The Heart Surgery Forum 2022-4123
25 (3), 2022 [Epub May 2022]
doi: 10.1532/hsf.4123

Online address: http://journal.hsforum.com

Complete Revascularization Showed A Better Cardiac Function Improvement In Patients With Low Ejection Fraction

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ABSTRACT

Purpose: This study aimed to compare postoperative ejection fraction (EF) in response to coronary artery bypass grafting (CABG) among patients with preoperative EF <35% and >35%.

Methods: A retrospective study was conducted in a single institution using clinical data of 660 patients undergoing elective on-pump CABG in 2018-2019. Patients were classified into two groups based on preoperative left ventricle ejection fraction (<35% and >35%). The primary endpoint was the change of postoperative ejection fraction.

Results: In this study, 72 patients had preoperative left ventricle ejection fraction <35% (group A) while the other 588 patients had ejection fraction >35% (group B). Among both groups, the duration of cardiopulmonary bypass (CPB) and aortic clamp (AxC) were not significantly different (P > 0.05). The transformation of pre- and postoperative EF in groups A and B was significantly different (2.91+10.31 vs. -0.14+4.57, P < 0.001). There was a significant difference in the duration of ICU stay (73.42+112.55 vs. 34.43+64.99, P < 0.001) and postoperative ventilatory support (25.54+43.92 vs. 16.42+45.87, P < 0.008) between group A and B.

Conclusion: Low preoperative EF showed better improvement in cardiac function after surgery. We concluded that the result could be affected by revascularization of hibernating myocardium.

INTRODUCTION

There are 126 million individuals with coronary artery disease (CAD) with a global prevalence of approximately 5-8% and 9.14 million deaths in 2019 [Bauersachs 2019; Khan 2020; Roth 2020]. One of the most common complications of CAD is the cardiac function reduction indicated by low ejection fraction (EF). Low EF is linked to further reduced coronary flow and associated with a high mortality rate, thus effective treatment in increasing EF may reduce the mortality rate in patients with CAD [Mayala 2020; Sun 2018].

Coronary artery bypass grafting (CABG) is indicated for CAD patients and has been proven to effectively improve cardiac function [Hillis 2011; Koene 2017]. Numerous studies have shown significant improvement of postoperative EF in patients with preoperative EF <50%. On the other hand, the authors also identified a declining trend of postoperative EF in those with preoperative EF >50% [Koene 2017]. Based on this finding, our study aimed to compare the postoperative EF in response to CABG among patients with preoperative EF <35% and >35%.

METHOD

Data source: A database for all adult patients who underwent cardiac surgery in the National Cardiovascular Center Harapan Kita, Jakarta, was obtained for the years 2018-2019.

Study patients: All patients who underwent elective on-pump CABG were included. Patients with a history of previous cardiac surgery had a multiorgan failure, a history of intra-aortic balloon pump insertion, and who underwent combined surgery beside CABG were excluded. Patients who had EF <35% were assigned to group A, and the rest were assigned to group B.

Demographics and risk factors: The data evaluated in this study were gender, age, body weight, history of smoking, family history of coronary heart disease, diabetes mellitus, dyslipidaemia, hypertension, and New York Heart Failure classification for heart failure. Operative factors, such as three-vessel coronary disease, duration of cardiopulmonary bypass time, and aortic clamp time were also evaluated.

Surgical technique: All operative procedures were performed by senior surgeons qualified by the Indonesian Association of Cardiothoracic and Vascular Surgery. All operation begins with a median sternotomy incision. Greater saphenous vein and left internal mammary artery were harvested according to clinical indications. Cannulation was performed and heparin was administered. The cannulas were then connected to a cardio-pulmonary bypass (CPB) machine. A cardioplegic cannula was inserted, and cold cardioplegia was administered to induce asystole and hypothermia. All coronary vessels were evaluated, and anastomoses and endarterectomy were

Received July 13, 2021; accepted March 15, 2022.

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performed as needed. Core temperature slowly was increased after all the anastomoses correctly were done. After the core temperature was normal, the CPB machine was discontinued. We administer protamine according to the heparin dose that was given, then we release the cannulas. When the grafts' flow was adequate and haemostasis achieved, we closed the sternum and rounded off the operation.

Postoperative outcome: The primary endpoint of this study was the postoperative EF that was evaluated by an experienced cardiologist using trans-thoracic echocardiography three months post-CABG. The duration of postoperative ventilatory support and the length of stay in the intensive care unit (ICU) also were evaluated.

Statistical analysis: Statistical analysis was done using SPSS ver. 26. Kolmogorov-Smirnov was used to test of normality for numerical data. For numerical data, discrete variables were analysed using Mann Whitney, while continuous variables were analysed using the Wilcoxon test. Comparison of categorical data was done by Chi-square test.

RESULTS

Study population: The baseline demographic and clinical characteristics of this study are presented in Table 1. (Table 1) The mean age of this study group was 58.43+8.35 years and 563 patients in the study group were male. Risk factors that were observed in the patients include smoking, dyslipidemia, hypertension, family history of CAD, diabetes mellitus, grade III-IV NYHA, and three-vessel disease. In this study, 72 patients had preoperative left ventricle ejection fraction <35% (group A), while 588 patients' ejection fraction was >35% (group B). The mean duration of CPB in this study group was 105.773+55.77 and the aortic cross-clamp duration was 74.92+59.96.

Morbidity and mortality: There was a significant difference in the ICU stay among group A and group B (73.42+112.55 vs. 34.43+64.99, $P < 0.001$). The duration of postoperative ventilation support also had a significant difference among both groups (25.82+44.27 vs. 16.42+46.26, $P < 0.008$). The data is shown in Table 2. (Table 2)

Cardiac function evaluation: There was a significant increase in preoperative vs. postoperative EF observed in group A (27.85+5.48 vs. 30.76+10.39) compared with group B (58.36+11.78 vs. 58.23+12.21). The mean EF difference in group A vs. group B respectively were 2.91+10.31 vs. -0.14+4.59 ($P = 0.001$). Data on EF comparison is shown in Table 3. (Table 3)

DISCUSSION

Current evidence shows complete revascularization is a better option in treating patients with multivessel CAD because it reduces the risk of cardiovascular death and myocardial infarction [Mehta 2019]. Complete revascularization is defined as an intervention targeting all stenotic coronary vessels with a diameter greater than >1.5mm and >50% lumen narrowing in at least one angiographic view and can be done with either percutaneous coronary intervention or CABG [Ong 2006]. Several studies support the role of CABG in improving EF in this patient category [Khaled 2019; Koene 2017].

This study shows that there was a significant increment of EF in patients with preoperative EF < 35% compared with those with EF > 35%. Transformation of EF in group A seemed to be more widespread than in group B. On the other

Table 1. Demographic and clinical characteristics

Variable	All ($N = 660$)	Group A ($N = 72$)	Group B ($N = 588$)	*P*-value
Age (year)	58.43+8.35	55.24+8.37	58.86+8.25	<0.001
Male (n)	563	66	497	0.106
Smoking (n)	361	41 (56.9%)	320 (54.4%)	0.696
Dyslipidemia (n)	313	48 (66.7%)	265 (45.1%)	0.001
Hypertension (n)	437	52 (72.2%)	588 (89.1%)	0.253
Family history of CAD (n)	94	10 (66.7%)	84 (45.1%)	0.928
Diabetes mellitus (n)	278	33 (45.8%)	245 (41.7%)	0.499
History of infarction (n)	-	37 (51.4%)	204 (34.7%)	0.005
NYHA grade III-IV (n)	208	32 (49%)	176 (33.7%)	0.008
Three vessel diseases (n)	578	59	519	0.354
Preoperative LVEF	55.21+14.68	27.89+5.5	58.71+11.52	<0.001
CPB duration	105.773+55.77	113.42+66.03	104.6+54.54	0.665
AxC duration	74.92+59.96	80.87+63.63	74.31+589.57	0.876

Mann Whitney; CPB, cardiopulmonary bypass; AxC, aortic cross-clamp

hand, group B had tighter data dispersion. EF transformation in group A was 2.91+10.31, while there was no significant change in group B. Even though group A had a significant increase in EF, the length of ICU stay and ventilatory support was significantly longer than group B. These findings might be due to group A having lower preoperative EF than group B [Tunç 2018].

A similar study has been conducted to assess EF after CABG in patients with EF <50%. The patients were classified into two groups: group I, 76 (69%) patients with EF > 35%, and group II, 34 (31%) patients with EF < 35%. Both groups had a significant postoperative EF increase with an average EF of 29.76 ± 4.868 pre-CABG to 33.53 ± 9.655 postoperative ($P < 0.05$) [Khaled 2019]. This increase in EF is perhaps due to revascularization of hibernating myocardium caused by chronic low blood flow circulating the myocardium [Kloner 2020]. Hibernation of the myocardium is a physiologically adaptive process to preserve cardiac contractility function and can be found in other mammals [Ryan 2018]. Hibernating myocardium is a viable myocardium and can be reversed and recovered by adequate revascularization [Kloner 2020]. A study demonstrated revascularization in patients with viable myocardium improves the functional class (NYHA) and reverse left ventricle remodeling [Ribeiro 2005]. Several factors may influence cardiac function recovery following revascularization therapy, such as the volume of scar tissue, mass of viable cardiac myocyte, thickness of the myocardial wall, and left ventricle volume [Lakshman 2020].

The decrease in postoperative EF in group B appeared to be minuscule and insignificant in this study, but another study found a significant decrease in EF post-CABG in patients with preoperative EF ≥50% (59±5% to 56±9%, $P < 0.001$) [Koene 2017]. Decrease in postoperative EF perhaps due to intra-operative global ischemia, early postoperative graft failure, or if the flow was immediately restored after ischemia occurs, the myocardium may be stunned [Adabag; Koene 2017; Leung 1993]. Intra-operative global ischemia can be determined by measuring cardiac enzymes such as troponin I 24-hours postoperative, and the enzyme can also predict postoperative mortality [Adabag]. Consistent with our result, another study also found an increase in postoperative EF in patients with EF <50% (36±9% to 41±12%, $P < 0.001$) [Koene 2017].

There are several limitations while conducting this study, such as the sample size and the difficulty in determining myocardial viability. Although our study shows a significant increase in EF among group A, the sample size from this group is not equally comparable to group B (72 vs. 588). A larger sample size from group A may change the significance of this study. Determining myocardial viability can be done with several imaging techniques, such as echocardiography, cardiac magnetic resonance imaging, and positron emission tomography scan [Anavekar 2016]. Echocardiography with dobutamine infusion can be done to assess cardiac contractile reserve, thus myocardial viability [Afridi 1998]. Myocardial viability assessment cannot be done in this study because the imaging techniques mentioned earlier are not part of a routine examination. Myocardial viability can be a crucial factor to determine whether a patient needs complete revascularization therapy or not, thus further study is warranted.

Table 2. Morbidity comparisons

Variable	EF Group A (*N* = 72)	EF Group B (*N* = 588)	*P*-value
ICU stay duration (hour)	73.42+112.55	34.43+64.99	<0.001
Ventilator support duration (hour)	25.54+43.92	16.42+45.87	0.008

Mann Whitney

Table 3. Ejection fraction comparisons

Variable	Preoperative EF (mean)	Postoperative EF (mean)	*P*-value
Group A	27.85+5.48	30.76+10.39	0.019
Group B	58.36+11.78	58.23+12.21	0.468
	Paired T-test		

Variable	EF	*P*-value
Group A	2.91+10.31	0.001
Group B	- 0.14 ± 4.57	
	Mann Whitney	

CONCLUSIONS

CABG is a better option to improve EF in patients with low cardiac function. During the three-month evaluation, the improvement of EF after CABG was higher in patients with EF <35% than ≥35%. Myocardium hibernation from low EF has an important role in the myocardium adaptation from a chronic ischemic condition in CAD. Further study is required to evaluate myocardial viability in patients with coronary artery disease and reduced ejection fraction.

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