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Original Article

Survival and Long-Term Outcome of Coronary Artery Bypass Grafting in Patients With Heart Failure and Reduced Left Ventricular Ejection Fraction

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Background: Heart failure with reduced left ventricular ejection fraction (HFrEF) is associated with increased mortality and morbidity. This research was carried-out to explore the survival and long-term outcomes of coronary artery bypass grafting (CABG) in patients diagnosed with HFrEF

Materials and Methods: This retrospective cohort study was performed with reviewing the hospital databank related to all patients who underwent CABG in the state hospital affiliated to Babol University of Medical Sciences, north of Iran during 2011-2021. Adult patients who had EF lower than 40% were included by census, and followed for the research outcomes. Survival of the participants was considered as the primary outcome; and serious clinical complications were recorded as the secondary outcomes.

Results: Totally, 229 patients with HFrEF undergoing CABG were included. Mean age was 64.48±10.92 year; 153 subjects (66.8%) were male. The patients followed after the CABG surgery in a range from 1 to 68 months. Forty-five subjects (19.65%) died, and 184 (80.35%) survived during the study period; and 143 patients (62.45%) had re-admission in the hospital because of cardiac manifestations. Mean and standard error of survival time was 58.37±1.32 (95% CI: 55.78-60.95) months. Multivariable cox-regression analysis revealed the significant effect of age (adjusted HR: 1.288; 95% CI: 1.052-1.576; P=0.014) and LV size (adjusted HR: 58.847; 95% CI: 1.044-3316.247; P=0.048) on mortality of patients with HFrEF undergoing CABG

Conclusion: Given considerable proportion of death and cardiovascular manifestations in people with HFrEF undergoing CABG, more precise and regular care of these patients is emphasized.

Keywords: Coronary Artery Disease; Heart Failure; Coronary Artery Bypass Grafting, Survival

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Introduction

Heart failure (HF) as a life-threatening disease is associated with a significant morbidity and mortality rate, poor patients´ quality of life, and high health expenditure (1).

This syndrome affects more than 55.5 million people worldwide, and its prevalence is estimated to be increasing due to the ageing of the population, widespread availability of effective interventions, and improved treatments (1, 2).

Given the classification of HF according to left ventricular ejection fraction (LVEF), heart failure with reduced ejection fraction (HFrEF) is a type of this disease with LVEF ≤40% (3). This type of HF is a severe and progressive clinical condition with a high burden of mortality and readmission, and one of important global health challenges (4).

Considering the association of coronary artery disease (CAD) with HF, coronary artery bypass grafting (CABG) has been introduced as one of useful treatment options in patients with CAD and heart failure (5, 6). Some evidence demonstrated the significant effect of coronary revascularization on all-cause mortality of patients with chronic heart failure and CAD (7).

However, multiple factors might affect the survival and clinical outcome of patients with heart failure undergoing CABG; including concurrent comorbidities such as diabetes mellitus, renal failure, previous myocardial infarction, hemodynamic characteristics such as anemia or serum albumin, and the surgical aspects of CABG (8, 9). Also, some evidence has not supported the superiority of CABG over other interventions in patients with severely reduced ejection fraction (10).

Some previous studies investigated long-term (more than 5-year) outcome of coronary artery bypass grafting in patients with HFrEF (11-13); however, the evaluation of clinical outcomes in each region will help to identify the prognostic factors in that region, and to adopt intervention strategies for improvement of clinical impact. This research was conducted to explore 10-year survival and outcomes of coronary artery bypass grafting in patients with heart failure and reduced ejection fraction.

Materials and methods

Study design and setting

This retrospective cohort study was carried out with reviewing the hospital databank related to all patients who underwent CABG in the state hospital affiliated to Babol University of Medical Sciences, north of Iran during 2011-2021. Nearly 30% of patients undergoing CABG had LVEF ≤ 40%, and were included by census. The follow-up process was initiated in 2022. If the participant died during admission in the hospital, his/her death was recorded in the research datasheet; and if adequate data was not available, patients or their families were contacted by telephone using the call numbers recorded in the patients' file, and the survival status or other study outcomes such as the number of readmission after the CABG were followed.

Participants

Inclusion criteria were age ≥ 18 years, undergoing CABG in this hospital during 2011-2021, and left ventricular ejection fraction lower than 40% before CABG.

Patients with CABG and HFrEF whose hospital document was not complete, or had repeated heart surgery were excluded.

Variables and measurement

Basic characteristics including age; gender; occup-ation, previous history of chronic disorders such as diabetes mellitus, respiratory diseases, hyperlipi-demia, hypertension, stroke, or chronic kidney disease; smoking; substance and alcohol consumption were collected. Medications received before CABG including ACE- inhibitors, B-blockers, statins, and diuretics were recorded.

The participants´ body mass index, blood pressure, fasting plasma glucose and serum creatinine before CABG were extracted from the patient file in the hospital databank and recorded in the research data sheet.

Routinely, all patients undergoing CABG were examined through two-dimensional echocardiography before and after the surgery; and left ventricular ejection fraction, the condition of cardiac valves and presence of other cardiac disorders were assessed. The cardiac characteristics recorded as the research

variables were as following: 1- left ventricular ejection fraction (≤ 40% or < 30%); 2- LV size (normal or dilated); 3- LV diastolic dysfunction (grade 1-3); 4- mitral valve regurgitation (MR) (less than or ≥ moderate); 5- right ventricular function (normal or failure in function); and 6- pulmonary hypertension (yes or no).

Also, the summary result of pre-operative angiography; the number of coronary artery grafts; duration of CABG surgery; cross clamp time; on-pump, off-pump or use of intra-aortic balloon pump; and other cardiac surgical procedures conducted along with CABG was recorded. All patients were prescribed guideline-directed medical therapies for HFrEF (14).

Survival of the participants was considered as the primary outcome; and serious clinical complications including repeated hospitalization after the first CABG because of cardiac disorders, post-operative bleeding, acute kidney disorders, and stroke were recorded as the secondary outcomes.

Statistical methods

Data analysis was carried-out using SPSS-22 software package. Chi-square, t-test and multivariable cox-regression analysis were used for investigation of the research objectives.

Results

Before CABG findings

Totally, 229 patients with HFrEF undergoing CABG whose related data was complete were included in this study. Mean age was 64.48±10.92 (range of 30-86) year; 153 subjects (66.8%) were male, and 76 (33.2%) were female. Baseline demographic characteristics and past medical history of the participants is presented in Table 1; and a summary of substance use and medications the participants were taking before CABG has been reported in Table 2.

At baseline examination mean weight and BMI were 70.08±12.25 (range of 37-120) kg and 26.13±4.42 (16.21-53.33) kg/m2; mean systolic and diastolic blood pressure were 113.20±14.83 (range of 70-166) and 67.38±11.99 (40-110) mmHg, respectively. Mean fasting blood glucose was 159.30±62.75 (range of 75-430) mg/dL. Although, only one person reported previous chronic kidney disease, preliminary laboratory assessment of the participants revealed 184 (80.3%) persons had serum creatinine less than 1.5, and 45 individuals (19.7%) ≥ 1.5 mg/dL.

Echocardiographic finding of the participants before CABG has been summarized in Table 3.

The most frequent finding in pre-operative angiographic assessment of the participants was three-vessel disease (3VD); it was found in 159 (69.43%) of the patients.

Operative techniques and graft strategy

Among the examined patients 174 (75.98%) underwent only CABG surgery, and 55 (24.02%) persons underwent CABG in addition to mitral valve replacement or repair surgery; 221 (96.51%) had on-pump CABG, 5 (2.18%) intra-aortic balloon pump, and 3 (1.31%) individuals had off-pump CABG. Mitral valve repair was carried out for patients with moderate to severe mitral valve regurgitation.

Eighty individuals (34.93%) received more than three grafts during CABG; and 110 (48.03%) persons received more than three grafts in addition to left internal mammary artery graft. All patients had complete revascularization after the surgery.

Mean bypass time was 84.56±32.73 (range of 27-265); and mean cross clamp time was 48.11± 20.94 (8-185) minutes.

Post-CABG findings

The patients followed after the CABG surgery in a range from 1 to 68 months. Post-operative echocardiographic assessment of the participants showed that 95 persons (41.48%) had LVEF less than 40%; 140 (61.14%) had normal LV size; 168 (73.36%) < moderate mitral valve regurgitation, and 202 persons (88.21%) had normal RV function.

Twenty-three (10.04%) patients had acute kidney injury following the surgery; and 12 (5.24%) persons reported post-CABG stroke.

Thirty-two (13.97%) of the participants needed reoperation following the CABG surgery, because of bleeding; 143 patients (62.45%) had re-admission in the hospital because of cardiac manifestations: 73 subjects (51.05%) once readmission, 58 (40.56%) two times, 9 (6.29%) three times, 2 (1.39%) four times, and 1 person had five times readmission after CABG.

Among the examined people, 45 subjects (19.65%) died, and 184 (80.35%) survived during the study period. Mean and standard error of survival time was 58.37±1.32 (95% CI: 55.78-60.95) months. Multivariable cox-regression analysis for investigation of the factors affecting on mortality of the participants undergoing CABG has been presented in Table 4. This table shows the significant effect of age (adjusted HR: 1.288; 95% CI: 1.052-1.576; P=0.014) and LV size (adjusted HR: 58.847; 95% CI: 1.044-3316.247; P=0.048) on mortality of patients with HFrEF undergoing CABG. The significant effect of LV size on mortality of the participants has been represented in Figure 1.

Table 1. Baseline demographic characteristics, past medical history, and initial physical examination of patients with heart failure and reduced ejection fraction undergoing CABG during 2011-2021

Characteristics	Crude number	Valid percent
Occupation		
Farmer	86	38.6
Housekeeper	80	35.9
Staff of governmental organizations	24	10.8
Shopkeeper	13	5.8
Others	20	9.0
Previous history of diabetes mellitus		
No	122	53.3
Yes	107	46.7
Previous history of hypertension		
No	97	42.4
Yes	132	57.6
Previous history of dyslipidemia		
No	115	50.2
Yes	114	49.8
Previous history of bronchial asthma		
No	219	95.6
Yes	10	4.4
Previous history of chronic obstructive pulmonary disorders		
No	226	98.7
Yes	3	1.3
Previous history of chronic kidney disorders		
No	228	99.6
Yes	1	0.4
Previous history of stroke		
No	216	94.3
Yes	13	5.7
Past medical history of other chronic disorders		
No	151	65.9
Yes	78	34.1

Table 2. Previous history of substance use and medications in patients with heart failure and reduced ejection fraction undergoing CABG during 2011-2021

Previous history of….	Crude number	Valid percent
No smoking or substance use	162	70.7
Smoking	30	13.1
Opiates	20	8.7
Smoking and opiates use	15	6.6
Other substance use	2	0.9
Duiretics		
No	189	82.5
Yes	40	17.5
Statins		
No	89	38.9
Yes	140	61.1
B-blockers		
No	121	52.8
Yes	108	47.2
ACE-inhibitors*		
No	178	77.7
Yes	51	22.3
Aspirin		
No	115	50.2
Yes	114	49.8
Other drugs		
No	47	20.5
Yes	182	79.5

* Angiotensin-Converting Enzyme Inhibitors

Table 3. Baseline echocardiographic findings of patients with heart failure and reduced ejection fraction undergoing CABG during 2011-2021.

Characteristics	Crude number	Valid percent
LVEF		
≤ 40%	93	40.6
< 30%	136	59.4
LV size		
Normal	122	53.5
Dilated	106	46.5
LV diastolic dysfunction		
Grade I	197	59.5
Grade II	18	22.8
Grade III	14	17.7
Mitral valve regurgitation		
< moderate	166	73.1
≥ moderate	61	26.9
RV function		
Normal	180	78.9
Dysfunction	48	21.1
Pulmonary hypertension		
Yes	113	49.3
No	116	50.7

Table 4. Crude and adjusted hazard ratio of factors affecting on mortality of patients with heart failure and reduced ejection fraction undergoing CABG during 2011-2021

Research variables entered in the model	Crude hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
Female gender	0.682 (0.330-1.411)	0.302	2.728 (0.142-52.245)	0.505
Age	1.129 (1.082-1.177)	< 0.001	1.288 (1.052-1.576)	0.014
LVEF before CABG	1.159 (0.593-2.266)	0.666	0.220 (0.019-2.616)	0.231
LV size before CABG	1.408 (0.732-2.708)	0.306	58.847 (1.044-3316.247)	0.048
Mitral valve regurgitation before CABG	2.155 (1.084-4.286)	0.029	3.844 (0.332-44.567)	0.281
LV diastolic dysfunction (Grade II)	1.122 (0.330-3.808)	0.854	0.203 (0.008-5.134)	0.334
LV diastolic dysfunction (Grade III)	0.795 (0.189-3.341)	0.755	0.038 (0.001-2.697)	0.133
Pulmonary artery pressure	1.625 (0.629-4.201)	0.316	0.875 (0.077-9.874)	0.914
RV function before CABG	0.773 (0.333-1.792)	0.548	0.669 (0.048-9.299)	0.765

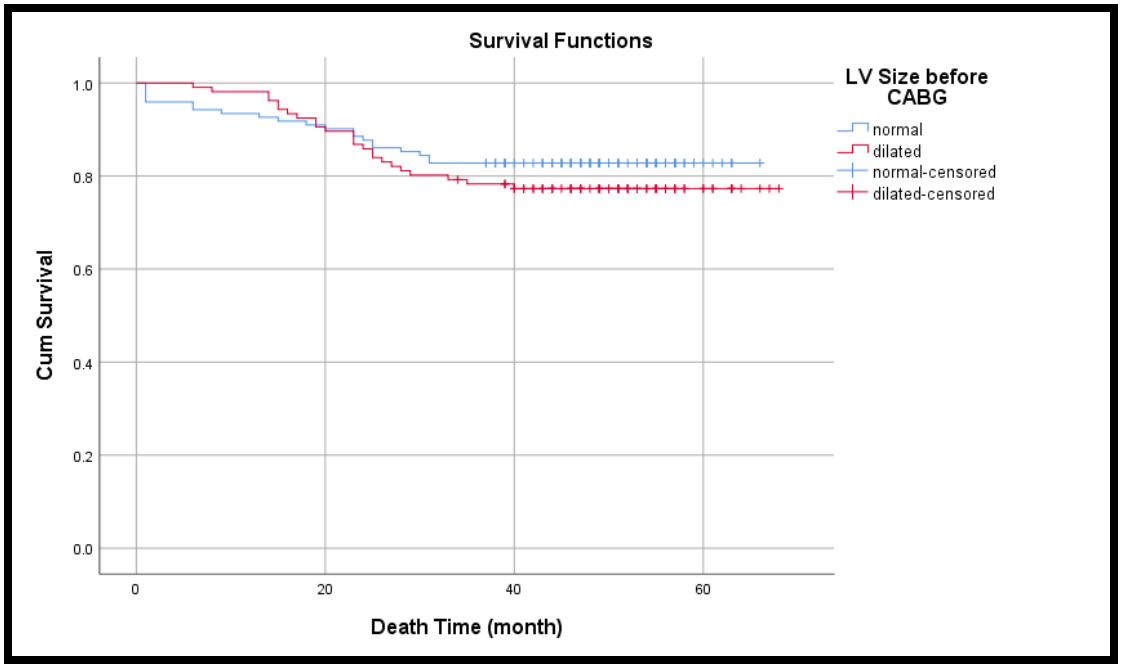

Fig. 1. LV size and survival of the patients with heart failure and reduced ejection fraction undergoing CABG during 2011-2021

Discussion

This follow-up study of people with HFrEF undergoing CABG showed a nearly 80% survival estimate of these patients. The average post-CABG survival time was 58 months (nearly 4.8 years). A recent systematic review and meta-analysis revealed that CABG resulted to better outcomes than percutaneous coronary intervention (PCI) in patients with HFrEF (15). A nationwide Swedish study among patients undergoing CABG (37000 persons without known HF and 5000 with known HF) during a mean follow-up time of 6.0 years, 19.0% of patients died, including 33.9% of individuals with HF and preserved EF (LVEF≥50%), and 42.9% with HFrEF (12).

Another research in Pittsburgh Medical Center in which 7218 patients who underwent multi-vessel CABG were included, the participants were followed for 4.81 (2.3-7.5) years. One-year and 5-year survival rate for RA and SV groups were reported as 96.0%,

94.3%, 87.9% and 83.2%, respectively (16). Another research examined the survival time in 2979 patients following CABG surgery in the United Kingdom during 20 years. They reported the cardiac function, preoperative dialysis, chest re-exploration, and redo surgery as significant factors affecting on postoperative mortality of the participants (17).

These two reviewed studies did not isolate the participants with heart failure. A research in Italy compared post-CABG outcomes between 215 patients without HF and 215 individuals with HF, and showed no significant difference between these two groups about in-hospital mortality (2.8%) (18). Another research assessed the survival rate and adverse cardiovascular events following CABG in patients with mid- range EF (LVEF > 40% and < 55%), and concluded that this range of myocardial dysfunction negatively affects survival time, and increases adverse cardiovascular events after CABG (8).

We found limited similar studies that focused on long-term outcome of patients with HFrEF undergoing CABG. Of course, the mentioned different findings can be due to difference in study design, participants, and pre-operative, surgical characteristics, and post-operative outcomes considered as research variables. Recent guidelines revealed significant reduction in all-cause, cardiovascular, and HF hospitalizations at 10 years in patients receiving CABG in addition to optimal medical treatment compared with medical treatment alone (3).

In current study, sixty-two percent of the participants had re-admission in the hospital because of cardiac manifestations; and fourteen percent needed reoperation following the surgery, because of bleeding. Ten percent of the patients had acute kidney injury following the surgery; and 5% reported post-CABG stroke. Chen et al reported the SYNTAX score (an invasive coronary angiography based score for quantifying the complexity of coronary artery disease)≥ 33 as an important factor for reduction in rehospitalization following CABG (19). Bianchi et al showed more frequently cardiogenic shock following CABG in patients with HF compared to those with HF, and reported a significant association between mortality and mechanical circulatory support and postoperative acute renal failure. Also, similar to us, age (HR: 1.28) had a significant impact on survival of these patients (18).

Among the examined characteristics LV size before the CABG, and age had a statistical significant impact on mortality of patients with HFrEF undergoing CABG. The impact of reduced LVEF on long-term prognosis and survival rate following CABG has been emphasized in previous studies (20, 21). A research in Canada concluded that although LVEF is more important than LV size in predicting outcomes after cardiac surgeries; in patients undergoing isolated CABG, LV size has an interactive effect with LVEF, and risk adjustment models using only LVEF may be inaccurate (21).

Despite evolving evidence and treatment strategies in patients with HF, multiple scientific gaps has been introduced for future clinical research (3).

The most important strong point of this research is long-term follow-up of the patients, and isolating individuals with HFrEF as the study group. The limitation of this work is not including laboratory assessment findings such as the profile of plasma glucose in research variables.

Conclusion

Regarding considerable proportion of death and cardiovascular manifestations in people with HFrEF undergoing CABG, more precise and regular care of these patients is emphasized.

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