ARAŞTIRMA MAKALESİ / *Research Article*

DOI: 10.5505/sakaryamedj.2015.30164

The Prognostic Value of The Platelet/Lymphocyte Ratio in Predicting Short-Term Mortality in Patients with Acute Pulmonary Embolism

Akut Pulmoner Emboli Tanısı Almış Hastalarda Platelet/Lenfosit Oranının Kısa Dönem Mortaliteyi Ön Gördürmedeki Prognostik Değeri

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Abstract

Objectives: *Pulmonary embolism (PE), which has an inflammatory component, has high mortality and morbidity rates. The platelet/lymphocyte ratio is a novel marker of inflammation that is an independent predictor of mortality in cardiac and various oncological diseases. The aim of the present study was to determine the prognostic value of the platelet/lymphocyte ratio for short-term mortality for patients with acute pulmonary embolism.*

Materials and Methods: *A total of 290 patients who were admitted to the emergency department and diagnosed with acute PE were enrolled retrospectively. Acute pulmonary embolism was confirmed via multislice computerized tomography.*

Results: *Of the 290 patients, 53 (18.2%) died within 1 month after the diagnosis was made. Age, malignancy, coronary artery disease, right ventricular dilatation, hemoglobin, white blood cell, neutrophil, and platelet counts, systolic pulmonary artery pressure, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and pulmonary embolism severity index were significantly higher in group 1 than in group 2. The platelet/lymphocyte ratio, hemoglobin, and simplified pulmonary embolism severity index were independent predictors of mortality in patients with acute pulmonary embolism. A platelet/lymphocyte ratio of more than 176.31 predicted the presence of mortality within 30 days after acute pulmonary embolism with a sensitivity of 79% and a specificity of 70%.*

Conclusion: *Platelet/lymphocyte ratios were higher in patients who died within 30 days of PE than those who did not. An inexpensive and practical parameter such as the platelet/lymphocyte ratio might be useful in mortality risk prediction in acute pulmonary embolism.*

(Sakarya Med J 2015, 5(4):204-208)

Keywords: *Platelet/lymphocyte ratio; pulmonary embolism; mortality*

Özet

Amaç Pulmoner emboli yüksek mortalite ve morbidite oranları ile inflamatuvar bileşeni iyi bilinen bir hastalıktır. Platelet / lenfosit oranı, kalp ve çeşitli onkolojik hastalıklarda mortalitenin bağımsız belirleyicisi olan inflamasyonun yeni bir belirtecidir. Bu çalışmanın amacı, akut pulmoner emboli hastalarında kısa süreli mortalite için platelet / lenfosit oranının prognostik değerini belirlemektir.

Materyal ve Metot: Acil servise başvuran ve akut PE tanısı toplam 290 hasta çalışmaya retrospektif olarak alındı . Akut pulmoner emboli çok kesitli bilgisayarlı tomografi ile teyit edildi.

Bulgular: Pulmoner emboli tanısı alan 290 hastanın, tanı aldıktan sonra 53'ü (%18,2) 1 ay içinde öldü. Yaş, malignite, koroner arter hastalığı, sağ ventrikül dilatasyonu, hemoglobin beyaz kan hücresi nötrofil ve trombosit sayımları sistolik pulmoner arter basıncı nötrofil / lenfosit oranı platelet / lenfosit oranı ve pulmoner emboli ciddiyet indeksi grup 1'de grup 2'ye göre anlamlı derecede yüksek bulundu. Platelet / lenfosit oranının 176.31 ve üzerinde olması akut pulmoner emboli sonrası 30 günlük mortaliteyi predikte ettirmedeki duyarlılığı %79 ve özgüllüğü %70'ti. Platelet / lenfosit oranı, hemoglobin ve basitleştirilmiş pulmoner emboli ciddiyet indeksi, akut pulmoner emboli tanısı almış hastalarda mortalitenin bağımsız bir belirleyicisiydi.

Sonuç: Platelet / lenfosit oranı, pulmoner emboli sonrası erken dönemde mortalite gelişen hastalarda, mortalite gelişmeyenlere göre daha yüksekti. Bu sebeple, platelet / lenfosit oranı gibi ucuz ve pratik bir parametre akut pulmoner embolide mortalite risk tahmininde kullanılabilir. ***(Sakarya Med J 2015, 5(4):204-208)***

Anahtar Kelimeler: Platelet / lenfosit oranı, pulmoner emboli, mortalite

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Geliş Tarihi / *Received* : 07.12.2015

Kabul Tarihi / *Accepted* : 13.11.2015

INTRODUCTION

Pulmonary embolism (PE) is a well-known condition with high mortality and morbidity rates. The annual incidence has been reported to be 60–70/100 000, and PE is a common cause of in-hospital deaths[1]. Thus, early predictors of mortality should be found in patients with PE.

Currently, hemodynamic instability, massive thrombus burden, and right ventricular dysfunction are commonly used as prognostic indicators[2-4]. Brain natriuretic peptide (BNP) and N-terminal brain natriuretic peptide (NT-proBNP) that can suggest right ventricular dysfunction are also used for prognosis[5]. Recent guidelines demonstrated that the simplified pulmonary embolism severity index (sPESI) score could be useful for the prediction of prognosis and mortality in patients with acute PE[6].

A venous thromboembolism with resulting PE triggers an inflammatory reaction characterized by cytokine and/or chemokine increase and inflammatory cell flow in the pulmonary arterial wall[6]. In this context, biochemical and hematological markers of systemic embolism may also be used for prognosis in PE.

Systemic inflammation can be evaluated with markers as C-reactive protein (CRP), albumin, and the neutrophil/lymphocyte ratio (NLR)[7]. The NLR is associated with mortality in patients with PE[8]. Recently, it has been reported that the platelet/lymphocyte ratio (PLR) is a potential marker of inflammation that is an independent predictor of mortality in cardiac and various oncological diseases[9-13]. In this study, we investigated whether the PLR was associated with mortality after acute PE and had a predictive value for mortality in patients with acute PE.

MATERIALS and METHODS

A total of 290 patients who were admitted to the emergency department and diagnosed with acute PE between October 2012 and February 2014 were enrolled retrospectively in this study. The diagnosis of acute PE was confirmed with multislice computed tomography (MSCT) (Toshiba multislice Aquilion 16 system, Toshiba Medical Systems, Otawara, Japan) in the radiology clinic, using the PE protocol (field of view: 35 cm, section thickness: 3 mm, pitch: 2, and intravenous 120 mL contrast material). The pulmonary arteries, their branches, and lung parenchyma were evaluated in detail. Ventilation-perfusion scintigraphy was not used for diagnosis because this diagnostic test is impractical in an emergency department. The study was approved by the local ethics committee. Patients with hematological (white blood cell < 3.0 K/μL or > 25.0 K/μL), infectious, or inflammatory diseases or severe renal or hepatic disease were excluded from the study. Patients who died after acute PE within 30 days are described as group 1, and the patients who survived after acute PE within 30 days are described as group 2.

Basal clinical characteristics and laboratory parameters were reviewed in the patients' files by using the hospital's electronic database. Laboratory parameters, including complete blood count (CBC), routine biochemistry, and cholesterol panel were recorded for all study participants. For CBC analysis, an automatic blood counter (A Cell-Dyn 3500, Abbot, IL, USA) was used. The blood samples were routinely centrifuged, and serum samples were collected and analyzed with an Immage 800 (Beckman Coulter Inc, CA, USA). The PLR was calculated as the ratio of platelets to lymphocytes in peripheral blood.

All patients or respective relatives were contacted via telephone and were queried regarding 30-day mortality.

Statistical Analysis

Statistical analysis was performed with SPSS 17.0 Statistical Package for Windows (SPSS Inc, Chicago, IL, USA). The median and standard deviation of the continuous variables were given, and the categorical variables were defined as percentages. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Categorical variables were compared with the chi-square test. The Student t-test was used to compare continuous variables, and the Mann-Whitney U test was used to compare noncontinuous variables. To define the relationship between short-term mortality after acute PE and possible confounding factors, multiple logistic regression analysis was performed. The receiver operating characteristics (ROC) curve was used to demonstrate the sensitivity and specificity of the PLR and the optimal cut-off point for predicting short-term mortality after acute PE. A value of $p < 0.05$ was

accepted as statistically significant.

RESULTS

The demographic, clinical, and laboratory characteristics of group 1 and group 2 are shown in Table 1. The basal patient characteristics, age, malignancy, coronary artery disease, right ventricular dilatation, hemoglobin, white blood cell, neutrophil, and platelet counts, systolic pulmonary artery pressure, sPESI, NLR, and PLR were significantly higher in group 1 than group 2 ($p<0.001$, $p=0.025$, $p=0.024$, $p=0.011$, $p=0.069$, $p=0.025$, $p=0.019$, $p=0.026$, $p=0.003$, $p<0.001$, $p<0.001$, and $p<0.001$, respectively). Diastolic blood pressure was significantly higher in group 2 than group 1 ($p=0.046$). Forty (13.7%) patients who were diagnosed with high-risk PE received thrombolytic therapy. The remaining 248 (85.5%) patients received low molecular weight heparin therapy. Fifty-three (18.2%) of the 290 patients had died within 1 month after the diagnosis was made. Nine (16.9%) of them had received applied thrombolytic therapy. One patient died after thrombolytic therapy because of major bleeding. Forty-one patients (77.3%) died during hospitalization, and 12 patients (23.7%) died after discharge.

In the ROC curve analysis, a PLR of more than 176.31 predicted the presence of mortality within 30 days after acute PE with a sensitivity of 79% and a specificity of 70% (Figure 1).

Multivariate logistic regression analyses showed that hemoglobin, PLR > 176.31, and sPESI > 2.5 were independent predictors of mortality ($p=0.045$, $p<0.001$, and $p=0.039$, respectively; Table 2).

DISCUSSION

Previous studies have reported that the neutrophil/lymphocyte ratio in patients with acute PE predicts mortality (8, 15). The present study showed that the PLRs of group 1 were significantly higher than those of group 2. Studies have demonstrated that the PLR predicts mortality in various cardiac and oncological diseases (9-12, 16-19). In the present study, the PLR was an independent predictor of 30-day mortality after acute PE as well as hemoglobin levels and the sPESI. PLR>176.31 had acceptable sensitivity and specificity of 79% and 70%, respectively, according to the ROC analysis.

Previous studies demonstrated that right ventricular dilatation was associated with mortality in patients with acute PE[20]. Right ventricular dysfunction may lead to platelet activation by impairing left ventricular filling and reducing cardiac output[21]. This in turn leads to reduced excretion of platelet-activating mediators and increased platelet activation by interfering with renal and hepatic perfusion[22]. Vasoconstrictor agents such as thromboxane that are released from platelets heighten pulmonary vascular resistance and worsen right ventricular ischemia and dysfunction[23]. Activated platelets facilitate monocyte adhesion and transmigration by inducing the release of inflammatory mediators from endothelial cells and leucocytes and thus worsen the inflammatory state[24,25]. In addition, the expression of plasminogen activator inhibitor-1, a potent inhibitor of fibrinolysis, is directly proportional to the platelet count. Therefore, a high platelet count may indirectly create a tendency for a thromboresistant state[26]. In the present study, the platelet levels were higher in group 1, and right ventricular dilatation was frequently observed in group 1.

Zhou et al. concluded that the PESI has discriminative power to predict short-term mortality and adverse outcome events in patients with acute pulmonary embolism[4]. In the present study, the sPESI was also related to short-term mortality, but sPESI>2.5 was an independent predictor of mortality after logistic regression analysis.

Acanfora et al. compared basal relative lymphocyte counts in patients older than 65 years of age who had congestive heart failure. Patients with a lower basal relative lymphocyte count had a higher 3-year all-cause mortality[27]. Thrombocytosis and lymphopenia are correlated to the degree of systemic inflammation, and a PLR that involves both hematological factors was presented as a novel inflammatory marker[28].

Kundi et al. showed that a high PLR is independently associated with a high risk of mortality in patients with acute PE[29]. In another study, Celik et al. demonstrated that the PLR is higher in patients with PE[30]. Similar to Kundi et al., in the present study, a higher PLR (PLR>176.31) was an early predictor of mortality in patients with PE (sensitivity of 79% and specificity of 70%).

This study has several major limitations. First, it was an observational, single-center, retrospective study. Second, the PLR could not be compared with any of the inflammatory markers such as C-reactive protein, fibrinogen, and myeloperoxidase since they were not studied. Moreover, the long-term outcomes of the discharged patients are unknown. Finally, no autopsy procedure was performed to verify the cause of death in the PE-related deaths.

In conclusion, this study investigated the relationship between the PLR and short-term mortality after acute PE. The results of this study showed that the PLR is an independent predictor of mortality among patients diagnosed with acute PE. These results are encouraging regarding the use of the PLR in risk prediction in acute PE as an inexpensive, readily available, and practical parameter. Other large-scale, randomized, prospective studies are needed to better clarify the role of the PLR in the pathophysiology of PE.

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