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Lembe Study: Left Main PCI in Belgaum

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Abstract

Objectives: To study left main registry for Indian population, demographic and procedural characteristic of patient outcomes after unprotected left main percutaneous coronary intervention (uLMPC) and identify the predictors of prognosis.

Methods: A total of 109 consecutive patients, who underwent uLMPCI, were analyzed in this single-center registry. All data related to the patient's clinical presentation, procedure and follow-up were collected. Syntax score and medina score were calculated for all patients. Mean follow-up duration of the study was 1 year. Procedural success rate for left main intervention was 100%. Primary endpoint was composite of major adverse cardiovascular and cerebrovascular events (MACCE), including cardiac death (CD), cerebrovascular accident (CVA), myocardial infarction (MI), and need for repeat revascularization and intervention.

Results: There was no primary end point noted in our study. Overall one year MACCE-free survival rate was 100%. Secondary end points were seen in 9 (8.2%). Secondary end point were lower in non diabetic patients who underwent uLMPCI with left main alone intervention, single stent in a vessel. Patients with syntax score ≤ 32 had higher event-free secondary end point rate than those with syntax score >32 . Syntax score >32 was found to be significantly correlated to prior PCI/CABG patients, patients with multiple stenting and multiple vessel stenting. Syntax score >32 was the only independent predictor of adverse outcome.

Conclusion: uLMPCI is safe and effective treatment alternative to CABG in non diabetic patients with selected LM alone, single vessel and single stent patients with low and intermediate syntax score (≤ 32).

Keywords: Coronary artery diease; Left main disease; Left main stenting; Syntax score

Summary

What is already known about this subject?

CABG still remains the procedure of choice for treatment in patients with left main disease (Class I indication). All randomized controlled trials (RCTs), registries and meta-analysis have proved the use and safety of DES, especially in patients with high surgical risk, PCI for ULMCA lesion is a class IIa indication.

What does this study add?

Multiple multicentric studies have been done in the western world but there is very minimal data of uLMPCI in the Indian population. The left main registry for Indian population assessed the demographic and procedural characteristic of patient outcomes after uLMPCI and identifies the predictors of prognosis in Indian subcontinent.

How might this impact on clinical practice?

There is minimal data on uLMPCI in Indian population. The LEMBE study showed uLMPCI is safe and effective treatment alternative to CABG in non diabetic patients with selected LM alone, single vessel and single stent patients with low and intermediate syntax score(≤ 32) in Indian subcontinent. This study will help the clinicians with evidence based decisions for left main diseases in Indians.

Introduction

The incidence of Left Main (LM) Disease is 6% [1]. In view of the large territory of supply, LM interventions have potential for major ischemic injuries and hence remain a huge therapeutic challenge for specialists.

In patients with high surgical risk, PCI for ULMCA lesion is a class IIa indication according to recent guidelines [2]. Various randomized controlled trials (RCTs), [3-6] registries, [7-9] and meta-analysis [10] have proved the use and safety of DES, though CABG still remains the procedure of choice for treatment in patients with high-risk anatomy (Class I indication).

Multiple multicentric studies have been done in the western world but there is very minimal data of uLMPCI in the Indian population. Hence, our objective was to evaluate the demographic features, angiographic variables, predictors of procedural success and one year outcome of uLMPCI with drug-eluting stents (DES) in Indian subcontinent.

Methods

Study population

A total of 109 consecutive patients, who underwent LMPCI between 2006 and 2015, were analyzed in this single-center registry. The study was approved by the Ethical committee of the institution. A written informed consent was obtained prior to the procedure in all patients as per institution protocol. All data related to the patient's clinical presentation, procedure and follow-up were collected. Syntax score [11] and medina score were calculated for all patients.

All patients were pre treated with loading dose of aspirin and clopidogrel/ticagrelor. Unfractionated heparin was administered during the procedure and ACT >250 seconds was maintained intraprocedurally. GpIIb/IIIa inhibiting agents were given at discretion of the operator. Post-procedure, all patients were continued on dual antiplatelets. Other cardiac medication (betablockers and statins) was prescribed post procedure.

All patients were followed up in cardiology outpatient department at 1, 3, 6 months and one year after PCI. Only symptomatic patients were evaluated, first subjected to stress testing and then if required, check angiography.

Endpoints

The primary endpoint of the study was a composite of major adverse cardiovascular and cerebrovascular events (MACCE) which was nonfatal Myocardial infarction (MI), Cardiac death (CD), including Target lesion revascularization (TLR)/Target vessel revascularization (TVR) and any new vessel revascularization or cerebrovascular accident (CVA).

Secondary endpoint was angina in addition to nonfatal Myocardial infarction (MI), Cardiac death (CD), including Target lesion revascularization (TLR)/Target vessel revascularization (TVR) and any new vessel revascularization or cerebrovascular accident (CVA) MACCE.

Definitions

Complete revascularization: Complete anatomic revascularization was defined as treatment of all coronary artery segments >1.5 mm in diameter with ≥ 50% diameter stenosis [12].

Target lesion revascularization (TLR): TLR was defined as repeat intervention of target lesion up to 5 mm segment proximal and distal to stent.

Target vessel revascularization (TVR): TVR was defined as repeat intervention of any segment of coronary vessel proximal or distal to the target lesion, involving its branches and/or target lesion itself.

Cardiac death (CD): Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure- related deaths, including those related to concomitant treatment, will be classified as CD [13].

Myocardial infarction (MI): MI was defined as increase in CPK-MB level of more than three times the upper limit of normal range associated with typical chest pain and fresh ST elevation or new onset LBBB.

Major adverse cardiovascular and cerebrovascular events (MACCE): MACCE was defined as occurrence of nonfatal MI, CD, including TLR/TVR and any new vessel revascularization or cerebrovascular accident (CVA) during follow-up period.

Stent thrombosis (ST): Stent thrombosis was labeled as acute, subacute, late, and very late when event occurred within 24 h, 30 days, <1 year, or >1 year, respectively after procedure. Definite, probable, and possible stent thrombosis was defined according to ARC definition [13].

Statistical analysis

Statistical analysis was done using univariate and multivariate analysis. Chi square testing was used to assess the equality of survival distribution at different levels. p values ≤ 0.05 were considered significant. Demographic, clinical, angiographic, and procedural variables were tested to determine significant ($p<0.05$) univariate correlates of immediate and long-term poor outcomes. Results of multiple variable analyses are reported as hazard ratios with 95% confidence intervals (CI) and p values. Kaplan–Meier survival analysis was used to analyse actuarial survival rates, and a log-rank test was used to compare different survival curves. Kaplan–Meier estimates were used to determine event-free survival (survival with freedom from CD, MI, ST, RI, and CVA). Mean survival time was reported.

Results

Basic demographic profile

A total of 109 patients were included in the study. Mean age of the patients was 58.06 years with 80.7% males and 19.3% females. The major risk factor associated was Hypertension in 58.7% followed by Diabetes mellitus 43.1% and smokers 15.6%. Multiple conventional cardiovascular risk factors were seen in 32.35% patients.

The most common clinical presentation was stable angina in 43%, followed by TMT positive in 33.02%. Non ST Elevation MI and ST Elevation MI were seen in 7.3% and 28.4% patients.

78 (71.5%) had normal Left ventricular (LV) function with LV dysfunction seen in 31 (28.4%) patients, mild (Ejection fraction 50-60%) 9 (8.2%), moderate (Ejection fraction 40-50%) 7 (6.4%) and severe (Ejection fraction<40%) 15 (13.7%).

Baseline characteristics of study group are summarized in Table 1.

Baseline characteristic (n=109)	
Age	58.06
Male	88 (80.7%)
Female	21 (19.2%)
DM	47 (43.1%)
HTN	64 (58.7%)
Current smoking	17 (15.5%)
Prior MI/CABG	17 (15.5%)
Clinical presentation (n=109)	
Unstable angina	47 (43.1%)

NSTEMI	8 (7.3%)
STEMI	31 (28.4%)
TMT+	36 (33.02%)

Table 1: Patients demographics.

Procedural and angiographic characteristics

The decision for unprotected left main intervention for all patients included in the study instead of coronary artery bypass surgery was based upon Syntax score, Heart team unanimous decision and patient refusal for surgery.

All patients underwent Drug eluting stent (DES) implantation, First generation DES in 62.5% (68), second generation in 34.8% (38) and bare metal stent in 2.7% (3).

Ostial LM lesion was seen in 25.6%, mid in 8.2%, and distal LM in 66.05% patients.

Bifurcation lesions were done in 58.4% patients. Medina scoring was done for all bifurcation lesion patients.

LM stenting alone was done in 37.6% with additional vessel stenting done in 62.3%. LM with one additional vessel stenting was done in 49 whereas LM with two additional vessel stenting in 19 patients. Single stent was used in 32 (29.3%) patients with multiple stents (>2 stents) were used in 77 (70.6%) patients.

All procedures were done with 7F/8F catheter, transfemoral route. Rotablation was used in 3.6% patients and IVUS in 9.1% to image the LM pre and post procedure.

Angiographic and procedural characteristics of all patients is summarised in Table 2.

SITE OF LESION	
Ostial	28 (25.6%)
Distal	72 (66.05%)
Mid	9 (8.2%)
NUMBER OF STENTS	
Single stent	32 (29.3%)
Multiple stent (>2)	77 (70.6%)
(a) bifurcation site alone	45/77 (58.4%)
(b) additional site	32/77 (41.5%)
NUMBER OF VESSELS INTERVENED	
Single vessel (LM alone)	41 (37.6%)
Multivessel	68 (62.3%)
(a) LM+1 additional vessel	49
(b) LM+2 or more vessels	19
Guiding catheter size	
7F	51 (46.7%)
8F	58 (53.2%)
Syntax score (n=109)	
<22	70 (64.2%)
22-32	23 (21.1%)
>32	16 (14.6%)
Other procedural details	
Mean stent diameter(mm)	3.81+0.6
Mean stent length(mm)	14.5+7.1
Kissing balloon	75 (68.8%)
Rotablation	4 (3.6%)
IVUS	10 (9.1%)

Table 2: Angiographic and procedural characteristics among patients (n=109).

Procedural and in-hospital outcome

There was no intraprocedural and post-procedural MACCE. Flow limiting dissection was noted in 23 (21%) patients, which were managed with by stent implantation. Minor groin haematoma were seen in 7 (6.4%). Average hospital stay was 3.51 ± 1.2 days.

Follow-up clinical outcome

Follow-up was terminated at the first occurrence of a MACCE (CD, MI, CVA). Asymptomatic patients were followed upto 1 year on outpatient basis(OPD) [13]. (11.9%) patients reported with symptoms. These patients were subjected to stress testing (treadmill testing TMT), 4 reported with TMT positive. Check angiography in all these patients revealed good stent patency with TIMI 3 flow and no instent restenosis. A significantly diffuse disease was noted in other vessels in these patients.

None of the patients had any CD/CVA/Repeat revascularization in hospital at 30 days and at the end of one year.

There was no loss to follow up in the patients.

Predictors of adverse outcome (MACCE)

Syntax score >32, multivessel stenting, and use of multiple stent have been noted to be predictors of MACCE [14]. In our study none of these variables were found to be predictors of primary outcome.

Secondary outcome

It is composite of CD, MI, CVA, and recurrent angina after procedure. A total of 9 patients presented with angina post procedure on follow up. These patients underwent stress testing of which 4 (44.4%) were found to be positive. Check angiography in all these patients showed patent LM stent with TIMI III flow and noncritical disease in other vessels. The non critical disease in the other vessels could be attributed to the positive stres s test.

Predictors of secondary outcome

The 9 patients which presented with recurrent angina, 4 patients undewent coronary angiography .Syntax score >32 was found in 7

(77.7%) and 2 (22.2%) patients had syntax score <32. 75% of the patients with secondary outcomes were found to be diabetics with 25% non diabetics. Diabetes was found as an independent predictor of secondary outcomes of the LM interventions. Kaplan–Meier survival curve in diabetics and non diabetics showed non diabtics with better survival outcome (Figure 1).

High syntax score (>32) was found to have significant corelation with positive TMT, multiple vessel stenting , multiple stents in a vessel and in patients with prior PCI/CABG (Tables 3-6).

		SYNTAX		Total		
		Low & Intermediate	High	p Value	Significance	
Prior PCI/CABG	NO	83 (87.37)	9 (64.29)	92 (84.4)	0.026	Significant
	YES	12 (12.63)	5 (35.71)	17 (15.6)		
Total		95 (100)	14 (100)	109 (100)		

Table 3: Syntax score corelation with prior pci/cabg patients.

		SYNTAX		Total		
		Low & Intermediate	High	p Value	Significance	
TMT	Negative	93 (97.89)	12 (85.71)	105 (96.33)	0.024	Significant
	Positive	2 (2.11)	2 (14.29)	4 (3.67)		
Total		95 (100)	14 (100)	109 (100)		

Table 4: Syntax score corelation with TMT.

		SYNTAX		Total		
		Low & Intermediate	High	p Value	Significance	
Multiple Stents	No	82 (86.32)	1 (7.14)	83 (76.15)	<0.001	Significant
	Yes	13 (13.68)	13 (92.86)	26 (23.85)		
Total		95 (100)	14 (100)	109 (100)		

Table 5: Syntax score correlation with multiple stents in patients.

		SYNTAX		Total		
		Low & Intermediate	High	p Value	Significance	
Multiple Vessels	No	71 (74.74)	2 (14.29)	73 (66.97)	<0.001	Significant
	Yes	24 (25.26)	12 (85.71)	36 (33.03)		
Total		95 (100)	14 (100)	109 (100)		

Table 6: Syntax score correlation with stents in multiple vessels in patients.

Discussion

In this present study we found significant correlation of the secondary end points with diabetes, single or multiple stents and multiple vessel stenting.

Syntax score >32 has been reported to be a predictor of outcomes in left main interventions [14]. Various studies have shown high syntax (>32) to be a predictor for outcome compared to low and intermediate score (<32). In our study we found the same correlation of syntax score with secondary outcomes in left main interventions. Survival curve was better in patients with low and intermediate syntax score compared to high syntax score (Figure 2).

In our study we found a strong correlation between patients with history of prior PCI/CABG with high syntax score ($p<0.01$). Patients who had undergone prior coronary interventions had significant correlation with high syntax score which in turn predicted outcomes of left main intervention (Table 3).

Patients which multiple stents in a vessel, multiple vessel stenting were also found to have significant correlation ($p<0.01$) with high syntax score and thus were predictors of secondary outcomes of left main interventions (Tables 5 and 6).

Patients with syntax score ≤ 32 had higher mean event-free secondary outcomes compared to patients with syntax score >32, Kaplan–Meier curve (Figure 2).

Patients who underwent singe stent implantation compared to patients with multiple stents had better Kaplan–Meier survival curve (Figure 3).

LM alone PCI *vs.* LM plus additional vessels PCI showed Kaplan–Meier curve of event-free survival better in aptients with LM alone PCI (Figure 4).

Numerous trials had been performed between PCI and CABG for left main disease. Among them, four randomized controlled trials (study of unprotected Left Main stenting versus bypass surgery) LEMANS Study, SYNTAX Trial, PRECOMBAT Trial and MAIN COMPARE have proved efficacy of PCI in Left Main disease.

LEMANS Study showed MACCE at 30 days was lower with PCI versus CABG (0.2% *vs.* 13%) and at one year (31% *vs.* 25%). SYNTAX Trial concluded that PCI was not non inferior to CABG for prevention of MACCE. It also concluded that in patients with syntax score of less than 32 PCI and CABG, MACCE was similar at 3 years and in unprotected Left Main disease, but in patients with syntax score of more than 32, CABG was found to be better than PCI of Left Main. PRECOMBAT Study, further reiterated that PCI was non inferior to CABG.

Our study is a single-center registry of ULMCA PCI with drug-eluting stent (DES) in Indian population. The primary outcome of this study was that uLMPCI is safe and effective treatment alternative to CABG in low to moderate-risk anatomy patients (syntax score <32). Patients' selection was done at the discretion of the primary operator after informed consent about the pros and cons in individual cases.

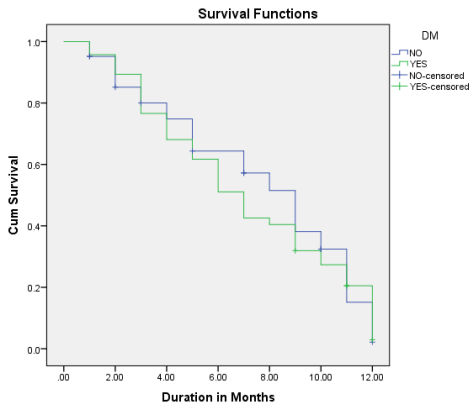

Figure 1: Survival curve in diabetics *vs.* non diabetics

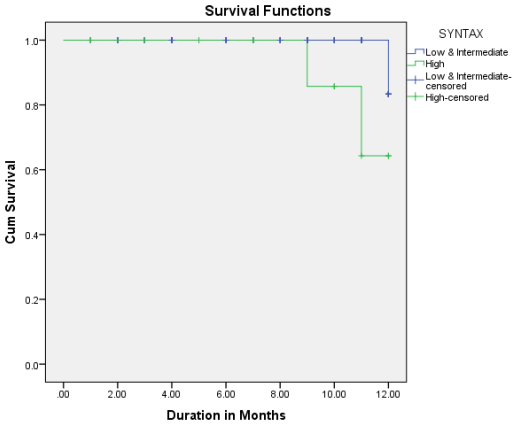

Figure 2: Survival curve in high syntax score *vs.* low and intermediate syntax score.

The high event free survival rate observed in the study may be attributed to selection bias as per the operator. Patients with combination of triple vessel and LM disease were not included in the study. Interventions in LM with involvement of other vessels may have operator bias.

Syntax score being <32 may also be one of the reasons for no primary outcomes of MACCE in our study.

The absence of MACCE at 30 days of follow up which is significant against the PCI arm of LEMANS study (4.8%) 3 may be due to the fact of excluding high risk patients due to operator based selection.

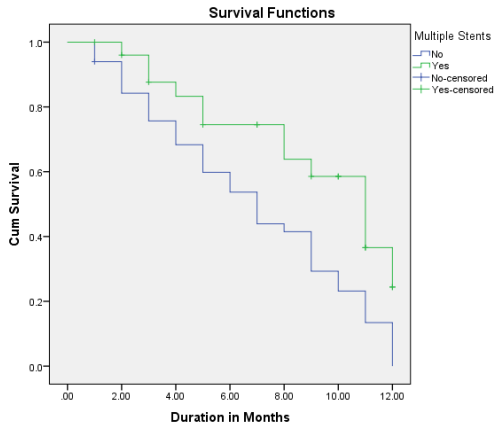

Figure 3: Survival curve in patients with multiple stents.

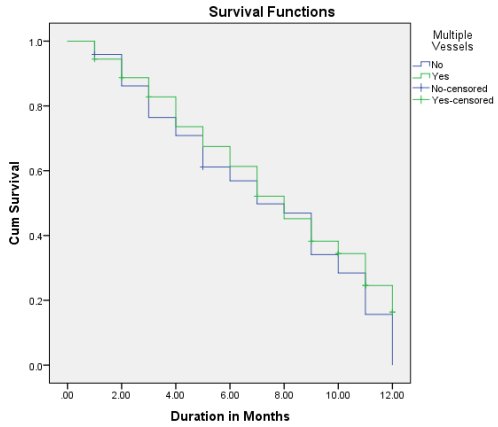

Figure 4: Survival curve in patients with stenting to multiple vessels.

Higher complete revascularization (92%) was achieved in our patients as compared to other studies [3,4,15]. Average hospital stay was also less in our study in comparison to PCI arm of other studies [4].

The one-year incidence of MACCE in our patients was nil, which is lower comparable to PCI arm of SYNTAX trial [4], the study by Buodriot et al. [5], DELFT7 registry and other studies [16]. The higher event rate in these studies may be explained by higher lesion complexity as compared to our population because our mean syntax score was lesser. Mean syntax scores in SYNTAX trial [4] and Boudriot et al. study [5] were 29.6 ±13.5 and 23.5, respectively.

In the recent NOBLE study: 5-Year Risk of PCI *vs.* CABG in Left Main CAD, it showed that CABG was superior to PCI in patients with left main CAD. Comparing PCI with CABG, five-year estimates were 11.6 *vs.* 9.5 percent for all-cause mortality; 6.9 *vs.* 1.9 percent for non-procedural MI; 16.2 *vs.* 10.4 percent for any revascularization; and 4.9 *vs.* 1.7 percent for stroke [17]. EXCEL Study showed that at 5 years, no difference in overall MACCE was found between treatment groups. PCI-treated patients had a lower stroke but higher revascularization rate versus CABG. These results suggest that both treatments are valid

options for LM patients. The extent of disease should accounted for when choosing between surgery and PCI as patients with high SYNTAX scores seem to benefit more from surgery compared to the lower terciles [18].

A lower rate of repeat revascularization may contribute to higher event-free survival rate in our study as compared to other reports. The fact that may be contributing to the better results might be a good case selection with lower mean syntax score which was shown as a predictor of secondary outcome in our study. Our study involved only the indian population compared to the above data which was mainly european patients. There may be racial and ethnic differences in these two population which may contribute to the predictors of outcome of the LM interventions.

Limitation

There are a few limitations in our study.

The study is a single-center experience with multiple primary operators.

There could be a selection bias in patient population.

It is an observational analysis with total number of patients being small.

The use of Intravascular Imaging (IVUS) being was very low in the population which may be attributed to operator discretion.

Conclusion

We conclude that uLMPCI is safe and effective treatment alternative to CABG in non diabetic patients with selected LM alone, single vessel and single stent patients with low and intermediate syntax score (≤ 32).

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