Correlation between Troponin I Level and Major Adverse Cardiovascular Events (MACE) in Patients with Acute Myocardial Infarction at Gotong Royong Hospital Surabaya

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Abstract
Acute coronary syndromes (ACS) are critical medical emergencies that can disrupt the progression of coronary artery disease at any given time. Cardiac troponin I levels are precise and sensitive markers for detecting acute myocardial infarction (AMI). Assessing the incidence of Major Adverse Cardiovascular Events (MACE) in patients experiencing AMI is pivotal for guiding medical interventions. This study investigates the association between cardiac troponin I levels and the frequency of MACE in individuals diagnosed with AMI. Employing an observational analytic approach with a cross-sectional design, the research focuses on patients diagnosed with AMI, including both ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI), admitted to Gotong Royong Hospital in Surabaya from January to December 2023. The relationship between troponin I level and MACE was examined through bivariate analysis using the Chi-square test within SPSS 23.0 software. Among the 76 participants, the majority were aged over 65 years (39.5%), with 51 males (67.1%), and 59 patients were diagnosed with NSTEMI (77.6%). MACE occurred in 39 individuals (51.4%) with AMI, notably including heart failure in 69.2% of cases. Regarding cardiac troponin I (cTnI) values, 17 patients had STEMI, while 59 were diagnosed with NSTEMI. Within the AMI group, 6.6% were classified in Group 1, 26.3% in Group 2, and 67.1% in Group 3. Remarkably, a significantly higher proportion of patients with MACE exhibited markedly elevated cTnI levels in Group 3 (78.3%). In summary, the study highlights a significant association between cardiac troponin I levels and the occurrence of major adverse cardiovascular events (MACE) in patients with acute myocardial infarction at Gotong Royong Hospital in Surabaya.

Keyword: *Acute Myocardial Infarction, Troponin I, Major Adverse Cardiovascular Events (MACE)*

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of death worldwide. In 2019, around 17.9 million people died from CVDs, representing 32% of all global deaths. Among these fatalities, 85% were linked to heart attacks and strokes (Lilly, 2012). Based on the 2018 Riskesdas data, the prevalence of cardiovascular disease in Indonesia was reported

Winda Diah Nugraheni[1], Lenny Kartika Sari[2]

at 1.5%, suggesting that roughly 1,017,290 individuals had been diagnosed with heart disease by healthcare professionals (Putri et al., 2022)

Acute coronary syndromes (ACS) present critical situations that can disrupt the progression of coronary artery disease suddenly. These syndromes cover a range from unstable angina pectoris to the emergence of a significant acute myocardial infarction (MI) characterised by irreversible damage to the heart muscle (Naik et al., 2007). They were distinguishing between AMI, based on electrocardiogram (ECG) alterations, results in two classifications: ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI). The primary initial symptom of AMI is chest pain resembling angina pectoris, requiring prompt identification through ECG and myocardial markers. Cardiac troponin (cTn) and creatine kinase-MB isoenzymes (CK-MB) are presently the predominant biomarkers for diagnosing AMI. Unstable angina shares similarities with NSTEMI, but the difference lies in the absence of elevated cardiac markers (Sandoval et al., 2020).

The definition of Major Adverse Cardiovascular Events (MACE) lacks a precise standard, leading to varied interpretations in cardiovascular research over time. MACE is frequently chosen as the primary or secondary study endpoint (Poudel et al., 2019). In one definition, MACE refers to a combination of outcomes, including overall mortality, recurrent myocardial infarction, stroke, hospitalisation resulting from heart failure, and revascularisation procedures such as percutaneous coronary intervention and coronary artery bypass graft (Choi et al., 2019). Additionally, MACE may include left ventricular dysfunction, recurrent ischemia, early reinfarction, severe coronary disease, stroke, and malignant arrhythmias (Nasution et al., 2022). Recognising the incidence of MACE in acute myocardial infarction patients holds significance for guiding medical management, influencing factors such as the duration and intensity of hospitalisation, and optimising appropriate therapy during treatment (Nasution et al., 2022).

Troponin is a regulatory protein in muscle cells that coordinates the interactions between myosin and actin. It consists of three subunits: TnC, TnI, and TnT; cardiac muscle-specific troponin I (cTnI) and troponin T (cTnT) exhibit structural distinctiveness from their skeletal muscle counterparts. Specialised assays have been developed for the serum detection of these cardiac forms (Lilly, 2012). cTnI is exclusively expressed in the myocardium during human development, lacking expression in any skeletal muscle type irrespective of developmental or disease-related stimuli. This exclusive myocardial specificity renders cTnI a highly sensitive and specific marker for acute myocardial infarction (AMI) (Ahmad et al., 2013).

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from their skeletal muscle counterparts. Specialised assays have been developed for the serum detection of these cardiac forms (Lilly, 2012). cTnI is exclusively expressed in the myocardium during human development, lacking expression in any skeletal muscle type irrespective of developmental or disease-related stimuli. This exclusive myocardial specificity renders Cardiac troponin I (cTnI) as a marker with high sensitivity and specificity for detecting acute myocardial infarction (AMI) (Ahmad et al., 2013).

Although the usefulness of cTnI in diagnosing AMI is well-known, there is a lack of comprehensive data establishing a direct relationship between cardiac troponin I levels and the incidence of Major Adverse Cardiovascular Events (MACE) in AMI patients. Therefore, our study sought to explore the association between cardiac troponin I levels and the occurrence of MACE in individuals diagnosed with acute myocardial infarction, aiming to provide valuable insights into this area of research that is still inconclusive.

MATERIAL AND METHODS
Study Design
This research adopted an observational analytic approach employing a cross-sectional design. It was a retrospective cohort study, utilising secondary data from the medical records of individuals diagnosed with acute myocardial infarction (STEMI and NSTEMI) at Gotong Royong Hospital in Surabaya from January to December 2023.

Study Participants
During the period spanning January to December 2023, a collective of 95 patients were subjected to analysis. The study's population comprised individuals diagnosed with acute myocardial infarction, while the sample population specifically included STEMI and NSTEMI patients admitted to Gotong Royong Hospital in Surabaya. Inclusion criteria stipulated that subjects must be STEMI and NSTEMI patients diagnosed in the emergency room and amenable to follow-up. Exclusion criteria encompassed patients with significant comorbidities such as chronic kidney disease, acute complications of sepsis, liver cirrhosis, malignancy, pulmonary embolism, those with incomplete medical records, and individuals with troponin I levels assessed within less than 3 hours of angina onset.

The dependent variables of the study included Major Adverse Cardiovascular Events (MACE), which comprised heart failure, recurrent myocardial infarction, arrhythmias, cardiogenic shock, stroke, and overall mortality. The independent variable scrutinised at admission was the troponin I level. Other variables examined in this study included age, sex, and the classification of acute myocardial infarction (STEMI or NSTEMI). Ultimately, the study included 76 patients who met the inclusion and exclusion criteria.

Data Collection
Troponin I concentrations were evaluated using ELISA kits, with a specified threshold for diagnosing acute myocardial infarction (AMI) set at >0.01 ug/L. The analysis included 76 patients whose troponin I levels were measured within 3 hours to 14 days after

Winda Diah Nugraheni[1], Lenny Kartika Sari[2]

the onset of angina. These patients were then divided into three groups based on the severity of troponin I levels.

Statistical Analysis

Patient characteristics were examined using univariate analysis with frequency distribution method. In contrast, the correlation between troponin I level and MACE was examined using bivariate analysis with the Chi-square test in the SPSS 23.0 version program.

RESULT & DISCUSSION

The study included 76 patients, with the majority being individuals aged over 65 years (39.5%), comprising 51 males (67.1%), and 59 patients diagnosed with non-ST-segment elevation myocardial infarction (NSTEMI) (77.6%). Detailed patient characteristics are presented in Table 1.

Table 1 Patient Characteristics

Characteristic	N	%
Age (y.o) :		
- 26-35	3	3,9
- 36-45	4	5,3
- 46-55	16	21,1
- 56-65	23	30,2
- >65	30	39,5
Gender :		
- Male	51	67,1
- Female	25	32,9
Types of AMI :		
- STEMI	17	22,4
- NSTEMI	59	77,6
Total	76	100

Table 2 shows the occurrence of MACE in patients with acute myocardial infarction (AMI) in 39 patients (51,4%), with the more significant proportion of patients with heart failure (69,2%). Thirty-seven patients did not experience MACE (48,6%).

Table 2 MACE in patients with Acute Myocardial Infarction

MACE	N	%
Yes :	39	51,4
- Heart failure	27	69,2
- Recurrent myocardial infarction	2	5,2

- Arrhythmia	5	12,8
- Cardiogenic shock	4	10,2
- Stroke	0	0
- Death	1	2,6
No	37	48,6
Total	76	100

The levels of cardiac troponin I (cTnI) were categorized into three groups according to the severity of troponin I levels. Group 1 with mild elevation of cTnI (cTnI level baseline (0,5) to ten times), group 2 with moderate elevation of cTnI (cTnI level ten times to hundred times), and group 3 with severe elevation of cTnI (cTnI level more than hundred times). Table 3 shows cardiac troponin I level in Acute Myocardial Infarction (MI) patients. Based on the cTnI value, 17 patients were diagnosed with STEMI and 59 were found to have NSTEMI. Among these patients with AMI, 6,6% belonged to group 1, 26,3% to group 2, and 67,1% to group 3.

Table 3 Cardiac Troponin I Level in Patients with Acute Myocardial Infarction

Cardiac Troponin I level	N	%
Group 1 (0,5 – 5)	5	6,6
Group 2 (5 – 50)	20	26,3
Group 3 >50	51	67,1
Total	76	100

Correlation between troponin I level and MACE were examined using bivariate analysis with the Chi-square test, which is shown in Table 4. A significantly more significant proportion of patients who have MACE had severely elevated cTnI levels in group 3 (78,3%).

Table 4 Correlation between troponin I level and MACE in Patients with Acute Myocardial Infarction

Cardiac Troponin I level	MACE				p
	Yes		No		
	N	%	N	%	0,016
Group 1	1	2,6	4	10,8	
Group 2	7	17,9	12	32,4	
Group 3	31	79,5	21	56,8	
Total	39	100	37	100	

Winda Diah Nugraheni[1], Lenny Kartika Sari[2]

DISCUSSION

This finding aligns with a systematic review and meta-analysis conducted by Salari et al., which investigated the global prevalence of myocardial infarction (MI) across two age groups: those under 60 years and those over 60 years. The review revealed a prevalence of MI in individuals under 60 years of age to be 3.8%, based on 22 studies with a total sample size of 29,826,717 individuals. Additionally, the prevalence among individuals over 60 years of age was found to be 9.5% in 20 studies involving 5,071,185 patients. The increase in coronary heart disease (CHD) risk associated with aging is primarily attributed to a decrease in the HDL/total cholesterol ratio and an increase in systolic blood pressure. Moreover, an increase in body mass index (BMI) and diabetes prevalence correlates with elevated CHD incidence and mortality as individuals age (Jousilahti et al., 1999). As the demographic profile of acute coronary syndrome (ACS) patients increasingly includes older adults, advanced age becomes associated with frailty, multimorbidity, and a heightened risk of both ischemic and bleeding events in ACS patients.

Following gender categorization, the prevalence of MI in males was found almost 2 folds greater (67,1%) than the females (32,9%). This study was consistent with Schulte KJ *et al* showing that males have a higher incidence than females, with males accounting for approximately 70% of MIs and having an MI 7-10 years earlier than females (Schulte & Mayrovitz, 2023). Estrogen has many important effects on the cardiovascular system. Estrogen can impact cardiovascular health and disease by direct effects on the vascular cells or cardiomyocytes or indirectly by systemic effects (Murphy, 2011). Both men and women produce estrogen but men and postmenopausal women have lower circulating level than premenopausal women. Estrogen receptors and estrogen are responsible for cardioprotective mechanism observed in females.

Our study shows 59 patients (77,6%) out of 87 presenting NSTEMI and 17 patients (22,4%) out of 87 presenting STEMI. Sim et al observed the incidence of STEMI decreased from 60,5% in 2006 to 48,1% in 2013, while the incidence of NSTEMI increased from 39,5% in 2006 to 51,9% in 2013 (Sim & Jeong, 2017). In a similar study, Khera et al observed from 2002 to 2011 that among patients with AMI, the proportion of those presenting with NSTEMI increased from 52,8% in 2002 to 68,6% in 2011 (Khera et al., 2014).

In our study, the occurrence of MACE in patients with acute myocardial infarction (AMI) were 39 patients (51,4%), with proportion of patients were heart failure (69,2%), followed by arrhythmia (5,2%), cardiogenic shock (12,8%), recurrent myocardial infarction (10,2%), stroke (0%) and death (2,6%). There were 37 patients who did not experience MACE (48,6%). This finding is consistent with Kusumawati et al that shows the greater proportion of MACE in patient with ACS was heart failure 24 out of 47 patients (51%) (Kusumawati et al., 2018). In a similar study, Aprilia et al observed that the most common type of MACE in patient with ACS was heart failure in 20 out of 30 patients (66,7%) (Aprilia

et al., 2023). Acute heart failure may occur as a complication of ACS. Acute HF as a result of ACS significantly increases the risk of other in-hospital complications, including worsening of renal function, respiratory failure, pneumonia, and death (Byrne et al., 2024).

In this study, patients with MI who belonged to group 1 (mild elevation of cTnI) were 5 patients (6,6%), patients belonged to group 2 (moderate elevation of cTnI) were 7 patients (17,9%), and patients belonged to group 3 (severe elevation of cTnI) were 31 patients (79,5%). Among 39 patients (51,4%) who presenting MACE, 1 patient (2,6%) belonged to group 1, 7 patients (17,9%) belonged to group 2, and 31 patients (79,5%) belonged to group 3.

Our statistical study showed that there was a significant association between cardiac troponin I level and the incidence of MACE (p value = 0,016, p <0,05). This finding is consistent with Kusumawati et al that showed that elevated cardiac troponin I level can lead to MACE (p<0,002, p value <0,05) (Kusumawati et al., 2018). In similar study, Kim et al observed that there was a higher risk of MACCE (adjusted HR: 3.12; 95% CI: 2.33–4.17; $p < 0.01$) in elevated high sensitive troponin I (hs-TnI) group, compared to non-elevated hs-TnI group. There is indication of a heightened cardiovascular risk in individuals under primary prevention who exhibit elevated levels of high-sensitive troponin (hs-cTn). Moreover, it is established that alterations in hs-cTn levels over time correlate with an elevated risk of cardiovascular events (Kim et al., 2023).

The limitation of this study was retrospective design and performed by a single healthcare system, so the results may not be generalizable and the bias of the information was quite large.

CONCLUSION

The study included 76 patients with acute myocardial infarction (AMI), the majority of whom were individuals aged over 65 years (39.5%), comprising 51 males (67.1%), and 59 patients diagnosed with non-ST-segment elevation myocardial infarction (NSTEMI) (77.6%). The occurrence of major adverse cardiac events (MACE) in patients with AMI was 51.4%, with heart failure being the most common (69.2%). The levels of cardiac troponin I (cTnI) were categorized into three groups, with 6.6% in group 1, 26.3% in group 2, and 67.1% in group 3. There was a significant association between cTnI level and MACE (p=0.016). The study's limitations include its retrospective design and single healthcare system, potentially limiting the generalizability of the results.The research outcomes indicate a significant association between cardiac troponin I levels and the incidence of major adverse cardiovascular events (MACE) among patients diagnosed with acute myocardial infarction who received treatment at Gotong Royong Hospital in Surabaya.

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