Frequency of Low Cardiac Output Syndrome Following on Pump Coronary Artery Bypass Grafting Surgery and it's Association with Degree of Pre-operative Left Ventricular Dysfunction

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ABSTRACT

Background

Low cardiac output syndrome (LCOS) is a serious complication after coronary artery bypass grafting (CABG) surgery. It is associated with 10 times to 17 times increase in mortality and markedly increase morbidity.

Objective

To find out the frequency of Low cardiac output syndrome following on pump coronary artery bypass grafting surgery, to determine the association of Low cardiac output syndrome with degree of pre-operative left ventricular dysfunction and to compare in hospital outcomes of coronary bypass surgery with and without low cardiac output syndrome.

Method

This prospective, descriptive study enrolled 200 patients who underwent on pump coronary artery bypass grafting surgery using antegrade St Thomas blood cardioplegia. Pre-operatively grouped into two groups consisting Group A of 100 patients with pre-operative left ventricular ejection fraction (LVEF) ≥ 40% and group B of 100 patients with pre-operative left ventricular ejection fraction (LVEF) < 40%. Post-operatively frequency of low cardiac output syndrome was compared between the groups and in-hospital outcomes were studied.

Result

The mean age of the patients in the study was 53.50±7.57 years. Male to female ratio was 1.8:1. Results showed overall frequency of low cardiac output syndrome was 21.5%. The frequency of LCOS was 15 vs 28% (p - 0.038) in patients with pre-operative LV EF ≥ 40% and < 40% respectively. The outcomes of coronary artery bypass grafting surgery were stroke (3.82 vs. 30.23%, p - 0.001), acute kidney injury (5.09 vs. 23.25%, p - 0.001), respiratory failure (6.36 vs. 34.88%, p - 0.001), ICU stay days (4.75 ± 1.28 vs. 7.44 ± 4.66, p - 0.018), hospital stay days (9.56 ± 2.40 vs. 15.22 ± 3.89, p - 0.001) and mortality (4.45 vs. 32.55%, p - 0.001) in patients without and with low cardiac output syndrome respectively.

Conclusion

The frequency of low cardiac output syndrome following coronary artery bypass surgery is 21.5%. Left ventricular dysfunction pre-operatively is associated with high frequency of low cardiac output syndrome following surgery. There is significantly poor outcome of coronary artery bypass surgery with low cardiac output syndrome in terms of stroke, respiratory failure, acute kidney injury, mortality and significant ICU stay, hospital stay in compare to patients without low cardiac output syndrome.

KEY WORDS

Coronary artery bypass, Low cardiac output, Ventricular dysfunction, Coronary artery disease

INTRODUCTION

Coronary Artery Bypass Grafting (CABG) surgery is the optimal approach and remains superior to medical therapy in symptomatic multivessel coronary artery disease patients and severe left ventricle dysfunction. But CABG in patients with depressed LV function remains a surgical challenge. There is higher morbidity and mortality with LV dysfunction cases than for normal LV function cases.[1] Low cardiac output syndrome (LCOS) is a clinical condition which is resulted by decrease in systemic perfusion due to myocardial dysfunction. This results in an imbalance between oxygen delivery and oxygen consumption at the cellular level which leads to metabolic acidosis. It occurs commonly in patients after cardiac surgery.[2] LCOS is identified by need of postoperative inotropic support or intra-aortic balloon pump support to maintain a systolic blood pressure > 90 mmHg or to maintain cardiac index ≥ 2.2 L/min/m^2.[3]

LCOS is one of the very important complications after CABG which accounts 13.5% and leads to higher morbidity and mortality accounting 25.4%.[4] The development of LCOS after CABG is associated with 10 times to 17 times increase in mortality and markedly increase morbidity.[5] It results in higher rates of morbidity in the forms of respiratory failure, stroke, acute kidney failure, and need for reoperation. In addition, patients who develop LCOS have prolonged ventilator support and longer time of intensive care unit (ICU) stay and hospital stay. Poor ventricular function is the important predictors of postoperative morbidity and mortality.[6] Patients with poor ventricular function have a limited margin for myocardial protection, which makes patients more intraoperative myocardial injury and develop LCOS after surgery.[7] LV dysfunction is the most significant independent predictor of low-output syndrome in post-operative period and is significantly greater in patients with impaired LV function.[8] The limitations of our research in terms of generalizing the finding to larger population is required to be stated. The invasive measures for continuous measuring of cardiac output, cardiac index and systemic vascular resistance following CABG surgery are the limitations in our study.

We aim to conduct this study to identify the frequency of LCOS and the outcomes of CABG with and without LCOS and their association with pre-operative LV function in our hospital facilities.

METHODS

This is a prospective comparative study conducted in the department of Cardiac Surgery, Punjab Institute of Cardiology, Punjab, Pakistan. The study duration was from 15, June 2016 to 14, June 2018 (2 years). Sample size calculated by using 95% confidence interval with 5% margin of error by taking expected 13.5% incidence of low cardiac output syndrome in patients undergoing CABG. The study enrolled 200 patients fulfilling inclusion criteria. The non-probability, consecutive sampling technique was used in this study. The author and members of the research team do not have any conflict of interest. Ethical clearance from ethical committee and preoperatively consent from every patient was taken. Preoperatively grouped into two groups consisting Group A of 100 patients with pre-operative LVEF ≥ 40% and group B of 100 patients with pre-operative LVEF < 40% undergoing CABG. Postoperatively frequency and outcomes of LCOS were compared between the groups.

Inclusion criteria

1. All patients undergoing isolated elective on pump CABG using antergrade St. Thomas blood cardioplegia.

2. Inclusion criteria for Low cardiac output syndrome: Need for inotropic support with vasoactive drugs (dopamine ≥ 4 µg/kg/minute at least for a minimum of 12 hours and/or dobutamine and/or milrinone and/or epinephrine and/or noradrenaline) or mechanical circulatory support using an intra-aortic balloon pump (IABP) to maintain systolic blood pressure more than 90 mmHg after correction of all electrolytes and arterial blood gas abnormalities with adjusting preload volume to its optimal values.[4]

3. Cardiac index measured by transthoracic echocardiography. CI < 2.2 L/min/m^2 is considered as LCOS.[5,10-12]

Exclusion Criteria

1. Patients undergoing CABG with valve replacement surgery.

2. Patients having prior LCOS e.g. on pre-operative IABP, Inotropic supports.

3. Patients with pre-operative renal failure.

4. Patients in cardiac tamponade (rule out by echocardiography).

5. Preoperatively ventilated patients.

Data was collected in a self- designed performa which include demographic information (like name, age, sex, height, weight, address). Then the low cardiac output syndrome and in hospital outcomes were noted. Data was analyzed using SPSS 20. P value ≤ 0.05 was taken as significant.

RESULTS

The mean age of patients in group A was 52 ± 7.48 years and male is to female ratio of 2.3 is to 1. In group B it was 54.84 ± 7.44 years and male is to female ratio of 1.5 to 1. There was significant difference in age (p - 0.009) and gender (p - 0.001) between the Group A and group B. In group A smokers were 35% and in group B 50% (p - 0.044). Patients with hypertension in group A was 32% and in group B 43% (p - 0.143). Patients with DM in group A was 30% and

in group B 45% (p - 0.029). The mean LVEF in group A was 51.0 ± 6.27%. In group B the mean LVEF was 28.19 ± 4.58% (p - 0.001) (Table 1).

Table 1. Preoperative characteristics of the patients

Characteristics	Group A (LVEF ≥ 40%)	Group B (LVEF < 40%)	P value
Age(Years)	52 ± 7.48	54.84 ± 7.44	0.009
Gender	2.3 : 1	1.5 : 1	0.001
Smoking (%)	35	50	0.044
Hypertension (%)	32	43	0.143
Diabetes mellitus (%)	30	45	0.029
LVEF %	51.0 ± 6.27	28.19 ± 4.58	0.001

LIMA was used in 96% (96 patients) of cases in group A and 78% (78 patients) of cases in group B (p - 0.002). The number of grafts in group A was mean 3.18 ± 0.71 and in group B it was 2.98 ± 0.87 (p - 0.001). The mean aortic cross clamp time in this study in group A was mean 47.00 ± 11.15 minutes. In group B it was mean 50.01 ± 9.66 minutes (p - 0.001). The mean cardiopulmonary bypass time in this study in group A was 91.46 ± 22.52 minutes. Similarly in group B it was 94.92 ± 21.80 minutes (p - 0.001) (Table 2).

Table 2. Intra-operative characteristics

Characteristics	Group A (LVEF ≥ 40%)	Group B (LVEF <40%)	P- value
LIMA	96 %	78%	0.002
Number of grafts	3.18 ± 0.71	2.98 ± 0.87	0.001
Aortic cross clamp (minutes)	47.00 ± 11.15	50.01 ± 9.66	0.001
Cardiopulmonary bypass time (minutes)	91.46 ± 22.52	94.92 ± 21.80	0.001

The mean dose of adrenaline used in the patients with LVEF ≥ 40% with LCOS was 0.46 ± 0.27 µg/kg/minute. The mean duration of adrenaline used was 33.53 ± 6.12 hours. In the patients with LVEF < 40% with LCOS was 0.83 ± 0.38 µg/kg/minute. The mean duration of adrenaline used was 54.73 ± 23.64 hours. There is significant difference in dose (p - 0.02) and duration (p - 0.005) of adrenaline between the groups (Table 3).

Table 3. Postoperative inotropic support dose and duration and IABP used in the study in patients with LCOS.

Supports Dose and duration	LCOS with LVEF ≥ 40%	LCOS with LVEF < 40%	P-value
Adrenaline µg/kg/minute	0.46 ± 0.27	0.83 ± 0.38	0.020
Duration (in hours)	33.53 ± 6.12	54.73 ± 23.6	0.005
Nor-adrenaline µg/kg/minute	0.12 ± 0.03	0.17 ± 0.01	0.002
Duration (in hours)	27.93 ± 5.35	48.80 ± 9.87	0.001
Dopamine µg/kg/minute	7.03 ± 1.32	8.56 ± 0.91	0.002
Duration (in hours)	29.06 ± 5.44	43.00 ± 4.79	0.001
IABP	2 (13.3%)	10 (35.71%)	0.163

The mean dose of nor-adrenaline used in the patients with LVEF ≥ 40% with LCOS was 0.12 ± 0.03 µg/kg/minute and mean duration of nor-adrenaline used was 27.93 ± 5.35 hours. The mean dose of nor-adrenaline used in the patients with LVEF < 40% with LCOS was 0.17 ± 0.01 µg/kg/minute. The mean duration of nor-adrenaline used was 48.80 ± 9.87 hours. There is significant difference in dose (p - 0.002) and duration (p - 0.001) of nor adrenaline between the groups.

The mean dose of dopamine used in the patients with LVEF ≥ 40% with LCOS was 7.03 ± 1.32 µg/kg/minute. The mean duration of dopamine used was 29.06 ± 5.44 hours. The mean dose of dopamine used in the patients with LVEF < 40% with LCOS was 8.56 ± 0.91 µg/kg/minute. The mean duration of dopamine used was 43.00 ± 4.79 hours. There is significant difference in dose (p - 0.002) and duration (p-0.001) of Dopamine between the groups.

IABP was required in 2 cases (13.3%) in patients with LVEF ≥ 40% with LCOS and in 10 cases (35.71%) in patients with LVEF < 40% with LCOS. IABP was required in 27.90% of patients (12 patients) out of 43 patients who developed LCOS.

The mean CK-MB level in this study was preoperatively 12.58 ± 5.52 IU/L and postoperatively (12-18 hours after surgery) was 59.80 ± 27.08 IU/L. Postoperatively, five patients (2.5%) of the cases had CK-MB level more than 125 IU/L with pathological Q wave and were identified as perioperative myocardial infarction. There is significant difference in CK-MB level pre and postoperatively (p - 0.001) (Table 4).

Table 4. Pre-operative and post-operative CK-MB level

	Preoperative	Postoperative	P-value
CK-MB level (IU/L)	12.58 ± 5.52	59.80 ± 27.08	0.001

The mean Cardiac Index in this study was 1.73 ± 0.14 L/min/m^2 with maximum CI of 2 L/Min/m^2 and minimum CI of 1.5 L/min/m^2 (Table 5).

Table 5. Cardiac Index in patients with LCOS

	Cardiac Index (L/minute/m^2)
Mean	1.73
Standard Deviation	0.14
Maximum	2
Minimum	1.5

The overall frequency of LCOS 21.5% with 15% in LVEF ≥ 40% and 28% with LVEF < 40% (Fig. 1).

The frequency of LCOS in patients with LCOS with pre-operative LVEF ≥ 40 was 15% (15 cases) and in patients with pre-operative LVEF < 40% was 28% (28 cases) (p - 0.038) (Table 6).

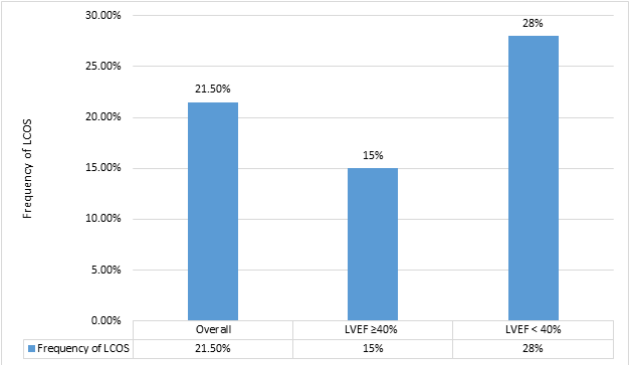

Figure 1. **Frequency of LCOS**

Table 6. **LCOS in association with LV dysfunction**

	Group A (LVEF ≥ 40%)	Group B (LVEF < 40%)	P-Value
Frequency	15% (15)	28% (28)	0.038

The significant difference in outcomes in terms of stroke, respiratory failure, Acute kidney failure, mortality, ICU stay and hospital stay between the groups with no LCOS and LCOS (Table 7).

Table 7. **Table showing outcome of LCOS**

	No LCOS (157)	LCOS (43)	P-Value
Stroke	3.8% (6)	30.23% (13)	<0.001
Respiratory failure	6.36% (10)	34.88% (15)	<0.001
Acute Kidney failure	5.09% (8)	23.25% (10)	<0.001
ICU stay(days)	4.75 ± 2.28	7.44 ± 4.66	0.018
Hospital stay (days)	9.56 ± 2.40	15.22 ± 3.89	0.001
Mortality	4.45% (7)	32.55% (14)	<0.001

DISCUSSION

This descriptive study was conducted in Cardiac Surgery Department/Punjab Institute of Cardiology, Lahore, Punjab, Pakistan to determine the frequency of Low cardiac output syndrome (LCOS) in post CABG surgery patients and its association with pre-operative LV dysfunction.

In this study the mean age of patients was 53.50±7.57 years. The male population was 64.5% and female population was 35.5%. A study by Murtaza et al. found the mean age undergoing CABG was 55.33 ± 9.59 years.[13] A study by Hussain et al. found the male patients undergoing CABG was 82.7% and female population was 17.3%.[14]

In our study the mean age in group A was 52 ± 7.48 years and male to female ratio of 2.3:1 and in group B the mean age was 54.84 ± 7.44 years and male to female population of 1.5:1.

Low Cardiac Output syndrome is known as a common complication after CABG and reduced EF has been reported as a significant predictor of LCOS following isolated CABG.[15]

In a study by Ding et al. included 1524 patients, single center, found the frequency of LCOS following isolated CABG as 13.5%.[4] Similarly, another prospective study by Sa et al. included, 605 patients found the frequency of LCOS 14.7%.[8] Another Brazilian study included 814 patients and criteria for LCOS was CI the cardiac index < 2.1 L/min/m^2, at the patient's admission to the ICU found the frequency of LCOS 16.1%.[16] In a study in 2017 by Kamal and colleagues, prospective study including 100 patients found the frequency of LCOS 35.0%.[17] In our study frequency of LCOS was 21.5% which is similar to study by Kumon and colleagues including 4179 patients, criteria of LCOS was CI to less than 2.2 L/min/m^2, necessitating the administration of large doses of inotropic agents with or without an assist circulation, found frequency of LCOS 21.2%.[18]

The frequency of LCOS increases with reduction of EF.[17] The study found the frequency of LCOS 26% with LVEF > 50% and 44% with LVEF < 50% and 76% with LVEF ≤ 35%. But study by Sa et al. found it was 22.4% with LVEF < 50% and Ding et al. found 49.3% with LVEF < 50%.[4,8] In a prospective study comprising 4558 patients, the frequency depending on LVEF is 6% in LVEF > 60%, 8% in LVEF 40-60%, 21% in LVEF < 40%.[19] Similarly, a study from Egypt by Elassy et al. reported LCOS in 77.5% with EF <35% versus 46.4% with EF > 50%.[20] In our study, there was 15% versus 28% occurrence of LCOS in patients with LVEF ≥ 40% versus < 40% respectively. This is statistically significant with p value 0.038.

John et al. reported the frequency of stroke after CABG is between 1.4% and 3.8%.[21] Another study by Ding et al. compared the frequency of stroke in patients who develop LCOS and those did not following CABG surgery which was found 32.2% and 3.6% respectively.[4] Similarly, Sa et al. found patients who developed LCOS following CABG presented higher rates of stroke that is 41.6% versus 3.5% who don't develop LCOS.[8] These studies shows incidence of stroke is higher in patients who have LCOS following CABG surgery. Similar finding in our study was observed where incidence of stroke was 30% (13 patients) and 3.8% (6 patients) patients who had no LCOS and with LCOS with respectively (p - 0.001).

Ding et al. in their study found that in patients who acquired LCOS following CABG surgery showed higher rates of respiratory failure that is 38.1% in compare to those who didn't developed LCOS that is 7.2%.[4] Our study showed that frequency of respiratory failure in patients with LCOS was 34.88% (15 patients) and 6.36 %(10 patients) without LCOS p - 0.001).

A study by Ding et al. showed patients who had LCOS following CABG surgery showed higher rates of acute renal failure 22.4% versus 5.7% in compare to those who didn't develop.[4] A study by Sa et al. found that patients who had LCOS after CABG presented more rates of renal failure 23.6% versus 5.8% in compare to the group that did not

have postoperative LCOS.[8] None of the above studies have mentioned about the need of dialysis for ARF in patients with or without LCOS. Similar finding in our study was found that none of patients required dialysis. In our study the frequency of ARF was 23.25% (10 patients) and 5.09% (8 patients) of patients who developed LCOS and without LCOS respectively (p - 0.001).

A prospective study by Algarni et al. found patients with LCOS had significantly longer intensive care unit stay and hospital stay.[5] Another study by Rao et al. reported that patients whom LCOS developed had longer duration of postoperative intensive care unit stay and longer hospital stay.[19] Sa et al. in their study showed that ICU stay was 2.38 ± 1.21 days in whom no LCOS developed but it was 8.45 ± 3.26 days who had developed LCOS.[8] Similarly, Ding et al. found that ICU stay was 2.1 ± 1.0 days versus 7.3 ± 2.8 days in patients who didn't develop LCOS and those who developed LCOS respectively.[4] Similarly in our study the ICU stay was longer in patients who developed LCOS post CABG surgery which was 4.75 ± 1.28 days and 7.44 ± 4.66 days with no LCOS and with LCOS respectively (p - 0.01).

The total hospital stays prolongs in patients with LCOS in compare to those who didn't develop LCOS. In a study by Sa et al., it was found that longer hospital stay in patients who developed LCOS and that was 21.87 ± 7.24 days versus 10.54 ± 5.23 days in those who had not develop LCOS after CABG.[8] Another study by Ding et al. found hospital stay was 21.3 ± 6.4 versus 8.4 ± 2.3 days in patients who developed LCOS and those who didn't developed LCOS post CABG respectively.[4] Our study showed that in patients with no LCOS and with LCOS, hospital stay was observed 9.56±2.40 days and 15.22±3.89 days respectively p - 0.001).

The Society of Thoracic Surgeons database found the overall operative mortality of CABG across North American centers is 3.0%. In two contemporary randomized trials, the SYNTAX trial and the FREEDOM trial reported that the operative mortalities for CABG patients were 3.5% and 1.7% respectively.[22,23] According to study by Rao et al. patients who had low cardiac output syndrome, the mortality was 17% compared with 0.9% in those patients without low cardiac output syndrome.[19] Algarni et al. found the development of LCOS after CABG is associated with 10 times to 17 times increase in mortality.[5] In a study by Sa et al. it was reported that the mortality in patients who developed LCOS was 52.8%.[8] Similarly, Ding and associates found operative mortality was 25.4% in patients who developed LCOS.[4] Our study showed that operative mortality in patients with LCOS was 32.55% (14 patients) and with no LCOS was 4.45% (7 patients) (p - 0.001).

CONCLUSION

The frequency of LCOS following CABG is 21.5%. LV dysfunction pre-operatively is associated with high frequency of LCOS following CABG. There is statistically significant difference in frequency of LCOS in patients with pre-operative LVEF < 40% in compare to LVEF ≥ 40%. There is significantly poor outcome of CABG with LCOS in terms of stroke, respiratory failure, acute kidney injury, mortality and significant ICU stay, hospital stay in compare to patients without LCOS.

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