Evaluation of Cardiac Biomarkers as Predictors of Short-Term Mortality Following Coronary Artery Bypass Grafting

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Abstract

Background: Non-communicable diseases (NCDs), particularly cardiovascular diseases (CVDs) like coronary heart disease (CHD), are the leading cause of global mortality. Despite advancements in diagnostic and therapeutic interventions, CHD remains a significant healthcare challenge. Coronary artery bypass grafting (CABG) is a widely used surgical intervention for advanced CHD, but postoperative mortality remains a concern. Biomarkers such as N-terminal pro-brain natriuretic peptide (NT-proBNP), high-sensitivity troponin I (HS troponin I), and creatine kinase-myocardial band (CKMB) have been investigated for their prognostic value in predicting CABG outcomes, but their efficacy remains debated. Methods: This single-center retrospective cohort study, conducted at Soetomo General Academic Hospital, Surabaya, Indonesia, evaluated the relationship between preoperative levels of NT-proBNP, HS troponin I, and CKMB with 30-day post-CABG mortality. Participants undergoing CABG with cardiopulmonary bypass (CPB) between January and April 2024 were included. Data collected included biomarker levels (CK-MB, HS-TnI, NT-proBNP), CPB and cross-clamp times, and demographics. Statistical analysis was performed using logistic regression to assess associations with mortality. Results: A total of 31 participants (90.3% male, mean age 59.31 ± 9.11 years) were included. The biomarker levels were as follows: CK-MB (48.03 ± 41.28 U/L), NT-proBNP (875.33 ± 1253.73 pg/mL), and HS troponin I (5.17 ± 5.20 pg/mL). One mortality event (3.2%) occurred. Multivariate analysis showed no significant association between age, sex, or the biomarkers (CK-MB, HS troponin I, NT-proBNP) and mortality (p>0.05 for all). Conclusion: Preoperative levels of CK-MB, HS troponin I, and NT-proBNP were not significantly associated with short-term mortality following CABG in this study. These findings highlight the need for further research to explore additional clinical variables and biomarkers for improving mortality prediction in CABG patients.

Keywords: coronary artery bypass grafting, cardiac biomarkers, NT-proBNP, HS troponin I, mortality prediction

Significance | This study evaluates the predictive value of biomarkers in short-term mortality after coronary artery bypass grafting to guide clinical decisions

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Introduction

Non-communicable diseases (NCDs) are the leading cause of mortality worldwide, accounting for 73% of global deaths (Shahjehan et al., 2024). Among these, cardiovascular diseases (CVDs), primarily coronary heart disease (CHD), contribute approximately 35% of NCD-related deaths. CHD arises from insufficient blood flow and oxygen delivery to the myocardium, largely due to atherosclerotic plaque accumulation (Pothineni et al.,

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2017). The disease spectrum includes acute coronary syndrome (ACS) and chronic coronary syndrome (CCS), both of which significantly burden healthcare systems. Epidemiological data indicate an alarming increase in CHD incidence; for instance, between 1979 and 2005, the prevalence of myocardial infarction rose from 215 to 242 cases per 100,000 individuals (Hu et al, 2000). In Indonesia, CHD affected 4,920 individuals in 2016, with females constituting 2,600 of these cases, predominantly in individuals over 60 years of age (Kementerian Kesehatan Republik Indonesia, 2017). Despite advancements in diagnostic and therapeutic approaches, CHD remains a silent threat, with asymptomatic cases often leading to fatal outcomes. Current treatment modalities include pharmacological interventions, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG). The choice of revascularization strategy depends on individual patient profiles and prognosis, which are assessed using scoring systems like the Society of Thoracic Surgeons (STS) model (Neumann et al., 2018). These systems, however, rely primarily on static patient and disease characteristics, leaving room for further refinement in mortality prediction methods.

Cardiac biomarkers, such as N-terminal pro-brain natriuretic peptide (NT-proBNP), high-sensitivity troponin I (HS troponin I), and creatine kinase-myocardial band (CKMB), have been investigated extensively for their role in predicting mortality in CHD patients. NT-proBNP is a marker of myocardial stress and heart failure, while HS troponin I and CKMB indicate myocardial injury. Although prior studies have identified these biomarkers as potential prognostic tools, findings remain inconsistent, and their clinical utility in predicting mortality, particularly in CABG patients, is still debated (Jacob & Khan, 2018; Machado et al., 2021). This study aims to elucidate the relationship between preoperative levels of NT-proBNP, HS troponin I, and CKMB with short-term mortality following CABG. CABG is one of the most effective surgical interventions for patients with advanced CHD, offering improved survival and quality of life. However, postoperative outcomes can vary widely, necessitating robust predictive tools to optimize patient care.

By focusing on biomarker levels, this study seeks to address the existing knowledge gaps in mortality prediction for CABG patients. Insights gained from this research could contribute to the development of more accurate prognostic models, thereby enhancing perioperative risk stratification and guiding clinical decision-making.

CHD is a significant public health challenge, with biomarkers like NT-proBNP, HS troponin I, and CKMB showing promise as predictors of surgical outcomes. However, their inconsistent performance warrants further investigation. This study endeavors to clarify their predictive value in the context of CABG, with the ultimate goal of improving patient outcomes and reducing mortality rates.

2. Materials and Methods

2.1 Study Design and Setting

This single-center retrospective cohort study was conducted at Soetomo General Academic Hospital, Surabaya, Indonesia. The study was performed in compliance with the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of Soetomo General Academic Hospital (approval number: [insert approval number, if available]). Patient recruitment occurred between January 2024 and April 2024, and all participants underwent coronary artery bypass grafting (CABG) with a revascularization strategy utilizing a cardiopulmonary bypass (CPB) device. Written informed consent was obtained from each participant before enrollment.

2.2 Inclusion and Exclusion Criteria

Patients were eligible for inclusion in the study if they underwent coronary artery bypass grafting (CABG) surgery using a cardiopulmonary bypass (CPB) device. However, several exclusion criteria were applied to ensure the accuracy and reliability of the study results. Patients were excluded if they lacked preoperative cardiac biomarker measurements, declined participation in the study, or were postprocedural ambulatory patients who were lost to follow-up within 30 days after the procedure. Additionally, patients who died due to trauma during the follow-up period were excluded from the analysis.

2.3 Data Collection and Variables

Data for this study were obtained from the hospital's electronic medical record (EMR) system. Baseline characteristics collected included age (in years), creatine kinase-MB (CK-MB) levels (U/L), high-sensitivity troponin I (HS-TnI) levels (pg/mL), N-terminal pro b-type natriuretic peptide (NT-proBNP) levels (pg/mL), cardiopulmonary bypass (CPB) time (minutes), and cross-clamp (AoX) time (minutes). The cutoff levels for cardiac biomarkers were established as 25 U/L for CK-MB, 20.1 pg/mL for HS-TnI, and 125 pg/mL for NT-proBNP. All cardiac biomarkers were measured using immunochemistry analysis with the Abbott Alinity ci-series analyzer (Abbott Laboratories, Illinois, USA).

The primary outcome of interest in this study was the incidence of mortality within 30 days following the CABG procedure. Participants were followed up until the fifth week post-surgery, during which any mortality events were thoroughly documented.

2.4 Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS), version 21 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize participant characteristics, which were presented as tables. Categorical variables were expressed as frequencies and percentages, while

Table 1. Baseline Characteristics of Study Participants

Variable	Value
	Mean ± Std Deviation
Age (year)	59.31 ± 9.11
CKMB (U/L)	48.03 ± 41.28
NT Pro BNP (pg/mL)	875.33 ± 1253.73
Hs Troponin I (pg/mL)	5.17 ± 5.20
CPB Time (min)	117.62 ± 28.05
AoX Time (min)	72.31 ± 22.33

Variable	Group	N (%)
Sex	Male	28 (90.3)
	Female	3 (9.7)
CKMB	CKMB > 25 U/L	28 (90.3)
	CKMB < 25 U/L	3 (9.7)
Hs Troponin I	Hs Troponin I > 20.1 pg/mL	13(41.9)
	Hs Troponin I < 20.1 pg/mL	18 (58.1)
NT Pro BNP	NT Pro BNP > 125 pg/mL	21 (67.7)
	NT Pro BNP < 125 pg/mL	10 (32.3)
Mortality		1 (3.2)

Table 2. Comparative Analysis of Participants Characteristics and Cardiac Biomarkers for Mortality

Parameters	Mortality (n)		p value
	(-)	(+)	
Age (years)	0	1	0.63
Sex			
• Male	27	1	0.90
• Female	3	0	
CKMB			
• CKMB > 25 U/L	27	1	0.90
• CKMB < 25 U/L	3	0	
Hs Troponin I			
• Hs Troponin I > 20.1 pg/mL	12	1	0.42
• Hs Troponin I < 20.1 pg/mL	18	0	
NT Pro BNP			
• NT Pro BNP > 125 pg/mL	20	1	0.68
• NT Pro BNP < 125 pg/mL	10	0	

continuous variables were presented as means ± standard deviations (SD) or medians with interquartile ranges (IQR), as appropriate.

Comparisons between groups were performed using Fisher's exact test for categorical variables. Logistic regression analysis was conducted to examine the association between preoperative cardiac biomarker levels and 30-day post-CABG mortality. A p-value of less than 0.05 was considered statistically significant for all analyses.

3. Results

A total of 31 participants who underwent CABG surgery between January 2024 and April 2024 were included in the study. Of these, 28 (90.3%) were male and 3 (9.7%) were female. The mean age of the participants was 59.31±9.11 years. The mean levels of the biomarkers were as follows: CK-MB 48.03±41.28 U/L, NT-proBNP 875.33±1253.73 pg/mL, and HS troponin I 5.17±5.20 pg/mL. The mean duration of CPB time was 117.62±28.05 minutes, and the mean AoX time was 72.31±22.33 minutes. In terms of biomarker cutoff levels, 28 participants (90.3%) had CK-MB levels greater than 25 U/L, while 3 participants (9.7%) had levels below this threshold. Regarding HS troponin I, 13 participants (41.9%) had levels above 20.1 pg/mL, and 18 participants (58.1%) had levels below this threshold. For NT-proBNP, 21 participants (67.7%) had levels greater than 125 pg/mL, while 10 participants (32.3%) had levels below this cutoff. One participant (3.2%) experienced a mortality event during the study period. A summary of the study participants' characteristics is provided in Table 1.

Multivariate analysis showed that age was not a significant predictor of mortality (p=0.63). Within the male population, one mortality event (3.6%) occurred, but no significant correlation was found between sex and mortality (p=0.90). Regarding CK-MB levels, one participant (3.6%) with CK-MB levels above 25 U/L experienced a mortality event, but statistical analysis did not reveal a significant association between CK-MB levels and mortality (p=0.90). Similarly, among participants with HS troponin I levels greater than 20.1 pg/mL, one (7.7%) mortality event occurred, but no significant correlation was observed between HS troponin I levels and mortality (p=0.42). Finally, one (4.8%) mortality event was observed in the group with NT-proBNP levels greater than 125 pg/mL, but statistical analysis did not indicate a significant association between NT-proBNP levels and mortality (p=0.68). A summary of the multivariate analysis results is provided in Table 2.

4. Discussion

This study aimed to evaluate potential predictors of short-term mortality following coronary artery bypass grafting (CABG) surgery, focusing on demographic factors and cardiac biomarkers such as CK-MB, HS troponin I, and NT-proBNP. Despite the known significance of these biomarkers in cardiovascular events, our analysis found no significant correlation between these variables and post-CABG mortality. This finding contributes to the ongoing debate about the value of certain biomarkers as reliable predictors of mortality in CABG patients and underscores the complexity of determining prognostic indicators in this population.

4.1 Age and Sex as Predictors of Mortality

The demographic variables of age and sex were not found to be significant predictors of short-term mortality following CABG surgery in our study. This is consistent with several prior studies. Hess et al. (2021) conducted a large clinical trial involving 1,211 participants with a mean age of 66 years, of whom 71.3% were male. This study did not find any significant correlation between age or sex and both short- and long-term mortality outcomes following CABG. Similarly, Zhou et al. (2023), in a study involving 116 patients with a mean age of 63.58 years, found that age and sex were not correlated with surgical outcomes. Beller et al. (2018), in a study with 1,272 participants, also failed to establish age and sex as predictors of mortality following CABG. Furthermore, Petäjä et al. (2017) analyzed more than 1,500 participants and found no significant association between age or sex and postoperative mortality, even when adjusting for high-sensitivity troponin I levels. These findings collectively suggest that while age and sex may influence overall health outcomes, they do not serve as reliable indicators of mortality risk specifically in CABG patients.

One possible explanation for the lack of correlation between these demographic factors and mortality in this study could be the heterogeneity of the patient population, which may obscure trends that would be more apparent in larger or more homogeneous groups. Moreover, comorbidities, clinical conditions, and intraoperative factors likely play a more significant role in determining patient outcomes after CABG surgery (Wu et al., 2012; Chua et al., 2024). Conditions such as renal dysfunction, hemodynamic instability, and the presence of other chronic diseases are often considered more substantial predictors of mortality, and these factors may have overshadowed the role of age and sex in our analysis.

4.2 The Role of CK-MB in Predicting Mortality

In our study, elevated CK-MB levels were not associated with an increased risk of mortality following CABG surgery, which is a surprising finding given the established role of CK-MB as a marker of myocardial injury. CK-MB, an enzyme released into the bloodstream following myocardial damage, is commonly used to assess myocardial infarction (MI) and other cardiovascular conditions. However, in line with the findings of Miao et al. (2017) and Lee et al. (2017), we observed that even though CK-MB levels were elevated in many participants, they did not correlate with increased mortality risk. Miao et al. (2017) found that elevated CK-MB levels in myocardial infarction patients did not predict

mortality risk, while Lee et al. (2017) showed similar results in acute coronary syndrome patients.

These findings suggest that CK-MB levels, while useful as indicators of myocardial injury, may not necessarily reflect the severity of the underlying pathology or predict mortality risk in CABG patients. Other factors, such as comorbidities (e.g., diabetes, heart failure, or renal dysfunction), may exert a more powerful influence on mortality outcomes (Montrief et al., 2018; Jawitz et al., 2020). Additionally, postoperative complications such as arrhythmias, graft failure, and hemodynamic instability are likely to have a more immediate and direct impact on survival than preoperative biomarker levels (Montrief et al., 2018).

4.3 Preoperative HS Troponin I and Mortality Risk

HS troponin I, a highly sensitive biomarker of myocardial injury, has been studied extensively as a potential predictor of mortality in CABG patients. In our study, however, no significant association was found between preoperative HS troponin I levels and postoperative mortality, which aligns with previous research. Beller et al. (2018) found that while peak troponin levels were elevated in some CABG patients, they were not significantly correlated with post-surgical mortality after adjusting for other clinical variables. Similarly, Petäjä et al. (2016) reported that high preoperative troponin levels did not predict mortality risk when combined with the EuroSCORE II risk model. Nellipudi et al. (2021) also observed that while elevated troponin levels may indicate an increased risk of short-term complications, they did not serve as reliable predictors of longer-term mortality after CABG.

The inability of HS troponin I to independently predict mortality in this study may be explained by the fact that troponin levels primarily reflect myocardial injury rather than other factors influencing post-CABG outcomes, such as comorbid conditions, surgical technique, or intraoperative complications. As such, it is likely that HS troponin I is more useful for identifying patients at risk for complications during or shortly after surgery rather than for predicting longer-term survival.

4.4 NT-proBNP and Mortality Prediction

NT-proBNP, a biomarker associated with heart failure and myocardial stress, was also not found to correlate with short-term mortality in our study. This result is consistent with several other studies examining the predictive value of NT-proBNP in CABG patients. Hess et al. (2021) concluded that preoperative NT-proBNP levels were not associated with either short-term or long-term mortality in patients with non-ST elevation myocardial infarction (NSTEMI). Beller et al. (2018) also reported that NT-proBNP did not predict postoperative mortality after adjusting for patient clinical profiles. Nellipudi et al. (2021) found that while NT-proBNP levels were linked to short-term complications, they were not reliable in predicting long-term mortality.

These findings suggest that while NT-proBNP may provide useful information regarding heart failure severity and myocardial injury, it is not an independent predictor of mortality following CABG surgery. The lack of association between NT-proBNP and mortality may reflect the multifactorial nature of mortality risk after CABG, which involves not only the extent of myocardial injury but also factors such as hemodynamic stability, comorbidities, and postoperative complications (Wu et al., 2012).

4.5 Limitations of the Study

There are several limitations to this study. First, the small sample size may have reduced the power to detect significant associations between the biomarkers and mortality. Larger studies with more diverse patient populations would be needed to validate these findings and explore potential interactions between biomarkers and clinical characteristics. Additionally, the study only included demographic factors such as age and sex, which are less comprehensive than other clinical variables, such as comorbidities, vital signs, and preoperative medication use, which may play a larger role in predicting mortality following CABG surgery. Finally, the study focused on only three cardiac biomarkers (CK-MB, HS troponin I, and NT-proBNP) due to resource limitations, but other biomarkers such as high-sensitivity C-reactive protein (hs-CRP) and lactate dehydrogenase (LDH) may offer additional prognostic value.

6. Conclusion

In conclusion, our study found no significant association between age, sex, or the cardiac biomarkers CK-MB, HS troponin I, and NT-proBNP, and short-term mortality following CABG surgery. These findings are consistent with the results of previous studies and highlight the complexity of predicting postoperative mortality. Future studies should consider incorporating a broader range of clinical variables and biomarkers, as well as utilizing larger sample sizes and longer follow-up periods, to better understand the predictors of mortality after CABG surgery.

Author contributions

P.A.A. contributed to the conceptualization, methodology, and writing of the original draft. Y.E.S. was responsible for data curation, validation, and formal analysis. O.R.S.P. assisted with investigation, software, and visualization. P. supervised the study, provided resources, and reviewed and edited the manuscript. All authors have read and approved the final version of the manuscript.

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Competing financial interests

The authors have no conflict of interest.

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