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Relationship Between Pulmonary Thromboembolism and Neutrophil Albumin Ratio

Pulmoner Tromboemboli ve Nötrofil Albümin Oranı Arasındaki İlişki

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ABSTRACT

Objective: *Pulmonary Thromboembolism (PTE) is a serious clinical condition and is common all over the world, requiring early diagnosis and treatment. Laboratory data and radiological imaging provide support in its diagnosis. The purpose of the present study is to investigate the clinical significance of neutrophil to albumin ratio (NAR) in patients who are diagnosed with PTE.*

Material and Method: *A total of 150 cases who of 100 patients with a diagnosis of PTE and 50 healthy volunteers without a history of smoking or any comorbidities were included in the study. Complete Blood Count (CBC) and biochemical data were evaluated retrospectively. NAR was calculated as the ratio of neutrophil to albumin.*

Results: *A total of 150 cases (84 male (56%) and 66 (44%) female) were included in the study. Neutrophil Albumin Ratio (NAR), were found to be statistically and significantly elevated in the patient group (p<0.001).The Serum NAR value showed a positive correlation with the Serum d-dimer value (r:0.488, p<0.001).*

Conclusion: *It is possible to argue that NAR, which is a novel, cheap, and easily calculable biomarker, can be a useful parameter for the diagnosis of patients with PTE.*

ÖZET

Amaç: *Pulmoner tromboemboli (PTE), tüm dünyada sık görülen ve erken tanı ve tedavi gerektiren ciddi bir klinik tablodur. Tanı koymada, hem laboratuvar verileri hem de radyolojik görüntüleme destek sağlamaktadır. Çalışmanın amacı, PTE tanılı hastalarda nötrofil albumin oranının (NAR) klinik önemini araştırmaktır.*

Gereç ve yöntem: *Çalışmaya, PTE tanılı 100 hasta ve sigara içme öyküsü ve komorbidite öyküsü olmayan 50 sağlıklı gönüllü olmak üzere toplam 150 olgu dahil edildi. Tam kan sayımı ve biyokimyasal veriler retrospektif olarak elde edildi. NAR, nötrofilin albumine oranı olarak hesaplandı.*

Bulgular: *Çalışmaya 84'ü erkek (%56) ve 66'sı (%44) kadın olmak üzere toplam 150 vaka dahil edildi. NAR, hasta grubunda istatistiksel olarak anlamlı düzeyde yüksek bulundu (p<0,001). Serum NAR değeri, serum d-dimer değeri ile pozitif korelasyon gösterdi (r:0,488, p<0,001).*

Sonuç: *Yeni, ucuz ve kolay hesaplanabilen bir biyobelirteç olan NAR, PTE hastalarının tanısında yararlı bir parametre olabilir.*

Keywords:
Pulmonary embolism
Inflammation
Albumin
Neutrophil

Anahtar Kelimeler:
Pulmoner emboli
İnflamasyon
Albumin
Nötrofil

INTRODUCTION

Pulmonary Thromboembolism (PTE) is a serious clinical condition and is common all over the world, requiring early diagnosis and treatment. PTE is characterized by pulmonary circulatory disorder that results from partial or complete occlusion of the pulmonary artery by thrombi that originate from the deep veins of the lower extremities (1). Laboratory data and radiological imaging provide support in its diagnosis (2,3).

Intense inflammation develops in PTE after the rapid release of inflammatory cells in the pulmonary artery wall and peaks in two days (4). It was reported in previous studies that some novel biomarkers in this inflammatory response play important roles in the diagnosis of PTE and predicting its prognosis (5-7). Neutrophils initiate the early inflammatory response after the acute infection. In this respect, an elevated neutrophil count is an important marker for systemic infection (8). Albumin is a negative acute phase reactant, decreases in acute infection, and is an important marker of mortality (9). Many studies are emphasizing the importance of neutrophils and albumin in the pathogenesis of PTE (10,11).

Neutrophil Albumin Ratio (NAR) is a novel inflammatory biomarker and was reported in many previous studies to be an important prognostic biomarker (12-14). When the literature was reviewed, no study was detected examining the relationship between PTE and NAR. The purpose of the present study is to investigate the NAR value in patients who are diagnosed with PTE and to pioneer future studies to be conducted on this subject.

MATERIAL AND METHOD

A total of 120 patients who were followed up with a diagnosis of PTE in our hospital between June 2019 and May 2023 were reviewed in this retrospective study. The

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study was approved by the Institutional Ethics Committee of Harran University, Faculty of Medicine (Approval No. HRU/23.12.19, Date: 10.07.2023). The patients who were under 18 years of age, those with acute or chronic inflammatory diseases, active cancer, a history of acute attacks of Chronic Obstructive Pulmonary Disease (COPD), and patients with a history of nephrotic and/ or hepatic disease that would cause hypoalbuminemia were excluded from the study. A total of 20 patients were excluded from the study according to these criteria. As a result, a total of 100 patients and 50 healthy volunteers without a history of smoking or any comorbidities were included. The demographic data and laboratory parameters of the patients were taken from the digital archive and recorded. The diagnosis of PTE was made with pulmonary angiographic computed tomography.

Blood samples were taken from the patients on the first day of their hospitalization. Complete Blood Count (CBC) and biochemical data were evaluated retrospectively. NLR was calculated as the ratio between the number of neutrophils and lymphocytes, LMR as the ratio between the number of lymphocytes and monocytes, CAR as the ratio of CRP to albumin, and NAR as the ratio of neutrophils to albumin.

Statistical Analysis

The SPSS for Windows version 22.0 (SPSS Inc., IL, USA) was used for statistical analyses. The Kolmogorov-Smirnov Test was used to evaluate whether the continuous data were distributed normally. The continuous data were expressed as Mean ± SD or Median (25-75 IQR) and were compared by using the Student's t or Mann-Whitney U Tests depending on their distributions. Receiver Operating Characteristics (ROC) Curve Analysis was used to determine the optimal cutoff value of NAR to predict PTE. The correlation between NAR and d-dimer parameters was determined by using the Spearman Test and a p-value of <0.05 was considered statistically significant.

RESULTS

A total of 150 cases (84 male (56%) and 66 (44%) female) were included in the study. The demographic and laboratory data of the patients are given in Table 1. When compared to the Control Group, C-Reactive Protein (CRP), White Blood Cell (WBC), leukocyte and d-dimer values were significantly higher in the patient group, and albumin and lymphocyte values were statistically lower. Among the patients who were diagnosed with PTE, 28% had Congestive Heart Failure (CHF), 18% had Hypertension (HT), 18% had Chronic Obstructive Pulmonary Disease (COPD), and 15% had Diabetes Mellitus (DM).

As novel biomarkers, Neutrophil Lymphocyte Ratio (NLR), Lymphocyte Monocyte Ratio (LMR), C-RP Albumin Ratio (CAR), and Neutrophil Albumin Ratio (NAR), were found to be statistically and significantly elevated in the patient group ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, respectively) (Table 1).

The correlation between the variables was given by using the Spearman Test. The Serum NAR value showed a positive correlation with the Serum d-dimer value (r:0.488, $p<0.001$) (Table 2).

The ROC Curve Analysis was performed to determine the cut-off value of NAR in predicting PTE, which was found to be ≥ 1.09 with 81% sensitivity and 72% specificity (AUC: 0.859, $P < 0.001$) (Figure 1).

Table 1: Comparison of demographic and laboratory data between groups.

	PATIENT GROUP (n=100)	CONTROL GROUP (n=50)	p
Age, year	63.0 (47.2-73.7)	56.0 (47.7-59.0)	0.16
Gender, (m/f)	43/57	41/9	<0.001
Urea, mg/dL	39.0 (29.0-54.5)	26.5 (23.0-34.0)	<0.001
Creatinine, mg/dL	0.8 (0.6-1.0)	0.8 (0.7-1.0)	0.82
Albumin, g/ dL	3.4 (3.1-3.8)	4.4 (4.1-4.7)	<0.001
CRP, mg/dL	19.3 (10.5-47.2)	0.3 (0.1-0.4)	<0.001
WBC, x103/mL	10.7 (7.6-14.0)	6.6 (6.0-7.6)	<0.001
Neutrophil, x103/mL	8.0 (5.0-11.3)	3.7 (3.1-4.9)	<0.001
Lymphocyte, x103/mL	1.7 (1.0-2.4)	2.2 (1.8-2.5)	0.001
Monocyte, x103/mL	0.7 (0.5-1.0)	0.4 (0.3-0.5)	<0.001
Platelet, x103/mL	249.5 (190.2-316.5)	253.8 (221.5-331.0)	0.350
MCV, fL	85.9 ± 9.4	87.3 ± 5.4	0.236
RDW, %	14.4 ± 3.5	12.6 ± 1.5	0.001
d-dimer	3.6 (1.4-6.6)	0.2 (0.1-0.3)	<0.001
CAR	5.8 (3.6-13.2)	0.06 (0.02-0.93)	<0.001
NLR	4.6 (2.2-8.4)	1.7 (1.3-2.2)	<0.001
LMR	2.9 (1.6-4.3)	5.2 (3.9-8.0)	<0.001
NAR	2.2 (1.6-3.5)	0.9 (0.7-1.1)	<0.001

CRP, C-reactive protein; WBC, white blood cell; MCV, mean corpuscular volume; RDW, red cell distribution width; CAR, C reactive protein to albumin ratio; NLR: Neutrophil to lymphocyte ratio; LMR: Lymphocyte to monocyte ratio; NAR: Neutrophil to albumin ratio.

Table 2: Spearsman correlation of variables.

		NAR
D-dimer	Correlation Coefficient	.488*
	p	<0.001
	n	150

** p<0,001.*

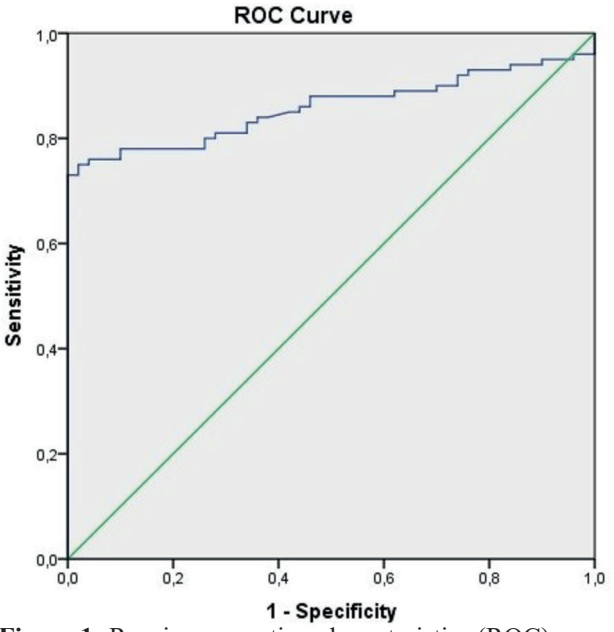

Figure 1: Receiver operating characteristics (ROC) curve of NAR for predicting the PTE.

DISCUSSION

In the present study, the clinical importance of NAR, which is a novel inflammatory marker, was investigated in patients with PTE. The important results of the study were that NAR had high sensitivity in the diagnosis of PTE and showed a positive correlation with d-dimer. Also, this study is the first to investigate the relationship between NAR and PTE.

The role of systemic inflammation in PTE was investigated in many previous studies. It was reported that an inflammatory reaction characterized by increased cytokines and inflammatory cell influx occurs in the pulmonary artery wall because of endothelial damage caused by thrombus (15). Therefore, it is possible to argue that biochemical and hematological parameters can play important roles in the diagnosis, follow-up, and prognosis evaluation of PTE. In their study, Gülen et al. compared the NLR, MPV, and WBC values in patients with PTE at the time of diagnosis and after treatment and found that these values decreased significantly at the end of treatment, and they argued that NLR, MPV, and WBC could be important biomarkers that can be used in the diagnosis and follow-up of PTE (16). Çaltekin et al. argued that LMR can be used as a prognostic biomarker in stroke cases (17). Several studies examining the relationship between CAR and patients with PTE emphasized that CAR may be both a risk-increasing factor for the disease and an independent predictive factor of mortality (7,18,19). In the present study, as a result of the examination of the blood samples taken at the time of diagnosis of patients with PTE, the NLR, LMR, and CAR values were found to be significantly higher than in the Control Group. Novel inflammatory markers can be used in the diagnosis, follow-up, and prognosis evaluation of PTE because this result supports previous studies.

NAR is a novel inflammatory biomarker and was considered an important prognostic factor in different pathologies such as cancer, sepsis, and diabetic retinopathy (20-22). It is an inflammatory cell initiating the stimulus for the development of neutrophils and thrombus and is necessary for their spread (23,24). In addition to the anti-inflammatory characteristics of albumin, which is a negative acute phase reactant, it also plays important roles in antioxidant, anticoagulant, and anti-platelet aggregation (25,26). Many studies emphasized that elevated serum neutrophil and low serum albumin values are strong and independent markers for mortality in patients who are diagnosed with PTE (27-29). However, no study has been conducted yet on NAR in patients diagnosed with PTE. In the present study, the relationship between PTE and NAR was investigated for the first time, and statistically significant high NAR values were detected in PTE patients. According to the results of the present study, we think that NAR may be an important marker in the diagnosis of PTE. Early diagnosis and treatment are vital in PTE because it is associated with high mortality. The d-dimer, a fibrin degradation product formed by the endogenous fibrinolytic system, is among the most frequently used laboratory parameters in its diagnosis and follow-up (30). The relationship between PTE and d-dimer was reported in many previous studies (31,32). In the present study, d-dimer levels were found to be significantly elevated in patients with PTE. For the first time, the present study showed a positive correlation between NAR as a novel inflammatory parameter and d-dimer levels. Based on this result, evaluating both parameters together may be more effective and helpful in the diagnosis of PTE.

The present study had some limitations, which include the fact that the study had a single-centered design, the lack of long-term follow-up data of the patients, and the inability to make clinical classifications because of insufficient data.

In conclusion, it is possible to argue that NAR, which is a novel, cheap, and easily calculable biomarker, can be a useful parameter for the diagnosis of patients with PTE. We also think that the present study, which investigated the relationship between PTE and NAR for the first time, will guide future studies to be conducted with larger populations.

Conflict of Interest: No conflict of interest was declared by the authors.

Ethics: This study was conducted with the approval of the Harran University Faculty of Medicine Clinical Research Ethics Committee (HRU/23.12.19, date: 22.07.2023).

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