Role of dobutamine-stress echocardiography in prediction of clinical and functional improvement after coronary artery bypass grafting in patients with low ejection fraction

Faisal A. Mourad, Gamal S. Sayed, Mostafa A.-A.A. El-Gawad, Mostafa E.K. Abdelkareem, Mohammed N.A. Jawad

Department of Cardiothoracic Surgery, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence to Mostafa E.K. Abdelkareem, MSc, Department of Cardiothoracic Surgery, Faculty of Medicine, Aswan University, Aswan 81528, Egypt. Tel: (+2) 01066880063; e-mail: mostafactsu@gmail.com

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Background
The aim of this study was to assess the results after coronary artery bypass graft (CABG) in patients with reduced ejection fraction (EF; ≤40%) but viable myocardium and to determine the possible predictors of postoperative outcome, depending on preoperative dobutamine-stress echocardiography (DSE) results.
Patients and methods
The study included 110 patients who underwent isolated elective on-pump CABG with left ventricular ejection fraction (LVEF) less than 40%. This study was conducted at the Department of Cardiothoracic Surgery in Ain Shams University Hospital, Nasr City Insurance Hospital, and Minia University Hospital. This prospective observational study was conducted over 1 year with a follow-up period of 6 months.
Results
The study approved a statistically significant increase in New York Heart Association class I and Canadian Cardiovascular Society grades I and II. Changes in the findings of trans-thoracic echocardiography postoperatively and at the end of the follow-up period in survivors compared with preoperative values were statistically significant in the form of improvements in LV dimensions, LVEF, and segmental wall motion abnormalities. On univariable analysis of the predictors of in-hospital mortality, the significant predictors were age more than 60 years, peak wall motion score index on DSE more than 1.5, improvement of LVEF on DSE less than 10%, insertion of intra-aortic balloon pump (intraoperative or postoperative), and incomplete revascularization. On multivariable analysis of the predictors of in-hospital mortality, insertion of intra-aortic balloon pump was the only significant predictor of mortality.
Conclusion
CABG for dysfunctioning 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.

Keywords:
coronary artery bypass grafting, dobutamine-stress echocardiography, low ejection fraction

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Introduction

Surgical coronary artery revascularization has significantly improved the survival of patients with ischemic heart disease by reducing mortality by 25% and the incidence of sudden cardiac death by 50% [1].

The increased operative risk in patients with poor ejection fraction (EF) is offset by the benefits resulting from viable myocardium in the area subjected to revascularization [2]. In addition, it has been demonstrated that in patients with low EF but viable myocardium, the benefit of coronary artery bypass graft (CABG) is higher than the benefit of conservative treatment [3].

The current tools used for predicting recovery of ventricular function include low-dose dobutamine-stress echocardiography (DSE), single-photon emission tomography with thallium-201, and F-18 fluorodeoxyglucose positron emission tomography. Of these techniques, DSE is a safe, widely available, and relatively inexpensive method for identifying viable myocardium [3].

Impaired regional function resulting from myocardial stunning or hibernating myocardium can be reverted with adrenergic stimulation by dopamine, isoproterenol, and dobutamine [4].

The test was considered positive if improvement in contractility was achieved in at least four segments [5].

The greater the degree and extent of viable myocardial segments preoperatively, the more likely the probability of improved regional wall motion and LV function, improved New York Heart Association (NYHA) class, and enhanced survival following successful surgical coronary revascularization [6].

Patients and methods

This study was conducted at the Department of Cardiothoracic Surgery in Ain Shams University Hospital, Naser City Insurance Hospital, and Minia University Hospital. This prospective observational study was conducted over 1 year with a follow-up period of 6 months.

The study included adult patients of both genders, patients with chronic stable coronary artery disease undergoing isolated, elective, on-pump CABG, and patients with low EF (≤40%) on trans-thoracic echocardiography, and excluded 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, and recent myocardial infarction or acute coronary artery syndrome. During the study period, 110 patients fulfilled our selection criteria. The study considered the ethical principles of the Helsinki Declaration. Approval from a research ethics committee and informed consent from patients were obtained.

Routine preoperative laboratory and radiological investigations for cardiac surgery were performed for all patients, including angiographic and echocardiographic studies. In addition, determination of preoperative myocardial viability was done by DSE.

All patients underwent conventional on-pump CABG with standardized anesthetic technique. Surgeons preferred to use blood cardioplegia in most cases with combined antegrade and retrograde routes. Echocardiography was repeated in the first week after surgery and in the sixth month during the follow-up period.

The collected data included preoperative risk factors: age, female gender, NYHA class, obesity, smoking, chronic obstructive pulmonary disease, hypertension, diabetes mellitus, hypercholesterolemia, chronic systematic diseases, myocardial infarction, the extent of coronary-artery disease, transient ischemic attack or stroke, and European System for Cardiac Operative Risk Evaluation.

The collected data from DSE included EF (resting, low dose, and peak dose), wall-motion score index (total score divided by the number of analyzable segments), and myocardial viability. The test was considered positive for myocardial viability if an improvement in contractility was achieved in at least four segments.

The collected postoperative echocardiographic data included EF, wall motion abnormalities, and any significant findings.

All statistical analyses were carried out using the SPSS program (IBM Corp., Armonk, NY, USA). Data were expressed as mean and standard deviation for continuous data or number and percentage for categorical data. Comparison of independent data groups was made using —Student's t-test for continuous data or χ^2 for categorical data. Predictors of outcome were estimated using multivariate regression analysis. A P-value less than 0.05 was considered significant.

Results

Preoperative characteristics of the studied patients are presented in Table 1. Preoperative findings of DSE revealed an averaged rest wall motion score index (WMSI) of 1.63 ± 0.18 and averaged peak WMSI of 1.40 ± 0.11. The average improvement in LVEF on DSE was 10.04 ± 2.51% per patient, with a higher frequency of improvement more than 10% (64.5%) (Table 2).

The postoperative outcome and complications are presented in Fig. 1. There was a significant improvement in NYHA class I and Canadian Cardiovascular Society (CCS) grades I and II (Table 3). Regarding the changes in postoperative echocardiographic findings, there were statistically significant improvements in the LF dimensions, LVEF, and segmental wall motion abnormalities (Table 4). On univariable analysis of the predictors of functional nonrecovery (Table 5), the significant predictors were peak WMSI on DSE more than 1.5, improvement of LVEF on DSE less than 10%, and incomplete revascularization. On multivariable analysis of the predictors of functional nonrecovery (Table 6), improvement of LVEF on DSE less than

Table 1 Demographic characteristics of the studied patients

Variables	Patients with low EF (*n*=110)
Age (years)	55.42±7.92
Age groups	
>60 years	28 (25.5)
<60 years	82 (74.5)
Sex	
Male	74 (67.3)
Female	36 (34.7)
Height (cm)	168.2±5.85
Weight (kg)	86.88±12.32
BMI (kg/m^2)	30.78±4.69
Obesity	
BMI >30 kg/m^2	58 (52.7)
BMI <30 kg/m^2	52 (47.3)

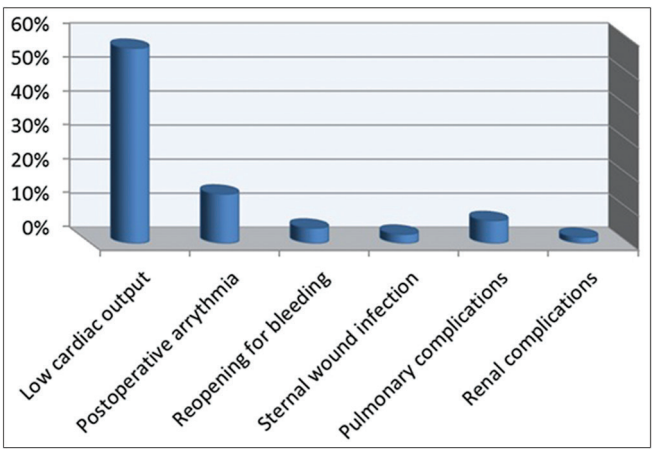
Data are presented as mean±SD or number (%). BMI, body mass index; EF, ejection fraction.

Table 2 Preoperative findings of dobutamine-stress echocardiography (DSE)

Variables	Patients with low EF (*n*=110)
Wall motion on rest DSE (per patient)	
Normal segments	9.41±1.97
Hypokinetic segments	3.98±1.67
Akinetic segments	1.55±0.94
Dyskinetic segments	1.04±0.68
Wall motion on peak DSE (per patient)	
Normal segments	11.77±0.96
Hypokinetic segments	2.22±0.69
Akinetic segments	1.66±0.72
Dyskinetic segments	0.33±0.47
Rest WMSI	1.63±0.18
Peak WMSI	1.4±0.11
Improvement in LVEF % (per patient)	10.04±2.51
Improvement in LVEF	
<10%	39 (35.5%)
>10%	71 (64.5%)

Data are presented as mean±SD or number (percent). DSE, dobutamine-stress echocardiography; LVEF, left ventricular ejection fraction; WMSI, wall motion score index.

Fig. 1



Distribution of postoperative complications.

Table 3 Comparison of preoperative and follow-up dyspnea and angina states in survivors (*n*=100)

Variables	Preoperative	Follow-up	*P* value
NYHA functional class			
I	0	58 (58)	<0.001*
II	28 (28)	31 (31)	0.64
III	69 (69)	11 (11)	<0.001*
IV	3 (3)	0	0.24
CCS angina scores			
I	0	59 (59)	<0.001*
II	20 (20)	41 (41)	0.001*
III	71 (71)	0	<0.001*
IV	9 (9)	0	0.003*

Data are presented as numbers (%). Fisher's exact test was used to compare qualitative data. CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association. *Significant difference.

10% and incomplete revascularization were significant predictors of functional nonrecovery.

Discussion

An increasing number of patients with ischemic heart disease and impaired function are being qualified for cardiac surgery. In these patients, coronary revascularization can lead to clinical improvement and reversal of LV remodeling, which led to the concept of viable myocardium to select patients in whom recovery of LV function and improvement of prognosis will outweigh the risk of the surgical maneuver [5,7].

The selection of patients with reduced EF for CABG is considered crucial in achieving a favorable outcome. Therefore, our selected criterion of viable myocardium determined by DSE was following meta-analysis performed by Allman *et al.* [3], which demonstrated improved survival rate after revascularization in patients with LV dysfunction and viable myocardium.

Various noninvasive imaging techniques are available to detect viable myocardium, including magnetic resonance imaging, DSE, and nuclear imaging with single-photon emission computed tomography or positron emission tomography [8].

DSE has the highest specificity for detecting viable myocardium and remains the most widely available test [9].

In our patients, LVEF significantly improved from 37.23%±2.37% preoperatively to 53.22%±4.09% after CABG. Also, left ventricular end-diastolic diameter and left ventricular end-diastolic diameter significantly improved after CABG. A study by Hirose *et al.* [10] also reported improvement of LVEF improved after surgery in 64.9% of patients with low preoperative LVEF. The mean EF increased from 33%±5.9% preoperatively to 40.3%±11.3% postoperatively.

Table 4 Changes in the findings of trans-thoracic echocardiography postoperatively and at the end of the follow-up period in survivors (*n*=100)

Variables	Preoperative	Postoperative	Follow-up	*P* value
LVEDD (cm)	4.97±0.51	4.77±0.38	4.75±0.53	0.01*
LVESD (cm)	3.91±0.46	3.49±0.23	3.36±0.36	<0.001*
LVEF (%)	37.23±2.37	53.22±4.09	56.8±4.48	<0.001*
SWMA				
Normal	0	47 (47%)	53 (53%)	<0.001*
Hypokinesia	27 (27%)	48 (48%)	43 (43%)	0.006*
Akinesia	47 (47%)	5 (5%)	4 (4%)	<0.001*
Dyskinesia	26 (26%)	0	0	<0.001*

The nonparametric Friedman test (for related samples) was used to compare quantitative data, and the χ^2 test was used to compare qualitative data. LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-diastolic diameter; SWMA, segmental wall motion anomalies. *Significant difference.

Table 5 Univariable analysis of the predictors of functional nonrecovery after CABG in patients with low LVEF

Variables	OR	95% CI	*P* value
Age >60 years	0.29	0.03–2.38	0.29
Female gender	1.45	0.42–4.97	0.53
Obesity (BMI >30)	0.87	0.26–2.91	1
Smoking	1.25	0.31–5	1
CCS >2	1.28	0.25–6.39	1
NYHA >2	0.75	0.20–2.72	0.73
DM	2.28	0.57–9	0.35
Hypertension	2.38	0.60–9.42	0.23
Hypercholesterolemia	2.02	0.59–6.87	0.35
Pulmonary disease	7.90	0.46–135.6	0.22
Left main disease	2.92	0.66–12.82	0.15
Apical contraction on TTE: dyskinesia	1.50	0.41–5.46	0.50
Rest WMSI on DSE >1.5	4.86	0.59–39.62	0.17
Peak WMSI on DSE >1.5	8.77	2.33–33.02	0.002*
Improvement of LVEF on DSE <10%	15.95	3.23–78.64	<0.001*
Insertion of IABP	1.05	0.11–9.38	1
Incomplete revascularization	39	7.45–204	<0.001*

BMI, body mass index; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; CI, confidence interval; DM, diabetes mellitus; DSE, dobutamine-stress echocardiography; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OR, odds ratio; TTE, trans-thoracic echocardiography; WMSI, wall motion score index. *Significant predictor.

Table 6 Multivariable analysis of the predictors of functional nonrecovery after CABG in patients with low LVEF (binary logistic regression analysis)

Variables	OR	95% CI	*P* value
Peak WMSI on DSE >1.5	4.69	0.53–41.43	0.16
Improvement of LVEF on DSE <10%	9.19	1.35–62.24	0.02*
Incomplete revascularization	29.63	4.59–190	<0.001*

CABG, coronary artery bypass graft; CI, confidence interval; DSE, dobutamine-stress echocardiography; LVEF, left ventricular ejection fraction; OR, odds ratio; WMSI, wall motion score index. *Significant predictor.

In the present study, the significant predictors of in-hospital mortality on univariable analysis were age more than 60 years, peak WMSI on DSE more than 1.5, improvement of LVEF on DSE less than 10%, insertion of intra-aortic balloon pump (IABP; intraoperative or postoperative), and incomplete revascularization. Sawada *et al.* [11] examined the value of wall-motion scores by preoperative DSE to predict outcome and benefit from revascularization in patients with ischemic heart disease. In patients with scores 2.00–2.49, revascularized patients had a significantly lower frequency of cardiac death than nonrevascularized patients (15 vs. 41%, *P*<0.05). The frequency of death in those with low-dose scores more than or equal to 2.50 was very high in both revascularized (75%) and nonrevascularized (56%, *P*=0.42) patients.

In our study, there was a statistically significant increase in NYHA class I and a statistically significant decrease in NYHA class III at the end of the follow-up period. In addition, there was a statistically significant increase in CCS grades I and II, with a statistically significant decrease in CCS grades III and IV. Similarly, Knapp *et al.* [3] reported that most of the patients had experienced anginal symptoms corresponding to CCS classes II and III before the procedure. One year after the procedure, 26 patients manifested anginal symptoms in CCS class I and 20 in CCS class II.

Although insertion of IABP is an effective means of supporting failing circulation in patients at high risk of cardiovascular events postoperatively improving the chance of survival [12], IABP can be accompanied by complications, including limb ischemia, aortic or iliac dissection bleeding, infection, hemolysis, paraplegia, and stroke, that have an impact on mortality after CABG [13].

Incomplete revascularization was a significant predictor of NYHA functional nonrecovery on univariable and multivariable analysis in the present study.

In the study by Boeken *et al.* [14], incomplete revascularization affected the early outcome after CABG

in patients with impaired preoperative LV function. The potential benefit of the shorter aortic cross-clamping time with incomplete revascularization does not overweigh the advantages of complete revascularization.

The beneficial effects of complete revascularization on patients' outcomes have been described by other authors [15].

Conclusion

In conclusion, successful results of CABG in patients with EF less than 40% can be achieved by careful selection of patients and management. Evidence of myocardial viability is necessary to determine the beneficial effect of CABG. Postoperative improvement of EF and NYHA functional class reflects the high benefit of CABG in patients with reduced EF. Insertion of IABP, wall-motion scores on DSE, incomplete revascularization, and postoperative low cardiac output syndrome were significant predictors of adverse outcomes.

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Conflicts of interest

No conflict of interest.

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