DOI: https://doi.org/10.3329/cardio.v14i2.58782

Review Article

Percutaneous Coronary Intervention of Bifurcation Lesion

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Key Words : *IHD, bifurcation lesion, PCI.*

Abstract:

Bifurcation lesion whether it is left main (LM) stem disease with left main to left anterior descending artery (LM-LAD) or left main to left circumflex (LM-LCX), LAD-Diagonal or LCX-Obtuse marginal or right coronary artery- posterior descending artery (RCA-PDA); are not uncommon lesion type that needs to be revascularized either by percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) to establish the coronary flow and relieved patient anginal symptoms. Even though, many of the literature maintained non-inferiority of bifurcation lesion PCI over CABG and is Class IIb indication for PCI by coronary stent. In literature, bifurcation lesions commonly encountered in PCI and are regarded as most technically challenging lesions to treat, in up to 20% of PCI cases. With the advent of interventional procedures and the availability of cardiac catheterization laboratory facilities, skilled interventionist, many of the Bangladeshi patients are being treated for coronary artery diseases (CAD). With the advent of drug eluting stents, availability of IVUS (Intravascular Ultrasound), FFR (Fractional Flow Reserve) and individual expertise, treating bifurcation lesion may not be difficult task. Interventionist must be expert enough in doing PCI, before to proceed for bifurcation lesion PCI. We need to work together to develop common consensus in developing updated skill in treating bifurcation lesion which will prove bifurcation PCI in our population.

(Cardiovasc j 2022; 14(2): 168-175)

The incidence of Myocardial infarction (MI) and death from MI is one of the leading causes of death in Bangladesh. Coronary revascularization either by PCI or CABG are the mainstay of treating coronary artery disease (CAD). Individual lesion type, length, tortuosity of the vessel, calcification, presence of thrombus, previous stenting or CABG are the key determinant of procedure related outcome and thus alleviation of angina or dyspnea. Among the different angiographic lesion characteristics, bifurcation lesion especially distal LM with ostial LAD and ostial LCX lesion is predominant and most important complex lesion than compared to LAD-Diagonal or LCX-OM bifurcation lesion. Literature mentioned, Coronary bifurcation lesions are encountered in up 20% of patients undergoing PCI.[1] They are challenging, complex and often encountered in high-risk surgical candidates, such as the elderly frail or those with high SYNTAX scores[2] where bifurcation stenting is the only realistic revascularization. LM bifurcation lesion is the commonest bifurcation PCI among all bifurcation lesion and represents approximately 15% to 20% of PCI.[3,4] PCIs in these circumstances are renowned for being technically challenging and historically have been associated with lower procedural success rates and worse clinical outcomes than when used to treat non-bifurcation lesions. In addition, there has also been a large amount of uncertainty and debate as to the most appropriate strategy when treating bifurcations.

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A proper analysis and classification of both lesions localization at the coronary bifurcation site and the side branch (SB) angulation are crucial in individual PCI technique for the treatment of coronary bifurcation stenosis. Several coronary artery bifurcation lesion (CABG) classification systems have been described in literature.[5-8] Currently the most applied classification of Bifurcation lesion is proposed by Medina[9] et al. which uses binary number system for each branch of bifurcation but does not consider bifurcation angle. Descriptive, intelligible, and ordered (DINO) classification by *Hassan SY*[10] gives information about SB angulation relative to main branch and extent of lesion distribution and its localization.

True distal LM bifurcation lesion may be treated by a single or two stent strategies. A Y-shaped lesion with <60 degree allows easier wire access to SB than a T angle. Precise stent placement at the ostial SB is more difficult in Y-lesion than T-angle lesion. LM-bifurcation (LAD/LCX) often T shaped with 80-degree angulation. Therefore, potential difficulty in rewiring the SB after MB stenting, strategy is an important consideration in selecting the stenting strategy for LM bifurcation lesion. One must keep the procedure simple and safe. Two stent strategies if side branch is >2.5 mm in diameter and > 7 mm in length.[11] Elective unprotected LM stenting is Class IIB recommendation in ACC/AHA guide. A provisional Single stent strategy with T and small protrusion (TAP) is most currently recommended and widely used strategy. Asian bifurcation club pioneering work with double kissing (DK) crush technique that specifically looks at the LM cohort in the DKCRUSH -III study.[12]

Results of randomized trials and observational studies found that PCI is a potential alternative to bypass surgery for patients with unprotected LM coronary artery stenosis.[13] However, PCI for LM bifurcation is technically demanding and has been associated with high rates of adverse clinical events.[14] In addition, a lack of randomized clinical trials focusing on distal LM intervention has often led to uncertainties regarding the optimal stenting strategy. In general, based on non-randomized studies and extrapolations from the results of non-LM bifurcation trials, the provisional one-stent approach has been considered as a preferred strategy over the elective two-stent technique for patients with LM bifurcation disease. In practice, however, two-stent techniques are chosen more frequently for LM bifurcation than for non-LM lesions due to concerns regarding the ischemic myocardial volume, which would be jeopardized by adverse events.[15]

The provisional approach is a single-stent strategy that allows the positioning of a second stent, if required. Like non-LM bifurcations, several studies reported that, compared with two-stent techniques, the provisional one-stent approach for distal LM bifurcation was associated with more favorable outcomes, including lower risks of major adverse cardiac events, death, myocardial infarction, and target vessel revascularization.[16] In addition, the provisional one-stent approach was found to reduce the risk of stent thrombosis. Based on these results, the provisional one-stent approach has been preferred in the treatment of LM bifurcation stenosis with more than 60 % of patients with LM bifurcation in real-world practice treated using the provisional one-stent technique.[17,18]

The European Bifurcation Club (EBC) has endorsed the Medina classification to describe the bifurcation lesions and the MADS (main, across, distal side) classification to describe the various ways to start bifurcation PCI.[19]

The Medina classification[9] consist of three numbers. Within this a score of 1 denotes to >50% stenosis, otherwise a score of 0 is given. The first number is denoting to proximal MV, the second distal MV and third SB. A true bifurcation lesion regarded as 1,1,1; 0,1,1; 1,0,1. It is important to appreciate that Medina classification only provides anatomical location of lesion and not physiological. Studies by using FFR have demonstrated that a negative correlation between the percentage stenosis of the SB after MV stenting as determined by quantitative coronary angiography (QCA); demonstrating that only 27% of lesion deemed significant by QCA are functionally significant.[20]

Coronary Bifurcation Lesion is complex by its anatomy and physiology. It accounts 15-20% of all PCIs.[21] Stenting of bifurcation associated with a high risk of stent thrombosis and restenosis even in the era of drug eluting stent (DES).[22] Coronary bifurcation lesions represents one of the most

technically challenging lesions ion interventional cardiology. Bifurcation lesions are heterogenous with great variation in morphology, plaque distribution, disease extension, and angulation. It is accepted that optimum current strategy in treating bifurcation lesion is main branch (MB) stenting with provisional side branch (SB) stenting.[23,24] Side branch lesions are associated with negative remodeling and seldom longer than 5 mm. SB > 2mm in size are worth wiring since it straightens the angle between the MB and SB and reduces the snow-plow effect.

Side branch pre-dilatation prior MB stenting diminishes the likelihood of SB occlusion, it can also create dissection that may limit SB rewiring. SB suboptimal results after MB stenting may suggest need for SB stenting, patient with jailed wire but patent SB do well and may not need stenting.[24]

Provisional approach (1 stent technique) proved non-inferior to 2 stent techniques,[25] better in terms of periprocedural MI, thus make it as standard strategy of treating bifurcation lesion PCI.[26] There are still lack of evidence of multiple steps of procedures; wiring, predilatation, main vessel (MV) PCI, side branch (SB) proximal optimization, SB ballooning, SB stenting, final kissing ballooning.

Studies showed considerable discrepancy between angiographic stenosis and FFR that less than one-third of angiographically isolated LCX ostia where FFR <0.8. These findings suggest that FFR >0.8 is a strong predictor of favorable survival and low event rate in patient with coronary artery disease including low or intermediate LM Disease.[27,28]

The decision to use a one or two-stent strategy should be made before starting PCI. With a single stent or provisional technique, the MV stent first, then If SB compromised and if it is significant then might be stented with T technique. With a two stent or complex procedure, operator decides if both MV and SB need to be stenting.

Understanding the vessel anatomy and physiology of coronary bifurcation lesions should be the most important goal. The relationship of vessel diameter between branches and anatomical and functional significance of plaque shifts and carina shift are two important concepts to understand. They are the science behind the predictors of SB occlusion, the rationale of proximal optimization (POT).

For better procedural outcome, all routine cases one must analyze the lesion character, proper plan, several techniques have been described in literature. Arrangement of available hardware and bail out if any complication is mandatory. The options for multiple stents include T-stenting, T and protrusion (TAP), which is a modified version of T-stenting, Crush technique, modified T-stenting, Culotte, V-stenting, simultaneous kissing stent technique, Y technique and reverse crush technique.[29-32] This will give comfort to operator but also prevent procedure related cost to patient and thus reduce the possible early or late stent thrombosis.

Lesion preparations are the key factor of procedural success and survival outcome. Specially in case of severe calcification lesion, scoring, cutting balloon or atherectomy or IVL if available can be considered. Sequential balloon inflations or simultaneous kissing balloon inflations can be performed. Jail wire when provisional stenting is chosen to prevent SB occlusion. During pull back of jailed wire one must be care full as it may cause proximal coronary dissection. Jailed balloon should avoid as it may distort the stent during pull out. Stent diameter should always correspond with the distal reference diameter. In appropriate apposition might be solved by POT. Usually, POT should be done with a small NC balloon just proximal to side branch. After POT, flow in the side branch improves. In case of wire recrossing to side branch, this provides more opening of strut and allows wire to recross to SB in case of kissing strategy. DOT can be performed across the side branch in caution so, it may not distort the Carina. Kissing ballooning should be done by non-compliant balloon. For better optimization of SB, high pressure dilatation of SB, followed by MV and finally low-pressure kissing inflation for carina optimization should be done. If patient is stable, downstream lesion should be stented first, since stenting of LM may make opening of downstream lesion more difficult. If not stable, then LM disease should be treated first.[33]

The EBC consensus, states that the provisional approach should be the preferred technique for most bifurcation. However, if there is significant SB ostial disease or if the vessel is particularly

large and supplies a large area of myocardium then complex strategy should be used.[18]

Ideally one stent strategy should be used whenever possible in treating bifurcation lesion. Disadvantage is that SB might be compromised by plaque shift. If this occurs, KB angioplasty can be performed. If results are suboptimal (residual stenosis > 50%, FFR <0.75, dissection is present or there is <TMI 3 flow), side branch should be stented.[29] Kissing balloon (KB) angioplasty or simultaneous inflation of balloons in both branches, is used to avoid plaque shifting to side branch and thus to avoid acute ischemia. With simultaneous KB inflation followed by final KB; restenosis of the side branch may be reduced.[34]

Current Two stent techniques commonly used in distal LM bifurcation lesion PCI include Crush technique, and its variant, culotte and simultaneous kissing techniques. Proper stent techniques depend on patients LM lesion morphology (diameter of two branches, angle of bifurcation, severity of ostial SB stenosis, extent of MV disease and operator discretion).

Crush is a modified version of T or kissing stent technique, in which MV stent crushes the SB stent against MV wall. Classic crush technique is performed by retracting the SB stent 4-5 mm into lumen, followed by crushing by the MV stent.

The mini-crush technique involves minimal (usually 1–2 mm) retraction of the SB stent into the MV before crushing, thus avoiding a large area with three strut layers, and minimizing residual metallic stenosis at the SB ostium.[35]

The double-kissing crush technique, another variant of the classic crush method, includes additional kissing balloon inflation between SB crushing and MB stenting and can further enhance stent apposition and facilitate FKI.

The culotte technique consists of the sequential implantation of two stents into both branches, with the MB stent implanted through the SB stent and protruding into the MB lumen. Consequently, the proximal MB is covered by two overlapping stents. This technique is suitable for all angles of bifurcations and provides near-perfect coverage of the SB ostium. However, it may cause intra-procedural acute closure of the MB after SB stenting, which can be catastrophic during interventions for distal LM disease. Since the proximal double stent layers can lead to delayed reendothelialization and subsequent stent thrombosis, the stents should be overlapped minimally in the proximal MB segment whenever possible. Finally, the distal MB stent at the ostial left anterior descending artery can be under-expanded because of the positioning through the SB stent strut.

A retrospective study compared culotte with T stenting, showed improved MACE (13.3% vs 27.3%, p=0.051) and lower residual stenosis at SB ostium (3.44+7.39% vs 12.55+11.47%, p<0.001).[36] Malapposition leads to an increases risk of late stent thrombosis. Higher rate of mal-apposition within the bifurcation with crush compared to culotte or T /TAP (41.5+8.2%, 31.4+5.2%, 36.7+8.0%). [37]

The simultaneous kissing stent technique consists of the delivery and implantation of two stents, together with a two-barrel metallic carina, in the LM. The main advantage of this technique is that it guarantees the patency of both branches during the procedure and does not require rewiring for FKI. This technique is preferable in narrow-angle bifurcations, where the LM diameter is much larger than the diameters of the LAD and LCX.

Mini crush techniques involve minimal 1-2 mm retraction of SB stent into MB before crushing, thus avoiding a large area with three strut layers and thus residual metallic stenosis at the SB ostium.[35] Mini crush vs. T-provisional techniques in bifurcation lesions met high procedural success with low complication rates and similar major adverse cardiac events long-term outcome. Mini crush techniques have a lower restenosis rate at both main and side branches.[38]

DK crush and mini crush were found to be associated with fewer events and complications compared to the other techniques reviewed, including the provisional approach. Further, Culotte and Crush were associated with an increased risk of stent thrombosis when compared to the provisional approach.[39]

Recently, several dedicated stents for bifurcations have been recently adopted for the treatment of LM disease.[40] These devices offer common advantages over conventional DES to cover the

LM bifurcation segment. The design of these dedicated bifurcation stents and balloons conforms to the natural anatomy of the bifurcation and can facilitate a more effective scaffolding of the SB ostium. Furthermore, these devices provide easier access to the main and side branch which lowers the risk of SB loss during the procedure. Several studies have shown that stenting of LM with these new-dedicated stents is safe and effective both at short and mid-term follow-up.

Stent under expansion is the most important issue in LM bifurcation lesion PCI outcome, as there is potential risk of stent thrombosis and subsequent complications. IVUS guidance LM bifurcation PCI with stent optimization is deem mandated. The best IVUS minimal stent area criteria predicted for angiographic restenosis on a segmental basis were 5.0 mm^2 for LCX, 6.3 mm^2 for LAD ostium, 7.2 mm^2 for POC and 8.2 mm^2 for LM.[41] Stent under expansion is more frequent in two-stent than in single stent group Whatever two stent technique is chosen for the LM bifurcation, achieving sufficient post-stenting cross-sectional are important for favorable clinical outcomes.

Thus, IVUS guidance PCI of LM bifurcation is essential in reducing late thrombosis and subsequent long-term mortality. Optical coherence tomography (OCT) is another imaging tool stent optimization. OCT offers superior resolution and can identify stent malposition, edge dissection, tissue protrusion, thrombus more clearly than IVUS.[42] For OCT imaging, blood must be replaced by iodine contrast to get clear images, evaluation of LM ostium or large LM is often problematic. Although there are no standardized OCT criteria for optimizing stent implantation, particularly for LM bifurcation which hinders the use of this novel imaging modality to guide LM intervention.

Recently, EBC (European Bifurcation Club) Main, has published its trial in the recent past EuroPCR2021. The European Bifurcation Club Left Main (EBC Main) study done on 467 patients in 31 countries with 43 operators. Fewer major adverse events were occurred with a stepwise layered provisional approach than with planned dual stenting. The stepwise provisional strategy should remain the default for distal LM bifurcation intervention. EBC MAIN trial addressed the issue of provisional single stent versus upfront double stenting in 467 patients with true bifurcation distal left main disease.[43]

The multicenter and randomized DKCRUSH-V (Double Kissing Crush versus Provisional Stenting for Left Main Distal Bifurcation Lesions): carried on 482 patients. The DKCRUSH-V Randomized Trial) study showed fewer 1-year TLF after DK crush for UPLMb (Unprotected Left Main Bifurcation) lesions compared with provisional stenting. The study reports the 3-year clinical outcome of the DKCRUSH-V study. Provisional stenting for UPLMb lesions was associated with significantly increased rates of TLF and ST over 3 years of follow-up. Further randomized study is warranted to confirm the benefits of DK crush stenting for complex UPLMb lesions.[44]

EBC main study was superiority trial, found to be negative as many of the operators don't have enough expertise of doing LM bifurcation PCI compared to DK Crush V; IVUS imaging was not done in all cases; in addition POT was lacking. Of note, 22% of patients randomized to a planned single-stent strategy were ultimately treated with two stents.

DKCRUSH-V (n=482), has addressed the same research question, showing better outcomes with an upfront two-stent strategy, more specifically the double-kissing crush (DK CRUSH) technique.

Coronary bifurcation lesion impacts the zone in which the main vessel divides into the main branch and the side branch. Bifurcation lesions represent 20% of all coronary lesions treated with percutaneous coronary intervention (PCI) and are associated with a higher risk of stent thrombosis and restenosis. Current guidelines recommend the provisional technique which involves placing one stent in the main branch and performing balloon angioplasty of the side branch as the primary approach. However, due to anatomical features, patient symptoms, ongoing ischemia, or electrical instability secondary to side branch (SB) compromise, two stent techniques are frequently needed. Multiple anatomical features such as the caliber of the main vessel, caliber of the side branch, calcification, tortuosity, angulation of the side branch, and extension of the disease into the side branch should be considered when selecting what technique to employ. Further, the interventionists preference should be taken in

consideration when selecting the technique to use as he or she must have expertise and confidence in the chosen technique. Although several randomized trials have been performed comparing the various stenting techniques, most studies are rather small, are single center, are underpowered, and do not provide conclusive evidence to support any one bifurcation technique over the others.

Provisional MB stenting or two-stent deployment still debatable. As the potential risk of stent thrombosis in two-stent technique, provisional stenting is recommended as first line strategy in bifurcation lesion. [45] Although provisional stenting has potential risk of side branch occlusion. One must expertise before doing bifurcation PCI as in the EBC Main, many of the operator has experiences with 150 PCI whereas in DK-Crush V most had more than 300 PCI.

Our Perspective:

Bangladesh pioneering its experiences in excellence in treating coronary artery disease more than a decade. Many centers of excellences have established with state-of-the-art interventionist at home and had footprint in international level. Many centers doing complex PCI cases including all types of bifurcation lesion. Primary PCI is in doorstep of every affordable patient. Like primary PCI, Complex CTO PCI, bifurcation lesion PCI is one of the common strategies in treating especially distal LM to LAD and LCX lesion. We need to develop common consensus in treating bifurcation lesion in our population subset. If possible, needs to form a database and guideline in treating bifurcation lesion. This will improve not only the quality but also survival outcome of patient with complex bifurcation lesion with the reduction of MACE in terms of death, MI, restenosis and target lesion revascularization.

Conflict of Interest - None.

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