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Original Article

Relation of monocyte-to-HDL-cholesterol ratio with prognosis in patients with pulmonary embolism

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Abstract

Background: Pulmonary embolism is a thromboembolic disease with high rates of morbidity and mortality. Monocyte-to-HDL-cholesterol ratio (MHR) can show the inflammatory status of patients. The objective of this study was to investigate the relationship of monocyte-to-HDL-cholesterol ratio, which is a new marker in predicting the prognosis of cardiovascular diseases, with prognosis and Pulmonary Embolism Severity Index (PESI) test in patients with pulmonary embolism.

Methods: Patients followed-up with the diagnosis of pulmonary embolism in our hospital between January 2016 and December 2018 were included in this study. Patients' demographic data such as age and gender, vital findings, hemogram outcomes at admission, lipid profiles, liver function tests, renal function tests, electrolyte values and cardiac markers were recorded and analyzed. Patients' pulmonary embolism (PE) clinical classes were determined and PESI test values were calculated. The correlations between monocyte-to-HDL-cholesterol ratio, PE severity and PESI test were analyzed.

Results: A total of 50 patients followed up in our hospital due to PE were included in the study. Of all patients 8% (n=4) were diagnosed with massive, 32% (n=16) sub-massive and 60% (n=30) non-massive PE. There was a positive correlation between MHR and PE severity, and MHR and PESI index, although these correlations were not statistically significant (r=0.011, p=0.940; r=0.043, p=0.767). Of all patients included in this study, one patient (2%) died in the hospital and 49 patients (98%) were discharged with recovery.

Conclusions: Although there were positive correlations between monocyte-to-HDL-cholesterol ratio, which is an inexpensive marker easily available in all centers, and the severity of acute pulmonary embolism and PESI test, these correlations were not statistically significant. Monocyte-to-HDL- cholesterol ratio may not be related to PE, however, further longitudinal studies are needed to clarify this finding.

Keywords: HDL, monocytes, pulmonary embolism

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Introduction

Pulmonary embolism (PE) is an acute thromboembolic disease with high rates of morbidity and mortality [1,2]. According to a study from the USA, 42 million deaths occurred within 20 years with 600.000 (1.5%) of these being due to PE [3]. As in many emergencies, an early and correct diagnosis is vital in PE. However, since clinical features of PE are not specific, it is not easy to establish the diagnosis of PE. The rate of mortality decreases below 10% if the diagnosis is established correctly and in an early stage in PE [4].

Various indexes have been developed for the classification of risks and predicting mortality in PE patients. Among these, the pulmonary embolism severity index (PESI) and recently recommended simplified pulmonary embolism severity index (sPESI) are quite beneficial recommended and validated tools in predicting mortality and prognosis of PE patients [5]. PESI test has been introduced as a prognostic and predictive index in 2005, and studies have shown that this model can determine low-risk patients who can be treated on an outpatient basis [6]. Because PESI test is calculated based on numerous parameters and it is difficult to be performed in an emergency setting, Jimenez et al. recommended its simplified form (sPESI) in 2007 [7].

Venous thromboembolism, which results in PE, causes a series of inflammatory reactions in the pulmonary arterial wall with the increased cellular flow and release of cytokines and chemokines [8]. Therefore, studies are investigating the effectiveness of various inflammatory markers in the determination of vascular inflammation. Studies have reported that systemic inflammation resulted from PE will be determined with neutrophils/lymphocytes ratio (NLR) in the near future, and NLR will be used in predicting mortality in PE [9].

One of the recently recommended parameters in the determination of systemic inflammation is monocyte-to-HDL-cholesterol ratio (MHR). As a source of various cytokines and molecules, monocytes interact with circulating platelets and endothelial cells, causing accumulation of inflammatory, and pro-thrombotic pathways [10]. Whereas HDL-C eliminates these pro-inflammatory and pro-oxidant effects of monocytes by inhibiting the migration of macrophages. Therefore, MHR can show the inflammatory status of a patient. Previous studies have investigated MHR as a novel cardiovascular prognostic marker [11,12]. However, the number of studies investigating the effectiveness of MHR in predicting prognosis and severity of PE is limited.

The objective of this study was to investigate the relationship of MHR, which is a new marker in predicting the prognosis of cardiovascular diseases, with prognosis and PESI test in patients with pulmonary embolism.

Methods

This study was designed as a retrospective cohort study. Patients followed-up and treated with the diagnosis of PE in our hospital between January 2016 and December 2018 were included in the study. Patient files were screened via the hospital registry system and patient's data were retrospectively screened and recorded. Patients' demographic data such as age and gender, vital findings, hemogram outcomes at admission (hemoglobin, neutrophils, platelets, lymphocytes, monocytes), lipid profiles (triglycerides, HDL, LDL), liver function tests (ALT, AST, albumin), renal function tests (urea, creatinine), electrolyte values (magnesium, calcium, phosphorus) and cardiac markers (troponin I) were recorded and analyzed. In addition, echocardiography (ECG) findings, blood gas values and patient outcomes at follow-up (follow-up in ward, referral to intensive care, exitus) were also recorded.

Patients' pulmonary embolism (PE) clinical classes were determined and PESI test values were calculated. PE severity was determined in accordance with the Turkish Thoracic Society Thromboembolism Guidelines and classified based on ECG findings as massive (high risk), sub-massive (moderate risk) and non-massive (low risk) [13]. Accordingly; patients with hypotension refractory to treatment were considered as massive PE, those with normal systemic blood pressure, but right ventricular dysfunction on echocardiography as sub-massive PE, and patients with normal systemic blood pressure and right ventricular function as non-massive PE.

Pulmonary Embolism Severity Index (PESI)

PESI scores of all patients included in the study were calculated as described by Aujesky et al. [6]. This index is calculated using 11 parameters including age, gender, history of cancer, heart failure and chronic pulmonary disease, heart rate, systolic blood pressure, respiratory rate, fever, altered mental status and oxygen saturation. The total score that can be obtained from this scale varies between 1 and 330. Based on the calculated score, patients are divided into five risk groups as I: 0-65 points, II: 66-85 points, III: 86-105 points, IV: 106-125 points and V: 126-330 points. PESI scale was developed to support clinicians in the determination of PE patients who can be treated on an outpatient basis.

Ethics Statement

Before the beginning of the study, the study protocol was approved by the local ethics committee of our hospital. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Statistical analysis

Data obtained in this study were analyzed using PASW 20 (SPSS/IBM, Chicago, IL, USA) statistical software. Descriptive statistics such as frequency distribution, mean and standard deviation were used to describe the sample. The difference of two independent group means was investigated with student t-test and differences among more than two groups with variance analysis where parametric test assumptions were met. Non-parametric alternatives of these tests, namely Mann-Whitney U and Kruskal-Wallis tests were used where parametric test assumptions were not met. Categorical data were analyzed with Chi-square or Fisher's Exact test. $p<0.05$ values were considered statistically significant at a 95% confidence interval.

Results

A total of 50 patients followed-up and treated with the diagnosis of PE were included in this study. The mean age of the patients was 59.2 (16.6) years (range: 19-86). Of all patients, 32 (64%) were female and 18 (36%) were male. Massive PE was found in 8% (n=4), sub-massive PE in 32% (n=16) and non-massive PE in 60% (n=30) of the patients [Figure 1].

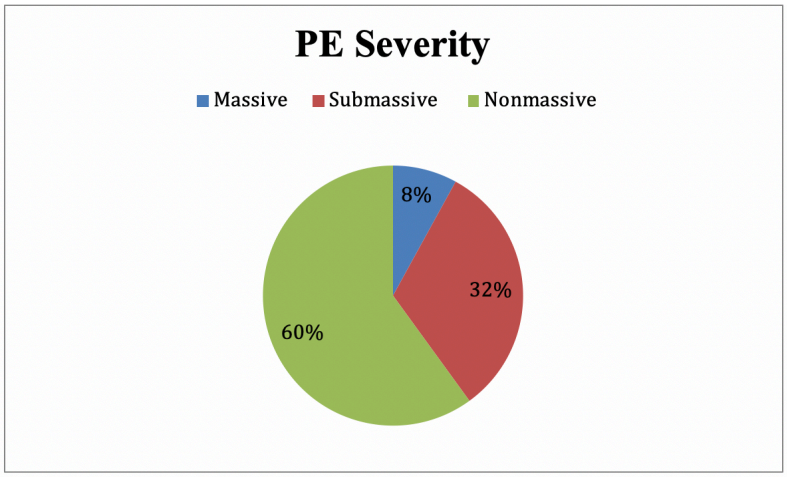

Figure 1. Distribution of pulmonary embolism severity

When comorbidities of the patients were examined; hypertension was found in 25 patients (50%), cancer in four patients (8%), COPD in 12 patients (24%), chronic heart failure in 13 patients (26%), diabetes mellitus in 14 patients (28%), coronary artery disease in 23 patients (46%), deep vein thrombosis in 15 patients (30%) and blood disorder in 20 patients (40%). 52% of the patients (n=26) used statins. PESI test scores of the patients are given in Table 1.

Table 1. PESI test values of the patients

PESI Index	n	%
1	25	50
2	17	34
3	5	10
4	2	4
5	1	2

PESI: Pulmonary Embolism Severity Index.

When biochemical laboratory outcomes of the patients were evaluated; the mean glucose value was found as 136.90 ± 69.64 mg/dL, creatinine as 0.92 ± 0.50 mg/dL, ALT as 26.64 ± 33.48 U/L, AST as 23.54 ± 12.35 U/L, GGT as 48.56 ± 56.09 U/L, ALP as 100.48 ± 94.92 U/L, WBC as 10646.02 ± 4366.41 10e3/ul, hemoglobin as 12.54 ± 1.99 g/dL, hematocrit as 39.96 ± 5.69 and platelet as 284.008.00 ± 104.851.8 10e3/ul. Lipid profiles of the patients showed the following mean values: LDL 115.03 ± 33.73 mg/dL, total cholesterol 187.30 ± 45.56 mg/dL and triglycerides 71.06 mg/dL. The mean pulmonary artery pressure was found as 42.08 ± 13.67 mmHg, systolic blood pressure as 126.60 ± 23.79 mmHg and diastolic blood pressure as 76.02 ± 11.21 mmHg. Among cardiac markers, the mean value of troponin I was found as 0.064 ± 0.205 ng/mL. The mean d-dimer value was found as 659.96 ± 523.30 ng/mL [Table 2].

Table 2. Clinical features of the patients

	Mean	Standard deviation	Minimum	Maximum
LDL (mg/dL)	115.03	33.73	66.0	192.40
Total cholesterol (mg/dL)	187.3	45.56	111.0	283.0
Triglycerides (mg/dL)	145.22	71.06	58.0	438.0
Pulmonary artery pressure (mmHg)	42.08	13.67	20.0	65.0
Pulse	94.72	17.20	58.0	130.0
Systolic blood pressure (mmHg)	126.6	23.79	95.0	190.0
Diastolic blood pressure (mmHg)	76.02	11.21	60.0	95.0
Troponin (ng/mL)	0.06	0.20	0.0	1.28
d-dimer (ng/mL)	659.96	523.3	80.0	2819.0
PO2 (mmHg)	70.46	16.59	41.20	95.90
PCO2 (mmHg)	38.94	6.67	27.9	55.9
HCO3 (mmol/L)	25.56	3.95	14.40	34.60
pH	7.42	0.5	7.23	7.55
SAT (%)	88.65	5.0	74.8	96.9

LDL: Low density lipoprotein, PO2: Partial oxygen pressure, PCO2: Partial carbon dioxide pressure, HCO3: Bicarbonate, pH: Potential hydrogen, SAT: Oxygen saturation.

There was a positive correlation between MHR and PE severity, and between MHR and PESI index, although these correlations were not statistically significant (r=0.011, p=0.940; r=0.043, p=0.767). The linear correlation between MHR and other variables are given in Table 3. Of all patients included in this study, one patient (2%) died in the hospital and 49 patients (98%) were discharged with recovery.

Table 3. The correlation analysis between MHR and other variables

	r	p
PE severity	0.011	0.940
PESI index	0.043	0.767
d-dimer	-0.134	0.354
PO2	0.110	0.448
PCO2	-0.04	0.978
HCO3	0.141	0.328
pH	0.214	0.136
SAT	0.058	0.687
Pulmonary artery pressure	0.055	0.799

PE: Pulmonary embolism, PESI: Pulmonary Embolism Severity Index, PO2: Partial oxygen pressure; PCO2: Partial carbon dioxide pressure, HCO3: Bicarbonate, pH: Potential hydrogen, SAT: Oxygen saturation.

Discussion

In this study, we investigated the relationship between MHR, which is among readily available laboratory markers, and the severity of PE and PESI test. In our study, 8% (n=4) of the patients were diagnosed with massive PE, 32% (n=16) patients with sub-massive PE and 60% (n=30) patients with non-massive PE.

Acute PE is a disease with significant morbidity and mortality. Studies have reported the rate of mortality due to PE between 8% and 30% [14]. In our study, one patient died in the hospital. We think that a lower rate of mortality in our study compared to the literature resulted from the small number of patients with massive PE.

Timely evaluation and treatment are the mainstays of successful outcomes in PE patients. However, some patients may present as asymptomatic depending on the localization of thrombus [15]. In addition, standard evaluation methods used for the diagnosis of PE may be time-consuming, and this causes delays in the diagnosis and initiation of the treatment. Therefore, research is continuing on novel markers that can be simply used in PE patients.

The most widely recommended mechanism in order to explain the relationship between PE and hematological parameters is inflammation. Inflammation plays a primary role in the pathophysiology of PE [16]. In inflammatory diseases, monocytes counts increase, while HDL-C levels decrease. Monocytes are a distinct type of leukocytes, migrate to the tissue macrophages and initiate inflammation. Previous studies have found that monocyte count is associated with the prediction of coronary artery disease [17].

On the other hand, HDL-C inhibits the activation of monocytes, prevents the transformation of monocytes to macrophages and decreases inflammation. In conclusion, the combination of these two parameters as MHR is thought to represent an inflammatory process. This relationship between monocytes and HDL-C has led researchers to investigate whether MHR is more effective than monocyte count or HDL-C alone in predicting cardiovascular events.

Kanbay et al. reported that MHR acts as an independent predictor for cardiovascular events and increases in parallel with the decrease in eGFR in patients with chronic kidney disease [18]. It has been proposed that MHR is associated with systemic infection and endothelial dysfunction, and it can be used as a novel inflammation-based diagnostic and prognostic marker in cardiovascular diseases [18,19]. In a study by Pamukcu [20], MHR was associated with mitral annulus calcification. MHR has also been associated with blood flow-mediated brachial artery dilatation in patients with Behcet's disease [21]. Taken together these findings, the predictive value of MHR for cardiovascular diseases is increasing in chronic inflammatory diseases such as pulmonary embolism. In a study by Dolapoglu et al. [22] investigating the effect of MHR on postoperative outcomes following coronary bypass surgery, MHR was found to be higher among patients who developed PE among postoperative outcomes. Canpolat et al. [23] reported that MHR was associated with adverse cardiac events and increased mortality following coronary angiographic intervention in patients with ST-elevation MI (STEMI). In a study investigating prognostic value of MHR in predicting short term mortality in patients with acute PE, 26 of 99 patients (25.2%) died within the first month of the diagnosis and MHR was found to be significantly higher in these patients. The authors found that MHR was an independent predictor of mortality in patients with acute PE [8].

In a study by Zhu et al. preoperative MHR value was significantly higher in patients who developed acute deep vein thrombosis following total joint arthroplasty [24].

In the present study, we evaluated the correlations of MHR with the severity of PE and PESI index. We found that the severity of PE and PESI test increased as MHR increased. However, no statistically significant correlation was found with Spearman's correlation analysis. Nevertheless, because the number of studies investigating the predictive value of MHR in acute PE is limited, our findings should be evaluated with further multicenter comprehensive studies.

Limitations

This study has several limitations. The study was designed as an observational, retrospective and single-center study. In addition, repeating MHR measurements with certain intervals possibly would affect the results. We could not compare MHR with the other markers used in pulmonary embolism. Finally, we could not make a comparison between the patients using statins and those not using in order to avoid the confounding effect of statins on HDL-C values. Further comprehensive studies are needed to better clarify this relationship.

Conclusion

In conclusion, although there were positive correlations between MHR, which is an inexpensive marker readily available in all centers, and the severity of PE and PESI test, these correlations were not statistically significant. We believe that these relationships will be better enlightened with further prospective and comprehensive multi-center studies.

Conflict of interest

The authors declare that they have no competing interests with regards to authorship and/or publication of this paper.

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