelevant (see Figure 4). It is performed as follows:

1. Wire both branches
2. Dilate MB if needed but not SB
3. Stent MB and leave wire in the SB



4. Perform post-dilatation of the MB with jailed wire in the SB
5. Do not re-wire SB or post-dilate SB

This 'jailed wire' strategy allows protection of a SB that may not require treatment but where the need to maintain patency is important. This strategy can be utilised as a stand-alone technique or as part of the provisional strategy when the operator may need to eventually dilate or stent the SB.

Provisional approach

This strategy is quick, safe, easy to perform and has been shown to be associated with results comparable to a more complex approach. The provisional approach is utilised when the SB has minimal disease or disease at the ostium only **and** the SB is suitable for stenting. A 6F guide catheter is generally used but if implanting Xience V (Abbott Vascular Devices, Redwood City, CA, USA) or Promus™ (Boston Scientific, Natick, MA, USA), a 7F guide is preferred. The provisional approach is performed as follows:

1. Wire both branches
2. Pre-dilate the MB and the SB as required; many SBs without significant disease do not require pre-dilatation
3. Stent the MB, leaving the SB wire in place. If the angiographic results in MB and SB are satisfactory, the procedure is complete and the SB wire jailed behind the MB stent struts can be removed gently
4. Re-wire SB and then remove jailed wire. In our experience, re-crossing into the SB through the MB stent struts is usually possible using the Rinato-Prowater wire (Asahi Intecc Co Ltd, Nagoya, Japan/ Abbott Vascular Devices, Redwood City, CA, USA) and in extremely difficult cases the ACE fixed wire balloon (Boston Scientific, MA, USA). In difficult situations, we have also successfully used the Pilot 150 (Abbott Vascular Devices, Redwood City, CA/Guidant Corporation, Santa Clara, CA, USA) or the Miracle 3 or 4.5 gm (Asahi Intecc Co Ltd, Nagoya, Japan/Abbott Vascular Devices, Redwood City, CA, USA) wires. The jailed wire in the SB should always be left in place as a marker until complete re-crossing has been done
5. SB balloon dilatation and FKI. FKI is mandatory if the SB is dilated through the MB stent struts to correct MB stent distortion and expansion[14]
6. If the result remains unsatisfactory (suboptimal result, plaque shift with >75% residual stenosis or TIMI <3, in a SB ≥2.5 mm) or SB balloon dilatation is complicated by a flow-limiting SB dissection, then perform SB stenting (see below)

There is some uncertainty as to whether FKI is mandatory when a provisional approach is used. Theoretically, and from the benchmark studies, FKI has the advantage of opening stent struts that potentially can scaffold the SB ostium and thus facilitate future access to the SB. There is also concern that stenting across a bifurcation without opening the stent struts into the SB results in 'malapposed' struts across the SB ostium that are not endothelialised.

Two-stent approach

The main difference between the 2S approach as 'intention-to-treat' or as 'crossover' from a provisional approach is whether the SB is stented at the same time or before the MB (in the former case) or after the MB stent (the latter). There is a learning curve in the treatment of bifurcations and we have found at our institution that, as our experience with implanting two DES in a bifurcation has increased rates of restenosis and repeat revascularisation have decreased.[15] Thus, we stress that meticulous attention to performing the specific bifurcation technique is important and improves long-term results.[16,17]

Intention-to-treat. When the operator decides that the 2S approach is needed as 'intention-to-treat', the guide catheter should ideally be an 8F. The two techniques we recommend are the V technique – when the disease does not extend proximal to the bifurcation (less than 20% of the time) – or the modified-T (also called mini-crush).

Performance of the V technique (Figure 5a) requires deploying the two stents simultaneously, with some operators performing a true simultaneous stent deployment while others prefer to alternate balloon inflation. However, it is important to avoid simultaneously inflating the two stents at high pressure, a manoeuvre which may traumatise the proximal un-stented vessel. A practical approach is to perform the FKI with two short non-compliant balloons, being careful not to protrude proximally to the stents.

The modified-T or mini-crush (Figure 5b) is performed by positioning the two stents in both branches with the SB stent minimally protruding into the MB. The SB stent is inflated first, and following a check for patency of the SB, the deploying balloon and wire are removed from the SB. The MB stent is then deployed. The final step is to re-cross into the SB, perform a high-pressure inflation with a non-compliant balloon in the SB (usually at 20 atm or more) and then perform a FKI utilising another non-compliant balloon in the MB. The FKI is also performed at high pressure, usually 20 atm or more. This manoeuvre is called the 'two-step kiss'.

Bench-testing of this two-step kiss technique by Dr Ormiston's group (presented at TCT, 2006), has shown that this technique results in improved opening of and less obstruction by stent struts at the SB ostium.[18]

Provisional, requiring a second stent in the SB (including 'bail-out' or 'crossover'). When there is the need to implant a second stent in the SB, we now use the T-stenting with protrusion technique (TAP). TAP (Figures 5c and 6) requires advancement of a second stent in the SB following re-crossing of the MB stent. A non-compliant balloon is placed in the MB stent. We then pull back the SB stent into the MB using the MB balloon as a marker. This results in full coverage of the ostium with some minimal protrusion. The final step is to inflate the delivery balloon in the SB and the MB balloon at 20 atm or more. An alternative crossover 2S technique is the reverse crush.[16]

Management of bifurcation lesions *continued*

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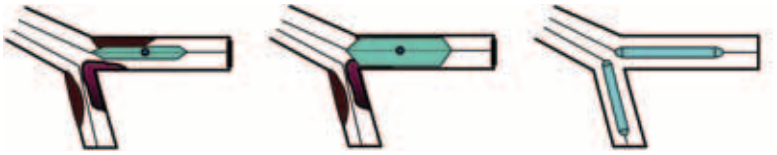
(a) The V Technique

Step 1:

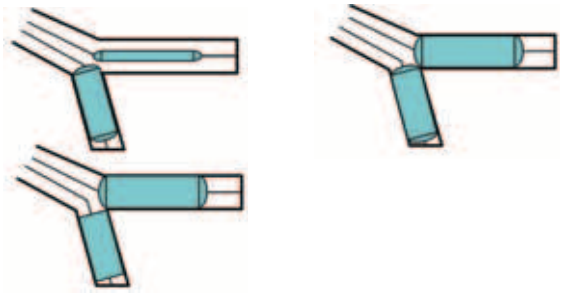


(a) Wire and pre-dilate both branches

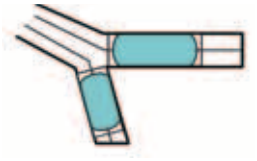
(b) Two parallel stents are positioned covering both branches

Step 2: The stents are deployed either

alternately or **simultaneously**



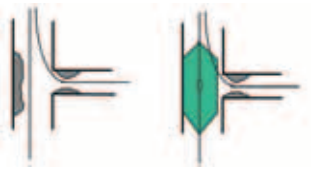
Step 3:



Final kissing balloon inflation with 2 short non-compliant balloons using the same pressure for both balloons

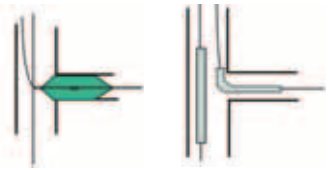
(b) The Mini-Crush Technique

Step 1:



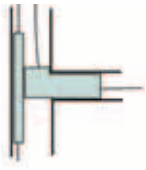
Wire and dilate both branches

Step 2:



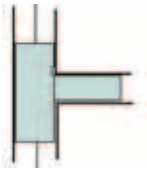
Position both unexpanded stents. SB stent is positioned with only minimal protrusion into MB but ensuring coverage of ostium

Step 3:



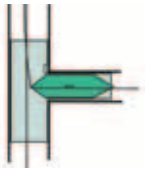
Dilate SB stent

Step 4:



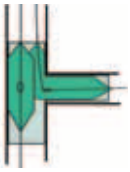
Remove the wire and balloon from SB and dilate stent in MB

Step 5:



Re-cross into SB, and perform high pressure dilation with non-compliant balloon

Step 6:



Final kissing balloon dilation at high pressure with non-compliant balloons

(c) The T-stenting with protrusion technique (TAP) as a cross-over from the provisional approach

Step 1:

Wire both branches and pre-dilate the main and the side branch as required

Stent the MB jailing the SB wire

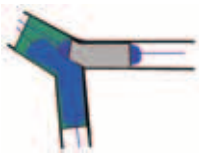
Step 2:

If the result in the SB is unsatisfactory due to plaque shift or dissection and the SB has to be stented, then re-cross into the SB through the MB stent struts

Step 3:

Position stent in the SB ensuring coverage of ostium with minimal protrusion into MB and place non-compliant balloon in MB stent

Step 4:



Inflate the delivery balloon in the SB and the MB balloon simultaneously

Final Result:

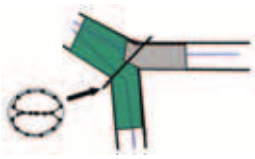


Figure 5. Explanatory diagrams of the V-stenting, Mini-Crush and T-stenting with protrusion techniques. Adapted from Iakovou et al.[16]

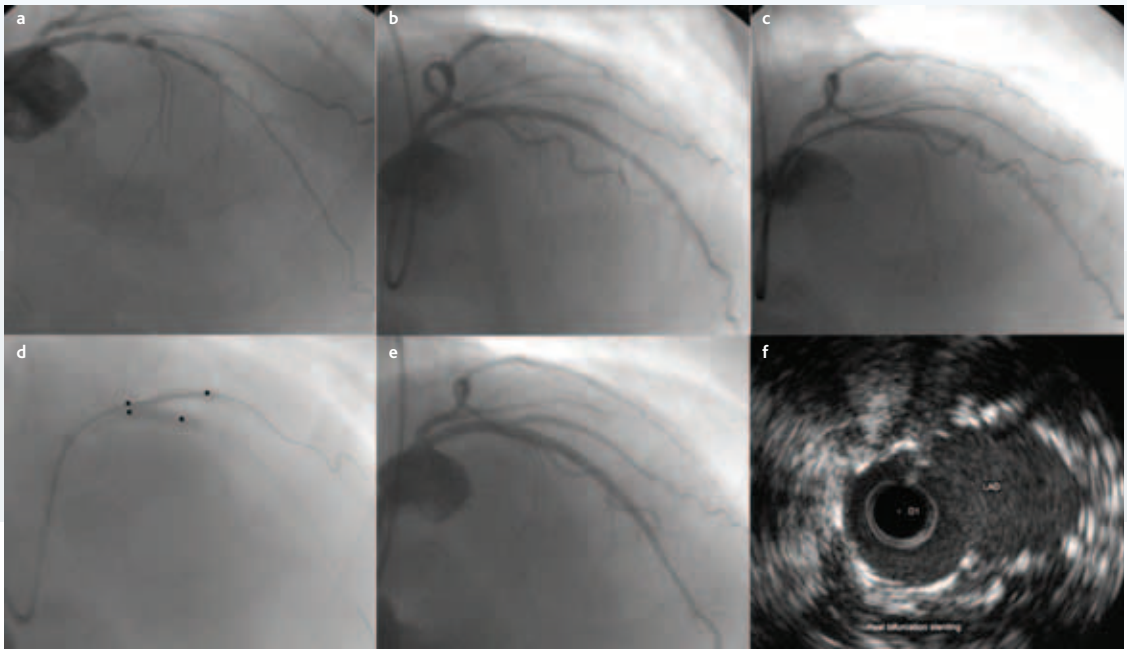


Figure 6. An example of the T-stenting with protrusion technique used to stent a flow-limiting dissection in the side branch after a provisional approach: (a) baseline angiogram showing diffusely diseased left anterior descending (LAD) artery with true bifurcation lesion of LAD/diagonal; (b) plaque shift and decreased flow in diagonal artery after stenting of LAD; (c) flow-limiting dissection in diagonal after balloon dilatation; (d) placement of Quantum™ Maverick® (Boston Scientific, Natrick, MA, USA) in LAD and Cypher® (Cordis Corporation, Miami, FL, USA) 2.5 x 18 mm stent in diagonal with slight protrusion of stent into LAD, followed by simultaneous inflation of both balloons (black dots are balloon markers); (e) final angiographic result; (f) intravascular ultrasound pull-back in diagonal confirming full coverage of ostium and 'figure of eight' appearance to LAD/diagonal.

Safety of DES in bifurcation stenting

The current controversy on the safety of DES and the risk of stent thrombosis (ST), especially in off-label indications, has placed the use of DES in bifurcations under the spotlight. We have previously shown that DES implantation in bifurcations is a predictor of ST (HR 6.42; 95% CI 2.93–14.07; p<0.001) with a ST incidence of 3.5% among patients whose bifurcations were treated with DES.[19] However, the use of two stents was not an independent predictor of ST.[19] Further, the reported rates of ST in some bifurcation studies are higher than seen in less-complex lesions, although there is no uniform definition of ST across these studies. This has raised concerns about the safety of DES in bifurcations.

The study by Hoye *et al*. deepened concerns when the authors reported a ST rate of 4.3% with the crush technique.[20] However, of the 10 patients who had a ST, only two were documented angiographically and four had discontinued dual antiplatelet therapy within 7 months of the procedure. As this was a 2S study, the findings cannot be extrapolated to conclude that double stenting carries a higher risk than a single-stent strategy.

The Nordic Bifurcation Study is reassuring in that only one patient had a definite ST and this patient was treated with one stent.[1] However, this study has reported 6-month clinical data only, and it will be important to know what the rate of ST is at 2 and 3 years. In the ARTS II study, five

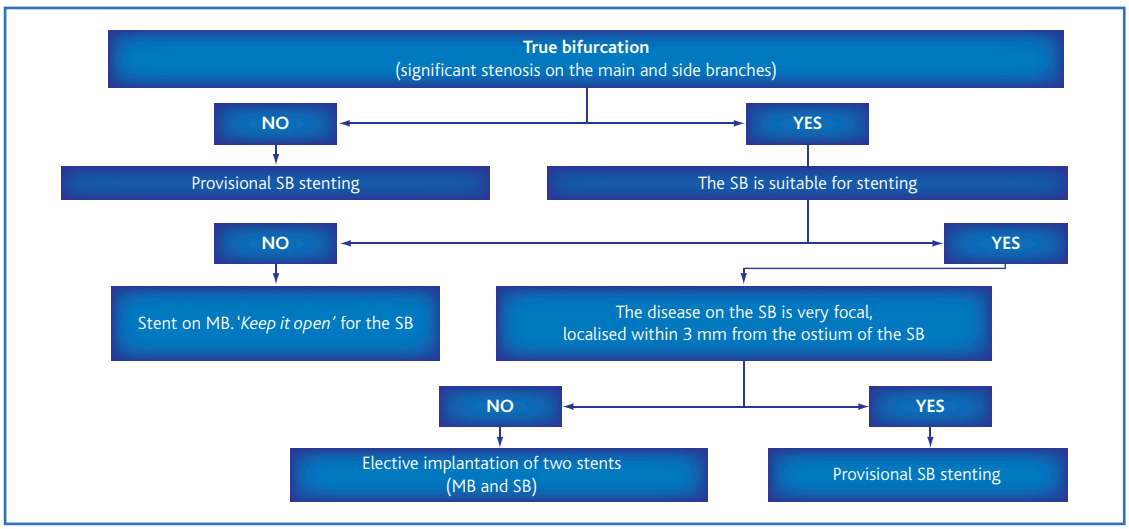


Figure 7. A proposed approach to treat coronary bifurcations.

cases of ST (1.5%) occurred in a total of 465 bifurcations in 324 patients treated with DES.[4] Four of these were sub-acute ST, with three of the bifurcation lesions having had a poor angiographic result at the end of the procedure and the only case of late ST occurring in a non-bifurcation lesion. Thus, there is currently no convincing evidence to suggest that we should refrain from using DES in bifurcations or that a two-stent strategy is associated with a greater risk of ST.

Despite these statements, we should take into consideration the fact that implanting two stents always demands more attention and expertise in order to obtain the best result in both MB and SB. Currently, we continue to recommend 1 year of dual antiplatelet therapy in patients undergoing bifurcation stenting with DES.

Conclusions

DES have had a major impact on how we treat complex coronary lesions and have been shown to be more efficacious than BMS in the treatment of bifurcations. The majority of bifurcations can be treated with a provisional approach but there are still situations when a 2S approach is required, either as 'intention-to-treat' (left main or diffuse disease in SB ≥2.5 mm in diameter) or as a 'crossover' procedure from the provisional approach (because of dissection, suboptimal result or plaque shift). Figure 7 summarises our approach to deciding the stenting strategy when treating a coronary bifurcation.

Key Learning

- Bifurcations have variable anatomy and complexity, and the approach to percutaneous coronary intervention is tailored to each lesion, based on the extent of disease, suitability for stenting and importance of the side branch
- Drug-eluting stents (DES) are more efficacious than bare metal stents and are the preferred stent platform for the treatment of coronary bifurcations, irrespective of whether a one-stent or two-stent strategy is utilised
- A provisional strategy of stenting the main branch only is the preferred approach in the majority of bifurcations
- After treatment of bifurcations with DES, 12 months of dual antiplatelet therapy is recommended

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