CURRENT PERCUTANEOUS MANAGEMENT OF CORONARY BIFURCATION DISEASE

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ABSTRACT

Coronary bifurcation disease (CBD) is frequently found in patients undergoing coronary interventions. Optimal management of CBD is technically demanding and therefore requires experience with different techniques, which should be tailored case-by-case. Provisional T-stenting is the recommended initial approach in most cases, however several two-stent techniques are described either as elective or as bailout strategy. This review describes the most common percutaneous techniques used to manage CBD, with advantages, drawbacks, and up-to-date medical evidence.

Keywords: Coronary disease, coronary bifurcation disease (CBD), stents, kissing balloon (KB).

INTRODUCTION

One of the hottest and most controversial topics in the recent history of interventional cardiology is the optimal management of coronary bifurcation disease (CBD). Percutaneous coronary interventions (PCI) of CBD account for 15–20% of all procedures.1 CBD interventions are technically demanding and often associated with complications including periprocedural (Type 4a) myocardial infarction (MI), stent thrombosis (ST) (Type 4b MI), and in-stent restenosis.1,2

Definition, Anatomy, and Classifications

CBD is defined as an obstructive atherosclerotic lesion occurring at a significant division of a major epicardial coronary artery.3 The atherosclerotic burden in CBD is closely related to blood shear stress,4-6 and it is more prevalent in lower shear stress zones such as the lateral wall. Nakazawa et al.7 investigated the axial distribution of coronary plaques using a longitudinal autofluorescent sectioning method.7 In their series, the lateral wall showed significantly larger coronary plaque with higher prevalence of necrotic core as compared with the flow-divider zone, also known as the carina (high-shear stress area). This anatomic background should always be taken into consideration when approaching CBD and planning PCI.

During the last two decades, several CBD classifications were proposed, the most intuitive and commonly used is the Medina classification. The Medina is an angio-based classification that defines CBD with three ciphers.8 The first one indicates the proximal vessel or main vessel (MV), the second one the distal MV, and the third one the side branch (SB). The binary score attributed to the lesion is ‘1’ if there is a ≥50% lumen diameter stenosis, otherwise it is ‘0’. The advantage of this simple classification is counterbalanced by the lack of some valuable information that should not be ignored for PCI planning such as: SB disease length, MV and SB reference diameters, angle between the MV and SB, distribution of calcifications, presence of thrombus or ulcerations, and SB thrombolysis in myocardial infarction (TIMI) flow grade. For all the above reasons, while Medina classification is still the most used by interventional cardiologists and in clinical trials, a limited standardisation of CBD lesions is often encountered in this setting and should be considered when interpreting clinical trial results.

THE PROVISIONAL STENTING TECHNIQUE

The European Bifurcation Club (EBC) recommends the provisional stenting technique as the preferred initial approach for most CBD PCI.9
Table 1: Studies comparing provisional T-stenting with elective two-stent techniques.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of publication</th>
<th>Number of patients (simple/complex)</th>
<th>Type of DES</th>
<th>Complex technique used</th>
<th>Primary endpoint</th>
<th>Main result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan et al.10</td>
<td>2004</td>
<td>47/44</td>
<td>RES</td>
<td>T-stenting</td>
<td>MACE and occurrence of angiographic restenosis at 6 months</td>
<td>No differences in clinical outcome.</td>
</tr>
<tr>
<td>Colombo et al.11</td>
<td>2004</td>
<td>22/63</td>
<td>SES</td>
<td>T-stenting, V-stenting, Y-stenting</td>
<td>Binary in-segment restenosis of both the MV and SB (stented or not stented) evaluated at the follow-up angiogram</td>
<td>The total restenosis rate at 6 months was 25.7%, and it was not significantly different between the double-stenting (28.0%) and the provisional SB-stenting (18.7%) groups. 14 of the restenosis cases occurred at the ostium of the SB and were focal.</td>
</tr>
<tr>
<td>Nordic12</td>
<td>2006</td>
<td>207/206</td>
<td>SES</td>
<td>Crush, culotte, or other</td>
<td>MACE (cardiac death, MI, TVR, or ST) at 6 months</td>
<td>There were no significant differences in rates of MACE between the groups (MV+SB 3.4%, MV 2.9%; p=NS).</td>
</tr>
<tr>
<td>BBK13</td>
<td>2008</td>
<td>101/101</td>
<td>SES</td>
<td>T-stenting</td>
<td>Diameter stenosis of the SB at 9-month angiographic follow-up</td>
<td>The SB binary restenosis rate was 9.4 with provisional T-stenting and 12.5% after provisional T-stenting (p=0.32). In the main branch, binary restenosis rate was 7.3% after provisional and 3.1% after routine T-stenting (p =0.17). Routine T-stenting with SES did not improve the angiographic outcome of PCI of CBD as compared with stenting of the MV followed by kissing-balloon angioplasty and SB stenting.</td>
</tr>
<tr>
<td>CACTUS14</td>
<td>2009</td>
<td>173/177</td>
<td>SES</td>
<td>Crushing</td>
<td>MACE (cardiac death, MI, or TVR) at 6 months</td>
<td>MACE was similar in the two groups (15.8% in the crushing group versus 15% in the provisional stenting group, p=NS). Angiographic restenosis rate was not different between the crush group (4.6% and 13.2% in the MV and SB, respectively) and the provisional stenting group (6.7% and 14.7% in the MV and SB, respectively; p=NS).</td>
</tr>
<tr>
<td>BBC One15</td>
<td>2010</td>
<td>250/250</td>
<td>PES</td>
<td>Culotte or crushing</td>
<td>MACE (death, MI, and TVF) at 9 months</td>
<td>Two-stent techniques result in higher rate of in-hospital and 9-month MACE (8% versus 2%, p=0.002). This difference is largely driven by Type 4a MI. (9.9% versus 3.5% in the simple strategy group [p&lt;0.001]).</td>
</tr>
<tr>
<td>Lin et al.16</td>
<td>2010</td>
<td>54/54</td>
<td>SES, PES</td>
<td>DK crush, culotte, or T-stenting</td>
<td>MACE (cardiac death, MI, TVR, and ST) at 8 months</td>
<td>The overall 8-month incidence of TVR was 31.5% after provisional and 7.4% after routine stenting (p&lt;0.01), and cumulative MACE was 38.9 and 11.1% (p&lt;0.01), respectively. Routine stenting significantly improved the MACE outcome in true coronary bifurcation compared with PS.</td>
</tr>
</tbody>
</table>
This recommendation is based on several randomised trials, registries, and meta-analyses, which are outlined in Table 1.

In the provisional technique the MV is stented first. MV stent measures should be sized to the reference distal MV diameter, considering a minimum of 8–10 mm protrusion in the proximal MV to permit post-dilatation to the proximal reference diameter (proximal optimisation technique [POT], explained below). A ‘protection’ wire in the SB is usually placed before MV-stenting, especially if the SB supplies a large territory or if the operator considers rewiring after MV-stenting to be potentially difficult. The ‘protection’ wire can also be used as a radiopaque marker that helps to reduce contrast usage and may straighten the proximal SB, which in turn may help rewiring. MV-stenting ‘jails’ the protection wire between the stent struts and the vessel wall: this implies that rewiring through MV stent (preferably to the distal) struts is necessary before proceeding to any further SB interventions like final kissing balloon (KB) or bailout stenting. SB pre-dilatation should not be routinely performed unless severe calcifications, tortuosity, or extensive ostial SB disease may decrease the likelihood of rewiring or recrossing with a balloon after MV-stenting. In case of SB pre-dilatation, an undersized balloon should be used to avoid dissection. Final KB is not routinely required in provisional stenting technique unless tight (>75% diameter) stenosis or TIMI flow <3 is persistently observed after MV-stenting. bailout SB-stenting may be required in case of persistent flow limitation, dissections, or persistent tight stenosis after final KB. Before proceeding with bailout SB-stenting, a pre-dilatation is usually required to open the MV struts laterally, and final KB is mandatory at the end of the procedure.

### Table 1 continued.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of publication</th>
<th>Number of patients (simple/complex)</th>
<th>Type of DES</th>
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<th>Primary endpoint</th>
<th>Main result</th>
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<tbody>
<tr>
<td>DKCRUSH-II</td>
<td>2011</td>
<td>185/185</td>
<td>SES</td>
<td>DK crush versus culotte</td>
<td>MACE (cardiac death, MI, or TVR)</td>
<td>TVR was 6.5% in the DK group, occurring significantly less often than in the PS group (14.6%, p=0.017). There was NS difference in MACE and definite ST between the DK (10.3% and 2.2%) and provisional stenting groups (17.3%, and 0.5%, p=0.070 and p=0.372, respectively).</td>
</tr>
<tr>
<td>Nordic-Baltic IV</td>
<td>2013</td>
<td>221/229</td>
<td>SES, EES</td>
<td>Crushing, culotte, other</td>
<td>All-cause death, cardiac death, non-procedure-related MI, TVR, TLR, ST, and the combined endpoint of cardiac death, non-procedure-related MI, TVR, and ST</td>
<td>At a 5-year follow-up the rate of the events was 15.8% in the optional SB stenting group as compared to 21.8% in the MV and SB stenting group (p=0.15). All-cause death was seen in 5.9% versus 10.4% (p=0.16) and non-procedure-related MI in 4% versus 7.9% (p=0.09) in the optional SB stenting group versus the MV and SB stenting group, respectively. The rate of TVR was 13.4% versus 18.3% (p=0.14) and the rate of definite ST was 3% versus 1.5% (p=0.31) in the optional SB stenting group versus the MV and SB stenting group, respectively.</td>
</tr>
</tbody>
</table>

protrusion (TAP) (explained forthwith) is usually the preferred technique to optimise lesion coverage and metal distortion in bailout SB-stenting; however, other techniques such as internal culotte or internal crushing may be considered and tailored case-by-case.

In randomised trials, patients treated with the provisional stenting technique as compared with more complex, elective, two-stenting techniques, had reduced procedure and fluoroscopy times, lower rates of procedure-related biomarker elevation, and lower rate of MI at follow-up. However, the elective two-stenting approach may still be valuable when managing true CBD (Medina 1,1,1) with a sizeable SB. In DKCRUSH-II, Tryton IDE study, and Nordic-Baltic IV trial (TCT 2013), a trend towards improved midterm outcome using a two-stent technique was observed in the subgroup of patients with a large SB (reference diameter ≥2.75 mm) and with large atherosclerotic burden i.e. stenosis diameter ≥50%, extending more than 5 mm from the SB ostium.

**TWO-STENT TECHNIQUES**

There are several techniques to manage a bifurcation lesion with two stents, either as an elective procedure (intention-to-treat) or as bailout of a provisional stenting strategy.

**Culotte**

In the culotte technique, the first stent is deployed in the MV across the bifurcation. A proximal inflation with oversized balloon POT should be used before a second stent is deployed from the proximal MV in the SB. Final KB inflation is mandatory as in all two-stent techniques. The use of this technique may be quite demanding because it implies rewiring of the stent struts twice.

**Figure 1: Elective double kissing crushing technique.**

A) Main vessel (MV) and side branch (SB) are wired and pre-dilated, a stent is advanced in the SB with a small (few millimetres) protrusion in the MV and a balloon is advanced in the MV. The proximal markers are juxtaposed. B) SB stent is inflated. C) MV balloon is inflated and SB struts are crushed to the proximal MV wall. D) First kissing balloon (KB) inflation is performed. E) A stent is advanced and inflated in the MV. F) Final KB is performed.
The culotte technique is best performed in large Medina 1,1,1 CBD with similar MV and SB reference diameter and bifurcation angles between 45° and 60°. The unfavourable metal-to-vessel ratio resulting from the two struts layers in the proximal MV may lead to under-expansion and malapposition of the stent in the MV and at the bifurcation site, despite the highly recommended use of KB inflation, and may be one of the main reasons for acute and follow-up failure associated with this technique.

Crushing, Mini-Crush, and Double Kissing Crushing Techniques

In the crushing technique, as originally described, a stent is advanced in the SB with one-third of its length protruding into the MV and a second stent is positioned in the MV at the same time. Once the SB stent is deployed, the SB wire is removed and the MV stent is inflated. By inflating the MV stent, the SB struts are ‘crushed’ to the proximal MV wall. The SB is then rewired and a final KB, preferably with a non-compliant balloon, is performed. This technique results in three stent struts layers from the proximal MV to the SB ostium, which may lead to difficult recrossing with wires and balloons. Sometimes multiple inflations with step-up caliper balloon are necessary to advance non-compliant balloon in the SB for final KB. The impossibility to perform final KB is an independent predictor of poor outcome.

Figure 2: T and protrusion technique.

A) Main vessel (MV) and side branch (SB) are wired and pre-dilated. B) A first kissing balloon (KB) to open lateral MV struts without deforming the stent is performed. C) A balloon is advanced in the MV and a stent is advanced in the SB with minimal protrusion in the proximal MV, the SB stent is then inflated. D) SB stent balloon is retrieved a few millimetres and a final KB inflation is performed.
6 Fr guiding catheters, usually used in radial approach. Another modification of the crushing technique is the so called double kissing (DK) crush. With this approach a first KB inflation is performed before deploying the second stent in the MV. This aids proximal MV expansion, apposition of the struts to the vessel wall, and maximises the likelihood of SB recrossing to perform a final KB inflation. An example of DK crush is shown in Figure 1.

The crushing technique was studied in the CACTUS trial as (Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus Eluting Stents). This study was designed to test whether the crushing technique could improve the outcome of patients undergoing CBD interventions as compared with provisional T-stenting. After 6-month follow-up, the primary angiographic outcome of in-stent restenosis was comparable between the two study arms as well as the primary clinical outcome of major adverse cardiac events (MACE) that occurred in 15.8% of the crushing group versus 15% of the provisional group (Table 1). Of note, a bailout SB stent was performed in one-third of patients randomised to provisional T-stenting. The DKCRUSH-III Study compared the DK crush versus culotte stenting for distal left main disease bifurcation (LMDB) lesions. After 3 years follow-up, MACE incidence was 8.2% in patients randomised to DK crush and 23.7% in patients randomised to the culotte technique (p<0.001). The composite endpoint was mainly driven by a higher incidence of MI (3.4% versus 8.2%, p=0.037), definite ST (0% versus 3.4%, p=0.007), and target-vessel revascularisation (TVR) (5.8% versus 18.8%, p<0.001) in the culotte arm. Further studies comparing DK crush with provisional T-stenting in patients with complex LMDB lesions are ongoing.

**SIMULTANEOUS KISSING STENTS**

The simultaneous kissing stent (SKS) technique was first proposed by Sharma et al. as a modified V-stenting technique. SKS involves two stents, one in the MV and one in the SB, with a short overlapping segment in the proximal MV, which creates a neo-carina. The advantage of this technique is that it allows complete coverage of the SB ostium in few steps, avoiding extensive deformation of the stent struts, but can be used only in large-size vessel bifurcations with a large proximal MV that can accommodate two parallel stents and using 7 Fr or 8 Fr guiding catheters. In selected left main CBD with favourable anatomy, the SKS technique may provide management of both the MV and the SB, in a few simple steps, without the need for rewiring, which is particularly useful in unstable patients.

Siotia et al. published the midterm outcome of 150 consecutive patients with unprotected bifurcation left main treated with SKS. The mortality rate at 1 year was 11.3%, and at 2 years 12.7%. The (ischaemia-driven) target-lesion revascularisation rate was 4.3% at 1 year and 6.2% at 2 years. This demonstrates that the SKS technique for treating unprotected LMBD is simple, feasible, effective, and durable. It is also interesting to note that the SKS has been proposed in managing bifurcation coronary aneurysms. Crimi et al. reported successful coronary bifurcation aneurysm closure with the implantation of two polyethylene terephthalate covered MGuard stents in accordance with the SKS technique.

**DEDICATED BIFURCATION STENTS**

Several dedicated bifurcation devices have been developed to simplify the percutaneous procedure of CBD with two-stents, optimise metal-to-vessel ratio, and improve clinical outcomes.

The Tryton SB Stent is a dedicated SB bare-metal stent which simplifies the culotte technique. It is composed of three different zones: a distal zone (5.5–6.5 mm) deployed within the SB, a transition zone (4.5 mm), which fits the SB ostium and the carina, and a MV zone (8 mm). The implantation
technique requires pre-dilatation of the SB. The Tryton stent is then inflated into the SB and the wire is removed. A second stent is advanced and inflated in the MV, the SB rewired, and final KB closes the procedure.

The TRYTON Trial was designed to evaluate the clinical impact of a dedicated SB stent\textsuperscript{25} in patients with Medina classification 1,1,1; 1,0,1; or 0,1,1 CBD located in a de novo native coronary artery with a SB of at least 2.5 mm. Lesion evaluation was based on visual estimates of the baseline angiography. The primary endpoint at 9-month follow-up was the rate of target-vessel failure, defined as the composite of cardiac death, target-vessel MI (Q-wave or non-Q-wave), and clinically-driven TVR of the MV or SB. This endpoint was not met in the TRYTON group, mainly for an increased rate of peri-procedural (Type 4a) MIs.

**PROcedure Optimisation**

**Proximal Optimisation**

The POT was described by Hildick-Smith et al.\textsuperscript{33} as a method of expanding the stent from the proximal stent edge to the carina, using a short, oversized, non-compliant balloon. After implantation of the MV stent, the proximal MV is post-dilated using a non-compliant balloon whose size matches the proximal MV diameter. The POT has shown advantages when there is a consistent difference in reference diameter between proximal and distal MV. It might also be used when the operator encounters difficulties in recrossing into the SB with either a wire or a balloon.

**Final Kissing Balloon**

Final KB consists in the simultaneous dilatation of two balloons in the MV and SB. This aimed to restore stent strut geometry and to minimise areas of malapposition or underexpansion. The selection of the balloon diameter must be made according to the distal reference diameter of each branch (ratio 1:1:1). Balloons must be shorter than the stent and preferably be non-compliant balloons. Sometimes a first final KB with undersized compliant balloon is required to ensure SB recrossing with non-compliant balloons. While final KB is mandatory in any of the aforementioned two-stent techniques, the routine use of final KB in provisional T-stenting is less established. The Nordic-Baltic Bifurcation Study III compared final KB with controls in patients with coronary bifurcations treated with MV-stenting.\textsuperscript{34} The two strategies were associated with similar clinical outcomes. However, final KB reduced the rate of angiographic SB restenosis, while simple non-final KB technique resulted in shorter procedure and fluoroscopy times and in reduced use of contrast media.

**Conclusions**

CBD is frequently found in patients undergoing coronary interventions. The optimal management of CBD is technically demanding and requires considerable experience with different techniques which should be tailored case-by-case. Provisional T-stenting is the first preferred approach for most bifurcation lesions. However, when a large SB is involved, an elective two-stent technique may be considered. When using a two-stent technique, a final KB is mandatory, but may be challenging. For this reason, TAP and DK crush, which were designed to increase the likelihood of performing a final KB and inflation, should be considered.

**References**


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