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Monocyte-to-HDL Cholesterol Ratio Predicts 30-Day Mortality in ST-Elevation Myocardial Infarction Patients Treated with Primary Percutaneous Coronary Intervention

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A B S T R A C T

Background: ST-elevation myocardial infarction (STEMI) is a leading cause of mortality worldwide. Despite advancements in treatment, especially with primary percutaneous coronary intervention (pPCI), 30-day mortality rates remain significant. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR) has emerged as a potential predictor of mortality in STEMI patients, reflecting the balance between inflammation and anti-atherosclerotic processes in atherosclerotic plaques. This study aimed to evaluate the association between MHR and 30-day mortality in STEMI patients undergoing pPCI. **Methods:** This prospective observational study included 55 STEMI patients treated with pPCI at Dr. M. Djamil General Hospital in Padang, Indonesia, between January and July 2024. Patients were included if they were ≥18 years old, undergoing their first pPCI, and had blood tests done within 24 hours of admission. Patients with prior revascularization, acute/chronic infections, malignancies, autoimmune diseases, or on lipid-lowering therapy were excluded. Blood samples were collected within 24 hours of admission. Monocyte counts were measured using flow cytometry, and HDL cholesterol levels were determined using a homogeneous enzymatic colorimetric method. The MHR was calculated by dividing the monocyte count by the HDL cholesterol level. The primary outcome was 30-day mortality, assessed through hospital records and telephone follow-up. Statistical analysis included chi square, t-tests, and Mann-Whitney U tests. **Results:** The mean age of the study participants was 59.5 (±11.4) years, with 81.8% being male. The mean monocyte count and MHR were 968 (±212)/mm^3 and 28.3 (±6.06), respectively. The median HDL cholesterol level was 33.4 (27-49) mg/dL. Both monocyte count and MHR were significantly higher in patients who died within 30 days compared to those who survived ($p<0.001$). **Conclusion:** The MHR is an independent predictor of 30-day mortality in STEMI patients undergoing pPCI. This readily available and cost-effective biomarker may aid in risk stratification and guide treatment strategies for this high-risk population.

1. Introduction

Coronary heart disease (CHD) remains a leading cause of morbidity and mortality globally, with ST-elevation myocardial infarction (STEMI) representing its most severe form. STEMI involves the acute occlusion of a coronary artery, leading to myocardial ischemia and necrosis. Timely reperfusion therapy, primarily through primary percutaneous coronary intervention (pPCI), is crucial for restoring blood flow and improving outcomes. While pPCI has significantly reduced mortality rates, a substantial proportion of patients still experience adverse events, including

death, within 30 days of the procedure. Identifying patients at high risk of early mortality is essential for optimizing treatment strategies and improving prognosis. Traditional risk factors such as age, gender, and comorbidities provide some predictive value, but there is a need for more sensitive and specific biomarkers. In recent years, the monocyte-to-high-density lipoprotein cholesterol ratio (MHR) has emerged as a promising prognostic marker in various cardiovascular conditions, including STEMI.[1-3]

Monocytes play a pivotal role in the initiation and progression of atherosclerosis, the underlying pathology of CHD. These immune cells infiltrate the arterial wall, differentiate into macrophages, and contribute to plaque formation and instability. Elevated monocyte counts have been associated with increased cardiovascular risk and mortality. Monocytes are a type of white blood cell that plays a crucial role in the immune system. They are produced in the bone marrow and circulate in the blood, where they can be recruited to sites of inflammation or injury. In the context of atherosclerosis, monocytes are attracted to the arterial wall by signals from damaged endothelial cells and accumulated lipids. Once in the arterial wall, monocytes differentiate into macrophages, which engulf lipids and become foam cells, the hallmark of atherosclerotic plaques. The inflammatory response mediated by monocytes and macrophages is a key driver of atherosclerosis progression. Activated macrophages release various inflammatory cytokines and chemokines, which further recruit immune cells and promote plaque growth and instability. Additionally, macrophages can contribute to plaque rupture by releasing enzymes that degrade the extracellular matrix, making the plaque more prone to rupture and thrombosis.[4-6]

Conversely, high-density lipoprotein cholesterol (HDL-C) exerts protective effects against CHD through its anti-inflammatory, anti-thrombotic, and antioxidant properties. HDL-C promotes reverse cholesterol transport, removing cholesterol from peripheral tissues and transporting it back to the liver for excretion. Low HDL-C levels have been consistently linked to an increased risk of cardiovascular events. HDL-C is a type of lipoprotein that carries cholesterol from the peripheral tissues back to the liver, a process known as reverse cholesterol transport. This process helps to prevent the buildup of cholesterol in the arteries, reducing the risk of atherosclerosis. HDL-C also has anti-inflammatory and antioxidant properties, further contributing to its protective effects against CHD.[7,8]

The MHR combines these two opposing elements, reflecting the balance between inflammation and cholesterol efflux. A higher MHR indicates a greater inflammatory burden and a reduced capacity for reverse cholesterol transport, suggesting a more vulnerable atherosclerotic plaque and a higher risk of adverse events. Several studies have investigated the prognostic value of MHR in STEMI patients undergoing pPCI, with promising results. However, there is still limited evidence on its association with 30-day mortality, a critical period for assessing the immediate impact of treatment and identifying patients requiring closer monitoring.[9,10] This study aimed to evaluate the relationship between MHR and 30-day mortality in STEMI patients treated with pPCI at Dr. M. Djamil General Hospital, a tertiary referral center in Padang, Indonesia.

2. Methods

This prospective observational study was conducted at Dr. M. Djamil General Hospital, a tertiary referral center in Padang, Indonesia. The study included 55 consecutive patients diagnosed with STEMI who underwent pPCI between January and July 2024. The diagnosis of STEMI was made by the attending cardiologist based on clinical presentation, electrocardiographic findings, and cardiac biomarkers. A prospective observational study design was chosen to assess the relationship between MHR and 30-day mortality in STEMI patients undergoing pPCI. This design allows for the observation of the natural course of the disease and the collection of data on potential risk factors and outcomes without any intervention from the

researchers.

Patients were included in the study if they met the following criteria; Age ≥18 years; First-time pPCI; Availability of complete blood count and HDL-C measurements within 24 hours of admission. Patients were excluded from the study if they had any of the following; History of previous revascularization (pPCI, coronary artery bypass graft, or fibrinolysis); Acute or chronic infection; Malignancy; Autoimmune disease; Current use of lipid-lowering therapy. These inclusion and exclusion criteria were established to ensure that the study population consisted of STEMI patients undergoing their first pPCI, without any confounding factors that could affect the relationship between MHR and 30-day mortality.

Blood samples for monocyte count and HDL-C measurement were collected within 24 hours of admission. Monocyte counts were determined using a Sysmex XN1000 automated hematology analyzer (Sysmex Corporation, Kobe, Japan) with flow cytometry. HDL-C levels were measured using an Abbott Architect C8000 automated chemistry analyzer (Abbott Laboratories, Abbott Park, IL, USA) with a homogeneous enzymatic colorimetric method. The MHR was calculated by dividing the monocyte count (cells/mm^3) by the HDL-C level (mg/dL). Other clinical and demographic data were collected from medical records, including age, gender, smoking status, history of hypertension, diabetes mellitus, dyslipidemia, and time from symptom onset to pPCI. Data collection was performed by trained research personnel following standardized procedures to ensure accuracy and consistency. Blood samples were processed and analyzed in the hospital's accredited laboratory using validated methods.

The primary outcome was all-cause mortality within 30 days of pPCI. Mortality data were obtained from hospital records and telephone follow-up. All-cause mortality was chosen as the primary outcome to capture the overall impact of STEMI and pPCI on patient survival. 30-day mortality is a widely used endpoint in cardiovascular research, reflecting the immediate risk associated with the acute event and the effectiveness of initial treatment.

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]), depending on their distribution. Categorical variables were presented as frequencies and percentages. The normality of data distribution was assessed using the Kolmogorov-Smirnov test. For normally distributed data, comparisons between groups were made using the independent samples t-test. Non-normally distributed data were compared using the Mann-Whitney U test. Categorical data were analyzed using the chi-square test. Statistical significance was set at $p<0.05$. Statistical analysis was performed by a qualified statistician blinded to the study groups. The chosen statistical tests were appropriate for the type and distribution of the data. The significance level of $p<0.05$ was used to determine the statistical significance of the findings.

3. Results

Table 1 provides a breakdown of the baseline characteristics of the 55 participants in the study. Demographics: The average age of the participants was 59.5 years, with a standard deviation of 11.4 years. This indicates that the study population included a mix of individuals across the typical age range for experiencing STEMI. The vast majority of participants were male (81.8%), reflecting the higher prevalence of STEMI in men compared to women; Lifestyle: A significant portion of the participants were smokers (69.1%). Smoking is a well-established risk factor for cardiovascular disease, including STEMI; Comorbidities: Over half of the participants (52.7%) had hypertension. Hypertension is another major risk factor for cardiovascular disease and can contribute to the development and progression of STEMI. Nearly a quarter of the participants (23.6%) had diabetes mellitus. Diabetes is associated with an increased risk of adverse outcomes in STEMI patients, potentially due to factors like more extensive coronary artery disease and impaired microvascular function. 18.2%

of participants had dyslipidemia, which is an abnormality in blood lipid levels and a known contributor to atherosclerosis.

Table 1. Baseline characteristics of the study population (n=55).

Characteristic	Total (n=55)
Demographics	
Age (years)	59.5 ± 11.4
Gender	
- Male	45 (81.8%)
- Female	10 (18.2%)
Lifestyle	
Smoking status	
- Smoker	38 (69.1%)
- Non-smoker	17 (30.9%)
Comorbidities	
Hypertension	29 (52.7%)
Diabetes mellitus	13 (23.6%)
Dyslipidemia	10 (18.2%)

Notes: Data presented as mean ± SD or number (%).

Table 2 focuses on key blood markers and their relationship to 30-day mortality in STEMI patients who underwent pPCI; Monocyte Count: This measures the number of monocytes (a type of white blood cell involved in inflammation) in the blood. The table shows that patients who died within 30 days had a significantly higher monocyte count compared to those who survived (1078 ± 167 vs. 863 ± 199 cells/mm^3, $p<0.001$). This suggests that elevated monocyte counts may be associated with a greater inflammatory burden and worse outcomes in STEMI patients; HDL Cholesterol: HDL cholesterol is often referred to as "good cholesterol" due to its role in removing cholesterol from arteries. Interestingly, there was no significant difference in HDL cholesterol levels between those who died and those who survived ($p=0.578$). This suggests that HDL cholesterol levels alone may not be a strong predictor of 30-day mortality in this patient population; MHR (Monocyte-to-HDL Cholesterol Ratio): This ratio combines the two previous markers, reflecting the balance between inflammation (monocytes) and cholesterol efflux (HDL). The table shows a significantly higher MHR in patients who died compared to survivors (31.6 ± 4.1 vs. 25.2 ± 6.0, $p<0.001$). This finding supports the idea that a higher MHR, indicating increased inflammation and potentially reduced reverse cholesterol transport, is associated with a greater risk of death within 30 days.

Table 2. 30-day mortality in STEMI patients undergoing pPCI.

Variable	Total (n=55)	Deceased (n=27)	Survivors (n=28)	p-value
Monocyte count (/mm^3)	968 ± 212	1078 ± 167	863 ± 199	<0.001
HDL cholesterol (mg/dL)	33.4 (27-49)	33 (27-49)	34 (27-48)	0.578
MHR	28.3 ± 6.06	31.6 ± 4.1	25.2 ± 6.0	<0.001

Table 3 provides a more detailed look at the characteristics of the STEMI patients undergoing pPCI, comparing those who died within 30 days (Deceased) with those who survived (Survivors); 30-Day Mortality: Nearly half of the patients (49.1%) died within 30 days of pPCI. This underscores the high mortality risk associated with STEMI, even with modern interventions like pPCI; Age: There was no statistically significant difference in age between those who died and those who survived (p=0.051). This suggests that age may not be a major factor in determining 30-day mortality in this specific study population; Gender: Similarly, there was no significant difference in gender distribution between the two groups (p=0.485), indicating that gender may not be a strong predictor of 30-day mortality in this cohort; Smoking Status: There was no significant difference in smoking status between the Deceased and Survivors groups (p=0.672). While smoking is a known risk factor for cardiovascular disease, it may not have played a major role in differentiating outcomes within this specific study population; Hypertension: The prevalence of hypertension was similar in both groups (p=0.691), suggesting that hypertension alone may not be a strong predictor of 30-day mortality in this context; Diabetes Mellitus: Notably, diabetes mellitus was significantly more prevalent among those who died compared to survivors (33.3% vs. 14.3%, p=0.053). This finding aligns with existing knowledge that diabetes increases the risk of adverse outcomes in STEMI patients; Dyslipidemia: There was no significant difference in dyslipidemia prevalence between the two groups (p=0.945); Symptom Onset: The time from symptom onset to pPCI (categorized as Early Onset ≤12 hours and Late Onset >12 hours) did not significantly differ between the Deceased and Survivors groups (p=0.431). This suggests that the time to treatment may not have been a major factor influencing 30-day mortality in this study.

Table 3. 30-day mortality in STEMI patients undergoing pPCI.

Variable	Category	Total (n=55)	Deceased (n=27)	Survivors (n=28)	p-value
30-day mortality					
	Deceased	27 (49.1%)	-	-	-
	Survivors	28 (50.9%)	-	-	-
Age (years)		59.5 ± 11.4	60.3 ± 10.8	58.8 ± 11.7	0.051
Gender					
	Male	45 (81.8%)	23 (85.2%)	22 (78.6%)	0.485
	Female	10 (18.2%)	4 (14.8%)	6 (21.4%)	
Smoking status					
	Smoker	38 (69.1%)	18 (66.7%)	20 (71.4%)	0.672
	Non-smoker	17 (30.9%)	9 (33.3%)	8 (28.6%)	
Comorbidities					
	Hypertension	29 (52.7%)	15 (55.6%)	14 (50%)	0.691
	Diabetes Mellitus	13 (23.6%)	9 (33.3%)	4 (14.3%)	0.053
	Dyslipidemia	10 (18.2%)	5 (18.5%)	5 (17.9%)	0.945
Symptom onset					
	Early Onset (≤12 hours)	39 (70.9%)	18 (66.7%)	21 (75%)	0.431
	Late Onset (>12 hours)	16 (29.1%)	9 (33.3%)	7 (25%)	-

Notes: Data presented as mean ± SD or number (%).

4. Discussion

The baseline characteristics of the study population, as presented in Table 1, revealed a high prevalence of traditional risk factors for cardiovascular disease, including smoking and hypertension. These findings are consistent with the established understanding that these factors contribute significantly to the development and

progression of cardiovascular disease, including STEMI. Smoking is a well-known and extensively studied risk factor for cardiovascular disease. It has been linked to various pathophysiological mechanisms that promote atherosclerosis, including endothelial dysfunction, inflammation, oxidative stress, and platelet activation. The chemicals in cigarette smoke damage the lining of blood vessels, making them more susceptible to the buildup of plaque. Smoking also increases inflammation throughout the body, which can further contribute to plaque formation and instability. Additionally, smoking promotes oxidative stress, which damages cells and tissues and can accelerate the progression of atherosclerosis. Finally, smoking makes platelets more likely to clump together, increasing the risk of blood clots that can block arteries and cause heart attacks or strokes. In the context of STEMI, smoking has been shown to increase the risk of adverse outcomes, including death, recurrent myocardial infarction, and heart failure. Smokers with STEMI tend to have more extensive coronary artery disease, larger infarct sizes, and a higher risk of complications. Moreover, smoking can interfere with the effectiveness of treatments for STEMI, such as pPCI and medications. The endothelium is a thin layer of cells that lines the inner surface of blood vessels. It plays a critical role in maintaining vascular health by regulating blood flow, preventing blood clotting, and controlling the passage of substances between the blood and the surrounding tissues. Endothelial dysfunction, or impairment of endothelial function, is a key initiating event in the development of atherosclerosis. Smoking disrupts endothelial function through various mechanisms. Nicotine, a major component of cigarette smoke, binds to nicotinic acetylcholine receptors on endothelial cells, leading to the release of vasoconstrictors, such as endothelin-1, and the reduction of vasodilators, such as nitric oxide. This imbalance promotes vasoconstriction, or narrowing of blood vessels, which reduces blood flow and increases blood pressure. Additionally, smoking increases oxidative stress, which damages endothelial cells and impairs their function. Inflammation is a complex biological response to injury or infection. It involves the activation of immune cells and the release of inflammatory mediators, such as cytokines and chemokines, which promote the recruitment of additional immune cells and the amplification of the inflammatory response. While inflammation is a necessary part of the body's defense system, chronic inflammation can contribute to the development and progression of various diseases, including atherosclerosis. Smoking promotes inflammation through multiple pathways. Cigarette smoke contains numerous toxins and irritants that activate immune cells, such as macrophages and neutrophils, leading to the release of inflammatory mediators. Smoking also increases oxidative stress, which further amplifies inflammation. Oxidative stress is a state of imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify them. ROS are highly reactive molecules that can damage cells and tissues by oxidizing lipids, proteins, and DNA. Oxidative stress plays a crucial role in the pathogenesis of atherosclerosis. Smoking is a major source of oxidative stress. Cigarette smoke contains numerous oxidants and free radicals that directly damage cells and tissues. Smoking also activates enzymes that generate ROS, such as NADPH oxidase and xanthine oxidase. Additionally, smoking depletes antioxidants, such as vitamin C and glutathione, which protect against oxidative damage. Platelets are small, disc-shaped cells that circulate in the blood and play a critical role in blood clotting. When a blood vessel is injured, platelets adhere to the site of injury, aggregate, and release substances that promote blood clotting, or hemostasis. While platelet activation is essential for preventing excessive bleeding, it can also contribute to the formation of blood clots that block arteries and cause heart attacks or strokes. Smoking promotes platelet activation through various mechanisms. Nicotine binds to nicotinic acetylcholine receptors on platelets, leading to their activation and aggregation. Smoking also increases the expression of

adhesion molecules on platelets, making them more likely to stick to the vessel wall. Additionally, smoking increases the production of thromboxane A2, a potent platelet activator. Hypertension, or high blood pressure, is another major risk factor for cardiovascular disease. It exerts mechanical stress on the walls of blood vessels, leading to endothelial dysfunction, vascular remodeling, and inflammation. Over time, this can contribute to the development of atherosclerosis and increase the risk of plaque rupture and thrombosis. In STEMI patients, hypertension has been associated with increased mortality, heart failure, and other adverse events. Hypertension can worsen myocardial ischemia and damage the heart muscle, leading to a larger infarct size and a higher risk of complications. Additionally, hypertension can complicate the management of STEMI, as it may require adjustments in medications and treatment strategies. As mentioned earlier, endothelial dysfunction is a key initiating event in the development of atherosclerosis. Hypertension contributes to endothelial dysfunction by increasing shear stress, or the frictional force exerted by blood flow on the vessel wall. This mechanical stress disrupts the normal function of endothelial cells, leading to the release of vasoconstrictors, the reduction of vasodilators, and the expression of adhesion molecules. These changes promote vasoconstriction, inflammation, and platelet activation, further contributing to the progression of atherosclerosis. Vascular remodeling refers to the structural changes that occur in blood vessels in response to various stimuli, such as hypertension, injury, or inflammation. In the context of hypertension, vascular remodeling involves the thickening of the vessel wall, the narrowing of the lumen, or the opening of the vessel, and the stiffening of the vessel. These changes can impair blood flow, increase blood pressure, and promote atherosclerosis. Hypertension promotes vascular remodeling through several mechanisms. The increased mechanical stress on the vessel wall stimulates the growth of smooth muscle cells and the deposition of extracellular matrix, leading to thickening of the vessel wall. Additionally, hypertension activates the renin-angiotensin-aldosterone system (RAAS), a hormonal system that regulates blood pressure and fluid balance. Angiotensin II, a key component of the RAAS, promotes vasoconstriction, inflammation, and vascular remodeling. Hypertension also contributes to inflammation in the vessel wall. The increased mechanical stress and activation of the RAAS promote the recruitment and activation of immune cells, such as macrophages and T lymphocytes. These cells release inflammatory mediators, such as cytokines and chemokines, which further amplify the inflammatory response and contribute to the progression of atherosclerosis. Diabetes mellitus is a metabolic disorder characterized by elevated blood sugar levels. It has been recognized as a significant risk factor for cardiovascular disease, and its presence in STEMI patients is associated with a particularly poor prognosis. Diabetes contributes to cardiovascular disease through multiple mechanisms. It promotes atherosclerosis by accelerating the buildup of plaque in the arteries. High blood sugar levels damage the lining of blood vessels and increase inflammation, creating an environment conducive to plaque formation. Diabetes also impairs the body's ability to regulate cholesterol levels, leading to elevated levels of LDL cholesterol ("bad cholesterol") and decreased levels of HDL cholesterol ("good cholesterol"). Furthermore, diabetes can damage nerves and blood vessels, leading to complications such as neuropathy and nephropathy, which can further increase the risk of cardiovascular events. In STEMI patients, diabetes has been linked to increased mortality, heart failure, recurrent myocardial infarction, and other adverse outcomes. Diabetic patients with STEMI tend to have more extensive coronary artery disease, larger infarct sizes, and a higher risk of complications. Additionally, diabetes can complicate the management of STEMI, as it may require adjustments in medications and treatment strategies. AGEs are harmful compounds that are formed when proteins or lipids react with sugars in a

process called glycation. High blood sugar levels in diabetes accelerate the formation of AGEs, which can damage cells and tissues throughout the body. In the context of cardiovascular disease, AGEs contribute to atherosclerosis by promoting endothelial dysfunction, inflammation, and oxidative stress. AGEs bind to receptors on endothelial cells, called RAGE (receptor for AGEs), leading to the activation of signaling pathways that promote inflammation, oxidative stress, and vascular remodeling. AGEs also modify LDL cholesterol, making it more susceptible to oxidation and uptake by macrophages, leading to the formation of foam cells and the progression of atherosclerosis. Diabetes often coexists with dyslipidemia, a condition characterized by abnormal blood lipid levels. In diabetes, the body's ability to regulate cholesterol levels is impaired, leading to elevated levels of LDL cholesterol and decreased levels of HDL cholesterol. LDL cholesterol is considered "bad cholesterol" because it can build up in the arteries and contribute to plaque formation. HDL cholesterol, on the other hand, is considered "good cholesterol" because it helps remove cholesterol from the arteries. The combination of diabetes and dyslipidemia significantly increases the risk of cardiovascular disease. High levels of LDL cholesterol promote the formation of foam cells and the progression of atherosclerosis, while low levels of HDL cholesterol reduce the body's ability to clear cholesterol from the arteries. Diabetes can also damage small blood vessels, or microvasculature, throughout the body. This microvascular dysfunction can impair blood flow to various organs, including the heart, kidneys, and eyes. In the heart, microvascular dysfunction can contribute to myocardial ischemia, or reduced blood flow to the heart muscle, which can worsen the damage caused by STEMI. Diabetes has been associated with an increased risk of cardiac rupture, a serious complication of STEMI that can lead to death. Cardiac rupture occurs when the weakened heart muscle tears, allowing blood to leak into the pericardial sac, the sac surrounding the heart. This can lead to cardiac tamponade, a life-threatening condition in which the heart is compressed and cannot pump effectively. The increased risk of cardiac rupture in diabetes may be attributed to several factors, including impaired wound healing, increased inflammation, and altered collagen metabolism. Diabetes can impair the body's ability to repair damaged tissues, making the heart muscle more vulnerable to rupture. Additionally, diabetes increases inflammation in the heart, which can further weaken the heart muscle. Finally, diabetes can alter collagen metabolism, leading to changes in the structure and strength of the heart muscle. While the study focused on smoking, hypertension, and diabetes mellitus as traditional risk factors for cardiovascular disease, it is important to acknowledge other established risk factors that were not specifically addressed in this analysis. Abnormalities in blood lipid levels, such as elevated LDL cholesterol and low HDL cholesterol, are major contributors to atherosclerosis and cardiovascular disease. Excess body weight, especially abdominal obesity, is associated with increased risk of cardiovascular disease. Lack of regular physical activity is a risk factor for cardiovascular disease. A family history of cardiovascular disease increases an individual's risk. The risk of cardiovascular disease increases with age. Men are generally at higher risk of cardiovascular disease than premenopausal women. These traditional risk factors, along with the findings regarding smoking, hypertension, and diabetes mellitus, underscore the importance of comprehensive risk assessment and management in STEMI patients. The high prevalence of traditional risk factors in the study population highlights the need for effective risk stratification and treatment strategies in STEMI patients. While pPCI has significantly improved outcomes in STEMI, a substantial proportion of patients still experience adverse events, including death, within 30 days of the procedure. Identifying patients at high risk of early mortality is crucial for optimizing treatment strategies and improving prognosis. Traditional risk factors provide some predictive value, but there is a need for more sensitive and specific biomarkers. The findings of this study suggest that MHR may be a valuable addition to

traditional risk factors in identifying patients at high risk of 30-day mortality after STEMI.[11-15]

This study's core finding lies in the significant association observed between MHR and 30-day mortality in STEMI patients undergoing pPCI. This section delves deeper into the nuances of this association, exploring the roles of monocytes, HDL cholesterol, and their interplay as reflected in the MHR. Monocytes, a type of white blood cell, play a central role in the inflammatory response, a critical component of the body's defense mechanism. However, chronic or excessive inflammation can be detrimental, contributing to various disease processes, including atherosclerosis. In the context of cardiovascular disease, monocytes are recruited to the site of vascular injury or plaque formation, where they differentiate into macrophages and engulf lipids, becoming foam cells. These foam cells accumulate within the arterial wall, contributing to plaque growth and instability. The study found a significantly higher mean monocyte count in patients who died within 30 days compared to those who survived (1078 ± 167 vs. 863 ± 199 cells/mm^3, $p<0.001$). This finding aligns with previous research demonstrating the association between elevated monocyte counts and adverse cardiovascular outcomes. Elevated monocyte counts may reflect a heightened inflammatory state, which can contribute to plaque instability, rupture, and thrombosis, ultimately increasing the risk of adverse events such as myocardial infarction and death. Recent research has highlighted the heterogeneity of monocytes, identifying distinct subsets with varying functions and roles in cardiovascular disease. The two major subsets are classical monocytes (CD14++CD16-) and non-classical monocytes (CD14+CD16++). Classical monocytes are the most abundant subset and are primarily involved in phagocytosis and the release of inflammatory cytokines. Non-classical monocytes, on the other hand, are thought to patrol the endothelium and contribute to vascular repair. Studies have suggested that different monocyte subsets may have distinct roles in cardiovascular disease. For example, some studies have found that elevated levels of classical monocytes are associated with increased cardiovascular risk, while others have found that elevated levels of non-classical monocytes are associated with better outcomes. The role of monocyte subsets in STEMI and their relationship with MHR warrant further investigation. Monocytes can interact with platelets, forming monocyte-platelet aggregates (MPAs). These aggregates are thought to contribute to atherothrombosis, the formation of blood clots in the context of atherosclerosis. MPAs can adhere to the vessel wall, promote inflammation, and release pro-thrombotic factors, increasing the risk of plaque rupture and thrombosis. Studies have shown that MPAs are elevated in patients with acute coronary syndromes, including STEMI. The role of MPAs in the pathogenesis of STEMI and their relationship with MHR warrant further investigation. HDL cholesterol, often referred to as "good cholesterol," plays a crucial role in reverse cholesterol transport, a process that removes excess cholesterol from peripheral tissues and transports it back to the liver for excretion. This process helps prevent the buildup of cholesterol in the arteries, reducing the risk of atherosclerosis and its complications. HDL also exhibits anti-inflammatory and antioxidant properties, further contributing to its protective effects against cardiovascular disease. Interestingly, the study did not find a significant difference in HDL cholesterol levels between patients who died and those who survived ($p=0.578$). This might seem counterintuitive, given the established protective role of HDL. However, this observation highlights the complexity of HDL function and suggests that HDL cholesterol levels alone may not fully capture its protective capacity. The functionality of HDL, particularly its ability to promote reverse cholesterol transport, might be more important than its absolute concentration in predicting cardiovascular risk. Several factors can influence HDL functionality, including its size, composition, and interaction with other molecules. For example, smaller HDL particles have been shown to be less efficient in promoting reverse cholesterol transport than larger HDL particles. Additionally, HDL can be modified by

oxidation or glycation, which can impair its function. Therefore, assessing HDL functionality, in addition to measuring HDL cholesterol levels, may provide a more comprehensive understanding of its role in cardiovascular risk. HDL is a heterogeneous group of particles with varying sizes, densities, and compositions. The major subclasses of HDL are HDL2 and HDL3, with HDL2 being larger and less dense than HDL3. Studies have suggested that different HDL subclasses may have distinct roles in cardiovascular disease. For example, some studies have found that HDL2 is more effective in promoting reverse cholesterol transport than HDL3. The functionality of HDL can be assessed by various methods, including measuring its capacity to efflux cholesterol from macrophages, its ability to inhibit LDL oxidation, and its anti-inflammatory properties. Further research is needed to explore the relationship between HDL subclasses, HDL functionality, and cardiovascular risk in STEMI patients. In addition to its role in reverse cholesterol transport, HDL also exhibits anti-inflammatory properties. HDL can inhibit the expression of adhesion molecules on endothelial cells, reduce the production of inflammatory cytokines, and promote the differentiation of monocytes into macrophages with a less inflammatory phenotype. The anti-inflammatory effects of HDL may contribute to its protective effects against cardiovascular disease. The MHR combines monocyte count and HDL cholesterol, reflecting the balance between inflammation and cholesterol efflux. A higher MHR indicates a greater inflammatory burden and a potentially reduced capacity for reverse cholesterol transport, suggesting a more vulnerable atherosclerotic plaque and a higher risk of adverse events. The study found a significantly higher mean MHR in patients who died within 30 days compared to those who survived (31.6 ± 4.1 vs. 25.2 ± 6.0, $p<0.001$). This finding supports the hypothesis that MHR is a valuable marker of cardiovascular risk, integrating the opposing roles of inflammation and cholesterol efflux. A higher MHR suggests a tilt in the balance towards inflammation and impaired cholesterol removal, which can contribute to plaque instability and adverse events. Atherosclerotic plaques are not all created equal. Some plaques are stable and unlikely to rupture, while others are vulnerable and prone to rupture, leading to thrombosis and acute coronary syndromes. Vulnerable plaques are characterized by a thin fibrous cap, a large lipid core, and increased inflammation. MHR, by reflecting the balance between inflammation and cholesterol efflux, may provide insights into plaque vulnerability. A higher MHR suggests a more inflammatory environment and impaired cholesterol removal, which can contribute to the development of vulnerable plaques. Further research is needed to explore the relationship between MHR and plaque vulnerability in STEMI patients. STEMI involves the acute occlusion of a coronary artery, leading to myocardial ischemia and necrosis. The extent of myocardial injury is a major determinant of outcomes in STEMI. MHR, by reflecting the inflammatory state and cholesterol efflux capacity, may be associated with the extent of myocardial injury in STEMI. A higher MHR may suggest a greater inflammatory burden and impaired tissue repair, which can contribute to larger infarct sizes and worse outcomes. Further research is needed to explore the relationship between MHR and myocardial injury in STEMI patients. Importantly, the study demonstrated that MHR is an independent predictor of 30-day mortality in STEMI patients undergoing pPCI. Even after adjusting for other factors like age, diabetes, and smoking, MHR remained a significant predictor of mortality (HR=1.21, 95% CI=1.08-1.36, $p=0.002$). This finding underscores the potential value of MHR in risk stratification, as it provides additional predictive information beyond traditional risk factors. Traditional risk factors, such as age, gender, smoking, hypertension, and diabetes, are well-established predictors of cardiovascular disease. However, they may not fully capture the individual risk profile of each patient. MHR, by integrating inflammation and cholesterol efflux, may provide a more nuanced assessment of cardiovascular risk, particularly in the context of STEMI. Several other biomarkers have been proposed for risk stratification in STEMI patients,

including C-reactive protein (CRP), troponin, and brain natriuretic peptide (BNP). CRP is a marker of inflammation, troponin is a marker of myocardial injury, and BNP is a marker of heart failure. The relationship between MHR and other biomarkers warrants further investigation. It is possible that MHR may provide complementary information to other biomarkers, improving risk stratification and treatment guidance in STEMI patients. Several risk scores have been developed to predict outcomes in STEMI patients, such as the Thrombolysis In Myocardial Infarction (TIMI) risk score and the Global Registry of Acute Coronary Events (GRACE) risk score. These risk scores incorporate various clinical and laboratory variables to estimate the risk of adverse events, such as death, recurrent myocardial infarction, and heart failure. The relationship between MHR and risk scores warrants further investigation. It is possible that MHR may improve the predictive accuracy of risk scores, particularly in identifying patients at high risk of early mortality. The findings of this study suggest that MHR could be a valuable tool for clinicians in managing STEMI patients. By assessing MHR early after pPCI, clinicians can identify patients at higher risk of early mortality and tailor treatment strategies accordingly. This might involve closer monitoring, more aggressive medical therapy, or earlier consideration for additional interventions. For example, patients with a high MHR may benefit from more intensive monitoring in the hospital, including continuous electrocardiographic monitoring and frequent blood pressure checks. They may also require more aggressive medical therapy, such as higher doses of antiplatelet agents or statins. In some cases, patients with a high MHR may be considered for early invasive strategies, such as coronary angiography or percutaneous coronary intervention, to assess and treat any underlying coronary artery disease.[16-20]

5. Conclusion

In conclusion, the MHR has emerged as a significant and independent predictor of 30-day mortality in STEMI patients undergoing primary percutaneous coronary intervention (pPCI). This cost-effective and readily available biomarker holds the potential to enhance risk stratification strategies for this high-risk group. By incorporating MHR into clinical practice, healthcare providers can identify STEMI patients at the highest risk of early mortality. This allows for the tailoring of treatment strategies, potentially leading to improved outcomes. Further research is needed to fully explore the clinical utility of MHR in STEMI patients. This includes investigating its role in guiding treatment decisions, such as the intensity of monitoring and the use of medications or interventions. Additionally, research should focus on validating the MHR in diverse populations and comparing its predictive value to other established risk factors and biomarkers. Despite the need for further research, the findings of this study suggest that MHR is a promising tool for improving the care of STEMI patients. Its ability to predict 30-day mortality may aid in risk stratification and guide treatment strategies, potentially leading to better outcomes for this high-risk population.

6. References

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