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Original Article

Relationship between neutrophil-to-lymphocyte ratio, d-dimer and troponin-I values and pulmonary embolism severity index

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Abstract

Aim: We aimed to determine whether Neutrophil-to-Lymphocyte Ratio (NLR), Monocyte-to-Lymphocyte Ratio (MLR), Platelet-to-Lymphocyte Ratio (PLR), D-dimer, and troponin values were correlated with the simplified Pulmonary Embolism Severity Index (sPESI) in patients diagnosed as having Pulmonary Embolism (PE) in the emergency room.

Material and Methods: Forty-three patients diagnosed as having PE in the emergency department were divided into low and high-risk groups according to the sPESI. We investigated whether NLR, MLR, and PLR, d-dimer, troponin-I, and Pulmonary Artery Pressure (PAP) had any effect in determining the severity of PE. Also, patients were divided into groups as those with PAP ≤20 or >20 mm Hg, Systolic Blood Pressure (SBP) ≤100 or >100 mm Hg, and those receiving or not receiving thrombolytic treatment, and compared.

Results: There was a statistically significant difference between patients with low sPESI (n=10) and those with high sPESI (n=33) in terms of age (p=0.001), pulse (p=0.016), oxygen saturation (p=0.039), troponin-I (p=0.029) and PAP (p=0.032), but there was no difference between the groups in terms of NLR (p=0.796), MLR (p=0.656), PLR (p=0.863), and d-dimer (p=0.343). There was a statistically significant difference between patients who did (n=6) and did not (n=37) receive thrombolytic treatment in terms of troponin-I (p=0.012), but there was no difference between the groups in terms of NLR (p=0.861), MLR (p=0.335), and PLR (p=0.277).

Conclusion: NLR, MLR, PLR and d-dimer levels were found not to be effective in determining the severity of PE. Troponin-I was associated with sPESI and was considered as an effective marker in determining the thrombolytic treatment.

Keywords: D-Dimer; Emergency; Neutrophil-To-Lymphocyte Ratio; Pulmoner Embolism; Pulmonary Embolism Severity Index; Troponin.

INTRODUCTION

Venous Thromboembolism (VTE), including Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT), is a major health problem in the world and is the most common cardiovascular disease in Western countries(1). A number of risk classification models have been developed to predict mortality in PE (2). The most commonly used model for predicting 30-day mortality is the Pulmonary Embolism Severity Index (PESI) (3). D-dimer is a fibrin destruction product and is another parameter used as a clinical diagnostic tool in patients with a clinical suspicion of PE. D-dimer can increase in many cases such as older age, malignancy, infections, and major surgery, and has low specificity in PE. Therefore, d-dimer cannot be used as a single marker in PE. The Neutrophil-to-Lymphocyte Ratio (NLR), Monocyte-to-Lymphocyte Ratio (MLR) and Platelet-to-Lymphocyte Ratio (PLR) are emerging as promising prognostic markers in acute coronary syndromes and atherosclerotic diseases (4-6). Recently, there have been a number of studies suggesting that there is a potential relationship between high NLR and short-term mortality in PE (7). However, whether the NLR is useful in the treatment of patients with PE is an important issue of research. In this study, we investigated the relationship between NLR, MLR, and PLR, d-dimer and troponin-I values, which were measured in serum samples at admission and sPESI in patients diagnosed as having PE in the emergency room.

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MATERIAL and METHODS

In this study, 68 patients diagnosed as having PE in the emergency room of Samsun Training and Research Hospital, University of Health Sciences between January 1st, 2016, and June 30th, 2018, were investigated. Patients with a diagnosis of PE according to the International Classification of Diseases (ICD-10) diagnostic code were identified through the hospital automation system and the files of the patients were accessed. A data collection form was created so that data could be collected in a standardized way. Age, sex, vital signs, laboratory findings, and specific scores were recorded in the data collection form. Patients under the age of 18 years, patients in whom hematologic parameters could change, those with hematologic malignancies, receiving treatment for infection or having findings of active infection for the last 2 weeks, with known collagen tissue diseases, and patients using immunosuppressive drugs were excluded from the study. Twenty-five patients were excluded from the study according to these exclusion criteria and 43 patients were included. For the diagnosis of PE, the gold standard test, Multi-Slice (64-segment) Computed Tomography (MSCT) was performed using a Philips Brilliance. The patients were radiologically confirmed as having PE. Patients were divided into low and high-risk groups according to the sPESI. We investigated whether NLR, MLR, PLR, d-dimer, troponin-I, and pulmonary artery pressure (PAP) had an effect in determining the severity of PE. Also, patients were divided into groups as those with PAP ≤20 or >20 mm Hg, blood pressure (SBP) ≤100 or >100 mm Hg, and those receiving or not receiving thrombolytic treatment, and the groups were compared.

Biochemical analysis

In the emergency room admission, the Complete Blood Count (CBC) was measured using a Beckman Coulter-Coulter LH780 analyzer. Arterial and venous blood gases were analyzed using a GEM® Premier™ 4000. Troponin-I values were measured using an Advia Centaur® CP. Other biochemical parameters such as Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), urea, creatinine, and glucose levels were measured using a Beckman Coulter®AU 680. Laboratory results were obtained by scanning the patient files, retrospectively. The reference values used in our laboratory are as follows: glucose, 74-109 mg/dL, urea, 17-43 mg/dL, creatinine (in blood), 0.5-1.1 mg/dL, AST, 0-35 U/L; ALT, 0-35 U/L; Troponin-I, 0-0.06 µg/L; d-dimer, 0-0.55 mg/L, hemoglobin (female), 11-15 g/dL hemoglobin (male), 12-16 g/dL, platelets, 130-400 10^3/µL, neutrophils, 2-7 10^3/µL, lymphocytes, 0.8-4 10^3/µL, and monocytes, 0.12-1.2 10^3/µL.

Statistical analyses

After the data gathered from the study were encoded, they were analyzed using the SPSS statistics software package (Version 22 for Windows, SPSS Inc, Chicago, IL, USA). Parametric continuous variables are expressed as mean ± standard deviation, nonparametric continuous variables are expressed as median (minimum and maximum values), and frequency variables were expressed as numbers and percentages (%). In statistical analyses, the Shapiro-Wilk test was used to evaluate whether measurable variables had normal distribution. If not, the nonparametric Mann-Whitney U test was used to compare the groups. P<0.05 was considered statistically significant.

RESULTS

There were 43 patients including 21 females (48.8%) and 22 males (51.2%). There was a statistically significant difference between patients with low sPESI (n=10) and those with high sPESI (n=33) in terms of age (p=0.001), pulse (p=0.016), oxygen saturation (p=0.039), troponin-I (p=0.029) and PAP (p=0.032), but there was no difference between the groups in terms of NLR (p=0.796), MLR (p=0.656), PLR (p=0.863), and d-dimer (p=0.343) (Table 1).

Table 1. Correspondence of clinical findings and laboratory results with low and high sPESI

	sPESI low (1.1%)	sPESI high (8.9%)	p
Number of patients	n = 10	n = 33	
Age	48.30 ± 15.88	68.84 ±15.21	0.001
Systolic Blood Pressure	114.00 ± 16.46	114.54 ± 27.62	0.704
Pulse	80.50 ± 12.50	98.81 ± 22.53	0.016
O_2 Saturation	94.30 ± 2.94	90.03 ± 6.52	0.039
Glucose	131.70 ± 26.18	158.30 ± 81.45	0.785
Urea	27.90 ± 11.65	44.30 ± 20.16	0.005
Creatinine	0.76 ± 0.17	1.00 ± 0.40	0.007
AST	36.70 ± 15.57	32.93 ± 25.70	0.185
ALT	27.90 ± 29.98	27.84 ± 27.67	0.730
HGB	12.63 ± 1.93	12.66 ± 2.02	0.999
Platelet (PLT)	273.40 ± 151.75	230.18 ±113.20	0.301
Neutrophil (NE)	6.90 ± 2.23	7.43 ± 3.89	0.863
Lymphocyte (LY)	2.22 ± 0.99	2.07 ±1.71	0.215
Monocyte (MON)	0.67 ±0.29	0.70 ± 0.43	0.919
NE/LY	3.72 ±1.96	5.35 ± 5.46	0.796
MON/LY	0.33 ±0.14	0.42 ± 0.26	0.656
PLT/LY	139.78 ± 77.34	141.71 ± 74.24	0.863
D-dimer	4.58 ± 3.73	6.14 ±4.84	0.343
Troponin	0.08 ± 0.16	0.42 ± 0.36	0.029
Pulmonary Artery Pressure	30.50 ± 13.63	43.12 ± 17.13	0.032

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase, HGB: Hemoglobin. Data are shown as mean±standard deviation. p<0.05 was considered statistically significant

There was a statistically significant difference between patients with PAP ≤20 (n=9) and with PAP >20 (n=34) in terms of d-dimer (p=0.028), but no difference between the groups in terms of NLR (p=0.743), MLR (p=0.929), and PLR (p=0.232) (Table 2). There was a statistically significant difference between patients with SBP ≤100 (n=17) and with SBP >100 (n=26) in terms of PAP (p=0.022), but no difference between the groups in terms of NLR (p=0.398), MLR (p=0.813), and PLR (p=0.168) (Table 3). There was a statistically significant difference between patients who did (n=6) and did not (n=37) receive thrombolytic treatment in terms of troponin (p=0.012), but there was no difference between the groups in terms of NLR (p=0.861), MLR (p=0.335), and PLR (p=0.277) (Table 4).

Table 2. Correspondence of clinical findings and laboratory results with PAP

	PAP ≤ 20	PAP > 20	p
Number of patients	n = 9	n = 34	
Age	60.44 ± 15.29	65.02 ±18.16	0.282
Systolic Blood Pressure	116.66 ± 23.97	113.82 ± 25.93	0.832
Pulse	91.66 ± 19.05	95.32 ± 22.85	0.630
O_2 Saturation	91.88 ± 5.18	90.79 ± 6.40	0.764
Glucose	125.44 ± 25.50	159.17 ± 79.89	0.317
Urea	30.33 ±10.92	43.17 ± 20.72	0.062
Creatinine	0.76 ± 0.22	1.00 ± 0.39	0.046
AST	31.22 ± 10.66	34.50 ± 26.08	0.510
ALT	29.11 ± 31.58	27.52 ± 27.30	0.709
HGB	12.47 ± 2.19	12.70 ± 1.94	0.881
PLT	258.88 ± 90.18	235.29 ± 130.57	0.199
Neutrophil	6.37 ± 1.78	7.56 ± 3.88	0.687
Lymphocyte	1.85 ± 1.06	2.17 ± 1.68	0.742
Monocyte	0.57 ± 0.25	0.72 ± 0.43	0.251
NE/LY	4.51 ± 2.78	5.09 ± 5.35	0.743
MON/LY	0.39 ± 0.24	0.40 ± 0.24	0.929
PLT/LY	180.22 ± 104.60	130.95 ± 61.65	0.232
D-dimer	3.40 ± 3.31	6.41 ± 4.74	0.028
Troponin	0.06 ± 0.12	0.16 ± 0.34	0.074
Pulmonary Artery Pressure	20.00 ± 0.00	45.52 ± 15.23	<0.001

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; HGB: Hemoglobin. Data are shown as mean±standard deviation. p<0.05 was considered statistically significant

Table 3. Correspondence of clinical findings and laboratory results with SBP

	SBP ≤ 100	SBP > 100	p
Number of patients	n = 17	n = 26	
Age	64.82 ± 23.50	63.57 ± 12.74	0.345
Systolic Blood Pressure	92.94 ± 9.85	128.46 ± 22.21	<0.001
Pulse	95.58 ± 21.13	93.88 ± 22.85	0.680
O_2 Saturation	90.05 ± 7.90	91.65 ± 4.70	0.960
Glucose	140.23 ± 50.98	159.88 ± 84.47	0.941
Urea	40.47 ± 24.43	40.50 ± 16.42	0.419
Creatinine	0.92 ± 0.46	0.96 ± 0.31	0.175
AST	30.52 ± 28.65	35.96 ± 19.99	0.041
ALT	21.82 ± 19.74	31.80 ± 31.83	0.196
HGB	12.57 ± 1.79	12.71 ± 2.12	0.921
PLT	267.41 ± 140.15	222.46 ± 108.93	0.184
Neutrophil	7.83 ± 3.95	6.97 ± 3.31	0.551
Lymphocyte	2.27 ± 2.25	2.00 ± 0.92	0.463
Monocyte	0.68 ± 0.37	0.70 ± 0.42	0.980
NE/LY	5.99 ± 6.45	4.30 ± 3.56	0.398
MON/LY	0.41 ± 0.25	0.39 ± 0.23	0.813
PLT/LY	163.89 ± 88.24	126.46 ± 60.42	0.168
D-dimer	5.33 ± 4.28	6.08 ± 4.88	0.682
Troponin	0.18 ± 0.45	0.11 ± 0.17	0.732
Pulmonary Artery Pressure	32.52 ± 10.36	45.19 ± 18.89	0.022

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; HGB: Hemoglobin, SBP: Systolic Blood Pressure. Data are shown as mean±standard deviation. p<0.05 was considered statistically significant

Table 4. Correspondence of clinical findings and laboratory results with thrombolytic treatment

	Receiving Thrombolytic Treatment	Not Receiving Thrombolytic Treatment	p
Number of patients	n = 6	n = 37	
Age	57.66 ± 19.78	65.10 ± 17.21	0.461
Systolic Blood Pressure	125.00 ± 29.49	112.70 ± 24.56	0.311
Pulse	108.16 ± 17.73	92.35 ± 21.96	0.054
O_2 Saturation	88,83 ± 6.61	91.37 ± 6.07	0.378
Glucose	136.16 ± 37.86	154.70 ± 77.28	0.861
Urea	50.83 ± 34.26	38,81 ± 16.39	0.505
Creatinine	1.16 ± 0.66	0.91 ± 0.30	0.357
AST	52.16 ± 50.41	30.83 ± 15.25	0.661
ALT	38.16 ± 34.74	26.18 ± 26.77	0.483
HGB	13.25 ± 2.51	12.56 ± 1.90	0.410
PLT	174.66 ± 35.29	250.86 ± 128.61	0.099
Neutrophil	8.33 ± 5.32	7.14 ± 3.26	0.847
Lymphocyte	1.75 ± 0.43	2.16 ± 1.67	0.986
Monocyte	0.58 ± 0.43	0.71 ± 0.40	0.264
NE/LY	5.40 ± 4.86	4.90 ± 4.97	0.861
MON/LY	0.30 ± 0.17	0.41 ± 0.25	0.335
PLT/LY	104.93 ± 32.80	147.15 ± 77.40	0.277
D-dimer	8.42 ± 5.62	5.35 ± 4.37	0.123
Troponin	0.48 ± 0.71	0.08 ± 0.15	0.012
Pulmonary Artery Pressure	55.83 ± 23.54	37.64 ± 14.73	0.058

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; HGB: Hemoglobin. Data are shown as mean±standard deviation. p<0.05 was considered statistically significant

DISCUSSION

PE is one of the most serious clinical conditions that may require hospitalization and has an average mortality rate of 15% (8). Therefore, defining PE with risk classifications is very important for physicians (9). The most widely used and accepted scale is PESI (10). The PESI scale consists of 11 different variables, but it is difficult to use per bed, so the sPESI has been improved (Table 5) (11).

Table 5. Simplified pulmonary embolism severity index (sPESI)

Variables	Points
Age >80 years	+1
Cancer	+1
Chronic cardiopulmonary disease	+1
Heart rate ≥110 beats/min	+1
SBP < 100 mm Hg	+1
SaO_2< 90%	+1

SBP, systolic blood pressure; SaO_2, oxygen saturation. The total score is calculated as the sum of the points assigned to each variable. Patients with a score of 0 were determined to be low risk, while those with a score of 1 or more were considered high risk

The NLR representing the balance between neutrophils and lymphocytes is suggested as a new marker in systemic inflammation (12). In previous studies, a high NLR was reported to be associated with cardiovascular mortality (13). The inflammation process accelerates neutrophil production and lymphocyte apoptosis (14). In a meta-analysis by Quian Wang et al., the authors investigated the prognostic value of NLR and PLR in PE and found a significant correlation with short and long- term prognosis (7). Kayrak et al. investigated the prognostic value of the NLR in PE and concluded that it could be a 30-day mortality marker (15). Karataş et al. assessed the prognostic value of NLR and PLR in PE and concluded that both ratios might be related with short and long-term mortality in PE(16). Akgüllü et al. investigated early mortality markers in PE and found that the NLR was significantly different in patients with PE (17). In a meta-analysis by Galliazzo et al., the authors found that the NLR was useful in providing prognostic value in PE, reporting that it could be a valuable tool in combination with other prognostic markers (18). In our study, we found that NLR, MLR and PLR were not correlated with sPESI, unlike other studies. We believe that this result was due to our exclusion criteria, which caused exclusion of a wider population of patients compared with other studies. Ghaffari et al. investigated high levels of cardiac troponin-I–associated factors in patients with PE and found that cardiac troponin was an independent marker for the short-term consequences of PE (19). Spirk et al. investigated the relation between cardiac troponin and sPESI and found that troponin levels were higher in patients with high-risk sPESI scores (20). In our study, we found that troponin-I was associated with sPESI in patients with PE. We concluded that troponin-I was an effective biomarker in determining thrombolytic therapy when we examined two groups of patients who did and did not receive thrombolytic treatment.

D-dimer levels rise in plasma in the presence of acute thrombosis due to concurrent activation of coagulation and fibrinolysis. The negative predictive value of the D-dimer test is high and a normal d- dimer level makes PE or DVT unlikely, however, because D-dimer levels can be elevated due to other reasons and the positive predictive value is low. The D-dimer test is not a useful test for the validation of PE (21). In a study conducted by Kozlowski et al., the authors investigated whether D-dimer contributed to sPESI in PE, the in-hospital risk classification, and reported that high plasma D-dimer levels were correlated with sPESI scores (22). Coşkun et al. explored the relationship between D-dimer and the severity of PE and found that there was a significant difference between massive and non-massive PE cases (23). PE diagnosis was confirmed with MSCT and D-dimer was positive in our patients, and we did not classify our patients as massive and non-massive PE, which may have caused the lack of difference between patients with low-risk sPESI and high-risk sPESI in our study, unlike in other similar studies (22,23). We also found that D-dimer levels were not associated with sPESI, but that D-dimer had a significant correlation with high PAP values.

CONCLUSION

NLR, MLR, PLR and D-dimer were not effective in determining the severity of PE. Troponin-I was associated with sPESI and it was an effective marker in determining thrombolytic therapy.

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