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Comparison of the validity of Myeloperoxidase and Troponin I in short-term acute outcomes for patients with Myocardial Infarction

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ABSTRACT

Inflammation is involved in formation stages to rupturing the atherosclerotic plaque. One of the enzymes involved in inflammatory processes is Myeloperoxidase (MPO) which is effective in predicting the prognosis of Myocardial Infarction (MI). Myeloperoxidase enzymes have various polymorphisms. This study has addressed the MPO serum level related to the short-term outcome in patients with MI for the first time in Iran. This is a perspective cohort study. The sample size was calculated as 90 subjects considering the possible loss. Blood samples were taken from patients on admission and before taking the drug, and evaluated in terms of MPO and troponin I levels (TnI) as the gold standard test. Before discharge, Echocardiography was done on patients and after discharge within 30 days after the occurrence of MI, patients were followed up in terms of Major Adverse Cardiac Events (MACE) including death, Re-MI, unstable angina, Cerebrovascular Accident (CVA) and doing Revascularization including Coronary Artery Bypass Grafting (CABG) and Percutaneous Coronary Intervention (PCI). The obtained results were analyzed by statistical t-test on two independent samples (or Mann – Whitney test) and Chi-square using SPSS software. To determine the sensitivity of MPO, the analysis was done using the curve of Receiver-operating-characteristic curves (ROC). Among from 90 patients in the study, 54 cases were with ST elevation MI (STEMI) and 36 ones with Non-ST elevation MI (NSTEMI). In patients without MACE (3.70±5.61 ng/dl), the mean level of MPO was higher than that in patients with MACE (4.09±5.45 ng/dl); however, it was not statistically significant. The Area under Curve (AUC) was equal to 0.456 (0.662-0.250: CI 95%) for MPO in dead patients that their clinical diagnostic value was not statistically significant. In cases with revascularization in STEMI group (3.91±5.49 ng/dl), the mean level of MPO was more than that in cases without revascularization (3.93±5.38 ng/dl) and in NSTEMI group (3.97±4.47 ng/dl), it was less than that in cases without revascularization (3.28±5.84 ng/dl) that they were not statistically significant. Although patients with higher TnI level were more likely to have higher rate of mortality, unlike other studies, MPO level had no predictive ability for mortality or MACE in short-term. However, MPO level had lower sensitivity and specificity to predict revascularization in making decision for early invasive strategy.

Keywords: Myeloperoxidase, Myocardial Infarction, Outcome

INTRODUCTION

Coronary Artery disease (CAD) and its outcome, Myocardial Infarction (MI), is one of the major causes of mortality and morbidity all over the world. Over the past 50 years, the cascade of thrombotic events following atherosclerotic rupture has well been known. Therapies such as Fibrinolysis, Coronary Artery Bypass Grafting (CABG) and Percutaneous Coronary Intervention (PCI) have improved the outcome [1]. Inflammatory events are involved in at all formation stages of atherosclerotic plaque from endothelial dysfunction to the formation of adult atheroma and its

rupture. One of the involved enzymes is Myeloperoxidase which is a member of heme peroxidase superfamily. This enzyme is stored in granules of Azurophilic leukocytes and excretes from them in the activation of leukocytes [2]. Several studies have shown that Myeloperoxidase serum level is effective in predicting short- and long-term prognosis after Acute Coronary Syndrome (ACS), MI and cardiac failure [3, 4, 5 and 6]. Various studies have revealed Myeloperoxidase polymorphisms related to premature ischemic heart disease [7], intensity of ischemic disease [8] and mortality of heart failure [9]. Also, some studies have reported the diagnostic and prognosis disability of Myeloperoxidase serum level [10].

In individuals over 40 years in Iran, the rate of ACS incidence has annually been reported as 8% that 10% of them will die after discharge, and 24% of them will suffer from another heart attack [11]. In the present study, MPO serum level related to Major Adverse Cardiac Events (MACE) is studied during 30 days after the first MI in Iran.

MATERIALS AND METHODS

The framework of the study and patients:
This study is a prospective cohort study conducted on patients referred to hospitals affiliated to Isfahan Medical School from March 2011 to May 2012. By assuming that the sensitivity found from previous studies was equal to 0.8, the minimum sensitivity accepted for the study 0.9, the confidence level 95% and power 80%, the sample size was 84 subjects among from 90 studied patients. Sampling method was as available.

Inclusion criteria:
patients over 18 years old and referred to the emergency center with chest pain and the doctor diagnosed of the possibility of MI.

Exclusion criteria:
1-negative Troponin I after 6 hours from referring
2-Impossibility of following-up the patient

Procedure:
At initial entering and before taking the medication, a blood sample was taken from patient and sent to a laboratory after centrifuging. MPO tests were done by ELISA (Enzyme-Linked Immunosorbent Assay) kit of Boster Biological Technology Company made in Canada and TnI tests were done by ELISA kit of Dia-Plus Company made in USA. After the occurrence of MI at hospital and discharge, within 30 days, patients were followed in terms of major adverse cardiac events (MACE) including death, unstable Angina, Re-MI, Cerebrovascular Accidents (CVA) and doing Revascularization. After providing the explanation about the study, the patients and their accompanies were given the written consent based on guidelines of University Research Ethics Committee matched with Ethics Center regulations for medical research in Ministry of Health and Medical Education. The questionnaire including cardiovascular risk factors and also the patient's clinical condition on admission was filled. Before discharge, Echocardiography was performed on the patient.

Statistical analyses:
The numerical variables were reported as mean and standard deviation and the qualitative variables were reported as frequency and percentage. The statistical t-test was applied on independent samples, and Chi-squre test was applied to compare the groups in terms of numeric and qualitative variables, respectively. To determine MPO sensitivity, the analysis was performed using TnI test as standard by ROC curve. In all conducted tests, the significance level of P was considered as less than 0.05. All analyses were performed using SPSS software.

RESULTS AND DISCUSSION

From March 2011 to April 2012, 112 patients suspected to myocardial infarction (MI) were admitted to the emergency centers of hospitals under study that 6 hours after admission, in following-up, the result of qualitative Troponin I (TnI) was positive for 90 patients that MI was absolutely diagnosed (Fig. 1).

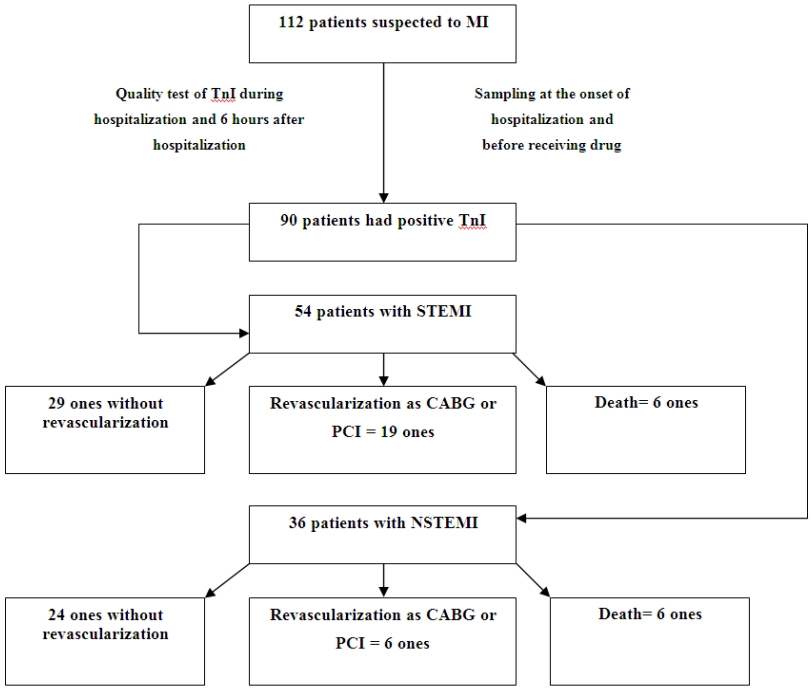


Figure 1: The sample raw status of patients admitted in emergency centers under study

ST-segment elevation Myocardial Infarction (STEMI) was diagnosed in 54 (60%) patients and no ST-segment elevation Myocardial Infarction (NSTEMI) was diagnosed in 36 (40%) patients. The mean age of the study population was (12.21 ± 61.89) years at the age range of 29-87 years. 32.2% of them were female and all were married. The mean BMI of patients was (0.56 ± 25.75) at the range of 17.33 to 44.44. The risk factors of MI were 31.1% for hyperlipidemia (HLP), 36.7% for Hypertension (HTN), 23.3% for diabetes mellitus (DM) and 24.4% for current smoking. There was the ischemic history disease (IHD) in 25.6% of the patients. The mean onset of symptoms to admission was (0.38 ± 3.88) hours. Only 5 patients (5.6%) had the history of cerebrovascular attack (CVA). NSTEMI was more common in women. The history of HLP, HTN, DM, IHD and mean of left ventricular ejection fraction (LVEF) was higher in NSTEMI and smoking and the mean onset of symptoms to admission was higher in STEMI. The mean levels of troponin I (TnI) and Myeloperoxidase (MPO) were higher in STEMI and NSTEMI, respectively (Table 1).

Table 1: Basic and clinical properties of patients who were hospitalized with an MI diagnosis

Properties/Group	STEMI	NSTEMI	P-Value	All patients
Age	12.19 ± 60.44	12.09 ± 64.06	0.171	12.21 ± 61.89
Sex (female)	11 (20.4)	18 (50)	0.003	29 (32.2)
Rural residence	10 (18.5)	5 (13.9)	0.392	15 (16.7)
BMI	26.23 ± 0.72	25.03 ± 0.89	0.300	0.56 ± 25.75
HLP history	16 (29.6)	12 (33.3)	0.442	28 (31.1)
HTN history	16 (29.6)	17 (47.2)	0.071	33 (36.7)
DM history	12 (22.2)	9 (25)	0.476	21 (23.3)
Smoking history	15 (27.8)	7 (19.4)	0.260	22 (24.4)
IHD history	11 (20.4)	12 (33.3)	0.129	23 (25.6)
the mean onset of the symptoms to admission (hour)	4.38 ± 3.75	3.14 ± 3.41	0.115	3.88 ± 0.38
LVEF level	± 11.07	± 11.07	0.084	± 11.17
TnI level	3.76 ± 5.11	2.54 ± 3.50	0.071	2.94 ± 0.34
MPO level	5.30 ± 3.78	5.89 ± 4.04	0.334	5.54 ± 0.41

** Mean (±SD) for continuous variables and the numb er (percentage) for qualitative variables.*

MPO level in comparison with TnI in types of MI:

In NSTEMI, the mean MPO level was higher than that in STEMI; however, it was not statistically significant. The mean level of STEMI troponin was higher than that of NSTEMI that was statistically partially significant (P= 0.071) (Figure 2).

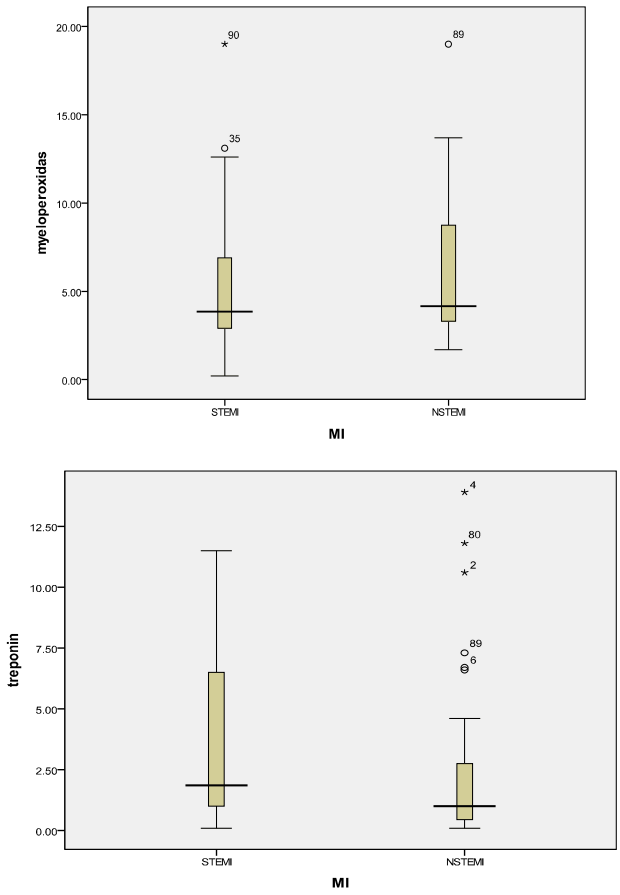


Figure 2: The mean MPO level compared with TnI in STEMI and NSTEMI

MPO level in comparison with TnI in the prediction of MI cases with MACE:
No case had CVA or TIA. 12 individuals (13.3%) died that 9 and 3 cases died during admission and one month after discharge, respectively and 6 (11/1%) cases were in STEMI group and 6 cases (16.7%) were in NSTEMI group.

25 (27.8%) patients underwent PCI that 19 (35.2%) and 6 (16.7%) individuals were in STEMI and NSTEMI groups, respectively. 3 (3.3 %) patients underwent CABG that 1 case was in STEMI group and 2 cases were in NSTEMI group.

After discharge, 46 (51.1%) individuals were without problems that 26 (48.1%) and 20 (55.6%) cases were in STEMI and NSTEMI groups. 4 (4/4 %) patients were re-admitted with the diagnosis of unstable angina (UA) (2 individuals per group) and there was no case of re-MI.

In patients without MACE (3.70 ± 5.61 ng/dl), the mean MPO level was higher than that in patients with MACE (4.9 ± 5.45) that it was 5.43 ± 4.07 versus 5.17 ± 3.55 in STEMI group and 3.24 ± 5.87 versus 5.92 ± 4.97 in NSTEMI group that it was not statistically significant.

In patients without MACE (3.42 ± 2.86), the mean TnI level was lower than that in patients with MACE (5.45 ± 4.01) that was 2.86 ± 3.42 versus 4.60 ± 6.24 in STEMI group and 3.44 ± 2.1 versus 2.97 ± 3.65 in NSTEMI group. None of them were statistically significant (Fig. 3).

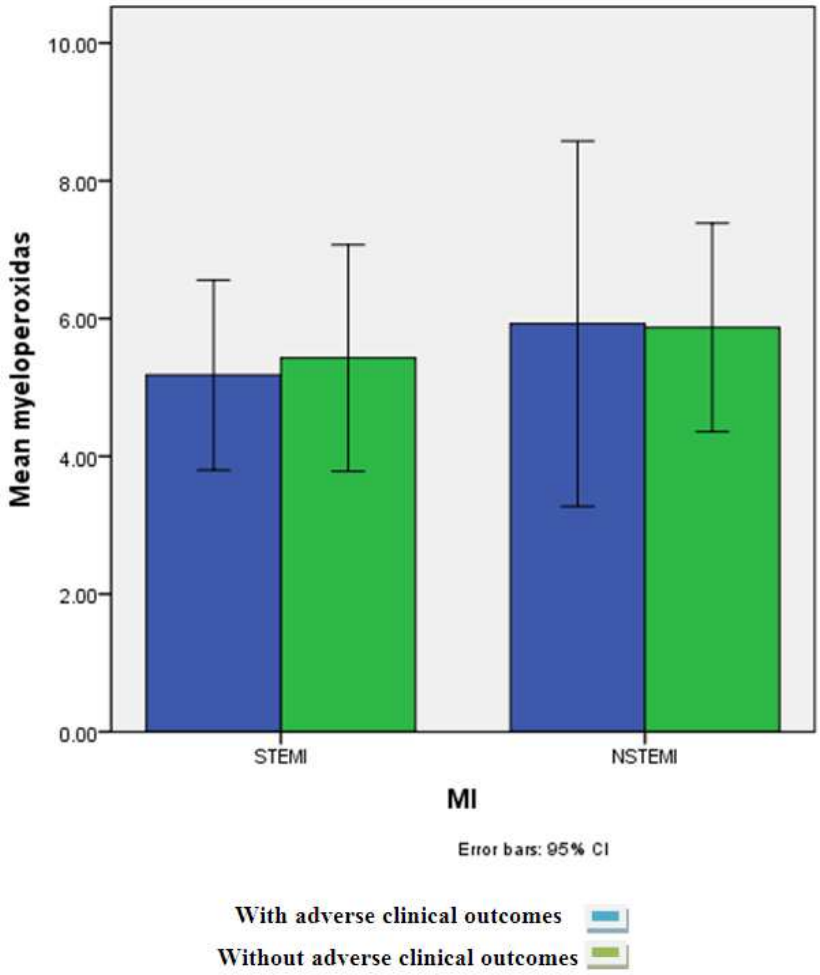


Figure 3: The mean MPO level compared to TnI in terms of adverse clinical outcomes

The MPO level compared with TnI level in predicting mortality during one month after MI:
In STEMI group (4.27 ± 2.94), the mean MPO level in dead patients was less than that in the alive patients (3.87 ± 5.43) and in NSTEMI group, this level in dead patients (3.53 ± 4.87) was more than that in the alive patients (5.29 ± 3.62); however, it was not statistically significant.

In STEMI group, the mean TnI level in the dead patients (3.53 ± 4.87) was more than that in alive patients (3.62 ± 5.29) which was not statistically significant while in NSTEMI group, the mean TnI level in dead patients (5.45 ± 4.61) was more than that in alive patients (1.95 ± 3.01) which was statistically significant (P = 0.023).

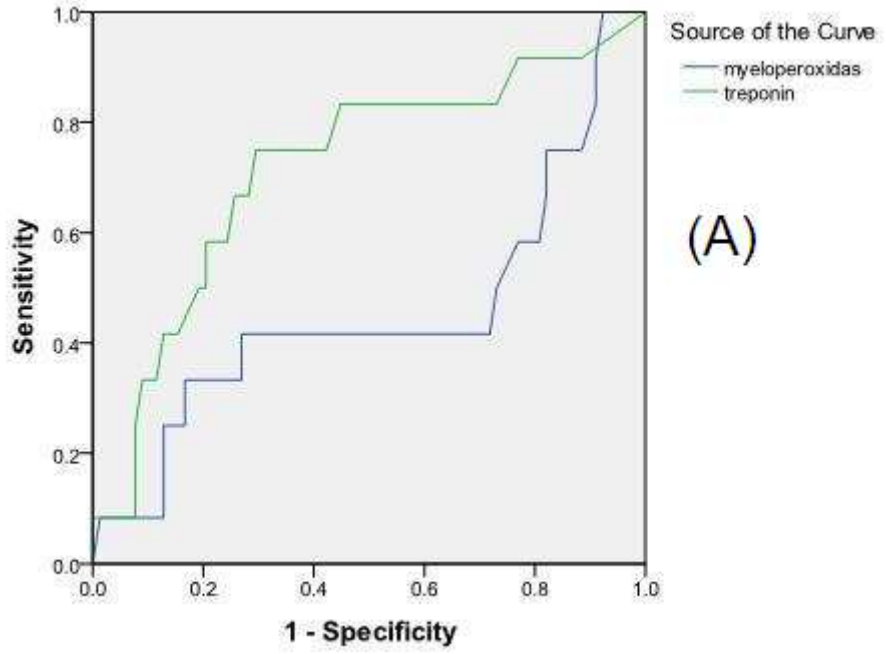
In dead patients, area under curve (AUC) was equal to 0.456 (0.250 – 0.662: CI 95%) for MPO and 0.716 (0.549 – 0.884: CI 95%) for TnI that had statistically no significant clinical diagnostic value. MPO cutoff median was equal to 4.20 ng/ml with sensitivity of 42% and specificity of 65% and for TnI, it was equal to 1.35 ng/ml with the sensitivity of 83% and specificity of 54% (Figure 4).

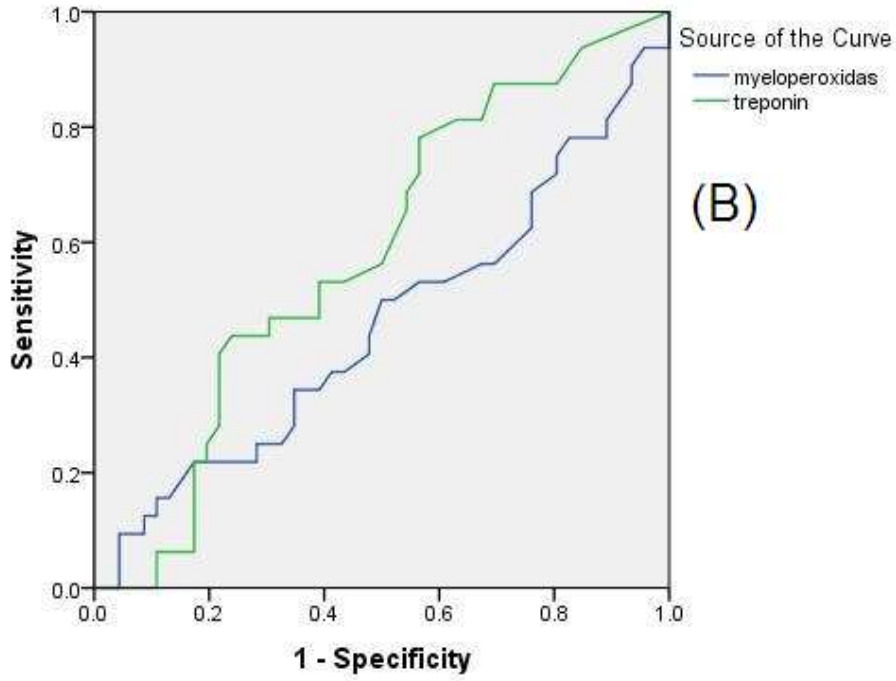
MPO level in comparison with TnI level in predicting cases of revascularization in patients alive:
In STEMI group, the mean MPO level in cases with revascularization (3.91 ± 5.49) was more than that in cases without revascularization (3.39 ± 5.49) and in NSTEMI group, the mean MPO level in cases with revascularization (4.48 ± 3.97) was less than cases without revascularization (3.28 ± 5.84) that all were not statistically significant.

In STEMI group, the mean TnI level in cases with revascularization (7.12 ± 4.87) was more than that in cases without revascularization (3/33 ± 2.74) and in NSTEMI group, the mean MPO level in cases with revascularization (1.65 ± 2.15) was less than cases without revascularization (2.06 ± 3.20) that all were not statistically significant.

In patients with revascularization, area under curve (AUC) was equal to 0.448 (0.586 – 0.310: CI 95%) for MPO and 0.613 (0.741 – 0.485: CI 95%) for TnI that it statistically showed no significant clinical diagnostic value. Median of MPO cutoff was equal to 4.20 ng/ml with the sensitivity of 43% and specificity of 52% and for TnI, it was equal to 1.35 ng/ml with the sensitivity of 54% and specificity of 54% (Figure 4).

MPO level in comparison with TnI level in predicting MI patients with moderate to severe decline in LVEF:
In STEMI group, the mean MPO level was (4.07 ± 5.54) in patients with moderate to severe decline in LVEF versus (3.55 ± 5.07) in patients with normal or mild decline in LVEF and in NSTEMI group, was (5.49 ± 3.59) versus (4.66 ± 6.47) that no differences were statistically observed.





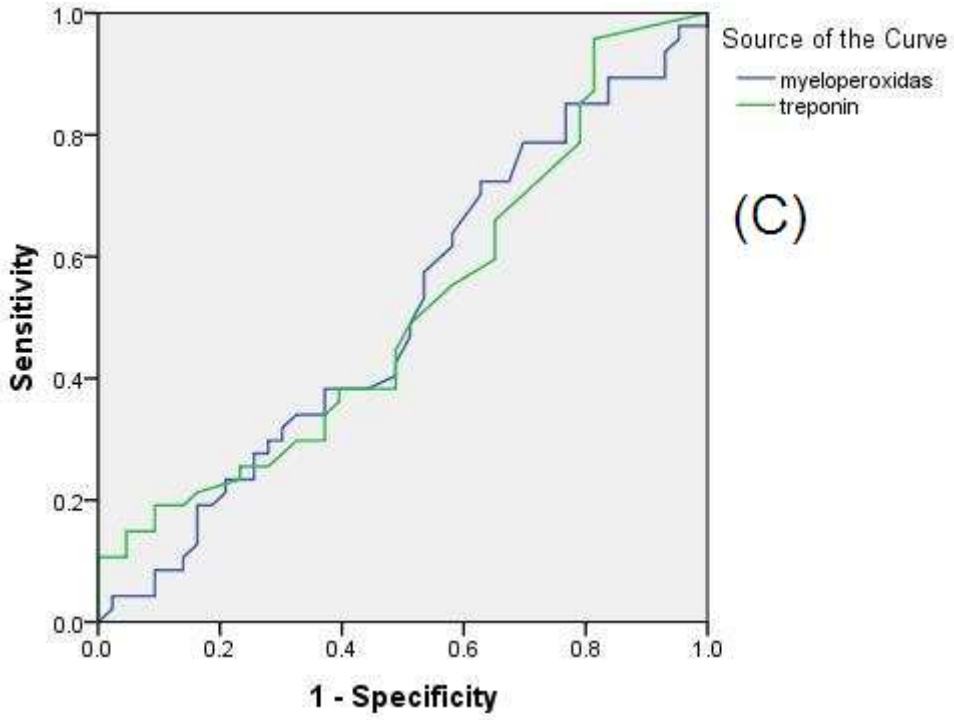


Figure (4): Receiver-operating-characteristic curves (ROC), MPO and TnI levels to predict outcomes: a) the mortality of patients b) need for revascularization c) moderate to severe decline in LVEF

In STEMI group, the mean TnI level was (3.37 ± 3.28) in patients with moderate to severe decline in LVEF versus (4.21 ± 6.35) in patients with normal or mild decline in LVEF and in NSTEMI group, was (2.96 ± 4.12) versus (1.94 ± 2.40) that it was no statistically significant.

In patients with moderate to severe decline in LVEF, AUC was equal to 0.509 (0.630 – 0.388: CI 95%) for the diagnostic value of MPO and 0.508 (0.629 – 0.387: CI 95%) for TnI. MPO cutoff was 4.20 ng/ml with the sensitivity of 43% and specificity of 52% and for TnI, it was 1.65 ng/ml with the sensitivity of 45% and specificity of 52% (Figure 4).

DISCUSSION

In the study by Brennan et al on chest pain, MPO level and Hyperlipidemia were higher in men which did not differ in our study. Meanwhile, MPO level was higher in patients who faced with mortality or MACE during 30 days and 6 months following-up and also MPO level was the predictor of revascularization in 30-days and 6-months follow-up after chest pain which was not statistically significant in our study. For MI, sensitivity and specificity from ROC curve were reported with 0.1 ng/ml < a cutoff point (0.58%, 100%) in TnI, and 198 ng/ml < a cutoff point (60.7%, 65.7%) in MPO [6].

On the other hand, in the study by Eggers et al on patients with chest pain, the median MPO level in patients with acute MI was more than that with unstable angina which was higher than that in non-cardiac patients. But MPO level was not associated with MACE in 6-months and even long-term of 4.9-years follow-up [12]. In the study by Mocatta et al, higher MPO level in patients with MI (81.19% as STEMI) was associated with mortality of patients at the onset of admission and this difference revealed more as the time passed [13] that in our study, the difference may also be revealed in long-term.

In a study, Dominguez-Rodriguez et al showed that patients who suffered from STEMI with cardiogenic shock and died in CCU had higher MPO level compared to those survived [14]. The study by Esporcatte et al revealed that in NSTEMI and unstable angina, MPO level was statistically and significantly higher than that in non-cardiac patients. For the diagnosis of AMI as 100 pg/ml, MPO level with a cutoff point obtained ROC curve was equal to area under the curve equal to 0.662 (with 0.793 – 0.532: CI 95%) with the sensitivity of 92.3% and specificity of 40.2%. However, similar to our study, MPO level had no relation to age, sex, risk factors such as HTN, DM, hyperkalemia, smoking and SBP at the onset of admission [15]. Unlike our study, in the study by Ndrepepa et al, the mean MPO level in patients with STEMI was more than that in patients with NSTEMI. In their study, MPO level was associated with hsCRP, based Creatinine, LVEF and smoking; however, there were no statistically significant differences

between STEMI and NSTEMI cases, in our study, there was difference between LVEF and smoking in the two above-mentioned groups [16]. Also, in the study by Peacock et al in patients either without complications or with MACE, the median serum MPO level in patients with STEMI has been higher than patients with NSTEMI at 30-day follow-up [17].

In TACTICS-TIMI 18 trial, it was indicated that patients with 884 pg/ml <MPO level faced with higher risk of death, Re-MI and re-hospitalization in 30-days follow-up which was not relation to ST-segment changes at all. This risk was also not related to or conservative early invasive strategy [18]. Meanwhile, MPO level was not related to TnT level and 330 micg/L < MPO level increased the risk of MACE at 6-month follow-up. MPO level was higher in the diabetes and IHD history [5]. In our study, MPO level was not related to TnI level.

In a study on NSTEMI patients in the CAPTURE trial, MPO level with cutoff point> 350 micg/ml was associated with an increase in MACE cases in a 4-year period of follow-up in which predictive ability was higher in the case of combining its results with TnT level, IL10 and PIGF (placental growth factor) [4].

Ferrante et al demonstrated that plaques with erosion have much higher MPO level than ruptured plaques [20]. This issue may explain higher MPO level in NSTEMI in our study, although the difference of MPO level between STEMI and NSTEMI was not statistically proved. IHD history had no difference in the two groups. Although some studies showed higher MPO level in stable CAD and related to the MACE [21, 22], other studies rejected it [23].

CONCLUSION

Although patients with higher TnI level were more likely to have higher rate of mortality, MPO level had no predictive ability of mortality or MACE despite studies in other countries. On one hand, MPO level had low sensitivity and specificity for predicting revascularization in making-decision on early invasive strategy; however, its reason can be related to the genetic polymorphisms or small sample size. On the other hand, its effect may be specified on long-term follow-up. Another reason may pertain to the method and type of laboratory kit because in our study, the mean MPO level was about the first quintile of the other studies.

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