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 (uLMPCI) 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) in Indian subcontinent. This study will help the clinicians with evidence based decisions for left main diseases in Indians.

Keywords: Coronary artery disease; 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 institutional protocol. All data related to 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 levels with ≥50% increase in MB fraction with ≥50% CK-MB fraction.

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 31.85% 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.

<table>
<thead>
<tr>
<th>Baseline characteristic (n=109)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58.06</td>
</tr>
<tr>
<td>Male</td>
<td>88 (80.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>21 (19.2%)</td>
</tr>
<tr>
<td>DM</td>
<td>47 (43.1%)</td>
</tr>
<tr>
<td>HTN</td>
<td>64 (58.7%)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>17 (15.5%)</td>
</tr>
<tr>
<td>Prior MI/CABG</td>
<td>17 (15.5%)</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>47 (43.1%)</td>
</tr>
</tbody>
</table>
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.

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 stress test.

Predictors of secondary outcome

The 9 patients which presented with recurrent angina, 4 patients undrewon coronary angiography. Syntax score >32 was found in 7
High syntax score (>32) was found to have significant correlation with positive TMT, multiple vessel stenting, multiple stents in a vessel and in patients with prior PCI/CABG (Tables 3-6).

### Table 3: Syntax score correlation with prior PCI/CABG patients.

<table>
<thead>
<tr>
<th>SYNTAX</th>
<th>Total</th>
<th>Low &amp; Intermediate</th>
<th>High</th>
<th>p Value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior PCI/CABG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>83 (87.37)</td>
<td>9 (64.29)</td>
<td>92 (84.4)</td>
<td>0.026</td>
<td>Significant</td>
</tr>
<tr>
<td>YES</td>
<td>12 (12.63)</td>
<td>5 (35.71)</td>
<td>17 (15.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>95 (100)</td>
<td>14 (100)</td>
<td>109 (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 4: Syntax score correlation with TMT.

<table>
<thead>
<tr>
<th>SYNTAX</th>
<th>Total</th>
<th>Low &amp; Intermediate</th>
<th>High</th>
<th>p Value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>93 (97.89)</td>
<td>12 (85.71)</td>
<td>105 (96.33)</td>
<td>0.024</td>
<td>Significant</td>
</tr>
<tr>
<td>Positive</td>
<td>2 (2.11)</td>
<td>2 (14.29)</td>
<td>4 (3.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>95 (100)</td>
<td>14 (100)</td>
<td>109 (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>SYNTAX</th>
<th>Total</th>
<th>Low &amp; Intermediate</th>
<th>High</th>
<th>p Value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Stents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>82 (86.32)</td>
<td>1 (7.14)</td>
<td>83 (76.15)</td>
<td>&lt;0.001</td>
<td>Significant</td>
</tr>
<tr>
<td>Yes</td>
<td>13 (13.68)</td>
<td>13 (92.86)</td>
<td>26 (23.85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>95 (100)</td>
<td>14 (100)</td>
<td>109 (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>SYNTAX</th>
<th>Total</th>
<th>Low &amp; Intermediate</th>
<th>High</th>
<th>p Value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Vessels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>71 (74.74)</td>
<td>2 (14.29)</td>
<td>73 (66.97)</td>
<td>&lt;0.001</td>
<td>Significant</td>
</tr>
<tr>
<td>Yes</td>
<td>24 (25.26)</td>
<td>12 (85.71)</td>
<td>36 (33.03)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>95 (100)</td>
<td>14 (100)</td>
<td>109 (100)</td>
<td></td>
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</tbody>
</table>

Discussion

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

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.

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]. 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 populations 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 uLM PCI 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).

References