Original Article

Serum Myeloperoxidase Level in Patients with Chronic Heart Failure

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Abstract

Background: Evidence suggests that the serum myeloperoxidase level has a diagnostic and predictive role in patients with chronic heart failure (CHF). We evaluated the association between the serum myeloperoxidase level and the severity and prognosis of CHF.

Patients and Methods: In a prospective observational study, patients with CHF were evaluated. The myeloperoxidase serum level was measured at baseline by enzyme-linked immunosorbent assay. Transthoracic echocardiography was done at baseline and then after 6 months. History and duration of admission and also mortality were recorded during follow-up.

Results: Fifty patients at a mean age of 64.7±1.8 years (70% male) were evaluated. The mean serum myeloperoxidase level was 51.0±6.5µg/dL. Accordingly, the patients were classified into two groups of A and B with a serum myeloperoxidase level of less and more than 51µg/dl, respectively. No differences were found between the two groups in New York Heart Association functional class (NYHA III 20.5% vs. 27.3%; p value=0.456), left ventricular ejection fraction (30.3±10.0 vs. 29.8±10.1%; p value=0.873), systolic dysfunction (48.7% vs. 54.5%; p value=0.500), or diastolic dysfunction (38.5% vs. 63.6%; p value=0.127) neither at baseline, nor at 6 months' follow-up. The serum myeloperoxidase level was not associated with admission history or mortality.

Conclusion: We found no significant association between the serum myeloperoxidase level and echocardiography parameters, admission history, or mortality in patients with CHF. Further studies with larger samples of patients are required in this regard. ***(Iranian Heart Journal 2015; 16(1):20-25)***

Keywords: ■Chronic heart failure; ■Myeloperoxidase; ■Outcome

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Heart failure (HF) affects more than 5 million people in the United States with a mortality rate of 5–10% in mild and 30–40% in severe cases.[1] The incidence and prevalence of HF is increasing worldwide, and it is the most frequent cause of hospitalization in patients older than 65 years.[1] Chronic heart failure (CHF) is a major public health problem, and understanding the factors related to its mortality and morbidity may help the better management of the disease.[2]

Cardiac biomarkers play an important role in the diagnosis and management of patients with cardiovascular diseases.[3]

Myeloperoxidase (MPO), one novel biomarker, is a leukocyte-derived enzyme that catalyzes the formation of reactive oxidants and diffusible radical species.[4] Studies have suggested that MPO provides a link between inflammation and impaired cardiac remodeling.[5] In patients with CHF, MPO has a diagnostic role and also is important in the prediction of long-term outcomes.[4,6] Elevated serum MPO levels are associated with worsening functional class in patients with CHF.[4] The MPO level is reported to be increased in stable CHF patients and is predictive of adverse clinical outcomes.[7] However, there are limited studies conducted on the MPO level and its association with the outcomes of patients with CHF. The aim of the current study was to evaluate the association between the MPO serum level and CHF severity and its complications during a 6-month follow-up of patients.

Patients and Methods

Study Population

This prospective observational study was conducted on patient diagnosed with CHF referred to the Isfahan Cardiovascular Research Institute. The inclusion criteria were comprised of age older than 18 years, New York Heart Association (NYHA) functional class II or III,[8] and left ventricular ejection fraction (LVEF) < 49%. Patients with a history of recent myocardial infarction, unstable hemodynamic status, severe valvular disease, and uncontrolled arrhythmia were not included into the study. The study was approved by the Ethics Committee of Isfahan University of Medical Sciences, and an informed consent was obtained from all the participants.

Assessments

Demographic characteristics, including age, sex, past medical history, and drug history, were recorded. To determine the MPO serum concentration, blood samples were taken at the beginning of the study. Five ml fasting blood samples were obtained. The serum samples were stored at -70°C. After sampling, the serum was separated using a centrifuge tool. The enzyme-linked immunosorbent assay (ELISA) technique was used for the determination of the serum MPO concentration according to the procedures recommended by the manufacturer (Bio Techno Lab).

All the patients underwent transthoracic echocardiography to determine the LVEF, diastolic dysfunction (DD), systolic dysfunction (VD), left ventricular end-diastolic volume (LVDV), left ventricular end-systolic volume (LVSV), and valvular problems. Six months after the enrollment of the individuals, for those who were available the NYHA functional class was evaluated and echocardiography was done again. Also histories of admission due to cardiac problems, death, or other problems such as stroke, ischemic or non-ischemic cardiomyopathy, arrhythmia, and valvular disorders were asked and recorded. All the examinations were done by the same physician using the same instruments.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows (Version 16.0, SPSS Inc., Chicago, IL, USA). The independent t-test and paired t-test (for the continuous variable) and the chi-square test (for the categorical variables) were used for comparing the variables. Statistical significance was assessed at the 0.05 probability level in all the analyses. All the values are given as mean ± standard deviation (SD or Standard Error for non-parametric data) or numbers (%).

Results

In this study, 50 CHF patients at a mean age of 64.7±13.2 years were included. Thirty-five (70%) patients were male. Of the participants, 11 (22%) had diabetes, 22 (44%) hypertension, 26 (52%) ischemic heart disease, and 8 (16%) dyslipidemia. The subjects were classified according to the NYHA classification: 39 (78%) patients had functional class II and 11 (22%) had functional class III. The drug history of the patients showed that 37 (74%) took Aspirin, 27 (54%) statins, 31 (62%) beta-blockers, 3 (6%) calcium channel blockers, 16 (32%) angiotensin- converting enzyme inhibitors, 11 (22%) angiotensin receptor blockers, 16 (32%) diuretics, and 14 (28%) Digoxin.

The mean (SE) of the serum MPO level of all the subjects was 51.0±6.5µg/dL. The MPO level in the patients with functional class II and III were 52.7±8.0 and 45.1±8.9µg/dL, respectively (p value =0.634). According to the mean of the MPO level, we classified all the subjects into two groups: group A (MPO serum level < 51 µg/dL) and group B (MPO serum level > 51 µg/dL). Groups A and B consisted of 39 (78%) and 11 (22%) patients, respectively. There was no significant difference between the two groups in age (63.9±14.4 vs. 67.2±8.1 years; p value =0.472) or sex (male 71.8% vs. 63.6%; pvalue=0.430). An MPO serum level > 51 µg/dL was associated with a higher frequency of diabetes (p value = 0.033), hypertension (p value=0.026), and ischemic heart disease (p value=0.019) (Table 1).

Table 1. Association between the serum myeloperoxidase level and the comorbidities of the patients

	Serum Myeloperoxidase Level		OR (95% CI)	P Value
	Less than 51µg/dl	†More than 51µg/dl		
Diabetes	6 (17.1%)	5 (50%)	4.83 (1.05, 22.09)	0.033
Hypertension	14 (40%)	8 (80%)	6.00 (1.10, 32.53)	0.026
Ischemic heart diseases	17 (48.6%)	9 (90%)	9.52 (1.08, 83.43)	0.019
Hyperlipidemia	6 (17.1%)	2 (20%)	1.20 (0.20, 7.17)	0.835

Data are reported as number (%). OR, Odds ratio; CI, Confidence interval; †is the selected class for calculating OR

Systolic dysfunction was present in 19 (48.7%) and 6 (54.5%) and diastolic dysfunction was present in 15 (38.5%) and 7 (63.6%) of the patients in groups A and B, respectively (p values =0.500 and 0.127, respectively). After 6 months, no change was seen in the systolic and diastolic dysfunction distribution of the subjects. According to Table 2, there were no significant differences between the two groups in the comparison of the EF, LVDV, and LVSV (p values =0.873, 0.679, and 0.750, respectively) at baseline. After 6 months, there were no significant differences regarding these variables (p values = 0.763, 0.506, and 0.503, respectively) or their changes (p values =0.248, 0.516, and 0.978, respectively) between the two groups. The serum MPO level was not associated with admission history or mortality during the 6 months' follow-up period.

Table 2. Association between the serum myeloperoxidase level and cardiac parameters at baseline and after 6 months' follow-up

	Serum myeloperoxidase level		
	Less than 51 µg/dl	**More than 51 µg/dl**	***P Value**
Ejection fraction (%)			
First day	30.3±10.0	29.8±10.1	0.873
After 6 months	32.1±10.9	30.6±10.7	0.763
**P Value	0.752	0.118	
Increasing	0.42±1.32	3.80±2.01	0.248
LVDV, mL			
First day	148.6±47.1	156.5±63.3	0.679
After 6 months	144.7±50.1	129.9±37.5	0.506
**P Value	0.198	0.361	
Decreasing	11.49±8.65	25.65±24.89	0.516
LVSV, mL			
First day	100.3±44.4	106.3±69.1	0.750
After 6 months	80.0±40.3	92.5±40.4	0.503
**P Value	0.002	0.393	
Decreasing	22.93±6.54	23.42±24.48	0.978

Data are given as mean±SD, *P-value is calculated by the independent t-test,
** P-value is calculated by the paired t-test, LVDV, Left ventricular end-diastolic volume; LVSV, Left ventricular end-systolic volume

Table 3. Association between the serum myeloperoxidase level and admission history during the 6 months' follow-up

	Serum Myeloperoxidase Level		
	Less than 51 µg/dl	**More than 51 µg/dl**	**P Value**
Hospital admission	29 (74.4%)	10 (90.9%)	0.232
Admission duration, day	3.89±0.99	4.40±1.26	0.206
Mortality	3 (7.7%)	0 (0.0%)	0.343

Data are given as mean±SD or numbers (%)

Discussion

The aim of the current study was to evaluate the association between the serum MPO level and the severity and outcome of CHF during a 6-month period. According to our results, the serum MPO level was the same in patients with the NYHA functional classes II and III. Also, no association was found between the serum MPO level and echocardiography parameters, admission history, or mortality in the CHF patients. We found only an association between the serum MPO level > 51 µg/dL with comorbidities such as diabetes, hypertension, and ischemic-heart disease. The MPO serum level indicates an inflammatory process associated with oxidative stress. The oxygen species will cause ventricular injuries. Studies have shown that diseases such as diabetes and hypertension are associated with such inflammatory processes, and this chimes in with our results.[9] Also studies have revealed that the serum MPO level is associated with the incidence of the acute coronary syndrome.[10-12]

Some previous studies have shown that the serum MPO level is significantly higher in patients with CHF. They also have reported that patients with a higher NYHA class have significantly higher serum levels of MPO,[4,13] but our results did not show the same difference between the NYHA class II and class III. We found no association between the MPO level and systolic or diastolic dysfunction or EF. In a study conducted on non-HF individuals, the results showed that the MPO level is associated with LV dysfunction.[14] Also, we found no association between the serum MPO level and admission history during the 6-month follow-up. In contrast to our results, Tang et al.[15] showed that elevated levels of plasma MPO are

associated with more advanced HF. These authors also reported that elevated MPO levels are associated with increased adverse clinical outcomes. Some studies have reported that the MPO level is a marker of risk prediction in HF. Studies have reported that the MPO level is predictive of future long-term outcomes and is highly diagnostic.[4, 6] According to our results, the MPO level was not associated with the mortality rate after 6 months in CHF patients; however, our study sample size was small and its follow-up was short in this regard. A study conducted by Reichlin et al.[7] revealed that the MPO serum level is an independent predictor of one-year mortality in patients with acute HF.[7] Previous studies have divided the plasma MPO level into quartiles and tertiles.[4,15] Nevertheless, given our small sample size, we divided them into two groups of more/lower than the mean of the study sample. Also, the mean plasma MPO level in the previous studies [15] was much higher than that in the current study (431±337µg/dL).

There are some limitations to our study. Our study sample size was small and the follow-up duration was not long enough to evaluate some outcomes such as mortality.

Conclusions

We found no significant association between the serum MPO level and echocardiography parameters, admission history, or mortality in our patients with CHF. Further studies with larger samples of patients are required in this regard. We found only an association between the serum MPO level > 51 µg/dL and comorbidities including diabetes, hypertension, and ischemic-heart disease. Further studies with larger samples of patients and longer follow-up periods are required in this regard.

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