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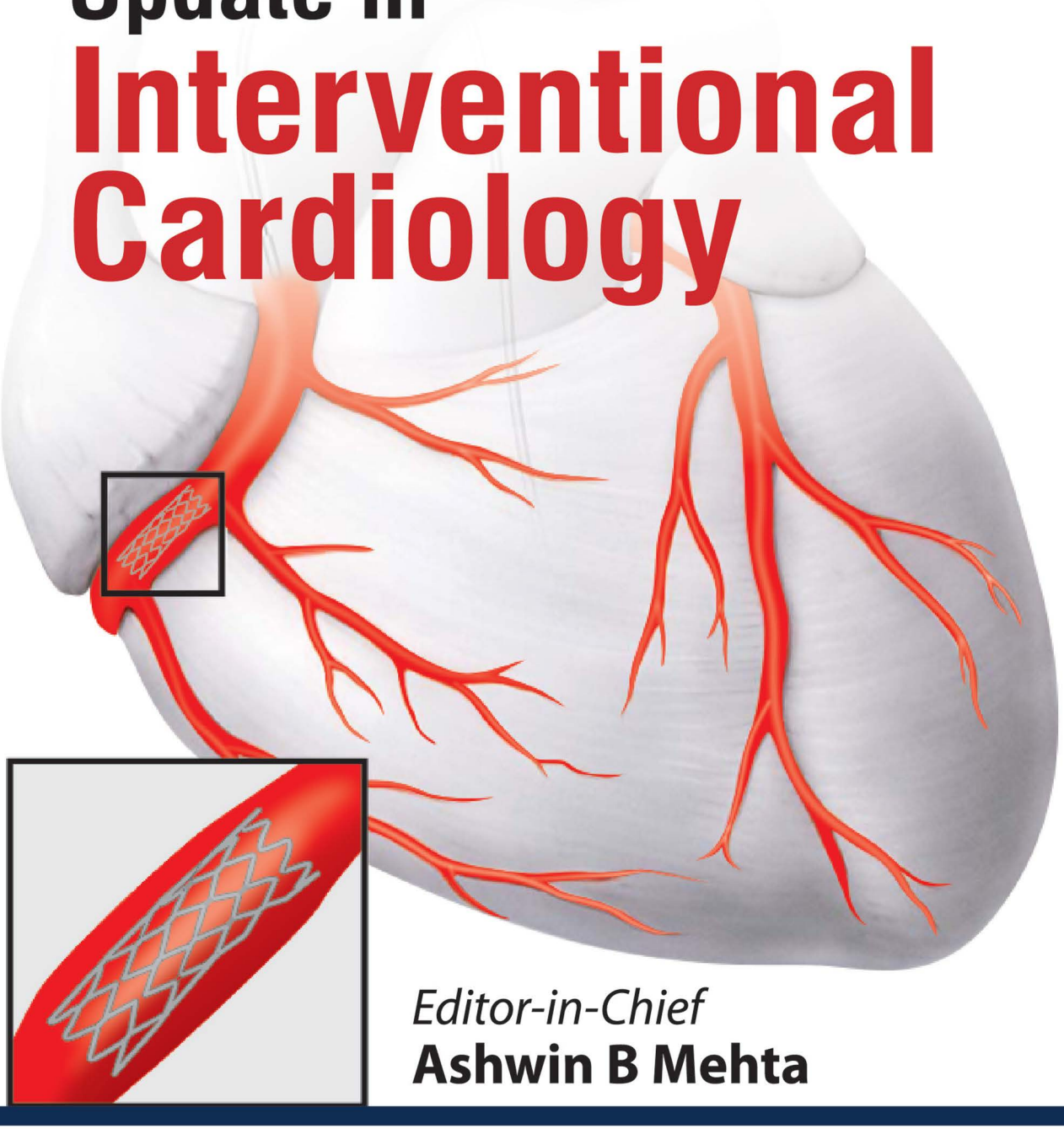
Update in Interventional Cardiology



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4 Left Main Coronary Intervention

Vinay K Bahl, Anunay Gupta

INTRODUCTION

Left main coronary artery (LMCA) involvement is seen in up to 5 % patient in patients undergoing coronary angiography.[1] Inolvement of LMCA is associated with worse prognosis with 50% mortality at three years in patients who are treated medically. LMCA lesion is important clinically as it supplies 100% of myocardium in case of left dominant circulation and around 75% in case of right dominant or balanced circulation.[2] Coronary artery bypass grafting (CABG) has been the standard of care of treatment of LMCA disease. However, recent studies have shown that due to advances in stents technology and use of drug eluting stents, percutaneous coronary intervention (PCI) can be an alternative to CABG. This review highlights the emerging role of PCI in left main disease.

INITIAL EXPERIENCE WITH PCI

Andreas Gruentzig performed first PCI of left main in 1979, however that patient died after four months. Later on it was seen that plain old balloon angioplasty (POBA) alone was associated with poor outcomes in these patients. O Keffe et al. reported 3 years mortality of 64% in patients of LMCA treated with balloon angioplasty. However, later on with development of bare metal stents procedural success rate increased but still over all events rate remain unacceptably high. In a study of 279 patients undergoing left main PCI Tan WA et al reported 1-year incidence of 24.2% for all-cause mortality, 20.2% for cardiac mortality and 9.8% for myocardial infarction.[3]

TRIALS COMPARING PCI WITH CABG

There have been a few randomized control trials which have compared DES with CABG in LMCA disease which are discussed in Table 1.

The Study of Unprotected Left Main Stenting versus Bypass Surgery (LE MANS) was the first randomized controlled trial (RCT) which compared CABG with DES. The primary endpoint of study was change in left

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Table 1: Summary of major RCT comparing PCI with CABG in patients with LMCA disease.

Name	*Number of patients*	*Primary outcome*	*PCI*	*CABG*	*P*
LEMANS 2008	105	Change in LVEF	3.3%	0.5%	0.04
SYNTAX 2009/2014	705	MACE	36.9%	31.0%	NS
PRECOMBAT 2011	600	MACE	8.7%	6.7%	0.01

(MACE: Major adverse cardiovascular events; LMCA: Left main coronary artery; PCI: Percutaneous coronary intervention; LVEF: Left Ventricular efectige graction; CABG: Coronary artery bypass grafting).

ventricular ejection fraction (LVEF) at 12 months and secondary endpoint were major adverse cardiac and cerebrovascular event (MACCE) at 30 days and 1 year. Trial results showed statistically significant improvement in LVEF with patients treated with PCI versus CABG (58% vs. 54%). PCI was also associated with a lower MACCE rate at 30 days (2% vs. 13%), however MACCE were equal at 1 year in the two groups.

The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial is the largest RCT which compared PCI to CABG in patients with LMCA disease. PCI with DES (Taxus) was non-inferior to CABG at one year of follow-up. Five-year follow-up of the trial was published recently which also showed non-inferiority of CABG of PCI vs CABG. Rate of MACE at 5 years were 36.9% in PCI versus 31% in CABG which was statistically not significant. It was seen that when patient were subdivided according to there complexity of coronary anatomy, CABG was found to be superior in complex subsets. When stratified by SYNTAX tertiles (0-22, 22-32, >32), the MACE rates were similar between PCI and CABG in the lower two tertiles; in highest tertile, PCI had significantly higher rate of MACCE.[4]

The Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease (PRECOMBAT) randomized patients with LM disease to first-generation Cypher sirolimus-eluting stents (SES) versus CABG. At 2 years of follow-up rate of MACE were not significantly different between the groups (12.2% for PCI vs. 8.1% for CABG; p = 0.12), however ischemia-driven TVR was significantly more common in the PCI group (9.0% vs. 4.2%; p = 0.02). Similar findings were noted in recently published five-year follow-up.[5]

To summarize, results of above discussed trials conclude that PCI is a possible alternative to CABG in selected subsets of patients. However, these trials have their own limitations such as use of first generation stents and having softer primary end points instead of having harder end points such as mortality.

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In a meta-analysis which was published in 2013, MACE rates were not different between PCI and CABG group up to 5 years as discussed above. However, PCI was associated with a lower rate of stroke and CABG was associated with lower rate of target vessel revascularization (TVR).

ROLE OF IMAGING AND FFR

Newer imaging modalities such as intravascular ultrasound (IVUS) and optical coherence topography (OCT) plays a significant role in performing left main intervention. Angiographic assessment of stenosis of left main is challenging. Fractional flow reserve (FFR) and IVUS helps in such situation to take decision regarding revascularization. Minimum lumen area (MLA) of 6 mm^2 has been set as criteria for revascularization in angiographically indeterminate stenosis. However, in Asian population criteria of MLA 4.5 mm^2 has been proposed.

IVUS remains crucial for assessing the degree of lumen compromise and the extent, distribution, and morphology of plaque. IVUS also helps in assessment post PCI of Left main. IVUS can differentiate between plaque versus carinal shift and stent underexpansion versus malapposition. Stent underexpansion has been a predictor of adverse events post LM stenting. It has been seen that long-term mortality in patients who undergo IVUS-guided LM stenting may be lower compared to those who undergo LM stenting under angiographic guidance alone. OCT have higher resolution than IVUS. However, its penetration is poor. Its use is LM intervention developing, importantly in LM Bifurcation PCI.

FFR is the standard method to assess physiological significance of stenosis. In FAME II FFR guided strategy in Non-LM stenosis improved outcomes. Hamilos et al. evaluated the role of FFR in angiographically indeterminate stenosis. Patients with FFR < 0.80 underwent CABG and FFR > 0.80 received optimal medical therapy. There was no significant difference in 5 years survival estimates between two groups. Hence FFR helps in guiding therapy in patients with indeterminate stenosis.

Key Practical Points

- Adjunctive imaging techniques (IVUS and/or FFR) should be used liberally to assess the underlying significance of ambiguous LMCA lesions on angiography
- IVUS guidance should be strongly recommended as the standard of care during LMCA PCI.

OSTIAL LM PCI

Ostial lesions are usually favorable for stenting. However, few points to be kept in mind while performing PCI are summarized in Box 1.

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Box 1: Tips and tricks for ostial LM PCI.

- AO/RAO cranial views are best to visualize ostium of left main.
- Avoid Amplatz guides
- Keep guide disengaged after wire has been crossed to avoid damage to ostium
- Deploy stent 1-2 mm in aorta and flare it with balloon
- Use IVUS post stenting to ensure optimal results

MANAGEMENT OF LM BIFURCATION

Distal LM lesions are mostly bifurcation lesions involving either Left anterior descending or left circumflex ostium. LM bifurcation can be treated with single or two stent strategy.

Provisional stenting is a single stent strategy which allows placement of second stent if required. In this strategy both the LAD and LCX are wired. LM to LAD is stented. LCX may be or not be treated by final kissing balloon inflation. *Final kissing balloon inflation is must in two stent strategy*. *NORDIC II trial* compared routine final kissing versus no final kissing in patients undergoing provisional stenting. It was seen that there was reduction in angiographic SB restenosis at 8-month follow-up. However, there was no differences in 6-month MACE 2.1% vs. 2.5. But duration of procedure, and contrast use were greater with final kissing balloon inflations.[6] If LCX develops less than TIMI3 flow or patient developed ST/T changes or chest pain or FFR in LCX is less than 0.8, LCX may be stented. After placement of second stent FKBD is must.[4]

Double stent strategy uses either culotte technique, T or the T And Protrusion (TAP) technique, crush stenting or V stenting.

Culotte technique is suitable when angulation of LCX is less than 60° and LCX ostium is diseased. For culotte stenting there should not be more than 1.5 mm difference in vessel diameter between main vessel and side branch. It provides a full coverage of distal LM bifurcation but a significant area of stent overlap.

Crush stenting is preferred when angulation is less than 60 degree and main vessel is larger than side branch. It requires stenting of side branch first with 1-2 mm protrusion in LM which is than crushed by LM to LAD stent. A modification of crush technique is DK crush technique which requires double kissing. In this side branch stent is crushed by balloon instead of stent followed by kissing balloon inflation. First kissing balloon inflation facilitates side branch crossing for final KBI.

V stent technique is used for distal LM bifurcation in which distal LM is not significantly diseased (Medina 0,1,1). Both the stents are simultaneously deployed with minimal protrusion into left main. In *simultaneous kissing*

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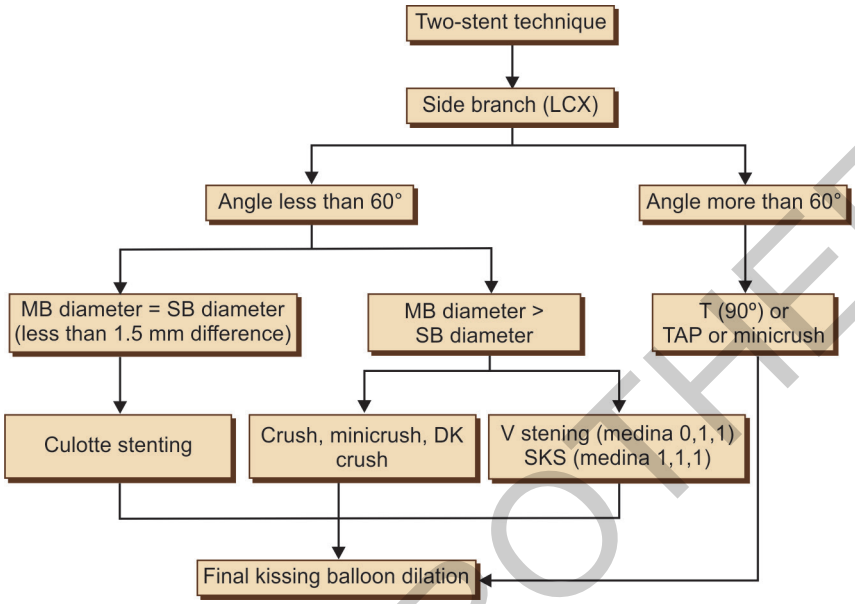
Flowchart 1: Approach to LM bifurcation stenting in two-stent technique.



(MB: Main branch; SB: Side branch).

stent (SKS) technique there is 4-5 mm overlap of stents in left main. SKS is used when distal left main is significantly diseased (Medina 1,1,1). SKS is uncommonly used these days. Flowchart 1 summarizes the approach to LM bifurcation disease.

Key Practical Point

- It is important to remember that when there is no significant lesion in the SB (LCX artery), stenting the LM artery with a jailed wire in the SB followed by provisional T-stenting if required is the most reasonable and successful strategy.

WHAT GUIDELINES SAY?

Latest guidelines of European Society of Cardiology were released in 2014.[7] Table 2 summarizes the management of left main coronary artery disease. Heart team approach is recommended when considering LM revascularization.

ACC/AHA guidelines which were updated in 2011 recommends PCI for LM as Class II A in low syntax score versus ESC/EACTS guidelines which recommends PCI as Class I. Ostial or trunk LM is class IIa and LM bifurcation is recommended as II b irrespective of SYNTAX score.

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Table 2: 2014 ESC/EACTS guidelines for LM revascularization.

	PCI		*CABG*	
	Class	*LOE*	*Class*	*LOE*
LMCA disease with syntax score ≤ 22	I	B	1	B
LMCA disease with syntax score 23-32	IIa	B	I	B
LMCA disease with syntax score >32	III	B	I	B

(LOE: Level of evidence, Modified from 2014 ESC/EACTS guidelines on myocardial revascularization).

RECENTLY PUBLISHED TRIALS

Current recommendations of PCI in LM disease solely rely on subgroup analysis of SYNTAX trial. Two major trials EXCEL and NOBLE whose results were published recently had added both clarity and confusion in LM intervention. Table 3 summarizes both the clinical trials.

The Evaluation of XIENCE Prime or XIENCE V vs. CABG for Effectiveness of Left Main Revascularization (EXCEL) was multicenter RCT enrolling patients with a low or intermediate SYNTAX score (<32) with use of the second generation Xience (Abbott Vascular) DES. The composite primary end point of all-cause death, stroke, or MI at 3 years occurred in 15.4% of patients treated with PCI and in 14.7% of patients undergoing CABG. The difference was significant for noninferiority (p = 0.018); but not for superiority (hazard ratio [HR] 1.00, 95% CI 0.79–1.26; p = 0.98). Authors concluded that PCI may be considered an acceptable revascularization modality for selected patients with LM CAD.[8]

Second major trial was The Nordic-Baltic-British Left Main Revascularization Study (NOBLE) trial. It compared PCI using the bioabsorbable polymer biolimus-eluting BIOMATRIX with CABG patients with LM CAD with ≤3 additional noncomplex lesions. Kaplan-Meier 5-year estimates for MACCE at 5 years were 28.9% for the PCI group and 19.1% for the CABG group. The hazard ratio was 1.48, which exceeded the limit for noninferiority and was significant for superiority for CABG compared with PCI (p = 0.006). Major differences between the two trials include a *lower rate of IVUS use post stent deployment in NOBL*E which might have ntributed to the higher stent thrombosis rates and *use of repeat revascularization as one of the end points* which is softer end point as compared to MI or Death and *81 % of patients in NOBLE* had LM bifurcation disease.[9]

To conclude these two landmark trials provide us enough evidence in management of LM disease but they are unlikely to change current guidelines.

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Table 3: Salient features of EXCEL and NOBEL trials.

Trial design	*Excel*	*Nobel*
	Prospective, multicentre, open label, randomized	
Number of Patients	1905	1200
SYNTAX	<32	Low
Primary end point	Death/MI/CVA	MACE
Follow up	3 years	2 years
IVUS	Recommended	Recommended
FFR	Recommended	Recommended
Stent	EES (Xience)	BES (Biomatrix)
Angiographic follow up	Not recommended	Not recommended
Periprocedural MI	Included	Excluded

CONCLUSION

To summarize left main coronary intervention has evolved from Class III recommendation to Class I recommendation over last one decade. PCI requires careful selection of patients. Heart team approach is must while selecting the patient for LM intervention. Recently published two land mark trials have yielded conflicting results. Still LM PCI should be a suitable alternative to CABG in carefully selected patients. Longer follow-up of these two large trials might add to additional valuable information.

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Update in Interventional Cardiology

This book is intended to provide recent trends and practical approach to interventional procedures in the management of occlusive coronary artery disease. Detailed full reviews of randomized trials are deliberately avoided. Our intention is to provide ability of decision-making in the cath lab on the basis of the most recent data.

In addition, the book also aims at providing practical hints and guidance for achieving success in the procedures and preventing or managing complications with the help of the latest devices. We hope the book will serve its purpose.



Ashwin B Mehta MD FACC, presently the Director of the Department of Cardiology at Jaslok Hospital and Research Centre, Mumbai, Maharashtra, India, is a distinction-holder and a Gold Medalist in 19 various subjects during his MBBS and MD from University of Mumbai. Thereafter, he received specialized training in Cardiology from USA. After returning to India, he introduced various new technologies in India. In 1973, he performed the first Cardiac Catheterization and Angiography in newborn babies in India. In the same year, he was the first to start his Bundle Electrography in India. He also performed the first systematic trial on primary angioplasty in Acute Myocardial Infarction in India.

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