CORONARY ARTERY BIFURCATION LESIONS: A REVIEW OF CONTEMPORARY TECHNIQUES IN PERCUTANEOUS CORONARY INTERVENTION

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ABSTRACT

Percutaneous intervention of coronary bifurcation lesions continues to challenge interventional cardiologists. Nonetheless, the past decade has seen an explosion in the development of clinical novel techniques and well-conducted trials validating the relative efficacy and safety of these techniques. For the most part, consensus has emerged regarding the preferred technique, that being provisional stenting of the side-branch (SB), based on the results of several randomised trials that, with the exception of one, have shown no benefit of a two-stent approach, utilising any one of several techniques, including the crush, culotte, or other modifications. Only the double-kiss (DK) crush appears to confer better clinical outcomes, possibly because of the superiority of the technique in optimising access to the SB. Trial data are still pending regarding the efficacy of two-stent techniques in patients with complex SB lesions and with large-calibre SBs. The use of second-generation drug-eluting stents is associated with better results compared to historical data. Preliminary data from studies utilising dedicated bifurcation stents similarly shows favourable results. Bifurcation stenting using bioresorbable vascular scaffolds is at an early stage, with prospective trial data needed to validate this technology for the use in this subset of patients. Modern imaging tools such as intravascular ultrasound and optical coherence tomography, as well as physiological assessment of SB lesions, are now utilised in decision-making regarding stent strategy, though trial data showing better outcomes with routine use of these tools are lacking.

Keywords: Bifurcation, stenting, crush, culotte, provisional stenting.

INTRODUCTION

Coronary artery bifurcation lesions comprise one of the more complex lesion subsets routinely faced in interventional cardiology, accounting for up to 20% of all coronary disease treated by percutaneous coronary intervention (PCI).¹

The technical difficulties inherent in the treatment of bifurcation lesions, associated with their lower success and higher complication rates compared with non-bifurcation lesions, have always been the object of intense research activity, with publication of contemporary studies in the past few years contributing significantly to the decision-making process.²⁻⁸ In this review article we will examine the main techniques for the treatment of bifurcation lesions and discuss the evidence to support their use.

Anatomical Classification

Bifurcation lesions are challenging to categorise, since they are variable not only in their anatomy (location of plaque, plaque burden, angle between branches, site of bifurcation, and size of branches), but also in the dynamic anatomic changes during treatment caused by dissections and carina shift.⁹ Despite these challenges complicating classification of bifurcation lesions, many definitions have been proposed in an effort to unify this common clinical situation. Louvard and colleagues⁹ proposed that a bifurcation lesion is a coronary artery narrowing occurring adjacent to, and/or involving, the
origin of a significant side-branch (SB); being a significant SB it should not be lost in the global patient context (symptoms, location of ischaemia, branch responsible for symptoms or ischaemia, viability, collateralising vessel, left ventricular function, and so forth). Indeed, the Medina classification, a simple and straightforward classification that provides all the information contained in other systems, has prevailed and is nowadays used worldwide (Figure 1). The classification entails recording any narrowing exceeding 50% in each of the three arterial segments of a bifurcation in the following order: proximal main vessel (MV), distal MV, and the SB; 1 is used to indicate the presence of a significant stenosis and 0 the absence of stenosis (Figure 1). Based on the Medina classification, lesions classified as 1,1,1, 1,0,1, and 0,1,1 are considered ‘true bifurcation’, as they involve a significantly diseased SB.

BIFURCATION STENT TECHNIQUES

The introduction of drug-eluting stents (DES) in the last decade has created an expectation of better long-term outcomes when treating bifurcation lesions. Despite reducing the incidence of restenosis in comparison with balloon angioplasty and/or bare metal stent deployment, the majority of contemporary studies have failed to demonstrate a benefit in routinely choosing a two-stent technique over a provisional SB stent approach. Although the provisional technique has been the prevailing strategy for many years, various two-stent techniques have become popular in the DES era. Below is a brief description of the most commonly used bifurcation techniques.

Provisional SB Stent Technique

This technique, considered by the majority of experts to be the preferred strategy for the majority of bifurcation interventions, consists of deploying a single stent in the MV, with a second stent then being deployed in the SB only in case of an unsatisfactory SB result (thrombolysis In myocardial infarction [TIMI] flow <3 or residual angiographic stenosis >70% after balloon dilatation). A common variation includes pre-dilatation of the SB. In case of dilation of the SB, a final kissing balloon inflation (FKBI) is recommended.

Crush Technique Variations

The crush technique, first reported by Antonio Colombo and colleagues, consists of placing one stent in the MV and one in the SB, with the main-vessel stent being positioned more proximally in order to completely cover the crushed proximal end of the SB stent. After the SB stent is deployed, it is crushed by the stent positioned in the MV, flattening the protruding cells of the SB stent. Hereafter, the wires are recrossed and FKBI is performed. The downsides of this technique lie in the difficulty in recrossing the SB through the multiple layers of metal after deployment of both stents, and residual stenosis of SB ostium.

The mini-crush modification simply consists of protruding less SB stent material in the MV, this being associated with greater success in recrossing the struts. The crush technique requires the use of a 7 or 8 French (Fr) guiding catheter. The development of the balloon crush technique, whereby the SB stent is initially crushed by a balloon rather than a stent in the MV, has allowed the use of a 6 Fr guiding catheter, and thus, the ability to perform the crush utilising radial access. Subsequent variations have included the DK crush and the modified balloon or double crush. In both techniques, access to the SB is improved by first dilating the struts of the crushed SB stent with a balloon prior to deployment of the MV stent. In the DK crush, kissing balloon (KB) inflation is performed after crushing the SB stent with a balloon. This technique facilitates access to the SB in addition to optimising stent apposition at the SB ostium; it has been shown to perform favourably.
against provisional stenting in a randomised trial.\textsuperscript{4} In the double crush technique, the dilated SB stent struts are crushed by a balloon to prevent winging of the MV portion of the stent, and thus, facilitating positioning of the MV stent. Following deployment of the MV stent (the second crush), the SB struts are again recrossed and dilated using a high-pressure inflation. The procedure is then completed with a FKBI. Registry data have shown excellent long-term results using this technique.\textsuperscript{19}

A final crush variation is the reverse crush technique, the main indication for which is as bailout in a provisional SB stenting strategy, with unacceptable SB result after main-vessel stenting, when the SB angle is too narrow for an effective T-stent approach. In this case, a second stent is advanced into the SB, after balloon dilatation to open the MV struts. The SB stent should be deployed no more than 2-3 mm into the MV, with a balloon positioned at the bifurcation level in the MV. For the most part, this technique has been supplanted by the T and protrusion (TAP) technique in which, rather than protruding the provisional SB stent so far into the MV that it needs to be crushed, the SB stent is deployed with a slight protrusion in the carinal aspect of the bifurcation, resulting in slight protrusion of the SB stent into the MV.\textsuperscript{20} If the SB is large, and the bifurcation angle acute, this procedure could potentially result in excessive protrusion of the SB stent into the MV lumen. In such unusual cases, a reverse crush may remain a better option.

**The Culotte Technique**

This consists of deploying two stents in vessels of somewhat similar luminal diameters.\textsuperscript{21} It results in complete coverage of the bifurcation at the expense of an excess of metal covering of the proximal segment. After balloon predilatation of both branches, the first stent should be delivered in the more angulated vessel, facilitating access into the other vessel. After opening the stent struts, a second stent is advanced through them and deployed in overlap with the first stent at the proximal segment. The procedure is completed with a FKBI. The culotte technique provides excellent coverage of the SB ostium. Similar to the crush technique, it leads to a high concentration of metal with a double-stent layer at the carina and at the proximal part of the bifurcation. The main disadvantage of the technique is that rewiring both branches through the stent struts can be difficult and time consuming.

**T-Stenting and Modified T-Stenting Techniques**

The original T-stenting technique consists of positioning a stent first at the ostium of the SB, without stent protrusion into the MV. After deployment of the stent and removal of balloon and wire from the SB, a second stent is advanced in the MV. A wire is then re-advanced into the SB, and a FKBI is performed.\textsuperscript{22} Modified T-stenting is done by simultaneous positioning of stents at the SB and MV. The SB stent is deployed first, then after wire and balloon removal from the SB, the MV stent is delivered.\textsuperscript{12} This technique is best suited for a right angle bifurcation, although the TAP modification allows for the use of this technique when the bifurcation angle is more acute.

**A Systematic Approach**

The European Bifurcation Club has devised a systematic classification and approach to the treatment of coronary bifurcation lesions.\textsuperscript{9} This classification of techniques, MADS (main, across, distal, side) is based on the manner in which the first stent is implanted, which often corresponds to a technical strategy related to the importance of the vessel treated first\textsuperscript{9} (Figure 2).

All considerations regarding the best treatment strategy for bifurcation lesions are based on the premise that the SB is large enough (≥2 mm) with a sufficient territory of distribution to justify preoccupation with its patency. If the SB is small (<1.5 mm) and supplies a small area of myocardium, it can be ignored, and a stent can be placed in the MV across the SB ostium. In the medium size SB (2-2.75 mm), a strategy of wiring and reassessment after MV pre-dilatation is appealing. In general, predilation of the SB prior to stent deployment is not recommended, as predilation can cause a dissection of the ostium and render subsequent recrossing of the ostium through MV stent struts problematic.\textsuperscript{23} If an unsatisfactory result of the SB is observed after stenting the MV, balloon dilatation of the SB is the first option. A stent placement in the SB is generally required only when flow in the SB is reduced. In the NORDIC study, patients randomised to provisional SB stenting had further intervention in the SB only if the TIMI flow was <3.\textsuperscript{6}

Treatment of coronary bifurcations frequently requires simultaneous insertion of two balloons or two stents; therefore, an appropriately sized guiding catheter should be selected. With the currently available low-profile balloons, it is possible to insert
two balloons inside a large-lumen 6 Fr guiding catheter with an internal lumen diameter of more than 0.070 in (1.75 mm). If two stents are needed, they can only be inserted one after the other, not simultaneously, in a large-lumen 6 Fr guiding catheter. Because most commonly used two-stent techniques do not require simultaneous deployment of the MV and SB stents, 6 Fr access is usually the first option, especially because it allows a radial approach in virtually all patients.

The Evidence

Several randomised trials utilising DES have compared multiple strategies for the treatment of bifurcation lesions. The larger, contemporary trials are summarised in Table 1. Most of these studies did not demonstrate different clinical outcomes when comparing provisional SB stenting with complex strategies. However, the majority reported higher use of contrast, longer procedural times, and consequently radiation exposure with two-stent approaches. In addition, having similar clinical outcomes, procedures requiring use of more materials (guidewires, balloons, stents) imply higher costs.

Target lesion revascularisation (TLR) rates are comparable between simple versus complex strategies, with a trend towards lower angiographic restenosis rates in the two-stent approach techniques when considering only true bifurcation lesions. The general concept that in true bifurcations a provisional SB stent approach has worse outcomes than an upfront two-stent strategy was not seen in a post-hoc analysis of true bifurcations in the NORDIC Study, which demonstrated better clinical outcomes with the provisional approach (19.9 versus 30.1, p=0.044). The primary outcome of the study also suggested a trend towards a lower incidence of major adverse cardiac events (MACE) in the provisional arm.

On the other hand, the DKCRUSH-II trial, enrolling mostly patients with true bifurcations, demonstrated significantly less TLR and a trend towards less MACE with the two-stent technique. However, this strategy had a numerically higher incidence of stent thrombosis. In addition, Colombo and colleagues failed to demonstrate a clinical benefit of the crush technique over provisional SB stenting in a study including only true bifurcation lesions. Provisional SB stenting and two-stent strategies using DES were tested in another two large randomised trials. Ferenc and colleagues showed, in an elegant study, that routine T-stenting technique did not improve angiographic outcome when compared to stenting of the MV followed by KB angioplasty and

Figure 2: MADS classification of different bifurcation treatment techniques. Adapted from Stankovic et al.23

<table>
<thead>
<tr>
<th>M</th>
<th>Main prox. first</th>
<th>A</th>
<th>Main Across side first</th>
<th>D</th>
<th>Distal first</th>
<th>S</th>
<th>Side branch first</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st stent</td>
<td>PM stenting</td>
<td>MB stenting across SB</td>
<td>DM stenting</td>
<td>SB ostial stenting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After balloon</td>
<td>Skirt</td>
<td>MB stenting + SB balloon</td>
<td>Provisional SKS</td>
<td>SB minicrush</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 stents</td>
<td>Skirt + DM</td>
<td>MB stenting + kissing</td>
<td>MB stenting + kissing</td>
<td>SB crush</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 stents</td>
<td>Extended V</td>
<td>V stenting</td>
<td>SKS</td>
<td>Minicrush</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Culotte Tap</td>
<td>Syst. T Stenting</td>
<td>Crush</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For the full table and classification, please refer to the original source.
provisional SB stenting. Clinical outcomes, a secondary endpoint in this trial, revealed no difference between the two strategies.

Another large randomised study that compared simple versus complex strategies, the British Bifurcation Coronary Study trial showed higher rates of in-hospital and 9-month MACE with a systematic two-stent technique. Nevertheless, this difference was largely driven by periprocedural myocardial infarction (MI), an endpoint of questionable significance not reported in other recent bifurcation trials.

Two contemporary randomised trials compared different complex strategies for the treatment of bifurcation lesions. The NORDIC Stent Technique Study compared crush versus culotte techniques and, at 36-month follow-up, found similar clinical outcomes. It is important to accentuate that in this study only 10% of lesions were located in the left main and around 80% of all lesions were true bifurcations. Furthermore, Chen and colleagues published in 2013 the DK Crush-III Study, a comparison of DK crush versus culotte stenting for unprotected distal left main bifurcations lesions. Besides only involving left main lesions, this trial enrolled basic medina 1,1,1 bifurcations. The major finding at 1-year follow-up was that culotte stenting was associated with significantly increased MACE (6.2 versus 16.3, p<0.05), mainly because of higher TLR rates (4.3 versus 11, p<0.05).

In two-stent techniques, such as culotte and crush, FKBI is considered mandatory. The impact of FKBI in provisional SB stenting was assessed in the NORDIC-III Study, which demonstrated similar 6-month clinical outcomes with and without FKBI. However, in a subgroup of patients that underwent quantitative coronary assessment at 8 months, FKBI reduced angiographic SB restenosis, 7.9% versus 15.4% (p=0.039), especially in patients with true bifurcation lesions, 7.6% versus 20.0% (p=0.024). Nevertheless, a small sample of these patients also had fractional flow reserve (FFR) performed immediately after the procedure and at follow-up. FKBI improved acute functional outcome in the SB compared to leaving the SB jailed, but no significant difference was detected at follow-up.

### New Stents and Platforms

The majority of randomised trials comparing simple versus two-stent strategies to date were conducted utilising first-generation DES. Data regarding the efficacy of second-generation DES are derived from registries and sub-group studies.

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**Table 1: Randomised trials using DES that compared different bifurcation lesion treatment strategies.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Technique</th>
<th>N</th>
<th>Follow-up (months)</th>
<th>MACE (%)</th>
<th>TVR (%)</th>
<th>Definite ST (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferenc et al.</td>
<td>2008</td>
<td>T stent vs. provisional</td>
<td>202</td>
<td>9</td>
<td>11.9 vs. 12.9</td>
<td>8.9 vs. 10.9</td>
<td>2 vs. 1</td>
</tr>
<tr>
<td>CACTUS³</td>
<td>2009</td>
<td>crush vs. provisional</td>
<td>350</td>
<td>6</td>
<td>15.8 vs. 15</td>
<td>7.9 vs. 7.5</td>
<td>1.7 vs. 1.1</td>
</tr>
<tr>
<td>BBC ONE²</td>
<td>2010</td>
<td>crush / culotte vs. provisional</td>
<td>500</td>
<td>9</td>
<td>15.2 vs. 8*</td>
<td>5.6 vs. 7.2</td>
<td>2.0 vs. 0.4</td>
</tr>
<tr>
<td>DKCRUSH-II⁴</td>
<td>2011</td>
<td>DK crush vs. provisional</td>
<td>370</td>
<td>12</td>
<td>10.3 vs. 17.3</td>
<td>6.5 vs. 14.6</td>
<td>2.2 vs. 0.5</td>
</tr>
<tr>
<td>NORDIC-III³²</td>
<td>2011</td>
<td>FKBI vs. no FKBI</td>
<td>477</td>
<td>6</td>
<td>2.5 vs. 3</td>
<td>1.3 vs. 1.7</td>
<td>0.4 vs. 0.4</td>
</tr>
<tr>
<td>NORDIC⁶</td>
<td>2013</td>
<td>simple vs. complex</td>
<td>413</td>
<td>60</td>
<td>15.8 vs. 21.8</td>
<td>13.4 vs. 18.3</td>
<td>3 vs. 1.5</td>
</tr>
<tr>
<td>NORDIC-II⁴⁰</td>
<td>2013</td>
<td>crush vs. culotte</td>
<td>424</td>
<td>36</td>
<td>22 vs. 19.1</td>
<td>11.5 vs. 6.5</td>
<td>1.4 vs. 4.7</td>
</tr>
<tr>
<td>DK-III²⁵</td>
<td>2013</td>
<td>DK crush vs. culotte</td>
<td>419</td>
<td>12</td>
<td>6.2 vs. 16.3</td>
<td>4.3 vs. 11</td>
<td>0 vs. 1</td>
</tr>
</tbody>
</table>

TVR: target vessel revascularisation; ST: stent thrombosis; MACE: major adverse cardiac events (cardiac death, myocardial infarction, and TVR); DK: double-kiss; FKBI: final kissing balloon inflation; DES: drug-eluting stents.

*All-cause death, myocardial infarction, and TVR.
analyses of randomised trials. In a substudy of the RESOLUTE All Comers Trial, comparing the resolute zotarolimus-eluting stent (ZES, Santa Rosa, CA, USA) and the Xience V everolimus-eluting stent (Santa Clara, CA, USA), randomised patients undergoing bifurcation PCI had similar outcomes at 2 years compared to those undergoing non-bifurcation PCI only, with the exception of the occurrence of any MI, that tended to occur more frequently in the bifurcation group (7.3% versus 4.7%, p=0.068). Similar results were reported by the SPIRIT V prospective registry. In a retrospective comparison of patients treated with first-generation compared with second-generation DES with 2-year follow-up, Costopoulos et al. reported a significantly lower MACE rate in the second-generation group (14.4% versus 23.1%, p=0.02). The comparison, of course compared different eras that differed not only in DES type and platform, but also in technical advances and concomitant medical therapy, that are likely also responsible for these observations.

Several recent reports have suggested the feasibility of treating bifurcation lesions with bioresorbable vascular scaffolds (BVS). To date these consist of isolated cases of complex stenting procedures (Figure 3) performed with the Absorb BVS (Santa Clara, CA, USA), and small case series. While treating bifurcation lesions with material that resorbs over time appears attractive, caution must be exercised as the poly-lactic acid material can fracture when dilated 0.5 mm or more beyond the rated diameter of the device. This area is evolving rapidly.

Dedicated Bifurcation Stents

Alongside the evolution of bifurcation techniques there has been the development of several dedicated bifurcation stents. The most advanced of these in terms of evidence base is the Tryton Side Branch Stent, a bare-metal device utilising two guidewires and a bifurcating balloon that scaffolds the SB in the proximal aspect and allows for potential deployment of a second regular stent through the opening, resulting in complete coverage of the SB ostium, the use of which has in a pooled analysis of eight registries been shown to result in outcomes at 1 year similar to those reported in other contemporary trials and registries. 3-year results were recently reported in the DIVERGE study, a prospective registry of 302 patients, 77% of whom had true bifurcation lesions, treated with the AXXESS, a nitinol self-expanding biolimus A9-eluting stent, showing a MACE rate of 16.1% and an ischaemia-driven TLR rate of 10.1%, again, comparing favourably with randomised trial results at shorter duration follow-up.

ANATOMICAL AND FUNCTIONAL ASSESSMENT OF BIFURCATION LESIONS

Intra-Vascular Ultrasound Imaging (IVUS)

IVUS has been incorporated into clinical practice for the treatment of bifurcation lesions for many years, especially in left main lesions. It allows detailed assessment of plaque burden in the MV as well as in SB, helping decide the necessity of an upfront two-stent strategy.

Figure 3: A) Left anterior descending-diagonal bifurcation just distal to the carina after deployment of a 3.0x28 mm Absorb BVS; B) at the carina; C) proximal to the carina after proximal optimisation and gentle kissing balloon inflation.
Stent apposition can also be assessed by this imaging modality. Two large Korean observational studies demonstrated a significant advantage of IVUS-guided over angiographic guided PCI in bifurcations lesions. However, no randomised trials have tested this strategy in this scenario.

**Optimal Coherence Tomography (OCT)**

OCT’s potential role for bifurcation lesions is very promising. Its ability of defining anatomical details of the bifurcation allows precise measurement of the angle, plaque burden, size of the vessel, and plaque characteristics. In addition, stent apposition and mechanical complications can easily be identified by OCT. It can also be used to create 3D reconstructions of implanted stent structures with excellent quality and at resolutions much higher than what is currently possible using IVUS. Furthermore, the expected ability of OCT to assess the risk of carina shift or SB closure may influence the decision to protect a SB with a wire and whether or not to predilate it. To date, there is no systematic evaluation for its use in guiding the treatment of bifurcation lesions.

**FFR**

FFR has a defined role in the percutaneous treatment of bifurcation lesions. It has been used to assess the severity of residual stenosis in the SB after deployment of the MV stent, when using the provisional SB stent technique. Koo and colleagues demonstrated in an elegant study that only 30% of lesions which appear >75% on quantitative coronary angiography are physiologically significant when assessed by FFR.

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**SUMMARY**

Contemporary evidence from randomised clinical trials that compared different treatment strategies for bifurcation lesions using DES demonstrated similar clinical outcomes: less use of contrast, shorter procedural times, and consequently less radiation exposure with provisional SB stenting compared to complex strategies, even in true bifurcations. Also, most ostially narrow-jailed SBs are not functionally significant as assessed by FFR, and the operator should resist the temptation to improve the final angiographic appearance.

Among two-stent strategies, the DK crush technique has shown better results compared to the original crush and culotte techniques, and comparable results to provisional SB stent approach. The DK crush technique provides full coverage of the SB ostium as well as expansion of the SB stent. In addition, it allows the use of 6 Fr guides, permitting radial approach in virtually all patients. Newer DES platforms appear to confer better long-term safety compared to older generation stents. The BVS has been shown to be a feasible tool for bifurcation treatment; however, further studies are needed to ascertain its long-term safety and efficacy in this patient subset.


