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Monocyte to High-Density Lipoprotein Ratio (MHR) as A Predictor of Major Cardiovascular Events in Acute Myocardial Infarction Patients with ST-Segment Elevation in Patients Undergoing Primary Percutaneous Coronary Intervention at Haji Adam Malik Central General Hospital

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ABSTRACT

Introduction: IMA-EST is a cardiovascular disease with high mortality and morbidity. Therefore, tools (markers) to efficiently predict mortality rates are essential to reduce these rates for effective management. Since most of the available literature suggests that MHR value can be used as a predictor of MACE, we are interested in examining MHR as a predictor of MACE in IMA-EST patients undergoing primary PCI
Methods: This type of study was an observational analytic study with the research design used is an ambispective cohort. namely assessing the role of MHR Ratio as a predictor of prognosis after primary MACE in IMAEST patients. This study was conducted at HAM Hospital Medan from April-June 2023. Patients who met the inclusion and exclusion criteria were assessed for laboratory parameters such as triglyceride levels and calculated MHR index, then MACE was observed in patients who underwent primary IKP. The MACE assessed was cardiovascular death, malignant arrhythmia, cardiogenic shock, and acute heart failure during hospitalisation and 30 days post-treatment either through control at the polyclinic or by telephone and interview.
Results: A total of 55 samples were obtained. The GRACE Score and MHR parameters have an area under the ROC curve > 0.7. The MHR parameter had a sensitivity of 69.2% and specificity of 64.3% and a p value <0.05. Based on ROC curve analysis, the cut-off-point parameter for estimating predictors of MVC was 22.48. The GRACE Score coefficient is 0.466 with a significance value (p value) of 0.001 that there is a correlation between the GRACE Score parameters and MHR parameters.
Conclusion: High monocyte counts have an association of low HDL-C levels in the development of atherosclerosis and MACE.

Keywords

Monocyte to High-Density Lipoprotein Ratio, Major Cardiovascular Events (MACE), Primary Percutaneous Coronary Intervention

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INTRODUCTION

Myocardial infarction with ST segment elevation (IMA-EST) and patients with equivalent findings (posterior MI, hyperacute T wave changes, anterior ST depression with ST elevation on aVR leads, and others) account for 30-50% of myocardial infarctions and are associated with short- and long-term morbidity and mortality. Myocardial ischaemic reperfusion is the primary therapeutic goal and can be achieved by primary angioplasty with stent implantation or intravenous fibrinolytic therapy. Timely MACE (≤90 minutes from first medical contact) is the more recommended approach in hospitals that can perform PCI (ACC/AHA recommendation class I, level of evidence A) resulting in more complete reperfusion and lower rates of early death, recurrent infarction, and bleeding, including intracranial haemorrhage, compared with fibrinolysis therapy.[1-6]

Evaluation of care in IMA-EST patients requires assessment from the onset of initial symptoms, reperfusion measures to hospital discharge and return home. Risk stratification should be performed due to the complications of death, acute kidney injury and haemorrhage which are strongly influenced by the characteristics of the patient on initial admission as well as subsequent clinical events. One of the things that needs to be evaluated and assessed is major cardiovascular events (MACE) both in terms of the course of the disease and the interventions performed such as MACE until the occurrence of complications. Major cardiovascular events (MACE) themselves do not have a concrete definition. Over time, various definitions have evolved and MACE continues to be researched as a noteworthy complication. Major cardiovascular events include heart failure, non-fatal recurrent cardiac infarction, recurrent chest pain, recurrent hospitalisation due to heart disease, recurrent SCI, CABG, and all events resulting in mortality.[7,8]

Various scores to assess the risk of developing MACE have been developed and used for risk stratification in IMA-EST events. Many complex multivariable models have been developed to predict mortality in IMA-EST patients by identifying independent clinical predictors and quantifying the relative contribution to mortality risk. One widely used and easily performed risk stratification is the TIMI score which has been routinely applied and can predict early and late mortality. However, monocyte to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) is emerging as a new prognostic marker that has been reported to be associated with cardiovascular prognosis outcomes in various cardiovascular diseases. Monocytes are the source of various cytokines associated with inflammatory processes. It has been found that different monocytes and macrophages can modulate inflammatory cytokines and tissue remodelling in the pathophysiology of coronary artery disease. In contrast, the main function of HDL-C is to protect peripheral tissues through cholesterol elimination and to suppress monocyte activation and proliferation and differentiation of monocyte progenitors.[9-14]

IMA-EST is a cardiovascular disease with high mortality and morbidity. Therefore, tools (markers) to efficiently predict mortality rates are essential to reduce these rates for effective management. Since most of the available literature suggests that MHR value can be used as a predictor of MACE, we are interested in examining MHR as a predictor of MACE in IMA-EST patients undergoing primary PCI.[15]

METHODS

This type of study was an observational analytic study with the research design used is an ambispective cohort. namely assessing the role of MHR Ratio as a predictor of prognosis after primary MACE in IMAEST patients. This study was conducted at HAM Hospital Medan since April 2023. Data collection was carried out from April-June 2023.

Inclusion criteria in this study were patients with a diagnosis of IMAEST based on diagnostic criteria who underwent Primary MACE, IMAEST patients who were willing to undergo a complete blood test and lipid profile. Patients with 2nd and 3rd degree AV block, anaemia (Hb<8) and history of haemoglobinopathy, IMA patients with KILLIP II - IV, incomplete medical record data, and patients with severe infectious diseases, were included in the exclusion criteria.

Before the study began, the researcher requested ethical clearance from the Standing Committee for Research Ethics Assessment of the Faculty of Medicine, University of North Sumatra. Each subject included in the research sample was explained and all samples of this study were patients with a diagnosis of IMAEST who were treated at Adam Malik Hospital Medan. The diagnosis of IMAEST was based on PERKI guidelines.

The researcher examined the patient's medical record to see the history, physical examination, electrocardiography (ECG), blood laboratory, echocardiography, then recorded data, observation during and after treatment and primary percutaneous coronary intervention then MACE that occurred was recorded until the patient was discharged or died. Blood samples for diagnosis were taken during the first admission to the emergency room. The blood was examined through the Clinical Pathology Laboratory of Hajj Adam Malik

Hospital Medan using Architech C4000 and C8000 equipment. ECG assessment using Bionet Cardiotouch 3000 with a speed of 25 mm/s and amplitude of 10 mV.

Patients who met the inclusion and exclusion criteria were assessed for laboratory parameters such as triglyceride levels and calculated MHR index, then MACE was observed in patients who underwent primary IKP. The MACE assessed was cardiovascular death, malignant arrhythmia, cardiogenic shock, and acute heart failure during hospitalisation and 30 days post-treatment either through control at the polyclinic or by telephone and interview. The management of patients was based on the existing medical service standards at HAM General Hospital. After all the data obtained, data processing, analysis, and hypothesis testing will be carried out using SPSS ver.25.

RESULTS

Table 1. Baseline Characteristics Data

Variable	N = 55
Type Gender (n/%)	
Man	44 (80%)
Woman	11 (20%)
Age	54.16 ± 9.0
Location	
Anterior	8 (14.5 %)
Anterolateral	9 (16.4%)
Anteroseptal	9 (16.4%)
Anteroextensive	11 (20%)
Inferior	6 (10.9%)
Inferiolateral	4 (7.3%)
Inferoposterior	7 (12.7%)
Inferoposteriolateral	1 (1.8%)
Onset, hour	7 (2 -11)
GRACE SCORE	100.93 ± 29.44
TIMI SCORE	6.7 ± 2.8
Leukocytes	13110 (8790 – 24780)
Monocytes	770 (220 – 2200)
HDL	35 (21-70)
MHR	20.83 (6.9 – 66.7)
Mortality	
Survive	42 (76.4%)
Not survive	13 (23.6%)
MACE	
Fail Heart I	4 (7.3%)
Arrhythmia Malignant	3 (5.5%)
Shock Cardiogenic	6 (10.9%)
Died	13 (23.6%)
1 Month Evaluation	
Rehospitalization Consequence Fail Heart	3 (5.5%)
Rehospitalization Consequence Other Reasons	3 (5.5%)
Catheterization Results	
CAD1VD	30 (54.5%)
CAD2VD	9 (16.4%)
CAD3VD	13 (23.6%)
CAD3VD + LM	3 (5%)
Factor Risk	
Hypertension	27 (49.1%)
DM	23 (41.8%)
Smoke	31 (56.4%)

ROC curve analysis (Table 2) for the GRACE Score and MHR parameters against MACE displayed in Table 2 shows that the GRACE Score and MHR parameters have an area under the ROC curve > 0.7. However,

the MHR parameter curve (ROC curve > 0.8) has a higher area under the ROC curve than the GRACE Score parameter (ROC curve > 0.7). This indicates that the MHR parameter is used as a predictor of MACE incidence. Figure 4.1 shows that the area under the ROC curve of the MHR parameter for the predictor of MACE incidence was 0.810 (95% CI = 0.675-0.944). The MHR parameter had a sensitivity of 69.2% and specificity of 64.3% and a p value <0.05. Based on ROC curve analysis, the cut-off-point parameter for estimating predictors of MVC was 22.48.

Table 2. ROC analysis

Parameter	AUC	95%CI	p value	*Cut off*	Sensitivity	Specificity
MHR	0.810	0.675 -0.944	0.0001	22.48	69.2%	64.3%
GRACE	0.728	0.563 – 0.893	0.007	112.5	61.5%	81%

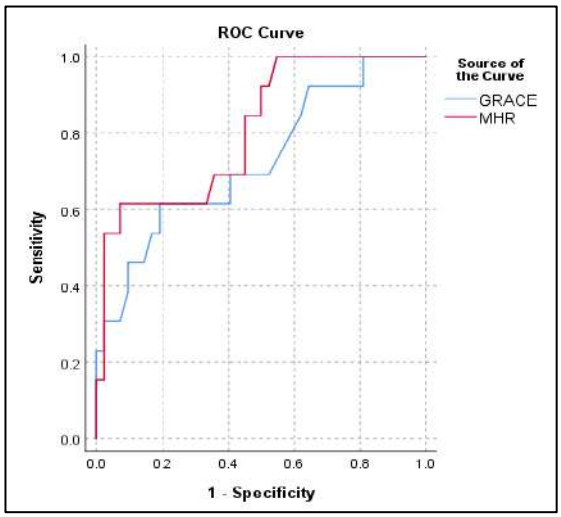

Figure 1. ROC and AUC Curves of GRACE Score and MHR Parameters against MACE

Table 3. Correlation analysis

Other Parameters	MHR parameters	
	Coefficient r	P value
Onset	0.055	0.691
GRACE Score	0.466	0.001
THYME	-0.170	0.216
Age	-0.158	0.249
Leukocytes	-0.125	0.361
HDL	-0.531	0.0001
Monocytes	0.760	0.0001

Table 3 shows the correlation analysis between the parameters of onset, GRACE Score, TIMI, age, monocytes, HDL, and leukocytes with MHR parameters. The onset coefficient is 0.055 with a significance value (p value) of 0.691, because the probability> 0.05, this indicates that there is no correlation between the onset parameters and MHR parameters.

The GRACE Score coefficient is 0.466 with a significance value (p value) of 0.001, because the probability < 0.05, this indicates that there is a correlation between the GRACE Score parameters and MHR parameters. TIMI coefficient of -0.170 with a significance value (p value) of 0.216, due to probability > 0.05, this indicates there is no correlation between TIMI parameters and MHR parameters. Age coefficient of -0.158 with a significance value (p value) of 0.249, due to probability > 0.05, this indicates there is no correlation between age parameters and MHR parameters.

Table 4. Bivariate Analysis of Overall MACE

Variable	MACE		P value
Type Gender (n/%)	Yes (N=13)	No (N=42)	
Man	9 (69.2%)	35 (83.3%)	0.427*
Woman	4 (30.8%)	7 (16.7%)	
Age	52.77 ± 9.43	54.6 ± 8.9	0.527***
Location			
Anterior	4 (30.8 %)	4 (9.5%)	
Anterolateral	3 (23.1%)	6 (14.3%)	
Anteroseptal	1 (7.7%)	8 (19%)	
Anteroextensive	3 (23.1%)	8 (19%)	
Inferior	1 (7.7%)	5 (11.9%)	0.423*
Inferiolateral	1 (7.7%)	3 (7.1%)	
Inferoposterior	0(0%)	7 (16.7%)	
Inferoposteriolateral	0 (0%)	1 (2.4%	
Onset	7 (2 -11)	6 (2-11)	0.08****
GRACE SCORE	122.92 ± 36.66	94.12 ± 23.4	0.001***
TIMI SCORE	7.14 ± 2.74	5.23 ± 2.52	0.03***
Leukocytes	13110 (9530 – 18860)	13045 (8790 – 24780)	0.905****
Monocytes	1000 (540 – 2200)	695 (220 – 1770)	0.012****
HDL	30 (21 – 45)	40 (22 – 70)	0.006****
MHR	39.58 (17.3 – 66.7)	17.99 (6.9 – 49.3)	0.001****
Catheterization Results			
CAD1VD	8 (61.5%)	22 (52.4%)	
CAD2VD	0 (0.0%)	9 (21.4%)	0.004*
CAD3VD	2 (15.4%)	11 (26.2%)	
CAD3VD + LM	3 (23.1%)	0 (0%)	
Factor Risk			
Hypertension	7 (53.8%)	20 (46.2%)	0.940**
DM	6 (46.2%)	17 (40.5%)	0.967**
Smoke	8 (61.5%)	23 (54.8%)	0.912**

Noted: *Fisher-Exact Test; **Chi Square Test; ***Independent T-test; ****Mann Whitney Test

Table 5. Multivariate Analysis of MACE Factors

Variable	P value	95%Cl
Step 1		
THYME	0.129	0.908 – 2.135
Monocytes	0.006	0.989 – 0.998
HDL	0.045	1.005 – 1.517
GRACE Score	0.628	0.090 – 4.274
MHR	0.078	0.736 – 339.008
Step 2		
THYME	0.134	0.905 – 2.110
Monocytes	0.004	0.989 – 0.998
HDL	0.022	1,033 – 1,532
MHR	0.047	1,046 – 392,678
Step 3		
Monocytes	0.003	0.989 – 0.998
HDL	0.043	1,056 – 1,546
MHR	0.023	1,101 – 394, 069

DISCUSSION

In this study, the most common ischaemic site was anterior (predominantly anterolateral and anteroseptal). A study by Ahmed et al. found that LAD lesions were the most common coronary artery lesions (36-38%), followed by RCA and LCX lesions (27-29%). Lesions in the LAD can cause anterior ischaemic events.[16] In

this study, ROC curve analysis was performed for the MHR parameter. ROC curve analysis showed that the cut-off value of MHR for estimating MVC was 22.48. The area under the ROC curve for the MHR parameter to predict MVC was 0.81, with a sensitivity of 69.2% and specificity of 64.3%. With a fairly good area under the curve result of 0.81, MHR is a fairly accurate marker as a predictor of MVCM. This result is in accordance with the study of Yu et al, who found that in the same population, the area under the curve was 0.827. This suggests that MHR has a high diagnostic value for KKVM.[17]

In this study, ROC curve analysis was also conducted for the GRACE score parameter, the ROC curve analysis showed that the cut-off value of the GRACE score for predicting KKVM was 112.5. The area under the ROC curve for the GRACE score parameter to predict the incidence of KKVM was 0.728, with a sensitivity of 61.5% and a specificity of 81%. With a good area under the curve result of 0.728, GRACE score is a good score as a predictor of MVC. The results found in this study are in accordance with a study by Hong and Zeng, where in a population with onset under 24 hours, it was found that the area under the ROC curve of the GRACE score parameter to predict MVC was 0.80, with sensitivity and specificity of MVC prediction being 76% and 69%, respectively.[18]

In this study, correlation analysis was conducted between the parameters of onset, GRACE Score, TIMI, age, monocytes, HDL, and leukocytes with MHR parameters. There was a significant correlation between MHR and GRACE score, HDL, and monocytes with r coefficients of 0.466, -0.531 and 0.760 respectively. Meanwhile, there was no correlation between MHR and onset, TIMI, age, and leucocytes. The results in this study are in accordance with research by Ma et al. where it was found that MHR was significantly and positively correlated with GRACE score ($r = 0.226$, $P < 0.001$) in a population with acute coronary syndrome who will undergo percutaneous coronary intervention.[19]

In IMA-EST with onset below 12 hours, correlation analysis was conducted between onset, GRACE Score, TIMI, age, monocytes, HDL, and leukocytes parameters with MHR parameters. There was a significant correlation between MHR and GRACE score, HDL, and monocytes with r coefficients of 0.466, -0.531 and 0.760 respectively. It can be concluded that an increase in MHR also correlates with an increase in GRACE score and monocytes. Meanwhile, an increase in MHR correlated with a decrease in HDL. There was no correlation between MHR and onset, TIMI, age, and leucocytes. The results in this study are in accordance with research by Ma et al. where it was found that MHR was significantly and positively correlated with GRACE score ($r = 0.226$, $P < 0.001$) in a population with acute coronary syndrome who will undergo percutaneous coronary intervention.[19]

Bivariate analysis was performed on this study population. In onset below 12 hours, there was a significant association between GRACE score, TIMI score, monocytes, HDL, MHR, and catheterisation result with MVC. In onset above 12 hours, bivariate analyses were conducted in this study population. In onset above 12 hours, it was found that there was a significant association between age, GRACE score, leucocytes, monocytes, HDL, MHR, catheterisation result and DM with CTD. The results in this study that showed an association between GRACE risk score and CTD are in accordance with the results in previous studies. According to the study by Yin et al, in the low-medium GRACE risk score group, there were 15 CVMs (2 cardiovascular deaths, 1 non-fatal myocardial infarction, 1 stroke, 0 heart failure, and 11 cardiovascular disease-related hospitalisations). In the high GRACE risk score group, there were 35 CVMs (12 cardiovascular deaths, 2 strokes, 3 heart failures, and 18 cardiovascular disease-related hospitalisations). The total incidence of CVM was significantly higher in patients with a high GRACE risk score than in patients with a low GRACE risk score.[20]

CONCLUSION

High monocyte counts have an association of low HDL-C levels in the development of atherosclerosis and MACE, called MHR. There was a significant correlation between MHR and GRACE score, HDL, and

monocytes. Variables that were independent predictors of MACE were MHR, monocyte, and HDL values in IMA-EST onset below 12 hours. While onset above 12 hours, only DM was an independent predictor of MACE.

DECLARATIONS

The research has received approval from the Universitas Sumatera Utara and Adam Malik Hospital of Health Research and Ethics Committee. All participants were informed about subject of the study.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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The authors declare that there is no conflict of interest in this research.

AUTHORS' CONTRIBUTIONS

All authors are responsible for conceptualization, manuscript preparation, manuscript editing, and manuscript assurance.

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