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**International Journal of Life Sciences**  
(ISSN: 2277-193x) (Scientific Journal Impact Factor: 6.106)

UGC Approved-A Peer Reviewed Quarterly Journal



## "Prognostic Value of Dobutamine Stress Echocardiography in Functional and Clinical Recovery after Coronary Artery Bypass Grafting in Patients with Impaired Left Ventricular Function"

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### ARTICLE DETAILS

### ABSTRACT

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**Key words:**  
Dobutamine stress echocardiography, coronary artery bypass grafting, low ejection fraction.

**Introduction:** Coronary artery bypass graft (CABG) decrease mortality by 25% and the occurrence of sudden cardiac death by 50% in patient with ischemic heart disease. The advantages of having viable myocardium in the revascularized area outweigh the higher surgical risk in patients with poor ejection fraction (EF). Additionally, it has been proven that (CABG) is more beneficial than conservative treatment in patients with low EF but viable myocardium, dobutamine-stress echocardiography use to predict surgical outcome of patients with multi-vessels disease with low EF. **Material and Methods:** this study is a descriptive cohort study that was conducted at the Al-Azhar University hospitals on 100 patients who underwent (CABG) with low ejection fraction to identify potential associated risk factors of postoperative outcome based on the results of dobutamine-stress echocardiography (DSE) with a follow-up period of 6 months. **Results:** The results showed that there was a statistically significant improvement in LVEDD, LVESD, and LVEF parameters after surgery. on univariable analysis of the associated risk factors of in-hospital mortality, the significant associated factors were age > 60 years, peak WMSI on DSE >1.5, improvement of LVEF on DSE <10%, insertion of IABP (intra- or post-operative) and incomplete revascularization. Low cardiac output (57.0%), arrhythmia (15.0%), reopening for bleeding (5.0%), sternal wound infection (3.0%), pulmonary problems and postoperative IABP (7.0% each), and renal complications (2.0%). Peak WMSI on DSE >1.5, improvement of LVEF on DSE 10%, and partial revascularization were the significant associated factors on univariable analysis of the associated factors of functional non-recovery. **Conclusion:** Patients with poor ejection fraction can experience considerable improvements in cardiac function and quality of life after undergoing coronary artery bypass grafting (CABG)

### 1. Introduction

In patients with ischemic heart disease, surgical coronary artery revascularization has considerably increased survival by lowering mortality rate and the occurrence of sudden cardiac death by of 25% and 50% respectively <sup>(1)</sup>. The advantages of having viable myocardium in the area undergoing revascularization outweigh the higher operational risk in patients with poor ejection fraction (EF). Additionally, it has been proven that coronary artery bypass graft (CABG) is more beneficial than conservative treatment in patients with low EF but viable myocardium <sup>(2)</sup>.

With adrenergic stimulation provided by dopamine, isoproterenol, and dobutamine, impaired regional function brought on by myocardial stunning or a hibernating myocardium can be reversed. If contractility was improved in at least four parts, the test was deemed successful. likelihood of improved regional wall motion and LV function, improved New York Heart Association (NYHA) class, and increased mortality following successful surgical coronary revascularization increases with the degree and extent of viable myocardial segments present prior to surgery <sup>(3)</sup>.

This study conducted on patients with multi-vessels disease with low EF undergo Coronary artery bypass graft (CABG) to predict surgical outcome and shows significant improvement of cardiac function after cardiac surgery based on the results of dobutamine-stress echocardiography (DSE) and follow up after six months.

## 2. Materials and Methods

### 2.1 Study design.

This study was a descriptive cohort study which was conducted at the Al-Azhar University hospitals in Cairo, Egypt. This study aimed to evaluate the outcomes following coronary artery bypass graft (CABG) in 100 patients with low ejection fraction and to identify potential associated factors of postoperative outcome based on the results of dobutamine-stress echocardiography (DSE).

### 2.2 Inclusion and exclusion criteria

100 Patients were recruited from Cardiothoracic Surgery and Cardiology Departments at Al-Azhar University during the study period of a year with a 6-month follow-up were included in the current study according to the following.

*Inclusion criteria:* patients with chronic stable coronary artery disease (CAD) undergoing isolated, elective, on-pump CABG with low ejection fraction ( $EF \leq 40\%$ ) on trans-thoracic echocardiography (TTE)

*The exclusion criteria* including Patients with concomitant valve replacement, previous cardiac surgery, Redo-CABG, emergency CABG, hepatic or renal failure, ventricular or aortic aneurysmal repair, overt peripheral vascular disease, surgery for arrhythmia, repair of ventricular septal perforation, concomitant carotid artery surgery, recent myocardial infarction, or acute coronary artery syndrome.

### 2.3 Sampling technique

A consecutive sample of all patients admitted to Cardiothoracic Surgery and Cardiology Departments at Al-Azhar University during the study period 2 years from September 2021 to august 2023 and meeting the inclusion criteria were selected to be participants in the current study.

### 2.4 Data collection

*All the study participants were subjected to the following:* Routine preoperative laboratory and radiological investigations for cardiac surgery including angiographic and echocardiographic studies. Dobutamine Stress Echocardiography (DSE) was performed using a 16-segment model analysis in which intravenous administration of Dobutamine was started at a dose of 5.0  $\mu\text{g}/\text{kg}/\text{min}$  and increased by 5–10  $\mu\text{g}/\text{kg}/\text{min}$  every 3 minutes up to a maximum of 40  $\mu\text{g}/\text{kg}/\text{min}$ , or until a study endpoint was achieved. Study participants were instructed to avoid taking drugs with a positive inotropic action 3 days prior to the test. Conventional on-pump CABG through median sternotomy with standardized anesthetic and surgical techniques. After surgery, patients were managed at Cardiothoracic Surgery ICU. Echocardiography was performed within one week after CABG and at the end of 6 months after surgery during the follow-up.

### 2.5 Ethical considerations

A written informed consent was obtained from all participants. Confidentiality of data was assured, and data collection forms were anonymous. The study protocol was approved by the Scientific Research Ethical Committee of Faculty of Medicine, Al-Azhar University under IRB Registration number.

### 2.6 Statistical analysis

Data were analyzed using IBM Statistical Package for Social Science (SPSS) Statistics for Windows version 20.0 and MedCalc software version 15.8.0. Quantitative data were expressed as median and inter quartile range. Qualitative data were expressed as number and percentage. Data were tested for normality using the Shapiro-Wilk test. Independent samples t test was applied for normally distributed data. The nonparametric Mann-Whitney test was used for data which were not normally distributed. Chi-square ( $\chi^2$ ) test and Fisher's Exact Test were used for comparison of qualitative variables as appropriate. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

**3. Results:**

In relation to the sociodemographic data of the studied patients, the current study estimates that mean age of study participants was  $50.32 \pm 6.32$  years, 35.0% were male while 65.0% were female, 62.0% and 58.0% had D.M and HTN with mean Euro score II of  $1.45 \pm 0.11$ . respectively. 47.0% of the studied patients were ex-smokers and 24.0% still smokers. there was a relative increase in the frequency of obese patients with body mass index (BMI) > 30 kg/m<sup>2</sup> (58.0%). Most of the patients were smokers (47.0% ex-smokers and 24.0% still smokers), In relation to the medical health history of the studied patients, the current study mentions that (70% and 72.0%,61% and 14%) of the studied patients had NYHA functional class III respectively .and CCS angina grade III, 3-vessels disease and left main stem disease. Also, the studied patients were receiving Beta-blockers and statins by (64% and 39%) respectively. Concerning the Changes in the findings of trans-thoracic echocardiography pre & postoperatively and at the end of follow-up period in survivors. The current study shows that the studied patients had preoperative left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD) and left ventricular ejection fraction (LVEF) of  $5.12 \pm 0.45$  cm of  $4.25 \pm 0.21$  cm and  $40.32 \pm 1.36$ . respectively. while the same parameters were  $4.97 \pm 0.37$ ,  $3.96 \pm 0.21$  and  $56.21 \pm 3.21$  postoperatively. Also, the studied patients had left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD) and left ventricular ejection fraction (LVEF) of  $4.95 \pm 0.42$ ,  $3.46 \pm 0.31$  and  $59.7 \pm 4.25$  respectively in the follow up period. Regarding SWAM, the apical contraction on TTE was presented as hypokinesia, akinesia and dyskinesia by (28.0%, 47.0% and 25.0%) respectively, while the same parameters were 48 %, 5% and 0%) postoperatively while the apical contraction on TTE was presented as hypokinesia, akinesia and dyskinesia by (43% ,4% and 0%) respectively in the follow up period. There was highly statistical significance between the findings of trans-thoracic echocardiography pre & postoperatively and at the end of follow-up period in which  $p < 0.001$ , All these results showed in Table (1).

**Table 1:** Changes in the findings of trans-thoracic echocardiography postoperatively and at the end of follow-up period in survivors

	Preoperative	Postoperative	Follow-up	Test Value	P-value	Sig.
LVEDD (cm)	$5.12 \pm 0.45$	$4.97 \pm 0.37$	$4.95 \pm 0.42$	5.021	0.007	HS
LVESD (cm)	$4.25 \pm 0.21$	$3.96 \pm 0.21$	$3.46 \pm 0.31$	259.957	0.000	HS
LVEF (%)	$40.32 \pm 1.36$	$56.21 \pm 3.21$	$59.7 \pm 4.25$	1059.459	0.000	HS
<b>SWMA</b>				-	-	-
- Normal	0 (0%)	47 (47%)	53 (53%)			
- Hypokinesia	28 (28.0%)	48 (48 %)	43 (43%)	170.538	0.000	HS
- Akinesia	47 (47.0%)	5 (5%)	4 (4%)			
- Dyskinesia	25 (25.0%)	0 (0%)	0 (0%)			

In relation to Multivariable analysis of the associated factors of in-hospital mortality after CABG in patients with low LVEF (Cox Proportional Hazards Regression Analysis, the current study shows that Insertion of IABP is highly significant associated factor within hospital mortality  $p < 0.001$ ), On multivariable analysis of the predictors of in-hospital mortality (**Table 2**), the insertion of IABP was the only significant predictor of mortality.

**Table 2:** Multivariable analysis of the predictors of in-hospital mortality after CABG in patients with low LVEF (Cox Proportional Hazards Regression Analysis)

	OR	95% CI	P-value
Age > 60 years	4.12	0.79-12.9	0.121
Peak WMSI on DSE >1.5	3.90	0.85-17.52	0.089
Improvement of LVEF on DSE <10%	2.31	0.35-14.67	0.420
Insertion of IABP	6.18	1.45-26.90	<b>0.001*</b>
Incomplete revascularization	5.66	0.47-72.99	0.190

About Multivariable analysis of the predictors of functional non-recovery after CABG in patients with low LVEF (Binary Logistic Regression Analysis) the current study mentions that Peak WMSI on DSE >1.5, Improvement of LVEF on DSE <10% and Incomplete revascularization were at odd ratio and 95% IC of (4.72, 9.45 and 29.89) respectively. The improvement of LVEF on DSE <10% and incomplete revascularization were significant associated factors of functional non-recovery. All these results are shown in Table (3). Regarding preoperative extent of coronary artery disease, the current study shows that coronary revascularization was complete in 74.0% and incomplete in 26.0%. Coming off bypass required inotropes in 49.0% and IABP in 10.0%.

**Table 3:** Multivariable analysis of the predictors of functional non-recovery after CABG in patients with low LVEF (Binary Logistic Regression Analysis)

	OR	95% CI	P-value
Peak WMSI on DSE >1.5	4.72	0.59-41.43	0.162
Improvement of LVEF on DSE <10%	9.45	1.39-62.58	<b>0.002*</b>
Incomplete revascularization	29.89	5.59-196	<b>&lt;0.001*</b>

In relation to the Postoperative complications, the current study showed that low cardiac output arrhythmia reopening for bleeding (Sternal wound infection, pulmonary complications (and renal complications were presented in (57.0%,15.0%,5.0%,3.0%,7.0% and 2.0%) of the studied patients respectively. The mean duration of mechanical ventilation and hospital stay was  $25.32 \pm 11.01$  hours and  $10.36 \pm 2.36$  days respectively. While the incidence of 30-day (in-hospital) mortality was 9.0%. Regarding the NYHA Functional class and CCS angina, there were highly statistically significant differences when comparing pre-operative and follow up after surgery  $p < 0.001$ .

### Discussion

Coronary artery disease (CAD) is one manifestation of ischemic heart disease, which is the leading cause of mortality in the world. In addition to preventive medical therapy and lifestyle changes, consideration of revascularization of obstructed arteries to reduce ischemia, alleviate angina, and improve quality of life is a mainstay of current practice <sup>(4)</sup>.

Coronary artery revascularization can be performed surgically or percutaneously. Surgery is associated with higher procedural risk and longer recovery than percutaneous interventions, but with long-term reduction of recurrent cardiac events. For many patients with obstructive coronary artery disease in need of revascularization, surgical or percutaneous intervention is indicated based on clinical and anatomical reasons or personal preferences. Medical therapy is a crucial accompaniment to coronary revascularization, and data suggest that, in some subsets of patients, medical therapy alone might achieve similar results to coronary revascularization <sup>(5)</sup>

CABG for dysfunction but viable myocardium enhances LV recovery of function and ensures acceptable survival. The results of DSE in patients with low LVEF are predictive for clinical improvement. Therefore, assessment of wall motion score index and LVEF with dobutamine echocardiography may be the optimal means of evaluating the impact of viability on prognosis <sup>(6)</sup>

The aim of this study was to evaluate the outcomes following coronary artery bypass graft (CABG) in 100 patients with low ejection fraction and to identify potential associated factors of postoperative outcome based on the results of dobutamine-stress echocardiography (DSE).

In relation to the sociodemographic data of the studied patients, the current study estimates that mean age of study participants was  $50.32 \pm 6.32$  years, 35.0% were male while 65.0% were female, 62.0% and 58.0% had D.M and HTN with mean Euro score II of  $1.45 \pm 0.11$ . respectively. 47.0% of the studied patients were ex-smokers and 24.0% still smokers. there was a relative increase in the frequency of obese patients with body mass index (BMI) > 30 kg/m<sup>2</sup> (58.0%). Most of the patients were smokers (47.0% ex-smokers and 24.0% still smokers) in this context, Escobar et al, 2023 <sup>(7)</sup> mentioned that in the overall HF population, mean age was 69.7 (19.0) years and 53.8% of patients were men. Regarding comorbidities, 59.1% of patients had hypertension, 27.6% type 2 diabetes, 33.1% coronary artery disease, 28.2% atrial fibrillation and 26.7% chronic kidney disease.

In relation to the medical health history of the studied patients, the current study mentions that (70% and 72.0%,61% and 14%) of the studied patients had NYHA functional class III respectively .and CCS angina grade III, 3-vessels disease and left main stem disease .this result is matched with Chandra et al,2018 <sup>(8)</sup> who mentioned that most of the patients had dilated cardiomyopathy (61 [73.5%] with an EF<0.5), CCS functional class II-III, and sinus rhythm .Also, the studied patients were receiving Beta-blockers and statins by (64% and 39%) respectively. This result is mismatched with who Escobar et al, 2023 <sup>(7)</sup>, mentioned that 1% of the studied patients were taking beta-blockers, 56.3% renin-angiotensin system inhibitors, 11.8% mineralocorticoid receptor antagonists and 8.9% SGLT2 inhibitors.

Concerning the Changes in the findings of trans-thoracic echocardiography pre & postoperatively and at the end of follow-up period in survivors. The current study shows that the studied patients had preoperative left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD) and left ventricular ejection fraction (LVEF) of  $5.12 \pm 0.45$  cm of  $4.25 \pm 0.21$  cm and  $40.32 \pm 1.36$  respectively while the same parameters were  $4.97 \pm 0.37$ ,  $3.96 \pm 0.21$  and  $56.21 \pm 3.21$  postoperatively. In this context, Stankowski et.al, 2024 <sup>(9)</sup> stated that at discharge, the mean postoperative transvalvular

pressure gradient was  $15.1 \pm 8.4$  mmHg and was comparable between both groups. Paravalvular leak (PVL) occurred in 44 (38.6%) patients, however, nearly 90% of them presented mild PVL, and we did not observe any severe PVL after VIV-TAVI. Both LVEF and tricuspid annular plane systolic excursion did not significantly change after VIV-TAVI, and there were no differences between groups before and after PSM.

Also, the studied patients had left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD) and left ventricular ejection fraction (LVEF) of  $4.95 \pm 0.42$ ,  $3.46 \pm 0.31$  and  $59.7 \pm 4.25$  respectively in the follow up period. This result is in line with Stankowski et al, 2024<sup>(9)</sup>, who mentioned that in the follow-up period, 71 (62.3%) patients survived, 59 (70.2%) of them in the non-mild MR group, and 12 (40.0%) in the moderate MR group. The overall survival probabilities at one, three, and five years were 93.7%, 71.0%, and 53.8%. In the unmatched cohort, survival probabilities at one, three, and five years were 96.3% vs. 86.3%, 74.6% vs. 60.9%, and 66.0% vs. 25.0% in the none to mild MR group vs. moderate MR group, respectively (log-rank  $P=0.003$ ). In the matched cohort, survival probabilities at one, three, and five years were 95.7% vs. 87.0%, 85.0% vs. 64.5%, and 85.0% vs. 29.0% in the none to mild MR group vs. moderate MR group, respectively (log-rank  $P=0.035$ )

Regarding SWAM, the apical contraction on TTE was presented as hypokinesia, akinesia and dyskinesia by (28.0%, 47.0% and 25.0%) respectively, while the same parameters were 48%, 5% and 0% postoperatively while the apical contraction on TTE was presented as hypokinesia, akinesia and dyskinesia by (43%, 4% and 0%) respectively in the follow up period. In this context, Meo et al, 2020<sup>(10)</sup>, stated that Abnormal ventricular wall motion is a strong clinical predictor of sudden, arrhythmic, cardiac death. Dispersion in repolarization is a prerequisite for the initiation of re-entrant arrhythmia, The patient group with Wall motion abnormality was included six patients with hypokinesia and six patients with akinesia or dyskinesia in which dispersion of ARIs between the nine segments was significantly increased in the hypokinetic ( $84 \pm 7.4$  ms,  $p < 0.005$ ) and akinetic/dyskinetic group ( $94 \pm 3.5$  ms,  $p < 0.0005$ ) compared with the normal group ( $49 \pm 5.1$  ms)

There was highly statistical significance between the findings of trans-thoracic echocardiography pre & postoperatively and at the end of follow-up period in which  $p < 0.001$ . This result is mismatched with Papestiev et al, 2023<sup>(11)</sup> who mentioned that Preoperative global longitudinal strain was reduced (GLS  $< -17\%$ ) in 39% of the patients. Parameters of systolic LV function were significantly reduced in this group of patients compared to the patient group with  $GLS\% \geq -17\%$ . In both groups, 4 months after CABG there was a decline in LVEF but statistically significant only in the group with  $GLS\% \geq -17\%$  ( $p = 0.035$ ). In patients with reduced GLS, there was a statistically significant postoperative improvement ( $p = 0.004$ ). In patients with preoperative normal GLS, there was not a significant change in any strain parameters after CABG. There was an improvement in diastolic function parameters measured by Tissue Doppler Imaging (TDI) in both groups.

In relation to Multivariable analysis of the associated factors of in-hospital mortality after CABG in patients with low LVEF (Cox Proportional Hazards Regression Analysis, the current study shows that Insertion of IABP is highly significant associated factor with in hospital mortality  $p < 0.001$ ) this result is mis matched with Talukder et al, 2022<sup>(12)</sup> who illustrated that Preoperative factors that were identified as statistically significant predictors of 10-year mortality in the multivariable analysis (all  $P \leq 0.01$ ) were: left ventricular ejection fraction, atrial fibrillation, age, diabetes, prior cerebrovascular event (stroke or transient ischemic attack), serum creatinine and smoking status. The following variables were significantly associated in univariable models but did not retain significance in the multivariable model for mortality: non-Caucasian ethnicity, hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, and prior myocardial infarction. Also, he mentioned that independent predictors of 10-year mortality in the ART were identified including: heart function, renal function, cerebrovascular disease, age, atrial fibrillation, smoking status, and diabetes. Understanding which preoperative variables influence long-term outcome after coronary artery bypass grafting may help to target treatments to those at higher risk to reduce mortality. About Multivariable analysis of the associated factors of functional non-recovery after CABG in patients with low LVEF (Binary Logistic Regression Analysis) the current study mentions that Peak WMSI on DSE  $> 1.5$ , Improvement of LVEF on DSE  $< 10\%$  and Incomplete revascularization were at odd ratio and 95% IC of (4.72, 9.45 and 29.89) respectively. The improvement of LVEF on DSE  $< 10\%$  and incomplete revascularization were significant associated factors of functional non-recovery. In this context, Rijnhart-de Jong et al, 2020<sup>(13)</sup>, showed that (21.9%) did not display an improvement in the SF-36 physical domain score 1 year after cardiac surgery. In a multivariate analysis independent risk factors for non-recovery in the SF-36 physical domain were baseline SF36 physical domain score (OR 0.954 [0.942–0.965],  $P < 0.001$ ), diabetes (OR 0.437 [0.265–0.720],  $P 0.001$ ), female sex (OR 0.492 [0.307–0.789],  $P 0.003$ ), post-operative infection (OR 0.240 [0.109–0.525],  $P < 0.001$ ) and PCI within 1 year (OR 0.113 [0.036–0.349],  $P < 0.001$ ) For isolated CABG, 23.2% of patients did not display an improvement in the physical domain score and risk factors appeared to be identical.

In relation to preoperative extent of coronary artery disease, the current study shows that coronary revascularization was complete in 74.0% and incomplete in 26.0%. Coming off bypass required inotropes in 49.0% and IABP in 10.0%. In this context, Leviner<sup>(14)</sup> mentioned that Complete revascularization was more often achieved with CABG than with PCI and is associated with a 30% reduction in long-term mortality, a 22% reduction in MI, and a 26% reduction in repeat coronary revascularization procedures. The lower mortality associated with CR was seen in both PCI- and CABG-treated patients and was independent of the study design and definition of CR. This is arguably the most statistically powerful and rigorous assessment in the peer-reviewed literature of the impact of CR and IR among both PCI a CABG patients with multivessel CAD. In relation to the Postoperative complications, the current study showed that low cardiac output arrhythmia reopening for bleeding (Sternal wound infection, pulmonary complications (and renal complications were presented in (57.0%,15.0%,5.0%,3.0%,7.0% and 2.0%) of the studied patients respectively. The mean duration of mechanical ventilation and hospital stay was  $25.32 \pm 11.01$  hours and  $10.36 \pm 2.36$  days respectively. In this context, Montrief<sup>(15)</sup>, stated that post-CABG surgery complications can affect many different systems other than the cardiovascular system, as patients are at risk for common post-surgical complications, including respiratory failure, stroke, urinary tract infections, renal failure, coagulopathy, limb ischemia, wound dehiscence, pleural effusion, and hematologic abnormalities.

This result is in line with Montrief<sup>(15)</sup>, who mentioned that the incidence of 30-day (in-hospital) mortality was 9.0%. CABG surgery is often considered a high-risk procedure, associated with a 30-day morbidity and mortality rate up to 14.0% and 2.0%, respectively there has been a widespread institution of early extubation and fast track protocols, which has resulted in earlier hospital discharge, with an average post-op length of stay of 5.4 days.

### Conclusion

In conclusion, our study suggests that coronary artery bypass grafting (CABG) can lead to significant improvements in cardiac function and quality of life in patients with low ejection fraction. The study found an improvement in the patient's symptoms and functional limitations. Additionally, there was an overall improvement in cardiac function. However, the study also identified certain associated factors of postoperative outcomes, including age > 60 years, peak WMSI on DSE >1.5, improvement of LVEF on DSE <10%, insertion of IABP, and incomplete revascularization, which were associated with an increased risk of in-hospital mortality and functional non-recovery.

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