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Correlation of Ejection Fraction, Diastolic Function and Left Ventricular Volume Index Preoperative with Major Cardiovascular Events During Postoperative Treatment of Coronary Artery Bypass Graft

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ABSTRACT
Background: Technological advances in coronary artery bypass graft surgery can improve patient outcomes after CABG surgery. Echocardiography parameters indicate left ventricular function. In CABG, left ventricular function plays an important role in the occurrence of major cardiovascular events (MACE) after CABG. This study assesses the relationship between ejection fraction, diastolic function, and preoperative left ventricular index volume with MACE during post-CABG care. ***Methods:*** Retrospective cohort study. Independent variables are ejection fraction, diastolic function, and left ventricular volume index. MACE during treatment is cardiovascular death, cardiogenic shock, acute heart failure, arrhythmia, and myocardial infarction. ***Results:*** A total of 79 samples were enrolled in this study. There were 36 patients (45.6%) with EF <45%, 67 patients (84.8%) with diastolic dysfunction, and 39 patients (49.3%) with an index volume > 64 ml/m2. After follow-up during treatment, 23 patients (29.1%) experienced MACE. The cut-off value for EF was 45% (AUC 0.255; 95% CI 0.14 – 0.37; p 0.001, while the cut-off value for LVVi was 67 ml/m2 (AUC 0.680; 95% CI 0.6 – 0.8; p 0.012). Cox regression analysis showed EF < 45% (adjusted HR 3.2; 95% CI 1.2 – 8.1; p = 0.016), diastolic dysfunction (adjusted HARI 0.7; 95% CI 0.1 – 6.9; p = 0.769) and index volume > 67 ml/m2 (adjusted HR 1.0; 95% CI 0.3 – 3.1; p = 0.993). ***Conclusion:*** Ejection fraction < 45% is an independent predictor of MACE during postoperative care of CABG. Diastolic dysfunction and volume index > 67 ml/m2 are not significant enough as predictors of MACE during postoperative care of CABG.

Keywords: ejection fraction; diastolic function; volume index; CABG; MACE

INTRODUCTION
Cardiovascular disease is the leading cause of death globally, with 17.9 million deaths reported in 2019, representing 32% of global deaths. Of these, 85% were due to coronary heart disease (CHD). Healthcare costs related to cardiovascular disease are projected to exceed USD 1.044 billion globally by 2030. In Indonesia, heart disease consumes significant healthcare resources, with spending increasing to nearly 8.6 trillion rupiahs in 2021[1].

Coronary heart disease can be managed medically or through revascularization procedures, such as percutaneous coronary intervention and coronary artery bypass graft (CABG) surgery. Revascularization is indicated for patients with symptoms unresponsive to medical therapy, those with intolerable medical therapy, or those with high-risk anatomy. The 2020 ISCHEMIA trial showed that revascularization, followed by medical therapy, improved angina-related symptoms but did not reduce mortality or myocardial infarction rates[2].

Coronary artery bypass graft surgery is recommended for patients with obstructive coronary heart disease, improving survival rates compared to medical therapy or percutaneous intervention [3]. Mortality risk after CABG is influenced by factors such as comorbidities, postoperative complications, and hospital procedure volumes. The mortality rate varies by country, with lower mortality in high-volume hospitals compared to low-volume ones [4].

Echocardiography plays a crucial role in preoperative assessment for CHD patients, evaluating left ventricular function, which is essential for diagnosis, treatment planning, and prognosis.

Left ventricular ejection fraction (LVEF) is a key parameter in assessing ventricular efficiency and predicting clinical outcomes after CABG. Preoperative LVEF and other factors like LV volume index and diastolic function are strongly associated with postoperative morbidity and mortality [5].

Studies have identified several preoperative factors, including LVEF, as strong predictors of mortality after CABG. Low preoperative LVEF is linked to complications such as Low Cardiac Output Syndrome (LCOS), prolonged ICU stays, and increased mortality [6]. Other factors like advanced age, emergency surgery status, and procedure complexity also significantly impact postoperative outcomes [7]. Understanding these predictors helps optimize treatment strategies and improve cardiovascular care.

METHOD

This study was conducted using a retrospective cohort design. The assessment of independent variables, which include ejection fraction, diastolic function, and left ventricular volume index, was carried out through medical records. All research subjects were followed up through medical records to determine the incidence of major cardiovascular events during the post-CABG care period. Patients who underwent Coronary Artery Bypass Graft surgery at Prof. dr. I G. N. G. Ngoerah General Hospital consecutively and met the inclusion criteria were selected as samples for this study.

The inclusion criteria were: 1) Patients with coronary heart disease who underwent CABG surgery at Prof. dr. I G. N. G. Ngoerah General Hospital; 2) Patients aged ≥18 years; 3) Patients who had undergone echocardiography at Prof. dr. I G. N. G. Ngoerah General Hospital (a maximum of 6 months before surgery). The exclusion criteria were: 1) Patients with incomplete medical records; 2) Patients with stage V chronic kidney failure with or without routine hemodialysis; 3) Patients with acute hemorrhagic or ischemic stroke; 4) Patients with malignancy/cancer; 5) Patients with severe infections/sepsis; 6) Patients with autoimmune diseases (SLE, rheumatoid arthritis); 7) Patients with congenital heart disease.

Data on ejection fraction, diastolic function, and left ventricular volume index were obtained from the final full study echocardiography report, finalized by cardiologist echocardiography consultant at Prof. dr. I.G.N.G. Ngoerah General Hospital.

Data on major cardiovascular events (MACEs) were collected from the postoperative period until the occurrence of a MACE or in-hospital period, obtained from integrated patient records and medical summaries in both physical and electronic medical records. Mortality assessment was conducted by reviewing death certificates, ECGs to identify arrhythmias, hemodynamic assessments for cardiogenic shock, echocardiography, and chest X-rays for acute heart failure, as well as clinical ACS and/or dynamic ECG changes and/or elevated hs-Troponin levels to assess myocardial infarction.

Control variable data were collected from the preoperative, postoperative, or treatment period, obtained from integrated patient progress notes and medical summaries in both physical and electronic medical records. Data analysis was performed using SPSS version 26 for descriptive analysis, proportion comparison tests, survival analysis using survival rate comparison, and Cox regression tests. Conclusions were drawn based on a 95% confidence interval and a p-value of < 0.05. All data analysis was carried out with the assistance of SPSS software.

RESULT

This study is a retrospective cohort study using secondary data from electronic medical records of post-CABG patients at Prof. I.G.N.G Ngoerah General Hospital during the period from January to June 2024. Sample collection was carried out using consecutive sampling within the research population. A total of 103 samples were initially collected, followed by an evaluation of data completeness and the application of inclusion criteria. A total of 24 samples were excluded: 17 samples due to incomplete data and 7 samples due to echocardiography examinations conducted outside the hospital, resulting in 79 eligible samples. All eligible samples were then followed up during the postoperative care period. The variables analyzed in this study include ejection fraction, diastolic function, and left ventricular volume index as independent variables, and Major Adverse Cardiovascular Events (MACE), including cardiogenic shock, arrhythmia, acute heart failure, and death, as dependent variables.

The results of the descriptive analysis of the study population are presented in Tables 1 and 2. The samples were grouped based on independent variables, including ejection fraction, diastolic function, and left ventricular volume index (Table 1), as well as based on the occurrence of MACE (Table 2). The cut-off values used to define each independent variable were obtained from the Receiver Operating Characteristic (ROC) curve.

TABLE 1: Characteristics of study subjects based on independent variables.

Variable	Ejection Fraction		Diastolic Function		Index Volume	
	<45%	≥45%	Dysfunction	Normal	>64 ml/m2	≤64 ml/m2
	n= 36	*n*= 43	*n*= 67	*n*= 12	*n*= 39	*n*= 40
Sociodemographic						
Age*	60 ± 8.5	59 ± 7.9	60 ± 8.3	62 ± 7.1	60 ± 8.6	59 ± 7.7
Gender (Male)	34 (94.4)	35 (81.4)	59 (88.1)	10 (83.3)	37 (94.9)	32 (80.0)
BMI (overweight/obese)	25 (69.4)	36 (83.7)	51 (76.1)	10 (83.3)	29 (74.4)	32 (80.0)
Hypertension	18 (50.0)	33 (76.7)	41 (61.2)	10 (83.3)	22 (56.4)	29 (72.5)
DM Type 2	20 (55.6)	20 (46.5)	35 (52.2)	5 (41.7)	20 (51.3)	20 (50.0)
ACS	21 (58.3)	22 (51.2)	39 (58.2)	4 (33.3)	23 (59.0)	20 (50.0)
Dyslipidemia	15 (41.7)	7 (16.3)	20 (29.9)	2 (16.7)	14 (35.9)	8 (20.0)
Creatinine*	1.3 ± 0.5	1.4 ± 0.7	1.4 ± 0.7	1.1 ± 0.2	1.3 ± 0.5	1.3 ± 0.7
Intra-operative						
CPB Time*	145 ± 45	145 ± 30	147 ± 39	134 ± 25	145 ± 43	145 ± 32
Cross Clamp Time*	85 ± 37	84 ± 21	87 ± 30	73 ± 17	86 ± 32	84 ± 26
Amount of Bleeding*	720 ± 430	552 ± 159	655 ± 342	483 ± 94	700 ± 417	560 ± 167
Number of Grafts	3 (2 - 4)	3 (2 - 4)	3 (2 – 4)	3 (2 – 3)	3 (2 - 4)	3 (2 - 4)
Post-Operative						
Support Duration*	39 ± 31	18 ± 20	30 ± 29	12 ± 11	36 ± 32.8	19 ± 18.2
Ventilator Duration*	20 ± 24	13 ± 14	17 ± 21	10 ± 4	21 ± 26.4	10.5 ± 6.5
ICU stay*	5.3 ± 3.6	4.4 ± 1.6	4.8 ± 2.9	4.6 ± 1.6	5 ± 3.5	4.5 ± 1.7

*Numerical data are presented as mean ± standard deviation.

Based on the analysis of the Receiver Operating Characteristic (ROC) curve, the optimal cut-off value of left ventricular ejection fraction for predicting MACE is 45%, with a sensitivity of 35% and a specificity of 36%. The area under the curve (AUC) is 0.255; 95% CI (0.14 – 0.37); p-value 0.001.

Using the cut-off value of 45%, the study subjects were then categorized into two groups: ejection fraction < 45% and ejection fraction ≥ 45%. After categorization, 36 samples were found to have an ejection fraction < 45% and 43 samples had an ejection fraction ≥ 45%.

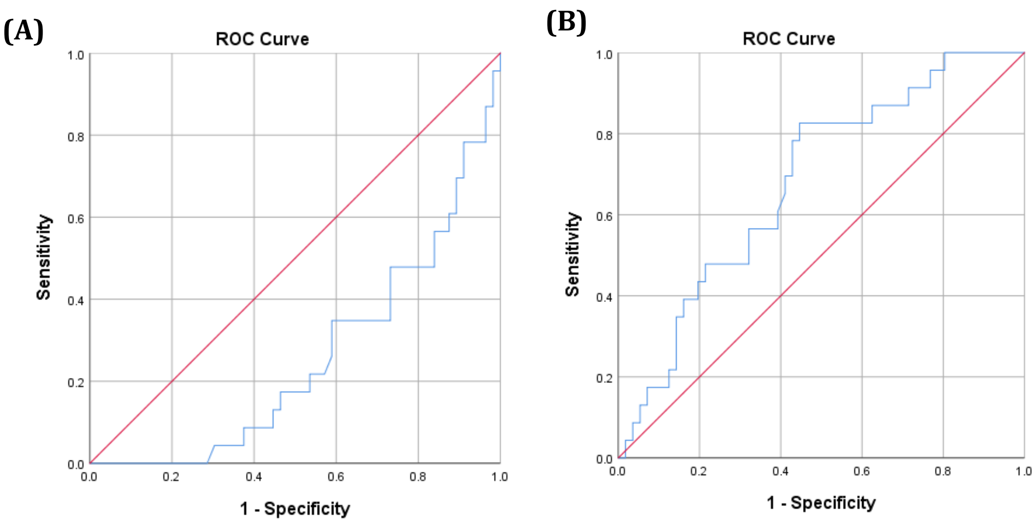

FIGURE 1: ROC Curve to obtain cut-off value for **(A)** left ventricular ejection fraction (LVEF) and **(B)** left ventricular index cut-off volume (LVVI).

The optimal cut-off value of the left ventricular volume index for predicting MACE is 67 ml/m2, with a sensitivity of 60% and a specificity of 61%. The area under the curve (AUC) is 0.680; 95% CI 0.6 – 0.8; p-value 0.012. Using the cut-off value of 67 ml/m2, the study subjects were then categorized into two groups: left ventricular volume index > 67 ml/m2 and left ventricular volume index ≤ 67 ml/m2.

After categorization, 39 samples were found to have a volume index > 67 ml/m2, and 40 samples had a volume index ≤ 67 ml/m2.

Out of 79 samples, 36 samples had an ejection fraction < 45%, and 16 samples (44.4%) of these experienced MACE. For diastolic function, 67 samples had diastolic dysfunction, and 22 samples

(95.7%) of these experienced MACE. Furthermore, 39 samples with an index volume > 67 ml/m^2 had 16 samples (69.6%) that experienced MACE.

The Kaplan-Meier survival estimate for the occurrence of MACE based on each category of independent variables is shown in Figure 3.

TABLE 2: Characteristics of research subjects based on MACE.

Variable	MACE		RR	*p*-value
	Yes	No		
Age (> 60 years)	16 (39.0)	25 (61.0)	2.1	0.051
Gender (Male)	22 (31.9)	47 (68.1)	0.3	0.266
BMI (overweight/obese)	16 (26.2)	45 (73.8)	0.7	0.378
Hypertension	14 (27.5)	37 (72.5)	0.9	0.661
DM Type 2	14 (35.0)	26 (65.0)	1.5	0.323
ACS history	13 (30.2)	30 (69.8)	1.1	1,000
Dyslipidemia	12 (54.5)	10 (45.5)	2.8	0.002
Creatinine (>1.2 mg/dL)	16 (50.0)	16 (50.0)	3.3	0.001
LV Ejection Fraction	**39.6 ± 10**	**50.3± 12**		
< 45%	16 (44.4)	20 (55.6)	2.7	0.006
≥ 45%	7 (30.4)	36 (64.3)		
LV Diastolic Function				
Dysfunction	22 (32.8)	45 (67.2)	3.9	0.085
Normal	1 (8.3)	11 (91.7)		
LV Index Volume	**78 ± 22**	**65± 23**		
> 67 ml/m2	16 (41.0)	23 (59.0)	2.3	0.021
≤ 67 ml/m2	7 (17.5)	33 (82.5)		
CPB Time	**165 ± 49**	**136± 28**		
> 150 min	17 (53.1)	15 (46.9)	4.2	< 0.0001
≤ 150 min	6 (12.8)	41 (87.2)		
Cross Clamp Time	**89 ± 42**	**82± 22**		
> 85 min	13 (34.2)	25 (65.8)	1.4	0.458
≤ 85 min	10 (24.4)	31 (75.6)		
Amount of Bleeding	**876 ± 447**	**527± 143**		
> 550 ml	18 (56.3)	14 (43.8)	5.3	< 0.0001
≤ 550 ml	5 (10.6)	42 (89.4)		
Support Duration	**52 ± 37**	**17± 13**		
> 24 hours	17 (63.0)	10 (37.0)	5.5	< 0.0001
≤ 24 hours	6 (11.5)	46 (88.5)		
Ventilator Duration	**31 ± 31**	**9.6± 5**		
> 12 hours	16 (57.1)	12 (42.9)	4.1	< 0.0001
≤ 12 hours	7 (13.7)	44 (86.3)		
ICU stay	**5.2 ± 4.5**	**4.6± 1.4**		
> 5 days	9 (34.6)	17 (65.4)	1.3	0.599
≤ 5 days	14 (26.4)	39 (73.6)		

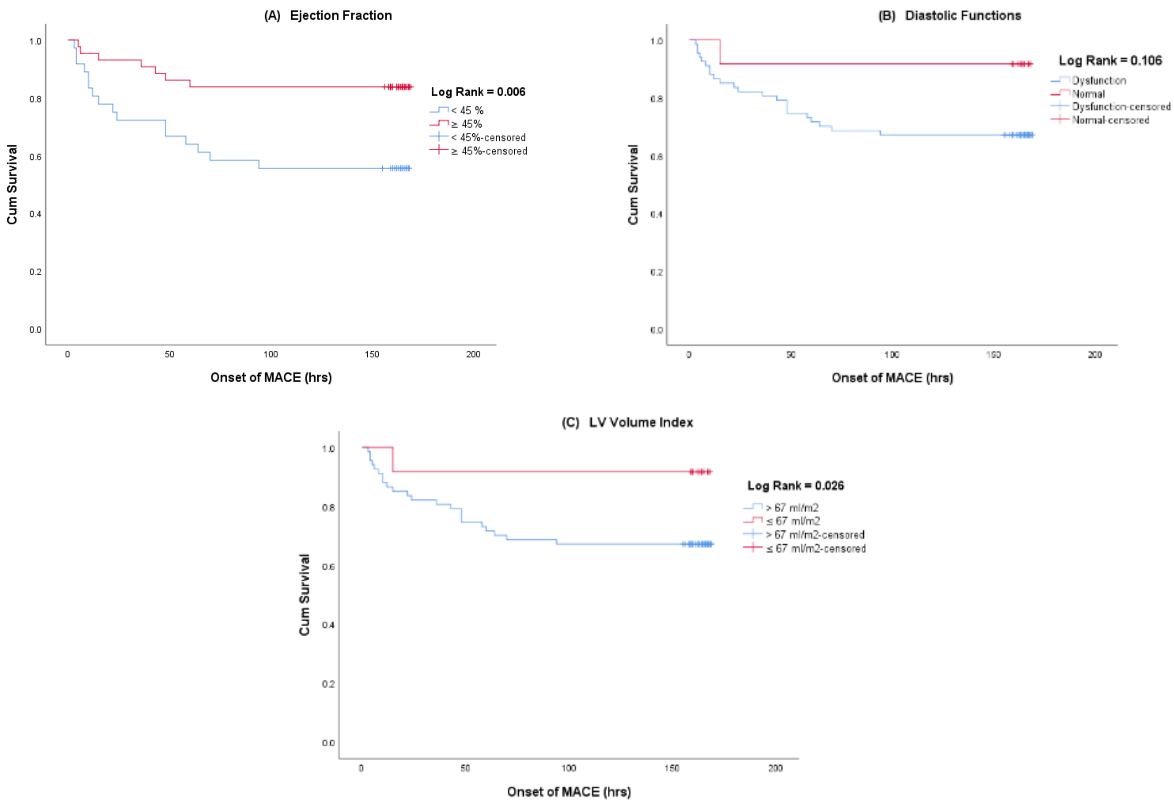

FIGURE 3: shows the Kaplan-Meier survival estimate curves for the occurrence of MACE based on left ventricular ejection fraction **(A)**, diastolic function of the LV **(B)**, and LV index volume **(C).**

Based on Table 3, the mean survival time for patients with an ejection fraction < 45% is 107.1 hours (95% CI 84.1 - 130.1), while the mean survival time for patients with an ejection fraction ≥ 45% is 146.4 hours (95% CI 131.1 - 162.1). The log-rank test shows a statistically significant difference in survival between patients with an ejection fraction < 45% and those with an ejection fraction ≥ 45%, with a p-value of 0.006.

For diastolic function, the mean survival time for patients with diastolic dysfunction is 123.8 hours (95% CI 108.1 - 139.7), whereas the mean survival time for patients with normal diastolic function is 155.2 hours (95% CI 131.3 - 179.1). The log-rank test did not show a statistically significant difference in survival between patients with diastolic dysfunction and those with normal diastolic function, with a p-value of 0.106.

TABLE 3: Survival rate and mean survival time based on categories of ejection fraction, LV diastolic function, and left ventricular index volume.

Variable	Mean Survival Time(hours)	95%CI	Survival Rate (%)	p-value
LVEF				
< 45%	107.1	84.1 - 130.1	55.6	0.006
≥ 45%	146.4	131.1 - 162.1	83.7	
Diastolic Function				
Dysfunction	123.8	108.1 - 139.7	67.2	0.106
Normal	155.2	131.3 - 179.1	91.7	
Volume Index				
> 67 ml/m2	113.3	91.6 - 135.1	59.0	0.026
≤ 67 ml/m2	143.1	126.1 - 160.1	82.5	

For the LV index volume variable, the mean survival time for patients with an index volume > 67 ml/m^2 is 113.3 hours (95% CI 91.6 – 135.1), while the mean survival time for patients with an index volume ≤ 67 ml/m^2 is 143.1 hours (95% CI 126.1 – 160.1).

The log-rank test shows a statistically significant difference in survival between patients with a left ventricular index volume > 67 ml/m^2 and those with an index volume ≤ 67 ml/m^2, with a p-value of 0.026.

In this study, LV ejection fraction, LV diastolic function, and LV index volume are used as independent variables, while other factors such as age, sex, hypertension, type 2 diabetes, history of ACS, dyslipidemia, creatinine levels, CPB time, cross-clamp time, amount of bleeding, duration of support, and duration of ventilator use are control variables. For control variables with numerical data scales such as age and creatinine levels, normality tests are conducted using the Kolmogorov-Smirnov test, and significance tests are performed using the independent sample t-test. For control variables with categorical data scales such as dyslipidemia, CPB time, amount of bleeding, duration of support, and duration of ventilator use, the association measure calculated is Relative Risk (RR) using the Chi-Square test.

TABLE 4: Cox regression analysis of LV ejection fraction, LV diastolic function, and LV index volume on MACE.

Variable	HR	95%CI	*p*	Adjusted HR	95%CI	*p*
Ejection Fraction < 45%	3.2	1.3 - 7.9	0.010	3.2	1.2 - 8.1	0.016
Diastolic Dysfunction	4.5	0.6 - 33.2	0.142			
Index Volume (> 67 ml/m2)	2.8	1.2 - 6.4	0.015			
Dyslipidemia	3.5	1.6 - 8.1	0.003			
Creatinine (> 1.2 mg/dL)	0.2	0.1 - 0.5	0.001	4.3	1.7 - 10.6	0.002
CPB Time (> 150 minutes)	5.6	2.2 - 14.3	<0.0001	7.0	2.7 - 18.8	<0.0001
Total Bleeding (> 550 ml)	7.4	2.8 - 20.1	<0.0001	4.4	1.5 - 12.6	0.006
Inotropic/pressor (> 24 hours)	6.9	2.7 - 17.6	<0.0001			
Ventilator Duration (> 12 hours)	5.0	2.0 - 12.1	<0.0001			

The multivariate analysis used to assess the independent effects of LV ejection fraction, LV diastolic function, and LV index volume on MACE is Cox regression. Variables included in the multivariate analysis are control variables that showed a p-value < 0.05 in univariate analysis. The multivariate analysis indicates that left ventricular ejection fraction is an independent predictor of MACE occurrence during post-CABG care (adjusted HR 3.2; 95% CI 1.2 – 8.1; p = 0.016). This suggests that in patients undergoing CABG, after adjusting for confounding variables, the risk of MACE during post-CABG care is 3.2 times higher in patients with an ejection fraction < 45% compared to those with an ejection fraction ≥ 45%.

The study also shows that after adjusting for confounding variables in the multivariate analysis, LV diastolic function (adjusted HR 0.7; 95% CI 0.1 – 6.9; p = 0.769) and LV index volume (adjusted HR 1.0; 95% CI 0.3 – 3.1; p = 0.993) are not significant predictors of MACE occurrence during post-CABG care. Control variables that are significant predictors of MACE during post-CABG care after adjusting for confounding variables include creatinine levels (adjusted HR 4.3; 95% CI 1.7 – 10.6; p = 0.002), CPB time (adjusted HR 7.0; 95% CI 2.7 – 18.8; p < 0.0001), and amount of bleeding (adjusted HR 4.4; 95% CI 1.5 – 12.6; p = 0.006).

DISCUSSION

Advancements in the science and techniques of CABG surgery have progressed rapidly in recent years, particularly in diagnostic aspects and management of patients with coronary artery disease. Nevertheless, the high complication rates in post-CABG patients remain a serious challenge. One of the main complications occurring in post-CABG patients is MACE, which has a significant impact on patient outcomes. MACE includes conditions such as cardiovascular death, cardiogenic shock, heart failure, malignant arrhythmias, and persistent angina. The high mortality and morbidity caused by MACE underscore the need for early prediction and prevention efforts.

In this regard, prognostic parameters are a key focus of research in CABG patients, with one prominent parameter being echocardiographic metrics, which are standard supportive tests routinely performed in these cases. A thorough understanding of echocardiographic parameters is expected to open new avenues for risk assessment and management of post-CABG patients. A good grasp of these echocardiographic parameters not only provides insight into cardiac function before surgery but also forms the basis for more effective MACE prevention strategies.

Research on preoperative echocardiographic parameters in CABG is highly relevant for a deeper understanding of the pathophysiological mechanisms, prognosis, and management of this condition. Ejection fraction measures the heart's ability to contract and pump blood from the left ventricle to the aorta and the rest of the body during systole, while diastolic function reflects the left ventricle's ability to relax during diastole, and left ventricular index volume describes the end-diastolic volume just before systolic contraction. All three are parameters that depict cardiac function, particularly left ventricular function. This study evaluates ejection fraction, diastolic function, and left ventricular index volume preoperatively in relation to MACE during post-CABG care.

In this study, 79 subjects were consecutively sampled from the research population. The average age of the study samples was 60 ± 8.5 years.

This is consistent with a study by Kamel et al. in 2018, which reported an average age of CABG patients as 60 years [8]. Another study conducted by Yan et al. in 2022 also found similar results, with an average patient age of 59 years [9]. Gender and BMI are common risk factors in patients with CAD. In this study, the majority of patients were male (69, or 87%) and 67 patients (61%) were classified as overweight/obese. This is consistent with a study by Albakri et al. in 2018, which found that the majority of CAD patients requiring CABG were male and had a BMI > 25 kg/m². This study identified risk factors such as hypertension, type 2 diabetes, dyslipidemia, and a history of ACS as major CAD risk factors in patients undergoing CABG. These findings are consistent with the study by Kao et al. in 2022, which reported that hypertension, type 2 diabetes, dyslipidemia, and a history of myocardial infarction are commonly found risk factors in patients with coronary artery disease undergoing CABG [10,11].

In this study, elevated preoperative serum creatinine (>1.2 mg/dL) was found in 32 patients (40%), with half of them, or 16 patients (50%), experiencing MACE during post-CABG care. In this study, patients with CKD stage V were excluded. The increase in preoperative serum creatinine may be attributed to worsening renal function due to cardiorenal syndrome, which is common in patients with chronic heart failure, where chronic CAD leads to decreased cardiac function in most patients in this study. Additionally, cardiogenic shock and/or acute heart failure resulting from acute coronary syndrome can also cause elevated preoperative serum creatinine. In this study, there were 8 patients with acute coronary syndrome who underwent urgent CABG. This is consistent with the study by Griffin et al. in 2022, which explains that elevated preoperative creatinine (>1.2 mg/dL) is a predictor of MACE. The proportion of MACE events was higher in the group with abnormal baseline creatinine levels (2.9% vs 1.4%) compared to the group with normal creatinine levels [12].

In this study, 23 patients (30%) experienced MACE during post-CABG care. In the MACE group, 69% or 16 patients had an ejection fraction < 45%, while 7 patients (31%) had an ejection fraction ≥ 45%. This is consistent with the study by Kamel et al. in 2018, which found that the average ejection fraction was 42 ± 4.1% in the low ejection fraction group and 50.6 ± 3.8% in the normal ejection fraction group, with MACE proportions in these ejection fraction groups being 21% and 7%, respectively (Kamel et al., 2018). Another study by Omer et al. in 2022, involving 128 patients, also found that the majority of patients had an ejection fraction < 50%, with 83 patients (65%), while 45 patients (35%) had an ejection fraction > 50% [13]. Optimal management according to heart failure and chronic coronary disease therapy guidelines should continue before surgery to prevent the worsening of ejection fraction, which increases the risk of MACE.

In this study, left ventricular diastolic dysfunction was observed in nearly all patients in the MACE group, with 22 patients (95.7%). This finding is consistent with the study by Kaw et al. in 2016, which found that 137 patients (87.9%) with diastolic dysfunction compared to those without diastolic dysfunction had worse post-CABG outcomes, including cardiac death and MACE [7]. This finding is also consistent with the theory that, in patients with coronary artery disease, a decline in left ventricular diastolic function is a common abnormality occurring early in the ischemic cascade. Diastolic dysfunction often does not present with significant symptoms and is therefore frequently overlooked, leading to patients presenting with more severe diastolic dysfunction and often accompanied by other cardiac functional or structural abnormalities [14].

In this study, a left ventricular index volume > 67 ml/m² was found in 16 patients (69.6%) in the MACE group, while only 7 patients (30.4%) with a normal left ventricular index volume experienced MACE. These results are consistent with the study by Salem et al. in 2006, which showed that the incidence of mortality/MACE in the left ventricular dilation group (LVVI > 70 ml/m²) was 21 patients (72%), compared to 9 patients (28%) with normal index volume [15]. Another study by Rahmat et al. in 2021 also found similar results, where a left ventricular index volume > 65 ml/m² was a predictor of low cardiac output syndrome and postoperative mortality (Rahmat et al., 2021).

For intraoperative parameters, this study collected data on cardiopulmonary bypass time (CPB time), cross-clamp time, and amount of bleeding. In this study, 17 patients (74%) in the MACE group had prolonged CPB time (> 150 minutes). The definition of prolonged CPB time in this study aligns with the study by Juca et al. in 2024, where CPB time > 140 minutes was defined as prolonged CPB time, with 228 patients (71.5%) experiencing prolonged CPB time[16]. Another study by Maharani et al. in 2017 found that 21 patients (46.7%) with a CPB time > 120 minutes experienced MACE (Maharani et al., 2017).

In this study, 13 patients (56.5%) in the MACE group had a cross-clamp time > 85 minutes. This result differs from the studies by Nissinen et al. in 2009 and Patel et al. in 2020, where prolonged cross-clamp times were defined as > 90 minutes and > 79 minutes, respectively. The difference in results may be due to the fact that this study only included patients undergoing isolated CABG procedures, whereas the two comparison studies included all types of cardiac surgeries, where the duration of cross-clamp time may vary depending on the type of surgical procedure performed [18,19].

In this study, 18 patients (78%) with a blood loss > 550 ml during surgery experienced MACE during the postoperative period. Similar results were found in the study by Nelson et al. in 2018, which identified blood loss > 600 ml as a risk factor for in-hospital mortality. Another study by Seetharama et al. in 2021 found that a blood loss > 500 ml during CABG surgery was an independent predictor of MACE during the intensive care unit stay following CABG [20,21].

For postoperative parameters, this study collected data on the duration of inotropic/vasopressor use. Among the patients, 27 (34%) had a duration of inotropic/vasopressor use > 24 hours after CABG surgery, and 17 of these patients (73.9%) experienced MACE during the postoperative period. These results are consistent with the study by Kontar et al. in 2023, which reported a mean duration of inotropic/vasopressor use of 21 ± 7.3 hours among 78 patients, with 36 patients (46.1%) experiencing MACE, including acute heart failure and cardiogenic shock. Another study by Patel et al. in 2020 on the duration of cardiac pharmacologic support following cardiac surgery involving 478 patients found a longer ICU stay (1 day vs. 3 days) in the group with cardiac pharmacologic support > 24 hours [19,22].

In this study, 28 patients had a duration of ventilator use > 12 hours, and 16 of these patients (69.6%) experienced MACE during the postoperative period. This aligns with the study by Zhang et al. in 2024, which reported a mean duration of ventilator use for patients after CABG as > 18 hours. For ICU stay, this study found that 53 patients (67%) had an average intensive care unit stay of 5 days. This is consistent with the study by Zhao et al. in 2022, which reported an average ICU stay of 3 ± 2.1 days for patients after open-heart surgery [23,24].

Based on the data analysis conducted, the overall characteristics of the study subjects did not show significant differences compared to previous studies. This finding indicates a uniformity in characteristics between the two subject groups, both in terms of demographic and clinical characteristics.

The Area Under the Curve (AUC) provides an overview of how well the classification model can distinguish between positive and negative groups. Determining the cut-off value using the ROC curve involves analyzing sensitivity and specificity at various cut-off points. The ROC curve visualizes this relationship. The intersection point of the curve provides the best balance between sensitivity and specificity. This cut-off point is the optimal threshold for separating two categories in the analyzed variable.

In this study, the AUC for ejection fraction against MACE was 0.255, with a cut-off value for ejection fraction of 45%, sensitivity of 35%, and specificity of 36%. A study by Kim et al. in 2021 reported different results, with an AUC for ejection fraction against MACE of 0.790, a cut-off value of 31.8%, sensitivity of 88.8%, and specificity of 58.2% [25].

Another study by Erdogan et al. in 2020 achieved an AUC of 0.629. The cut-off value for the ejection fraction was 44.4%, with a sensitivity of 74% and specificity of 64% [25,26]. In this study, the AUC result for the ejection fraction differs from the two comparative studies mentioned above. This discrepancy can be explained by the fact that a null AUC value is 0.5, indicating that the variable cannot be used as a predictor for the occurrence of an outcome. If the AUC value of a variable is > 0.5, a higher AUC value (> 0.7) indicates a greater risk of predicting the occurrence of the outcome of interest. Conversely, if the AUC value of a variable is < 0.5, a lower AUC value (< 0.3) indicates a higher risk of predicting the occurrence of the outcome of interest (Hajian, 2013). From this explanation, an AUC value of 0.255 with a cut-off ejection fraction of 45% has the same meaning in predicting the occurrence of MACE within the scope of this study.

The AUC value for the left ventricular index volume in relation to MACE is 0.680, with a cut-off value of 67 ml/m^2, and a sensitivity of 60% and a specificity of 61%. A similar result was reported in a study by Salem et al. in 2006, which found an AUC of 0.737, with a cut-off volume index of 70 ml/m^2, sensitivity of 71%, and specificity of 67%. Another study by Zhou et al. in 2022 reported an AUC for the left ventricular index volume of 0.67, with a cut-off value of 60 ml/m^2, sensitivity of 67%, and specificity of 63%. These results indicate consistency with previous studies [15,28].

In addition to the independent variables, the assessment of AUC values and cut-off points using ROC curves was also conducted for other statistically significant control variables in the univariate analysis, such as CPB time, amount of preoperative bleeding, duration of inotropic/vasopressor use, and duration of ventilation. In this study, the AUC for CPB time in relation to MACE was 0.717, with a cut-off value of 150 minutes, and sensitivity of 73% and specificity of 74%. This result is consistent with data from a study by Madhavan et al. in 2018, which reported an AUC of 0.721, with a cut-off value of 180 minutes, sensitivity of 70%, and specificity of 68% [29]. Furthermore, this study found that the AUC for intraoperative blood loss in relation to MACE was 0.821, with a cut-off value of 550 ml, sensitivity of 78%, and specificity of 75%. Similar results were obtained in a study by Nelson et al. in 2018, which reported an AUC of 0.793 with a cut-off value of 600 ml. Another study by Seetharama et al. in 2021 found a cut-off value of 500 ml with sensitivity of 77% and specificity of 73% [20,21].

The AUC for the duration of inotropic/vasopressor use in relation to MACE was 0.797, with a cut-off value of 24 hours, sensitivity of 74%, and specificity of 75%. This is consistent with a study by Howlett et al. in 2019, which reported an AUC of 0.749 for postoperative inotropic/vasopressor use, with a cut-off value of 22.7 hours, sensitivity of 76%, and specificity of 65%. Meanwhile, the AUC for the duration of ventilation in relation to MACE was 0.781, with a cut-off value of 12 hours, sensitivity of 74%, and specificity of 68%. A study by Rochayati et al. in 2023 reported similar findings, with an AUC of 0.697 for ventilation duration, a cut-off value of 24 hours, sensitivity of 70%, and specificity of 61% [30,31].

Thus, it can be concluded that the results of this study demonstrate consistency in the cut-off values for ejection fraction, left ventricular index volume, CPB time, amount of bleeding, duration of inotropic/vasopressor use, and ventilation duration post-operation, compared to previous studies.

This consistency enhances the validity and generalizability of the findings. The clinical implications of this research contribute positively to understanding the role of each variable as a risk factor for MACE and strengthen the argument for the success of the classification model in predicting this risk. From the cut-off values, an ejection fraction < 45% is identified as an independent predictor of MACE. The survival analysis in this study shows that a left ventricular ejection fraction < 45% is associated with MACE events during post-CABG operation care (log-rank p < 0.016).

In this study, a left ventricular ejection fraction < 45% was associated with a higher occurrence of MACE (RR 2.7; 95% CI 1.26 – 5.91; p = 0.007). The mean survival time for patients with EF < 45% was 107.1 days (95% CI 84.1 – 130.1) with a survival rate of 55.6%. For the EF ≥ 45% group, the mean survival time was 146.4 days (95% CI 131.1 – 162.1) with a survival rate of 83.7%. The log-rank test showed a significant result (p = 0.006). Multivariate analysis using Cox regression revealed that EF < 45% is associated with MACE with an adjusted HR of 3.2 (95% CI 1.2 – 8.1; p < 0.016). This indicates that patients with EF < 45% have a 3.2 times greater risk of MACE and have a lower survival rate and mean survival time compared to patients with EF ≥ 45%.

These findings are supported by a study by Kamel et al. in 2018, which found that low ejection fraction is associated with higher MACE (HR 2.5; 95% CI 1.97 – 2.73; p = 0.026). Multivariate analysis with logistic regression showed that low EF is a predictor of MACE with an HR of 3.4 (95% CI 2.62 – 8.94; p = 0.021)[8]. Another study by Omer et al. in 2022 found that low ejection fraction is associated with a higher incidence of MACE. The mean survival time for patients with low EF was 63.7 days (95% CI 58.1 – 79.3; p = 0.01), while for those with normal EF, it was 83.1 days (95% CI 78.4 – 101.2; p = 0.01). Multivariate analysis using Cox regression showed that low ejection fraction is associated with MACE with an HR of 1.88 (95% CI 1.80 – 1.96; p = 0.0043)[13].

The underlying mechanism is that the left ventricular ejection fraction reflects the heart pump function. A lower ejection fraction increases the risk of postoperative low cardiac output syndrome (LCOS). The occurrence of LCOS disrupts myocardial perfusion and other organ tissues, potentially leading to cardiogenic shock, acute heart failure, and malignant arrhythmias. Theoretically, this condition requires hemodynamic support, either mechanical or inotropic/vasopressor, and a longer duration of ventilation post-operation. This also necessitates additional management, which can lead to prolonged ICU stays and an increased risk of nosocomial infections, ultimately worsening postoperative outcomes (Kamel et al., 2018; Omer et al., 2022). Optimal management according to heart failure and chronic coronary disease guidelines should be continued before surgery to prevent worsening of the ejection fraction, which could increase the risk of MACE.

In this study, left ventricular diastolic dysfunction was statistically not associated with MACE (RR 4.0; 95% CI 0.59 – 26.5; p = 0.164). The mean survival time for patients with left ventricular diastolic dysfunction was 123.8 days (95% CI 108.1 – 139.7), while for those with normal diastolic function, it was 155.2 days (95% CI 131.3 – 179.1) with p = 0.106. Multivariate analysis using Cox regression showed that diastolic dysfunction was not significantly associated with MACE, with an adjusted HR of 0.7 (95% CI 0.1 – 6.9; p = 0.769). These results differ from a study by Kaw et al. in 2016, which found that patients with diastolic dysfunction had worse postoperative outcomes, including cardiac death (OR 2.4; 95% CI 1.54 – 2.71; p = 0.032) and an adjusted OR of 2.0 (95% CI 1.77 – 2.38; p = 0.0064)[7]. A study by Lee et al. in 2023 found a significant association between patients with HFmrEF and HFpEF and the occurrence of MACE (OR 1.52, 95% CI 0.85 – 2.73, p = 0.015). Multivariate analysis comparing the two EF groups with MACE and mortality showed an adjusted HR of 2.1 (95% CI 1.39 – 3.11; p = 0.044) [6].

The difference in findings between this study and the comparison studies may be due to the high proportion of diastolic dysfunction in the MACE patient group, with 22 patients (95%) affected. This high prevalence may have prevented achieving statistical significance. Theoretically, in patients with coronary artery disease, a reduction in left ventricular diastolic function occurs as an early abnormality in the ischemia cascade. Diastolic dysfunction often does not present with significant symptoms, leading to patients presenting with more severe diastolic dysfunction when symptomatic, which is frequently accompanied by other cardiac functional or structural abnormalities. Left ventricular diastolic dysfunction results from impaired relaxation and reduced myocardial recoil force during the diastolic phase, a consequence of chronic ischemic processes, which leads to suboptimal left ventricular filling. This results in suboptimal stroke volume and cardiac output, affecting coronary perfusion, particularly in patients with multi-vessel CAD who have pre-existing obstructions. This combination worsens myocardial viability and function globally, manifesting as symptoms like chest pain or shortness of breath during activity, which reduces the patient's quality of life [14].

In this study, a left ventricular index volume > 67 ml/m^2 was associated with the occurrence of MACE post-operation (RR 2.3; 95% CI 1.1 – 5.1; p = 0.027). The mean survival time for the group with a left ventricular index volume > 67 ml/m^2 was 113.3 days (95% CI 91.6 – 135.1), while for the group with a volume index ≤ 67 ml/m^2, it was 143.1 days (95% CI 126.1 – 160.1), with a p-value of 0.026. In multivariate analysis, after controlling for confounding variables, the left ventricular index volume did not show a statistically significant relationship with the occurrence of MACE post-CABG, with an adjusted HR of 1.0 (95% CI 0.3 – 3.1; p = 0.993).

These results suggest that a left ventricular index volume > 67 ml/m^2 is associated with a lower survival time compared to patients with a volume index ≤ 67 ml/m^2, with a statistically significant p-value.

These findings are consistent with a study by Zhou et al. in 2022, which found that patients with left ventricular dilation (LVVI > 60 ml/m^2) had a higher incidence of MACE post-CABG. However, after adjusting for confounding variables, the multivariate analysis yielded an adjusted HR of 0.78 (95% CI 0.65 – 0.94), which was not statistically significant [28]. This study's results differ from those of a study by Fukunaga et al. in 2020, which found that left ventricular dilation could predict mortality and morbidity post-CABG, with an OR of 5.5 (95% CI 2.0 – 15.7; p = 0.01). Survival analysis of MACE, after controlling for confounding variables, showed an adjusted HR of 3.4 (95% CI 1.2 – 10.3; p = 0.026). These results indicate that left ventricular dilation is an independent predictor of mortality in patients post-CABG [32].

In this study, the left ventricular index volume did not show a statistically significant effect on the occurrence of MACE post-CABG, which may be due to the presence of more significant confounding variables affecting MACE. Theoretically, the relationship between left ventricular index volume and MACE can be explained by chronic ischemia in patients with CAD, leading to the expansion of ischemic areas (scars) and subsequent myocardial fibrosis. This myocardial fibrosis increases the left ventricular index volume because scar tissue, resembling inelastic fibrous tissue, does not contract effectively. This results in increased wall stress on the myocardium, which ultimately reduces myocardial contractility and recoil force. This process decreases stroke volume and cardiac output, which cumulatively impairs coronary and global organ/tissue perfusion, thereby increasing the risk of MACE post-CABG [28,32,33].

This study, utilizing a retrospective design with secondary data from medical records, has limitations including the restricted availability of preoperative, intraoperative, and postoperative data. Several confounding factors could not be clearly evaluated, which may affect the results.

The research was conducted at a single referral center hospital. The patient characteristics were predominantly complex in terms of disease severity, and comorbid factors, and were relatively homogeneous. Thus, the findings may not fully represent all patients undergoing CABG.

Another limitation is the short follow-up period for MACE, which only covered the postoperative care period. Future research could involve a prospective design, a larger sample size, a broader range of variables, and a longer follow-up period to obtain more representative results that can be more widely applied to the general population.

CONCLUSION

This study is a retrospective cohort study aimed at examining the relationship between preoperative left ventricular ejection fraction, diastolic function, and left ventricular index volume with MACE during postoperative care following CABG at RSUP Prof. I.G.N.G. Ngoerah. Based on the results of the analysis, the following conclusions can be drawn:

(1) Preoperative left ventricular ejection fraction < 45% is associated with major cardiovascular events during postoperative care following CABG at RSUP Prof. I.G.N.G. Ngoerah.
(2) Preoperative left ventricular diastolic function is not associated with major cardiovascular events during postoperative care following CABG at RSUP Prof. I.G.N.G. Ngoerah.
(3) Preoperative left ventricular index volume is not associated with major cardiovascular events during postoperative care following CABG at RSUP Prof. I.G.N.G. Ngoerah.

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