

Research Progress of Percutaneous Interventional Therapy For Bifurcation Lesions of Coronary Heart Disease

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Abstract: Compared with non-bifurcation lesions, even if the new generation of percutaneous coronary intervention (PCI) technology is used to treat coronary bifurcation lesions, the incidence of adverse cardiovascular events is still higher. The evaluation of related clinical data and computer virtual modeling before surgery can guide the implementation of bifurcation PCI in a more precise manner. The new understanding of bifurcation PCI may further improve the clinical prognosis and outcome of patients with bifurcation disease. This review aims to summarize the assessment methods of PCI for coronary heart disease non-left main bifurcation disease and the treatment plan supported by clinical evidence. The treatment plan depends on three parameters: the diameter of the three parts of the bifurcation lesion; the length of the lesion and plaque distribution; and the angle of the bifurcation. To this day, the best technique for PCI for bifurcation lesions is still controversial, and a personalized approach using temporary collateral stent implantation schemes seems to be suitable for 75% to 95% of patients. For more complex bifurcation lesions, it may be necessary to use two stents at the same time. More and more evidence supports the practicability of the DK-crush technique.

Keywords: Coronary Heart Disease Non-Left Main Bifurcation Disease; Percutaneous Coronary Intervention; Progress

1. Introduction

Coronary artery bifurcation disease (coronary bifurcation lesion, CBL) is defined as severe coronary artery stenosis, which mainly occurs at the opening of adjacent and /or cumulative larger branches, which has obvious functional value for patients. Percutaneous coronary intervention (percutaneous coronary intervention, PCI) is still the main treatment. Compared with non-bifurcated PCI, bifurcated PCI has lower success rate and higher cardiovascular adverse events. In addition, coronary bifurcation lesions accounted for 15%-20% of all PCI [1]. Although advances have been made in the treatment of drug-eluting stents, the incidence of adverse cardiovascular events after treatment of bifurcated coronary artery lesions is still higher than that of non-bifurcated lesions.[1,2] The risk of perioperative acute collateral obstruction after bifurcated percutaneous coronary intervention (PCI) and the long-term ischemic risk associated with stents are higher [3]. SYNTAXII studies have shown that bifurcated PCI (the most advanced PCI) using physiologically guided thin biodegradable polymer drug-eluting stents optimized by intravascular ultrasound still increases the risk of target lesion failure by 70% compared with non-bifurcated PCI. In addition, in the EXCEL trial, prognostic analysis showed that the left main bifurcation technique of choice for patients with complex bifurcation disease was associated with an increased risk of cardiac death compared with single stenting [4, 5]. The purpose of this article is to review the research progress of PCI in the treatment of non-left main and left main bifurcation lesions of coronary artery.

2. Bifurcation anatomy of coronary artery

The bifurcation anatomy of coronary artery can be divided into three different segments (proximal main branch, distal main branch and lateral branch). Coronary artery bifurcation lesions mainly include anterior descending branch, diagonal branch, circumflex branch, blunt marginal branch, distal right coronary artery bifurcation and left trunk bifurcation. The branching model of the coronary artery: the main branch becomes thinner at the starting point of the lateral branch. At present, the academic circles define the geometric relationship between the main branch and the side branch by Murray, Finett or Hou

and Kassab formula (figure 1)[9]. There were geometric differences between left main coronary artery (LMCA) bifurcation and non-left main coronary artery bifurcation (NLMCA) in distal bifurcation (left anterior descending branch [LAD] and diagonal, left circumflex branch [LCx] and obtuse angle [OM], right posterior descending branch and posterolateral artery). The curvature between the distal branches in LAD and LCx bifurcation is significantly different from that observed in LMCA. Moreover, compared with LAD and LCx bifurcation, LMCA bifurcation has the smallest proximal bifurcation angle and the largest distal bifurcation angle. Therefore, different anatomical structures should be considered when evaluating the distal bifurcation of LMCA and NLMCA [8].

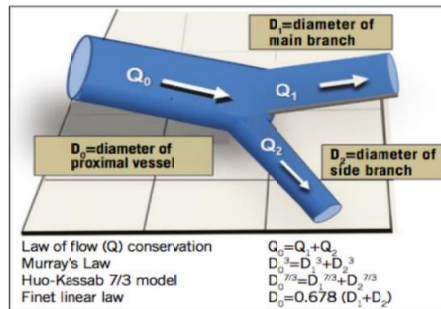


Figure 1: Diameter relationship between bifurcated segments

3. Evaluation of PCI bifurcation lesion

3.1 Functional Assessment

The first step in evaluating bifurcation lesions is to determine the applicability of revascularization. The effect of angiography in distinguishing the functional state of bifurcated lesions is not ideal.[10,11] In addition, commonly used techniques including flow reserve fraction (FFR) and dedicated bifurcated quantitative coronary angiography (QCA) software are to some extent related to the presence of ischemia [12]. IVUS and optical coherence tomography (OCT) have limitations in the application of bifurcation lesions. Studies have shown that invasive pressure guide wire evaluation is essential for determining the best treatment for PCI, especially in cases of moderate stenosis (30% to 70% of the stenosis diameter). In the FIESTA study, systematic FFR evaluation of bifurcation lesions with diameter stenosis > 50% of the main branches before PCI showed that almost half of the target lesions were not functionally important[13], suggesting that FFR was not accurate in evaluating bifurcation lesions.

3.2 Anatomical Evaluation

Once the indications for revascularization are determined, the clinical treatment plan mainly depends on three parameters: (1) the diameter of the three bifurcated segments; (2) the lesion length and plaque distribution; and (3) the bifurcation angle [3]. At present, these parameters can be evaluated by the application of Finet or Hou and Kassab formulas, or ideally through dedicated bifurcation QCA software, angiographic evaluation of the treatment plan [8]. A dedicated bifurcation QCA package can also help select the best angiographic projection to show bifurcation lesions [14]. However, conventional angiography and other imaging techniques are usually limited in the evaluation of collateral vessels [8]. Intravascular ultrasound imaging (IVUS) or optical coherence tomography (OCT) in the main and lateral branches may provide key information about the lesions and choose the best treatment. Studies have shown that for LM coronary artery disease, the IVUS minimum lumen area (MLA) criterion is 6mm², which can be used to determine the importance of coronary artery disease [15]. Similarly, the risk of collateral damage after stent implantation can be evaluated by intravascular imaging. It has been found that the Atheromatous plaque load adjacent to the lateral branch orifice can predict acute collateral occlusion [16]. In addition, intravascular imaging can accurately determine the lesion length of the three bifurcated segments, the percentage of stenosis and the reference vessel diameter.

In the case of severe vascular calcification, intra-plaque determination by IVUS or OCT can

provide a reference for clinicians to use cutting balloon or plaque rotational surgery for more aggressive lesion management, which is conducive to stent implantation and dilatation [17]. The use of non-invasive imaging techniques derived from coronary computed tomography angiography (CTA) in conjunction with flow reserve to assess plaque distribution and characteristics may also play a role in the selection of treatment options. In addition, a prospective study must be conducted to determine the usefulness of non-invasive surgery in bifurcation lesions. Studies have shown that the complexity of bifurcation lesions will seriously affect the clinical outcome after PCI. After percutaneous coronary intervention with drug-eluting stents, the definition of complex bifurcation lesions and their impact on clinical outcomes (DEFINITION) established the criteria for bifurcation complexity: the primary and at least two secondary criteria of bifurcation complexity. In the case of complex bifurcation lesions, the one-year cardiac death and in-hospital MACE incidence of dual-stent implantation was lower than that of temporary stent implantation [20]. In view of the above research, the double stent technique is more suitable for complex bifurcation lesions, and the DEFINITIONII test is testing this hypothesis [21].

4. Progress of PCI technique in the treatment of bifurcation lesions

4.1 Temporary Support Technology

At present, temporary lateral stent implantation is considered to be the “first choice” for the treatment of non-left trunk bifurcation disease [6]. A step-by-step guide to the temporary stent placement strategy is shown in figure 2. Temporary stent technique is suitable for PCI of single main artery (MV) stent. Either the SB is not treated, or the blood vessels are treated only by balloon expansion. The guidelines recommend temporary single-stent technology as the standard method for most bifurcated PCI [5]. Recent trials support temporary stent implantation as a first-line treatment and have been shown to reduce the risk of mortality, major cardiovascular adverse events (MACE), stent thrombosis (ST), and target disease failure (TLF) [7, 11]. At the beginning of surgery, it is important to recognize the risk factors that the use of temporary stents may cause obstruction of SB, such as SB stenosis, especially prolonged 9-10mm or reduced blood flow in TIMI, and the risk of unstable plaque or acute SB occlusion [12,17]. Current PCI guidelines recommend the use of SB side branch guide wire protection and proximal optimization technique (POT) during temporary stent implantation, which can reduce the risk of SB occlusion due to eminence displacement and facilitate the entry of SB after MV stent implantation [18]. However, it should be recognized that these techniques do not completely alleviate the risk of SB occlusion caused by temporary stent implantation.

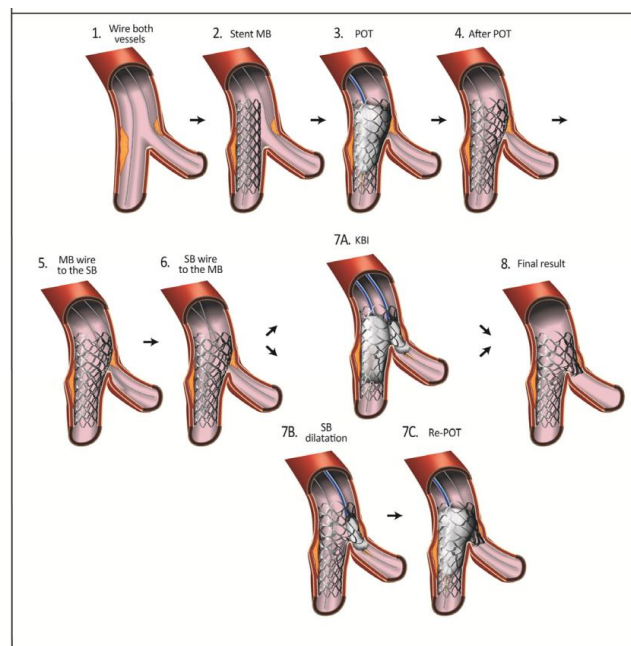


Figure 2: Temporary side support technology

For bifurcated vessels of clinical importance, and in the treatment of true bifurcated lesions (that is, diameter stenosis > 50%), collateral rewiring (guide wire reentry stent mesh technique) [6] is recommended. The stent diameter of the main branch should be selected according to the diameter of

the distal main branch reference vessel. After that, the main branch and lateral guide wire protection and main branch stent implantation were carried out at the same time, and proximal optimization (POT) was carried out to facilitate access to the lateral branches. At this point, the clinician should determine whether there is a need for collateral intervention [6]. The principle is that collateral branches should not be interfered unless there are obvious blood flow restrictions or clear angiographic results (lateral branch orifice diameter stenosis > 70%). In the latter case, you need to replace the guide wire and use a balloon or a series of high-pressure POT for balloon inflatable dilatation, lateral balloon dilatation and re-POT [3, 6]. If there are suboptimal results or flow restrictions, lateral stent implantation can be performed.

4.1.1 The best stent technique for collateral bifurcation lesions

After temporary stent implantation and POT, clinicians may need to further intervene collateral branches due to poor results. If collateral dilatation and re-POT or eventual anastomotic balloon occur, a more distal stent implantation (near the Carina) is recommended. The guide wire is usually pushed into the distal main blood vessel and pulled backward to cover the farthest blood vessel, which has the preformed distal end of the MB guide wire to match the angle of the SB and the diameter of the MB. Through the cross display of the support bar closest to the protuberance and the steel wire, it is better to push the support rod inward toward the main vein lumen than the proximal cross, and the support of the lateral branch mouth is better. If it is clinically decided to use a dual stent technique (for example, extrusion, skirt stent (Culotte) or TAP), lateral stents can be better established in a simple way [6].

4.2 Double Stent Implantation

Several randomized clinical trials compare double-stent techniques with single stent and temporary collateral therapy (for example, collateral insufficiency or collateral complications that include anatomical or severe residual collateral stenosis) [22, 28]. Although there was no difference in the target vascular / lesion revascularization rate between the two regimens in the trial, the myocardial infarction rate (perioperative) and the use of contrast media were higher after the use of the two stents. It is suggested that stent approach (temporary collateral therapy) should be used as the first choice [6, 29]. In addition, in LM lesions, matching analysis showed that patients treated with temporary stent implantation on the left trunk showed a similar rate of revascularization to the target stent during 10-year follow-up compared with the two stent regimens [30]. In some cases, the use of dual stents can be considered in advance; however, before considering a more complex approach, the clinical relevance of collateral should be determined and potential hazards should be balanced. Important collateral branches are defined according to the patient's clinical manifestations and symptoms, complications, collateral length and diameter (and the myocardial functional status of the collateral), local ischemia through non-invasive testing of the collateral region or pressure line to evaluate the location of the myocardium, collateral vessels and left ventricular function, etc. [6].

4.2.1 T stent and TAP (T-stenting and small protrusion technique) technology

In order to obtain the best angiographic effect, it is recommended to use T-stent and TAP technique as collateral stent implantation technique [6]. In the bifurcation with an obtuse angle greater than 90 °, the T-shaped stent can completely cover the lateral branch opening. The TAP technology is an improvement of the T-stent, which is based on the minimum protrusion of the SB stent inside the MB stent and is suitable for bifurcation at an angle of about 70 ° [3] (figure 3) when the SB stent is implanted, the uninflatable balloon will cover the SB opening and be placed in the MB. After the SB stent is implanted, the balloon of the SB stent should be pulled into the MB for a few millimeters, and then the inflatable dilatation will be reserved at the opening of the MB to open the protuberant part of the SB stent. Immediately after the deployment of the SB stent, the stent delivery balloon and the balloon already placed in the MB were used for balloon-to-kiss dilatation (KBI) [3].

4.2.2 Skirt support technology (Culotte) and double kiss extrusion support technology

Double stents are usually needed in bifurcated lesions, where the branches of these lesions are large and the diseased lateral branches extend 5-10mm from the mouth of the lateral branches, or in cases where it is difficult to enter the lateral branches. The commonly used dual-stent techniques are Culotte and double-kiss extruded stent technology. Figures 4 and 5 show step-by-step guidelines for Culotte and double-kiss extruded stent technology [6]. After the double stents were implanted into the PCI, the balloon was first dilated through the balloon kiss, and then POT was performed [6]. In 2017, FDA approved Tryton collateral stents for the treatment of distal bifurcation lesions involving large collateral branches (for stents ≥ 2.5mm) [31]. Different from traditional coronary artery stents, Tryton stents are

characterized by fewer stents in the proximal part of the stents to facilitate the implantation of other stents by techniques similar to Culotte [32]. Under the guidance of angiography, the Tryton stent was located according to four opaque markers. The manufacturer recommends that the bracket be expanded so that the distance between the bifurcation bulge position and the distal intermediate mark is 1/3[32].

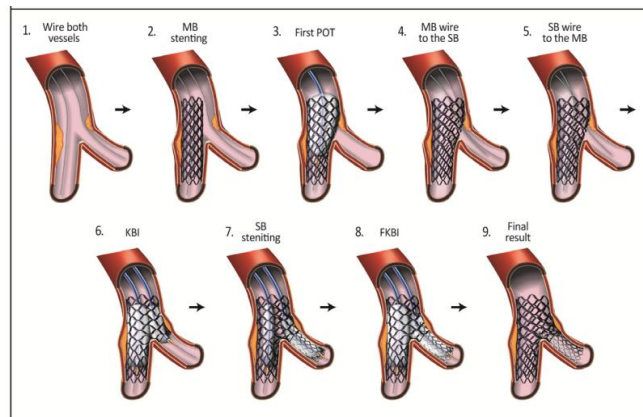


Figure 3: T-stent and TAP technology

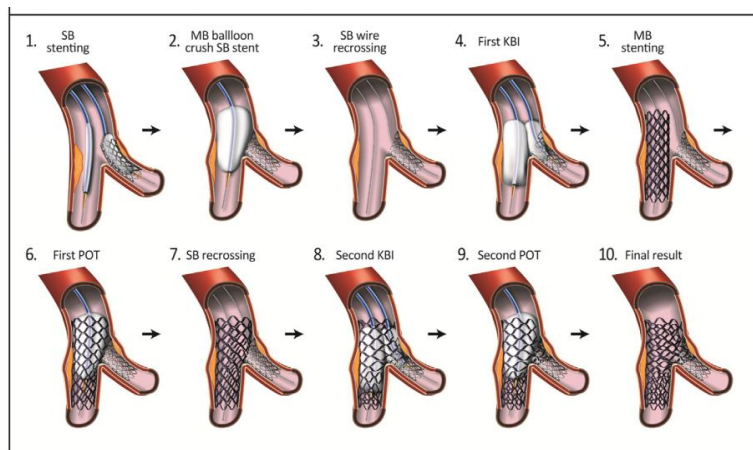


Figure 4: Culotte stent technology

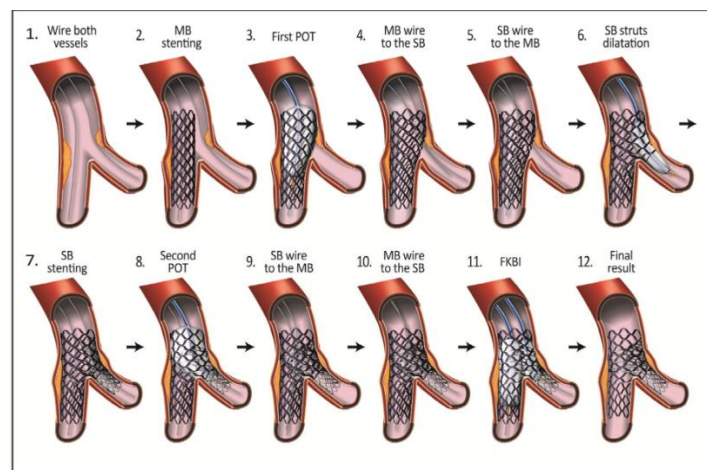


Figure 5: double kiss extrusion stent technique

4.2.3 DK-crush technology

DK-crush technology is a new type of Crush double stent developed by Professor Chen Shaoliang. Its safety and effectiveness have been confirmed by clinical studies, and it has also been recognized and recommended by many intervention experts at home and abroad. DK-crush technique is superior to classical Crush technique in reducing branch restenosis, target lesion revascularization and major

cardiovascular adverse events. The key to this technique is to include two Crush and two kiss expansions. In the first rewire, the guide wire passes through the proximal mesh of the side support; the second rewire position is located in the middle of the side branch opening as far as possible, and the guide wire passes out from the middle mesh. When choosing the position of the side guide wire to enter the edge branch opening, with the help of OCT, IVUS and other imaging equipment, the positioning of the guide wire can be realized more easily. In addition to paying attention to the position of the side branch guide wire entering the side branch opening twice, a non-compliant balloon should also be used to complete high-quality kiss expansion.

4.3 The Latest Side Support Technology

Recently, several new methods have been reported to help reduce the risk of SB occlusion through temporary stent implantation, including aortic plaque transfer technique, balloon stent kissing technique and detention balloon (JBT) technique. The method of active plaque transfer includes pushing the drug-eluting balloon (the size of the SB diameter) into the SB, pre-expanding the SB plaque to actively transfer the SB plaque into the MV, protruding 2 mm to the proximal MV, and placing an appropriate size unexpanded stent in the MV[23]. First, the SB balloon was dilated to pre-dilate the SB. Then, expand the MV stent to nominal pressure to kiss the inflated SB airbag. Then deflate the SB balloon and stent balloon, and remove the SB balloon and guide wire. Then the MV stent is completely expanded and optimized by POT. Although pre-dilation may lead to risks such as SB intimal dissection, a large observational study recently found that active plaque transfer improved TIMI flow in SB and reduced the risk of SB occlusion and SB stent implantation. There was no difference in target lesion failure rate (TLF) within 1 year between the two groups [19].

A technique similar to the active plaque transfer method is the improved balloon-stent kissing method, in which the SB airbag and the MV stent are inflated simultaneously rather than sequentially. A small randomized study (n = 89) [20] and propensity matching study (n = 120) [21] showed that the occlusion rate of SB [20,21] and perioperative MACE decreased [21]. However, there is no evidence of long-term improvement in clinical efficacy [20, 21]. A large multicenter observational registry study (n=1083) reported that prior to temporary MV implantation SB dilatation and angiographic success rates were higher and were associated with higher SB stent implantation rates while long-term MACE did not decrease significantly [24].

A smaller propensity matching study (n=192) found that prior to temporary stent implantation, the use of smaller balloon pre-dilatation in MV and SB (balloon diameter smaller than distal reference vessel 0.5mm) reduced SB blood flow abnormalities, increased rewire success rate and reduced SB dilation failure [22].

Detention balloon techniques (pre-placement of undilated balloons[25] or low-pressure 4-6 mmHg dilated balloons in the SB before temporary stent implantation in the SB to help SB avoid occlusion during posterior balloon dilatation without re-rewire) have also been evaluated in many small case studies (nude 60[25]; n=70 [26];n= 82 [27]). In two studies, there was no vascular occlusion, MACE or SB occlusion [25, 26], successful angiography [25, 26] and TIMI grade 3 blood flow [27]. The incidence of SB occlusion was low in the third study. However, there is no appropriate comparative study to evaluate the technology [25, 27].

4.4 Design And Characteristics Of The Support Platform

No matter which technique is used, the clinician must be familiar with the stent design features and understand the maximum expansion capacity and stent hole size [33]. In patients receiving LM bifurcation PCI, the new generation of DES can significantly improve the clinical effect compared with the early DES. Improved stent metal thickness, biocompatibility of coated or biodegradable polymers, and improvements in new antiproliferative drugs have played a role in reducing acute and late adverse events [34].

5. Postoperative evaluation of PCI

5.1 Physiological And Anatomical Assessment

Studies have shown that invasive physiological assessment after PCI is associated with long-term clinical outcomes. In bifurcated PCI, FFR measurement in the lateral branch after stent implantation in

the main branch may help to determine whether further intervention of the contralateral branch is needed. Double kiss squeeze technique and temporary stent technique in the treatment of coronary bifurcation lesions the VIDKCRUSH-VI trial verified the hypothesis of temporary stents in patients with true and false bifurcation lesions treated by FFR-guided collateral intervention. Compared with angiography-guided PCI, FFR measurement is feasible in 90.6% of cases, resulting in a reduction in the number of stents implanted. The incidence of major adverse cardiovascular events in both groups within one year was 18.1% (hazard ratio: 0.91, 95% confidence interval: 0.48 to 1.88, paired 1.00). The 1-year target revascularization rate and stent thrombosis rate in the vascular-guided and FFR-guided groups were 6.9% and 5.6% (paired 0.82) and 1.3% and 0.6% (paired 0.56)[37], respectively. It was found that IVUS-guided stent optimization could reduce major adverse cardiovascular events. In bifurcated PCI, IVUS or OCT may be valuable in identifying underexpansion, dislocation, edge peeling of stents, verifying the position of wires after collateral crossing, eliminating unexpected re-rewire without tube, and evaluating lateral branch holes[6].

In the bifurcation of the left main coronary artery, IVUS-guided PCI is associated with reduced mortality in non-randomized trials, so the guidelines recommend IIa-level evidence B [40, 41] in bifurcated PCI that appropriate dilatation with a larger minimum stent area can lead to better clinical results [42].

5.2 Drug Treatment

The duration of dual antiplatelet therapy (DAPT) after drug-eluting stent implantation is recommended to be 6 months after selective PCI and 12 months after acute coronary syndrome. Prolonged DAPT can reduce ischemic events and increase the risk of bleeding [41]. After bifurcation lesion PCI, especially after the use of double stent technique, the incidence of ischemic complications is higher [2]. Therefore, the 2017 European Society of Cardiology dual antiplatelet Therapy focus Update (DAPT) points out that for patients with bifurcated lesions implanted with double stents, DAPT ≥ 6 months can be considered [43]. It has been reported that patients with complex bifurcation lesions who receive PCI may benefit from effective or prolonged DAPT. However, there is little clinical evidence to support the study. In accordance with the recommendations of the guidelines, when determining the DAPT regimen and duration, it is recommended to consider personalized treatment options, which should take into account clinical and procedural factors that affect the risk of ischemic and bleeding complications [44].

6. Complications after PCI

6.1 PCI Technology Has Made Great Progress

The benchmark test of bifurcated PCI provides a reference for the acute complications of bifurcated PCI. Finet and others performed final POT after balloon-to-kiss dilatation to prevent poor stent attachment during bifurcation stenting and optimize stent distribution [45]. Finet and others studied the effect of balloon dilatation sequence on acute complications. Compared with the classical balloon-to-kiss dilatation, the circular geometry can be maintained by performing POT (and re-POT), while significantly reducing the incidence of collateral opening stent obstruction and poor overall stent attachment [46]. In addition, Gwon and others reported data from the COBISII registry and analyzed the subgroup of people with a tendency to match scores with a larger SB (≥ 2.5 mm). Comparing 665 patients without POT with 204 patients with POT, there was a significant difference in end point events (MACCE) during 36-month follow-up, and the POT group was better [6].

Computational bifurcation PCI modeling has also been shown to help assess vascular responses to different PCI techniques and to identify potential mechanisms for treatment failure [47]. Chiastra and others used a virtual bifurcation experimental device to describe the effects of the position of the Tryton stent on the obstruction of the lateral opening, the displacement of the boundary ridge and the wall shear stress. Inappropriate proximal or distal position can lead to obstruction of higher lateral opening pillars, which has been shown to be associated with thrombosis [48, 50]. Moreover, poor fit is related to blood flow disorder and platelet activation [51]. In addition, Chatzizisis developed a virtual bifurcation model to predict the side branch response to bifurcated PCI [52]. The tool may assist interventional cardiologists in choosing PCI techniques, stents, and even have an impact on treatment decisions. Although special bifurcated stents were initially concerned, these devices did not show obvious advantages over conventional stents in clinical studies, so they were not widely used in conventional

clinical practice. Therefore, the vast majority of bifurcated PCI are still using conventional stents.

At present, the implantation technique has been improved by using the information of Tryton bifurcation test as a guide. From T stent to lateral stent, double kiss compression technique (DK-crush) is superior to temporary collateral stent strategy and Culotte technique in left main coronary artery bifurcation. In patients with DKCRUSH-V who received bifurcated LMCA PCI, patients who randomly received double-kiss dilatation and extruded stents had a lower risk of target lesion failure, myocardial infarction, and definite or possible stent thrombosis after one year [53]. In the distal (non-left trunk) bifurcation, the five-year follow-up of the DKCRUSH III trial also confirmed that the double-kiss extruded stent technique was superior to the temporary lateral stent technique in revascularization of the target lesion [54]. Nevertheless, it must be recognized that the double-kiss extruded stent technique is technically challenging and is supported by clinical data from a group of experienced doctors. The repeatability of these results is necessary for the technology to be widely adopted.

7. Conclusion

In the past decade, percutaneous coronary intervention (PCI) techniques have undergone great changes, thus improving the treatment strategies and management of bifurcation lesions. The PCI strategy guided by coronary physiology has been shown to optimize the selection of surgical patients who can undergo revascularization. In bifurcation lesions, the ideal treatment should depend on the presence of significant lesions indicated by pressure line-derived index-hemodynamic tests, especially in the case of moderate stenosis. For preoperative anatomical evaluation, computed tomographic angiography can provide a comprehensive anatomical (lumen and plaque) and physiological assessment for interventional physicians in a non-invasive environment. In the catheterization laboratory, special bifurcation quantitative coronary angiography and intravascular imaging have been shown to contribute to treatment decision-making and strategy. Moreover, a new generation of drug-eluting stents has improved the long-term prognosis of patients who have received PCI, and has been used in the PCI of bifurcation lesions to make it have better short-term and long-term effects.

The understanding of bifurcation PCI technology in the industry is constantly developing, and the bifurcation test further improves the technology, thus supporting the usefulness of proximal balloon optimization technology (POT). Sequence POT, collateral expansion and re-POT as an alternative to balloon-to-kiss expansion highlight the importance of using non-compliant balloons for material selection and can be better used for stent optimization. The TRYTON clinical trial indicates that temporary stent strategy is the first choice for non-left main bifurcation lesions of coronary heart disease. However, ongoing studies will further clarify which bifurcation lesions can achieve the best results from the more complex PCI double stent technique. Special bifurcation evaluation techniques have been introduced into clinical practice, and these devices are designed to simplify bifurcation PCI, especially when double stents are needed due to complex bifurcation anatomy. In addition, in many randomized clinical trials comparing double-stent technology, the superiority of double-kiss extrusion (DK-crush) has been proved compared with other double-stent techniques. Therefore, the replicability of these results ensures the wide adoption of DK-crush in clinical practice. Prolonged dual antiplatelet therapy (i.e. > 6 months) should be considered for the best DAPT drug treatment after PCI, especially after complex bifurcation PCI and double stent techniques. Statins intensive lipid-lowering therapy and secondary prevention should be part of the clinical management of patients with bifurcation lesions. Within five years, the treatment of bifurcation lesions will achieve special bifurcation angiography analysis, and have the function of automatically determining the location of the lesions. Pre-operative virtual modeling based on bifurcation technology will provide personalized treatment strategies and suggestions. In addition, even in complex anatomical structures, special bifurcation equipment can simplify the PCI program. At the same time, the development of personalized treatment will further improve the short-term and long-term prognosis of patients with bifurcation lesions.

8. The key issues addressed in this review

Although the technology based on the new generation of percutaneous coronary intervention is constantly improving, the PCI treatment strategy for coronary bifurcation lesions is still associated with a higher incidence of adverse cardiovascular events than non-bifurcation lesions. The first step in the evaluation of bifurcation lesions is to determine the appropriateness of revascularization, and it is very important to determine the best scheme of PCI by invasive stress line assessment. The treatment of

bifurcation lesions depends on the bifurcation shape of the lesion site. Special bifurcation QCA and intravascular imaging are recommended for accurate anatomical evaluation. For most bifurcation lesions, temporary collateral stent implantation is recommended as the first choice.

References

- [1] Grundeken MJ, Wykrzykowska JJ, Ishibashi Y, et al. First generation versus second generation drug-eluting stents for the treatment of bifurcations: 5-year follow-up of the LEADERS all-comers randomized trial. *Catheter. Cardiovasc. Interv.* 2015; 87: E248-E260.
- [2] Gao X-F, Zhang Y-J, Tian N-L, et al. Stenting strategy for coronary artery bifurcation with drug-eluting stents: a meta-analysis of nine randomised trials and systematic review. *EuroIntervention.* 2014; 10:561-569.
- [3] Milasinovic D, Wijns W, Ntsekhe M, et al. Step-by-step manual for planning and performing bifurcation PCI: a resource-tailored approach. *EuroIntervention.* 2018; 13: e1804-e1811.
- [4] Escaned J, Collet C, Ryan N, et al. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. *Eur. Heart J.* 2017; 38: 3124-3134.
- [5] Modolo R, Collet C, Chichareon P, et al. Clinical outcomes with the state-of-the-art approach for treating bifurcation lesions in the SYNTAX II trial. *EuroPCR. Paris;* 2018.
- [6] Flensted Lassen J, Burzotta F, Banning AP, et al. Percutaneous coronary intervention for the left main stem and other bifurcation lesions: 12th consensus document from the European Bifurcation Club. *EuroIntervention.* 2018; 13: 1540-1553.
- [7] Sawaya FJ, Lefèvre T, Chevalier B, et al. Contemporary Approach to Coronary Bifurcation Lesion Treatment. *JACC Cardiovasc. Interv.* 2016; 9: 1861-1878.
- [8] Collet C, Onuma Y, Cavalcante R, et al. Quantitative angiography methods for bifurcation lesions: a consensus statement update from the European Bifurcation Club. *EuroIntervention.* 2017; 13: 115-123.
- [9] Ormiston JA, Kassab GS, Finet G, et al. Bench testing and coronary artery bifurcations: a consensus document from the European Bifurcation Club. *EuroIntervention.* 2018;13:e1794- e1803. De Bruyne B, Pijls NHJ, Kalesan B, et al. Fractional Flow Reserve-Guided PCI versus Medical Therapy in Stable Coronary Disease. *N. Engl. J. Med.* 2012; 367: 991-1001.
- [10] Girasis C, Onuma Y, Schuurbiens JCH, et al. Validity and variability in visual assessment of stenosis severity in phantom bifurcation lesions: A survey in experts during the fifth meeting of the European bifurcation club. *Catheter. Cardiovasc. Interv.* 2012; 79: 361-368.
- [11] Sarno G, Garg S, Onuma Y, et al. Bifurcation lesions: Functional assessment by fractional flow reserve vs. anatomical assessment using conventional and dedicated bifurcation quantitative coronary angiogram. *Catheter. Cardiovasc. Interv.* 2010; 76: 817-823.
- [12] Vassilev D, Dosev L, Collet C, et al. Intracoronary electrocardiogram to guide percutaneous interventions in coronary bifurcations - a proof of concept: the FIESTA (Ffr vs. IcEcgSTA) study. *EuroIntervention.* 2018; 14: e530-e537.
- [13] Tu S, Jing J, Holm NR, et al. In vivo assessment of bifurcation optimal viewing angles and bifurcation angles by three-dimensional (3D) quantitative coronary angiography. *Int. J. Cardiovasc. Imaging.* 2012; 28: 1617-1625.
- [14] De La Torre Hernandez JM, Hernández Hernandez F, Alfonso F, et al. Prospective Application of Pre-Defined Intravascular Ultrasound Criteria for Assessment of Intermediate Left Main Coronary Artery Lesions: Results From the Multicenter LITRO Study. *J. Am. Coll. Cardiol.* 2011; 58: 351-358.
- [15] Sakamoto N, Hoshino Y, Mizukami H, et al. Intravascular ultrasound predictors of acute side branch occlusion in coronary artery bifurcation lesions just after single stent crossover. *Catheter. Cardiovasc. Interv.* 2015; 87: 243-250.
- [16] Barbato E, Carrié D, Dardas P, et al. European expert consensus on rotational atherectomy. *EuroIntervention.* 2015; 11: 30-36.
- [17] Nørgaard BL, Leipsic J, Gaur S, et al. Diagnostic Performance of Noninvasive Fractional Flow Reserve Derived From Coronary Computed Tomography Angiography in Suspected Coronary Artery Disease: The NXT Trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). *J. Am. Coll. Cardiol.* 2014; 63: 1145-1155.
- [18] Park JJ, Chun EJ, Cho Y-S, et al. Potential Predictors of Side-Branch Occlusion in Bifurcation Lesions after Percutaneous Coronary Intervention: A Coronary CT Angiography Study. *Radiology.* 2014; 271: 711-720.
- [19] Chen S-L, Sheiban I, Xu B, et al. Impact of the Complexity of Bifurcation Lesions Treated With Drug-Eluting Stents: The DEFINITION Study (Definitions and impact of complex bifurcation lesions)

- on clinical outcomes after percutaneous coronary intervention using drug-eluting stents). *JACC Cardiovasc. Interv.* 2014; 7: 1266-1276.
- [20] Zhang J-J, Gao X-F, Han Y-L, et al. Treatment effects of systematic two-stent and provisional stenting techniques in patients with complex coronary bifurcation lesions: rationale and design of a prospective, randomised and multicentre DEFINITION II trial. *BMJ Open.* 2018; 8: e020019.
- [21] Steigen TK, Maeng M, Wiseth R, et al. Randomized Study on Simple Versus Complex Stenting of Coronary Artery Bifurcation Lesions: The Nordic Bifurcation Study. *Circulation.* 2006; 114: 1955-1961.
- [22] Colombo A, Bramucci E, Saccà S, et al. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: The CACTUS (Coronary bifurcations: Application of the Crushing Technique Using Sirolimus-eluting stents) study. *Circulation.* 2009; 119: 71-78.
- [23] Hildick-Smith D, de Belder AJ, Cooter N, et al. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British Bifurcation Coronary Study: old, new, and evolving strategies. *Circulation.* 2010; 121: 1235-1243.
- [24] Pan M, de Lezo JS, Medina A, et al. Rapamycin-eluting stents for the treatment of bifurcated coronary lesions: A randomized comparison of a simple versus complex strategy. *Am. Heart J.* 2004; 148: 857-864.
- [25] Ferenc M, Gick M, Kienzle R-P, et al. Randomized trial on routine vs. provisional T-stenting in the treatment of de novo coronary bifurcation lesions. *Eur. Heart J.* 2008; 29: 2859-2867.
- [26] Behan MW, Holm NR, Curzen NP, et al. Simple or complex stenting for bifurcation coronary lesions: A patient-level pooled-analysis of the nordic bifurcation study and the british bifurcation coronary study. *Circ. Cardiovasc. Interv.* 2011; 4: 57-64.
- [27] Maeng M, Holm NR, Erglis A, et al. Long-Term Results After Simple Versus Complex Stenting of Coronary Artery Bifurcation Lesions: Nordic Bifurcation Study 5-Year Follow-Up Results. *J. Am. Coll. Cardiol.* 2013; 62: 30-34.
- [28] Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J. Am. Coll. Cardiol.* 2011; 58: e44-e122.
- [29] D'Ascenzo F, Iannaccone M, Giordana F, et al. Provisional vs. two-stent technique for unprotected left main coronary artery disease after ten years follow up: A propensity matched analysis. *Int. J. Cardiol.* 2016; 211: 37-42.
- [30] Górecki P, Kumsars I, Lesiak M, et al. A Randomized Trial of a Dedicated Bifurcation Stent Versus Provisional Stenting in the Treatment of Coronary Bifurcation Lesions. *J. Am. Coll. Cardiol.* 2015; 65: 533-543.
- [31] Grundeken MJ, Górecki P, Wykrzykowska JJ, et al. The Tryton Side Branch Stent. *EuroIntervention.* 2015; 11: V145-V146.
- [32] Foin N, Sen S, Allegría E, et al. Maximal expansion capacity with current DES platforms: a critical factor for stent selection in the treatment of left main bifurcations? *EuroIntervention.* 2013; 8: 1315-1325.
- [33] Cho S, Kang TS, Kim J-S, et al. Long-Term Clinical Outcomes and Optimal Stent Strategy in Left Main Coronary Bifurcation Stenting. *JACC Cardiovasc. Interv.* 2018; 11: 1247-1258.
- [34] Piroth Z, Toth GG, Tonino PAL, et al. Prognostic Value of Fractional Flow Reserve Measured Immediately After Drug-Eluting Stent Implantation. *Circ. Cardiovasc. Interv.* 2017; 10: 1-9.
- [35] Li S-J, Ge Z, Kan J, et al. Cutoff Value and Long-Term Prediction of Clinical Events by FFR Measured Immediately After Implantation of a Drug-Eluting Stent in Patients With Coronary Artery Disease: 1- to 3-Year Results From the DKCRUSH VII Registry Study. *JACC Cardiovasc. Interv.* 2017; 10: 986-995.
- [36] Chen S-L, Ye F, Zhang J-J, et al. Randomized Comparison of FFR-Guided and Angiography-Guided Provisional Stenting of True Coronary Bifurcation Lesions: The DKCRUSH-VI Trial (Double Kissing Crush Versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions VI). *JACC Cardiovasc. Interv.* 2015; 8: 536-546.
- [37] Buccheri S, Franchina G, Romano S, et al. Clinical Outcomes Following Intravascular Imaging-Guided Versus Coronary Angiography-Guided Percutaneous Coronary Intervention With Stent Implantation: A Systematic Review and Bayesian Network Meta-Analysis of 31 Studies and 17,882 Patients. *JACC Cardiovasc. Interv.* 2017; 10: 2488-2498.
- [38] D'Ascenzo F, Chieffo A, Cerrato E, et al. Incidence and Management of Restenosis After Treatment of Unprotected Left Main Disease With Second-Generation Drug-Eluting Stents (from

Failure in Left Main Study With 2nd Generation Stents-Cardiogram III Study). *Am. J. Cardiol.* 2017; 119: 978-982.

[39] Park S-J, Kim Y-H, Park D-W, et al. *Impact of Intravascular Ultrasound Guidance on Long-Term Mortality in Stenting for Unprotected Left Main Coronary Artery Stenosis*. *Circ. Cardiovasc. Interv.* 2009; 2: 167-177.

[40] members AF, Windecker S, Kolh P, et al. *2014 ESC/EACTS Guidelines on myocardial revascularization*The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of. *Eur. Heart J.* 2014; 35: 2541-2619.

[41] Kang SJ, Ahn JM, Song H, et al. *Comprehensive intravascular ultrasound assessment of stent area and its impact on restenosis and adverse cardiac events in 403 patients with unprotected left main disease*. *Circ. Cardiovasc. Interv.* 2011; 4: 562-569.

[42] Valgimigli M, Bueno H, Byrne RA, et al. *2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS*. *Eur. J. Cardio-Thoracic Surg.* 2018; 53: 34-78.

[43] Levine GN, Bates ER, Bittl JA, et al. *2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines*. *J. Thorac. Cardiovasc. Surg.* 2016; 152: 1243-1275.

[44] Foin N, Secco GG, Ghilencea L, et al. *Final proximal post-dilatation is necessary after kissing balloon in bifurcation stenting*. *EuroIntervention.* 2011; 7: 597-604.

[45] Finet G, Derimay F, Motreff P, et al. *Comparative Analysis of Sequential Proximal Optimizing Technique Versus Kissing Balloon Inflation Technique in Provisional Bifurcation Stenting: Fractal Coronary Bifurcation Bench Test*. *JACC Cardiovasc. Interv.* 2015; 8: 1308-1317.

[46] Antoniadis AP, Mortier P, Kassab G, et al. *Biomechanical Modeling to Improve Coronary Artery Bifurcation Stenting: Expert Review Document on Techniques and Clinical Implementation*. *JACC Cardiovasc. Interv.* 2015; 8: 1281-1296.

[47] Chiastra C, Grundeken MJ, Collet C, et al. *Biomechanical Impact of Wrong Positioning of a Dedicated Stent for Coronary Bifurcations: A Virtual Bench Testing Study*. *Cardiovasc. Eng. Technol.* 2018; 9: 415-426.

[48] Hariki H, Shinke T, Otake H, et al. *Potential Benefit of Final Kissing Balloon Inflation After Single Stenting for the Treatment of Bifurcation Lesions*. *Circ. J.* 2013; 77: 1193-1201.

[49] Grundeken MJ, Chiastra C, Wu W, et al. *Differences in rotational positioning and subsequent distal main branch rewiring of the Tryton stent: An optical coherence tomography and computational study*. *Catheter. Cardiovasc. Interv.* 2018; 0: 1-10.

[50] Foin N, Gutiérrez-Chico JL, Nakatani S, et al. *Incomplete stent apposition causes high shear flow disturbances and delay in neointimal coverage as a function of strut to wall detachment distance implications for the management of incomplete stent apposition*. *Circ. Cardiovasc. Interv.* 2014; 7: 180-189.

[51] Chatzizisis YS. *FLOW ISR Study: Patient-specific bifurcation stenting simulations*. *Eur. Bifurc. Club. Porto*; 2017.

[52] Chen S-L, Zhang J-J, Han Y, et al. *Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions: DKCRUSH-V Randomized Trial*. *J. Am. Coll. Cardiol.* 2017; 70: 2605-2617.

[53] Chen S-L, Santoso T, Zhang J-J, et al. *Clinical Outcome of Double Kissing Crush Versus Provisional Stenting of Coronary Artery Bifurcation Lesions: The 5-Year Follow-Up Results From a Randomized and Multicenter DKCRUSH-II Study (Randomized Study on Double Kissing Crush Technique Versus Provisi*. *Circ. Cardiovasc. Interv.* 2017; 10: e004497-e004497.

[54] Chen S-L, Xu B, Han Y-L, et al. *Comparison of Double Kissing Crush Versus Culotte Stenting for Unprotected Distal Left Main Bifurcation Lesions: Results From a Multicenter, Randomized, Prospective DKCRUSH-III Study*. *J. Am. Coll. Cardiol.* 2013; 61: 1482-1488.