



**Research Article**

**CORONARY ARTERY BYPASS GRAFTING IN PATIENTS WITH DIFFUSE CAD AND ADVANCED LEFT VENTRICULAR DYSFUNCTION- CHANGES IN LEFT VENTRICULAR EJECTION FRACTION AND FUNCTIONAL STATUS -AN AMBISPECTIVE OBSERVATIONAL (COHORT) STUDY**

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**ABSTRACT**

**Objective and background** - This study evaluated the outcome of CABG in patients with advanced left ventricular dysfunction (EF<35%) with diffuse CAD, in terms of the change in their LV ejection fraction and the functional status postoperatively, since such a subset is regarded as high risk with poor outcome. **Material and method-** A total of 100 patients, of Coronary Artery Disease with diffusely diseased vessels and severe LV dysfunction, who underwent Coronary Artery Bypass Grafting in our center between 2010 and 2016, were included in this study. This study was an ambispective observational study. Patients were evaluated and analyzed retrospectively as well as prospectively followed up. Statistical analysis done using statistical software STATA 13 IC. **Results** - In our study group (N=100), 81 (81%) underwent on pump CABG, while 19, (19%) underwent off pump CABG with mean of 3.62 distal graft per patient. The intraoperative and the postoperative follow up data at 03, 06, and at the 12 month with median follow up period of 09 months, revealed that the improvement in mean LVEF (%) from 28.6% (SD= 2.8) to 37.3% (SD= 7) intraoperatively to 41.5(SD= 8.3)(Range : 20-55), at one year follow up, with p value of <0.001, which is statistically very significant. There is also a significant improvement in the NYHA Class in the study population. Preoperatively, 82, (82%) patients in the study group were in NYHA Class 3B, and 18(18%) were in class 2B However at 06 month postoperative follow up, 79, (81.4%) of the study population functionally improved to, class 1B, with p value of <0.001, which is statistically very significant. **Conclusion** -The outcome of this study shows definite improvement in the LVEF and in the NYHA class and suggests that, CABG in this setting of the patients is effective, safe and should be recommended.

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**INTRODUCTION**

In today's scenario, many patients with coronary artery disease are presenting for CABG surgery in advanced stage of left ventricular dysfunction (ejection fraction <35%) with diffusely diseased coronary vessels. CABG in such a subset, represents a surgical challenge, and has been often regarded as high risk with poor post operative outcome. However medical therapy for such patients has been unsatisfactory and causes poor long term survival [2, 3, 13, and 14].

Little information is available about relief of symptoms in patients with diffuse CAD and advanced LV dysfunction, post CABG in Indian setup.

We sought to quantify the changes, mainly in LVEF and NYHA class following CABG in such a subset of patients, keeping in mind that observations from this study might help in optimizing allocation of surgical choice in the subset of patients in the resource compromised Indian health system.

**MATERIALS AND METHODS**

A total of 100(N=100) patients, of Coronary Artery Disease with diffusely diseased vessels, and Left Ventricular Ejection Fraction (LVEF) of < 35 %, i.e. with severe LV dysfunction, who underwent Coronary Artery Bypass Grafting (CABG) in Dept of CTVS, AIIMS New Delhi between 2010 and 2016 were included in this study. This study was an ambispective observational study. Patients were evaluated and analyzed retrospectively as well as prospectively followed up.

Till one year post operative data were included for the statistical analysis and the minimum post operative follow up period was of three months and the median follow up period

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was of 09 months. 88, (88%) patients were operated by the single surgeon. No patient was lost during the follow up period. The study protocol was duly approved by the Institute Ethics Committee for the Post Graduate Research, and the informed consent was obtained from the patients.

The preoperative, intraoperative, and follow up at 03 Month, 06 Month and 12 Month data of clinical, operative and 2D echocardiography/ MUGA Scan(Multigated Acquisition Scan) for LVEF were collected through CTVS record center, and during follow up in opd. The patients were contacted telephonically, during routine follow up in opd, and through social media. Patients in whom, CABG with concomitant valve replacement surgery and LV aneurysmectomy was done, were excluded from the statistical analysis.

**Statistical analysis:-** was done using statistical software STATA I/C Version 13. Mean and standard deviation (SD) were used to describe continuous variables and percentage and frequency were used to describe categorical variables. Repeated measure ANOVA (Analysis of Variance) was used for statistical testing of continuous variable and chi square test was used for statistical testing of categorical variable. The p value of less than 0.05 was taken as significant.

## RESULTS

In the study group (N=100) 91 (91%) were male and only 9 (9%) were female, with mean age( Years) 57.6 (SD=7.8) (range: 42-76), and mean weight (kg) 64.8 (SD=9.4) (Range: 45-95). Preoperatively, as shown in tab 1, 48 (48%) were diabetic, 75 (75%) were hypertensive, 26 (26%) had suffered recent myocardial infarction, 04 (04%) had severe ischemic MR, 03 (03%) had ventricular sepal rupture or defect, and 82 (82%), and 18 (18%) of the study population were in NYHA class 3 and 2 respectively.

All the patients in the study group (N=100), were having CAD with diffusely diseased vessels, and severe LV dysfunction (LVEF<35%) with mean LVEF (%) of 28.6 (SD = 2.9) (Range: 19-33). 96, (96%) having triple vessel disease (TVD), 02 (02%) had double vessel disease(DVD)and only 1 (1%) had single vessel disease (SVD). As per intraoperative data as shown in Tab 2, 80 (80%) of the patients underwent on pump CABG, 19 (19%) underwent off pump CABG, and 01 (01%) was undergone on pump beating heart surgery and Minimally Invasive Direct Coronary Artery Bypass (MIDCAB) was performed in 01 (01%) patient with mean of 3.62 distal graft per patient. In 90 (90%) of cases LIMA was harvested and In 02 (02%) of patient's Radial artery conduit was also taken for the LAD anastomoses and in 01 (01%) case redo CABG was done. MV Repair for ischemic MR was done in 04 (04%) patients, and VSR repair done in 03 (03%) patients. Intra Aortic Balloon Pump (IABP) was used in 20 (20%).

As per post operative follow up data to reveal the outcome or change in Left ventricle Ejection Fraction (LVEF) in %, as shown in Tab 3 and in Fig 1, in the study group (N=100), preoperatively, the mean value of the LVEF (SD) (%) was 28.6% (2.8), intraoperative data of LVEF was available only for 95 (95%) patients, in whom the mean(SD) value of LVEF(%) was changed to 37.3 (7.0), at 03 months postoperative follow up period, data for 76 (76%) patients were available for analysis, in whom the mean(SD) value of LVEF(%) was 39.0 (8.0). Subsequently at 06 months and at 12 months postoperatively, 94 (94%), and 58 (58%) of the study

population were available for data analysis respectively, in whom the mean (SD) value of the LVEF (%) was found to be 39.8 (8.7) at 06 month and 41.5 (8.3) at 12 month post operatively with p value of <0.001 with 95% confidence interval.

The NYHA class of the study group (N=100), as shown in tab3 and in fig 2, preoperatively, 82, (82%) of the patients were in class 3B and 18, (18%) in class 2. At 03 month follow up, the data for 81, (81%) were available and out of which 63, (77.8%) were in NYHA class 1B and 18, (22.2%) were in class 2B. At 06 month follow up the data for 97, (97%) were available and out of which 79, (81.4%) were in NYHA class 1B and 18, (18.6%) were in class 2 and at 12 month follow up the data for 59, (59%) were available and out of which 49, (83%) were in NYHA class 1B and 10, (17%) were in class 2B, with p value <0.001.

As shown in Tab 3 and in Fig 3, the 88, (88 %) of the study population were having regional wall motion abnormality (RWMA), and 12, (12%) had Global Hypokinesia in 2D Echocardiography findings, preoperatively. At 03 month follow up, out of 78, (78%) available for data analysis, 17, (21.8%) had normal LV contraction with no RWMA, 56, (71.8%) had RWMA, and 5, (6.4%) were showing global hypokinesia in 2D Echocardiography/ MUGA scan. At 06 month follow up, out of 94, (94%) available for data analysis, 26, (27.7%) had normal LV contraction with no RWMA, 63, (67%) had RWMA, and 5, (5.3%) were showing global hypokinesia in 2D Echocardiography/ MUGA scan. At 12 month follow up, out of 56, (56%) available for data analysis, 22, (39%) had normal LV contraction with no RWMA, 32, (57%) had RWMA, and 2, (3.6%) were showing global hypokinesia in 2D Echocardiography/ MUGA scan, with p value < 0.001.

**Tab 1** Baseline Preoperative Demographic and clinical data

STUDY GROUP	N=100
<b>DEMOGRAPHIC PROFILE</b>	
SEX (%)	
MALE	91
FEMALE	09
AGE IN YEARS (MEAN,SD)	57.58, 7.75
WEIGHT IN KG (MEAN+SD)	64.82, 9.35
<b>CLINICAL PROFILE</b>	
DM (FREQUENCY, %)	48 (48%)
HTN (FREQUENCY, %)	75 (75%)
NYHA CLASS (FREQUENCY, %)	
CLASS 2	18 (18%)
CLASS 3	82 (82%)
RECENT MI (FREQUENCY, %)	26 (26%)
MR (FREQUENCY, %)	
NO MR	77 (77%)
MILD MR	17 (17%)
MODERATE MR	02 (02%)
SEVERE MR	04 (04%)
VSR (FREQUENCY, %)	03 (03%)
SEVERE LV DYSFUNCTION	100 (100%)
DIFFUSE CAD	100 (100%)
TVD	96 (96%)

(DM= Diabetes Mellitus, NYHA- NEW YORK HEART ASSOCIATION, MI- MYOCARDIAL INFARCTION, MR= MITRAL REGURGITATION, VSR= VENTRICULAR SEPTAL RUPTURE, CAD= CORONARY ARTERY DISEASE, LV= LEFT VENTRICLE)

**Tab 2** Operative Data

STUDY GROUP	N=100
<b>VARIABLES – FREQUENCY (%)</b>	
ON PUMP CABG	80 (80%)
OFF PUMP CABG	19 (19%)
ON PUMP BEATING HEART	1 (1%)

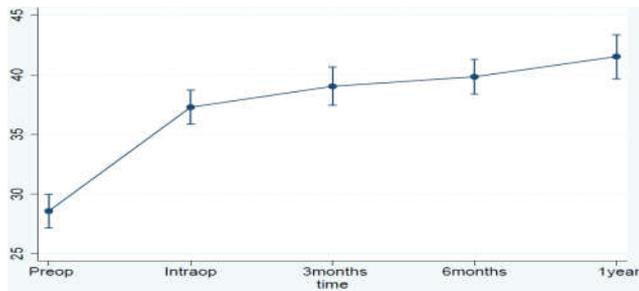
MEAN DISTAL GRAFT/PATIENT (MEAN, SD)	3.6,(1.2)
MIDCAB	1 (1%)
USE OF IABP	20 (20%)
MV REPAIR	04 (04%)
VSR REPAIR	03 (03%)

(CABG=CORONARY ARTERY BYPASS GRAFTING, MIDCAB= MINIMALLY INVASIVE DIRECT CORONARY ARTERY BYPASS, VSR= VENTRICULAR SEPTAL RUPTURE, LV= LEFT VENTRICLE)

**Tab 3** Post operative changes in the characteristics

S NO.	Characteristic	Pre OP	Intra OP	Post OP			P Value
				03 M	06 M	12 M	
1	N	100	95	76	94	58	
2	LVEF (%) (MEAN,SD)	28.6, (2.8)	37.3, (7.1)	39, (8.1)	39.8, (8.7)	41.5, (8.3)	<0.001
3	NYHA CLASS (FREQUENCY, %)						<0.001
	CLASS 1	0, (0%)	-	63, (77.8%)	79, (81.4%)	49, (83%)	
	CLASS 2	18, (18%)	-	18, (22.2%)	18, (18.6%)	10, (16.5%)	<0.001
	CLASS 3	82, (82%)	-	0, (0%)	0, (0%)	0, (0%)	
4	NO RWMA	0, (0%)	-	17, (21.8%)	26, (27.7%)	22, (39.3%)	
5	RWMA	88, (88%)	-	56, (71.8%)	63, (67%)	32, (57%)	<0.001
6	GLOBAL HK	12, (12%)	-	5, (6.4%)	5, (5.3%)	2, (3.6%)	

(OP= OPERATIVE, LVEF= LEFT VENTRICLE EJECTION FRACTION, RWMA= REGIONAL WALL MOTION ABNORMALITY, HK= HYPOKINESIA)

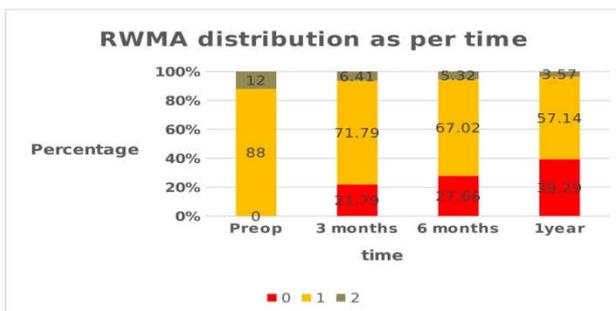


**Fig 1** Post operative changes in Ejection Fraction with 95% CI (line diagram)

(X- Axis= Follow up period, Y- axis= EF %)



**Fig 2** Post Operative Change in NYHA Class - Bar Diagram



(0= No RWMA, 1= RWMA+, 2= Global HK+)

**Fig 3** Post Operative Change in RWMA - Bar Diagram

## DISCUSSION

Severe LV Dysfunction has long been considered a contraindication for surgical coronary revascularization due to high operative risk and poor outcome. However medical therapy for such patients has been unsatisfactory and causes poor long term survival [1, 3, 7, 8-11].

In our study, all the patients in the study group (N=100), were having CAD with diffusely diseased vessels, with 96,(96%) having TVD, 02,(02%) had DVD, 1,(1%) had SVD, and severe LV dysfunction (LVEF<35%) with mean (SD) LVEF(%) of 28.6 (2.9) (Range: 19-33), 82 (82%) of the study population were in NYHA class 3B, since all of them were on medical therapy. 48 (48%) were diabetic and 26 (26%) had recent MI. 88 (88%) of the patients were operated by the single surgeon. 81 (81%) underwent on pump CABG, while 19, (19%) underwent off pump CABG and only 1, (1%) underwent on pump beating heart surgery with mean of 3.62 distal graft per patient. In 90, (90%) of cases LIMA was harvested and In 02, (02%) of patients Radial artery conduit was also taken for the LAD anatomizes and in 01, (01%) case redo CABG was done. In 20, (20%) of the patients, IABP was used to tide over the intra and immediate post operative hemodynamic instability.

The intraoperative and the postoperative follow up data at 03, 06, and at the 12 month with median follow up period of 09 months, revealed that the improvement in mean LVEF (%) from 28.6% (SD= 2.8) to 37.3% (SD= 7) intraoperatively to 41.5(SD= 8.3) (Range: 20-55), at one year follow up, with p value of <0.001, which is statistically very significant. There is also a significant improvement in the NYHA Class in the study population. Preoperatively, 82, (82%) patients in the study group were in NYHA Class 3B, and 18(18%) were in class 2B. However at 06 month postoperative follow up, 79, (81.4%) of the study population functionally improved to, class 1B, with p value of <0.001, which is statistically very significant. All the patients in this group were on antihypertensive, antiplatelet, and lipid lowering agents routinely and 18, (18%) of the study population were on antianginals, diuretics, carvedilol along with ACE inhibitors also. The abnormality in the LV contractility as RWMA or global hypokinesia as shown in the preop 2D Echocardiography was also significantly improved. Preoperatively, 88, (88%) had RWMA and 12, (12%) had Global HK, while at 06 month post op follow up, 26, (27.7%) had no RWMA, 63, (67%) had RWMA, and only 5, (5.3%) had Global HK, with p value of <0.001, which is also statistically significant. There is also nil mortality during the study period in the study group and no redo surgery was needed.

Many groups and studies have also reported improvements in survival, ventricular function, and functional status after coronary revascularization in patients with severe LV dysfunction [5-11]. From the clinical perspective, recovery of global function is more important than regional improvement [16, 17]. We compared our study and results with following studies, and found that our study outcome was comparable with good results.

Mehrdad Salehi *et al.* in their study, showed that CABG in patients with severe LV Dysfunction can be performed with low mortality. They enrolled 145 patients with severely impaired LV function (ejection fraction ≤ 30%) undergoing either on-pump or off-pump CABG. Different variables (preoperative, intraoperative, and postoperative) were

evaluated and compared. The mean preoperative LV ejection fraction was  $25.33 \pm 5.07\%$  (10 to 30%), which improved to  $26.67 \pm 5.38\%$  (10 to 40%) (P value < 0.001). Off-pump CABG was performed in 25(17.2%) patients[5]. They also showed that, patients who underwent off-pump CABG had higher operative mortality, compared to our study, in which 19(19%) of the patients underwent off pump CABG with comparable post operative results as in on pump CABG, however, it was observed that threshold of using IABP was less in the off pump group.

Sak Lee, MD *et al.* from republic of Korea studied a total of 120 patients with CAD and severe LV dysfunction (LV EF  $\leq 30\%$ ), who underwent CABG in last 15 years. Mean LVEF was 23.5%, and 75% of patients were in New York Heart Association functional class III or IV. Mean LVEF improved to 32% postoperatively, and further improved to 39% at a mean follow-up of 57.6 months ( $p < 0.05$ ). They concluded that CABG in such setting provides optimal survival with an improved EF and functional state [6].

Lynda L. Mickleborough *et al* in their study evaluated the experience with isolated revascularization in similar settings. In 79 patients of their study group, preoperative ejection fraction was  $18 \pm 5\%$ . Hospital mortality was 3.8% and intraaortic balloon pump was used in 18 of 79 (23%). Morbidity included myocardial infarction in 2 of 79 (2.5%) and stroke in 2 (2.5%). Post op, angina improved in 84% and heart failure improved in 26%. These data supported the bypass graft surgery in patients with severe LV dysfunction [7].

John A. Elefteriades *et al* retrospectively analyzed the data of 83 consecutive patients with a left ventricular ejection fraction of  $< 30\%$ , who underwent isolated CABG. The hospital mortality rate was 8.4%. NYHA class improved postoperatively by 1. Left ventricular ejection fraction improved from 24.6% preoperatively to 33.2% postoperatively with p value < 0.001[8].

With reference to the Meta analysis published by Underwood *et al* [9], it is also understood that the improvements in LVEF, and the LV contractility, along with improved NYHA class following CABG in such settings are related to postoperative myocyte recruitment. Basically, restoration of perfusion resuscitates dormant and viable myocardium and protects the previously functioning portions of the ventricle from further ischemic insults, arrhythmias, and infarction. Hence, the most important factor for successful surgical recovery may be the viability of revascularized myocardium [13, 14].

**Strength of the study** It is a single center study with similarities in the study population in terms of the demographic, clinical, angiographic and the 2D Echocardiography findings and the maximum number of the patients in the study group were operated by single surgeon, hence bias are less. Secondly patients in the study group were followed up strictly and 100 % of the patients were in contact through social media like whatsapp and face book for better coordination for postop follow up and investigations. Retrospective and prospective studies were combined. Postoperative changes were recorded carefully and LVEF changes in the maximum number of the patients were investigated by MUGA scan with better accuracy.

**Limitations:** It is an observational study, with analysis of short term and the early midterm results only.

**Research implication and future direction:** We should also consider preoperative investigations such as nuclear imaging studies like PET or SPECT imaging with Tc-99M labeled radiotracers derived myocardial viability information, in addition to the clinical, 2D Echocardiography and angiographic data into the process of selecting the patients with severe LV dysfunction for CABG with reference to the meta analysis published by Underwood *et al*[12] which clearly demonstrated an increase in LVEF in patients with evidence of hibernating myocardium, but no improvement in those with nonviable or scarred myocardium.

We should also evaluate and study the role of elective use of IABP, better myocardial preservation techniques, total arterial coronary conduits and off pump CABG in such setting. We can also undertake RCT's to remove the bias influencing the postoperative outcomes, like better compliance of the patients in terms of taking medicines, adopting disciplined and healthy lifestyle, with dietary modification, quitting smoking and strict blood sugar control.

## CONCLUSION

The outcome of this study shows definite improvement in the LVEF and in the NYHA class and suggests that, CABG in this setting of the patients is effective, safe and should be recommended. Furthermore, it also showed that off-pump CABG can be performed safely even in patients with low EF, provided it is done with good surgical technique with advanced off pump surgical equipments and good anesthesia support, along with elective and judicious use of IABP. However, in future, we may go for randomized controlled trials, or include multicenter studies to prove our point.

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