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Interventions for the Left Main Coronary Artery Disease

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ABSTRACT

The left main coronary artery disease (CAD) is a complex subset of CAD with constantly evolving guidelines in management and treatment. Indications for revascularization and the strategies of revascularization (Percutaneous intervention versus bypass surgery) are the subject of many trials and metanalysis. If percutaneous intervention is planned, meticulous planning and imaging to guide intervention are mandated. Step-wise layered provisional strategy is the treatment of choice with a systematic two-stent strategy reserved for complex bifurcation.

Keywords: Left main, Percutaneous coronary intervention, Bifurcation, Provisional strategy, Two-stent strategy

UPDATE ON LEFT MAIN (LM) CORONARY INTERVENTIONS

About 5–7% of the patients undergoing coronary angiography have LM coronary artery (LMCA) disease.[1] Coronary artery bypass surgery (CABG) has been the treatment of choice for patients with LMCA disease. LMCA percutaneous intervention is challenging and constantly evolving to achieve outcomes comparable to coronary bypass surgery. Second-generation stents, advances in dual antiplatelet therapy, evolution of techniques of percutaneous coronary intervention (PCI), and intravascular imaging led to improved outcomes with PCI.

CURRENT GUIDELINES FOR LMCA REVASCULARIZATION

In European guidelines, CABG is Class I while PCI has Class I indication in patients with Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score ≤22.[2] Patients with SYNTAX scores of 22–32 have a Class IIa and patients with SYNTAX >33 have a Class III recommendation for PCI. In the recently updated 2021 AHA/ACC/SCAI Guideline for coronary artery revascularization, CABG remains a Class I indication to improve survival relative to that likely to be achieved with medical therapy. PCI is a class IIa recommendation in selected patients with low to medium coronary anatomic complexity and LM disease that is equally suitable for surgical or percutaneous revascularization. CABG is recommended over PCI as the choice of revascularization, in patients with significant LM coronary artery disease (CAD) with high-complexity CAD.[3]

EVIDENCE COMPARING PCI WITH CABG

Registry data

An increase in LM PCI by 389% was noted in the nationwide Swedish (SCAAR) registry with a more profound increase in diabetic and male patients. There was a decrease in the 3-year major adverse coronary and cerebral events (MACCE) rate to 35.7% in this all-comer population with increasing use of second-generation stents and intracoronary imaging (48%). Compared to randomized trials, 79% had acute coronary syndromes.[4]

Randomized trials

Updated results of various trials comparing PCI and CABGs have been published. In the SYNTAX trial[5] which included 705 patients with LM disease, there was no significant difference in MACCE (death, myocardial infarction [MI], stroke, and repeat revascularization) at 5 years in the PCI and CABG groups. MACCE with PCI and CABGs was similar in low/intermediate SYNTAX (up to 32) scores but was significantly increased in PCI patients with high scores (≥33). In the SYNTAXES extended survival group, there was no difference in mortality at 10 years in the LM subgroup.[6] In the EXCEL (Evaluation of XIENCE versus CABG for Effectiveness of LM Revascularization) trial,[7] 1905 patients with unprotected LMCA (ULMCA) disease and SYNTAX score ≤32 were randomized to PCI or CABG if clinically and anatomically amenable to both procedures. The primary endpoint, the composite of death from any cause, stroke, or MI at 3 years and 5 years occurred in 15.4% and 22% of patients who underwent PCI and 14.7% and 19.2% of the patients who underwent CABG.[7,8] All-cause mortality was higher in the PCI group though cardiovascular death and MI were not different. Repeat revascularization was higher with PCI as expected. Hence, PCI was deemed non-inferior to CABGs.

Nordic-Baltic-British LM Revascularization Study (NOBLE) trial[9] randomized 1201 patients with significant ULMCA lesions visually assessed stenosis diameter ≥50% or fractional flow reserve (FFR) ≤0.80 and no more than three additional non-complex lesions to PCI or CABG. MACCE (death from any cause, non-procedural MI, repeat revascularization, or stroke) occurred in 28% of PCI patients and 18% of CABG patients (hazard ratio [HR] 1.48; 95% confidence interval [CI]: 1.11–1.98) with CABG being significantly better than PCI. PCI patients had higher rates of MI, revascularization, and stroke compared with CABG patients though mortality rates were similar. Repeat revascularization was higher due to *de novo* lesion and target non-LMCA lesion revascularization. Surprisingly, there was no association between the SYNTAX score and MACCE. Similar findings were noted in the updated 5-year results from the NOBLE trial[10] [Table 1].

Both the EXCEL trial and NOBLE trial enrolled predominantly males. Most patients were clinically at low risk (stable ischemic heart disease and normal ejection fraction). Most of the patients had distal LM disease. Provisional stenting was the default strategy. Imaging was used in approximately 75% of both trials. Despite these similarities, both trials yielded conflicting results.

Sabatine *et al*.[11] in an individual patient data meta-analysis of trials with follow-up of 5 years found no difference in mortality between PCI or CABG but repeat revascularization and spontaneous MI was higher with PCI.

Indications

LM intervention is recommended if LM diameter stenosis is ≥50%, FFR <0.80, and instantaneous wave-free ratio (iFR) <0.89 and intravascular ultrasound (IVUS) <6 mm^2. Coronary physiology is useful for assessing the functional significance of equivocal LMCA lesions. There is a poor correlation between angiography and FFR with an interobserver concordance of only 52% in one study.[12] A meta-analysis of eight trials[13] detected no significant difference in the primary endpoint (all-cause death, non-fatal MI, and revascularization) between revascularized and deferred groups. The rate of revascularization was higher in the deferred group and whether this was due to LMCA intervention was not reported. iFR is comparable to FFR in assessing equivocal LM stenosis with 0.89 as the cutoff value.[14] Deferral of LM PCI when iFR >0.89 is safe.[15] Downstream lesions

Table 1: Randomized Trials comparing PCI versus CABGs in Left main coronary artery disease *P*<0.05.

Trial	Population			Primary end point % (PCI vs. CABG)					
	Patients	Distal LM%	syntax score	Follow-up	MACCE	Death	MI	Repeat revasc	Stroke
Syntax trial	705	61	30	5 years	36.9 versus 31.0	12.8 versus 14.6	8.2 versus 4.8	26.7 versus 15.5	1.5 versus 4.3
				10 years		27 versus 28			
EXCEL trial	1905	80	20	3 years	15.4 versus 14.7	8.2 versus 5.9	8.0 versus 8.3	12.9 versus 7.6	2.3 versus 2.9
				5 years	22.0 versus 19.2	13.0 versus 9.9	10.6 versus 9.1	17.2 versus 10.5	2.9 versus 3.7
NOBLE trial	1201	81	22	3 years	28 versus 18	11 versus 9	6 versus 2	15 versus 10	5 versus 2
				5 years	28 versus 19	9 versus 9	8 versus 3	17 versus 10	

PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass surgery, MACCE: Major adverse coronary and cerebral events, MI: Myocardial infarction, LM: Left main lead to overestimation of LMCA FFR and hence, resting indices may be more useful in such cases.[16] IVUS helps in direct lumen visualization, which is useful in eccentric lesions and contrast streaming. IVUS was given a class IIa recommendation for diagnosing lesion severity in ACC guidelines.[3] IVUS measured minimal luminal area (MLA) of 5.9 mm^2 and a minimum lumen diameter of 2.8 mm correlated with FFR <0.75 with high sensitivity and specificity.[17] Park *et al*.[18] proposed an MLA cutoff of 4.5 mm^2 to predict an FFR ≤0.80 with 77% sensitivity and 82% specificity in Asian populations. A deferral strategy is safe if the IVUS-derived LMCA MLA is >6 mm^2, a cutoff used in the EXCEL trial.

Considerations in the choice of revascularization strategy

Both American and European guidelines recommend a multidisciplinary heart team approach in decision-making. Different risk scores delineate the clinical and anatomic complexity of the LM lesion. MEDINA classification depends on the plaque distribution into the branches with Medina classes 1,1,1; 1,0,1; and 0,1,1 denoting true bifurcation lesions.[19] SYNTAX score reflects the anatomic complexity of CAD with high scores reflecting higher burden and complexity of disease.[20] The SYNTAX score was incorporated into European guidelines. However, in both EXCEL and NOBLE trials, the SYNTAX score did not help predict outcomes. SYNTAX II and SYNTAX 2020 additionally incorporate clinical risk factors to predict 5- and 10-year outcomes of PCI and CABG. The DEFINITION (Definitions and impact of complex bifurcation lesions on clinical outcomes after PCI using drug-eluting stents)[21] criteria are the only specific risk score for LMCA disease. LMCA lesions are classified as simple if side branch (SB) diameter stenosis is <70% and lesion length <10 mm. A complex LM lesion has SB diameter stenosis >70% and lesion length >10 mm or if it satisfies two of the following six minor criteria: (1) Moderate-to-severe calcification; (2) multiple lesions; (3) left anterior descending (LAD)-left circumflex artery (LCX) bifurcation angle >70°; (4) main vessel (MV) reference vessel diameter <2.5 mm; (5) thrombus-containing lesion; and (6) MV lesion length >25 mm. CABG is more dependent on the clinical characteristics of patients rather than anatomic complexity as reflected in EuroSCORE and STS scores.

TECHNIQUE OF LM PCI

Stenting strategy—Provisional versus two stents

European bifurcation club (EBC) 13th consensus[22] recommends a stepwise layered provisional stenting (PS) strategy as the first choice for the majority of patients. This has been reiterated in subsequent EBC consensus documents,[23,24] particularly after the results of the EBC MAIN trial,[25] where similar outcomes were achieved with the PS versus a more complex systematic 2-stent strategy. The provisional approach is preferred in a simple lesion by DEFINITION criteria,[21] small LCX <2.5 mm especially in a right dominant coronary system and a wide angle between LAD and LCX [Figure 1].

The operator must choose a second-generation DES sized to the distal reference diameter to avoid carinal shift and should also consider the maximum expansion capability of the stent. Single-stent crossover from LM into the LAD is the most common approach [Figure 2]. An inverted provisional strategy with stenting from LM toward the LCX is performed in Medina 0,0,1 lesions (ostial LCX lesions).

Proximal optimization technique (POT)

POT is performed after stenting by inflating a short balloon just proximal to the carina, to change the tubular stent to a tapered device fitting the LM and distal MB, respecting the anatomy of the bifurcation.[23] Care must be taken so that at least 6–10 mm of stent length is proximal to the carina. Careful positioning of the balloon for POT is crucial. Ideally, the distal shoulder of the balloon should be placed immediately proximal to the carina, with the proximal shoulder reaching the proximal stent edge.[26] The position of the distal marker compared with the distal shoulder varies among the different balloons currently available. Compliant or noncompliant balloons sized 1:1 to the proximal reference diameter of the LM should be used. POT opposes the stent to LM, reduces the ellipticity of stented segment, and prevents accidental abluminal wiring. POT allows strut protrusion into the SB with a larger strut opening and minimizes carinal shifting for easier guidewire exchange.

Appropriate POT balloon positioning influences the final result. If too distal, it increases the risk of SB occlusion and SB ostial lumen reduction by carina shift. If too proximal, it leads to incomplete expansion of the SB ostium, no stent strut toward the SB, and increased risk of proximal stent edge dissection.[27] Kissing balloon inflation (KBI) in single stent strategy is controversial with conflicting results reported in different trials. In COBIS I registry (Korean Coronary Bifurcation Stenting registry), KBI was associated with a higher MACE rate due to higher target lesion revascularisation (TLR) rather than death or MI.[28] The COBIS II registry KBI reduced MACE and TLR.[29]

Surprisingly, EXCEL trial subgroup analysis revealed no difference in 4-year primary outcome with KBI in both provisional stenting and the two-stent groups.[30] In the RAIN registry,[31] there was no difference in MACE at 16 months in KBI and non-KBI groups in the provisional strategy group but KBI reduce MACE in the two-stent strategy group.

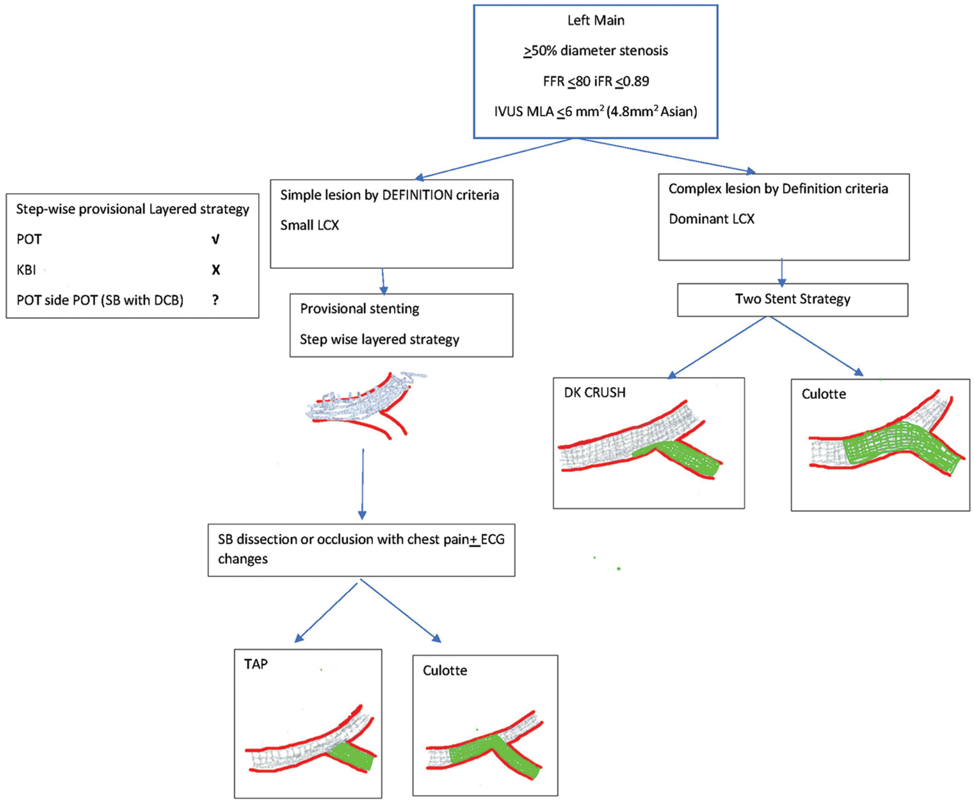

Figure 1: Left Main PCI Techniques

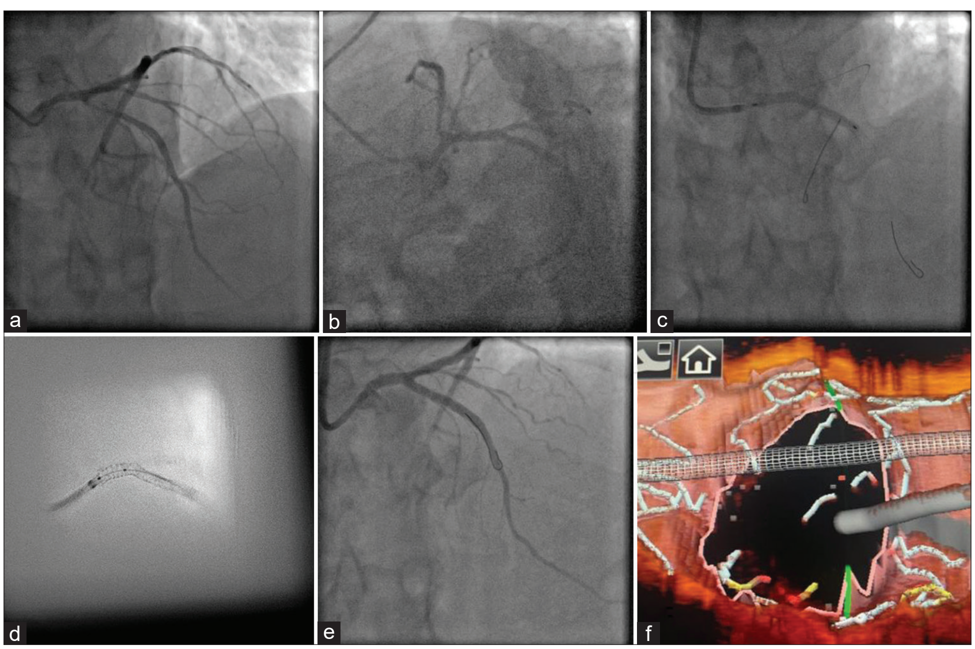

Figure 2: Provisional stenting. (a and b) Left main (LM) diffuse disease and left anterior descending (LAD) ostial 90% stenosis, (c) Cross over stenting LM to LAD, (d) proximal optimization technique, (e) Final result, and (f) optical coherence tomography showing no strut across left circumflex artery.

Furthermore, short overlap KBI (<3 mm) led to less TLR. Proper guidewire cross in the distal cell to optimize SB strut opening, and final POT to correct proximal malapposition are the key steps.[31] In the EBC MAIN trial, KBI was mandated by the protocol in the provisional strategy.[25] Drug-coated balloons in the SB is an emerging technique to further strengthen the concept of provisional stenting but randomized trials are lacking.

Conversion to two-stent strategies

After MV stenting SB intervention is performed in patients who develop ECG changes or ischemic symptoms due to SB compromise. A considerable discrepancy exists between angiographic stenosis (50%) and FFR values.[32,33] FFR-guided PCI strategy to treat the LCX reduces the incidence of unnecessary SB intervention.[34] Low FFR in the jailed LCX was associated with a higher rate of target lesion failure (TLF) at 5 years while angiographic stenosis did not predict clinical outcomes.[35] SB stenting can be performed by T, T and small protrusion (TAP), or culotte techniques. If the wire recrosses through the distal strut, T-stenting or T-TAP is preferred, and if the wire crosses through the proximal strut, culotte stenting is preferred [Figures 3 and 4].

Two-stent techniques

Systematic two-stent techniques are preferred in complex LM lesions according to DEFINITION criteria[21] or true bifurcation lesions (Medina classification 1,1,1 or 1,0,1 or 0,1,1). T/TAP, double kissing (DK) Crush, and Culotte are the commonly used two stent techniques.[27]

DK crush technique

Chen *et al*. modified mini crush as the DK-crush technique.[36]

This technique consists of stenting the SB, completely crushing the SB stent with MV balloon sized 1:1 to the proximal vessel diameter, proximal SB recross, first KBI (FKBI), MV stenting, second SB recross, and second KBI, followed by final POT [Figure 5]. Another key step in the procedure is sequential inflation at high pressure (≥16 atm) with non-compliant balloons followed by simultaneous KBI.[27] First kissing can optimize the distorted SB stent, enlarge the cell of the SB stent, and leave only one layer

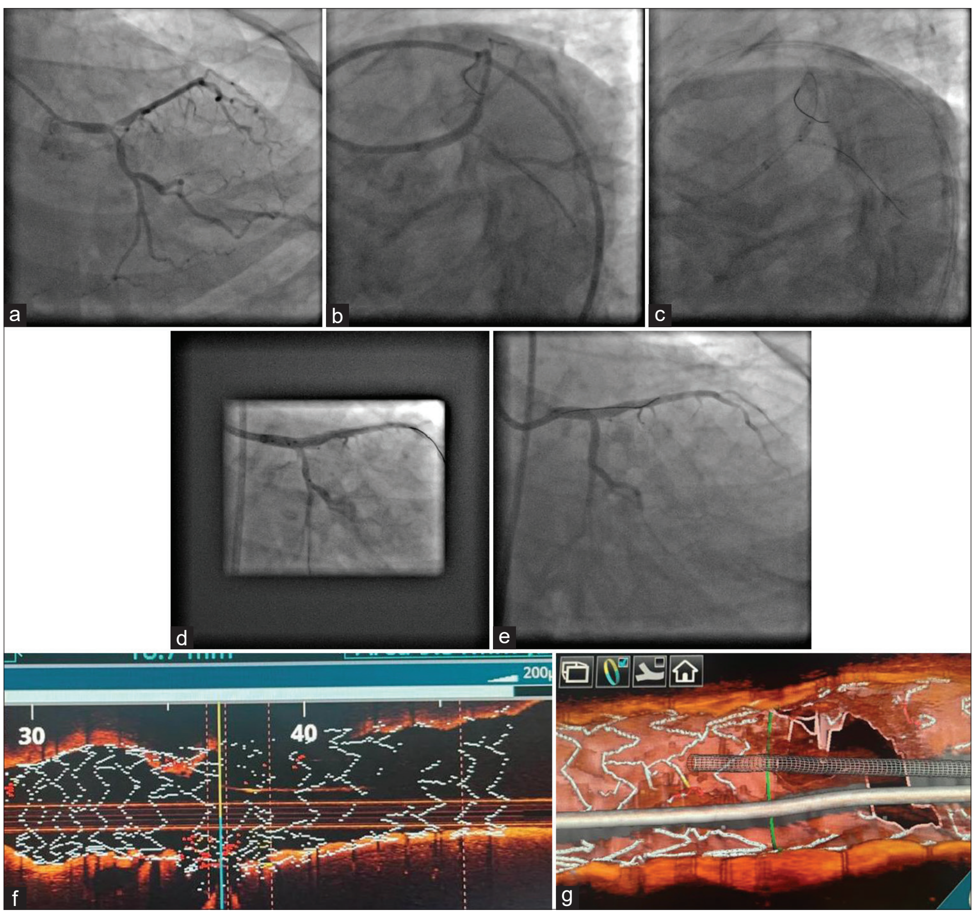

Figure 3: Provisional stenting converted to T and small protrusion (TAP). (a) Left main (LM) Medina 1,1,1 with LCX lesion <10 mm, (b) Post-cross over stenting LM to left anterior descending (LAD), (c) LCX stenosis treated with kissing balloon inflation, (d) LCX dissection treated with TAP stenting, (e) Final result, (f) Optimal stent expansion on optical coherence tomography (OCT), and (g) OCT showing no strut across LCX.

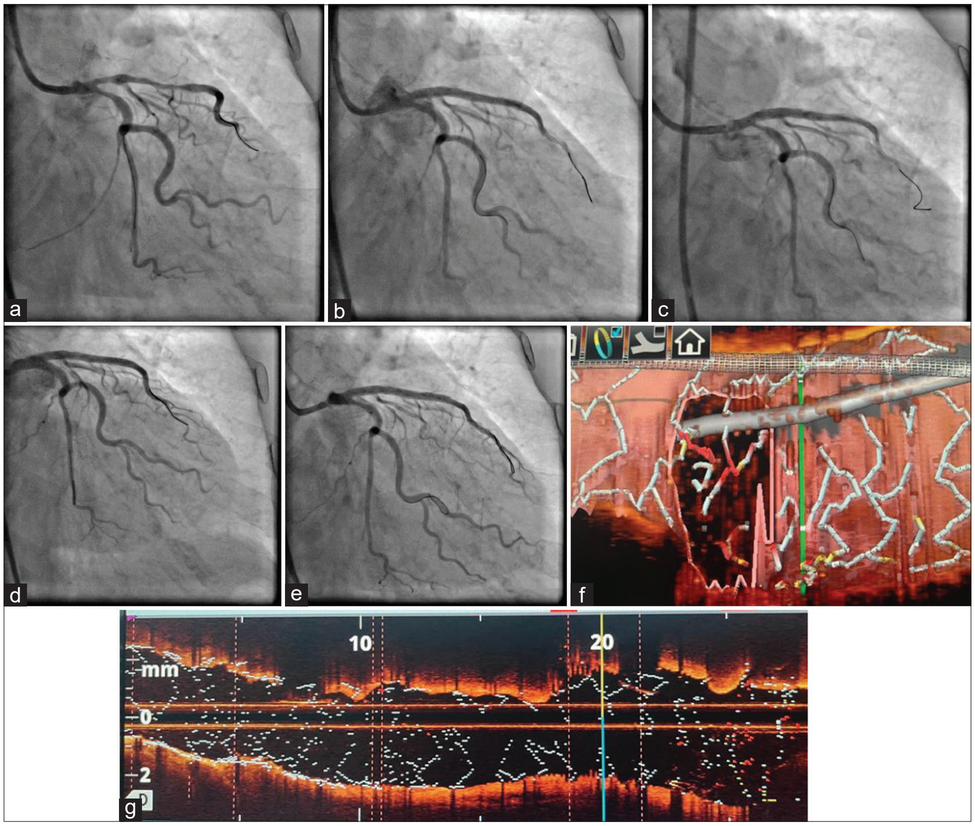

Figure 4: Provisional stenting converted to double kissing Culotte. (a) Left main (LM) Medina 0,1,1 with the left circumflex artery (LCX) lesion <10 mm, (b)Post-cross over stenting LM to LAD, (c) LCX dissection post kissing balloon inflation, (d) LCX dissection treated with Culotte stenting, (e) Final Result, (g) optical coherence tomography (OCT) showing LCX ostium, and (g) Optimal stent expansion on OCT.

of struts at the ostial SB, which probably facilitates the second kissing after stenting the MV. FKBI was successfully performed in 100% of cases by DK crush.

Culotte technique

The Culotte technique has undergone recent evolution into DK-Culotte,[37] and DK-Mini-Culotte,[38] and can be employed as part of a provisional strategy or as a systematic two-stent strategy. Culotte stenting is preferred as part of a provisional strategy when the SB result is unacceptable and the wire recrosses through a proximal strut.[24] In the systematic two-stent strategy MV and SB are wired first. The SB is then ideally stented first. After POT, the MV is then rewired through a distal stent strut and the jailed wire is removed. Stent struts are opened with a balloon, a sequential KBI is performed (DK-Culotte).[38] The MV is stented according to the diameter of the distal vessel. After a further POT, the SB is rewired, and a systematic KBI is made at the bifurcation followed by a final POT. The limitations of Culotte are two overlapping stent layers in LM causing delayed reendothelialization and subsequent stent thrombosis. Disadvantages of Culotte stenting include catastrophic intraprocedural acute closure of the MB after SB stenting and the distal MB stent at the ostial LAD can be under-expanded due to positioning through the SB stent strut.

Provisional strategy (PS) versus systematic two-stent strategy for lm bifurcation PCI

Two major randomized and controlled trials investigated PS versus two-stent approaches in unprotected LM bifurcation PCI. The DK Crush V trial by Chen *et al*., randomized 482 patients with true distal LM bifurcation lesions (Medina 1,1,1 or 0,1,1) to PS ($n = 242$) or DK crush stenting ($n = 240$).[39] Patients were enrolled from 26 centers predominantly from China, but also from Indonesia, Thailand, the United States, and Italy. The primary endpoint of the 1-year composite rate of TLF, cardiac death, target vessel MI, or clinically driven target lesion. Revascularization (TLR) occurred in significantly fewer patients assigned to a planned DK crush strategy (5.0%) versus a provisional stenting strategy (10.7%) (HR: 0.42; 95% CI: 0.21–0.85; $P = 0.02$). At 3 years, the favorable results persisted with TLF occurring in 8.3% in the

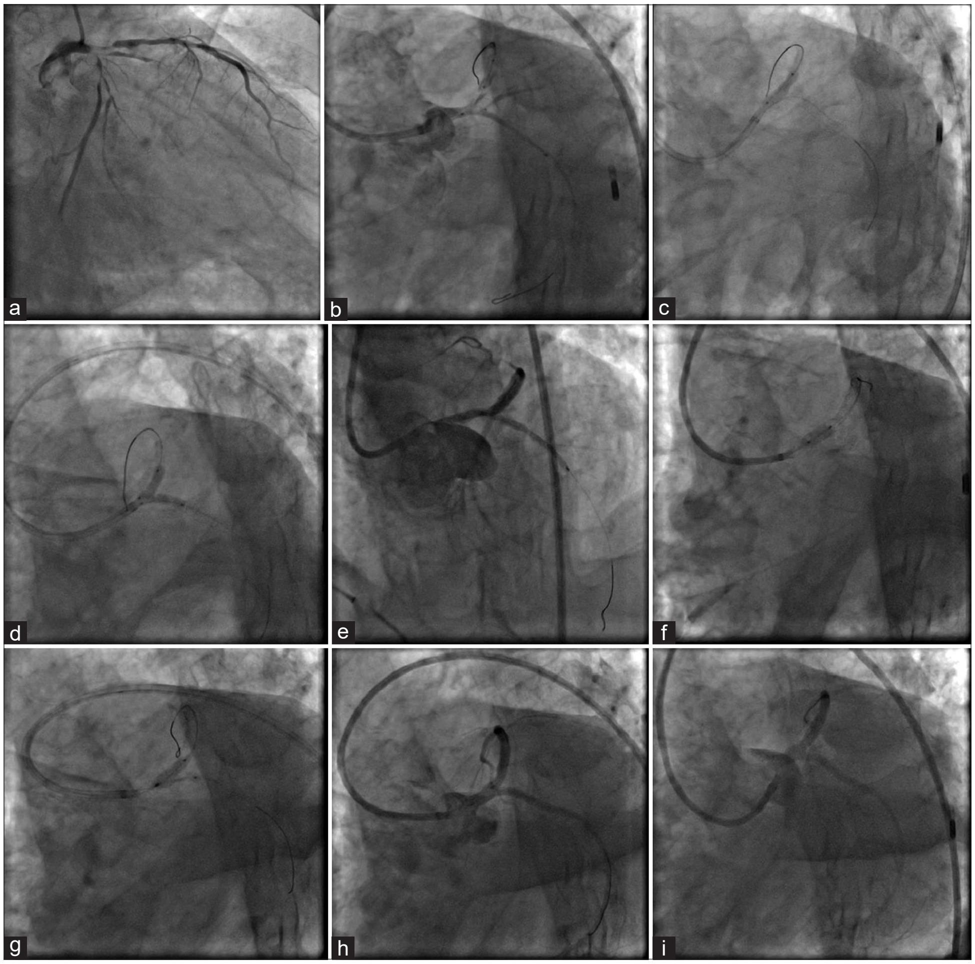

Figure 5: Double kissing Crush technique. (a) Left main (LM) Medina 1,1,1 percutaneous coronary intervention on Intra aortic balloon pump (IABP), (b) stenting left circumflex artery, (c) First crush, (d) First kissing balloon inflation after distal wire recross, (e) Stent LM to left anterior descending second crush, (f) proximal optimization technique (POT), (g) Second KISS, (h) Final POT, and (i) Final result.

provisional group versus 16.9% in the DK crush group.[40] DK Crush strategy also resulted in lower rates of target vessel MI and stent thrombosis.[40] Previously, this same group by Chen *et al.* had demonstrated the superiority of the DK crush technique over culotte stenting in LM bifurcation lesions in the DK Crush III trial.[41]

The EBC main trial randomized a similar number of patients (n = 467) with true LM bifurcation lesions (Medina 1,1,1 or 0,1,1) were randomized 1:1 to a stepwise layered provisional strategy (n = 230) or a systematic two-stent strategy (n = 237) at 31 sites in 11 European countries.[25] There were no differences in the primary endpoint, a composite of death, MI, and TLR at 1 year, which was met in 14.7% versus 17.7% in the provisional and dual stent groups, respectively (HR 0.8, 95% CI 0.5–1.3, P = 0.34), with numerically fewer major adverse cardiac events occurring with a step-wise layered provisional approach. There was a 22% cross-over to a two-stent strategy from provisional. Notably, the only two-stent strategy applied in DK Crush V was indeed the DK crush technique.[39] In EBC MAIN, where the two-stent strategy of choice was left to operator discretion, the predominant upfront two-stent strategy adopted was Culotte (53%), followed by T or TAP (33%), with only a small minority undergoing DK Crush (5%).[27] Equal proportions of Culotte and TAP were observed among the 22% who were randomized to provisional but required a bail-out 2nd stent.[25]

In addition to this geographical variation in two-stent strategy preference, there were differences in lesion complexity between these two pivotal trials: in EBC MAIN, the lesion subset was less complex, with mean Syntax Scores of 23 versus 31 for EBC MAIN and DK Crush V, respectively. Further, SB lesion length in DK crush (16 mm) was also more than double that in EBC MAIN (7 mm). In both trials, however, intravascular imaging was not mandated by protocol, with approximately 40% of each receiving IVUS guidance in PCI.[25,39]

In a recent meta-analysis including 8318 patients comparing different bifurcation techniques found that DK Crush technique was associated with lower MACE compared to provisional stenting and was superior to other two-stent techniques. Two-stent strategy was superior to PS in subgroup with SB length >10 mm.[42]

Intracoronary imaging in the LM PCI

Post-procedure imaging with IVUS has a Class IIa (level of evidence B) recommendation in both the European and American myocardial revascularization guidelines.[2,3] Imaging identifies stent malapposition, dissections, or significant residual disease. Kang *et al*.[43] reported the best IVUS-MSA criteria that predicted angiographic restenosis on a segmental basis included 5.0 mm^2 for the LCX ostium, 6.3 mm^2 for the LAD ostium, 7.2 mm^2 for the polygon of confluence POC, and 8.2 mm^2 for the proximal LM above the POC; 33.8% had under expansion of at least one segment, and angiographic ISR was more frequent in lesions with the under expansion of at least one segment versus lesions with no under expansion (24.1 vs. 5.4%, $P < 0.001$). Analysis of the British Cardiovascular intervention society database of PCI revealed that IVUS use in LM PCI was increasing and was associated with lower 1-year mortality.[44] The benefits of lower MACE with IVUS-guided PCI persisted even at 10 years in the MAIN-COMPARE registry.[45] Meta-analysis[46,47] of trials comparing IVUS-guided with angiography-guided LM PCI consistently demonstrated significantly lower risks of all-cause death, cardiac death, target lesion revascularization, and in-stent thrombosis. Furthermore, de la Torre Hernandez *et al*.[48] showed that achieving protocol-based IVUS optimization criteria yielded additional clinical benefits. In the EXCEl IVUS sub-study the primary endpoint of all-cause death, MI, and stroke was19.4% in the lowest MSA tertile (4.4–8.7 mm^2) compared to 9.6% in the highest MSA tertile (11.0–17.8 mm^2).[49] In the NOBLE IVUS sub-study, adequate stent expansion was not associated with reduced MACCE but reduced repeat revascularization and LM target lesion revascularization.[50] Optical coherence tomography (OCT) has better spatial resolution and provides not only stent apposition parameters but also information on proximal or distal SB wire recross. OCT is comparable to IVUS though long-term data are lacking.[51] Three-dimensional reconstruction of OCT identifies not only the wire cross but also delineates any strut across the LCX ostium needing further treatment. Systematic OCT-guided LM PCI is being evaluated in LEMON study.[52]

CONCLUSIONS

LM PCI is constantly evolving and when done systematically in the hands of experienced operators has comparable outcomes to CABG. Step-wise layered provisional strategy is the treatment of choice in majority of cases with two-stent strategy reserved for complex cases. POT is a crucial step in LM PCI. Intravascular imaging is useful in optimizing outcomes.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. DeMots H, Rösch J, McAnulty JH, Rahimtoola SH. Left main coronary artery disease. Cardiovasc Clin 1977;8:201-11.
2. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, *et al.* 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87-165.
3. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, *et al*. 2021 ACC/AHA/SCAI Guideline for coronary artery revascularization: A report of the American college of cardiology/American heart association joint committee on clinical practice guidelines. J Am Coll Cardiol 2022;79:E21-129.
4. Mohammad MA, Persson J, Buccheri S, Odenstedt J, Sarno G, Angerås O, *et al.* Trends in clinical practice and outcomes after percutaneous coronary intervention of unprotected left main coronary artery. J Am Heart Assoc 2022;11:e024040.
5. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Ståhle E, Colombo A, *et al.* Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. Circulation 2014;129:2388-94.
6. Thuijs DJ, Kappetein AP, Serruys PW, Mohr FW, Morice MC, Mack MJ, *et al.* Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. Lancet 2019;394:1325-34.
7. Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, *et al.* Everolimus-eluting stents or bypass surgery for left main coronary artery disease. N Engl J Med 2016;375:2223-35.
8. Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC,

Puskas J, *et al.* Five-year outcomes after PCI or CABG for left main coronary disease. N Engl J Med 2019;381:1820-30.
9. Mäkikallio T, Holm NR, Lindsay M, Spence MS, Erglis A, Menown IB, *et al*. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): A prospective, randomized, open-label, non-inferiority trial. Lancet 2016;388:2743-52.
10. Holm NR, Mäkikallio T, Lindsay MM, Spence MS, Erglis A, Menown IBA, *et al.* Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: Updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. Lancet 2020;395:191-9.
11. Sabatine MS, Bergmark BA, Murphy SA, O'Gara PT, Smith PK, Serruys PW, *et al.* Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: An individual patient data meta-analysis. Lancet 2021;398:2247-57.
12. Hamilos M, Muller O, Cuisset T, Ntalianis A, Chlouverakis G, Sarno G, *et al.* Long-term clinical outcome after fractional flow reserve-guided treatment in patients with angiographically equivocal left main coronary artery stenosis. Circulation 2009;120:1505-12.
13. Mallidi J, Atreya AR, Cook J, Garb J, Jeremias A, Klein LW, *et al.* Long-term outcomes following fractional flow reserve-guided treatment of angiographically ambiguous left main coronary artery disease: A meta-analysis of prospective cohort studies. Catheter Cardiovasc Interv 2015;86:12-8.
14. De Rosa S, Polimeni A, De Velli G, Conte M, Sorrentino S, Spaccarotella C, *et al.* Reliability of Instantaneous Wave-Free Ratio (iFR) for the evaluation of left main coronary artery lesions. J Clin Med 2019;8:1143.
15. Warisawa T, Cook CM, Rajkumar C, Howard JP, Seligman H, Ahmad Y, *et al.* Safety of revascularization deferral of left main stenosis based on instantaneous wave-free ratio evaluation. JACC Cardiovasc Interv 2020;13:1655-64.
16. Fearon WF, Yong AS, Lenders G, Toth GG, Dao C, Daniels DV, *et al.* The impact of downstream coronary stenosis on fractional flow reserve assessment of intermediate left main coronary artery disease: Human validation. JACC Cardiovasc Interv 2015;8:398-403.
17. Jasti V, Ivan E, Yalamanchili V, Wongpraparut N, Leesar MA. Correlations between fractional flow reserve and intravascular ultrasound in patients with an ambiguous left main coronary artery stenosis. Circulation 2004;110:2831-6.
18. Park SJ, Ahn JM, Kang SJ, Yoon SH, Koo BK, Lee JY, *et al.* Intravascular ultrasound-de- rived minimal lumen area criteria for functionally significant left main coronary artery stenosis. JACC Cardiovasc Interv 2014;7:868-74.
19. Medina A, de Lezo JS, Pan M. A new classification of coronary bifurcation lesions. Rev Esp Cardiol 2006;59:183.
20. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, *et al.* The SYNTAX Score: An angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005;1:219-27.
21. Chen SL, Sheiban I, Xu B, Jepson N, Paiboon C, Zhang JJ, *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;7:1266-76.
22. Burzotta F, Lassen JF, Banning AP, Lefèvre T, Hildick-Smith D, Chieffo A, *et al.* Percutaneous coronary intervention in left main coronary artery disease: The 13th consensus document from the European Bifurcation Club. EuroIntervention 2018;14:112-20.
23. Burzotta F, Lassen JF, Lefèvre T, Banning AP, Chatzizisis YS, Johnson TW, *et al.* Percutaneous coronary intervention for bifurcation coronary lesions: The 15(th) consensus document from the European Bifurcation Club. EuroIntervention 2021;16:1307-17.
24. Lassen JF, Albiero R, Johnson TW, Burzotta F, Lefèvre T, Iles TL, *et al.* Treatment of coronary bifurcation lesions, part II: Implanting two stents. The 16th expert consensus document of the European Bifurcation Club. EuroIntervention 2022;18:457-70.
25. Hildick-Smith D, Egred M, Banning A, Brunel P, Ferenc M, Hovasse T, *et al.* The European bifurcation club Left Main Coronary Stent study: A randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN). Eur Heart J 2021;42:3829-39.
26. Hildick-Smith D, Arunothayaraj S, Stankovic G, Chen SL. Percutaneous coronary intervention of bifurcation lesions. EuroIntervention 2022;18:e273-91.
27. Burzotta F, Lassen JF, Louvard Y, Lefèvre T, Banning AP, Daremont O, *et al.* European Bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. Catheter Cardiovasc Interv 2020;96:1067-79.
28. Gwon HC, Hahn JY, Koo BK, Song YB, Choi SH, Choi JH, *et al.* Final kissing ballooning and long-term clinical outcomes in coronary bifurcation lesions treated with 1-stent technique: Results from the COBIS registry. Heart 2012;98:225-31.
29. Hahn JY, Chun WJ, Kim JH, Song YB, Oh JH, Koo BK, *et al.* Predictors and outcomes of side branch occlusion after main vessel stenting in coronary bifurcation lesions: Results from the COBIS II Registry (COronary BIfurcation Stenting) J Am Coll Cardiol 2013;62):1654-9.
30. Kini AS, Dangas GD, Baber U, Vengrenyuk Y, Kandzari DE, Leon MB, *et al.* Influence of final kissing balloon inflation on long-term outcomes after PCI of distal left main bifurcation lesions in the EXCEL trial. EuroIntervention 2020;16:218-24.
31. Gaido L, D'Ascenzo F, Imori Y, Wojakowski W, Saglietto A, Figini F, *et al.* Impact of kissing balloon in patients treated with ultrathin stents for left main lesions and bifurcations: An analysis from the RAIN-CARDIOGROUP VII study. Circ Cardiovasc Interv 2020;13:e008325.
32. Mortier P, Hikichi Y, Foin N, De Santis G, Segers P, Verhegghe B, *et al.* Provisional stenting of coronary bifurcations: Insights into final kissing balloon post-dilation and stent design by computational modeling. JACC Cardiovasc Interv 2014;7:325-33.
33. Kang SJ, Ahn JM, Kim WJ, Lee JY, Park DW, Lee SW, *et al.* Functional and morphological assessment of side branch after left main coronary artery bifurcation stenting with cross-over technique. Catheter Cardiovasc Interv 2014;83:545-52.
34. Nam CW, Hur SH, Koo BK, Doh JH, Cho YK, Park HS, *et al.*

Fractional flow reserve versus angiography in left circumflex ostial intervention after left main crossover stenting. Korean Circ J 2011;41:304-7.
35. Lee CH, Choi SW, Hwang J, Kim IC, Cho YK, Park HS, *et al.* 5-year outcomes according to FFR of left circumflex coronary artery after left main crossover Stenting. JACC Cardiovasc Interv 2019;12:847-55.
36. Chen SL, Zhang JJ, Ye F, Chen YD, Patel T, Kawajiri K, *et al.* Study comparing the double kissing (DK) crush with classical crush for the treatment of coronary bifurcation lesions: The DKCRUSH-1 Bifurcation Study with drug-eluting stents. Eur J Clin Invest 2008;38:361-71.
37. Toth GG, Sasi V, Franco D, Prassl AJ, Di Serafino L, Ng JCK, *et al.* Double-kissing culotte technique for coronary bifurcation stenting. EuroIntervention 2020;16:e724-33.
38. Hu F, Tu S, Cai W, Jiang Z, Zheng H, Xiao L, *et al.* Double kissing mini-culotte versus mini-culotte stenting: Insights from micro-computed tomographic imaging of bench testing. EuroIntervention 2019;15:465-72.
39. Chen SL, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, *et al.* Double kissing crush versus provisional stenting for left main distal bifurcation lesions: DKCRUSH-V randomized trial. J Am Coll Cardiol 2017;70:2605-17.
40. Chen X, Li X, Zhang JJ, Han Y, Kan J, Chen L, *et al.* 3-year outcomes of the DKCRUSH-V trial comparing DK crush with provisional stenting for left main bifurcation lesions. JACC Cardiovasc Interv 2019;12:1927-37.
41. Chen SL, Xu B, Han YL, Sheiban I, Zhang JJ, Ye F, *et al.* Clinical outcome after DK crush versus culotte stenting of distal left main bifurcation lesions: The 3-Year follow-up results of the DKCRUSH-III study. JACC Cardiovasc Interv 2015;8:1335-42.
42. Park DY, An S, Jolly N, Attanasio S, Yadav N, Rao S, *et al.* Systematic review and network meta-analysis comparing bifurcation techniques for percutaneous Coronary intervention. J Am Heart Assoc 2022;11:e025394.
43. Kang SJ, Ahn JM, Song H, Kim WJ, Lee JY, Park DW, *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;4:562-9.
44. Kinnaird T, Johnson T, Anderson R, Gallagher S, Sirker A, Ludman P, *et al.* Intravascular imaging and 12-month mortality after unprotected left main stem PCI: An analysis from the British cardiovascular intervention society database. JACC Cardiovasc Interv 2020;13:346-57.
45. Kang DY, Ahn JM, Yun SC, Park H, Cho SC, Kim TO, *et al.* Long-term clinical impact of intravascular ultrasound guidance in stenting for left main coronary artery disease. Circ Cardiovasc Interv 2021;14:e011011.
46. Ye Y, Yang M, Zhang S, Zeng Y. Percutaneous coronary intervention in left main coronary artery disease with or without intravascular ultrasound: A meta-analysis. PLoS One 2017;12:e0179756.
47. Wang Y, Mintz GS, Gu Z, Qi Y, Wang Y, Liu M, *et al.* Meta-analysis and systematic review of intravascular ultrasound versus angiography-guided drug eluting stent implantation in left main coronary disease in 4592 patients. BMC Cardiovasc Disord 2018;18:115.
48. de la Torre Hernandez JM, Garcia Camarero T, Baz Alonso JA, Gómez-Hospital JA, Veiga Fernandez G, Lee Hwang DH, *et al.* Outcomes of predefined optimisation criteria for intravascular ultrasound guidance of left main stenting. EuroIntervention 2020;16:210-7.
49. Maehara A, Mintz G, Serruys P. impact of final minimal stent area by IVUS on 3-year outcome after PCI of left main coronary artery disease: The excel trial. J Am Coll Cardiol 2017;69:963.
50. Ladwiniec A, Walsh SJ, Holm NR, Hanratty CG, Mäkikallio T, Kellerth T, *et al.* Intravascular ultrasound to guide left main stem intervention: A NOBLE trial substudy. EuroIntervention 2020;16:201-9.
51. Cortese B, de la Torre Hernandez JM, Lanocha M, Ielasi A, Giannini F, Campo G, *et al.* Optical coherence tomography, intravascular ultrasound or angiography guidance for distal left main coronary stenting. The ROCK cohort II study. Catheter Cardiovasc Interv 2022;99:664-73.
52. Amabile N, Rangé G, Souteyrand G, Godin M, Boussaada MM, Meneveau N, *et al.* Optical coherence tomography to guide percutaneous coronary intervention of the left main coronary artery: The LEMON study. EuroIntervention 2021;17:e124-31.

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