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Current Evidence and Future Perspective for Coronary Bifurcation Stenting

Koroner Bifürkasyon Stentleme için Güncel Kanıtlar ve Gelecek Perspektifi

REVIEW
DERLEME

ABSTRACT

Coronary bifurcation lesions account for 15%-20% of all percutaneous coronary interventions and are associated with greater procedural complexity and consequently at higher risk for cardiac adverse events. Early clinical trials in the interventional approach to bifurcation lesions supported provisional stenting. However, the most recent randomized studies have indicated potentially superior results using a double-kissing crush technique, particularly for unprotected distal left main bifurcation lesions. Moreover, many operators recently favor double-kissing mini-culotte, nanocrush, and double-kissing nanocrush stenting techniques for bifurcation lesions. In this review, we describe the traditional and novel bifurcation stenting techniques and the current evidence for each and review general principles for bifurcation percutaneous coronary intervention.

Keywords: Clinical trial, coronary bifurcation lesions, major adverse cardiac event, stenting

ÖZET

Koroner bifürkasyon lezyonları tüm perkütan koroner girişimlerinin %15-%20'sini oluşturur ve daha fazla prosedür karmaşıklığı ile ilişkilidir ve sonuç olarak olumsuz kardiyak olaylar için daha yüksek risk taşır. Bifürkasyon lezyonlarına girişimsel yaklaşımdaki erken klinik sonuçları, provizyonel stentlemeyi destekledi. Bununla birlikte, en son randomize çalışmalar, özellikle korumasız distal sol ana bifürkasyon lezyonları için 'double-kissing crush tekniği' kullanılarak potansiyel olarak üstün sonuçlar göstermiştir. Ayrıca, son zamanlarda birçok operatör bifürkasyon lezyonları için double-kissing mini culotte, nanocrush ve double-kissing nanocrush stentleme tekniklerini tercih etmektedir. Bu derlemede, geleneksel ve yeni bifürkasyon stentleme tekniklerini ve her biri için mevcut kanıtları ele alıyoruz ve bifürkasyon koroner girişimi için genel ilkeleri gözden geçiriyoruz.

Anahtar Kelimeler: Klinik araştırma, koroner bifürkasyon lezyonları, majör olumsuz kardiyak olay, stentleme

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Coronary bifurcation lesion (CBL) is a very intriguing topic in terms of treatment strategies and management. Coronary bifurcation lesions account for 15%-20% of all percutaneous coronary interventions (PCI).[1,2] The optimal treatment modality for CBL is still debated due to its complex anatomy and variable patient characteristics. The procedural success rate for CBL-PCI is lower, with a higher incidence of major adverse cardiac event (MACE) such as death, myocardial infarction (MI), stent restenosis, target vessel revascularization (TVR), and target lesion revascularization (TLR).[3] Provisional stenting (PS) or planned 2-stent strategy decision is controversial and multifactorial. PS seems to be non-inferior in non-left main coronary artery (LMCA) CBL-PCI. However, a planned 2-stent strategy such as double-kissing crush (DK-crush) may be preferred over PS in LMCA bifurcation lesions.[4] Some prognostic determinants such as side branch (SB) diameter and lesion length, SB length, occlusion risk, evidence of ischemia, bifurcation angle, patient's symptoms, and comorbidities also play an important role in the decision process.[5]

The advances in stenting technologies, the widespread use of intracoronary imaging (intravascular ultrasound [IVUS] and optical coherence tomography [OCT]), increased operator experience, and the development of novel techniques have resulted in improved clinical outcomes and increased procedural success rates.[2,4] The purpose of this review is to summarize the approach to CBLs and bifurcation stenting techniques and algorithms based on novel or major clinical trials.

Definition of Coronary Bifurcation Lesions and Anatomic Considerations

The term "bifurcation" identifies mainly 3-vessel segments: proximal main vessel (PMV), distal main vessel (DMV), and SB. The most common classification system for CBLs is the Medina classification.[6] This classification system is a 3-digit binary code used to define a bifurcation based on the presence of disease proximal and distal to the bifurcation in the main vessel (MV) and the presence/absence of disease in the SB.[6] There are alternative classifications that divide CBLs into simple and complex based on factors that include the lesion length, relative angulation of the vessels, and degree of calcification.

A basic physical principle for bifurcation PCI is the reduction in the diameter of the MV coronary artery following a major SB. The size of the PMV determines the size of MV and SB following bifurcation, and SB can be determined by Finet's formula and constant: [*PMV diameter*=(*DMV diameter*+*SB diameter*) × 0.678], which was arranged from Murray's law [$PMV\ diameter^3 = DMV\ diameter^3 \times SB\ diameter^3$].[7]

Two new dedicated 2-dimensional bifurcation quantitative coronary analysis (QCA) algorithms were developed: CAAS bifurcation software (Pie Medical Imaging, Maastricht, Hollanda) and QAngio XA bifurcation software (Medis Medical Imaging Systems, Leiden, Hollanda). They use the principles of fractal geometry based on mass conservation to address the "step-down" reduction in diameter in the bifurcation branches and they are more accurate than single vessel analysis. New guidelines recommend these new dedicated bifurcation QCA.[5]

The DEFINITION study (Definitions and Impact of Complex Bifurcation Lesions on Clinical Outcomes After Percutaneous Coronary Intervention Using Drug-Eluting Stents) reported some major and minor criteria to categorize complex CBL.[8] In distal LMCA bifurcation, SB lesion length ≥10 mm and SB diameter stenosis ≥70% are major criteria for complex CBL, while SB lesion length ≥10 mm and SB diameter stenosis ≥90% are major criteria for non-LMCA bifurcation lesion. Moreover, 2 minor criteria (multiple lesions, thrombus-containing, main vessel reference diameter ≤2.5 mm, main vessel lesion length ≥25 mm, moderate to severe calcification, bifurcation angle >70° or <45°) fulfill the complex bifurcation term. The DEFINITION II study demonstrated that the systematic 2-stent strategy was associated with improved clinical outcomes compared to PS.[9] The 1-year target lesion failure (TLF) incidence was higher in provisional group (11.4% vs. 6.1%, P=.019). Moreover, at 3-year outcomes of DEFINITION II trial, the TLF was also higher in provisional group (16.0% vs. 10.4%, P=.035) that was mainly driven by increased target vessel MI and TLR.[10]

ABBREVIATIONS AND ACRONYMS

CBL	Coronary bifurcation lesion
IVUS	Intravascular ultrasound
LMCA	Left main coronary artery
MACE	Major adverse cardiac event
OCT	Optical coherence tomography
PCI	Percutaneous coronary interventions
PS	Provisional stenting
TVR	Target vessel revascularization
TLR	Target lesion revascularization

Lesion Preparation

Plaque modification remains a critically important step prior to achieve full stent expansion in CBLs.[2,11,14] Predilatation with semi-compliant or non-compliant coronary balloons is usually the selected strategy for lesion preparation of many CBLs, and scoring/cutting balloons (SCBs) are commonly used for the preparation of fibrous and mild to moderate calcified lesions. For severely calcified lesions, rotational atherectomy (RA) may be required.[2] More recently, a new tool called shockwave intravascular lithotripsy (Shockwave Medical, Santa Clara, Calif, USA), which uses high-energy shock waves to break down calcified plaques to achieve optimal stent expansion, has been introduced to effectively treat circumferential calcification,[11] and several studies have recently suggested that intravascular lithotripsy is a feasible, effective, and safe technique for the treatment of heavily calcified coronary lesions.[12,13] A subgroup analysis of the PREPARE-CALC trial showed that side branch compromise was more frequently observed after lesion preparation with SCBs as compared to RA, and in calcified CBLs, an upfront debulking with an RA-based strategy might optimize the result in the side branch.[14] However, evidence regarding treatment of calcified CBL is minimal. Coronary bifurcation lesions tend to have more complex lesion characteristics, resulting in an increased need for revascularization due to several complex factors such as increased calcification and plaque burden, bifurcation angle, and critical and significant length and diameter of SB lesion.[15]

Physiological Lesion Assessment and Intracoronary Imaging

Fractional flow reserve (FFR) is an essential interventional diagnostic tool in evaluating the hemodynamic significance of angiographically moderate stenosis.[16] Intracoronary imaging provides detailed information on anatomical features of the bifurcation side and plaque characteristics.[17,18] Due to its key role in calcium on stent apposition, intracoronary imaging is of importance in pre-, peri, and post-procedural steps.[18] Post-PCI neocarina assessment, stent malapposition, residual plaque formation or edge dissection, SB osteal coverage, and optimum osteal patency can also be evaluated by intracoronary imaging.

Fractional Flow Reserve

In a study conducted by Koo[19] in 2008, a total of 110 patients who underwent PS were evaluated and FFR was measured in 91 patients. Side branch intervention was performed in 26 of 28 patients whose FFR value <0.75 and control FFR value >0.75 were achieved. During 6-month follow-up period, there was no difference in terms of FFR value in patients with and without balloon angioplasty. Those 110 patients were compared to 110 control patients without FFR evaluation, and there was no MACE difference in both groups (4.6% in FFR group, 3.7% in control; P=.7). The rates of SB intervention (30% vs. 45%, P=.03) and SB stenting (0% vs. 9%, P=.002) were lower in FFR group. In a study, 83 patients with LMCA to left anterior descending artery (LAD) crossover stenting were evaluated and 14 patients with

FFR (≤80) value in circumflex artery (LCX) were categorized as low FFR value.[20] Target lesion failure was higher in patients with low FFR group (33.4% vs. 10.7%, *P*=.029) in a 5-year follow-up period. Lower FFR was an independent predictor of TLF. Fractional flow reserve-guided intervention was compared to angiography-guided intervention in DK-crush VI trial[21] and SB stenting was lower in FFR group (38.1% vs. 25.9%, *P*=.01). At 1-year follow-up, there was no significant difference in MACE, cardiac death, TVR, and stent thrombosis in both groups.

Intravascular Ultrasound

Intravascular ultrasound (IVUS) gives important knowledge about plaque morphology and luminal evaluation, rewiring, stent expansion and apposition, residual stenosis, and complications. In a study, it was demonstrated that minimal luminal area (MLA) <3.7 mm^2 and atherosclerotic plaque burden >56% in LCX ostium were correlated with FFR <0.80 after stenting procedure in patients with LMCA crossover stenting.[22] Minimal luminal area of LMCA was evaluated in LITRO study, and the cut-off value of 6 mm^2 was demonstrated on 354 LMCA patients.[23] Previously, Kang et al[24] reported that lower value than MLA of 5.0 mm^2 for LCX ostium, 6.3 mm^2 for LAD ostium, 7.2 mm^2 for confluence zone of LAD and LCX, and 8.2 mm^2 for LMCA was associated with higher in-stent restenosis and MACE rates. Besides, in the MAIN-COMPARE study, patients with LMCA bifurcation lesions treated with PCI were divided into 2 groups (IVUS-guided and angiography-guided).[25] A total of 1668 patients were evaluated and categorized as IVUS-guided and angiography-guided PCI groups, and the mortality and MI rates were lower in IVUS-guided group (3.8% vs. 7.8%, *P*=.04).[26] The 3-year mortality rates were similar in both groups. However, 3-year mortality rates were lower in IVUS group (4.7% vs. 16.0%, *P*=.048) in patients treated with drug-eluting stents. A recent systematic review and meta-analysis evaluated 7830 patients undergoing bifurcation PCI and categorized them as IVUS-guided and angiography-guided groups, and the MACE rate was lower in IVUS group during the 1-year follow-up period.[27]

Optical Coherence Tomography

In the ILUMEN III study, patients were divided into 3 groups as optical coherence tomography (OCT)-guided PCI, IVUS-guided PCI, and angiography-guided PCI.[28] Mean MLA was 5.79 mm^2 in OCT group, 5.89 mm^2 in IVUS group, and 5.49 mm^2 in angiography group. This study indicated that OCT was found to be non-inferior to IVUS, however, not superior (*P*=.42). Moreover, OCT was also not superior to angiography group (*P*=.12). The incidence of MACE was 3% in OCT group, while it was 1% in IVUS and angiography groups. Besides, the OPINION study reported that there was no difference in cardiac death, MI, TVR, stent thrombosis, and MACE between the groups with or without OCT.[29] Moreover, the DOCTORS trial showed that post-procedural FFR values were higher in OCT group (0.94 vs. 0.92, *P*=.005).[30]

Selection of a Revascularization Strategy for Bifurcation Lesions

Surgical or Percutaneous Intervention

Revascularization approach with percutaneous or surgical treatment in only 1 CBL is unclear. However, there is a recent randomized trial that compared PCI to coronary artery bypass graft surgery (CABG) in patients with de novo 3-vessel disease (3VD) and/or LMCA disease.[31] Patients were categorized into 4 different groups according to their lesion anatomy and treatment strategy: (1) presence of at least 1 CBL and treatment with PCI; (2) no CBL and treatment with PCI; (3) presence of at least 1 CBL and treatment with CABG; and (4) no CBL and treatment with CABG. All-cause death at 10 years was significantly higher in patients with CBL in PCI arm (19.8% vs. 30.1%, *P*=.007) compared to those without CBL. However, there was no difference in CABG arm. While CABG was superior to PCI (hazard ratio [HR]: 0.61, 95% CI: 0.47-0.79; *P* < .001) in terms of 10-year mortality in patients with 3VD with bifurcation. In the PCI group, 2-stent strategy was associated with higher mortality rates than 1-stent strategy (33.3% vs. 25.9%, *P*=.021). In patients with at least 1 CBL, there was an equipoise for all-cause mortality between PCI and CABG groups in 2 quartiles of Syntax score-2020, while CABG was superior to PCI in the 2 remaining quartiles. Some concerns regarding this study should be highlighted. First, 10-year follow-up was only for the survival status; second, it was unclear how many of the outcomes were cardiac death; third, paclitaxel-eluting stents were used for treatment with PCI; lastly, technological improvements, surgical techniques, and adjunctive optimal pharmacologic therapies could change the results.

Percutaneous Intervention for Bifurcation Lesions

An intentional (upfront) PS or the 2-stent strategy is usually considered in the foreground for the treatment of a CBL. The lesion characteristics and complexity are determinative in deciding on an approach to CBLs (Figure 1). The current European Bifurcation Club (EBC) guidelines recommend PS as the treatment of choice for most lesions and an upfront 2-stent strategy for more complex lesions with an extensive SB supplying a larger myocardial territory.[2] However, the adoption of the PS approach in fact provides foreseeable results in both MV and SB. In most cases, a stent is placed only in MV, with the deployment of additional SB stents if required. It is well known that PS is non-inferior to the 2-stent strategy.

Provisional Stenting

The EBC recommends PS as the initial strategy for non-complex CBLs.[2,15] The procedural steps of PS are demonstrated in Figure 2. In many studies, single or 2-stent strategies have been evaluated for CBLs (Table 1). In the DK-crush II trial, 370 patients with CBL were randomized to PS and DK-crush groups. The results showed no differences between the groups in terms of MACE (10.3% vs. 17.3% for DK-crush and PS, respectively) and definite stent thrombosis (2.2% vs. 0.5% for DK crush and PS, respectively). However, DK-crush technique was associated with reduced TLR and TVR (6.5% vs. 14.6%, *P*=.017) at 12 months.[18] There was also no difference in terms of MACE in an analysis of the EBC TWO trial (10.3% vs. 7.7% for single and 2-stent approach, respectively)[32] and Nordic-Baltic IV trial (12.9% vs. 8.4% for single and 2-stent approach, respectively).[33] On the other hand, the British Bifurcation Club 1 (BBC 1) trial demonstrated PS was associated with lower MACE (8% vs. 15.2% for single and 2-stent approach, respectively).[34] A patient-level meta-analysis of Nordic 1 and BBC 1 showed more frequent periprocedural MI with the complex stenting approach compared to PS.[35] In the

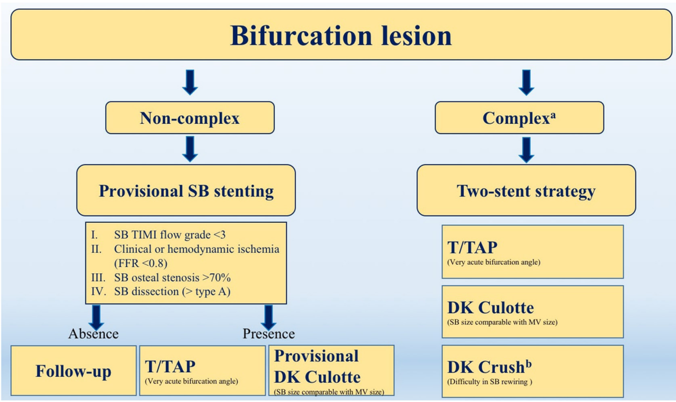

Figure 1. Treatment algorithm of bifurcation lesions. (A) In distal LMCA bifurcation, SB lesion length ≥10 mm and SB diameter stenosis ≥70% are major criteria for complex CBL, while SB lesion length ≥10 mm and SB diameter stenosis ≥90% are a major criteria for non-LMCA bifurcation lesion. Moreover, 2 minor criteria (multiple lesions, thrombus-containing, main vessel reference diameter ≤2.5 mm, main vessel lesion length ≥25 mm, moderate to severe calcification, bifurcation angle ≥70° or ≤45°) fulfill the complex bifurcation term. (B) DK crush stenting may be preferred for both complex and non-complex LMCA bifurcation lesion. CBL, complex bifurcation lesion; DK, double kissing; LMCA, left main coronary artery; SB, side branch; TAP, T and small protrusion.

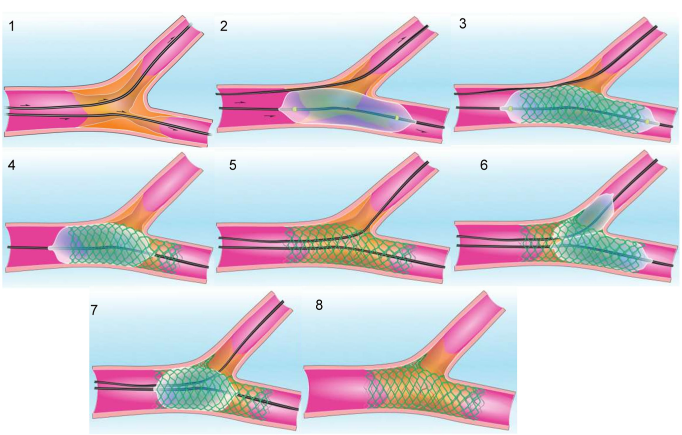

Figure 2. Procedural steps of provisional stenting technique. (1) Wire both MV and SB. (2) Predilate the MV and the SB as required; many SBs without significant disease or calcification do not require predilatation. (3, 4) Stent the MV and perform a POT, leaving the SB wire in place. If the angiographic results in the MV and SB are satisfactory, the procedure is complete and the SB wire jailed behind the MV stent struts can be gently removed. (5) Rewire the SB and then remove the jailed wire and recrossing through the distal strut following the MV stenting and the POT should be liberally utilized to facilitate rewiring of the SB. (6) Perform SB balloon dilatation and Simultaneous KBD with moderate pressure in the SB, until the balloon is fully expanded. (7, 8) Final POT is performed at the proximal MV upper level of the carina. KBD, double kissing balloon dilatation; MV, main vessel; POT, proximal optimization technique; SB, side branch.

light of current knowledge, provisional SB stenting may be the preferred strategy for non-complex CBLs.

Inverted Provisional Stenting (Medina 0,0,1)

Medina 0,0,1 bifurcation type represents <5% of lesions identified in published reports and is generally excluded from PCI studies.[36] While optimal medical therapy is the preferred first-line treatment, the placement of a single stent in the ostium has also been recommended for ostium SB lesions. Several techniques, including predilation or atherectomy, placement of a non-inflated balloon in the MV, or the Szabo technique, were described for the treatment of SB osteal lesions.[2,15] However, despite the use of these techniques, the accurate placement of an SB stent at the ostium remains challenging, particularly when the angle between the DMV and the SB is <90°, with a potential risk of placement of the stent too distally, leaving a gap in the scaffolding and drug delivery to the proximal SB, or too proximally, leaving the proximal struts protruding into the MV. The "inverted" PS technique, with cross-over stenting from the PMV into the SB, offers the advantage of complete coverage of the ostium.[2] The majority of challenges with this technique are (i) exact placement of the stent despite different PMV and SB diameters and (ii) optimal opening of the strut in front of the DMV. The kissing balloon (KB) maneuver can help overcome these disadvantages. However, it is suggested that the KB maneuver creates lesions in the endothelium that may cause dissection or restenosis. The stent boost acquisition or intravascular imaging (IVUS or OCT) may help us to confirm if the stent was well opened. In 2010, Brunel et al[36] examined the feasibility and safety of inverted PS for isolated osteal SB CBLs and was associated with 100% procedural success. At a mean follow-up of 22 months, they did not observe death, MI, or stent thrombosis. Repeat revascularization was required in 7.5% of the patients, while TVR and TLR rates were 2.5% and 2.5%, respectively. Moreover, Jang et al[37] have previously demonstrated that the 2-stent technique seems to be associated with a better clinical outcome [TLR: (3.2% vs. 12.0%, $P=.03$), TLF: (4.8% vs. 12.0%, $P=.05$)] compared to the single stent technique in patients with a medina 0,0,1 lesion.[37] However, it should be noted that only 60% of the patients selected for the single-stent strategy in this registry were treated with the "inverted" PS technique. The preferred strategy for the treatment of medina 0,0,1 lesion is still debated. Hence, "inverted" PS technique should only be considered for use after failed optimal medical treatment.

Prevention of Side-Branch Occlusion

In the provisional SB stenting technique, the major determinant of procedural success is the risk of SB occlusion. The optimal SB approach is still controversial. Systematically, wiring both branches in all PCI procedures with CBL is strongly recommended regardless of the selected strategy. Lesion preparation with SB predilatation can protect SB flow after MV stenting, with less requirement for performing an intervention to SB despite the risk of SB dissection.[38] An observational study indicated that SB predilatation (called as "active plaque transfer technique") improved thrombolysis in myocardial infarction (TIMI) flow in the SB, with a reduced risk of SB occlusion and less requirement for performing stenting to SB. There was no difference in TLF at 1-year follow-up.[39] Even though the standard approach is the sequential predilatation of the SB and MV, the simultaneous "pre-kissing

Table 1. Comparison of Provisional with 2-Stent Strategies

Trial	Technique	Follow-Up Period	TLR/TVR	Cardiac Death	MI	TLF[(a)] or MACE
DEFINITION II[9]	Provisional (325 patients) vs. 2-stent techniques (328 patients, 77.8% DK crush, 17.9% culotte, 4.3% others)	12 months	5.5% vs. 2.4%*	2.5% vs. 2.1%	7.1% vs. 3.0	11.4% vs. 6.1%*,[a]
DEFINITION II[10] **	Provisional (325 patients) vs. 2-stent techniques (328 patients, 77.8.% DK crush, 17.9% culotte, 4.3% others)	36 months	8.3% vs. 4.3%*	1.6% vs. 4.1%	8.0% vs. 3.7%*	16.0% vs. 10.4%*,[a]
DK crush II[18]	Provisional (185 patients) vs. DK crush (185 patients)	12 months	14.6% vs. 6.5%*	1.1% vs. 1.1%	2.2% vs. 3.2%	17.3% vs. 10.3%
EBC TWO[32]	Provisional (103 patients) vs. culotte (97 patients)	12 months	2.9% vs. 1.0%	2.0% vs. 1.1%[b]	4.9% vs. 10.3%	7.7% vs. 10.3%
Nordic-Baltic IV[33]	Provisional (218 patients) vs. 2-stent strategy (228 patients, culotte was recommended initially)	24 months	10.5% vs. 6.6%	0.9% vs. 0.9%	5.1% vs. 3.1%	12.9% vs. 8.4
British Bifurcation Club 1 (BBC 1)[34]	Provisional (249 patients) vs. 2-stent strategy (248 patients, 75 culotte, 169 crush and 4 provisional)	9 months		0.4% vs. 0.8%[b]	3.6% vs. 11.2%*	8.0% vs. 15.2%*
Ruiz-Salmeron et al[51]	Provisional (33 patients, 34 lesions) vs. T stenting (36 patients and lesions)	9 months	8.1% vs. 10.7%	0% vs. 0%	2.7% vs. 0%	8.1% vs. 10.7%
Bifurcations Bad Krozingen (BBK) I[52]	Provisional (101 patients) vs. T stenting (101 patients)	5 years	16.2% vs. 16.3%	7.9% vs. 10.0%[b]	9.9% vs. 13.9%[c]	22.8% vs. 22.9%
Zhang et al[54]	Provisional (52 patients) vs. culotte (52 patients)	9 months	1.9% vs. 7.7%	0% vs. 1.9%	5.8% vs. 0%	7.7% vs. 7.7%
Fan et al[56]	Provisional (66 patients) vs. DK mini-culotte (66 patients)	12 months	12.12% vs. 1.52%*	0% vs. 1.52%	3.03% vs. 1.52%	13.6% vs. 4.55%
CACTUS[60]	Provisional (173 patients) vs. crush (177 patients)	6 months	7.5% vs. 7.9%	0.5% vs. 0%[b]	8.6% vs. 10.7%	15.0% vs. 15.8%

MACE, major adverse cardiac events; MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization.
*$P < .05$, [a]TLF; [b]Non-cardiac death or all-cause death; [c]The composite of death and MI; **3-year follow-up results.

technique" is an alternative approach. It protects the SB ostium from the risk of carina displacement and plaque shift. Burzotta et al[40] have recently found that the pre-kissing technique using under-sized balloons to protect dissection risk was associated with a lower risk of SB-related complications. The other technique to protect SB flow is the jailed semi-inflated balloon technique. Briefly, the MV stent is implanted, while the semi-inflated balloon with low pressure is positioned in the SB ostium to protect SB occlusion following proximal optimization technique (POT).[41] Although the SB has osteal or diffuse disease, in some cases, it is not suitable for intervention due to the small vessel diameter. Protection of SB with the jailed wire strategy may be performed in these patients, called as "keep it open strategy." In this technique, neither rewiring nor balloon dilatation is recommended for SB.[42]

Consideration of Side-Branch Intervention

After performing cross-over stenting with a provisional approach, SB dilatation or KB dilatation is challenging. In this technique, SB intervention may be required when TIMI flow of SB is limited or severe osteal SB narrowing is present, resulting in hemodynamic impairment with insufficient FFR. Main vessel stenting followed by POT and then isolated SB dilatation through the MV stenting is not recommended alone due to the risk of MV stent malapposition opposite to the SB take-off. To avoid this, 2 different modalities may be performed; side branch balloon dilatation followed by repeat-POT (re-POT) is a simple technique called "POT-side-POT." Distal rewiring and position of the re-POT balloon are key determinants of final SB obstruction. The other technique is the KB dilatation. The impact of KB dilatation on TLR or MACE is controversial. In the COBIS II trial, KB dilatation is associated with reduced MACE (6.8% vs. 8.6%; KB vs. non-KB, respectively, $P = .048$), with no difference in MI and TLR.[43] On the other hand, the RAIN-CARDIOGROUP VII trial showed no significant difference in MACE (15.0% vs. 12.4% for KB vs. non-KB, respectively) and TLR (5.3% vs. 3.2% for KB vs. non-KB, respectively).[44] The Nordic III trial also demonstrated that KB dilatation was not associated with improved clinical outcomes in terms of both MACE and TLR.[45] However, Yamawaki et al[46] demonstrated that KB dilatation was associated with a higher incidence of MACE (14.6% vs. 6.9%, $P = .07$) and increased TVR ratio (14.6% vs. 5.9%, $P < .05$).[46] It is also important to note that re-POT is also recommended after performing KB dilatation to prevent PMV stent malapposition. To date, POT-side-POT and KB dilatation are not advised routinely in the light of current clinical data. However, they may be performed if the SB TIMI flow and/or SB opening is affected. A recent PROPOT trial investigated POT followed by SB dilatation compared to KB dilatation. The rate of stent malapposition did not differ between the groups. Moreover, the TLR rate was the same for both groups.[47]

When Do We Need Side-Branch Stenting?

The SB stenting should be performed in cases where SB is affected, with clinically significant outcomes. Generally, it is recommended when SB TIMI flow is <3 or large-diameter SB dissection may result in significant ischemia or in the presence of hemodynamic impairment with a low FFR (<0.8) value. The DK-crush VI randomized trial evaluated a total of 320 patients with Medina 1,1,1 and 0,1,1 CBL, randomly assigning them into 2 groups at a ratio of 1:1: angio-guided or FFR-guided groups.[44] The rate of performing SB stenting was significantly higher in the angio-guided group (38.1% vs. 25.9%, $P = .01$), while the rate of SB treatment (balloon dilatation or stenting) was lower in the FFR-guided group (63.1% vs. 56.3%, $P = .07$). The incidence of MACE was 18.1% in both groups. Furthermore, the 1-year TVR and stent thrombosis rates were not different between both groups.[48] When SB stenting is required in the PS approach, the T/T and protrusion (TAP) and culotte stenting techniques are recommended as in bail-out management of SB by the EBC.[15]

Two-Stent Strategies

While provisional SB stenting may be used for many CBLs, the 2-stent strategies are recommended as an up-front approach in the presence of complex bifurcation characteristics.[2] Multiple different techniques have been described and investigated for the treatment of CBL (Table 2). The main, across, distal, side (MADS)-2 classification of bifurcation stenting has been described by the EBC according to the strategy of first stent implantation.[15] The 2-stent strategy to be used may vary depending on the bifurcation anatomy and the operator's experience. Meticulous lesion preparation, as well as final KB dilatation, the use of POT

Table 2. Trials of 2-Stent Strategies

Trial	Technique	Follow-Up Period	TLR/TVR	Cardiac Death	MI	TLF [(a)] or MACE
Bifurcations Bad Krozingen (BBK) II[55]	Culotte (150 patients) vs. TAP (150 patients)	12 months	6.0% vs. 12.0%	0.7% vs. 0.7%	1.3% vs. 0.7%	6.7% vs. 12.0%[a]
Yang et al[61]	classic crush (67 patients, 69 lesions) vs. mini crush (111 patients, 112 lesions)	3 years	18.8% vs. 10.7%	7.5% vs. 2.7%[b]	4.5% vs. 1.8%	25.4% vs. 12.6%*
DK crush I[62]	Classic crush (156 patients) vs. DK crush (155 patients)	8 months	18.9% vs. 9.0%*	1.7% vs. 0.6%	11.1% vs. 9.1%	24.4% vs. 11.4%*
Nanocrush[64]	52 patients	12 months	0%	0%	0%	0%
DK Nanocrush[66]	42 patients	12 months	4.76%	2.38%	0%	7.14%

MACE, major adverse cardiac events; MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization.
*$P < .05$, [a]TLF; [b]Non-cardiac death or all-cause death.

(1-3 times depending on the strategy), and SB optimization are strongly recommended for all 2-stent techniques. If there is a risk of SB occlusion or difficulty in SB rewiring, the SB first 2-stent techniques such as inverted T/TAP, DK-culotte, or DK crush can be selected. If there is no risk of SB occlusion, MV first 2-stent techniques such as T/TAP, and provisional DK-culotte stenting can be selected. Furthermore, culotte stenting should be selected for CBL-PCI with an SB size comparable to the distal MV size. On the other hand, the DK crush technique can be a suitable approach for anticipated difficulty in rewiring to SB.[2,15]

T/T and Protrusion Stenting Technique

T stenting was firstly described by Antonio Colombo, through the stent struts of a previously deployed stent, in 1995[49] while TAP stenting was first reported by Burzotta in 2007.[50] The T/TAP stenting is usually known to be a simpler strategy after PS. The procedural steps of TAP stenting are demonstrated in Figure 3. Several studies have compared provisional and T/TAP stenting. Previously, Ruiz-Salmeron et al[51] compared simple stenting with T-stenting. There was no difference between the groups in terms of MACE (cardiac death, MI, and TVR) (8.1% vs. 10.7% for simple and T-stenting, respectively). The Bifurcations Bad Krozingen (BBK) I study assigned 101 patients to routine T-stenting and 101 patients to provisional T-stenting. The 5-year incidence of TLR was 16.2% in the provisional group, while it was 16.3% in the routine T-stenting group, with no difference between the groups in terms of MACE, the composite of death and MI, and stent thrombosis.[52] The T/TAP stenting is recommended as a bail-out strategy after provisional SB stenting.

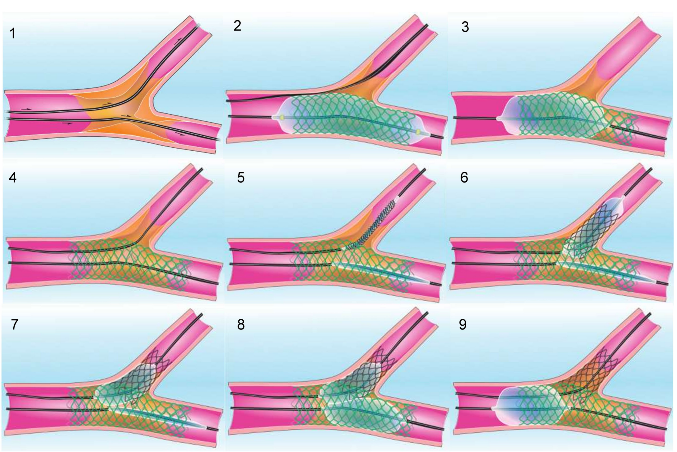

Figure 3. Procedural steps of TAP stenting technique. (1) Wire both branches and predilate if needed. (2) Stent the MV leaving a wire in the SB. The stent in the MV can be deployed at nominal pressure. (3) Stent the MV and perform a POT, leaving the SB wire in place. (4) Rewire the SB passing through the proximal struts of the MV stent. (5) SB stent is positioned with the aim to protrude as minimally as possible into the MV (1-2 mm) and a balloon is advanced in the MV. (6) The SB stent is deployed as nominal pressure, while the uninflated balloon remains parked in the MB at the bifurcation. (7) SB stent balloon is pulled back slightly then inflated (side branch optimization). (8) Simultaneous KBD is performed using the SB balloon and the previously positioned MB balloon at high pressure. (9) Final POT is performed at the proximal MV upper level of the carina. KBD, double kissing balloon dilatation; MV, main vessel; POT, proximal optimization technique; SB, side branch.

Culotte Stenting Technique

The culotte stenting technique was first described by Chevalier et al[53] in 1998, when a second stent was required after the provisional approach and called "classic culotte." In the routine daily practice, contrarily to this, the first stent implantation is performed from the PMV to SB. Nowadays, minimal protrusion to MV is also expected in this technique ("mini-culotte stenting"). The main limitation of the culotte stenting technique is the diameter mismatch between SB and DMV and PMV since both stents have to cover PMV. Hence, the selected stents have to be expanded enough to reach the PMV diameter. In the EBC TWO study, 200 true CBL patients with SB diameter ≥2.5 mm and significant osteal lesion length ≥5 mm were randomized to provisional T-stenting or culotte stenting.[32] Of the patients in the provisional group, 60% underwent T-stenting. The incidence of MACE at 12 months was 7.7% in the provisional group, while it was 10.3% in the culotte group.[32] Zhang et al[54] compared the PS and culotte stenting techniques, and MACE incidence was the same in both groups at a follow-up period of 9 months. The BBK II trial included a total of 300 patients and randomized them to TAP stenting or culotte stenting. The rate of re-stenosis was 17% and 6.5% in the TAP and culotte groups, respectively ($P=.006$). The 1-year incidence of TLR was 12.0% in the TAP group, while it was 6.0% in the culotte group ($P=.069$). The culotte stenting was associated with a lower incidence of angiographic restenosis compared to TAP.[55]

The DK practice and minimal stent protrusion to PMV appear to lead to better clinical outcomes. The procedural steps of DK mini-culotte stenting are demonstrated in Figure 4. Fan et al[56] compared the DK mini-culotte stenting technique with the T-provisional stenting technique using a propensity score matching analysis. The incidence of MACE (cardiac death, MI, and TVR/TLR) was 4.55% in the DK mini-culotte group, while it was 13.6% in the T-provisional group. The incidence of TLR/TVR was 1.52% and 12.12% in the DK mini-culotte and T-provisional groups, respectively ($P=.033$). The SB restenosis rate was 5.6% and 22.4% in the DK mini-culotte and T-provisional groups, respectively ($P=.014$).[56] Moreover, DK mini-culotte was compared with mini-culotte stenting in micro-computed tomography imaging bench testing.[57] The metal carina length, area of the SB ostium, and a maximum distance of malopposed struts for the wall facing the SB ostium were lower for the DK mini-culotte stenting technique. In the other bench test evaluation, the DK culotte technique was compared with the culotte and DK crush techniques. The overall rates of moderate (2.1 ± 1.9%, 8.1 ± 2.5%; $P < .001$) and significant malapposition (0.4 ± 0.2%, 3.7 ± 5.3%; $P=.002$) were lower for the DK culotte technique compared to the DK crush technique. The main difference of moderate and significant malapposition was observed in the PMV 0% vs. 14.0 ± 7.6%, $P < .001$ and 0.0 ± 0.0% vs. 4.2 ± 9.1%, $P=.026$ for DK culotte and DK crush techniques, respectively.[58] However, there are limited data for the DK culotte technique, and the clinical validity of this technique and its possible effects on long-term outcomes need to be evaluated.

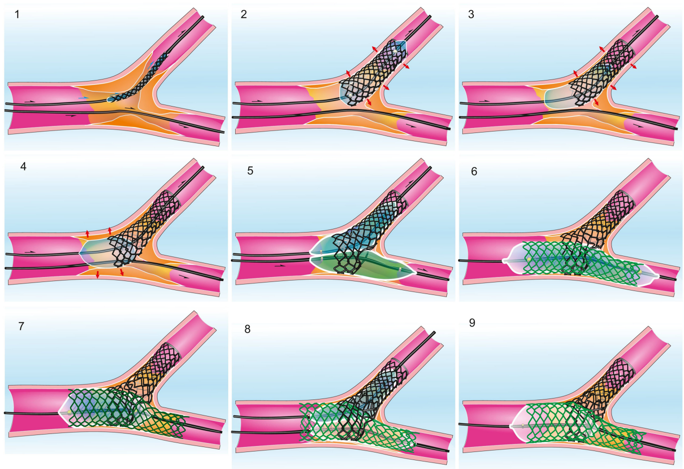

Figure 4. Procedural steps of DK mini-culotte stenting technique. (1) Both MV and SB are wired (predilatation may be performed for both vessels). (2) The first stent is implanted from MV to SB with a minimal protrusion to the PMV. (3) SB stent balloon is pulled back slightly then inflated (side branch optimization). (4) POT is performed at the proximal MV upper level of the carina. (5) After rewiring to DMV from distal cell, kissing balloon dilatation is performed (preferably with short non-compliant coronary balloons with the 1:1 size of distal MV and SB) with a minimal overlap into the PMV. (6) MV stent is implanted according to the 1:1 distal MV size (appropriate stent length should be allowed equal or longer than shortest available balloon for POT). (7) Second POT is performed at the proximal MV upper level of the carina. (8) After rewiring to DMV from distal cell, kissing balloon dilatation is performed (preferably with short non-compliant coronary balloons with the 1:1 size of distal MV and SB) with a minimal overlap into the PMV. (9) Third POT is performed at the proximal MV upper level of the carina. DK, double kissing; DMV, distal main vessel; MV, main vessel; PMV, proximal main vessel; POT, proximal optimization technique; SB, side branch.

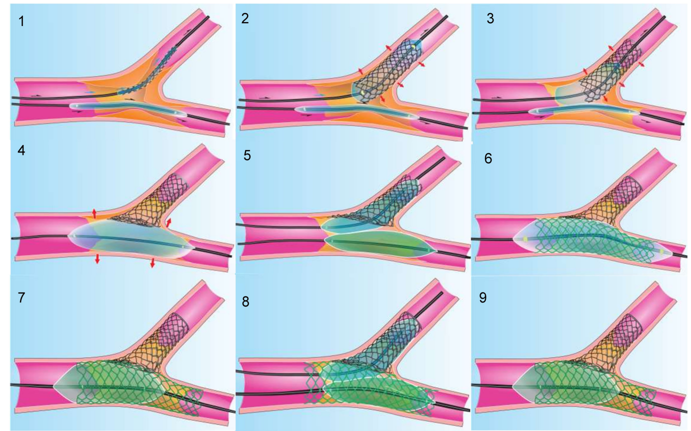

Figure 5. Procedural steps of DK crush stenting technique. (1) Both MV and SB are wired (predilatation may be performed for both vessels) and the SB stent (1:1 size with SB diameter) is advanced with a minimal (it should be limited to 2-3 mm) protrusion to the MV. (2) The SB stent is implanted while a coronary balloon is kept uninflated into the distal MV. (3) SB stent balloon is pulled back slightly then inflated (side branch optimization). (4) Balloon crush is performed with a balloon sized to distal MV (POT crush should be performed with a short balloon sized 1:1 to the PMV to warrant optimal crushing without PMV malapposition). (5) After rewiring to SB from non-distal cell, kissing balloon dilatation is performed (preferably with short non-compliant coronary balloons with the 1:1 size of distal MV and SB). (6) MV stent is implanted according to the 1:1 distal MV size (appropriate stent length should be allowed equal or longer than shortest available balloon for POT). (7) POT is performed at the proximal MV upper level of the carina. (8) After rewiring to SB from non-distal cell, kissing balloon dilatation is performed (preferably with short non-compliant coronary balloons with the 1:1 size of distal MV and SB) with a minimal overlap into the PMV. (9) Repeat-POT is performed at the proximal MV upper level of the carina. DK, double kissing; MV, main vessel; PMV, proximal main vessel; POT, proximal optimization technique; SB, side branch.

Crush Stenting Techniques

Colombo et al[59] first reported the "classic crush technique" in 2003. Over time, the "step crush technique," which was first crushed with a balloon, and then the "double kissing crush technique" were developed. The "mini crush" and contemporary "DK mini crush" techniques were developed with the aim of minimal protrusion in the current approach. Finally, novel techniques of "Nano crush" and "DK Nano crush," in which protrusion is reduced thoroughly, were developed. The procedural steps of DK crush, which is often performed in routine daily practice, are demonstrated in Figure 5. The Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting Stents (CACTUS) trial compared classic crush and PS for the first time.[60] In 6 months, the rates of angiographic stenosis of the main branch and SB and the incidence of MACE were not different.[60] Yang et al[61] compared classic crush and mini-crush and reported a lower MACE incidence with the mini-crush technique compared to the crush technique (12.6% vs. 25.4, $P=.030$) in 3-year outcomes. The DK crush I trial reported an 8-month MACE incidence of 24.4% for the classic crush technique and 11.4% for the DK crush technique ($P=.02$), and the TLR-free survival was 75.4% and 89.5% for the classic crush and DK crush techniques, respectively ($P=.002$).[62] The DK crush II trial compared DK crush and PS, the angiographic restenosis rates of MV (3.8% vs. 9.7%, $P=.036$) and SB (4.9% vs. 22.2%, $P<.001$) were lower for DK crush than PS at 8-month follow-up.[18] Moreover, the TVR rate was 6.5% in the DK crush group, while it was 14.6 in the provisional group ($P=.017$). However, there was no significant difference in terms of MACE.[18] A meta-analysis by Di Gioia et al[63] evaluated 5711 patients treated with 5 bifurcation techniques (provisional, T/TAP, crush, culotte, and DK crush). DK-crush was associated with a lower MACE incidence (OR: 0.39, 95% CI: 0.26-0.55), driven by a reduction in TLR (OR: 0.36, 95% CI: 0.22-0.57). Hence, the DK crush technique is recommended by the EBC as the initial strategy for complex CBLs, especially in patients with unfavorable angle for rewiring after MV stenting.[2,15] In the novel approach, the nanocrush technique allows for fewer stent protrusion in PMV. Rigatelli et al[64] evaluated 52 patients with large complex CBL who underwent nanocrush stenting and reported no death, MI, or TVR at a mean follow-up of 12 months. On the other hand, Morris et al[65] investigated the DK nanocrush technique and reported no adverse events occurred in a follow-up period of 12 months. Ray et al[66] also studied this novel technique in 42 patients in a follow-up period of 24 months. Major adverse cardiac event was noted in 3 patients (7.14%, 1 case of cardiac death at 9 months, and 2 cases of TVR due to in-stent restenosis). However, there is a need for further large-scale randomized trials to investigate the clinical outcomes of these techniques.

Other Techniques

Unfortunately, there are no clinical studies in the literature with strong evidence regarding other techniques including simultaneous kissing stent (SKS), Skirt, and Szabo 2-stent techniques. In 2012, Siotia et al[67] reported the 1- and 2-year results of the largest SKS series in the literature and they treated 150 consecutive, unselected patients with unprotected LMCA (ULMCA) with SKS and technical success was 99.3%. The mortality rate at 1 year was 11.3% and at 2 years was 12.7%. Target vessel revascularization rate was 4.3% at 1 year and 6.2% at 2 years. Skirt technique, so-called the "Y-stenting" technique, was first described in 1996 for lesions of medina 1,0,0, that is, lesions located just proximal to the bifurcation and it has historical importance as it is the first bifurcation stenting technique described in the literature.[68] Ding et al[69] described a modified Y-stent approach via the radial artery that allows the use of a 6 Fr guiding catheter and indicated long-term results of 167 consecutive coronary bifurcation stenting procedures using this technique. At 3-year follow-up, the modified skirt technique had an incidence of 6% cardiovascular mortality, 7% MI, 1% TLR, and 0.6% stent thrombosis.[70]

Ideally, full coverage of the SB osteal between main vessel and SB stents and minimal metallic load with minimal protrusion is desired. Improvement in clinical outcomes has been demonstrated due to the reduction in the incidence of TVR and stent thrombosis in the side branch ostia with the development of double stenting techniques such as mini-crush and TAP stenting, among others. However, considering the developmental stages of the technique, they did not meet the ideal criteria of "full coverage, minimal protrusion, and minimal disruption of stent structure." To overcome these challenging problems, Yang et al[71] have previously described the Szabo 2-stent technique for lesions of the medina 0, 1, 1, and 1,1,1 using the Szabo technique. At 6-month follow-up, no patients developed MACE, TVR, stent thrombosis, and MI. The authors also stated that the Szabo 2-stent technique is suitable for coronary anatomies with bifurcation angle >70˚ and without tortuosity and severe calcification.

Bifurcation Stenting Strategies for Left Main Coronary Artery

Left main coronary artery stenosis has been found in approximately 5%-7% of patients undergoing invasive coronary angiography.[2,15,72] Left main coronary artery-percutaneous coronary intervention is a challenging and important procedure as it supplies a large area of the myocardium. In the DK crush III trial, a total of 419 patients who underwent ULMCA-PCI were randomized to DK crush and culotte.[73] The 1-year MACE rate was higher in the culotte group, mainly driven by increased TVR. The in-stent restenosis rate in the SB was lower for the DK crush technique. Among patients with a bifurcation angle ≥70º, the MACE was significantly lower in the DK-crush group (3.8% vs. 16.5, *P* < .05).[73] At 3-year follow-up, TVR, MI, and MACE were statistically significantly lower in the DK-crush group.[74] The DK crush V study including 482 patients with Medina 1,1,1 or 0,1,1 ULMCA disease who underwent PCI were divided into two groups: provisional or DK crush stenting.[4] During the 1-year follow-up period, in the DK crush V trial, TLF was lower in the DK crush group (10.7% vs. 5.0%, *P*=.02), mainly driven by target vessel MI (2.9% vs. 0.4%, *P*=.03).[4] The rate of stent thrombosis was also lower in the DK crush group (3.3% vs. 0.4%, *P*=.02). Recently, 3-year outcomes of the DKCRUSH-V trial have been published.[75] These results showed that DK crush was associated with a significant reduction in ischemic event-driven (TLF, MI, TVR, definite, or probable stent thrombosis) endpoints for patients with complex lesions or at high risk. In the EBC MAIN trial, PS and 2 stent strategies were randomized (53% culotte, 33% T/TAP, and DK crush 5%).[76] There was no statistical difference (14.7% vs. 17.7%, *P*=.34) for MACE when the 2 randomization arms were compared. The main difference between the EBC MAIN trial and the DK crush V study was that the DK crush stenting was performed only in 5% of cases in the EBC MAIN study depending on the operator's experience. In a recent trial by Rigatelli et al[77], patients undergone ULMCA PCI were evaluated into 2 groups; nanocrush and culotte groups. Over 2-year follow-up period, TLR (0% vs. 12.2%, *P*=.04), MI (3.1% vs. 18.1%, *P*=.03), and cardiovascular death (6.2% vs. 24.2%, *P*=.04) were lower in nanocrush compared to culotte. Recent ESC/EACTS guidelines on myocardial revascularization preferred DK crush stenting over PS for LMCA true bifurcations and IVUS should be considered in ULMCA stenting to optimize the treatment.[78] The key clinical trials in LMCA bifurcation stenting are summarized in Table 3.

Kissing Balloon Dilatation

Provisional Stenting

In COBIS II trial, the impact of final kissing balloon dilatation (KBD) after PS procedure was evaluated in 1901 bifurcation patients with an SB diameter ≥2.3 mm.[43] Post-procedural MLA in MV and SB was found to be higher in 620 patients undergoing final KBD. In the 36th month, the incidence of MACE was lower in the final KBD group (6.8% vs. 8.6%, *P*=.048). In NORDIC III trial, 238 patients with final KBD were compared to 239 patients without final KBD after PS.[45] During the 6-month follow-up period, there were no differences in TVR, cardiac death, MI, and MACE in patients with and without final KBD, respectively. In RAIN-CARDIOGROUP VII study, 1123 patients with final KBD and 1619 patients without final KBD were compared after unprotected LMCA stenting.[44] During 16-month follow-up period, there were no differences in TVR, death, MI, and MACE in patients with and without final KBD, respectively. Contrary to these, Yamawaki et al[46] demonstrated that KB dilatation was associated with a higher incidence of MACE (14.6% vs. 6.9%, *P*=.07) and increased TVR rates (14.6% vs. 5.9%, *P* < .05).

Two-Stent Strategies

In the subgroup of the RAIN-CARDIOGROUP VII study, the incidence of TVR (7.8% vs. 15.9%, *P*=.03) and TLR (7.3% vs. 15.2%, *P*=.032) was lower in patients with final KBD.[44] Additionally, short overlap KBD was associated with lower TLR rates (2.6% vs. 5.4%, *P*=.034). There were no differences in

Table 3. The Key Clinical Trials in LMCA Bifurcation Stenting

Trial	Technique	Follow-Up Period	TLR/TVR	Cardiac Death	MI	TLF [(a)] or MACE
DK CRUSH III[73]	DK crush (210 patients) vs. culotte (209 patients)	12 months	4.3% vs. 11.0%*	1.0% vs. 1.0%	3.3% vs. 5.3%	6.2% vs. 16.3%*
DKCRUSH-III[74]**	DK crush (208 patients) vs. culotte (207 patients)	36 months	5.8% vs. 18.8%*	1.4% vs. 2.9%	3.4% vs. 8.2%*	8.2% vs. 23.7%*
DK CRUSH V[4]	Provisional (242 patients) vs. DK crush (240 patients)	12 months	7.9% vs. 3.8%	2.1% vs. 1.2%	2.9% vs. 0.4%*	10.7% vs. 5.0%*,[a]
DKCRUSH-V[75]**	Provisional (242 patients) vs. DK crush (240 patients)	36 months	10.3% vs. 5.0%*	5% vs. 3.3%	5.8% vs. 1.7%*	16.9% vs. 8.3%*,[a]
EBC MAIN[74]	Provisional (230 patients) vs. 2-stent strategy (237 patients, culotte 53%, DK crush 5%, T/TAP 33%)	12 months	6.1% vs. 9.3%	3.0% vs. 4.2%[b]	10.0% vs. 10.1%	14.7% vs. 17.7%
Rigatelli et al[75]	Nanocrush (32 patients) vs. culotte (33 patients)	27 months	0% vs. 12.1%*	6.2% vs. 24.2%*	3.1% vs. 18.1%*	

MACE, major adverse cardiac events; MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization.
**P* < .05; [a]TLF; [b]Non-cardiac death or all-cause death; **3-year follow-up results.

death, MI, and MACE in patients with and without final KBD. Previously, Grundeken et al[79] evaluated 717 patients who underwent dedicated bifurcation stenting. Cardiac death was found to be lower in patients with final kissing compared to non-final kissing group (1.7% vs. 4.6%, *P*=.017). Besides, in a study by Ge et al[80], a total of 181 patients treated with crush stenting technique were evaluated and divided into 2 groups (with or without final KBD); at 9-month follow-up period, MACE (19.8% vs. 38.5%, *P*=.008), TLR (9.5% vs. 24.6%, *P*=.008), and TVR (10.3% vs. 29.2%, *P*=.002) were lower in patients with final KBD.[80] Final KBD is recommended in all 2-stent strategies. Major clinical studies regarding final kissing balloon dilatation in bifurcation stenting are shown in Table 4.

Proximal Optimization Technique

The EBC strongly recommended final KB dilatation for all 2-stent strategies. Proximal optimization technique reduces the obstruction of SB and makes SB rewiring easier. Chevalier et al[81] studied

Table 4. The Impact of Final Kissing Balloon Dilatation in Bifurcation Stenting

Trial	Technique	Follow-Up Period	TLR/TVR	Cardiac Death	MI	MACE
Provisional stenting technique						
Yamawaki et al[46]	FKB (132 patients, 137 lesions) vs. no-FKB (121 patients, 124 lesions)	3 years	14.6% vs. 5.9%*	0% vs. 1.0%	0% vs. 0%	14.6% vs. 6.9%
NORDIC III[45]	FKB (238 patients) vs. no-FKB (239 patients)	6 months	1.3% vs. 1.7%	0.8% vs. 0%	0.4% vs. 1.3%	2.1% vs. 2.5%
RAIN-CARDIOGOUP VII[44]	FKB (1123 patients) vs. no-FKB (1619 patients)	16 months	5.3% vs. 3.2%	6.1% vs. 6.6%[a]	7.3% vs. 5.3%	15.0% vs. 12.4%
COBIS II[43]	FKB (620 patients) vs. non-FKB (1281 patients)	36 months	5.8% vs. 6.6%	0.6% vs. 1.2%	0.6% vs. 1.8%	6.8% vs. 8.6%*
Two-stent techniques						
Grundeken et al[79]	FKB (607 patients) vs. non-FKB (110 patients)	12 months	4.9% vs. 3.9%	1.7% vs. 4.6%*	6.6% vs. 9.2%	9.2% vs. 10.1%
RAIN-CARDIOGOUP VII[44]	FKB (1123 patients) vs. no-FKB (1619 patients)	16 months	7.3% vs. 15.2%*	6.6% vs. 3.9%[a]	5.6% vs. 6.6%	16.6% vs. 24.9%
Ge et al[80]	FKB (116 patients) vs. non-FKB (65 patients)	9 months	10.3% vs. 29.2%*	1.7% vs. 0%	8.3% vs. 8.6%	19.8% vs. 38.5%*

MACE, major adverse cardiac events; MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVR, target vessel revascularization.
**P* < .05, [a]Non-cardiac death.

the impact of POT on clinical outcomes of bifurcation stenting in 4395 patients who underwent PCI. They reported that POT was associated with a reduction in TLF (4.0% vs. 6.0%, $P < .01$) and stent thrombosis (0.4% vs. 1.3%, $P < .01$). The use of POT (1-3 times depending on the procedure) is also recommended for all 2-stent bifurcation techniques in all appropriate steps. The effect of POT on stent formation was evaluated in a study, which reported that POT led to significant longitudinal stent elongation in both bench test and in vivo evaluation.[82] The examination was performed on 2 different 3.0 and 3.5 mm stent platforms, and it has been shown that each 0.5 mm overexpansion of the stents results in a longitudinal stent elongation of 0.86 ± 0.74 on the 3.0 mm platform and 0.86 ± 0.73 mm on the 3.5 mm stent platform ($P = .71$). Longitudinal elongation of the stents on the 3.0 mm stent platform with 5.5 mm balloon dilatation was 4.31 ± 1.47 mm, and the stents on the 3.5 mm stent platform with 5.5 mm balloon dilation have been shown to elongate to 2.87 ± 0.94 mm. After the evaluation of 36 patients (61% distal LMCA patients), it was reported that stents elongate on average 2.22 ± 1.35 mm relative to their nominal length after 0.98 ± 0.36 mm of overexpansion. Thus, overexpansion by POT results in a longitudinal elongation of the proximal stent part. We are of the opinion that this elongation should be considered carefully, especially in cases of osteal stent implantation.

Bifurcation Lesion with Chronic Total Occlusion

Bifurcation lesions with chronic total occlusion (CTO) tend to have lower procedural success and a higher risk of long-term adverse clinical events due to the complex nature of CBLs. In 2017, Ojeda et al[83] indicated that SB rewire (OR: 0.10, 95% CI: 0.02-0.49; $P < .01$) and non-true CBLs (OR: 0.16, 95% CI: 0.04-0.68; $P < .05$) were associated with procedural success. In a multicenter registry, CBLs were detected in 238 of 922 CTO patients, and the patients were divided into groups including PS and 2-stent strategy,[84] and during follow-up, the incidence of MACE was 8% in the PS group and 10.8% in the 2-stent group. Event-free survival tended to be lower in the 2-stent group (80.1% in the PS group and 69.8% in the 2-stent group; $P = .08$). Insights from the PROGRESS-CTO registry indicated that patients with both proximal and distal CBLs have a higher J-CTO score than the others. Moreover, the technical success rate was lower in patients with both proximal and distal bifurcations.[85] In-hospital MACE, emergency surgery requirement, and pericardiocentesis were also observed at a higher rate in this group. In a study in which 146 patients undergoing CTO PCI were randomized to T-provisional stenting or mini-crush stenting techniques, a trend toward lower MACE rates was observed with T-provisional stenting in patients with a bifurcation away from the CTO lesion. In patients close to the CTO or with a bifurcation in the CTO region, higher MACE was observed in 1-year follow-up with mini-crush stenting (64.9% in T-provisional stenting and 89.1% in mini-crush stenting; $P = .007$). Although long-term clinical events are more common in CBLs containing CTO,[86] complex procedures tend to have negative consequences in terms of long-term MACE.

Future Directions

Dedicated Bifurcation Stents

The major problem with the contemporary 2-stent strategies is the risk of SB occlusion and SB rewiring difficulty.[15] To overcome this problem, some dedicated stents working with different mechanisms have been developed. In the first group, stents are implanted from PMV to DMV and have an aperture to access SB. They also protect the SB ostium from possible carina or plaque shift. Bioss LIM, Xposition Stentys, and Nile SIR are some examples of this stent group.[2] In the second dedicated stent design, the first stent is implanted to SB and then, a second stent is needed for MV treatment. The Capella Side-Guard and Tryton are stents that function with this mechanism.[87,88] Finally, in the third kind of dedicated stent, the first stent is implanted from PMV to the upper carina level. Two additional stents are needed to completely treat DMV and SB. Axxess Plus is the dedicated device of this stent group.[89]

Robotic Bifurcation Stenting

The first human trial of robotic PCI was conducted in 2006 by Beyar et al[90] and included 18 patients, most of whom had non-complex single-vessel lesions. The CORA-PCI study compared manual versus robotic PCI in patients with complex coronary lesions.[91] Although this study is the largest series in this field, CBLs requiring a planned 2-stent strategy were excluded. The robotic-PCI arm of the study had more complex anatomy (lesion complexity score 5.0 ± 2.3 vs. 4.9 ± 2.7, $P = .40$, SYNTAX score 19.6 ± 13.0 vs. 15.7 ± 10.9, $P = .01$), MACE, procedural MI, fluoroscopy time, and stent use; however, there was no statistical difference between the robotic-PCI and manual-PCI arms. Another study evaluated the 6-month and 1-year safety and efficacy of robotic-PCI for complex coronary lesions including bifurcation, and there was no difference between the 2 groups with regard to overall MACE at 6 months or at 12 months.[92] Larger series of data are needed to evaluate the role and ultimate benefit of robotic-PCI for more complex and elective double-stent procedures.[93] However, concerns about the complex procedural nature of robotics-PCI are intrinsically related to current technology limitations.

Artificial Intelligence

Artificial intelligence applications in the field of interventional cardiology are of 2 types: physical and virtual.[94] The physical domain is best represented by robotic interventional procedures as described above. The virtual domain includes informatics and automated clinical decision support systems such as machine learning, deep learning, natural language processing, and cognitive computing to control health management systems.[94] Previously, Macedo et al[95] reported a fully automated method (machine learning algorithms) to detect bifurcations in OCT sequences based on accurate segmentations of all common components of typical OCT images. This automated method can contribute to accurate stent positioning, 3-dimensional visualization, and many other quantitative analysis applications.

Current Guidelines for Coronary Bifurcation Lesions

The EBC has the following expert consensus recommendations[2]:

I. Coronary bifurcation lesions should be characterized using the Medina classification, and stenting procedure should be performed according to the MADS-2 classification.
II. A PS approach should be adopted for most CBLs; however, a 2-stent approach may be preferred for complex lesions with large SB supplying a large coronary territory.

III. Proximal optimization technique should be performed routinely for all BCLs.
IV. In cases where a 2-stent approach is used, lesion preparation should be performed in MV and SB first, and it is mandatory that final KBD is performed with subsequent POT. Optimization of the SB is also strongly recommended for 2-stent strategies as well as double KBD is recommended to avoid SB osteal stent deformation and improve outcomes.
V. A low threshold should be set for intracoronary imaging.

Conclusion

The treatment of CBLs is still challenging despite advanced techniques and novel technologies due to their complex anatomy and lack of a unique treatment approach. Although PS is successful in many non-complex CBLs, there is no standard treatment algorithm for complex CBL interventions as consequence of the complex lesion anatomy, variable operator's experience, and the presence of different 2-stent techniques. However, for LMCA stenting, DK crush stenting is superior to other conventional techniques whether the lesion is complex or not. There is a need for further studies on more up-to-date methods to be included in current treatment algorithms.

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