

## Association between Myeloperoxidase and High Sensitive Troponin I on Myocardial Contractility in Acute Myocardial Infarction Patients

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### ABSTRACT

**Background:** Myeloperoxidase (MPO) levels have been shown to have prognostic values for death events in acute myocardial infarction (AMI) patients. Increased levels of high sensitive troponin I (hs Trop I) are associated with poorer prognosis in AMI patients. This study aimed to determine the association between levels of MPO and hs troponin I at admission on myocardial contractility in AMI patients.

**Subjects and Method:** This was a prospective observational analytic study, conducted at Dr. Moewardi General Hospital, Surakarta, from November 1, 2018 to January 31, 2019. The study subjects were patients who were diagnosed with AMI. A total of 23 patients were included in this study; 15 patients with ST elevation myocardial infarction (STEMI) and 8 with non ST elevation myocardial infarction (NSTEMI). The dependent variable was myocardial contractility. The independent variables were MPO and hs Trop I. Blood tests for MPO and hs Trop I was measured at admission and the left ventricular ejection

fraction (LVEF) was measured when pre-discharge by the Simpson method to examine myocardial contractility. The data were analyzed by Pearson correlation run on SPSS 22.

**Results:** hs Trop I ( $r = -0.53$ ;  $p = 0.009$ ) and MPO ( $r = -0.15$ ;  $p = 0.487$ ) decreased LVEF.

**Conclusion:** Hs Trop I at admission has a correlation with myocardial contractility, and no correlation of MPO at admission with myocardial contractility in AMI patients.

**Keywords:** Myeloperoxidase, High sensitive Troponin I, Acute myocardial infarction

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### BACKGROUND

Coronary heart disease (CHD) is one of the most common and leading causes of death worldwide. Acute myocardial infarction (AMI) is triggered by systemic inflammatory process in the atherosclerotic plaques and myocardium. The incidence of AMI with ST segment elevation (STEMI) is in the range of 43 to 144 in 100,000 cases per year in Europe

(Widimsky et al., 2010). In Indonesia, the incidence of CHD is increasing, according to data from basic health research (Riskesdas) in 2013, the prevalence of CHD in Indonesia based on diagnosis and symptoms ranges from 0.5% - 1.5% (Balitbang Kemenkes RI, 2013). Acute myocardial infarction (AMI) is a form of severe cardiovascular disease which is the development of chronic atherosclerotic

lesions and acute thrombosis, due to atheroma plaque rupture formed by oxidation of low density lipoprotein (LDL), endothelial dysfunction, resulting in myocardial ischemia lesions and acute thrombosis (Pashkow, 2011).

Myeloperoxidase (MPO) is the largest protein component in azurophilic granulocytes, namely polymorphonuclear (PMN) leukocytes. MPO is a member of a subfamily of peroxidases; it is mostly expressed in immune cells such as PMN cells, lymphocytes, monocytes, and other macrophages and cells. It is stored in the cytoplasmic membrane and binds to azurophilic granules. It plays a potential role worsen the atherosclerosis process. It is produced when leukocytes are activated, and it plays a role in the formation of foam cells, endothelial dysfunction and apoptosis, matrix metalloproteinase (MMP) activation, and the expression of tissue factors to produce vulnerable plaque. Myeloperoxidase is part of heme peroxidase, causing various reactive oxidants and radical species that can diffuse so that it is able to initiate fat peroxidase and trigger post-translational modification of protein targets, including halogenation, nitration, and oxidative cross reactions (Podrez et al., 2000; Heinecke, 2003). High MPO plasma levels have been shown to have prognostic values for death events and major adverse cardiovascular events (MACE) in IMA patients (Kaya et al., 2012) with better prognostic values compared to NT-proBNP (Kacprzak and Zielinska, 2016).

Early diagnosis of IMA is necessary, therefore high-sensitive of Troponin I (hs-TnI) examination is still the first choice of biomarkers for diagnosing AMI. Complications of myocardial necrosis cause heart failure, myocardial rupture, and arrhythmia (Chan and Ng, 2010; Twerenbold et al., 2017). Decreased myocardial contractility is a complication of AMI that can result in a heart

failure or cardiogenic shock, and this event will increase the risk of morbidity and mortality in post-IMA patients by 81% within 30 days of treatment (Khan et al., 2013; Mello et al., 2014).

## SUBJECTS AND METHOD

### 1. Study Design

This study uses a prospective observational analytic study design. The study was conducted at the Emergency Room and Intensive Cardiovascular Care Unit (ICVCU) at Dr. Moewardi General Hospital Surakarta in STEMI and NSTEMI patients.

### 2. Population and Sample

A total of 23 patients with AMI were included in this study; 15 patients with ST elevation myocardial infarction (STEMI) and 8 with non ST elevation myocardial infarction (NSTEMI). This study was conducted from November 1, 2018 to January 31, 2019 at Dr. Moewardi General Hospital and selected by consecutive sampling.

### 3. Study Variables

The dependent variable was myocardial contractility by measuring the left ventricular ejection fraction (LVEF) using the Simpson method. The independent variables were myeloperoxidase (MPO) and hs troponin I (hs-TropI).

### 4. Study Instruments

Blood tests for MPO and hs Trop I was measured at the Emergency Room and the LVEF was measured when pre discharge using the Simpson method to examine myocardial contractility with the GE Vivid 6 echocardiography machine. MPO levels were measured using Human Myeloperoxidase Immunoassay Quantikine ELISA (R&D System, USA), conducted at the Prodia Clinical Laboratory. The level of hs-Trop I was measured using Vidas high-sensitive Troponin I (Biomerieux SA Tech, Lyon, France), done at the Clinical Pathology Laboratory of Dr. Moewardi Hospital.

**5. Data Analysis**

Pearson correlation analysis is used to determine the association between the MPO variable with the LVEF variable and the association between the hs-TropI variable and the LVEF variable. Pearson correlation coefficients are expressed in notation r. Data analysis was performed with SPSS 22.

**6. Research Ethics**

The research ethics include inside informed consent, identity confidentiality, and ethical clearance carried out in the Dr. Moewardi hospital, Surakarta.

**Table 1. Sample characteristics**

Variables	Mean	SD	Minimum	Maximum
Age	58.96	9.89	45	85
SBP	129.78	24.51	82	185
DBP	80.39	16.26	50	120
Heart Rate	80.35	17.80	55	140
Respiratory Rate	21.30	3.27	18	32
Hemoglobin	13.23	1.75	10.10	17.50
Hematocrit	40.26	5.49	31	52
Leukocyte	15.95	22.01	5.90	109.00
Platelets	238.80	76.91	234.50	386.00
Erythrocytes	4.53	0.66	3.39	5.72
eGFR	64.74	28.83	29	156
Total cholesterol	182.57	94.75	137	553
LDL	127.00	70.07	54	415
HDL	42.61	15.08	20	81
Triglycerides	113.61	49.24	11	240
<b>STEMI:</b>				
MPO (ng/mL)	181.49	74.67	44.70	271.90
hs-TnI (ng/L)	2,176.60	2,345.55	5.90	7,495.00
LVEF (%)	44.53	6.15	33	56
<b>NSTEMI:</b>				
MPO(ng/mL)	149.79	91.16	23.30	270.90
hs-TnI (ng/L)	946.56	1,473.65	9.20	4,000.00
LVEF (%)	43.50	9.37	34	61

SBP= Systolic blood pressure LDL= Low density lipoprotein.

DBP= Diastolic blood pressure

HDL= High density lipoprotein

Description of study characteristic variables are presented in Table 2. Table 2 showed that there was no difference between male (65%) and female (66.7%) to experience STMI (OR= 0.93; 95% CI= 0.07 to 12.14; p= 0.955).

Hypertension increased the risk of STMI and it was statistically significant (OR= 6; 95% CI= 0.87 to 41.22; p= 0.057).

**RESULTS**

The basic characteristics of the patients are presented in Table 1. The patients were 23 people with divided into two groups, namely STEMI for 15 and NSTEMI 8 patients. The average age of patients was 58.96 years (Mean= 58.96; SD= 9.89). They had ages ranging from 45 to 85 years. The average of systolic blood pressure was 129.78 mmHg (Mean= 129.78; SD= 24.51).

There was no difference between smoking (64.29%) and non-smoking (66.67%) to experience STMI (OR=0.90; 95% CI= 0.15 to 5.26; p= 0.907).

**Table 2. Bivariate analysis on the factors associated with acute myocardial infarction**

Independent Variables	Acute myocardial infarction				OR	95% CI		p
	STEMI		NSTEMI			Lower limit	Upper limit	
	n	%	n	%				
<b>Gender</b>								
Male	13	65	7	35	0.93	0.07	12.14	0.955
Female	2	66.67	1	33.33				
<b>Killip</b>								
Killip 1	10	76.92	3	23.08	3.33	0.56	19.95	0.179
Killip 2-4	5	50	5	50				
<b>Hypertension</b>								
Yes	10	83.33	2	16.67	6	0.87	41.22	0.057
No	5	45.45	6	54.55				
<b>Smoking</b>								
Yes	9	64.29	5	35.71	0.90	0.15	5.26	0.907
No	6	66.67	3	33.33				
<b>Dyslipidemia</b>								
Yes	1	50	1	50	0.50	0.03	9.24	0.636
No	14	66.67	7	33.3				
<b>DM</b>								
Yes	1	33.33	2	66.67	0.21	0.02	2.84	0.214
No	14	70	6	30				

STEMI= ST elevation myocardial infarction

NSTEMI= Non ST elevation myocardial infarction

The results of the correlation analysis between MPO, Hs-TnI, and LVEF were presented in Table 3. Table 3 showed that Hs-TnI decreased LVEF and it was

statistically significant ( $r = -0.53$ ;  $p = 0.009$ ). MPO decreased LVEF, but it was statistically non-significant ( $r = 0.15$ ;  $p = 0.487$ ).

**Table 3. Pearson correlation between MPO and Hs-TnI with left ventricular ejection fraction**

Independent Variables	r	p
MPO	-0.15	0.487
Hs-TnI	-0.53	0.009

## DISCUSSION

The subjects of this study were STEMI and NSTEMI patients, then measured blood myeloperoxidase (MPO) and hs-TnI levels, and left ventricular ejection fraction (LVEF) measurements with the Simpson method to see the role of MPO and hs-TnI on myocardial contractility. This study aims to determine the association between levels of MPO and hs troponin I on myocardial contractility in AMI patients.

Myeloperoxidase plays a role in the promotion of vasoconstriction, leukocyte recruitment and also myocardial fibrosis.

Increased levels of MPO are associated with diastolic disorders, due to excess ventricular pressure which may be associated with leukocyte activation (Deusch et al., 2014). MPO may contribute to myocardial dysfunction, a side effect of remodeling after acute myocardial infarction through several potential mechanisms. MPO secretes several cytotoxic species, including aldehydes that can modify residues that serve as key ionic channels or transporters to impair contractile function after an ischemic episode. Ischemic phenomena and myocardial reperfusion

stimulate polymorphonuclear (PMN) cell recruitment and are associated with microvascular dysfunction, contributing to decreased vascular bioavailability of nitric oxide (NO). The predominant mechanism is through rapid reaction with superoxide, which is a derivative of NADPH oxidase and PMNs, which accumulate and activate PMNs neutrophils in inflamed tissues (Baldus et al., 2004).

Myeloperoxidase can affect ventricular remodeling after infarction by activating proteases. Inactivation of PAI-1 with oxidation catalyzed with MPO, which increases plasmin activity will accelerate matrix degradation, which will thin the ventricular wall and dilate the heart chambers, while inhibition of MPO will result in decreased leukocyte infiltration, significant reduction in LV dilatation and good LV function (Askari et al., 2003).

Cardiac troponin I (cTnI) and T (cTnT) are components of the myocardial cell contractile apparatus and are expressed almost exclusively in the heart. An increase in troponin levels describes an injury to myocardial cells (Thygesen et al., 2018). Myocardial infarction can affect left ventricular function, wherein the extent or size of the infarct is directly related to left ventricular remodeling and is a stronger predictor of clinical outcome in patients with acute myocardial infarction than measurement of left ventricular systolic function (Wu et al., 2008).

Pearson correlation analysis showed that the MPO and LVEF variables did not have a significant correlation. The results of Pearson correlation analysis between the MPO variable and the LVEF indicate very weak negative correlation ( $r = -0.15$ ;  $p = 0.487$ ). Statistical analysis of data indicate no correlation between MPO at admission and myocardial contractility in patients with AMI.

Our results are in line with the study by Stankovic et al. (2012), who carried out serial examinations of MPO levels in AMI patients whose samples were taken at admission, 4, 8, 12, 24, and 48 hours of admission. All MPO levels taken at the time of the examination had a predictive value for mortality, except for MPO levels at admission. MPO levels associated with the incidence of heart failure were at 24 hours of admission. In addition, in a study by Kacprzak in 2016, MPO levels at admission were not associated with major cardiovascular events (PCI or unscheduled heart bypass surgery, stroke, reinfarction or death) in STEMI patients who underwent percutaneous coronary intervention (PCI). However, MPO levels at the time of treatment on the third and fourth days were predictors for major cardiovascular events (Stankovic et al., 2012).

The other results of this study indicate a negative correlation between hs-TropI and LVEF ( $r = -0.53$ ;  $p = 0.009$ ). This means, there is a correlation between hsTropI and myocardial contractility in patients with AMI. A high hsTropI level on admission correlates with low myocardial contractility in AMI patients conclusively.

Findings in our study are in line with research by Khan et al. (2017), where in NSTEMI patients, troponin levels were negatively correlated with LVEF, where high troponin levels were associated with low LVEF, while low troponin levels had better LVEF. In addition, high troponin levels are also associated with poor outcomes. In addition, a study by Chia et al. (2008), also proved similar results, where 378 STEMI patients who underwent primary Percutaneous Coronary Intervention (primary PCI) showed that the troponin I value 72 hours was associated with infarct size at 5 and 30 days of treatment. Troponin I levels  $>55$  ng/ml were 90% sensitive for large infarct

sizes ( $\geq 10\%$ ) and low LVEF ( $\leq 40\%$ ) with specificities of 70% and 52%, respectively.

Based on the results of this study, it can be concluded that there is a correlation between hs-TropI and myocardial contractility and no correlation between MPO at admission and myocardial contractility in acute myocardial infarction patients.

#### **AUTHOR CONTRIBUTION**

Budi Patria Meilus and Ahmad Yasa collected the data, measured myeloperoxidase level, high sensitive troponin I. Trisulo Wasyanto examined clinical changes, left ventricular ejection fraction (LVEF) to examine myocardial contractility with echocardiography, did data analysis, and wrote the manuscript.

#### **CONFLICT OF INTEREST**

The authors declare there is no conflict of interest.

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