

## Evaluate the Impact of Significant Left Main Stem (LMS) Stenosis on the Early Outcome of Coronary Artery Bypass Graft (CABG) Surgery: A Study in a Tertiary Cardiac Care Hospital, Dhaka, Bangladesh.

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### Abstract:

**Background:** The patients with significant left main stem (LMS) stenosis have a very high risk of major cardiovascular events because of the extent of ischemic myocardium. Coronary artery bypass grafting (CABG) is considered the gold standard for the treatment of complex significant LMS stenosis, especially if it is associated with multivessel coronary disease. In this study, main focus was to ascertain the impact of significant LMS disease on early outcome of CABG surgery. **Objective:** The main goal of this study was to assess the impact of significant LMS stenosis on the early outcome of coronary artery bypass graft (CABG) surgery. **Methods:** A retrospective non-randomized analytical study was conducted in Cardiac Surgery Department of a Tertiary Cardiac Care Hospital, Dhaka, Bangladesh. The data of patients who underwent isolated CABG at the institution from January 2017 to December, 2018 were analyzed. Two hundred and sixty (260) patients of isolated CABG were divided into 2 groups according to the Significant LMS disease. Group A (n=209): without significant LMS disease and Group B (n=51): with significant LMS disease. The groups were compared using Student's t-test for numeric variables. Chi-square test and Fishers Exact test were used for categorical variables. Statistically P-value  $\leq 0.05$  was considered as significant difference. **Results:** Out of two hundred and sixty (206), Two hundred and nine (209) patients were in non. significant LMS group (Control Group) and 51 fifty-one were in significant LMS Group (Study Group). Patients with significant LMS disease were older. In both non.significant LMS and significant LMS, there was no statistically significant difference regarding gender distribution, risk factors of ischemic heart disease (IHD), pre-operative renal function and preoperative CKMB levels. Significant number 5 (9.8%) of patients were unstable in Significant LMS group and they needed urgent surgery (p-value <0.0001). Need and duration for inotropic support and intra-aortic balloon counter-pulsation support were significantly high in significant LMS group (p-value <0.0001, 0.002, 0.003 respectively). Similarly, Mechanical ventilation time and hospital stay were higher in significant LMS group. Incidence of pulmonary complications and operative mortality were significantly higher in Significant LMS group (p-value 0.005 and 0.001 respectively). Mortality of CABG patients with significant left main coronary stenosis was 02 out of fifty-one (3.92%) as compared to just 2 out of two hundred and nine (0.96%) in control group. **Conclusion:** This study showed that significant LMS disease is an independent risk factor for early cardiopulmonary morbidity and mortality after CABG surgery.

**Key Words:** Coronary Artery Bypass Grafting; Significant Left Main Stem Disease; IHD; CKMB

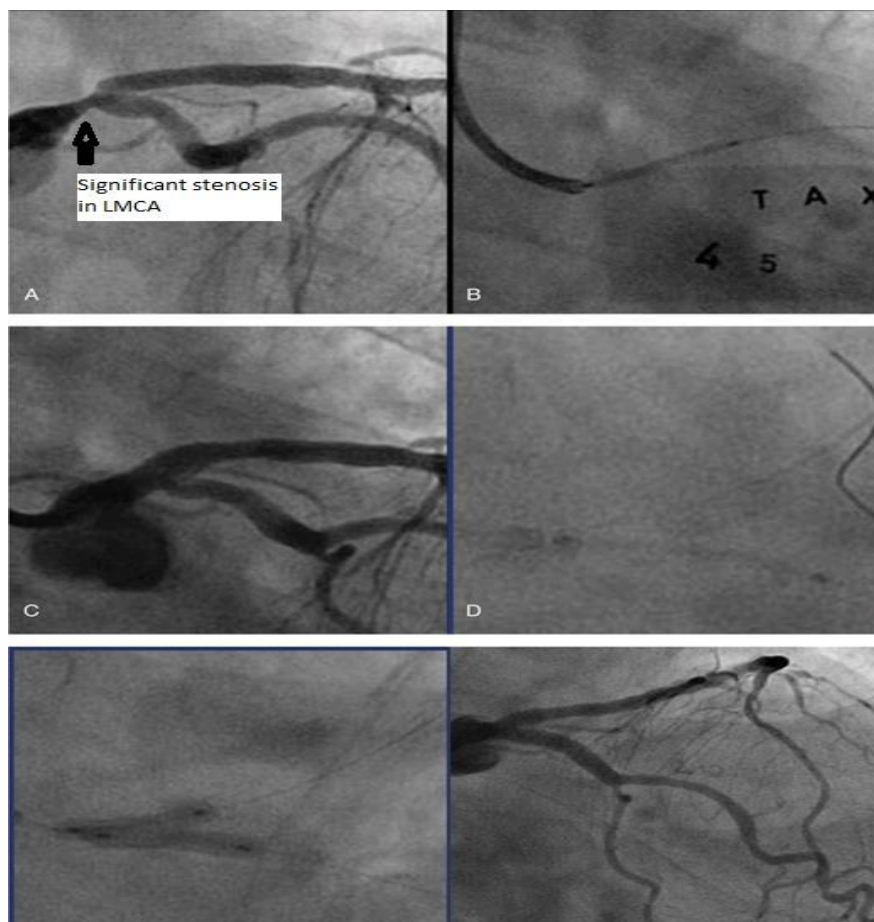
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### I. Introduction

A significant Left Main Stem (LMS) stenosis is considered when there is reduction of  $\geq 50\%$  of the vessel diameter at coronary angiogram. Significant LMS stenosis occurs in about 6% of patients undergoing coronary angiography,<sup>1</sup> and in 30% of coronary artery bypass grafting (CABG) patients.<sup>2</sup> Isolated Left main stem stenosis occurs in only 6% to 9% of patients, out of these over 70% to 80% of patients also have associated multivessel Coronary Artery Disease.<sup>1,3</sup> Patients with significant LMS disease are considered by many at high risk of mortality after CABG.<sup>2,4,5</sup> However, in many mortality risk estimation scoring systems like Parsonnet, Additive and logistic Euro-system, no one have identified significant LMS disease as an independent risk factor

for mortality.<sup>6</sup> The significant LMS disease is a poor prognostic factor with a 3-years survival as low as 37% depending on the degree of stenosis, left ventricular function, and associated distal coronary artery disease.<sup>7</sup> The magnitude of surgical benefit is influenced by both the degree of significant LMS stenosis and left ventricular function. The operative mortality is also associated with these factors as well as the emergent need for surgery, gender and left coronary dominance.<sup>8</sup> CABG in presence of significantly diseased left main coronary artery is likely to pose many challenges and patients with significant LMS disease are likely to become hemodynamically unstable at time of induction and during cardiac manipulation at time of surgery. In this study, main focus was to see the impact of significant LMS disease on early outcome of CABG surgery. 90% of all stenosis of the left main occurs from the distal left main into proximal LAD artery and/or the LCX artery and almost half of the lesions in the left main are calcified.<sup>9</sup> Significant diseases of the LMS, especially in the presence of multi-vessel disease, remains a strong indication for revascularization in both symptomatic and asymptomatic patients<sup>10</sup>. In the past, significant LMS stenosis was considered as a relative contraindication for CABG surgery mainly due to the haemodynamic changes occurring with changing the position of the heart during the method of grafting. For several decades, conventional CABG surgery done in arrested heart was regarded as the standard of care for significant LMS disease in patients eligible for surgical intervention<sup>11</sup>. OPCAB can be done for significant LMS stenosis but gold standard is conventional CABG/arrest heart CABG.



Source: Google

**Fig-1:** Significant Left Main Stem (LMS) stenosis

## II. Material And Methods

Study design:	A retrospective non-randomized analytical study.
Place of study:	A Tertiary Cardiac Care Hospital, Dhaka.
Study period:	January 2017 to December 2018.
Study population:	The study was carried out among all the patients to evaluate the impact of significant left main stem (LMS) stenosis on the early outcome of conventional coronary artery bypass graft (CABG) surgery during the given period.
Sample size:	Total number of patients –260 (Two hundred and sixty)
Sampling method:	A conventional or Purposive non-randomized sampling

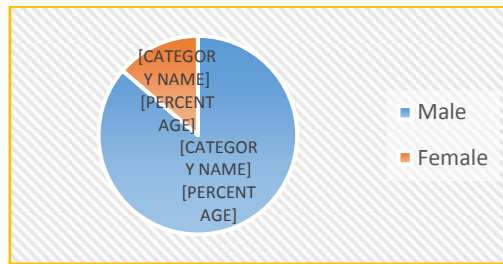
Grouping of Patients:

Group A:	Two hundred & nine (209) patients without significant LMS disease patients underwent isolated conventional CABG surgery.
Group B:	Fifty one (51) patients with significant LMS Disease underwent conventional CABG surgery.

A retrospective non-randomized analytical study was conducted at a Tertiary Cardiac Care Hospital, Dhaka, Bangladesh, presently performing over 400 coronary artery bypass surgery annually. The data of patients operated from January 2017 to December 2018 were analyzed. The data was retrieved from Cardiac Surgery DATA BASE of the institution. In the study, 260 patients' characteristics were prospectively entered in the electronic database of the cardiac care hospital. Patients undergoing isolated conventional CABG were included in the study and they were divided in two groups according to significant LMS disease. Group A: Patients without significant LMS disease (Control Group) and Group B: Patients with significant LMS disease (Study Group). General anaesthesia was used in all patients. Patients were pre-medicated with oral dose of 3mg bromazepam the night before surgery. Anaesthesia was induced with intra-venous morphine (0.1mg/kg), midazolam (0.05-0.1 mg/kg), and propofol (1.0-2.5 mg/kg) that titrated according to the response. They were given atracurium (1mg/kg) before endotracheal intubation. The anaesthesia was maintained with sevoflurane/isoflurane. Cold blood cardioplegia was used for myocardial protection in patients undergoing conventional CABG in both groups. The necessity of inotropic support and the choice of inotropic and dose of inotropic drugs to be administered during weaning from cardiopulmonary bypass (CPB) and in Intensive care unit (ICU) were noted. Inotropic support was defined as mild when dobutamine was administered at a rate <5 mg/kg/min, moderate when dobutamine was administered at 5-10 mg/kg/min and high dose when dobutamine was administered at >10 mg/kg/min. Need of adrenaline or noradrenaline as inotropic support <0.06 mg/kg/min was considered as mild support, 0.06 to 1.0 mg/kg/min as moderate and >1 mg/kg/min was considered as high inotropic support. Pre-op and maximum post-op CK-MB levels were noted. Enzymatic criteria were used to rule out peri-operative MI, a rise in CKMB Levels five times the designated reference value i.e. >125 IU/liter was considered as MI. The rise in serum creatinine levels two folds of preoperative value or the need for renal replacement therapy like hemo-dialysis was considered as renal complication. The development of significant pleural effusion and pneumothorax which need surgical intervention either paracentesis or chest tube insertion, Adult Respiratory Distress Syndrome (ARDS) and Pulmonary Embolism was recorded as pulmonary complication. The immediate need of surgery prior to next available routine operative list was defined as emergency surgery. If surgery has to be performed on immediate available list or patient has to be kept admitted in hospital to perform surgery was defined as urgent surgery. And patients whom routine operative time was given on outpatient basis was included in elective surgery. The statistical analysis was carried out using SPSS (SPSS version 16, SPSS Inc, Chicago, IL). The preoperative, operative and postoperative characteristics were summarized using means and standard deviation for the numeric variables. The groups were compared using Student's t-test for numeric variables. Chi-square test and Fishers Exact test were used to analyze categorical variables. The significance of differences between the groups was expressed as p-value and a value of  $\leq 0.05$  was considered statically significant.

## II. Results

Preoperative, operative and postoperative characteristics of patients are summarized in Table-I & II. A total of two hundred and sixty (260) patients underwent isolated conventional CABG surgery at our institution and their characteristics were retrieved from electronic data base. There were two hundred and nine (209) patients in non-significant LMS Group (Control Group) and fifty-one (51) in significant LMS Group (Study Group). Patients with significant LMS disease were older ( $57.74 \pm 9.71$  years) as compared to patients without significant left main stem disease ( $55.33 \pm 9.59$  years) (p-value <0.0001), majority of patients in both groups were in CCS (Canadian Cardiovascular Society) angina class III. However, significant number of patients were with unstable angina in significant LMS disease group (p-value <0.0001). Majority of patients (9.7%) underwent urgent surgery in significant LMS group (p-value <0.0001). All these findings are statistically significant.



**Fig 2:** Sex Distribution in the study for with significant LMS Group

**Table-I:** Comparison of demographic, echocardiographic and angiographic characteristics (n=260).

Name of Variable		Non-SLMS group (Control Group)	SLMS Group (Study Group)	P-Value
<b>Demographic Details:</b>				
No. of Patients		209	51	
Age (years)		55.33±9.59	57.74±9.71	<0.0001 <sup>s</sup>
Gender (%)	Male	177 (84.8)	44 (86.2)	0.435
	Female	32 (15.2)	7 (13.8)	
Body Mass Index		26.59±4.58	26.04±4.71	0.017
<b>Risk Factors of IHD:</b>				
Diabetic history (%)		71 (36.3)	15 (31.9)	0.06
Smoking history (%)		79(38.7)	17 (35.8)	0.22
History of Hypertension (%)		4 (7.4)	4 (7.0)	0.93
Family History (%)		43(21.9)	11 (22.2)	0.90
History of hyper-cholesterolemia (%)		12 (6.4)	4(8.9)	0.04
<b>Co-morbidities and Peri-operative Data:</b>				
Priority Status	Emergency	5 (0.2)	3(0.2)	
	Elective	201 (98.5)	42 (88.9)	
	Urgent	2 (1.2)	5(9.7)	<0.0001 <sup>s</sup>
	Salvage	1 (0.00)	1 (0.2)	
Type of Operation	CABG	202 (96.8)	50 (98.4)	0.05
	OPCABG	7 (3.2)	1 (1.6)	
Pul. Hypertension		8 (0.4)	1 (0.2)	1.0
Angina Class (CCS)*	Class I	28(13.3)	6 (9.9)	<0.0001 <sup>s</sup>
	Class II	18(8.4)	4 (8.8)	
	Class III	158 (75.6)	37 (72.8)	<0.0001 <sup>s</sup>
	Class IV	5 (2.7)	4 (8.6)	
Pre-op Creatinine levels (mg/dl)/Renal Function		1.00±0.31	1.00±0.24	0.89
Pre-op CKMB Levels (IU/L)		22.91±30.11	23.25±23.37	0.82
Category of Disease	SVD	11(5.2)	5(9.2)	<0.0001 <sup>s</sup>
	DVD	33(16.1)	7(13.8)	
	TVD	165 (78.70)	39 (76.5)	
Ejection Fraction (%)		51.02±10.13	52.94±9.72	<0.0001 <sup>s</sup>
L.V Function Grades	Grade I	135 (64.5)	37 (72.6)	0.001 <sup>s</sup>
	Grade II	47 (22.2)	9 (18.9)	
	Grade III	27 (13.4)	5 (8.6)	
Parsonnet score		4.15±3.58	4.12±4.40	0.86
Add-euro Score		1.18±1.23	1.27±1.37	0.14
Log-euro Score		1.38±.74	1.44±0.89	0.15

\*CCS= Canadian Cardiovascular Society. <sup>s</sup>=Significant

In both groups, there was no statistically significant difference regarding gender distribution, risk factors of IHD, Body Mass Index, pre-operative renal function and preoperative CKMB levels. The extent of coronary artery disease and LV dysfunction were more severe in non-significant LMS group A: (p-value <0.0001 and 0.001 respectively).

**Table-II:** Comparison of operative and post-operative characteristics.

Name of Variable		Non-SLMS group (Control Group)	SLMS Group (Study Group)	P-Value
Bypass time (min.)		108.81±30.47	111.35±32.13	0.114
Cross-Clamp time (min.)		62.83±20.20	64.07±19.90	0.219
Chest Drainage		667.81±381.81	693.84±357.07	0.157
Post-op CKMB* Levels (IU)		61.35±82.43	62.38±64.40	0.785
Duration of Support (hours)		11.08±19.50	14.47±26.25	0.002 <sup>s</sup>
Ventilation time (hours)		8.07±23.65	10.52±31.53	0.056

Hospital stay time (days)		7.12±3.16	7.47±3.22	0.032 <sup>s</sup>
IABP** (%)		6 (2.87)	3 (5.88)	0.003 <sup>s</sup>
Operative Mortality (%)		2 (0.96)	2(3.92)	0.001 <sup>s</sup>
Inotropic Support	Mild	125 (59.9)	27 (51.4)	<0.0001 <sup>s</sup>
	Moderate	46 (22.0)	15 (29.6)	
	High Dose	3 (1.9)	2 (5.4)	
	Nil	35 (16.3)	7 (13.6)	
Pul. Complications (%)		78 (3.7)	34 (6.6)	0.005 <sup>s</sup>
Neurologic complications	Transient Ischemic Attacks	2 (0.1)	2 (0.4)	0.259
	Permanent Local Paralysis	3 (0.1)	1 (0.2)	
	Brain death	3 (0.1)	2 (0.4)	
	Nil	298 (98.8)	42 (97.9)	
	Localized Paralysis	2 (0.1)	0 (0.0)	
	Acute Confessional State	1 (0.8)	4 (1.2)	
Renal Complications (%)		26 (1.2)	5 (1.0)	0.610

\*CKMB = Creatinine Kinase Myocardial Band, \*\* IABP= Intra-aortic Balloon Pump. <sup>s</sup>=Significant

Regarding preoperative operative mortality risk stratification scoring systems no difference was seen in both groups. All patients under went on pump CABG in non-significant LMS group. Both groups showed no significant difference in aortic cross clamp time and total Bypass time. The need, duration and dose of pharmacological inotropic support and intra-aortic balloon counter-pulsation were significantly higher in Group B: (Significant LMS Group). The mean length of ventilation and hospital stay time were significantly higher in group B. The peak CK-MB levels after surgery in 36 hours were not statistically different in both groups (p=0.785). Operative mortality was also significantly higher in group B:(p-value 0.001). There was no difference regarding postoperative neurological and renal complications in both groups.

### III. Discussion

In the era of medicated stents, stenosis of left main coronary artery still remains unchallenged indication for CABG. Indeed, current American College of Cardiology/American Heart Association (ACC/AHA) guidelines state that for significant LMS stenosis CABG is class I indication even in asymptomatic patients (class A evidence)<sup>5</sup> and PCI is a class III indication in those who are otherwise eligible for CABG.<sup>12</sup> In the recent years, the proportion of patient with stenosis of left main coronary artery referred for CABG has therefore increased sharply. In this study, the mortality of CABG in patients with significant left main coronary stenosis was 3.92% comparable with other reports of an early mortality in the range of 2–5%.<sup>13,14</sup> In our study group about 19.6% patients were with significant LMS disease. In this study, Patients with left main stem disease were older as compared to patients without left main stem disease, because elderly patient population admitted for surgery had more advanced coronary artery disease and more often Left Main Coronary Artery disease than younger patients.<sup>15,16</sup> About 80% patients with significant LMS disease had associated three vessel disease which is one of the limitation of PCI as alternative treatment option.<sup>17</sup> Several clinical trials<sup>18-20</sup> and data registries<sup>21, 22</sup> have revealed comparable procedural risks for both PCI and CABG, but the rates of subsequent re-intervention remained high with PCI in these studies. The complexity of the atherosclerotic lesions also has a prognostic impact on the outcome of PCI as the SYNTAX score has shown, which is not the case for CABG.<sup>23, 24</sup> Many studies have showed Significant LMS disease a risk factor for surgery. However, the different risk estimation scoring system like Additive Euro score and Logistic Euro score, no one has given any additional marks to Significant LMS disease. Our study showed that although the patients in non-Significant LMS group had more advanced LV dysfunction and extent of coronary disease but cardiac morbidity and mortality is more in Significant LMS group indicating significant LMS disease as independent operative risk factor for CABG surgery. Although Significant LMS disease had direct and indirect associations with operative morbidity and mortality, the operative results are acceptable and steadily improving. The higher risk in Significant LMS disease is probably because majority of patients are older and have unstable angina and frequently they need urgent surgery as in our study. The key message in the study is that operative team needs more vigilance in patients with Significant LMS disease during peri-operative period because of above mentioned risk profiles.

**Limitations of the study:** Like all retrospectivestudies, this study has some obvious limitations. It had some inherent limitations of the study design. Angiographic details, such as the anatomical sites of Significant LMS stenosis, were not available. The long-term follow-up data was not studied as the study only encompasses

early outcomes. The data revealed increased pulmonary morbidity in patients with Significant LMS disease but the contributing factors have not been studied.

#### IV. Conclusion

This study showed that significant left main stem (LMS) stenosis disease is an independent risk factor for early cardiopulmonary morbidity and mortality after coronary artery bypass graft (CABG) surgery.

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