Recent perspective on coronary artery bifurcation interventions

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ABSTRACT
Coronary bifurcation lesions are frequent in routine practice, accounting for 15–20% of all lesions undergoing percutaneous coronary intervention (PCI). PCI of this subset of lesions is technically challenging and historically has been associated with lower procedural success rates and worse clinical outcomes compared with non-bifurcation lesions. The introduction of drug-eluting stents has dramatically improved the outcomes. The provisional technique of implanting one stent in the main branch remains the default approach in most bifurcation lesions. Selection of the most effective technique for an individual bifurcation is important. The use of two-stent techniques as an intention to treat is an acceptable approach in some bifurcation lesions. However, a large amount of metal is generally left unapposed in the lumen with complex two-stent techniques, which is particularly concerning for the risk of stent thrombosis. New technology and dedicated bifurcation stents may overcome some of the limitations of two-stent techniques and revolutionise the management of bifurcation PCI in the future.

INTRODUCTION
Coronary bifurcation disease, which is difficult to deal with, is present in up to 15–20% of lesions undergoing percutaneous coronary intervention (PCI).1–2 PCI for bifurcation is associated with a higher incidence of procedural complications, a higher rate of restenosis and worse clinical outcomes than non-bifurcation PCI.3–7 Drug-eluting stents have contributed to a significant reduction in the incidence of restenosis and target vessel revascularisation in this subset of lesions.8–11 Based on several contemporary studies, interventionalists have settled on a ‘keep it simple’ approach which involves starting with a single-stent approach for the main branch (MB) and ignoring side branch (SB) disease unless the clinical situation warrants placement of an SB stent. Treatment of a bifurcation lesion as intention to treat is an acceptable approach in some situations. Dedicated bifurcation stents would probably result in a clear improvement in bifurcation stenting.

CORONARY BIFURCATION ANATOMY
How is a bifurcation lesion defined and which classification should be used?
A bifurcation lesion represents a coronary artery narrowing adjacent to and/or involving the origin of a significant SB. A significant SB is a branch that an interventionalist does not want to lose in the global context of a particular patient.12 Historically, several bifurcation classification schemes have been proposed, which are generally similar in describing specific bifurcation lesions and are sometimes difficult to remember. Although the Medina classification13 is easier to use and to remember, it does not include the description of angulation of branches and the size of the proximal healthy segment, as is the case in the classifications suggested by Movahed et al14 and Shams et al.15 However, a more specific and relevant classification should be developed based on intravascular ultrasound (US), taking into consideration the increasing use and more objective analysis of bifurcation lesions with intravascular US.

Anatomy and physiology
A coronary bifurcation consists of three distinct anatomical segments: the proximal MB (including the bifurcation carina), the distal MB and SB. The bifurcation carina or MB–SB ‘transition zone’ is the core of the coronary bifurcation anatomy. Each bifurcation presents with a unique anatomy characterised by (1) a conical shape connecting the proximal and distal segments; (2) larger proximal MB reference diameter compared with smaller reference diameter in distal branches; (3) negative remodelling at the SB ostium; (4) proximal to distal vessel diameter tapering; (5) non-uniform geometrical distribution of atherosclerotic plaque that can involve any anatomical segments, sparing the flow divider.16 Atherosclerotic changes usually occur in the lateral area of the bifurcation with low shear stress and rarely involve the carinal area where high flow is observed. A study by Russell et al17 reported an ex vivo characterisation of coronary bifurcation lesions demonstrating a complex and asymmetric geometry at the MB–SB transition zone (carina) of the bifurcation. The major forms of asymmetry included curvilinear junctions, tapering diameters and an elliptical SB take-off rather than spherical or round forms.

The physiological pattern of fluid diffusion through a branching system has been addressed by Murray. With regard to bifurcation lesions, Murray’s law is a function of the size of the proximal MB and the distal branches and is represented by the formula: $D_1^3 = D_2^3 + D_3^3$ where $D_1$ is the mother vessel and $D_2$ and $D_3$ are daughter vessels.18 A study by Finet et al19 investigated the bifurcational fractal geometry with angiographically normal coronaries. Finet’s law is used to determine the actual vessel size (diameter) of the three segments of bifurcation including the mother vessel and two daughter vessels. If two diameters are known, it is possible to derive the diameter of the third vessel by using the formula: mean ratio = $D_m/D_1 + D_d/2$, where $D_m$ is the mother vessel diameter and $D_1$ and $D_d$ are the respective diameters.
of the two daughter vessels. This might be helpful for sizing devices (balloon, stent), defining PCI strategy and preventing complications.

The impact of cardiac motion on bifurcation lesions should not be overlooked. There are constant movements and dynamic changes in the relationship between the MB and the SB, so attrition is maximal at the bifurcation carina where bending and twisting occur repeatedly. These sustained repetitive stresses may cause stent fracture, recoil or excessive injury to the vessel wall if a stent is deployed through the MB to the SB.

**IMAGING AND PHYSIOLOGICAL ASSESSMENT**

**Intravascular ultrasound (US)**

Furukawa et al.\(^2\) demonstrated that the presence and severity of ostial SB plaque on intravascular US is the most important predictor of SB occlusion after bifurcation PCI. Suboptimal stent deployment in bifurcation lesions, particularly with the two-stent strategy, increases the risk of stent thrombosis and restenosis (particularly at the SB ostium). Pre-intervention intravascular US can provide valuable information for the optimal selection of the bifurcation PCI strategy by assessing the morphology, burden and distribution of plaque at the SB ostium. In one study, with regard to non-left main coronary artery (LMCA) bifurcations, intravascular US-guided PCI with drug-eluting stents was associated with significantly lower rates of death and myocardial infarction than angiography guidance.\(^3\) Pre-intervention intravascular US of the SB is useful for predicting the likelihood of SB compromise due to plaque and/or carina shift after single-stent deployment in the MB. Post-procedural stent expansion and apposition, particularly at the carina level, is also important to guide optimal dilation of the SB ostium and kissing balloon dilatation that might enhance the long-term outcome of this technically challenging subset of lesions. Intravascular US of bifurcation lesions may be difficult because the image in the carina appears oval or irregular in shape. For a better understanding of the geometry of the bifurcation, especially the SB ostium, intravascular US pullback from both the MB and SB is recommended rather than one pullback.

**Optical coherence tomography**

Optical coherence tomography can assist the optimisation of bifurcation PCI. It may be useful in the detailed assessment of stent expansion, strut apposition, strut distribution, carina, overlap of stent struts, vessel trauma (dissection) and neointima growth pattern at follow-up. Optical coherence tomography can also assist with assessment of the lesion severity and plaque composition (calcific, lipid-laden, fibrotic or thrombotic) in the SB in order to predict the risk of SB closure and the need for the two-stent bifurcation technique.\(^4\) One study reported incomplete stent strut apposition in 60% of lesions, mostly in the MB proximal to the carina, which might explain the higher prevalence of restenosis in this area.\(^5\)

**Multislice CT**

Multislice CT (MSCT) is useful in studying and categorising the three-dimensional structure of coronary bifurcation anatomy. Optimal evaluation of the bifurcation angle is possible in the appropriate view when the angle is most widely opened in the MSCT. A previous MSCT study showed that the frequency of high-angled bifurcation (>80°) in the LMCA bifurcation was more than twice that in other bifurcations.\(^6\) There is a good correlation in the percentage plaque area between assessments by MSCT and by intravascular US.\(^7\) For planning the stenting strategy in bifurcation, MSCT might assist in pre-interventional assessment of plaque morphology, volume and distribution.

**Fractional flow reserve**

Fractional flow reserve (FFR) can be used to evaluate the functional significance of or the need for revascularisation in bifurcation lesions. An FFR study of the jailed SB showed the inherent limitations of angiographic assessment of SB narrowing after MB stenting.\(^8\) Only 30% of cases that showed >75% stenosis by angiography were <0.75 by FFR (the cut-off value for significant physiological ischaemia). FFR may avoid overtreatment and unnecessary deployment of the two-stent technique.

**WHAT HAVE RANDOMISED TRIALS TAUGHT US?**

The use of drug-eluting stents may be strongly recommended in the treatment of bifurcation lesions, considering the extensive clinical short- and long-term data on the on- and off-label use of drug-eluting stents versus bare metal stents.\(^9\) The overall conclusion from various studies comparing the one-stent and two-stent strategies is that the treatment of coronary bifurcations with drug-eluting stents is excellent with both stenting strategies.\(^10\) Thus, the rates of major adverse cardiac events are low and similar with both treatment strategies but procedure time, fluoroscopy time and the use of contrast are increased with the two-stent strategy. Also, procedure-related myocardial infarction is more frequent with the two-stent strategy, the prognostic significance of which remains a matter of debate. The results of the DKCRUSH-II study\(^11\) differ from the general finding of equally good results with the one-stent and two-stent strategies. However, the increased target vessel revascularisation and restenosis rates in the one-stent group of the DKCRUSH-II study did not translate into significantly increased rates of major adverse cardiac events. Thus, the overall clinical results are remarkably similar in these randomised studies, although there were significant differences in the two-stent techniques used. None of the studies have demonstrated an excess of stent thrombosis in these patients irrespective of the techniques used. To date, there are limited data from randomised clinical trials comparing the two-stent techniques. In the DKCRUSH-I study\(^12\), the additional kissing step reduced major adverse cardiac events at 8 months compared with the group treated with classical crushing. In the Nordic Stent Technique study\(^,13\) there was a similar 6-month clinical outcome and slightly improved 8-month angiographic SB result in the culotte stenting group compared with the crushing group.

**Final kissing balloon inflation**

Some interventionalists perform final kissing balloon inflation (FKBI) systematically in all patients while others do so only if required to correct the MB deformation that results from SB dilation. The role of FKBI was addressed in the Nordic-Baltic Bifurcation III study\(^14\) which demonstrated insignificant differences in binary restenosis rates in favour of FKBI at 8-month angiographic follow-up. However, in the subgroup of patients with a genuine bifurcation lesion there was significantly less restenosis in the SB in patients treated with FKBI. The results of this study suggest that, in non-true bifurcation lesions, FKBI should be performed in cases with compromised SB flow or severe ostial pinching after the MB stent. In true bifurcation lesions, FKBI should be recommended.

**APPROACH TO TREATMENT OF BIFURCATION LESIONS**

**Provisional stenting technique**

This is a one-stent strategy but allows the positioning of a second stent if required (figure 1). In this technique, after wiring both branches the MB should be predilated when
needed, whereas the SB without severe calcification, long significant lesion (>5 mm) does not require predilation. The MB stent is selected according to the distal reference and is deployed, jailing the SB wire. The wires are then exchanged. It is recommended that the wires cross through the distal strut following MB stenting. Proximal optimisation assists in optimising stent deployment proximal to the carina by using a short half-size bigger balloon. It may help to access the most distal strut during wire exchange. If, angiographically, the SB is pinched significantly after MB stenting, FFR or FKBI should be employed. High pressure proximal stent post-dilation may be considered for the correction of possible proximal stent distortion after FKBI. If the results in the SB remain unsatisfactory (>75% residual stenosis, Thrombolysis In Myocardial Infarction flow grade <3 in an SB ≥ 2.5 mm or FFR <0.75), SB stenting can be performed with T stenting, TAP (T stenting and protrusion) or culotte stenting followed by FKBI.

Classical T technique
This technique is suitable when the angle between the two vessels is close to 90°. A stent is deployed in the SB, making sure to cover the ostium with minimal protrusion into the MB. The MB lesion is then stented. The SB is rewired and dilated followed by FKBI. This technique provides good reconstruction of the carina but is associated with the risk of leaving a small gap between the branches, hence restenosis at the ostium of the SB. For this reason, this technique has largely been replaced by the modified T stenting technique. The T technique is most frequently used to cross over from provisional stenting to stenting the SB.

Modified T technique
This is a variation performed by simultaneously positioning stents at the SB and MB with the SB stent minimally protruding into the MB, when the angulations between the branches approach 90°. The SB stent is deployed first and then, after removal of the wire and balloon from the SB, the MB stent is deployed. The procedure is completed with FKBI.

Two-stent techniques
Culotte technique
This technique uses two stents and results in full coverage of the bifurcation at the expense of an excess of metal covering the proximal end. Both branches are wired and predilated. A stent in the more angulated branch (usually the SB) is deployed at nominal pressure. The non-stented branch is rewired through the stent struts and dilated. A second stent is advanced and deployed into the non-stented branch, usually the MB. The SB stent is rewired through the second stent struts followed by FKBI at moderate pressure using two non-compliant balloons of the same size (figure 2).

This technique is suitable for all angles of bifurcation and provides near-perfect coverage of the carina and SB ostium. It is excellent when the MB and SB have a similar diameter and for LMCA bifurcation. The main disadvantage of the technique is that rewiring both branches through stent struts can be technically demanding and time-consuming, and there is a limit to the maximum opening obtainable with a closed-cell design stent, so open-cell stents are preferred for this technique.
Mini-crush technique
The SB stent is deployed first and then ‘crushed’ by deployment of the MB stent. The mini-crush technique has replaced the standard crush technique to minimise the amount of metal overlap proximal to the SB origin. Both branches are wired and adequately predilated. The SB stent is positioned in the SB followed by advancement of the MB stent. The SB stent is pulled back into the MB about 2–3 mm (verified in at least two projections) and is deployed at 12 atm at least. After removal of the wire and balloon from the SB, the MB is stented at high pressure (usually >12 atm), which crushes the proximal SB stent. The SB is rewired through the MB stent at the middle part of the SB orifice. The SB stent is post-dilated at high pressure (≥12 atm) using non-compliant balloon sized to the diameter of this branch. This is followed by FKBI at moderate pressure (8–10 atm) using two non-compliant balloons sized to the respective vessel diameter (figure 4).

This technique can be used in almost all true bifurcation lesions but must be avoided in wide angle bifurcations. The immediate patency of both branches is assured and therefore it should be used in conditions of instability or complex anatomy. Compared with the culotte technique, there is a need to rewire only the SB and not both branches. This technique provides excellent coverage of the ostium of the SB. The main disadvantage is that, in order to perform FKBI, there is a need to re-cross multiple struts with wire and a balloon.

Double kissing crush
A stent is placed into the SB and a balloon placed in the MB. The stent and balloon are positioned as in the standard crush technique. The SB stent is deployed and then the wire and balloon from it are removed. The prepositioned balloon in the MB is inflated to crush the protruding segment of the SB stent against the vessel wall of the MB. The balloon is removed and a stent is deployed in the MB. The wire is then re-crossed into the SB and FKBI is applied to finish the procedure (figure 5). The double kissing crush technique results in less stent distortion, improved stent apposition and facilitates FKBI. It may be superior to classic crushing in optimising acute procedural results and possibly improves clinical outcomes by facilitating FKBI.29

Figure 2 Culotte stenting. (A) Baseline coronary angiogram showing a significant true bifurcation lesion involving the left anterior descending (LAD) artery and a large diagonal branch. (B) Both the LAD and the diagonal branch are wired and the diagonal branch is predilated. (C) The LAD is predilated. (D) The stent in the diagonal branch is deployed, jail the wire in the LAD. (E) Deployment of the stent in the LAD following dilation using a non-compliant balloon at high pressure after wire exchange. (F) Final kissing balloon inflation. (G) Final angiographic result.
DK-CRUSH II study is the only randomised trial to suggest that double stenting may be superior to provisional stenting and associated with a lower rate of restenosis and repeat revascularisation.

**Shunt technique**

In this technique the SB stent is positioned with the proximal end protruding minimally from the ostium while the MB balloon is positioned at the bifurcation. The SB stent is first inflated with low pressure and then the MB balloon is inflated. This leads to movement of the SB stent downstream to the appropriate position with minimal protrusion or overlap in the MB. Finally, the SB stent is inflated to a high pressure followed by MB stenting. The SB is rewired followed by FKBI. This technique protects the MB, SB patency and permits complete coverage of the SB ostium.

**Flower petal technique**

Flower petal stenting involves implanting a stent in the SB with a single strut protruding into the MB; the protruding strut closest to the carina is wired and dilated to create a larger strut or ‘flower petal’. This protruding petal is then flattened and reflected to the distal direction by the MB inflations, including an MB stent, followed by FKBI ensuring complete ostial scaffolding. It is a slightly more complex procedure and is not suitable in some lesions with stents already deployed in the MB as the stent struts in the MB adjacent to the SB ostium might interfere in creating the flower petal effect.

**V stent and simultaneous kissing stent techniques**

The V stent and simultaneous kissing stent techniques are performed by placing and deploying two stents together. When the two stents protrude minimally into the proximal MB creating a new carina the technique is called a V stent technique, whereas when the two stents protrude more deeply creating a rather long (≥5 mm) double barrel in the proximal MB it is called a simultaneous kissing stent technique. It is ideal to keep the length of the neocarina to <5 mm.

Wires are placed in both branches with or without predilation. The two stents are placed into respective branches and deployed by simultaneous inflation at ≥12 atm. This is followed by FKBI at ≥8 atm. The main advantage of this technique is that access to both branches is always preserved with no need for rewiring. V stenting is relatively easy and fast and thus ideal in emergencies. It is indicated in patients with Medina 0, 1, 1 bifurcation with a large proximal MB and an angle of <90° between both the branches and a short LMCA free from disease and critical disease of both the left anterior descending and left circumflex artery ostia.
TECHNICAL CHALLENGES

Accessing difficult SB

Successful wiring of SB that are difficult to access can be achieved with the use of an appropriate guidewire with an appropriately shaped curvature of the tip. A wide angle between the proximal MB and SB together with calcification and marked SB ostial disease makes wiring especially challenging. A useful solution is to shape the tip with a wide smooth bend or with a double bend, and to use a pullback wiring technique if an antegrade technique does not work.

The guidewire may be directed towards the SB after deflection of the tip of the Venture catheter (St Jude Medical, St Paul, Minnesota, USA) and then advanced into the SB over the strong support of the catheter.44 In cases of persistent failure to wire the SB, gentle low pressure predilation of the proximal MB using an undersized balloon may create enough space in the MB and change the angle for successful advancement of a bent wire towards the SB. This may happen because of modification of the plaque geometry at the bifurcation site. In some cases, debunking techniques such as rotational atherectomy or a scoring device can be used as a predilation tool. Another potential problem when using two or more guidewires is wire crisscrossing, which may lead to difficulty in negotiating balloons and/or stents into the vessel. To minimise this, it is advisable first to wire the branch with the more difficult access, where prolonged wire manipulation and rotation is expected, then the second wire should be advanced with minimal rotation into the vessel with easier access while keeping both wires separate on the table.

Rewiring SB with unfavourable anatomy after MB stenting

Difficult access to the SB or MB can occur either at the start of the procedure or after SB or MB stenting, especially with double-stenting techniques. Recrossing the SB through the MB stent struts is usually possible using the Rinato-Prowater (Asahi Intec, Nagoya, Japan), Whisper (Abbott Vascular Devices, California, USA) or the Runthrough NS (Terumo, Japan) guidewires. In difficult situations the author has successfully used the Pilot 50 and 150 (Abbott Vascular Devices), Fielder FC or Miracle 3/4.5 g (Asahi Intec) wires. Care is needed while using hydrophilic guidewires for recrossing into the SB because of the risk of wire-induced dissection or perforation. Until recrossing is complete, the jailed wire in the branch should always be kept in place as a marker. In cases of difficulty in negotiating the balloon through the struts, a 1.5 mm Ryujin (Terumo), Maverick (Boston Scientific, Massachusetts, USA) or Mini-Trek (Abbott Vascular Devices) balloon can be used to separate the struts and allow a larger balloon to pass. If a 1.5 mm balloon fails to cross, consideration must be given to recrossing with a second wire while the first wire remains in place to advance the stent struts in another location. If balloon insertion still proves unsuccessful, the stent should be further dilated. One should try to advance the balloon as close as possible to the stent struts, inflating the balloon to at least 12–14 atm for 20 s then deflating the balloon to attempt traversing it further. Repeating this manoeuvre often results in the balloon being slowly advanced through the stent struts.45 If it fails, a 1.5 mm balloon can be passed over the jailed wire (‘rescue’ jailed balloon technique) behind the stent struts to either redilate a less than totally occluded or dissected branch ostium and then another attempt can be made to advance the stent struts with a guidewire.

SCAFFOLDING VERSUS APPosition

Even if a simple provisional technique ensures adequate strut apposition and warrants preservation of the MB, the approach often fails to protect the SB ostium with the risk of late focal
Two-stent techniques such as culotte, crush, TAP and simultaneous kissing stenting provide continuous scaffolding in both the branches but are limited by the significantly higher rates of unopposed struts. Multiple layers of stent struts at the carina and in the proximal MB are a cause of concern for stent thrombosis. Neocarina after the simultaneous kissing stent and crush techniques can cause severe flow disturbance by juxtaposition of a large number of struts, grossly malapposed, with the high velocity component of the bloodstream giving concern for stent thrombosis.

DEDICATED BIFURCATION STENTS

The simple provisional approach to bifurcation PCI has many limitations such as maintaining the SB access at all times; jailing of the SB ostium by MB stent struts resulting in difficulty in rewiring the SB or advancing the balloon or stent into the SB through the stent struts; distortion of the MB stent by SB dilation; inability to fully cover the SB ostium; and operator experience and expertise. Dedicated bifurcation stents are expected potentially to overcome all these limitations of the simple provisional approach. Currently dedicated bifurcation stents can be divided broadly into the following:

1. Stents for provisional SB stenting facilitating or maintaining access to the SB after MB stenting and not needing recrossing of MB stent struts (eg, Petal, former AST stent (Boston Scientific, Natick, Massachusetts, USA); Multi-link Frontier/Pathfinder (Abbott Vascular Devices, Rewood City, California, USA); Invatec Twin-Rail (Invatec Brescia, Italy); Nile Croco/Pax (Minvasys, Genevilliers, France); Antares (Trireme Medical, California, USA); Stentys (Stentys SAS, Clichy, France)). These stents allow placement of a second stent in the SB if required.

2. Stents that usually need another stent deployed in the bifurcation (eg, Axxess Plus (Devax, Irvine, California, USA); Sideguard (Capella, Massachusetts, USA); Tryton (Tryton Medical, Massachusetts, USA)). The Tryton and Sideguard stents are designed to treat the SB first and need recrossing into the SB after MB stenting for FKBI. The Axxess Plus stent is the exception as it is implanted in the proximal MB at the level of the carina and does not need recrossing into the SB but may need additional implantation of stents to completely treat some types of bifurcation lesions.

Dedicated bifurcation stents are not without technical challenges. These devices tend to be bulkier and some of them rely on passive rotation. Some require two wires to be delivered, and wire wrap and bias remain important reasons for failure. Given the variability in the anatomy of bifurcations, no single device would fit into all lesions and a ‘family’ of dedicated bifurcation stents may be required. Even if the development of dedicated bifurcation stents is strongly encouraged and research is...
undertaken, none of the currently available systems can match the results offered by the provisional T stent approach in the majority of bifurcation lesions.

CONCLUSION
Coronary bifurcation lesions remain one of the most outstanding challenges of treatment with PCI. A remarkable improvement has occurred in the treatment with the advent of drug-eluting stents. The provisional approach of deploying one stent in the MB remains the default approach. However, two stents are required to be implanted as an intention to treat in several bifurcation lesions. Dedicated bifurcation stents are an exciting technology that may further facilitate the success of one of the most challenging frontiers in interventional cardiology.

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