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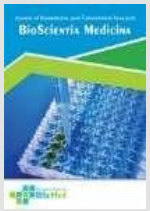

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Prognostic Factors for the Occurrence of Recurrent Major Adverse Cardiac Events after Isolated Coronary Arterial Bypass Graft

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A B S T R A C T

Background: Coronary heart disease (CHD), commonly known as coronary artery disease (CAD), is a heart disorder that occurs when the arteries supplying blood to the heart walls experience hardening and narrowing, leading to a reduced supply of oxygen and nutrients to the myocardial tissue due to limited coronary blood flow. The treatment of CHD requires revascularization or reperfusion procedures on the coronary blood vessels responsible for supplying the heart muscle. One recommended therapy is coronary artery bypass grafting (CABG). Patients post-CABG are at risk of experiencing major adverse cardiovascular events (MACE). **Methods:** This design is a cross-sectional study involving all patients who underwent CABG at Siloam Hospitals in Lippo Village and Kebon Jeruk from January to June 2023. Data analysis using a regression approach aims to evaluate the relationship between various prognostic factors and MACE occurrences, thereby identifying a cross-sectional association between these variables and MACE events. **Results:** Findings from this cross-sectional study indicate a correlation between overweight and the occurrence of recurrent MACE in patients with a history of CABG (p-value = 0.037). These results suggest that individuals with obesity undergoing CABG have a higher risk of experiencing recurrent MACE in CHD. **Conclusion:** The prognostic factor for recurrent CHD-related major adverse cardiovascular events (MACE) is body mass index (BMI). Monitoring body mass index (BMI) in CHD patients who have undergone CABG is essential to reduce the risk of recurring MACE in the future.

1. Introduction

Coronary heart disease (CHD) is a condition in which insufficient blood and oxygen supply to the myocardium. This is caused by the blockage of coronary arteries, resulting in a mismatch between oxygen demand and supply. Typically, this condition involves the formation of plaque in the coronary lumen, obstructing blood flow. Coronary heart disease is a multifactorial phenomenon. Etiological factors can generally be grouped into non-modifiable and modifiable factors. Non-modifiable factors include gender, age, family history, and genetics. Modifiable risk factors include smoking, obesity, lipid levels, and psychosocial variables. Changes in lifestyle patterns, characterized by increased consumption of fast food and unhealthy diets, have led to a rise in the prevalence of obesity, ultimately contributing to coronary heart disease. Males have a higher predisposition compared to females. Hypercholesterolemia remains a significant modifiable risk factor for coronary artery disease. Elevated low-density lipoproteins (LDL) increase the risk of this disease, while increased high-density lipoproteins (HDL) reduce its incidence.[1,2]

Coronary heart disease has become a leading cause of death worldwide, including in Indonesia. Many individuals experience heart attacks without prior symptoms. Over the past fifty years, the incidence of

coronary heart disease has been steadily increasing, and it is estimated that 30% of all global deaths are attributed to this condition. In 2004, the American Heart Association (AHA) estimated the prevalence of coronary heart disease in the United States to be around 13.2 million cases. By 2010, globally, it was projected to become the leading cause of death in developing countries, surpassing deaths from infections. In 2020, it is estimated that coronary heart disease will be the most common cause of death worldwide, accounting for approximately 36% of all deaths, a figure twice as high as cancer-related deaths. Currently, Coronary Heart Disease (CHD) or cardiovascular disease is one of the significant causes of death in both developed and developing countries, including Indonesia.[3,4]

The prevalence of coronary heart disease (CHD), according to the 2018 National Health Survey (Riskesdas), has remained stagnant over a period of 5 years (2013-2018), standing at 1.5% of the Indonesian population. The highest prevalence is observed in Central Sulawesi (0.8%), followed by North Sulawesi, DKI Jakarta, and Aceh, with a majority of 0.7%. Meanwhile, the prevalence of CHD based on doctor diagnoses or symptoms increases with age, reaching the highest rates in the 65-74 age group at 2.0% and 3.6%, and slightly decreasing in the ≥75 age group. CHD prevalence diagnosed by a doctor or based on symptoms is higher in females (1.5%) compared to males (0.5%).[5]

Treating coronary heart disease (CHD) necessitates revascularization or reperfusion of the coronary vessels, which supply blood to the heart muscle. One recommended therapy is coronary artery bypass grafting (CABG). Patients post-CABG are at risk of experiencing major adverse cardiovascular events (MACE). MACE represents the ultimate outcomes of cardiovascular disease, comprising death due to acute heart failure, stroke, and recurrent acute myocardial infarction or acute coronary syndrome. MACE is also used to assess the effectiveness of CABG procedures. A study conducted in Germany reported that the incidence of MACE in patients post-coronary artery intervention reached 53.7%. CABG is a revascularization procedure associated with the lowest risk of MACE. However, various comorbidities in CHD patients undergoing CABG can influence the prognosis of patients. A poor prognosis in patients may increase the risk of MACE. Consequently, it can be concluded that CHD patients with comorbidities will have an elevated risk of MACE following CABG procedures.[6,7] Research on prognostic factors for major adverse cardiovascular events (MACE) in patients undergoing coronary artery bypass grafting (CABG) is still limited. Therefore, a study has been conducted to investigate various prognostic factors in these patients, aiming to identify potential markers that could contribute to preventing MACE occurrences. The objective is to enhance our understanding of the factors influencing the prognosis of individuals post-CABG, ultimately allowing for more effective preventive measures against MACE. This research endeavors to fill the existing knowledge gap and provide valuable insights into the complex interplay of factors affecting cardiovascular outcomes in CABG patients.

2. Methods

The research design employed in this study is a cross-sectional investigation involving all patients who underwent coronary artery bypass grafting (CABG) at Siloam Lippo Village and Kebon Jeruk Hospitals from January to June 2023. The variable under scrutiny is major adverse cardiovascular events (MACE) as the dependent variable. In contrast, the independent variables encompass age, gender, diabetes mellitus, chronic kidney disease, diabetes mellitus concomitant with chronic kidney disease, smoking habits, dyslipidemia, blood pressure, body mass index, history of myocardial infarction, history of congestive heart failure (CHF), history of stroke, and history of peripheral artery disease.

Secondary data are extracted from patients' medical records to examine prognostic data available for each patient. The obtained data are analyzed descriptively, and further analysis is conducted

utilizing a multiple linear regression test. This test predicts the values of the dependent variable, recurrent MACE in coronary heart disease, based on the importance of the independent variables. The outcome of this analysis is expected to reveal relationships between various prognostic factors and the occurrence of MACE, providing deeper insights into the factors influencing cardiovascular outcomes in post-CABG patients.

3. Results

During the study period, 220 coronary heart disease (CHD) patients who had undergone coronary artery bypass grafting (CABG) were identified and willingly participated in the research. The study revealed a higher prevalence of male patients (84.5%) than female patients. Among the entire patient cohort, 69.1% experienced recurrent CHD-related major adverse cardiovascular events (MACE). Of the 2020 patients, comorbidities such as high blood pressure were present in 97.7% of cases, while diabetes mellitus was observed in 53.2% of patients. Additionally, 81.8% of the patients were classified as obese. The general characteristics of the subjects are presented in Table 1.

Table 1. Subject characteristics.

	N (%)	**Mean (SD)**	**Median (Min-Max)**
Age		59,2 (8,35)	59 (36-80)
Gender			
Male	186 (84,5%)		
Female	35 (15,5%)		
MACE - Recurrent CHF			
Yes	152 (69,1%)		
No	65 (30.9%)		
Diabetes mellitus			
Yes	117 (53,2%)		
No	103 (46.8%)		
Chronic kidney disease			
Yes	22 (10%)		
No	198 (90%)		
DM – CKD			
Yes	33 (15%)		
No	187 (85%)		
Smoking			
Yes	102 (46,4%)		
No	118 (53,6%)		
Dyslipidaemia			
Yes	73 (33,2%)		
No	147 (66,8%)		
Blood pressure			
Normal	5 (2,3%)		
Elevated	215 (97,7%)		
Body mass index			
Ideal	40 (18,2%)		
Non-Ideal	180 (81,8%)		
History of myocardial infarction			
Yes	130 (59,1%)		
No	90 (40,9%)		
History of CHF			
Yes	49 (22,3%)		
No	171 (77,7)		
History of Stroke			
Yes	45 (20,5%)		
No	175 (79,5%)		
History of peripheral artery disease			
Yes	6 (2,7%)		
No	97,3%)		

The results of the regression analysis are provided in Table 2. Based on the regression analysis, it was found that BMI (body mass index) has a significant positive correlation (positive coefficient = 0.998) with the occurrence of major adverse cardiovascular events (MACE) in coronary heart disease (0,037).

Table 2. Regression analysis of MACE.

	Coefficient	**Sig**
Age	.027	.201
Gender	.680	.180
Diabetes mellitus	-.060	.861
Chronic kidney disease	-1.140	.103
DM – CKD	.472	.380
Smoking	-.613	.067
Dyslipidemia	.054	.876
Blood pressure	-.741	.532
Body mass index	.998	.037
History of myocardial infarction	.022	.951
History of congestive heart failure (CHF)	-.257	.535
History of stroke	-.424	.347
History of peripheral artery disease	1.155	.236

4. Discussion

Cardiovascular disease is a leading cause of death, necessitating increased vigilance in preventing fatalities from this condition. Therefore, a combination of symptoms or abnormalities known as major adverse cardiovascular events (MACE) has become a focus in various studies on the prevention and awareness enhancement regarding cardiovascular-related deaths. MACE represents the culmination of a disease, encompassing systemic heart disease, acute myocardial infarction or acute coronary syndrome, stroke, heart failure, and cardiovascular or non-cardiovascular death. Despite the improved identification and definition of MACE, various risk factors associated with MACE still need further exploration to enhance preventive efforts. Findings from the current cross-sectional study indicate a correlation between overweight and the occurrence of recurrent MACE in coronary heart disease (CHD) patients with a history of coronary artery bypass grafting (CABG) (p-value= 0.037). These results suggest that individuals with obesity undergoing CABG have a higher risk of experiencing recurrent MACE in coronary heart disease.

There is a theory proposing a correlation between obesity and adverse inotropic effects on the human heart muscle. Fat cells contain more than 150 pro-inflammatory adipokines that impact the heart. Additionally, obesity is associated with an increase in leptin levels, which is linked to coronary heart disease. Elevated leptin levels serve as a predictor for increased mortality and morbidity rates in patients with coronary heart disease (CHD).[8] The study by Katja Buschmann et al. explores the influence of inflammation and leptin across various body mass index (BMI) ranges in patients undergoing elective coronary artery bypass grafting (CABG) in Germany. The study involved 45 male participants. The research findings indicate a significant relationship between BMI and leptin. Moreover, the study revealed that surgical wound infection is associated with higher BMI (29.4 ± 0.9 vs. 40.0 ± 3.1 kg/m², p-value=0.003) and elevated leptin levels (12.2 ± 2.2 vs. 27.7 ± 5, p-value=0.001).[9,10]

On the other hand, another study conducted by Babak Sattarbar et al. focuses on the differences in risk factors and long-term outcomes among patients undergoing isolated coronary artery bypass grafting (CABG) based on gender and age in Iran. This cross-

sectional study involved 24,318 patients from the years 2007 to 2017. The results indicated that hypertension (53%) and dyslipidemia (56%) were the most commonly observed risk factors in patients. Obesity (BMI >30 kg/m²) was found most frequently in women, and no association was found with the occurrence of major adverse cardiovascular events (MACE).[11,12] This is presumed to be because obesity is associated with excess fat mass. In contrast, patients with a higher body mass may have higher muscle mass, positively affecting heart health. In this study, the lowest survival rate was found in women under 55 years old (30.06%), and Cox regression analysis revealed that men are at a higher risk of experiencing major adverse cardiovascular events (MACE) compared to women (HR 0.72; 95% CI 0.57-0.91; p-value=0.006). However, no significant difference was found in mortality between genders (HR 1.00; 95% CI 0.79–1.28; P value 0.98).[12,13]

It is noteworthy that in this study, only body mass index (BMI) was found to be associated with the occurrence of major adverse cardiovascular events (MACE) in patients undergoing coronary artery bypass grafting (CABG). This result differs from some previous studies. Based on several studies, it has been found that hypertension, diabetes mellitus, dyslipidemia, history of myocardial infarction, RA-LAD surgery, old age at the time of surgery, prolonged aortic cross-clamping, female gender, prolonged use of the heart-lung machine, and prolonged ventilation are risk factors for MACE in patients undergoing CABG.[14–16] The limitations of this study include a small sample size and the use of a cross-sectional method. It is hoped that future research can overcome these limitations by conducting prospective cohort studies that analyze the risk factors for major adverse cardiovascular events (MACE) in patients undergoing coronary artery bypass grafting (CABG) across multiple hospital centers in Indonesia. This would provide a more comprehensive and in-depth understanding of the factors influencing MACE in this patient population.

5. Conclusion

In patients with coronary heart disease (CHD) who have undergone coronary artery bypass grafting (CABG), the prognostic factor for recurrent CHD-related major adverse cardiovascular events (MACE) is body mass index (BMI) with a p-value of 0.037. This indicates a correlation between obesity and adverse effects on the human heart, thereby increasing the risk of recurrent CHD-related events even after CABG. Therefore, it is crucial to monitor the BMI of CHD patients who have undergone CABG to mitigate the risk of recurrent MACE in the future. Regular BMI control can reduce the likelihood of recurrent adverse cardiovascular events in these patients.

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