

Pre-operative, Intraoperative, and Post-operative Determinants Associated with 30-day Mortality Post-Coronary Artery Bypass Graft: A Retrospective Cohort Study

Ikhwan Rinaldi¹, Mondastri K. Sudaryo²*, Arif Mansjoer³

¹Department of Internal Medicine, Division of Hematology and Medical Oncology, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia; ²Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, West Java, Indonesia; ³Department of Internal Medicine, Division of Cardiology, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Abstract

Edited by: Igor Spiroski Citation: Rinaldi I, Sudaryo MK, Mansjoer A. Pre-operative, Intraoperative, and Postoperative Determinants Associated with 30-day Mortality Post-Coronary Artery Bypass Graft: A Retrospective Cohort Study. Open-AccessMaced.MedSci.2022Apr/21.10(B):1022-1028. https://doi.org/10.3889/oamjms.2022.9563 Keywords: CABG, Mortality, Ischernic heart disease "Correspondence: Mondastri K. Sudaryo, Faculty of Public Health, Universitas Indonesia. E-mail: maqo19@gmail.com Received: 26-Mar-2022 Revised: 08-Apr-2022 Accepted: 11-Apr-2022 Copyright: © 2022 Ikhwan Rinaldi, Mondastri K. Sudaryo, Arif Mansjoer Funding: This research did not receive any financial support Competing Interest: The authors have declared that no competing Interest exists Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution.

NonCommercial 4.0 International License (CC BY-NC 4.0)

BACKGROUND: Various determinants of 30-day mortality risk in CABG patients have been formulated into certain scoring models such as the EuroSCORE and ACEF model. However, these models only consider pre-operative parameters while excluding intraoperative, post-operative, and perioperative parameters. At present, the prior research has increasingly emphasized the role of these excluded parameters as determinants of post-CABG mortality. Furthermore, there are differences in mortality rate of CABG procedures in Indonesia when compared with other countries.

AIM: This study aimed to identify pre-operative, intraoperative, and post-operative determinants of 30-day mortality after CABG surgery in Indonesian population.

METHODS: In this retrospective cohort study, secondary data were obtained from the medical records of 263 patients aged \geq 18 years who underwent CABG at a single center in Indonesia during the year 2012–2015. Selected pre-operative, intraoperative, post-operative, and perioperative determinants were analyzed in both bivariate and multivariate Cox regression models to identify determinants associated with 30-day mortality.

RESULTS: The 30-day mortality rate after CABG was 11.8%. Multivariate analysis identified neurological dysfunction (HR 6.16; 95% CI 2.42–15.66), renal impairment (HR 3.9; 95% CI 1.46–10.38), left ventricle dysfunction (HR 3.53;95% CI 1.55–8.03), aortic clamp duration (HR 3.7;95% CI 1.53–8.96), surgery duration (HR 3.85;95% CI 1.39–10.70), post-operative thrombocytopenia (HR 3.99;95% CI 1.72–9.23), and post-operative intra-aortic balloon pump (HR 10.98; 95% CI 4.77–25.28) as significant determinants associated with 30-day mortality after CABG

CONCLUSION: Neurological dysfunction, renal impairment, left ventricle dysfunction, aortic clamp duration, surgery duration, post-operative thrombocytopenia, and post-operative intra-aortic balloon pump were independent determinants for 30-day mortality after CABG.

Introduction

Coronary artery bypass grafting (CABG) is a surgical procedure commonly performed in patients with multiple occluded coronary vessels [1], [2]. There were 400,000 CABG procedures performed in the United States every year [1], [3] The CABG procedure is commonly used to bypass atheromatous blockages in coronary arteries with harvested arterial or venous conduits. The CABG procedure is indicated in highgrade blockage of coronary artery, provided the failure of percutaneous coronary intervention (PCI) procedure in myocardial infarction patients. The ACC/AHA guidelines also enlisted several indications of the procedure, with three-vessel coronary artery disease of greater than 70% with or without left anterior descending artery (LAD); LAD artery with one other major artery; or one artery with significant stenosis (>70%) with significant anginal symptoms or survivor of sudden cardiac death withisschemia-related ventricular tachycardia (VT) [1], [4].

Various determinants of 30-day mortality risk in CABG patients were formulated into certain scoring models such as European System for Cardiac Operative Risk Evaluation (EuroSCORE), risk model of Society of Thoracic Surgeon (STS), and age, creatinine, and ejection fraction (ACEF) model [5], [6] However, those models only use pre-operative parameters to predict the risk of mortality in CAGB patients.

Another interesting findings is that data from several studies in Indonesia have shown that mortality from CABG in Indonesia is relatively high when compared with other developing countries and from study that was used to develop EuroSCORE [7], [8]. A similar study to ours conducted in Indonesia by Ginting *et al.* showed CABG mortality rate of CABG of 18.6% [7]. Another study by Ariaty *et al.* had mortality rate of 15.15% [8]. Both of these numbers were higher than EuroSCORE study that had mortality rate of 4.7%. The differences are speculated to be caused by differences in baseline characteristics in the populations used for the studies such as ejection fraction and kidneyofunction of thus, infinistindex study aimed to identify pre-operative, intraoperative, post-operative, and perioperative determinants of 30-day mortality after CABG surgery in Indonesian patients as based on current data, it is suggested that there are unique factors that should be evaluated for their association with mortality. Furthermore, as EuroSCORE did not take into account operative and post-operative factors into analysis, we seek to analyze the role of operative and post-operative factors with mortality.

Methods

Study design

This retrospective cohort study was conducted using secondary data collected from manual and electronic medical records of patients at Cipto Mangunkusumo National General Hospital from the year 2012 to 2015. Inclusion criteria were adults (18 years of age or older) who underwent CABG procedure either elective or urgent. Exclusion criteria were CABG procedure performed with off-pump technique, patients who died during operation, and incomplete medical record.

The primary outcome of this study was 30-day mortality after CABG procedure, which was defined as mortality of any cause occurring within 30 days after the day of the procedure. Independent variables of this study were pre-operative, intraoperative, postoperative, and perioperative determinants of 30-day mortality after CABG procedure.

Pre-operative determinants

The pre-operative determinants used on this study include age, sex, body mass index (BMI), and presence of comorbidities such as chronic pulmonary disease, neurological dysfunction, history of cardiac surgery, impairment of renal function, extracardiac arthropathy, active endocarditis, unstable angina, extracardiac arthropathy, left ventricular dysfunction, history of myocardial infarction, pulmonary hypertension, urgency of surgery, thoracic aorta surgery, presence of anemia, leukocytosis, and thrombocytopenia.

Intraoperative determinants

Intraoperative determinants consisted of duration of aortic clamp, duration of cardiopulmonary bypass, and duration of surgery or procedure.

Post-operative and perioperative determinants

Post-operative anemia, leukocytosis, and thrombocytopenia, and the use of intra-aortic

balloon pump (IABP) were recorded as postoperative determinants while the need of red blood cell transfusion was recorded as a perioperative determinant.

Definition of determinants

Definition of determinants used in this study is presented in Table 1 of supplementary file.

Table 1: Subject characteristics and pre-operative, intraoperative,
post-operative, and perioperative determinants of 30-day
mortality after CABG at a single center during 2012–2015

after CA	3G	n (%)	
n	%		
31	11.8	263 (100)	
	0	50 (40 0)	
		50 (19.0)	
21	12.7	213 (81.0)	
7	54	130 (49.4)	
		68 (25.9)	
		46 (17.5)	
		10 (3.8)	
		9 (3.4)	
		- ()	
1	16.7	6 (2.3)	
30	11.7	257 (97.7)	
8	25.8	31 (11.8)	
23	9.9	232 (88.2)	
0	0	2 (0.8)	
31	11.9	261 (99.2)	
2	00.5	10 (0.5)	
		18 (6.8)	
25	10.2	245 (93.2)	
10	24 5	20 (11 0)	
		29 (11.0)	
		88 (33.5)	
10	0.0	146 (65.5)	
7	20	35 (13.3)	
		228 (86.7)	
24	10.0	220 (00.1)	
0	0	0 (0)	
31	11.8	263 (100)	
0	0	0 (0)	
31	11.8	263 (100)	
10	17.2	58 (22.1)	
21	10.2	205 (77.9)	
		8 (3.0)	
29	11.4	255 (97.0)	
21	15.7	134 (51 0)	
		134 (51.0) 129 (49.0)	
10	1.0	120 (40.0)	
1	100	1 (0.4)	
		262 (99.6)	
		202 (00.0)	
0	0	0 (0)	
31	11.8	263 (100)	
		. ,	
2	8	25 (9.5)	
29	12.2	238 (90.5)	
20	18.2	110 (41.8)	
11	7.2	153 (58.2)	
		17 (6.5)	
29	11.8	246 (93.5)	
0	0	1 (0 ()	
		1 (0.4)	
31	11.8	262 (99.6)	
10	40.0	25 (9.5)	
21	8.8	238 (90.5)	
	n 31 4 27 7 9 11 3 1 30 8 23 0 31 6 25 10 11 10 7 24 0 31 10 21 22 21 22 21 22 21 22 21 22 21 22 21 22 21 22 21 22 21 22 20 11 20 01 21 22 20 31 22 <td>n % 31 11.8 4 8 27 12.7 7 5.4 9 13.2 11 23.9 3 30.0 1 11.1 1 16.7 30 11.7 8 25.8 23 9.9 0 0 31 11.9 6 33.3 25 10.2 10 34.5 11 12.5 10 34.5 11 12.5 10 6.8 7 20 24 10.5 0 0 31 11.8 10 17.2 21 10.2 2 25.0 29 11.4 21 15.7 10 7.8 1 100 30 11.5</td>	n % 31 11.8 4 8 27 12.7 7 5.4 9 13.2 11 23.9 3 30.0 1 11.1 1 16.7 30 11.7 8 25.8 23 9.9 0 0 31 11.9 6 33.3 25 10.2 10 34.5 11 12.5 10 34.5 11 12.5 10 6.8 7 20 24 10.5 0 0 31 11.8 10 17.2 21 10.2 2 25.0 29 11.4 21 15.7 10 7.8 1 100 30 11.5	

Table 1: (Continued)

Predictive variable	Mortality after CA	within 30 days BG	n (%)	
	n	%		
Duration of cardiopulmonary bypass				
≥240 min	4	80.0	5 (1.9)	
<240 min	27	10.5	258 (98.1)	
Duration of surgery			. ,	
>260 min	25	19.1	131 (49.8)	
≤260 min	6	4.5	132 (50.2)	
Post-operative determinants Postoperative anemia**				
Anemia	31	12.8	242 (92.0)	
No anemia	0	0	21 (8.0)	
Post-operative leukocytosis				
Leukocytosis	26	11.4	229 (87.1)	
No leukocytosis	5	14.7	34 (12.9)	
Post-operative thrombocytopenia*				
Thrombocytopenia	9	64.3	14 (5.3)	
No thrombocytopenia Post-operative IABP	22	8.8	249 (94.7)	
Yes	18	40.9	44 (16.7)	
No	13	5.9	219 (83.3)	
Perioperative determinants Red blood cell transfusion				
Yes	30	14.0	215 (81.7)	
No	1	2.1	48 (18.3)	

Ethical statement

The work has been reported in line with the Declaration of Helsinki. Ethical clearance of this study was released by Ethical Committee of Faculty of Medicine-Universitas Indonesia, Ethical Committee of Faculty of Public Health-Universitas Indonesia, and Cipto Mangunkusumo National General Hospital-Universitas Indonesia (No. 0558/UN2.F1/ETIK/2018) 18-06-0646. The policy in our institution (Universitas Indonesia) stated that retrospective cohort study does not require informed consent. Medical records were not anonymized during access and data gathering. However, before commencing formal analysis, the medical records were anonymized.

Statistical analysis

The subjects' baseline characteristics and determinants are presented as means or medians for continuous data and as frequencies for categorical data. The pre-operative, intraoperative, post-operative, and perioperative determinant data were dichotomized according to the occurrence of mortality within 30 days after CABG.

All determinants were then tested for multicollinearity. Determinants which did not meet the criteria of multicollinearity were tested for its proportional hazard assumption using Kaplan–Meier estimator, Ln-Ln survival test, and global test. Every determinant that fit the proportional hazard assumption was then subjected to a Cox regression analysis.

Bivariate and multivariate Cox regression analyses of every determinant with p <0.25 were performed sequentially. The multivariate analysis was conducted using the 8-step backward logistic regression (LR) method. Determinants with the highest p value (>0.05) after each step were excluded from the upcoming steps. This multivariate analysis would result in several determinants that independently associated with the outcome (p<0.05). All statistical analyses were performed with SPSS ver. 14.0 (SPSS Inc., Chicago, IL, USA) and STATA (StataCorp Inc., College Station, Texas, USA).

Results

In total, 356 patients who underwent CABG during 2012–2015 were identified from medical records. Of these, 93 patients were ineligible due to incomplete medical records, resulting in 263 patients with complete medical records to be included for analysis in this study. All subjects were followed up for 30 days postoperatively or until death occurred. No patients were lost to follow-up. The subjects' characteristics and determinants factors contributing to 30-day mortality after CABG are described in Table 1.

About 11.8% of the subjects died within 30 days after CABG with 81% of which were male. Median number of days from the day of surgery to mortality was 2 days. The median age was 60 years old, with the age range from 31 to 79 years. Total number of patients who underwent CABG did not differ greatly between those aged <60 years and ≥60 years (49.4% and 50.6%). However, only 5.4% of those aged <60 years experienced mortality after CABG, whereas the group of patients aged ≥60 years had higher mortality. Nonelective CABG was performed in 134 patients (51%) with higher mortality as compared to the elective group (15.7% vs. 7.8%). Majority of patients in this study underwent the aortic clamp duration of < 150 min and cardiopulmonary bypass duration of < 240 min with total of 238 patients (90.5%) and 258 patients (98.1%), respectively. Two hundred and forty-two patients (92%) had post-operative anemia and 229 patients (87.1%) had leukocytosis post-operative. There was no mortality recorded in patients without anemia. Majority of patients in this study did not receive IABP support (83.3%). However, patients that received IABP support had higher 30-day mortality rate (40,9% vs. 5.9%). Most of the patients underwent red blood cell transfusion in the perioperative period with a total of 215 patients (92%). Of these, 14% experienced mortality within 30 days after CABG surgery while the group that did not undergo red blood cell transfusion after CABG surgery only had 2.1% mortality within 30 days after CABG surgery.

None of the determinants showed multicollinearity (r > 0.8). Therefore, all determinants were eligible for inclusion in the proportional hazard analysis of 30-day mortality after CABG. Determinants which met the assumption of proportional hazard were sex, age, chronic pulmonary disease, neurological dysfunction, renal function impairment, left ventricular

dysfunction, history of myocardial infarct, pulmonary pectoris. hypertension, unstable angina bodv mass index, pre-operative anemia, pre-operative leukocytosis, duration of aortic clamp, duration of cardiopulmonary bypass, duration of surgery, postoperative thrombocytopenia, post-operative IABP, and perioperative red blood cell transfusion. In contrast, a history of cardiac surgery, active endocarditis, extracardiac arteriopathy, thoracic aorta surgery, postinfarct septal rupture, post-operative anemia, and postoperative leukocytosis did not meet the assumption of proportional hazard. In addition, urgency of surgery did not meet the assumption of proportional hazard as the Kaplan-Meier analysis of this variable revealed constant survival from 15th day after surgery. Therefore, this variable was set as stratifying determinant.

Bivariate Cox regression analysis identified age, neurological dysfunction, renal function impairment, left ventricular dysfunction, pre-operative anemia, duration of aortic clamp, duration of cardiopulmonary bypass, duration of surgery, post-operative thrombocytopenia, and post-operative IABP support as factors associated significantly with 30-day mortality after CABG (Table 2). Meanwhile, gender, chronic pulmonary disease, and history of cardiac surgery were not associated with 30-day mortality after CABG. The highest hazard ratio obtained from bivariate analysis was the duration of cardiopulmonary bypass (HR 15.39; 95% CI 15.26–44.99).

Table 2: Bivariate cox regression model of pre-operative, intraoperative, post-operative, and perioperative determinants of 30-day mortality after CABG at a single center, 2012–2015

Determinants		Hazard ratio	p value
Gender	Female	1.58 (0.55-5.52)	0.391
	Male		
Age	≥ 60 years<60 years	3.47 (1.49-8.06)	0.004
Chronic pulmonary disease	Yes	1.39 (0.19-10.24)	0.743
	No		
Neurological dysfunction	Yes	2.87 (1.28-6.43)	0.010
	No		
Renal impairment	Yes	3.572 (1.46-8.71)	0.005
	No	,	
Left ventricular dysfunction	<30 EF≥30 EF	4.30 (2.02-9.15)	≤0.001
History of myocardial infarct	Yes	1.95 (0.84-4.52)	0.120
5 5	No		
Unstable angina pectoris	Yes	1.71 (0.80-3.64)	0.161
3 1	No	()	
Pulmonary hypertension	Yes	2.40 (0.57-10.07)	0.230
	No		
Urgency of surgery	Urgent	2.12 (1.00-4.51)	0.049
ergeney er eurgery	Elective	2.12 (1.00 1.01)	0.010
Body mass index	Obesity	0.65 (0.15-2.75)	0.566
Doug made made	No Obesity	0.00 (0.10 2.10)	0.000
Pre-operative anemia	Yes	2.66 (1.27-5.55)	0.009
	No	2.00 (1.27-0.00)	0.003
Pre-operative leukocytosis	Yes	0.98 (0.23-4.14)	0.988
Fie-operative leukocytosis	No	0.90 (0.23-4.14)	0.900
Pre-operative thrombocytopenia	Yes	n.a	n.a
Pre-operative thrombocytopenia	No	II.d	II.d
Duration of aortic clamp	≥150 min<150 min	5.34 (2.63–10.85)	≤0.001
Duration of cardiopulmonary bypass	≥130 min<130 min ≥240 min<240 min	15.39 (5.26–44.99)	
Duration of surgery	≥240 min≤260 min	4.51 (1.85–10.99)	≤0.001 ≤0.001
Post-operative thrombocytopenia	Yes	8.77 (4.02–19.14)	≤0.001 ≤0.001
r ost-operative thrombocytopenia	No	0.77 (4.02-19.14)	<u>⊐</u> 0.001
Post-operative IABP	Yes	8.77 (4.02–19.14)	≤0.001
Pust-operative IABP	No	0.11 (4.02-19.14)	≥0.001
Device weather and blood call	110	C 007 (0 05 51 00)	0.056
Perioperative red blood cell transfusion	Yes	6.987 (0.95–51.23)	0.000
transiusion	No		

These determinants together with other determinants with p < 0.25 were then included in an

8-step multivariate Cox regression analysis that ranged from the initial (Table 3) to the final model (Table 4).

Table 3: Initial multivariate Cox regression model of pre-operative, intraoperative, post-operative, and perioperative determinants of 30-day mortality after CABG at a single center, 2012–2015

	Coefficient	SE	p value	Цр	95% CI
	Coefficient	SE	p value	$HR_{_{adj}}$	95% CI
Age (≥60 years)	0.582	0.509	0.253	1.79	0.66-4.85
Neurological dysfunction (Yes)	1.641	0.524	0.002	5.16	1.85-14.42
Renal impairment (Cr >2.25 mg/dl)	1.064	0.563	0.059	2.90	0.96-8.74
Unstable angina pectoris	0.583	0.707	0.410	1.79	0.45-7.17
Left ventricular dysfunction (ejection	1.172	0.491	0.017	3.23	1.23-8.45
fraction <30%)					
New myocardial infarct within 3 months	-0.758	0.777	0.329	0.47	0.10-2.15
Pulmonary hypertension (Yes)	1.223	0.884	0.167	3.40	0.60-19.20
Pre-operative anemia (Hb <13 g/dL in	0.235	0.519	0.650	1.27	0.46-3.50
men; 12 g/dL in women)					
Duration of aortic clamp	1.336	0.521	0.010	3.81	1.37-10.57
(≥150 min)					
Duration of cardiopulmonary bypass	0.061	0.814	0.940	1.063	0.22-5.24
(≥240 min)					
Duration of surgery (>260 min)	1.269	0.542	0.019	3.56	1.23-10.30
Post-operative thrombocytopenia	1.250	0.485	0.010	3.49	1.35-9.02
Post-operative IABP	2.348	0.451	≤0.001	10.46	4.32-25.35
Perioperative red blood cell transfusion	1.029	1.039	0.322	2.80	0.37-21.46
SE: Standard error; HR _{ad} : Adjusted hazard ratio; CI: Confidence interval; Cr: Creatinine.					
ad a construction of the c					

Based on the final multivariate Cox regression analysis, neurological dysfunction, renal impairment, left ventricular dysfunction, duration of aortic clamp, duration of surgery, post-operative thrombocytopenia, and post-operative IABP support were identified as factors that significantly affect 30-day mortality after CABG. Out of these seven factors, post-operative IABP was the most significant one (HR 10.98; 95% CI 4.77–25.28).

Table 4: Final multivariate Cox regression model of pre-operative, intraoperative, post-operative, and perioperative determinants of 30-day mortality after CABG at a single center, 2012–2015

	Coefficient	SE	p value	$HR_{_{adj}}$	95% CI
Neurological dysfunction (Yes)	1.817	0.476	≤0.001	6.16	2.42-15.66
Renal impairment (Cr>2.25 mg/dL)	1.360	0.500	0.007	3.90	1.46-10.38
Left ventricular dysfunction (ejection	1.261	0.420	0.003	3.53	1.55-8.03
fraction <30%)					
Duration of aortic clamp (≥150 min)	1.309	0.451	0.004	3.70	1.53-8.96
Duration of surgery (>260 min)	1.349	0.521	0.010	3.85	1.39-10.70
Post-operative thrombocytopenia	1.383	0.429	0.001	3.99	1.72-9.23
Post-operative IABP	2.396	0.425	≤0.001	10.98	4.77-25.28

SE: Standard error; HR_{adj}: Adjusted hazard ratio; CI: Confidence interval; Cr: Creatinine

Discussion

The 30 day-mortality rate of CABG patients in this study was 11.8% which is higher than the study conducted by Hung *et al.* with mortality rate of 9.8% [9]. It is also higher overall mortality rate as compared to other 30-day mortality rate as reported by Adelborg *et al.* with 3.2% mortality rate and 2.44% reported by Hansen *et al.* [10], [11]. It should be noted that a significant proportion of the patients had urgent CABG instead of elective CABG. A possible reason for the high amount of urgent CABG instead of elective CABG is due to lack of tertiary centers able to conduct CABG in Indonesia, resulting in many patients not receiving elective CABG on-time. Another reason is due to a majority of our patients had low ejection fraction which may impact mortality. The proportion of patients with low ejection fraction in this study was 11% which is similar to an Indonesian study conducted by Ariaty *et al.* with a proportion of 12.6% [8].

Overall, the characteristics of the patients in this study are different from other countries and the research conducted on the development of EuroSCORE and STS. For example, fewer female patients in this study despite female gender being a protective factor. In addition, there were higher amounts of neurological dysfunction, kidney dysfunction, and left ventricular dysfunction in this study when compared with other studies [12], [13], [14]. For instance, the EuroSCORE study had only 7% of patients with ejection ratio <30% while this study had 11%. Another major difference is that this study had 6.8% of patients with impaired kidney function while EuroSCORE study only had 3.5%.

A similar study to ours conducted in Indonesia by Ginting *et al.* showed CABG mortality rate of CABG of 18.6% [7]. Another study by Ariaty *et al.* had mortality rate of 15.15% [8]. Thus, the mortality rate in Indonesia for CABG is higher than developed countries which suggested unique factors that should be evaluated for their association with mortality.

The multivariate Cox regression analysis identified neurological dysfunction, renal impairment, and left ventricular dysfunction as pre-operative determinants that were independently associated with 30-day mortality after CABG. In this study, 11.8% of the subjects presented with neurological dysfunction which is higher compared with rates of 1.4%, 2.4%, 6.3%, and 6.8% in the previous studies [13], [15], [16]. Thirty-day mortality in patients of this study with neurological dysfunction was 1.9% while mortality in patients without this condition is 0.6%. According to the previous study, pre-operative neurological dysfunction is a risk factor for fatal post-operative neurological complications and frequently present with comorbidities that lead to prolonged hospitalization [17]. They were also more prone to cardiac, pulmonary, and renal complications following surgery that leads into prolonged hospitalization [17]. We speculate that the increased prevalence of neurological dysfunction may have contributed to the relatively high 30-day mortality rate in our study.

We further note that 6.8% of our subjects presented with impaired renal function, a higher rate than those reported in the EuroSCORE, STS studies, and a study in Taiwan [12], [16]. Patients with this condition tend to have a higher incidence of three-vessel disease and involvement of the left main coronary artery. Furthermore, decreased renal function may also contribute to impaired oxygen delivery toward myocardium. Patients with renal impairment are also at higher risk of intraoperative and postoperative complications that might extend the duration of surgery [18]. This study identified aortic clamp duration and surgery duration as intraoperative determinants that were independently associated with 30-day mortality after CABG. A study by Al-Sarraf *et al.* (2011) also reported a similar finding in aortic clamp duration [odds ratio (OR), 5.2 (95% CI: 2.1–12.7)] [19]. It is speculated that the higher duration of aortic clamping would increase early mortality through longer duration of mechanical ventilation, reduction of cardiac output, and reduced blood flow to multiple organs. In addition, extracorporeal circulation during aortic clamping leads to reduced platelet and granulocyte counts, disrupted thrombocyte function, and caused coagulation disturbances that might contribute to the higher risk of early mortality in patients with prolonged aortic clamping.

In this study, we also observed that a duration of surgery <260 min was associated with an increased risk of 30-day mortality after CABG (hazard ratio [HR], 3.85; [95% CI 1.39–10.70]). The proportion of mortality 30-day after CABG surgery in patients with surgery time >260 min in this study was 19.1%, while subjects with ≤260 min of surgery were 4.5%. At present, there are no other studies that have examined the effect of surgery duration on 30 days after CABG.

In our bivariate analysis of intraoperative determinants, duration of cardiopulmonary bypass was identified as a significant factor contributing to 30-day mortality after CABG. However, we excluded this determinant from the multivariate analysis because the cutoff value of 240 min might have coincided with the effect of the duration of surgery. Furthermore, the small sample size might have also contributed to a lack of statistical significance in this regard.

post-operative determinants. As for thrombocytopenia and IABP were associated with 30-day mortality after CABG. Post-operative thrombocytopenia increased the risk of 30-day mortality after CABG by 3.99-fold, consistent with the results of the previous studies by Kertai et al. (2016), Rezende et al. (2011), and Selleng et al. (2009), despite the use of different cutoff values for thrombocytopenia [20], [21], [22]. Moreover, determinants such as the duration of aortic clamping, cardiopulmonary bypass, and post-operative IABP were previously reported to increase the risk of thrombocytopenia [20]. In CABG, heparin-induced thrombocytopenia should be considered as one of the causes of thrombocytopenia [23].

Patients who required IABP after CABG had a 10.98-fold higher risk of 30-day mortality, consistent with the study by Parissis *et al.* (2010) (OR, 19.19; 95% CI, 3.16–116.47) [24]. The requirement for postoperative IABP suggests poor left ventricular function and low cardiac output in patients, which are associated with worse hemodynamic status and prognosis [25]. Moreover, an ejection fraction of <50%, which predicts a low post-operative cardiac output, is also associated with a greater requirement for IABP [26], [27]. Although Kuduvalli *et al.* (2005) and Engoren *et al.* (2014) reported an increased risk of mortality in patients with perioperative red blood cell transfusion, our analysis did not identify association of perioperative red blood cell transfusion with 30-day mortality after CABG in our patient population [28], [29]. It is noted that Engoren *et al.* (2014) reported an increase of mortality only among subjects with anemia who received a transfusion, suggesting that the relationship between red blood cell transfusion and mortality was more likely attributable to anemia [29]. In our study, the lack of an association between transfusion and mortality can likely be attributed to the lack of an association of anemia with mortality.

This study had a limitation. First, the 95% confidence interval hazard ratio results of this study have a relatively wide range; however, it is not as wide as the study by Hung et al. [9]. While the wide range of confidence interval could be attributed to the small number of samples used in this study, however, the authors deemed the result as relevant. Another point to mention is the limited facilities of the study center in a developing country, which could attribute to the higher mortality rate as seen in this study, compared to the low mortality rate commonly reported in developed countries with sufficient support facilities. In addition, this study used a secondary data which may make it difficult to determine causal association. A further study with a larger sample size is needed to confirm the external validity of this study. Multicenter studies are also needed to determine the generalizability of our results to broader populations.

Conclusion

Our single-center study identified multiple significant independent determinants of 30-day mortality after CABG that was not included in the EuroSCORE and STS system. Those determinants are neurological dysfunction, renal impairment, left ventricle dysfunction, aortic clamp duration, surgery duration, post-operative thrombocytopenia, and post-operative intra-aortic balloon pump.

Acknowledgments

We would like to extend gratitude toward various people for their contribution to this study;

Maya Dorothea and Elizabeth Budiani for their help in collecting data and statistical analysis; Jessica Novia Hadiyanto and Kevin Winston for assistance with article writing.

Data Sharing Statement

All relevant data are within the manuscript and its Supporting Information files.

References

 Alexander JH, Smith PK. Coronary-artery bypass grafting. N Engl J Med. 2016;375:e22.

PMid:27602683

- Van Domburg RT, Kappetein AP, Bogers AJ. The clinical outcome after coronary bypass surgery: A 30-year follow-up study. Eur Heart J. 2009;30(4):453-8. https://doi.org/10.1093/ eurheartj/ehn530 PMid:19066209
- Roques F, Nashef SA, Michel P, Gauducheau E, de Vincentiis C, Baudet E, et al. Risk factors and outcome in European cardiac surgery: Analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg. 1999;15:816-22. https://doi.org/10.1016/s1010-7940(99)00106-2 PMid:10431864
- Bachar BJ, Manna B. Coronary Artery Bypass Graft. Card CT 2nd ed. Treasure Island (FL), USA: StatPearls; 2021;191-198.
- Metzler B, Winkler B. SYNTAX, ST, EuroSCORE-How good are they for risk estimation in atherosclerotic heart disease? Thromb Haemost. 2012;108:1065-71. https://doi.org/10.1160/ th11-06-0399

PMid:22187025

- Yohanes A. Validasi skor ACEF Sebagai Prediktor Mortalitas 30 Hari Pascabedah Pintas Koroner di RSUPN Dr Cipto Mangunkusumo Validation of ACEF Score as Predictor of 30-day Mortality Following Coronary Artery Bypass Grafting Surgery in Cipto Mangunkusumo National General Hospital. Indonesia: Universitas Indonesia; 2016. https://doi.org/10.7454/ msk.v23i2.10379
- Ginting AD. Karakteristik Pasien Penyakit Jantung Koroner Yang Dilakukan Coronary Artery Bypass Graft di Rumah Sakit Umum Pusat Haji Adam Malik Medan pada Tahun 2015-2016. Available from: https://www.repositori.usu.ac.id/handle/123456789/4782 [Last accessed on 2022 Mar 27]. https://doi.org/10.36911/ pannmed.v10i2.275
- Ariaty GM, Sudjud RW, Sitanggang RH. Angka mortalitas pada pasien yang menjalani bedah pintas koroner berdasar usia, jenis kelamin, Left ventricular ejection fraction, cross clamp time, cardio pulmonary bypass time, dan penyakit penyerta. J Anestesi Perioper. 2017;5(3):155-62. https://doi.org/10.15851/ jap.v5n3.1167
- Hung DQ, Minh NT, Vo HL, Hien NS, Tuan NQ. Impact of pre-, intra-and post-operative parameters on in-hospital mortality in patients undergoing emergency coronary artery bypass grafting: A scarce single-center experience in resource-scare setting. Vasc Health Risk Manag. 2021;17:211-26. https://doi. org/10.2147/vhrm.s303726 PMid:34040381
- Adelborg K, Horváth-Puhó E, Schmidt M, Munch T, Pedersen L, Nielsen PH, *et al.* Thirty-year mortality after coronary artery bypass graft surgery: A Danish nationwide population-based cohort study. Circ Cardiovasc Qual Outcomes. 2017;10(5):e002708. https://doi.org/10.1161/circoutcomes.116.002708 PMid:28500223

Open Access Maced J Med Sci. 2022 Apr 21; 10(B):1022-1028.

- Hansen LS, Hjortdal VE, Andreasen JJ, Mortensen PE, Jakobsen CJ. 30-day mortality after coronary artery bypass grafting and valve surgery has greatly improved over the last decade, but the 1-year mortality remains constant. Ann Card Anaesth. 2015;18(2):138-42. https://doi.org/10.4103/0971-9784.154462 PMid:25849679
- Nashef SA, Roques F, Hammill BG, Peterson ED, Michel P, Grover FL, *et al.* Validation of European system for cardiac operative risk evaluation (EuroSCORE) in North American cardiac surgery. Eur J Cardiothorac Surg. 2002;22(1):101-5. https://doi.org/10.1016/s1010-7940(02)00208-7 PMid:12103381
- Musa AF, Cheong XP, Dillon J, Nordin RB. Validation of EuroSCORE II in patients undergoing coronary artery bypass grafting (CABG) surgery at the National Heart Institute, Kuala Lumpur: A retrospective review. F1000Res. 2019;7:534. https:// doi.org/10.12688/f1000research.14760.2 PMid:32913630
- Shih HH, Kang PL, Pan JY, Wu TH, Wu CT, Lin CY, *et al.* Performance of European system for cardiac operative risk evaluation in Veterans General Hospital Kaohsiung cardiac surgery. J Chin Med Assoc. 2011;74(3):115-20. https://doi. org/10.1016/j.jcma.2011.01.025 PMid:21421205
- Nashef SA, Roques F, Sharples LD, Nilsson J, Smith V, Antony R, *et al.* EuroSCORE II. Eur J Cardiothorac Surg. 2012;41(4):734-5. https://doi.org/10.1093/ejcts/ezs043 PMid:22378855
- Khan JK, Shahabuddin S, Khan S, Bano G, Hashmi S, Shahid A, et al. Coronary artery bypass grafting in South Asian patients: Impact of gender. Ann Med Surg. 2016;9:33-7. https:// doi.org/10.1016/j.amsu.2016.05.018 PMid:27366322
- Ngaage DL, Dickson J, Chaudhry M, Cale AR, Cowen ME. Early and late prognostic significance of remote and reversible preoperative neurological events in patients undergoing coronary artery bypass grafting. Eur J Cardiothorac Surg. 2010;37(5):1075-80. https://doi.org/10.1016/j.ejcts.2009.11.050 PMid:20045345
- Cooper WA, O'Brien SM, Thourani VH, Guyton RA, Bridges CR, Szczech LA, et al. Impact of renal dysfunction on outcomes of coronary artery bypass surgery: Results from the society of thoracic surgeons national adult cardiac database. Circulation. 2006;113:1063-70. https://doi.org/10.1161/ circulationaha.105.580084

PMid:16490821

 Al-Sarraf N, Thalib L, Hughes A, Houlihan M, Tolan M, Young V, et al. Cross-clamp time is an independent predictor of mortality and morbidity in low-and high-risk cardiac patients. Int J Surg. 2011;9:104-9. https://doi.org/10.1016/j.ijsu.2010.10.007 PMid:20965288

- Kertai MD, Zhou S, Karhausen JA, Cooter M, Jooste E, Li YJ, et al. Platelet counts, acute kidney injury, and mortality after coronary artery bypass grafting surgery. Anesthesiology. 2016;124(2):339-52. https:// doi.org/10.1097/aln.00000000000959 PMid:26599400
- Rezende E, Morais G, Silva JM, de Oliveira AM, Souza JM, Richter I, *et al.* Trombocitopenia em cirurgia cardíaca: Importância diagnóstica e prognóstica. Braz J Cardiovasc Surg. 2011;26(1):47-53. https://doi.org/10.1590/ s0102-76382011000100011
- Selleng S, Malowsky B, Strobel U, Wessel A, Ittermann T, Wollert HG, *et al.* Early-onset and persisting thrombocytopenia in post-cardiac surgery patients is rarely due to heparininduced thrombocytopenia, even when antibody tests are positive. J Thromb Haemost. 2010;8(1):30-6. https://doi. org/10.1111/j.1538-7836.2009.03626.x PMid:19793190
- Greinacher A, Selleng K. Thrombocytopenia in the intensive care unit patient. Hematol Am Soc Hematol Educ Program. 2010;2010:135-43. https://doi.org/10.1182/ asheducation-2010.1.135
 PMid:21239783
- Parissis H, Leotsinidis M, Akbar MT, Apostolakis E, Dougenis D. The need for intra aortic balloon pump support following open heart surgery: Risk analysis and outcome. J Cardiothorac Surg. 2010;5:1-7. https://doi.org/10.1186/1749-8090-5-20
- Okonta K, Anbarasu M, Kanagarajan K. Intra-aortic balloon pump in coronary artery bypass graft-factors affecting outcome. J West Afr Coll Surg. 2011;1:28-40.
 PMid:25452970
- Lomivorotov VV, Efremov SM, Kirov MY, Fominskiy EV, Karaskov AM. Low-cardiac-output syndrome after cardiac surgery. J Cardiothorac Vasc Anesth. 2017;31:291-308. https:// doi.org/10.1053/j.jvca.2016.05.029
 PMid:27671216
- 27. Topkara VK, Cheema FH, Kesavaramanujam S, Mercando ML, Cheema AF, Namerow PB, *et al.* Coronary artery bypass grafting in patients with low ejection fraction. Circulation. 2005;112(Suppl 9):1344-50. https://doi.org/10.1161/ circulationaha.104.526277

PMid:16159844

- Kuduvalli M, Oo AY, Newall N, Grayson AD, Jackson M, Desmond MJ, *et al*. Effect of peri-operative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. Eur J Cardiothorac Surg. 2005;27:592-8. https://doi.org/10.1016/j.ejcts.2005.01.030
- Engoren M, Schwann TA, Habib RH, Neill SN, Vance JL, Likosky DS. The independent effects of anemia and transfusion on mortality after coronary artery bypass. Ann Thorac Surg. 2014;97:514-20. https://doi.org/10.1016/j.athoracsur.2013.09.019 PMid:24206967