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The relation between platelet-to-lymphocyte ratio and Pulmonary Embolism Severity Index in acute pulmonary embolism

Harun Kundi, MD *, Ahmet Balun, MD, Hulya Cicekcioglu, MD, Mustafa Cetin, MD, Emrullah Kiziltunc, MD, Zehra Guven Cetin, MD, Candan Mansuroglu, MD, Ender Ornek, MD

Department of Cardiology, Ankara Numune Education and Research Hospital, Ankara, Turkey

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ABSTRACT

Purpose: In this study, we aimed to investigate the value of the platelet-to-lymphocyte ratio (PLR) for predicting disease severity based on simplified Pulmonary Embolism Severity Index (sPESI), as well as in-hospital mortality in patients with acute pulmonary embolism (APE).
Materials and methods: Our hospital's electronic patient database was searched for the patients with ICD-9 code I26, and eligible 646 patients were included in the study.
Results: Univariate logistic regression analysis showed that PLR, pulmonary artery systolic pressure, right ventricular dysfunction, D-dimer level, and white blood cell, lymphocyte, platelet and neutrophil counts were significantly correlated with a high sPESI score in patients with APE.
Conclusions: To the best of our knowledge, this is the first study in the literature showing that a high PLR is independently associated with a high risk of mortality in patients with APE.

Introduction

Acute pulmonary embolism (APE) is a frequently seen disease associated with significant short- and long-term complications, and a mortality rate of 15–20%.[1] Therefore, identifying clinical prognostic markers for the disease is important.

Pulmonary Embolism Severity Index (PESI) is a validated clinical prognostic model for patients with APE.[2] Recently, Jimenez et al developed a simplified version of the PESI (sPESI), based on a study in which they reported that APE patients classified as low sPESI score had an in-hospital mortality of 1.1% compared to 8.9% in those classified as high sPESI score.[3]

Platelet activation and secretion of active chemokines play important roles in APE.[4] Previous studies have shown an association between major adverse cardiovascular outcomes, and both high and low platelet and lymphocyte counts.[5–7] In addition, the diagnostic and prognostic utility of a low lymphocyte count was noted in patients with myocardial infarction and chronic coronary artery disease.[8,9] Platelet-to-lymphocyte ratio (PLR) is a new prognostic marker that integrates those two parameters for risk prediction. It gives information about both aggregation and inflammatory pathways, and it may be more valuable than either platelet or lymphocyte count alone in prediction of thromboembolic events.[10] It was shown to predict critical limb ischemia in peripheral artery disease,[11] and shown to be strongly associated cardiovascular diseases.[12,13]

Since both inflammation and endothelial damage play role in the pathogenesis of APE, we aimed to investigate the value of PLR for predicting in-hospital mortality, and disease severity, as reflected by sPESI scores in patients with APE. To the best of our knowledge, this is the first study in the literature that investigated the prognostic utility of PLR in patients with APE.

Materials and methods

Our hospital's electronic patient database was searched for the patients with ICD-9 code I26, and a total of 710 patients were found. The data of the patients were analyzed. Sixty-four patients were excluded due to incomplete data, or presence of inflammatory diseases, rheumatologic diseases, or severe renal/liver disease. A total of 646 patients were included in the study. The study protocol was approved by Ankara Numune Education and Research Hospital's Ethics Committee.

The diagnosis of APE was confirmed in all patients with computerized tomography (CT) angiography that showed a partial intraluminal defect surrounded by contrast medium or complete occlusion of a pulmonary artery in two consecutive CT sections. All

* Corresponding author. Tel.: +90 532 352 93 93.
E-mail address: harunkundi@hotmail.com (H. Kundi).

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patients included had transthoracic echocardiography within 48 h of hospitalization, and pulmonary artery systolic pressure (PASP) was calculated using continuous-wave Doppler method. Tricuspid annular plane systolic excursion (TAPSE) was used to screen right ventricular (RV) dysfunction, and a value ≤15 mm was considered as RV dysfunction.

For PLR, complete blood counts and differentials that were obtained at presentation of the patients to emergency department were taken into account. In our hospital, peripheral blood samples are collected into calcium-EDTA tubes, and blood counts and differentials are analyzed using an auto-analyzer. PLR was calculated as the ratio of platelets to lymphocytes in the peripheral blood. Other routine laboratory parameters were obtained from our hospital's electronic patient database.

The sPESI scores of the patients were calculated using the data obtained from the electronic patient database. The patients with a sPESI risk score 0 were regarded to have low sPESI scores, and those with a sPESI score ≥1 were regarded to have high sPESI scores.

The statistical analysis of data was performed using SPSS v.22.0 for Windows (IBM Corp., Armonk, NY). Kolmogorov–Smirnov test was used to determine the normality of the distribution of data. Continuous data were presented as median and interquartile range (IQR) or mean ± SD. The effects of different variables on sPESI score were calculated via univariate logistic regression analysis. Variables with unadjusted P values <0.1 in logistic regression analysis were identified as potential risk factors, and included in the full model. We eliminated potential risk factors using likelihood ratio tests with reduced model, using multivariate logistic regression analysis. A P value <0.05 was considered as statistically significant. A receiver operating characteristics (ROC) curve was used to determine the sensitivity and specificity of the PLR, and the optimal cut-off value for predicting a sPESI score ≥1.

Results

The baseline clinical characteristics of the patients and univariate analysis results (P values) are shown in Table 1. Among 646 patients included in the study, 42 died during hospitalization.

A total of 238 (36.8%) patients had high sPESI scores. There were not any significant differences between low and high sPESI score groups in terms of age, smoking counts, diabetes mellitus (DM), levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), creatinine, total bilirubin, or hemoglobin (Hb), as well as monocyte count, red cell distribution width (RDW), or mean corpuscular volume (MCV).

Univariate analysis showed that PLR, PASP, RV dysfunction, WBC, D-dimer, lymphocyte, neutrophil, and platelet counts were all strongly correlated with high sPESI scores in APE patients. The in-hospital mortality rate was higher in patients with high sPESI scores when compared to the ones with low sPESI scores.

Multivariate logistic regression analysis of 9 study variables showed that PLR (coefficient β: 0.492; $P < 0.001$), PASP (coefficient β: 0.122; $P = 0.013$), RV dysfunction (coefficient β: 0.110; $P < 0.025$), and the WBC count (coefficient β: 0.495; $P = 0.015$) were significantly correlated with the risk of APE. All of those variables were significantly higher in high sPESI group (Table 2). Fig. 1 shows a significant difference for PLR between patients with low and high sPESI scores.

The PLR cut-off value at admission for predicting a high sPESI score in the entire study population based on receiver-operating characteristic curve (ROC) analysis was determined as 149, with a sensitivity of 77.1%, and a specificity of 76.3% (AUC: 0.860; $P < 0.001$) (Fig. 2).

Table 1
Baseline clinical characteristics of the study patients, and univariate analysis results.

	Acute pulmonary embolism			
	Overall ($n = 646$) (100%)	High risk sPESI ≥ 1 ($n = 238$) (36.8%)	Low risk sPESI = 0 ($n = 408$) (63.2%)	P
Gender Male, n (%)	294 (45.5%)	110 (46.2%)	184 (45.1%)	0.385
Age[a] (years)	60 ± 16	62 ± 14	59 ± 15	0.468
DM, n (%)	80 (12.4%)	40 (16.8%)	40 (9.8%)	0.083
Smoking, n (%)	166 (25.7%)	64 (26.8%)	102 (23.9%)	0.145
PASP[a] (mm Hg)	51 ± 19	59 ± 11	45 ± 13	**<0.001**
RV dysfunction, n (%)	210 (32.5%)	106 (44.5%)	104 (25.4%)	**<0.001**
D-dimer[a] (ng/mL)	5096 ± 2950	6038 ± 2008	4538 ± 2392	**<0.001**
WBC count[a] (μL)	11158 ± 4430	12162 ± 3426	9376 ± 2648	**<0.001**
Hemoglobin[b] (g/dL)	14.1 (12.6–15.5)	14 (12.1–15.2)	14.2 (13–16)	0.816
Neutrophil count[a] (μL)	8444 ± 4206	9566 ± 3084	7298 ± 3060	**<0.001**
Lymphocyte count[a] (μL)	2033 ± 1247	1748 ± 1312	2200 ± 1178	**0.002**
Monocyte count,[a] (μL)	803.55 ± 135.10	810.15 ± 128.5	785.00 ± 117.15	0.136
Platelet count[b] (1000 cells mm^{-3})	254 (207–298)	286 (236–350)	233 (189–273)	**<0.001**
MCV,[b] (fL)	87 (83.7–90)	86 (82–89)	88 (84–90)	0.351
PLR[b]	143 (113–176)	187 (152–231)	125 (96–148)	**<0.001**
Total cholesterol[a] (mg/dL)	170 ± 57	169 ± 58	170 ± 57	0.713
LDL[a] (mg/dL)	106 ± 37	108 ± 35	104 ± 35	0.556
HDL[a] (mg/dL)	$3^{-1}5$ ± 13	34 ± 12	36 ± 12	0.155
TG[a] (mg/dL)	129 ± 71	133 ± 67	127 ± 69	0.488
Creatinine[a] (mg/dL)	0.9 ± 0.4	0.87 ± 0.37	1.07 ± 0.23	0.322
Total bilirubin[a] (mg/dL)	0.565 ± 0.33	0.558 ± 0.33	0.569 ± 0.34	0.873
In-hospital mortality, n (%)	42 (6.5%)	32 (13.4%)	10 (2.3%)	**<0.001**

DM: Diabetes mellitus; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PLR: platelet-lymphocyte ratio; MCV: mean corpuscular volume; PASP: pulmonary artery systolic pressure; RDW: red blood cell distribution width; RV: right ventricular; SD: standard deviation; sPESI: simplified Pulmonary Embolism Severity Index; TG: triglyceride; WBC: white blood cell.
Statistically significant values are indicated in bold.
[a] Mean ± standard deviation.
[b] Median (IQR).

The patients were divided into two subgroups based on a PLR cut-off value of 149. In-hospital mortality rate was significantly higher in the patients with a PLR ≥149 ($P < 0.001$) (Table 3). In addition, PASP, RV dysfunction, the D-dimer level, the WBC, neutrophil, and platelet counts, and sPESI scores were significantly higher, whereas the lymphocyte count was significantly lower in the high PLR subgroup.

Table 2
Multivariate logistic regression analysis showing the independent predictors of sPESI ≥1 (high risk).

	P value	Coefficient β
Platelet count (1000 cells mm^{-3})	0.567	0.033
PLR	**<0.001**	0.492
Lymphocyte count (μL)	0.466	−0.046
Neutrophil count (μL)	0.722	0.073
D-dimer (ng/mL)	0.583	−0.023
PASP (mm Hg)	**0.013**	0.122
RV dysfunction	**0.025**	0.110
In-hospital mortality	**0.049**	−0.084
WBC count (μL)	**0.015**	0.495

PASP: Pulmonary artery systolic pressure; PLR: platelet-lymphocyte ratio; WBC: white blood cell.
Statistically significant values are indicated in bold.