

Is severely left ventricular dysfunction a predictor of early outcomes in patients with coronary artery bypass graft?

Seyed Hossein Ahmadi,¹ Abbasali Karimi,¹ Namvar Movahedi,¹ Mahmood Shirzad,¹ Mehrab Marzban,¹ Mokhtar Tazik,² Hermineh Aramin,² Samaneh Dowlatshahi,² Mahmood Sheikh Fathollahi²

¹Cardiovascular Surgery Department, Tehran Heart Center, Medical Sciences, University of Tehran, Iran
²Clinical Research Department, Tehran Heart Center, Medical Sciences, University of Tehran, Iran

Correspondence to
 Dr Hossein Ahmadi, Tehran Heart Center, North Kargar Street, Tehran, Iran;
 dr.ahmadi2006@yahoo.com

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ABSTRACT

Background Traditionally, the Coronary artery bypass grafting (CABG) surgery outcomes of patients with low ejection fraction (EF) have been worse compared to patients with moderate to good left ventricular function. During the past decade, despite improvements in surgical techniques, the trend in the outcomes of these patients remained unclear.

Aim We sought to determine the effect of left ventricular dysfunction on early mortality and morbidity and to specify predictors of early mortality of isolated CABG in a large group of patients EF \leq 35%.

Method We retrospectively analyzed data of 14 819 consecutive patients undergoing isolated CABG from February 2002 to March 2008 at Tehran Heart Center. Patients were divided into two groups based on their LVEF (EF \leq 35% and EF>35%). Differences in case-mix between patients with EF \leq 35% and those without were controlled by constructing a propensity score.

Results Mean age of our patients was 58.7 \pm 9.5 years. EF \leq 35% was present in 1342 (9.1%) of patients. In-hospital mortality was significantly increased univariate in EF \leq 35%, while this association diminished after confounders were adjusted for by using the propensity score ($p=0.242$). Following adjustment it was demonstrated that renal failure, cardiac arrest, heart block, infectious complication, total ventilation time, and total ICU hours were more frequent in patients with EF \leq 35%.

Conclusion We demonstrated EF \leq 35% was not predictor of in-hospital mortality in patients underwent CABG. Careful preoperative patient selection remains essential in patients with EF \leq 35% undergoing CABG.

INTRODUCTION

Traditionally, the operation outcomes of patients with a low ejection fraction (EF) have been worse compared with patients with moderate to good left ventricular (LV) function.¹ Coronary artery bypass grafting (CABG), ventricular remodelling and heart transplantation are current surgical treatment options for these patients.^{2–3} CABG is associated with improved early and long-term mortality and morbidity over the other therapies for low-EF patients.^{4–5} During the past decade, despite improvements in surgical techniques, the trend in the outcomes of these patients remained unclear. In the present study, we sought to determine the effect of left ventricular dysfunction on early mortality and morbidity, and to specify predictors of early

mortality of isolated CABG in a large group of patients with severely left ventricular dysfunction (LVD; EF \leq 35%).

MATERIAL AND METHODS

We retrospectively analysed data of 14 819 consecutive patients undergoing isolated CABG from February 2002 through March 2008 at Tehran Heart Center. All CABG patients, irrespective of whether they underwent conventional CABG or off-pump coronary artery bypass (OPCAB), were considered. Patients with other previous cardiac intervention/surgery (except percutaneous transluminal coronary angioplasty) and those who were admitted in cardiogenic shock or undergoing cardiopulmonary resuscitation before admission to the operating room were excluded. The preoperative EF was assessed by echocardiography ($n=10\,668$, 71.9%), LV angiogram ($n=4149$, 28.1%). Patients were divided into two groups based on their left ventricular ejection fraction (LVEF) (EF \leq 35% and EF>35%). For all patients, data recorded included information on patient characteristics and their preoperative comorbidities, operative variables (table 1) and their morbidity (any complications happen during this admission; table 2). The definition of low EF is somewhat variable across studies. To isolate patients with severely LVD in this study, low EF was defined as an EF \leq 35%. Early mortality was defined as death following the procedure before patient discharge regardless of the duration of hospitalisation. Any death that occurred after discharge from hospital but within 30 days of the procedure was also considered as early mortality. Infectious complications consisted of deep-sternal infection, thoracotomy, leg infection, septicæmia, urinary tract infection and pneumonia. The variables identified as predictors for EF \leq 35% along with the corresponding coefficients, standard errors and intercept value are listed in table 3. These variables were used to calculate a propensity score for each patient. By incorporating the established propensity score into the multivariable analyses, the effect of left ventricular dysfunction on early mortality and morbidity was assessed. A subgroup analysis to evaluate predictors of in-hospital mortality in patients with EF less than or equal to 35% undergoing conventional CABG was performed. All data were prospectively entered into the database. The definitions of Society of Thoracic Surgeons (<http://www.sts.org/file/CoreDef241Book.pdf>)⁶ were used for all entries in the database.

Table 1 Patient characteristics according to the ejection fraction in patients underwent isolated coronary artery bypass grafting*

Characteristics	Ejection fraction $\leq 35\%$ 1342 (9.1)	Ejection fraction $>35\%$ 13477 (90.9)	p Value
Preoperative risk factors			
Gender			<0.001
Male	1114 (83.0)	9944 (73.8)	
Female	228 (17.0)	3533 (26.2)	
Age (years)	58.51 \pm 9.44	58.74 \pm 9.52	0.403
BMI (kg/m ²)	26.62 \pm 3.83	27.26 \pm 4.01	<0.001
Smoke	613 (45.7)	5165 (38.3)	<0.001
Diabetes	493 (36.7)	4155 (30.8)	<0.001
Dyslipidaemia	865 (64.5)	9013 (66.9)	0.078
Family history	458 (34.5)	4980 (37.3)	0.053
Hypertension	702 (52.3)	7051 (52.3)	0.999
Cerebrovascular accident	74 (5.5)	835 (6.2)	0.340
Peripheral vascular disease	38 (2.8)	230 (1.7)	0.004
Renal failure	45 (3.4)	207 (1.5)	<0.001
Chronic lung disease (moderate)	17 (1.3)	128 (0.9)	0.245
Immunosuppressive therapy	30 (2.2)	231 (1.7)	0.188
Previous percutaneous transluminal coronary angioplasty	44 (3.3)	574 (4.3)	0.103
Myocardial infarction	912 (60.0)	4886 (36.3)	<0.001
Congestive heart failure	386 (28.8)	1326 (9.8)	<0.001
Angina	1306 (97.3)	13158 (97.6)	0.459
Arrhythmia	87 (6.5)	304 (2.3)	<0.001
CCS ≥ 3	1015 (87.3)	9669 (84.7)	0.019
No of diseased vessels >2	1037 (77.3)	9619 (71.4)	<0.001
Left main disease $\geq 50\%$	122 (9.1)	1202 (8.9)	0.845
Diuretic consumption	297 (22.1)	903 (6.7)	<0.001
Digoxin consumption	298 (22.2)	357 (2.7)	<0.001
ACE-inhibitor consumption	798 (59.9)	5354 (40.1)	<0.001
Operative risk factors			
Operation status			0.010
Elective or urgent	1344 (99.4)	13451 (99.8)	
Emergent	8 (0.6)	26 (0.2)	
Cardiopulmonary bypass	1323 (98.6)	13165 (97.7)	0.037
Intra aortic balloon pump insertion	90 (6.7)	239 (1.8)	<0.001
Blood transfusion	306 (23.0)	2326 (17.3)	<0.001
No of arterial grafts	1.10 \pm 0.369	1.10 \pm 0.350	0.480
No of vein grafts	2.63 \pm 0.947	2.48 \pm 0.935	<0.001
No of IMA used as graft	0.99 \pm 0.17	1.00 \pm 0.15	0.246
No of radial artery used as graft	0.11 \pm 0.34	0.11 \pm 0.33	0.624
Perfusion time (min)	75.64 \pm 25.25	70.26 \pm 24.30	<0.001

*Data are presented as mean \pm SD or n (%).

IMA: internal mammary artery, CCS: Canadian Cardiovascular angina Score.

ANAESTHETIC AND SURGICAL TECHNIQUES

All patients received standardised anaesthesia with isoflurane, fentanyl, midazolam, pancuronium bromide and propofol. The decision to perform off-pump or on-pump CABG was made by the surgeon. After general anaesthesia, median sternotomy was performed, and left internal mammary or radial artery and saphenous vein grafts were used; the minimum core temperature was 33°C during the cardiopulmonary bypass (CPB), the haematocrit concentration was above 20%, and the mean perfusion pressure was also 50–60 mm Hg. Active cooling was not performed, and patients were actively rewarmed to a nasopharyngeal temperature of 38°C before weaning off CPB. CPB was performed using a roller pump (flow rate 1.8–2.4 l/min/m²) and membrane oxygenator. Haemofiltration was used for all cases.

POSTOPERATIVE MANAGEMENT

All patients were brought to the cardiothoracic ICU while still intubated. Standard postoperative care involved mechanical

Table 2 Postoperative outcome according to the left ventricular function*

Variables	Ejection fraction $\leq 35\%$ 1342 (9.1)	Ejection fraction $>35\%$ 13477 (90.9)	p Value
Renal failure	36 (2.7)	95 (0.7)	<0.001
Cardiac arrest	31 (2.3)	102 (0.8)	<0.001
Bleeding (Re-operation)	21 (1.7)	141 (1.1)	0.071
Atrial fibrillation	102 (7.6)	786 (5.8)	0.010
Stroke	13 (1.0)	53 (0.4)	0.007
Pulmonary emboli	4 (0.3)	55 (0.4)	0.819
Heart block	15 (1.1)	46 (0.3)	<0.001
Infectious complication	29 (2.2)	112 (0.8)	<0.001
Prolonged ventilation	51 (3.8)	271 (2.0)	<0.001
Re-intubation	34 (2.6)	159 (1.2)	<0.001
Total ventilation time (h)	15.30 \pm 2.17	10.11 \pm 0.22	<0.001
Total ICU time (h)	59.00 \pm 4.12	41.69 \pm 0.35	<0.001
Mortality (in-hospital)	24 (1.8)	101 (0.7)	<0.001

*Data are presented as mean \pm SE or n (%).

ventilation in the assist control mode, with cardioactive drugs where indicated. Weaning from the ventilator was performed in the presence of haemodynamic and respiratory stability (no or decreasing use of cardioactive drugs), absence of significant bleeding (<100 ml/h), absence of significant arrhythmias and oxygen saturation $>95\%$ with FiO₂<0.50. In addition, the patient had to be sufficiently awake to follow simple commands.

STATISTICAL METHODS

Results were presented as mean \pm SD for numerical variables and were summarised by absolute frequencies and percentages for categorical variables. Continuous variables were compared using the Student t test, and categorical variables were compared using the χ^2 or Fisher exact test, as required. Differences in case mix between patients with severely left ventricular dysfunction and those without were controlled for by constructing a propensity score.⁷ A subject's propensity score is defined to be their conditional probability of having EF $\leq 35\%$ given a vector of their observed covariates and was constructed from the variables consisting of age, gender, body mass index, smoking, hypertension, diabetes, congestive heart failure, peripheral vascular disease, renal dysfunction, myocardial infarction, number of

Table 3 Propensity scores for severely left ventricular dysfunction (left ventricular ejection fraction $\leq 35\%$)

Variables	Coefficient	Standard error	p Value
Body mass index (kg/m ²)*	−0.0317	0.00794	<0.0001
Perfusion time (min)*	0.00547	0.00122	<0.0001
Diabetes	0.2902	0.0645	<0.0001
Congestive heart failure	1.2386	0.0708	<0.0001
Male gender	0.4555	0.0811	<0.0001
Renal dysfunction	0.5138	0.1805	0.0044
Myocardial infarction	1.2481	0.0630	<0.0001
Status			0.0367
Elective or urgent versus emergent	−0.9115	0.4362	
Conclusive			0.0300
2 versus 1	0.1148	0.1762	
3 versus 1	0.2875	0.1688	
Intercept	−3.1437	—	—

*For each additional unit.

Hosmer–Lemeshow goodness of fit test; p value=0.8506.

Area under the receiver operating characteristic curve; c=0.72805.

Table 4 Severely left ventricular dysfunction effect on mortality and morbidity in univariate and multivariable logistic regression analysis adjusted for confounders using propensity score

Variables	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
Renal failure	3.844	2.636 to 5.724	<0.001	2.313	1.498 to 3.572	<0.001
Cardiac arrest	3.109	2.072 to 4.666	<0.001	1.684	1.058 to 2.680	0.027
Bleeding (reoperation)	1.533	0.966 to 2.434	0.070	1.229	0.749 to 2.015	0.414
Atrial fibrillation	1.329	1.073 to 1.647	0.009	1.073	0.851 to 1.353	0.550
Stroke	2.484	1.351 to 4.569	0.003	1.675	0.859 to 3.267	0.129
Pulmonary emboli	0.730	0.264 to 2.017	0.544	0.644	0.224 to 1.857	0.415
Heart block	3.309	1.843 to 5.943	<0.001	2.761	1.459 to 5.225	0.001
Infectious complication	2.642	1.749 to 3.990	<0.001	2.242	1.431 to 3.512	<0.001
Prolonged ventilation	1.924	1.419 to 2.069	<0.001	1.307	0.934 to 1.829	0.118
Reintubation	2.187	1.503 to 3.181	<0.001	1.476	0.973 to 2.240	0.067
Mortality	2.412	1.540 to 3.777	<0.001	1.346	0.818 to 2.217	0.242

diseased vessels >2, CPB, operation status and perfusion time. Once the propensity score was estimated for each patient, we used regression adjustment because matching would reduce the study size, and stratification could be difficult to interpret. The propensity score was then taken along with the comparison variable (EF≤35% vs EF>35%) to multivariable analyses of outcomes. The propensity score could adjust for the case-mix differences between the two study groups.⁷ Multivariable logistic regression models for comparing postoperative complications and mortality across the two groups of patients along with the propensity score were then established, and the associations were presented as odds ratios (ORs) with 95% CIs. Multivariable linear regression models for comparing total ventilation and total ICU hours across the two groups of patients in the presence of the constructed propensity score were also established, and the associations were presented as β with 95% CIs. Multivariable forward logistic regression model for factors predicting mortality in severely left ventricular dysfunction patients was also constructed. Variables were included in the multivariable model if the p value was found to be less than or equal to 0.15 in univariate analysis. For the statistical analysis, the statistical software SPSS version 13.0 for Windows (SPSS, Chicago, Illinois) and the statistical package SAS version 9.1 for Windows (SAS Institute, Cary, North Carolina) were used. All p values were two-tailed, with statistical significance defined by $p \leq 0.05$.

RESULTS

Overall, 14819 patients were evaluated. The mean age was 58.7 ± 9.5 years, and 3761 (25.4%) were female. Severely depressed LV function (EF≤35%) was present in 1342 (9.1%) of patients. Significant differences were found in preoperative comorbidity and operative variables between cohort with EF≤35% and those with EF greater than 35% (table 1). Patients with EF≤35% were more likely to be male and present with lower BMI, and higher degree of smoking, diabetes, peripheral vascular disease (PVD), renal failure (RF), history of myocardial infarction (MI), congestive heart failure (CHF), arrhythmia,

number of diseased vessels >2, diuretic or digoxin or ACE-inhibitor consumption, need for intra-aortic balloon pump insertion (IABP), blood transfusion, number of vein grafts and longer perfusion time (except PVD, $p=0.004$, all p values were <0.001). Table 2 shows the crude postoperative outcomes in patients with EF≤35% versus those who EF>35%. In-hospital mortality was significantly increased in severely depressed LV function (EF≤35%), while this association diminished after confounders were adjusted for by using the propensity score ($p=0.242$) (table 4). Following adjustment, it was demonstrated that RF (OR=2.313, $p<0.001$), cardiac arrest (OR=1.648, $p=0.027$), heart block (OR=2.761, $p=0.001$), infectious complication (OR=2.242, $p<0.001$), total ventilation time ($\beta=2.644$, $p=0.009$) and total ICU hours ($\beta=12.074$, $p<0.001$) were more frequent in patients with EF≤35% (tables 4, 5). A multivariable analysis in a subgroup of patients with LVEF≤35% revealed that PVD (OR=7.013, $p=0.0025$), CHF (OR=2.355, $p=0.0472$), emergent operation (OR=25.207, $p<0.0001$), IABP insertion (OR=7.949, $p<0.0001$) and perfusion time (OR=1.014, $p=0.0414$) were predictors of in-hospital mortality (table 6).

DISCUSSION

The reported prevalence of severe LV dysfunction in patients undergoing CABG ranged from 3.4% to 15%;^{8–9} the differences may be partly explained by different definitions of severely depressed LV. In our study, we report a prevalence of 9.1% of patients with EF≤35% from a total patient population, confirming the apparent copious numbers of patients with severely depressed LV function referred for myocardial revascularisation. The prevalence of severe LVD in this study was greater than the repeated rates in the literature including a large registry of patients undergoing CABG in the UK that reported a consistent rate of 6–7% over a 6-year period.¹⁰ This is a disparity between higher rates of severe LVD (14.8% and 18%) reported elsewhere,¹¹ which may be explained in part by different definitions of severe LVD including LVEF less than 35% or less than 30% or sometimes less than 20%.^{12–14} CABG in these patients still constitutes a surgical challenge, and despite

Table 5 Severely left ventricular dysfunction effect on morbidity in univariate and multivariable logistic regression analysis adjusted for confounders

Variables	Univariate			Multivariate		
	β	95% CI	p Value	β	95% CI	p Value
Total ventilation 2time (h)	5.196	3.248 to 7.143	<0.001	2.644	0.645 to 4.642	0.009
Total ICU time (h)	17.314	13.942 to 20.687	<0.001	12.047	8.502 to 15.592	<0.001

Table 6 Factors associated with in-hospital mortality in patients with left ventricular ejection fraction less than or equal to 35%

Factors	OR	95% CI	p Value
Peripheral vascular disease	7.013	1.783 to 27.576	0.0025
Congestive heart failure	2.355	1.090 to 5.603	0.0472
Emergent operation	25.207	4.365 to 145.564	<0.0001
Intra-aortic balloon pump insertion	7.949	3.022 to 20.913	<0.0001
Perfusion time	1.014	1.006 to 1.027	0.0414

Hosmer–Lemeshow goodness of fit test; $p=0.5121$. Area under the receiver operating characteristic curve; $c=0.81821$.

the advanced myocardial protection and anaesthesia techniques, in-hospital mortality is still high. Some studies reported a mortality range from 5% to 25%.^{15–16} Luciani *et al*¹⁷ and De Carlo *et al*¹⁸ in a group of patients with LV EF \leq 35% reported a range of in-hospital mortality of 1.2–6.3%. In the present study, we report our experience in a large series of patients with EF \leq 35% undergoing CABG. One of the main findings of this study includes a very low operative mortality (1.8%), which is in the reported range of other studies. Univariately, severe left ventricular dysfunction carried approximately more than a twofold (1.7% vs 0.8%) increased mortality risk compared with patients who had impaired LVEF. Some studies showed older age, female gender, recent myocardial infarction, hypertension, previous cardiac surgery, left main disease and longer cross clamp time as predictors of in-hospital mortality.^{19–20} In the present study, female gender presented in only 17% of patients with EF \leq 35%. Hypertension was not significantly different in both groups. Furthermore, only 2.8% of low EF patients had PVD. Left main disease was found in 9.1% of low EF patients, 6.7% of them needed IABP insertion, and only 0.6% of the patients had emergent operation, which was considerably low. Thus, the low mortality in our study in comparison with those reported in previous studies may be due to the above reasons.

In this study, we were able to identify independent predictors of mortality in patients with low EF underwent CABG. We showed that CHF (OR=2.355, CI=1.090 to 5.603) and IABP insertion (OR=7.949, CI=3.022 to 20.913) are independent predictors of in-hospital mortality in patients with low EF underwent CABG. These results are in accordance with findings from the Patch trial database²¹ which identified congestive heart failure as an independent predictor of mortality in CABG patients with low EF. We also demonstrated PVD (OR=7.013, CI=1.783 to 27.576) and emergent operation (OR=25.207, CI=4.365 to 145.564) as independent predictors of in-hospital mortality in patients with low EF undergoing CABG. The results of Christakis *et al*²² were in line with the results of our study. Magee *et al*²³ demonstrated CPB in their study as a predictor of in-hospital mortality in patients who underwent CABG. Antunes *et al*²⁴ in their study showed that perfusion time is longer in patients with left ventricular dysfunction. Perfusion time in our study was longer in patients with EF \leq 35% compared with those without, and in this study we actuated perfusion time (OR=1.014, CI=1.006 to 1.027) as a predictor of mortality in patients with EF \leq 35%. However, the results of the multivariable analysis should be interpreted with caution because of the relatively small number of events in this subgroup, as reflected by large CIs. Despite the results from some studies,^{25–26} we showed that severely depressed LV function does not appear to be an independent predictor of early mortality in patients undergoing CABG in our practice. Our result was in agreement with Davierwala *et al*'s study²⁷. With respect to postoperative complications, multivariable logistic

regression analysis confirmed that EF of 35% or less was an independent risk factor for renal failure, cardiac arrest, heart block, total ventilation time, total ICU hours and infectious complication. Waleed *et al*²⁸ showed renal failure in their study as a postoperative complication in patients with left ventricular dysfunction. We showed in this study that infectious complication, cardiac arrest, heart block and total ventilation time, and total ICU stay occurred more often in our patients with EF \leq 35%. These findings were in accordance with the study reported by Davoodi and colleagues.²⁹

STUDY LIMITATIONS

Preoperative EF was not standardised for this study but rather was measured by different techniques in the context of usual care (ie, echocardiography, LV angiogram). A second limitation is that we did not separate different causes of deaths (cardiac or non-cardiac). We have not recorded data on the myocardial viability of our patients in this study. Therefore, our multivariable risk adjustment and propensity analyses provide partial adjustment for baseline differences and selection factors that would otherwise preclude a meaningful comparison between groups.

CONCLUSION

We demonstrated that an EF equal to or less than 35% was not a predictor of in-hospital mortality in patients undergoing CABG. Careful preoperative patient selection remains essential in patients with an EF equal to or less than 35% undergoing coronary artery bypass graft surgery.

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