Coronary bifurcations – anatomy, physiology and treatment with selected aspects of left main stem bifurcation

Bifurkacje wieńcowe – anatomia, fizjologia i leczenie z wybranymi aspektami bifurkacji pnia lewej tętnicy wieńcowej

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ABSTRACT

Coronary bifurcation remains a unique region of the coronary tree. The specific anatomy and blood flow determine the complex mechanisms of atherosclerotic plaque location. The treatment strategy should be chosen with caution as the failure of percutaneous coronary interventions (PCI) may expose a significantly larger area of the myocardium to ischamia than in the case of single vessel PCI. In order to understand the complexity of the clinical situation in patients after the treatment of coronary bifurcation, and the constantly evolving techniques of the procedure itself, this review presents basic information on the anatomy and classification, up-to-date step-by-step analysis of the optimal technique for PCI, beginning with qualification, planning and preparation for the procedure, through stent selection and ending with optimization techniques. Different PCI strategies are presented and explained, the indications for one- vs. two-stent techniques are evaluated, the available and recommended imaging and physiological methods for detailed bifurcation assessment are reviewed. Particular attention has been paid to left main stem bifurcation, a distinctive anatomical and physiological spot within the coronary circulation.

KEY WORDS
coronary bifurcation, left main coronary artery, percutaneous coronary angioplasty
Introduction

In recent years, we have witnessed exceptionally intensive development of technology or new imaging techniques, and the availability of medical materials of the future has become a fact. We currently have a new generation of coronary stents, drug-eluting balloons, bioreabsorbable scaffolds or dedicated bifurcation stents, and if necessary – it is practicable to use intravascular ultrasound to plan and verify the treatment effect. Increasingly better procedure techniques are being developed that allow the safer treatment of lesions located within bifurcation, but due to the complexity of the unique anatomy and physiology, coronary bifurcation treatment remains an extremely difficult challenge for interventional cardiologists.

Definition and classification

Coronary bifurcation remains a unique region of the coronary tree (Figure 1). The peculiar features of this area are connected with its specific anatomy and blood flow, which determine atherosclerotic plaque location [1,2].

There are three segments in every coronary artery bifurcation structure: the main vessel (MV), main branch (MB) and side branch (SB). Several mathematical models (Murray’s, Finet’s and the universal Huo-Kassab’s model), which describe the relationship between the diameters of these segments are very helpful in evaluating vessel reference sizes during percutaneous coronary interventions – PCI (the diameter of the distal part is always smaller than the proximal part) [3,4] (Figure 2). Atherosclerotic plaques usually develop in areas of minimal shear stress – mainly along inner curves of coronary arteries, near the side branches, especially in the region of lateral bifurcation walls [1,2,5]. Commonly, the carina is free of plaques (atherosclerosis involving the carina is only approximately 30%) [6].

A “coronary bifurcation lesion” as defined is a lesion that causes vessel diameter stenosis ≥ 50% and is contiguous to the division of a major coronary artery [3]. Additionally, the diameter of the side branch should be no less than 2.25 mm [7]. However, a “significant side branch” is arbitrarily defined by the operator’s subjective judgement and it means that we do not want to lose it during the PCI procedure [3].

Indeed, two classifications of coronary bifurcations: the universal Medina classification (describing a lesion, Figure 3) and the amended MADS classification (treatment description) [1,8,9,10] are accepted and recommended by the EBC to facilitate comparisons of the results between studies ongoing in different medical centers or countries [1,10,11]. Furthermore, coronary bifurcation lesions could also be classified into “true bifurcations” in the case that both the main vessel and the side branch, are significantly affected by atherosclerotic plaque (Icps-Lefevre types 1
Planning the PCI

According to the KISSS principle (Keep It Simple, Swift and Safe) [3] the fundamental approach for the treatment of a bifurcation is the single stent method with conditional SB stent implantation (provisional side branch stenting approach; provisional stenting strategy, reverse provisional stenting) that reflects rather a philosophy than a particular technique [13]. The most recommended and predominantly used technique is provisional T-stenting (PTS) consisting in single stent implantation into the MB followed by proximal optimization (POT) [10]. Any further procedures depend on the SB condition. In the presence of uncertain angiographic results, SB ostium balloon dilation or kissing balloon inflation (KBI) can be performed, always followed by subsequent proximal optimization (re-POT) [13]. Opening of the distal strut towards the SB ostium significantly improves ostium scaffolding and reduces the need for SB stent implantation. Indeed, the frequency of SB stenting could be remarkably decreased by using a non-compliant balloon (NC), which reduces the likelihood of vessel dissection [10].

The routine upfront use of the “two-stent technique” has no advantage over the single-stent implantation strategy and only conditional SB stenting [14,15]. Moreover, “two-stent techniques” are remarkably more complex, prolong the duration of the intervention, increase exposure to a higher dose of radiation and increase the costs of the procedure [14,16].

The “Jailing wire technique” is an important part of provisional stenting strategy that remains strongly recommended by the EBC. It involves MB stent implantation with another guidewire left in the SB in order to maintain SB patency. This technique brings some relevant advantages:

**Optimal treatment technique**

**Qualification**

Adequate lesion visualization, especially in the SB ostium is the essential point during every PCI procedure (optimally – at least two orthogonal projections). Evaluation of the stenosis in the side branch is a fundamental stage that affects the choice of further PCI strategy. The authors of the 14th EBC consensus highlight the importance of physiological assessment of the lesion and the usefulness of CT. Interestingly, an SB with a length > 73 mm (measured by CT) commonly supplies over 10% of the myocardial mass. Moreover, the first diagonal and obtuse marginal branches usually supply a substantial part of the myocardium and should be protected by a guidewire while the stent is being implanted in the main vessel [10].

The vast majority of bifurcation lesions can be treated by radial access using 6 French guiding catheters (Fr) (including bifurcation of the distal left main – LM) [10,11].

and 4\textsuperscript{12} or MEDINA types 1,1,1; 0,1,1; 1,0,1\textsuperscript{3} and “false bifurcations” in the case that the lesion involves the main vessel or the side branch (lcps-Lefevre types 2,3,4a and 4b) [7].

PCI for coronary bifurcation lesions account for 15–20% of all PCI. In spite of the fast development of interventional cardiology, these procedures still carry an increased risk of complications and remain a challenging field for operators [4,9]. For that reason, a group of the top European specialists in the field meets annually within the European Bifurcation Club (EBC) to discuss and establish the up-to-date EBC statement and recommendations for coronary bifurcation treatment strategies.
– It keeps the SB patent or in the case of SB occlusion after MB stent implantation, the guide wire remains the only SB marker.
– Changes the bifurcation angle and facilitates SB access.
– Helps guide catheter intubation.
– Gives stronger support to the balloon catheter.
– Allows a rescue procedure to be performed: SB bail-out dilation by a low-profile balloon catheter in the case of SB occlusion (to restore blood flow) [10]. The EBC recommends wiring first the vessel with the potentially most difficult lesions [10]. It should be kept in mind that pulling back a jailed wire from the SB can draw the guiding catheter deeply in the ostium. To minimize the risk of any complications (especially in the case of heavy calcifications) avoiding high pressure balloon inflation before wire removal is recommended. All the maneuvers should be performed extremely carefully as well [10].

**Lesion preparation**

MB predilation is likely to influence the long-term results of bifurcation treatment (it may facilitate vessel sizing, provide adequate MB stent expansion and an optimal effect after POT) [10]. It is emphasized that routine SB ostium predilation is not a recommended part of provisional stenting strategy. Nevertheless, certain situations justify this maneuver, such as:

– a significant flow reduction in the SB after wiring,
– severe/diffuse/calcified SB lesions,
– difficult SB access [10].

**Stent selection**

Drug-eluting stents (DES) are currently recommended to treat coronary bifurcation [11]. The diameter of the MV stent is sized according to the dimensions of the MB just after MV division. This type of stent sizing reduces the risk of MB dissection or vessel stenosis/closure due to carina shift when the stent diameter is too large. The key maneuver in this method of stent diameter selection is the use of the proximal optimization technique (POT). It involves the inflation of a short, non-compliant (NC) balloon in the MV, just before the carina (the ratio of the balloon to MV diameters should be 1:1). Anticipating the potential need to perform the POT technique, the length of the stent implanted into the MV (just before the carina) should be at least 6–10 mm (the length of the smallest commonly used balloons). Of note, the proximal section of the balloon should be entirely located within the stent [10,17].

**Procedure optimization**

The routine use of the KBI technique during single stent coronary bifurcation angioplasty has no clinical benefit [18,19,20,21]. The EBC experts allow this technique to be used in cases of significant ostial stenosis SB (> 75% or < TIMI III) after MV stent implantation. The use of non-compliant balloons (NC) is recommended for this purpose [3]. The advantages of this technique include proximal MV dilation, reconstruction of the carina (restoration of the natural anatomy of bifurcation) [22,23], SB ostial lesion dilation, stent strut extension (facilitating SB access) and stent apposition improvement. The potential disadvantages may include increased complexity of the procedure [18], exposure to possible complications such as SB dissection, stent deformation, stent crushing in the event of unintentional placement of the guidewire outside the vessel lumen and the formation of metal carina [24].

From among the two possible inflation sequences (POT-kiss-POT and POT-side-POT), the 14th EBC recommendations indicate POT-kiss-POT as more favorable (causes less stent deformation) [10]. Circular lumen restoration from the oval vessel formed after KBI can be achieved using the POT technique. If the SB condition is still unacceptable – bail-out SB stenting can be performed [13]. This accounts for about 10% of the cases of the originally intended technique using a single stent [10] and varies depending on the characteristics of the lesion, the significance of the SB, the possibility of passing the guidewire through the distal strut, or the degree of residual stenosis of the SB. For this purpose, the most commonly used techniques are T-stenting (passing the guidewire through the distal stent strut), T And Protrusion (TAP) and Culotte [13].

**Two-stent techniques**

The upfront implantation of two stents is recommended in the case of complex, extensive lesions, involving the MV and SB (especially ostial lesions, reaching > 5 mm deep into the SB), large side branches (especially with a diameter ≥ 2.75 mm) [3] with difficult access, current dissection or the high probability of occlusion [10]. The preferred two stent techniques, according to the EBC, are Culotte and DK-Crush, paying special attention to lesion preparation before stent implantation and obligatory optimization by KBI with subsequent final POT [10,13].

The issue of choosing the optimal technique as part of a two-stent strategy remains debatable. Analyzing the results of randomized clinical trials, it can be concluded that in the case of bifurcation lesions other than the left main coronary artery (LMCA), none of the techniques has a clear advantage in terms of the frequency of the main endpoints [28,29].

In techniques with the intended use of two stents, predilation of both the MV and SB is strongly recommended (balloon inflation should be limited to stent-covered vessel areas). SB protection (by another guidewire) may be considered first in the event of dissection during predilation, difficult SB access, the high probability of SB occlusion or in the presence of extensive SB lesions requiring stent implantation [3].
Culotte

Culotte is a versatile technique that can be used both as the intended two-stent method (with PREMIER SB stent implantation) and as a variant of the strategy with the primary intention of using a single stent – in the event of the need for “bail-out” SB stenting. The main limitation of the Culotte technique is the significant disproportion of MV and SB diameters [11]. At the same time, it is emphasized that when this technique is used, it is advisable to use a modification called “mini-culotte”, which is combined with minimizing the area of the double layer of stents within the MV [3]. Among the techniques using two stents, culotte has an advantage over the original crush technique, which is comparable in effectiveness to the mini-crush technique (minimizing the area of the double layer of the stent in the MV) in randomized trails and at the same time is preferred over T-stenting [30,31].

Crush

The modification of the original crush technique proposed by Colombo, which involves the use of double optimization via KBI (DK-Crush, double kissing crush) is associated with a reduced percentage of repeat revascularization compared to Culotte [32]. The limitation of the DK-Crush technique is undoubtedly the fact that it does not apply to the single stent strategy with only conditional SB stenting (provisional stenting) and that due to its rather complex form, it requires more experience from the operator.

T-stenting/TAP/SKS

Due to the current concerns regarding safety (long double-layer neocarina in SKS) and the lack of data on stent distortion or wall coverage – elective T-stenting and SKS (simultaneous kissing stenting) are currently not recommended by the EBC [10]. The modification of the T-stenting technique, consisting in a slight 1–2 mm SB-stent shift to the lumen of the MV (T And Protrusion – TAP), provides better coverage of the stent connection area and remains a part of provisional SB stenting strategy, especially when the SB leaves at an angle of less than 90° [33,34,35]. In the TAP technique, kissing balloon inflation (KBI) with final POT plays an extremely important role [13].

Intracoronary imaging techniques

The EBC highlights the various benefits of using particular endovascular imaging techniques. OCT provides accurate visualization of the vessel lumen, calcified plaques and ostial lesions, giving an opportunity for vessel evaluation after predilation, guidewire placement, and stent implantation. IVUS enables proper plaque load assessment, while not requiring additional contrast injections. Intravascular imaging usually extends the procedure duration; therefore the need for an intra-operative anticoagulation monitor must be greatly emphasized [10]. The key aspects of the particular stages of coronary bifurcation angioplasty in intravascular imaging are summarized in Table 1.

### Table 1. Key aspects of particular stages of coronary bifurcation angioplasty in intravascular imaging

| Before stent implantation | After stent implantation |
|--------------------------|--------------------------|
| • Evaluation of SB stenosis/occlusion likelihood after MB stent implantation, including location and nature of plaques adjacent to SB ostium. | • Evaluation of stent apposition and expansion. |
| • Assessment of MV and MB diameters to select optimal stent diameter. | • Exclusion of dissection and residual edge stenosis. |
| • Sient length assessment, including POT – balloon size. | • Assessment of guidewire position in SB – especially to rule out its course outside vessel lumen (assessment after rewiring). |
| • SB – side branch; MB – main branch; MV – main vessel; POT – proximal optimization | • Assessment of SB ostium, side branch condition, stent apposition and expansion. |

### Anatomical distinctions

**Left main coronary artery bifurcation**

**Anatomy**

A unique example of coronary bifurcation is the division of the left main coronary artery (LM). Usually when the right coronary artery dominates, this vessel supplies over 75% of the left ventricular myocardium [36,37]. In most cases, it originates by the left sinus of Valsalva; however, the anatomical variant is the take-off from the right sinus of Valsalva or above. In very rare cases, the LM may originate between the aorta and the pulmonary trunk, which is associated with a high risk of sudden death [36,38]. The LM is the only bifurcation proximal segment that extends directly from the aorta, which carries the risk of stent damage by the guide catheter or introducing a guidewire under the stent implanted into the LM [13]. The diameter of the LM is generally large and very variable; it usually fluctuates within 3.5–6.5 mm and is on average about 5 mm [39] (dimension often close to the upper limit of expansion of coronary stents [10,13]), while the average length is 10.5 mm [40]. This vessel is divided into two branches – the left anterior descending artery (LAD) and the left circumflex artery (LCX) (Figure 1). In approximately 10–25% of cases, the LM also provides an additional intermediate branch forming trifurcation [36]. The angle between the main branches of the LM (called angle B) is variable, but usually larger than in other coronary bifurcations (on average 70–80°) [40]. Commonly, the LCX is considered the side branch, which often takes off at a large angle and makes guidewire maneuvers dif-
Left main stenosis significance assessment

An LM lesion assessed in angiography as > 50%, in the case of documented myocardial ischemia, requires revascularization in order to improve the prognosis [14]. In practice, assessment of the ischemia may be ambiguous and the LM disease may be difficult to assess in coronary angiography (e.g. lack of proper projections, lack of a reference, uninvolved vessel segment or irritating effect of the catheter) [36]. In this case, we can use intravascular imaging (e.g. IVUS) and physiological assessment (FFR – fractional flow reserve).

In intravascular ultrasound, the decision making variable is the vessel lumen area (MLA – minimal lumen area) with the most commonly accepted (also by the EBC) cut-off of 6 mm² for the significance of LM stenosis [13,37,41]. Above this value, LM coronary angioplasty is not recommended.

Currently, there is insufficient data (lack of standardized values) to enable the practical use of optical coherent tomography (OCT) in LM lumen assessment, although this method may enable accurate imaging, especially in the case of the distal segment of this vessel, constituting a useful tool for assessing the effectiveness of LM angioplasty (min. accurate abluminal wire position assessment or stent strut identification during SB rewiring) [42].

Left main fractional flow reserve assessment

An isolated LM lesion occurs relatively rarely. It usually coexists with plaques spreading to both the LAD and LCX branches, which can also affect the results of physiological assessment. In that case, the use of the pullback method should be considered [43]. For the LM (as in the case of other vessels), the significance limit of the FFR is 0.8, above which LM revascularization may be safely deferred [14].

Moreover, the use of FFR can be helpful when it is necessary to assess the significance of ostial LCX stenosis, which is often troublesome, especially when the stent is implanted from the LM into the LAD branch [13]. Selected technical aspects of left main FFR assessment are summarized in Table II.
Provisional stenting strategy

In most cases of LM PCI, the provisional SB stenting approach is strongly recommended [10]. The technique might differ depending on the extent of plaque within the LM.

If only one branch of the LM is significantly diseased (Medina 1,1,0 or 1,0,1) the single-stent strategy can be performed (provisional stenting strategy), always by performing standard proximal optimization (POT).

It is recommended that the stent within the LM should have the proper length, depending on the lesion location, usually about 8–9 mm [13], indeed when necessary, including the LM ostium. The diameter of the stent is selected depending on the location of the lesions within the LM. In the case of ostial and medial changes, the stent diameter is selected based on the LM dimensions. During the percutaneous treatment of distal lesions predominantly involving LM branches, the diameter of the stent is determined by the dimension of the stented branch (usually about 3–4 mm) [13], then in order to achieve proper apposition within the LM, it is necessary to perform POT – always using a short, non-compliant balloon. Considering the often significantly larger diameter of the LM – knowledge of the maximum achievable stent diameters (expansion limits) seems to be the crucial point [36].

Optimization with the kissing-balloon technique should be performed in the case of a nonoptimal state of the SB in patients who are likely to require further coronary angioplasty in the future. KBI may be considered in younger patients and in the case of LCX stent implantation (when the LAD is recognized as a lateral branch) [36].

When both branches of the LM are involved – the choice of treatment strategy (upfront planned technique using 1 or 2 stents) should be individualized based on angiographic data taking into account the operator’s experience. According to the EBC statement, most LM lesions may be treated using a single stent (provisional stenting) with a conditional second stent.

Two stent strategy

When performing the intended technique using two stents in the treatment of LM bifurcation, DK-Crush is indicated by the EBC as the most advantageous choice due to the reduction in the frequency of failures of the final KBI compared to the crush technique as well as a lower risk of the main endpoint in the event of LM lesion treatment failure compared to provisional stenting [14,48,49,50].

Procedure evaluation – complications of left main stem bifurcation treatment

Patients undergoing PCI of the LM are a high-risk population, among which, in the case of symptom recurrence or documented ischemia, invasive diagnostics must be considered. In asymptomatic patients after left main PCI, late angiographic monitoring (3–12 months) may be considered [13].

In order to optimize the LM angioplasty effects, especially in the case of uncertain results or complications during the procedure, intravascular imaging (IVUS, OCT) and functional assessment (FFR) are extremely helpful [36]. Intravascular imaging methods allow inadequate stent apposition, edge dissection or stent underexpansion to be recognized, which are even more important in the case of the LM [13]. Incorrect stent size selection (usually too small) or its accidental deformation with the guidewire/guiding catheter, especially in the case of the LM may have serious consequences [10]. For that reason, EBC experts recommend using intravascular imaging techniques in every case of complications or an uncertain effect of the procedure within the LM [13].

A valuable test that allows quick assessment of LM stent patency is coronary CT angiography [51] (especially when a good image quality is expected, with a small number of artifacts, e.g. large, non-overlapping stents).

New technologies

Bifurcation dedicated stents

Bifurcation dedicated stents can be a valuable alternative to current treatment, especially in the case of significant MV and MB diameter disproportions [52]. There are several studies on these devices, whose angiographic and clinical results are encouraging, although the data from randomized controlled trials comparing these devices with the currently recommended treatment are limited [14,53].

Drug-eluting balloons

Drug-eluting balloons (DEB) used in bifurcation restenosis do not increase the number of stent layers, which especially applies to arteries previously treated with two-stent techniques [14,54,55]. The use of DEB in the case of de novo coronary bifurcation lesions may be an attractive alternative to DES; however, the current data of clinical trials remain inconclusive [14,55].

Bioresorbable stents

Taking into account the data on the safety of bioresorbable stents, currently the European Society of Cardiology (ESC) and European Association of Percutaneous Cardiovascular Interventions (EAPCI) recommend that these devices should not be used outside of well-controlled clinical trials [14].

Summary

Despite the growing knowledge of coronary bifurcations and systematic technological progress, in many cases the choice of the optimal technique of the procedure remains the subject of extensive discussions. This is dictated by the complexity of the lesions located within coronary artery bifurcation.
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