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Risk Factors for Mortality of Patients Waiting for Elective Coronary Artery Bypass Graft Surgery

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Abstract

Background: Insufficient capacity for cardiac surgery results in extensive waiting time for patients requiring coronary artery bypass grafting (CABG). Previous studies have reported a consequence of an increased risk of mortality while waiting for CABG. Identification of risk factors for mortality is important in patients waiting for CABG. **Objectives:** To assess mortality rates and identify risk factors for mortality of patients waiting for CABG. **Methods:** This retrospective cohort study was done on patients waiting for elective CABG in dr. Kariadi General Hospital from January 2018 to December 2020. Identification of risk factors associated with mortality was done on patients who were waiting for CABG using logistic regression methods. **Results:** There were 162 patients fulfilling the criteria, with a mean waiting time for surgery of 9.8 months. While waiting for CABG surgery, 32 (19.7%) patients died of any cause. Independent risk factors for death while waiting for CABG included left ventricular ejection fraction ≤ 45% (OR 4.75; 95% CI 1.76 - 12.78; p = 0.002), left main disease (OR 4.12; 95% CI 1.50 - 11.27; p = 0.006), serum creatinine ≥ 1.5 mg/dl (OR 3.71; 95% CI 1.41 - 9.74; p = 0.008), and a number of coronary artery disease risk factors ≥ 3 (OR 3.34; 95% CI 1.24 - 8.99; p = 0.017). **Conclusions:** Long waiting time for CABG is associated with a high mortality rate which is influenced by left ventricular ejection fraction ≤ 45%, left main disease, serum creatinine ≥ 1.5 mg/dl, and a number of coronary arteries disease risk factors ≥ 3.

Keywords

Waiting Time, Coronary Artery Bypass Graft Surgery, Risk Factor, Mortality

1. Introduction

Coronary Artery Disease (CAD) is the leading cause of death in the world today. The World Health Organization (WHO) states that CAD has become a global cause of death in the past 15 years because its prevalence continues to increase rapidly in developing and developed countries [1]. Coronary Artery Bypass Graft (CABG) surgery is one of the therapeutic modalities that has been shown to be effective in prolonging the life span of patients with stable CAD [2]. CABG can improve angina complaints in the majority of patients undergoing this procedure. The more severe the CAD, the stronger the indication for CABG [3].

As the increasing progress in health facilities and patient care for their health, causing CAD detection rates to increase and the need for surgical procedures such as CABG also increases, however, the contrast occurs where the economic constraints on the health system are developing less rapidly which means lack of resources and facilities to accommodate patients requiring CABG [4]. Patients on the waiting list are at high risk for acute coronary events. The natural history of CAD will imply a critical event that can occur at any time during the waiting time from the patient's first complaint until surgery [5]. Patients waiting for CABG have been reported to be at high risk of death and their risk of death increases when surgery is postponed because of the long waiting list [6].

Various risk factors have been known to influence mortality while waiting for surgery, including involvement of stenosis in the left main coronary artery, creatinine levels, history of myocardial infarction [7], CAD risk factors [8] [9], age [10], and impaired left ventricular function [10] [11]. No previous study was done in Indonesia to determine risk factors for mortality in patients waiting for CABG surgery, therefore it needs to be investigated further.

2. Materials and Methods

2.1. Study Design and Population

This study was a retrospective cohort study conducted using medical record data of patients waiting for CABG at Dr. Kariadi Hospital Semarang for the period January 2018 to December 2020. The inclusion criteria in this study were as follows: 1) Patients aged > 18 years to 80 years. 2) CAD patients who are candidates for CABG surgery are listed on the waiting list. Waiting time for surgery > 3 months. The exclusion criteria in this study were as follows: 1) Known to suffer from heart valve disease, congenital heart defects, malignancies, and autoimmune diseases which are thought to be the main causes of death. 2) Percutaneous Coronary Intervention (PCI) has been performed 3) Incomplete medical record data. Information about the variables was obtained from previous studies that have been shown as a risk factor for mortality in patients awaiting CABG surgery. There were 7 independent variables analyzed as independent predictors of risk factors for mortality in patients waiting for elective CABG surgery at Dr. Kariadi Hospital Semarang: 1) Age > 65 years old. 2) Number of CAD risk factors ≥ 3. 3) History of Myocardial Infarction. 4) Serum creatinine

level > 1.5 mg/dl. 5) Ischemic ECG. 6) Left ventricular ejection fraction ≤ 45%. 7) Stenosis of the left main coronary artery.

2.2. Endpoints and Definitions

The endpoint parameter was death, which death from all causes that occur any time before surgery after the patient was listed on the waiting list for CABG surgery and the patient will be removed from the waiting list. Deaths were obtained from telephone interviews with families or medical records. Waiting time was defined by the time a patient starts after being accepted for the CABG procedure and was listed on the waiting list until the CABG surgery was performed, the surgery was canceled, or the patient died [8] [9].

2.3. Statistical Analysis

Data analysis includes descriptive analysis. In a descriptive analysis of continuous scale, variable data were expressed as the mean and standard deviation if the distribution were normal or median and the minimum-maximum value if the distribution were not normal. Categorical scale variable data was expressed in number (n) and percentage (%). To test the hypothesis, the relationship between each independent variable and the dependent variable was analyzed using the unpaired t-test & Mann Whitney test. Multivariate analysis was performed by using linear regression predictive value with 95% confidence interval. The p-value was considered significant if it is <0.05. The magnitude of the risk was expressed as the odds ratio obtained from the multivariate logistic regression analysis.

3. Results

3.1. Baseline Characteristics

In the period January 2018 - December 2020, 191 patients were found, of which 162 patients met the inclusion criteria. There were 29 patients excluded from the study with details of 13 patients because the waiting time for surgery was less than 3 months, 6 patients because of involvement of heart valve disease, 6 patients because of a history of percutaneous coronary intervention, 2 patients due to ventricular septal rupture, 1 patient due to medical records incomplete, 1 patient died of rectosigmoid cancer (**Figure 1**).

Baseline characteristics of patients waiting for CABG Surgery were shown in **Table 1**. The study consisted of 135 men (83.3%) and 27 women (16.7%). The mean age ranged from 59.1 ± 6.66 years with a mean body mass index of 24.83 ± 3.78. 3 patients (1.9%) with BMI Underweight, 37 patients (22.8%) normal, 51 patients (31.5%), overweight, 71 patients (43.8%) obese. From laboratory examination data for kidney function, it was found that the mean serum creatinine level was 1.3 ± 0.32 with the lowest level of 0.75 and the highest at 3. Echocardiographic findings showed that the mean left ventricular ejection fraction (LVEF) was 48.12 ± 14.63 with the lowest ejection fraction at 14% and the highest at 78%. The angiographic data found that most of the patients had lesions on their three coronary arteries, namely 156 patients (96.3%) with CAD 3VD, and there

were 6 patients (3.7%) with CAD 2VD. From the coronary angiography results, it was also found that 77 patients (47.5%) had lesions involving the left main coronary artery, and 83 patients (51%) had lesions with chronic total occlusion of their coronary arteries. The mean SYNTAX Score was 30.24 + 3.66. All 162 patients (100%) received antiplatelets. Beta-blockers, ACEi or ARB, nitrates and statins each had reported use of more than 80% by the study cohort. Based on the length of waiting time for CABG surgery, the average waiting time was 9.8 ± 6.02 months.

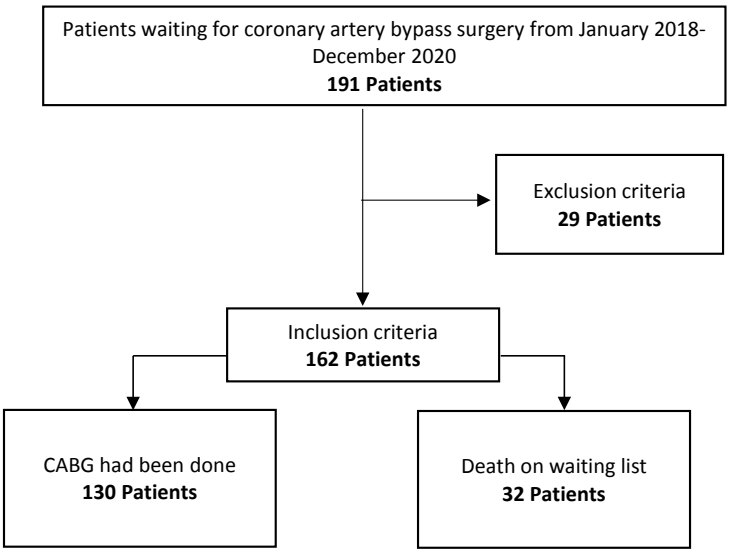

Figure 1. Process for selecting respondent.

Table 1. Baseline characteristics of patients waiting for CABG surgery.

Variables	Mean ± SD; Median (min-maks)	Patients (n = 162), %
Age (years)	59.11 ± 6.66; 59 (40 - 76)	
Gender		
Male		135 (83.3%)
Female		27 (16.7%)
History of Myocardial Infarction		75 (46.3%)
CAD Risk Factors		
DM		74 (45.7%)
Hypertension		113 (69.8%)
Dyslipidemia		75 (46.3%)
Family History		8 (4.9%)
Smoking		87 (53.7%)
Menopause		22 (81%)
Number of CAD Risk Factors ≥ 3		74 (45.6%)
BMI	24.83 ± 3.78; 24 (16 - 44)	
Underweight		3 (1.9%)

Continued

Normal		37 (22.8%)
Overweight		51 (31.5%)
Obesitas		71 (43.8%)
Ischemic ECG		117 (72.2%)
Serum Creatinine (mg/dl)	1.3 ± 0.32; 1.3 (0.75 - 3)	
Creatinine ≥ 1.5		50 (30.8%)
Creatinine < 1.5		112 (69.1%)
Ejection Fraction (%)	48.12 ± 14.63; 49 (14 - 78)	
EF ≤ 45%		59 (36.4%)
EF > 45%		103 (63.5%)
CAD		
CAD 2VD		6 (3.7%)
CAD 3VD		156 (96.3%)
LM Disease		77 (47.5%)
CTO		83 (51%)
LAD		15 (9.2%)
RCA		19 (11.7%)
LCx		6 (3.7%)
LAD and RCA		22 (13.5%)
LAD and LCx		5 (3%)
RCA and LCx		9 (5.5%)
LAD, RCA, LCx		6 (3.7%)
LM		1 (0.6%)
Syntax Score	30.24 ± 3.66; 30 (24 - 39)	
Medications		
Antiplatelet		162 (100%)
Beta-blocker		140 (86.4%)
Digoxin		7 (4.3%)
ACEi/ARB		136 (84%)
Nitrate		150 (92.6%)
Diuretics		54 (33.3%)
MRA		79 (48.8%)
Statin		158 (97.5%)
CCB		33 (20.4%)
Waiting time (Month)	9.8 ± 6.02; 8.0 (1 - 31)	

ACEi: Angiotensin-Converting Enzym inhibitor; ARB: Angiotensin Receptor Blocker; BMI: Body Mass Index; CAD: Coronary Artery Disease; CCB: Calcium Channel Blocker; CTO: Chronic Total Occlusion; DM: Diabetes Mellitus; ECG: Electrocardiograhy; EF: Ejection Fraction; LAD: Left Anterior Descending; LCx: Left Circumflex; LM: Left Main; MRA: Mineralocorticoid Receptor Antagonist; RCA: Right Coronary Artery; VD: Vessel Disease.

3.2. Mortality

While waiting for CABG surgery, 32 patients died with a mean age of 60.53 ± 4.84; 59 (54 - 70) and the mean duration from the time of registering for CABG surgery until the patient died was 147 + 144; 113 (0 - 606) days. The cause of death was shown in Table 2. The most causes of death were due to cardiac arrest in 21 patients (65.6%) and 2 patients (6.3%) died from a stroke.

Table 2. Data on causes of death in patients waiting for CABG surgery.

Patient	Age, y	Waiting, d	Cause of Death
1	60	52	Cardiac arrest
2	57	606	Cardiac arrest
3	63	20	Cardiac arrest
4	55	140	Sudden death
5	56	213	Cardiac arrest
6	60	24	Cardiac arrest
7	58	28	Stroke
8	58	26	Cardiac arrest
9	64	180	Sudden death
10	65	40	Cardiac arrest
11	54	265	Cardiac arrest
12	57	484	Sudden death
13	67	10	Cardiac arrest
14	58	229	Cardiac arrest
15	63	8	Sudden death
16	59	31	Sudden death
17	56	116	Cardiac arrest
18	70	111	Stroke
19	67	62	Sudden death
20	66	240	Cardiac arrest
21	59	398	Sudden death
22	69	156	Cardiac arrest
23	62	149	Cardiac arrest
24	59	183	Cardiac arrest
25	57	43	Cardiac arrest
26	55	213	Cardiac arrest
27	54	254	Cardiac arrest
28	67	68	Cardiac arrest
29	56	23	Cardiac arrest
30	55	235	Cardiac arrest
31	68	102	Sudden death
32	63	0	Sudden death

3.3. Bivariate Analysis

Furthermore, bivariate analysis of the variables associated with the incidence of mortality in patients waiting for CABG surgery was carried out (Table 3). For variables on an ordinal scale, the bivariate analysis of the Chi-Square test was carried out using a cut-off based on the theoretical basis of previous studies. In the bivariate analysis, a significant statistical correlation was observed in most variables: left ventricular ejection fraction ≤ 45% (RR 5.237; p = 0.000), serum creatinine ≥ 1.5 mg/dl (RR 4.276; p = 0.000), left main disease (RR 3.312; p = 0.001), number of coronary artery disease risk factors ≥ 3 (RR 3.039; p = 0.001), and ischemic ECG (RR 3.035; p = 0.017). No significant differences were observed in the history of myocardial infarction (RR 1.315; p = 0.432), and age ≥ 65 years (RR 1.210; p = 0.634).

3.4. Multivariate Analysis

The risk factor variables in the bivariate analysis which have p value < 0.25 then analyzed in the multivariate logistic regression test. These variables were serum creatinine levels ≥ 1.5 mg/dl, LM Disease, left ventricular ejection fraction ≤ 45%, number of CAD risk factors ≥ 3, and ischemic ECG. In the multivariate analysis, there were 4 risk factor variables: serum creatinine levels ≥ 1.5 mg/dl, LM Disease, left ventricular ejection fraction ≤ 45%, number of CAD risk factors ≥ 3 which reached statistical significance, and no association between ischemic ECG and mortality on the incidence of mortality in patients waiting for CABG surgery (Table 4).

Table 3. Bivariate analysis of risk factors for mortality in patients waiting for CABG surgery.

Variables		During waiting time		RR (95% IK)	p*
		CABG	Death		
Ejection Fraction (%)	≤45	35 (26.9%)	24 (75%)	5.237	0.000‡
	>45	95 (73.1%)	8 (25%)		
Serum Creatinine (mg/dl)	≥1.5	29 (22.3%)	21 (65.6%)	4.276	0.000‡
	<1.5	101 (77.7%)	11 (34.4%)		
LM Disease		53 (40.8%)	24 (75%)	3.312	0.001‡
Number of CAD Risk Factor ≥ 3		51 (39.2%)	23 (71.9%)	3.039	0.001‡
Ischemic ECG		85 (65.4%)	28 (87.5%)	3.035	0.017§
History of myocardial infarction		58 (44.6%)	17 (53.1%)	1.315	0.432‡
Age (years)	≥65	27 (20.8%)	8 (25%)	1.210	0.634‡
	<65	103 (79.2%)	24 (75%)		

‡ Chi-square test. § Fisher's exact test. CAD: Coronary Artery Disease; ECG: Electrocardiography; LM: Left Main.

Table 4. Multivariate analysis of risk factors for mortality in patients waiting for elective coronary artery bypass surgery.

Variabel	OR	95% IK (min-max)	p (<0.05)
Ejection fraction ≤ 45%	4.75	1.76 - 12.78	0.002
LM Disease	4.12	1.50 - 11.27	0.006
Serum creatinine level ≥ 1.5 mg/dl	3.71	1.41 - 9.74	0.008
Number of CAD risk factors ≥ 3	3.34	1.24 - 8.99	0.017

CAD: Coronary Artery Disease; LM: Left Main.

4. Discussion

This study demonstrated a high rate of mortality (19.7%) in CAD patients who died while waiting for CABG surgery. In comparison, previous studies reported lower mortality rates of 11.3% in Brazil [9], 0.02% in the Netherlands [8], 0.48% in Canada [10], and 1.3% in Sweden [7]. The sharp difference in the rate of mortality could be attributable to the availability of human resources and surgical facilities, a system for prioritizing patients where patients with high risk will be operated on earlier, and also clinical characteristics backgrounds. In this study, patients showed a higher proportion of risk factors and lower left ventricular ejection fraction. Furthermore, urgent cases were included in this study, meanwhile, in another study, the respondents included were only elective cases [12].

Left ventricular ejection fraction (LVEF) less than 45% was the strongest independent predictor of mortality in patients waiting for CABG. Fonseca *et al.* in their study found that ejection fraction ≤ 45% was an independent predictor of mortality in patients waiting for CABG surgery (HR 2.33; 95% IK; p = 0.039). There was also significant evidence that delaying surgery for patients with severe left ventricular dysfunction likely results in an increased number of deaths while waiting for CABG (OR 2.47; 95% CI; p < 0.001) [10]. Rexius *et al.* revealed that patients with a decreased ejection fraction of 10% were associated with a 28% increase in the risk of death while waiting for CABG (RR 1.27; 95% CI; p = 0.007) [7].

This study found that 82% of the population had a number of CAD risk factors ≥ 2, and even 45.6% of them had a number of CAD risk factors ≥ 3. Sub-analysis was performed and 2 variables were contributed significantly, dyslipidemia and smoking (data not shown). Suttorp *et al.* found that smoking history increased the risk of death 9-fold in CAD patients waiting for elective CABG surgery (OR 8.7; 95% CI) [13].

Among respondents, 77 patients (47.5%) had LM disease which contributed to a higher rate of mortality. A previous study found that LM disease or multivessel CAD was also associated with a 4-fold higher incidence of early death while waiting for CABG surgery (OR 4.1; 95% CI) [13].

Serum blood creatinine ≥ 1.5 mg/dl was an independent risk factor after the

multivariate logistic regression test with OR 3.71 (95% CI, p = 0.008). A previous study also found the same result, Rexius *et al.* found that the mean creatinine level of 104 + 53 (1.18 mg/dL) was associated with the risk of death while waiting for CABG surgery (p ≤ 0.001). It was also significantly associated with the incidence of CAD even though it was at normal values and in the absence of the metabolic syndrome.

There were 3 variables that were not proven to be independent risk factors for mortality in patients waiting for elective CABG surgery, including age; history of myocardial infarction; and ischemic ECG. In this study, patients were younger than in previous studies. A study by Cox *et al.* determined similar results in which there was no significant difference in age between study groups while waiting for CABG (p = 0.218) [14]. Seddon *et al.* in New Zealand also found that there was no significant difference in age between the priority groups while waiting for CABG (p = 0.9) [15].

This study found that the group of patients who died had a history of myocardial infarction higher than the CABG group. However, the difference between the two groups was not significant (p = 0.432). Cesena *et al.* reported that a history of extensive anterior myocardial infarction had no statistical effect in patients waiting for CABG (p = 0.19) [12]. Cox *et al.* in their study reported a high trend toward a history of myocardial infarction in patients who received priority of CABG, but statistically the results were not significant (p = 0.081) [14].

Ischemic ECG has a strong prognostic value for cardiovascular events [16], but in this study, it was not an independent predictor of patients waiting for CABG. Some of died patients had a normal ECG (9.4%) so it may affect the significance value of the ischemic ECG. The ECG examination in this study was carried out by tracing only a single ECG examination when the patient was admitted to clinic after the patient had received medical therapy. Some studies showed that a single ECG examination will be in changing conditions so that it will reduce the strength of its relative risk [17]. Several studies have reported that ST-segment abnormalities and T waves are unstable images due to the influence of drugs and other conditions such as electrolyte imbalance disorders. Study by Reykjavik *et al.* found that more than 36% of men with ST-T abnormalities did not show these abnormalities at subsequent follow-up [18].

The cause of death of most patients was related to the heart. Plomp *et al.* in their study divided 2 causes of death during waiting time: cardiac, and non-cardiac. All patients who died would be considered cardiac until the non-cardiac cause of death could be identified properly [19]. Rexius *et al.* reported that in about 95% of patients who died while waiting for CABG, the cause of death was cardiovascular-related as evidenced by their death certificates [7]. Ray *et al.* even described clearly about the cause of death in 2102 patients on the CABG waiting list. Among these patients, there were 14 (0.7%) patients who died with the cause of death mostly related to the heart [20].

Several limitations were found in this study. First, this study used retrospective secondary data that was dependent on the accuracy and completeness of

medical health records. Second, the absence of surgical priority on the patient waiting list and the surgical decisions that have been taken may be subjective depending on the patient and clinician so it can affect the clinical course of the patient. Third, some data on the causes of death were obtained from interviews with the patient's family that may not describe the exact cause of death.

5. Conclusion

Long waiting time for CABG is associated with a high mortality rate which is influenced by left ventricular ejection fraction ≤ 45%, left main disease, serum creatinine ≥ 1.5 mg/dl, and a number of coronary arteries disease risk factors ≥ 3.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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