Original Article

Percutaneous Coronary Intervention (PCI) of Left Main (LM) Stem Disease: Our Experiences in a Tertiary Care Hospital

AHM Waliul Islam[1], Shams Munwar[2], AQM Reza[2], Shahabuddin Talukder[2], Tamzeed Ahmed[2], Azfar H Bhuiyan[3], Kazi Atiqur Rahman[2]

Abstract:

Background: It is well known that coronary artery bypass graft (CABG) is considered as gold standard treatment of left main (LM) stem disease. Over the years PCI of left main (LM) stem disease, proved its non-inferiority to CABG in treating LM stem disease

Objectives: Exact data of LM stem PCI and its procedural success, in-hospital, and post-procedural one-year survival outcome in-terms of repeat hospitalization due to re-infarction, LVF and death, in our population not known clearly. Therefore, we have carried out this prospective observational cohort to see the overall outcomes of LM Stem, PCI in our population

Methods and materials: Patients who underwent elective CAG and found LM stem disease and planned for PCI, were enrolled in this non-randomized observational study between November 2013 to September 2019. Total 146 patient (F 29; Male 117) were enrolled in this study.

Results: Out of 146 patients, female :19.8% (n=29) vs Male: 80.1% (n=117). Among, these patient females were more obese (BMI: Female 29.8 ± 3.6 vs male 26.8 ± 3.8). Male patients were older than female; Male 59 yrs. vs female 56 yrs. Among the CAD risk factors Hypertension (HTN) 67.8% (n=99), dyslipidemia 56.2% (n=82), Diabetes Mellitus (DM) 51.4% (n=75), smoking 31.5% (n=46), Family history of CAD (FH) 21.2% (n=31). In this study, 19.2%(n=28) patient had CABG in the past. Common Stented territories were ostial LM 6.8%(n=10), shaft of LM 28.8% (n=42), distal LM-LAD 47.3% (n=69), distal LM-LCX 15.1% (n=22) and distal LM-RI 2.7% (n=4). Common DES were Everolimus 69.9% (n=102), Sirolimus 12.3% (n=18), Zotarolimus 9.6%(n=14), BMS 4.8% (n=7), Sirolimus with Epithelial Progenitor Cell 3.4% (n=5), and Biolimus 2.1% (n=3). In terms of post procedural dual antiplatelet therapy (DAPT), patients receiving Clopidogrel were 57.5% (n=85), Ticagrelor 28.8% (n=42), and Prasugrel 13.7% (n=20). Total 12 patient died due to acute, sub-acute stent thrombosis or re-infarction with or without arrhythmia. Relook CAG done was only in 14.4% (n=21) patients, Stent patency 80.9% (n=17), significant ISR, later went to CABG 14.3%(n=3) and mild ISR 4.7% (n=1). IVUS guided PCI were done only in 10.9% (n=16) patients. Major adverse cardiac events in terms of periprocedural MI, repeat hospitalization or death were not common in this study.

Conclusion: PCI of LM stem disease is one of the important treatment modalities over CABG in our patient population. Very few patients developed re-stenosis, that needs repeat revascularization either by PCI or CABG. Thus, we may conclude, PCI of LM stem disease might be an alternative to CABG and needs comparative multicenter study to justify its superiority outcome in our patient population.

Key Words: LM, PCI, CABG

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1. Consultant, Interventional Cardiology, Evercare Hospital, Dhaka.
2. Senior Consultant, Interventional cardiology, Evercare Hospital, Dhaka.
3. Specialist, Interventional cardiology, Evercare Hospital, Dhaka.

Address of Correspondence: Prof. Dr. AHM Waliul Islam, Interventional cardiology Department, Evercare Hospitals Dhaka. E-mail: Waliul.islam@evercarebd.com

Introduction:

Coronary artery bypass grafting (CABG) is considered as the gold standard in treating unprotected left main stem coronary artery (LMCA) disease.[1] Whereas percutaneous coronary intervention (PCI) was previously only performed as salvage treatment. Significant benefit

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of LM stem PCI with CABG over PCI and medical treatment shown has been shown in several studies.[2-3] Over the last 20 years, advancement of PCI technique, improvement of stent technology and adjunctive drug therapy has led to progressively improved PCI outcomes for LMCA disease.[4] In addition to different imaging modalities with intravascular ultrasound (IVUS), optical coherence tomography (OCT) and individual operators expertise has improved PCI of ULMCA. ULMCA disease is seen in 5-7% patients undergoing coronary angiography.,[5] 50% mortality those treated medically.[6-7]

Historically, the first reported balloon angioplasty of the LMCA was performed in 1979 by Gruntzig.[8] Later, in 1989, a series of 129 patients' cases were reported,[9] with 10% in hospital and 64% 3-year mortality. By the mid-1990s, development of stenting techniques, DAPT allowed interventionist to do LM stem PCI again. LM stem PCI by BMS characterized high procedural success rate with 17-20% and 10-20% mortality in 1st year.[10-11] The availability of drug eluting stents for the treatment of ULMCA stenosis showed significant reduction of restenosis and target lesion revascularization (TLR).[12-14] Several observational single and multicenter registries showed that PCI of ULMCA by second or third generation DES had a good efficacy and safety profile.

Bangladesh is a densely populated country where death from Cardiovascular disease is number one in all-cause mortality. Many of the centers, with the availability of imaging modalities IVUS, OCT, many of the centers are routinely doing LM stem PCI. There is insufficient data regarding the safety, in-hospital mortality, and morbidity. Therefore, we have carried out this prospective observational study, to investigate the outcome of PCI of ULMCA in our population, a single center experience.

Method:

Materials: Patients who underwent elective CAG and found to have significant LM stem disease and later, percutaneous coronary intervention by deploying drug eluting stent, were enrolled in the observational non-randomized prospective cohort study. Total 146 patient (F 29; Male 117) were enrolled in this study.

PCI Procedures:

LM stem PCI performed by using standard 6F guide catheter, guide wires, balloon catheters and DES via both Femoral and Radial routes. Patients received 5000-unit bolus of heparin, followed by an additional 2000 units during the procedure. Coronary stenting was performed with standard technique with contrast dose left to individual operator discretion. Further, stent optimization was done by post-dilatation whenever required. Successful PCI was defined as a visually assessed 20-30% residual stenosis with TIMI-III distal flow (ref0. After the PCI, patients were shifted to CCU. Patient were pre-loaded with either Ticagrelor or clopidogrel along with Aspirin. Most of the patients received loading and maintenance doses of GP IIb/IIIa receptor blocker abciximab unless any contraindication as a common strategy in our lab.

Statistical Analysis

All data were summarized and displayed as mean ± standard deviation and in percentage of distribution. No statistical comparison was made.

Results:

Total 146 patients were enrolled in this observational prospective cohort study. Among them, 19.8%(n=29) were female vs 80.1% (n=117) were male. Table 1. Shows the demographic profile of studied patient. Among, these patient females were more obese (BMI: Female 29.8 ± 3.6 vs male 26.8 ± 3.8). Male patients were older than females (59 vs 56 years respectively). Fig. 1 shows the distribution of CAD risk factors. Among the coronary artery

Table-I

Demographic Profile of patient

	Male	Female
Number	117	29
Age (yrs.)	59.0±11.0	56.0±14.0
BMI (kg/m^2)	26.8±3.8	29.8±3.6
SBP(mmHg)	125.0±14.8	124.0±17.7
DBP(mmHg)	76.2±8.9	75.0±9.9
No. of CAD Risk Factor	3.0±1.0	2.0±1.0
LVEF %	52.0±8.9	53.6±8.1

Data were presented as Mean±SD

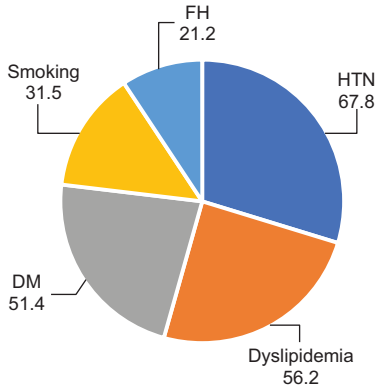


Fig.-1: *Percentage Distribution of CAD Risk Factors*

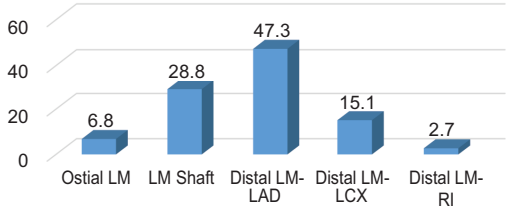
disease (CAD) risk factors for hypertension (HTN) 67.8% (n=99), Dyslipidemia 56.2% (n=82), diabetes mellitus (DM) 75 (51.4%), smoking 31.5% (n=46), family history (FH) 21.2% (n=31). Number of CAD risk factors were more in male, as all smokers in this study were male. In this study, 19.2%(n=28) patient had CABG in the past and not considered as or belong to UPLMCA. Table 2. Shows the average stent diameter according to location for ostial LM and LM shaft 3.7 mm, LM-LAD 3.4 mm, LM-LCX 3.3 mm and LM-RI 2.8 mm., indicating small size coronary vessel in this part of world. LVEF is almost same in both sex; in male 52 vs female 53%. Figure 2. Showed the distribution of lesion in the studied population.

Table-II

Average Size of Stent & Inflation Pressure at each segment of LM

	Diameter (mm)	Length (mm)	Inflation Pressure (ATM)
Ostial LM	3.7±0.4	14.9±5.9	16.0±1.13
LM Shaft	3.7±0.4	15.5±7.4	16.8±2.0
Distal LM-LAD	3.4±0.4	25.9±9.3	17.8±1.9
Distal LM-LCX	3.3±0.4	22.2±6.6	18.2±2.4
Distal LM-RI	2.8±0.7	26.7±8.1	16.5±4.1

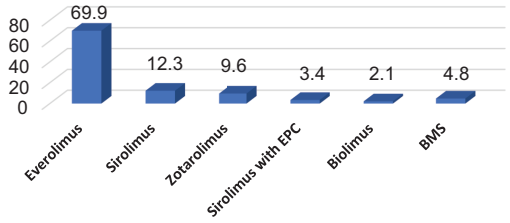
Data were presented as Mean ± SD



Common Stented territories were ostial LM 6.8%(n=10), shaft of LM 28.8% (n=42), distal LM-LAD 47.3% (n=69), distal LM-LCX 15.1% (n=22) and distal LM-RI 2.7% (n=4)

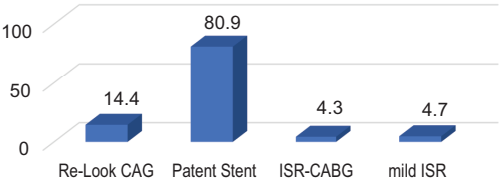
Fig.-2: *Percentage Distribution of Stented Territory of LM*

Common Stented territory were, Ostial LM 6.8% (n=10), shaft of LM 28.8% (n=42), distal LM-LAD 47.3% (n=69), distal LM-LCX 15.1% (n=22) and distal LM-RI 2.7% (n=4). LM-LAD lesion PCI followed by LM shaft lesion are the commonest LM segment lesions stented. Figure 3. Showed the distribution of common drug eluting stents. Common DES were, Everolimus 69.9% (n=102), Sirolimus 12.3% (n=18), Zotarolimus 9.6%(n=14), BMS 4.8%(n=7), Sirolimus with Epithelial Progenitor Cell 3.4% (n=5), Biolimus 2.1% (n=3). Among the P2Y12 inhibitors Clopidogrel were given in 57.5% (n=85), Ticagrelor in 28.8%(n=42), Prasugrel in 20 (13.7%). Total 8.2% (n=12) patient died due to acute, sub-acute stent thrombosis or re-infarction with or without arrythmia. Figure 4. Showed the findings of relook CAG done in a very small percentage of patients i.e., 14.4% (n=21). Among them, stent was patent in 80.9%(n=17), significant ISR, later went to CABG 14.3%(n=3) and mild ISR was found in in 4.7%(n=1). IVUS guided PCI were done only in 10.9%(n=16). Figure 5. Shows distribution of oral anticoagulant, Clopidogrel followed by Ticagrelor an Prasugrel were the commonest used oral P2Y12 inhibitors. Figure 6. Showed percentage distribution of status post CABG or who had CABG in the past were in 19.2%(n=28), IVUS guided PCI were done in 10.9% (n=16) and patient died after LM stem PCI in 8.2% (n=12). Figure 7. Showed IVUS guided LM stem PCI in a patient with 90% stenotic lesion from its distal 2/3rd segment by deploying a 3.5 x 48 mm Everolimus Eluting stents covering the LM ostium to proximal LAD lesion. Figure 8. Showed pre and Post PCI IVUS image of the same patient with well apposed expanded stent in LM stem. Figure 9. Shows PCI of LM-LAD and LCX by kissing (DK crush) technique. After ballooning both LM-LAD and LCX,



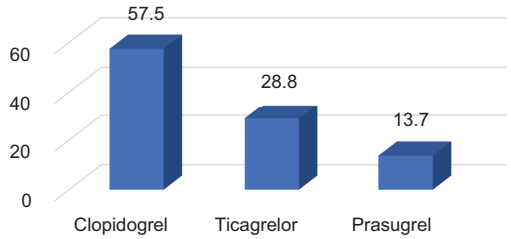
Common DES were Everolimus 69.9% (n=102), Sirolimus 12.3% (n=18), Zotarolimus 9.6%(n=14), BMS 4.8% (n=7), Sirolimus with Epithelial Progenitor Cell 3.4% (n=5), and Biolimus 2.1% (n=3)

Fig.-3: *Percentage distribution of different Drug Eluting Stents used*



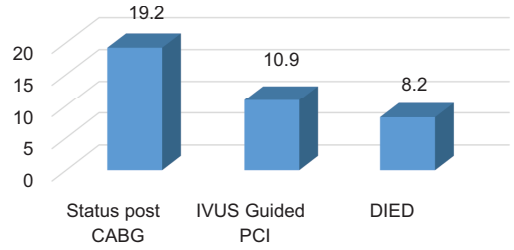
Relook CAG done was only in 14.4% (n=21) patients, Stent patency 80.9% (n=17), significant ISR, later went to CABG 14.3%(n=3) and mild ISR 4.7% (n=1)

Fig.-4: *Percentage Distribution of Re-look CAG in the Studied Patient*



Dual antiplatelet therapy (DAPT), patients receiving Clopidogrel were 57.5% (n=85), Ticagrelor 28.8% (n=42), and Prasugrel 13.7% (n=20)

Fig.-5: *Percentage Distribution of P2Y12 inhibitor as component of DAPT (n=146)*



status post CABG or who had CABG in the past were in 19.2%(n=28), IVUS guided PCI were done in 10.9% (n=16) and patient died after LM stem PCI in 8.2% (n=12)

Fig.-6: *Percentage distribution of SP CABG, IVUS guided PCI and patient died*

Fig.-7: *Showed LM stem lesion PCI in a patient with LM stem Disease*

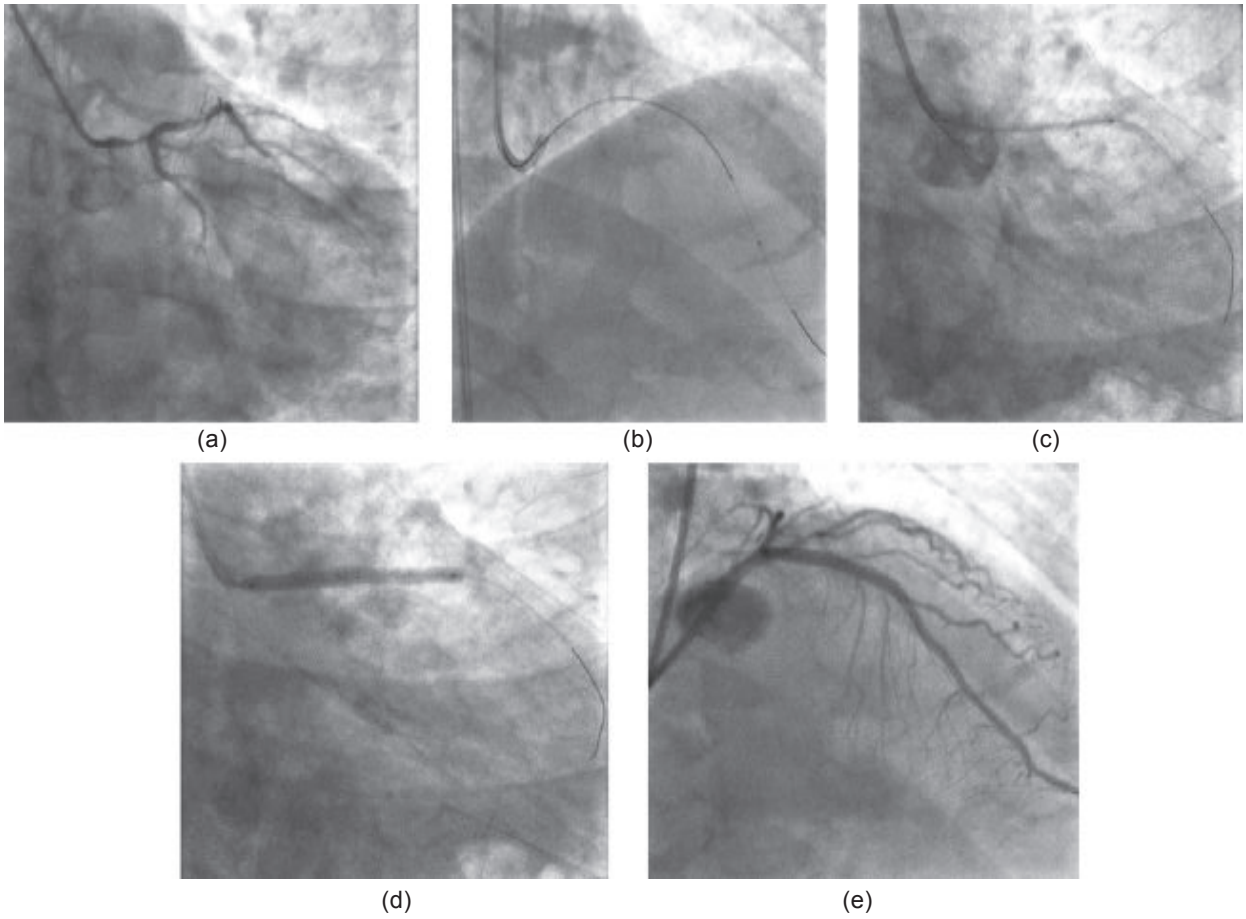
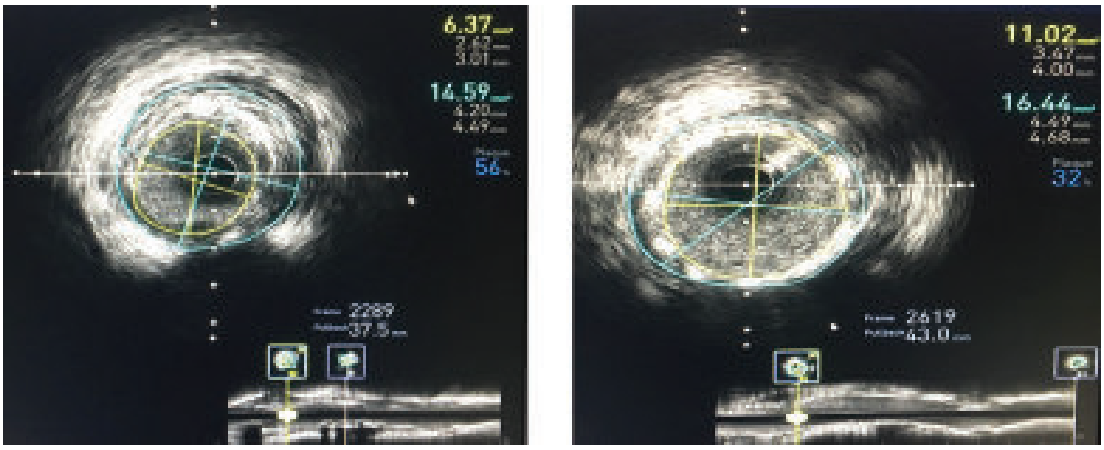


Fig.-7: *(a). 90% distal LM and 70Proximal LAD lesion, (b & c). 3.5 x 48 Everolimus Eluting Stent positioning, (d). Deployment of stent, while JL Catheter tip hanging at LM ostium, (e). Final cine after post dilation by 4.0 x 10mm NC balloon, showed well apposed stent*

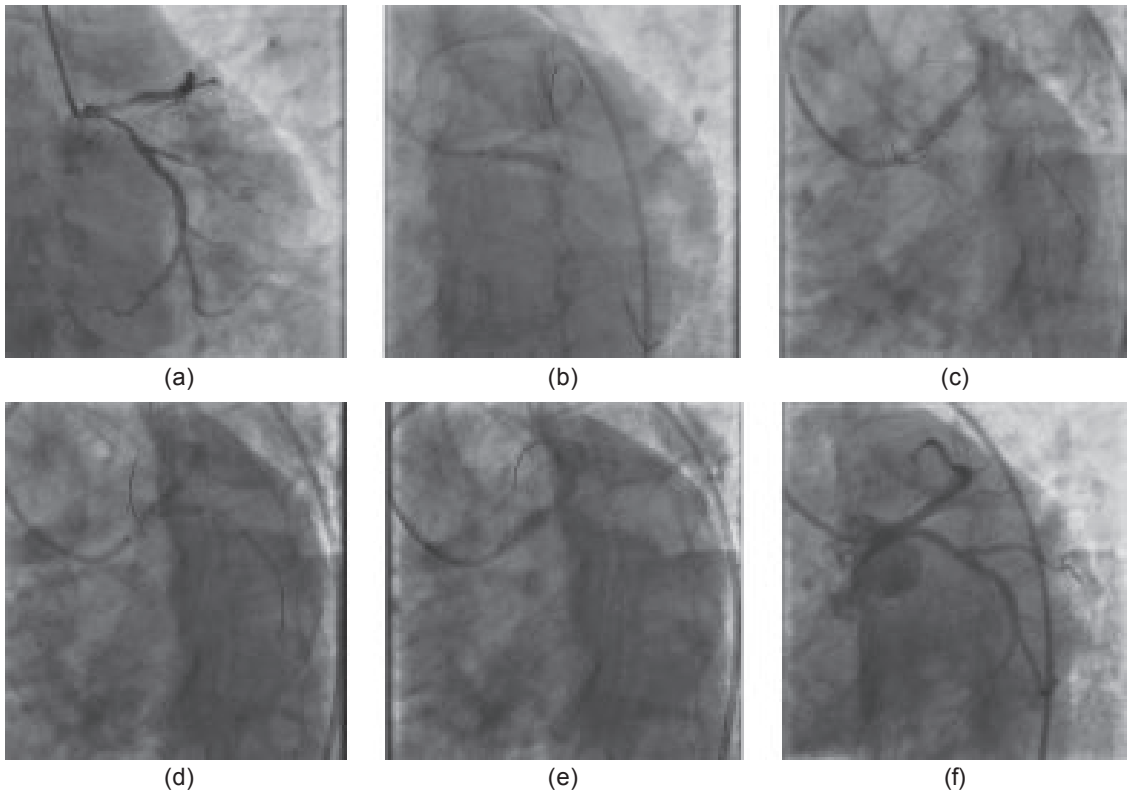
Figure 8. Shows both pre-post PCI IVUS Image of LM stem PCI
Left panel **Fig 8a**; showed Pre PCI IVUS images, showed stenotic lesion, Right Pane **Fig 8b.** post PCI IVUS image; well expanded stent and next one showed with complete apposition of and expansion of stent without edge tear.



(a) (b)

Fig.-8: *a. Pre PCI IVUS image of culprit LM lesion,* ***b.*** *Post PCI IVUS Image of LM Lesion*

Figure 9. Shows PCI of LM-LAD and LCX by Kissing (DK Crush) Technique



(a) (b) (c)

(d) (e) (f)

Fig.-9: *a. 50% distal LM and 90%Proximal LAD and 70% Proximal LCX lesion, b. 3.5 x 15 Everolimus Eluting stent in LCX deployed after kissing balloon, c. LM-LAD stenting by a 4.0 x23 Everolimus Eluting Stent, d. Further Kissing of both stent, e. POT of LM stent by 4.5 x 10 mm balloon at 18ATM, f. Final cine after post dilation by 4.0 x 10mm NC balloon showed well apposed stent.*

Everolimus Eluting 2.5 x 15 mm stent deployed covering the LCX ostium. Then, LM-LAD stenting done by 4 x 23 mm Everolimus eluting stent. Further optimization by kissing ballooning of both stent and POT of LM by a 4.5 x 10 mm balloon at 18ATM done. IVUS was done in LM-LAD which was showed LM-LAD & LCX were well dilated with clear bifurcation area.

Discussion:

With the growing number of cardiac catheterization laboratory facilities and the amount of expertise in the field of interventional cardiology, now a days many of the centers are performing percutaneous interventional procedures throughout the country. Availability of IVUS, OCT imaging facility and imaging physiology study by FFR, aids the needs of interventional procedures like stenting and details study of the lesion characterization and further stent optimization, thus, improving the quality of intervention and reduce the mortality and morbidity. We have carried out this observational prospective non-randomized study of LM stem PCI at our tertiary care center.

The *LMCA is responsible* for *supplying* about *75%* of the *left ventricular* (LV) *cardiac* mass in patients with *right dominant* type and 100% in the case of *left dominant* type. As a result, significant LM stem stenosis either, ostial, in shaft or distal segment disease will reduce flow to large portion of myocardium, thus may place patient at high risk for life threatening events of LV dysfunction or life-threatening arrhythmia. As we know, atherosclerotic lesion tends to occur where flow is disturbed specially in area of low shear stress.[15] In LMCA bifurcation, intimal atherosclerosis is accelerated in low shear stress area in lateral wall close to LAD/ LCX bifurcation.

Coronary artery bypass graft (CABG) or percutaneous coronary Intervention (PCI) are the well-known modalities in revascularizing the LM stem disease. Although, it is debatable, the superiority of CABG and PCI, and guideline recommendation has been updated time to time. Recent comparative studies of PCI and surgical revascularization for unprotected LM Stem PCI, demonstrated that PCI may be an alternative to CABG in treating ULMCA.[16] Clinical outcome may vary according to LM lesion site and complexity. Specially, disease of distal LM bifurcation increases PCI related complexity and is associated with worse clinical outcome compared to ostial LM or shaft segments.[17-18] Non-distal LM stem PCI is associated with favorable clinical outcomes.[19] Simple bifurcation lesions treated with one stent strategy more favorable than complex lesion treated with two-stent approach.[20-21] High plaque burden, patients with distal ULMCA PCI with two-stent approach showed TLR 25% with restenosis. two stents technique either crush, culotte, V- or T-stenting are mostly operator driven.

In the early era of DES, several randomized clinical trials, suggested that PCI achieved similar mortality and composite outcomes, more repeat frequent revascularization in PCI and frequent stroke in CABG.[21] These trials have been adequately powered or have included second generation DES with better safety and efficacy profile compared with first generation DES.[22] The EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Graft Surgery for Effectiveness of Left Main Revascularization) trial and the Noble (Nordic Baltic British left main revascularization study) trial are notable clinical trial on revascularization of LM stem disease. Excel found that PCI is noninferior to CABG and NOBLE shows CABG is superior to PCI.[23-24] The EXCEL trial shows similar 3-year outcomes for the composite primary endpoint of death, MI or stroke with PCI by using CoCr-EES compared with CABG. Repeat revascularization with 3 years for ischemia were more frequent in distal LM bifurcation PCI in previously reported studies distal LM lesion is shown as an important predictor of TLR after PCI.[25]

Multicenter registry study reported that patients with ostial or mid shaft LM CAD had a favorable prognosis after PCI with first Generation DES,[19] worse outcome in distal LM bifurcation lesion PCI than ostium or shaft.[26] In our present study, distal LM-LAD lesion represents 47.3% followed by shaft of LM 28.8%, distal LM-LCX lesion 15.1% , ostial LM 6.8% and distal LM-RI 2.7% and distal LM-LAD lesion PCI followed by LM shaft lesion are the commonest LM segment lesions stented. Although, many of the centers doing LM stem PCI routinely, exact data on survival outcome, stent patency or repeat revascularization is not well known in our patient perspectives. Average size of stent used for LM ostium and shaft 3.7 mm, LM-LAD / LM-LCX were 3.4 / 3.3 mm, indicating small size vessel in this part of world.[27]

Repeat revascularization rates during follow up after PCI compared to CABG were greater for lesion in distal LM but similar for LM ostium or shaft in previous studies. Metanalysis of several RCTS (PRE-COMBAT, SYNTAX, NOBLE, EXCEL) reported primary safety endpoint of death, MI, stroke was similar between PCI and CABG. Patients with UPLMCA disease, CABG and PCI results similar safety composite endpoint of death, myocardial infarction, or stroke. Among patients with isolated LM or + 1 vessel CAD PCI is associated with lower all-cause

mortality compared to CABG.[28] In our present observational study, only 14.4% (n=21) patients had relooked CAG and none of them underwent PCI, only three underwent CABG due to significant ISR. So, based on this finding, is very primitive to say that PCI is superior to CABG in our patient population. We need to have a set protocol for mandatory check CAG at least 3-6 months after PCI of LM and, need a multicenter LM registry. So, as to compare and better analyze, PCI outcome according to lesion location (shaft vs ostial vs distal LM).

ACC/AHA guideline recommends PCI of LMCA with stents a Class IIa recommendation for a SYNTAX score <22 and a class II b in patients with condition that associated with low risk in PCI or increased risk of surgical outcome with SYNTAX score 33.[29-30] Based on cumulative evidence of comparative studies of LMCA revascularization, guideline recommendation for LMCA PCI has been less stringent. CABG considered the standard of care in treating ULMC disease.[31] In ESC 2018 guideline CABG is a class of recommendation / Level of evidence IB for LM revascularization and PCI is IB, but a IIa recommendation, level of evidence B or III B based on SYNTAX score (SYNTAX score 23 to 32).[32]

The advent of coronary stents along with the evolutions of dual antiplatelet therapy has dramatically lowered the incidence of abrupt vessel closure, and the drug eluting stents further decreased the risk of in-stent restenosis.[33] PCI is increasingly used to treat ULMCA disease.[34] IVUS guidance is helpful in assessing vessel size, adequate stent expansion and absence of stent malapposition. In the MAIN-COMPARE registry, IVUS guidance was associated with improved 3-year mortality compared with angiography guided PCI.[35] OCT has been reported to assess vascular response to LMCA stenting.[36] Available IVUS and FFR and OCT guided PCI of LM stem diseases is associated with reduced major adverse cardiac events with further stent optimization.[37] Only 10.9% (n=16) of our patient had IVUS guided PCI in the studied group. Due to financial restrain, IVUS guided LM stem PCI was not carried out many of the patients of this study.

Unprotected LM stem disease is a heterogenous condition that includes various degrees of anatomic location and severity of LM lesions, and various possible sets of concurrent lesions of other coronary segments.[38]

Age is also an important predictor of LM stem PCI. Mortality was high > 60% in isolated LM PCI in patients over 75 years of age, as high as 75% in those with associated other coronary involvement among with LM stem, while being lower in younger patients.[39] when performing LM PCI, patient comorbidities such as diabetes, renal failure, acute coronary syndrome on presentation, left ventricular dysfunction, concomitant valvular disease, previous cerebro-vascular events are possible key important factor for procedural outcomes.

A recent metanalysis reported that based on totality of randomized clinical trial data (SYNTAX, EXCEL and NOBLE), at a mean follow up time of 5.6 years, there was no significant difference in overall mortality after PCI with DES and CABG for the treatment of LM coronary disease. There was no significant long-term difference between CABG and PCI for cardiac death MI or stroke.[1]

Conclusion:

In this preliminary observational prospective cohort study of LM stem PCI, we found that PCI is a reasonable option in LM lesion. LM stem disease is one of the important predictors of cardiovascular mortality and morbidity. Several studies have shown that revascularization of LM stem disease by PCI is not inferior to CABG. Although, LM stem PCI carries a risk of stent thrombosis or significant ISR development. Individual operator expertise, availability of IVUS, OCT, FFR helped to determine, character, lesion type and subsequent stent optimization. Proper size stent uses, pre- and post-dilation with upsize balloon may help well apposition of stent, thus reduce the risk of ISR and subsequent repeat revascularization.

We recommend check or relook CAG for all LM stem PCI patient at 3-6 months interval, if not possible, then at one year after PCI. We recommend, multicenter national database on LM stem PCI to better define outcomes in Bangladeshi population, facilitate comparative registry-based studies with CABG.

Limitations:

Due to financial issue, IVUS guided LM stem PCI with better lesion characterization and stent optimization not possible in most of the patients with LM stem disease. Limited numbers underwent relook CAG, no comparison of outcomes with CABG.

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