

Fibrinogen/Albumin Ratio in Patients with Pulmonary Embolism

Pulmoner Emboli Olan Hastalarda Fibrinojen/Albümin Oranı

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ABSTRACT

Objective: Pulmonary embolism is associated with a high mortality rate when it is not diagnosed emergently. Our aim was to investigate the relationship between the fibrinogen/albumin ratio and pulmonary embolism.

Material and Method: Patients who were suspected to have pulmonary embolism and who underwent routine blood testing to initiate the diagnostic process were included in this prospective study. Their fibrinogen and albumin values were evaluated.

Results: A total of 130 patients were included in the study. Pulmonary embolism was detected in 71 (54%) of the patients. Of those, 7 (9.9%) were subsegmental, 50 (70.4%) were segmental, and 14 (19.7%) were massive pulmonary. The fibrinogen/albumin ratio of the subjects in the control group was 99.1 (75.2–167.9), whereas the fibrinogen/albumin ratio in the pulmonary embolism group was 151 (125.1–220.5), significantly higher than the control value ($P < 0.001$). When ROC analysis was performed in the pulmonary embolism group, the fibrinogen/albumin ratio was found to be a significant predictive factor (AUC: 0.724; 95% CI = 0.635–0.814; $P < 0.001$). When the fibrinogen/albumin ratio was 119.3, the sensitivity was 77.5%, and specificity was 61.0%.

Conclusion: Fibrinogen levels and fibrinogen/albumin ratio were significantly higher in patients with pulmonary embolism.

ÖZET

Amaç: Pulmoner emboli teşhis edilemediğinde yüksek ölüm oranı ile ilişkilidir. Amacımız fibrinojen/albumin oranı ile pulmoner emboli arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: PE olduğundan şüphelenilen ve rutin kan testi yapılan hastalar bu prospektif çalışmaya dahil edilmiştir. Fibrinojenleri ve albumin değerleri değerlendirildi.

Bulgular: Çalışmaya toplam 130 hasta dahil edildi. PE, hastaların 71'inde (%54) tespit edildi. Bunlardan 7'si (%9,9) subsegmental, 50'si (%70,4) segmental ve 14'ü (%19,7) masif idi. Kontrol grubundaki deneklerin FAR(Fibrinojen albumin oranı) 'si 99.1 (75.2–167.9) iken, PE grubundaki FAR 151 (125.1–220.5) olup, kontrol grubundan anlamlı derecede yüksekti ($P < 0,001$). PE grubunda ROC analizi yapıldığında FAR önemli bir öngörücü faktör oldu (AUC: 0.724; %95 GA = 0.635-0.814; $P < 0.001$). FAR, duyarlılık %77.5 ve özgüllük %61.0 idi.

Sonuç: PE'li hastalarda fibrinojen düzeyleri ve FAR anlamlı olarak daha yüksekti.

Keywords:

Pulmonary embolism,
Fibrinogen/albumin ratio,
Mean platelet volume

Anahtar Kelimeler:

Pulmoner emboli,
Fibrinojen/albumin oranı,
Ortalama trombosit hacmi

INTRODUCTION

Pulmonary embolism (PE) is a general problem of deep vein thrombosis (1). Generally, part of the thrombus from the leg clogs the main pulmonary arteries or smaller pulmonary arteries (2). PE is associated with a high mortality rate when it is not diagnosed emergently. Treatment should be started immediately upon diagnosis. Differential diagnosis includes myocardial infarction, pneumonia, pericardial effusion, and aortic dissection (3,4).

Fibrinogen is a plasma protein synthesized in the liver that converts into fibrin during coagulation. It increases in infections, tissue damage, pregnancy, collagen tissue diseases, and many cancers. Fibrinogen levels are decreased in cases of haemolytic diseases, severe blood loss, phosphorus poisoning, disseminated intravascular

coagulation, blood transfusion, and burns. The main function of fibrinogen is to provide coagulation (5). Albumin, another protein synthesized in the liver, has a half-life of 21 days. It maintains osmotic pressure with its colloid structure. Serum albumin levels decrease in cases of liver diseases (cirrhosis), kidney diseases (renal excretion), malnutrition, burns, and infections (especially sepsis). It is a negative acute phase reactant (6).

This study was aimed to figure out the differences in fibrinogen, albumin, and the fibrinogen/albumin ratio (FAR) values between patients with and without PE, to identify a potential diagnostic marker to assist emergency physicians with diagnosis and decrease unnecessary pulmonary computed tomography angiography.

MATERIAL AND METHODS

The study was approved by Ethical Board (Meeting

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Table 1: Demographic characteristics of the groups and laboratory results

Characteristic	Control Group	Patient Group	P-value
Age	65.1 ± 11.6	68.2 ± 15.3	0.144
Sex (female)	32 (54.2%)	28 (39.4%)	0.093
Shortness of breath	24 (%40.7)	43 (%60.6)	
Syncope	4 (%6.8)	1 (%1.4)	
Leg swelling	4 (6.8%)	5 (7%)	
Chest pain	12 (20.3%)	2 (2.8%)	
Haemoptysis	4 (6.8%)	0	
Other complaint	11 (18.6%)	20 (28%)	
Malignancy (yes)	21 (35.6%)	20 (28.2%)	
Glucose	121.0 (105.0-136.0)	133.0 (100.0-180.0)	0.099
BUN	23.4 (16.0-29.4)	20.0 (14.5-32.7)	0.305
Creatinine	0.9 ± 0.4	0.9 ± 0.3	0.568
ALT	22.0 (12.0-30.0)	19.0 (12.0-29.0)	0.733
AST	20.0 (15.0-35.0)	22.0 (15.0-35.0)	0.582
LDH	264.0 (223.0-388.0)	270.0 (221.0-328.0)	0.893
Haemoglobin	11.3 ± 2.4	11.3 ± 2.5	0.984
Leukocytes	9.8 (6.7-13.8)	11.6 (8.2-15.4)	0.423
Neutrophils	7.1 (4.5-10.8)	9.0 (5.3-12.6)	0.283
Lymphocytes	1.5 (1.1-2.2)	1.4 (0.7-1.8)	0.283
RDW	16.9 ± 4.7	16.3 ± 2.9	0.389
MPV	9.6 ± 1.2	10.3 ± 1.8	0.021
Platelets	256.0 (183:0-313.0)	249.0 (190.5-343.0)	0.894
CRP	38.0 (18.3-121.0)	63.3 (30.6-134.0)	0.177
D-dimer	2633.3 ± 1441.3	3462.4 ± 1385.6	0.001
Albumin	3.2 ± 0.7	3.1 ± 0.6	0.302
Fibrinogen	379.5 ± 187.6	520.6 ± 191.1	<0.001
Fibrinogen/albumin ratio	99.1 (75.2-167.9)	151 (125.1-220.5)	<0.001
Neutrophil/lymphocyte ratio	4.7 (2.9-8.0)	5.6 (3.6-12.7)	0.061

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactose dehydrogenase; CRP: C-reactive protein; RDW: Erythrocyte distribution width in blood; MPV: Mean platelet volume in blood.

Decision No. 2018/1434). This prospective study was conducted with patients who were admitted to our university hospital emergency department with the suspicion of PE between July 1, 2018 and February 1, 2019. Patients with suspected pulmonary embolism who were consulted with chest diseases and had computed tomography pulmonary angiography (CTPA) were included in the study. One hundred thirty patients demographic data were collected. The age, gender, biochemistry, arterial blood gas, haemogram test results, and coagulation results of the patients were recorded. Patients who were under the age of 18 were excluded from the study.

Biochemical Markers

Coagulation tubes were centrifuged at 4000 rpm for 5 min. Fibrinogen was measured using a Siemens BCS XP haemostasis system (Siemens Healthcare Diagnostics, Los Angeles, CA, USA). Albumin was measured spectrophotometrically using an Abbott Architect Plus spectrophotometer (Abbott Park, IL, USA). Haemogram was analyzed using automatic blood counter (Beckman-

Coulter Co, Miami, Florida).

Statistics

Categorical variables were defined as the mean ± standard deviation or frequency and percentage. Student’s t-test was used to compare normally distributed variables. Normal distribution was evaluated with the Kolmogorov-Smirnov test (P < 0.05). Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic sensitivity and specificity of the FAR. Groups with non-normal distribution were evaluated using the Mann-Whitney U test. A P-value < 0.05 was considered significant.

RESULTS

The data of a total of 130 patients who were suitable for the working conditions were examined. The patients who evaluated within the scope of the study, 71 were included in the study group (PE), and 59 were placed in the control group (no PE). The mean ages of the PE group and the control group were 68.2 ± 15.3 years and 65.1 ± 11.6 years, respectively. Considering the ages, it was determined that

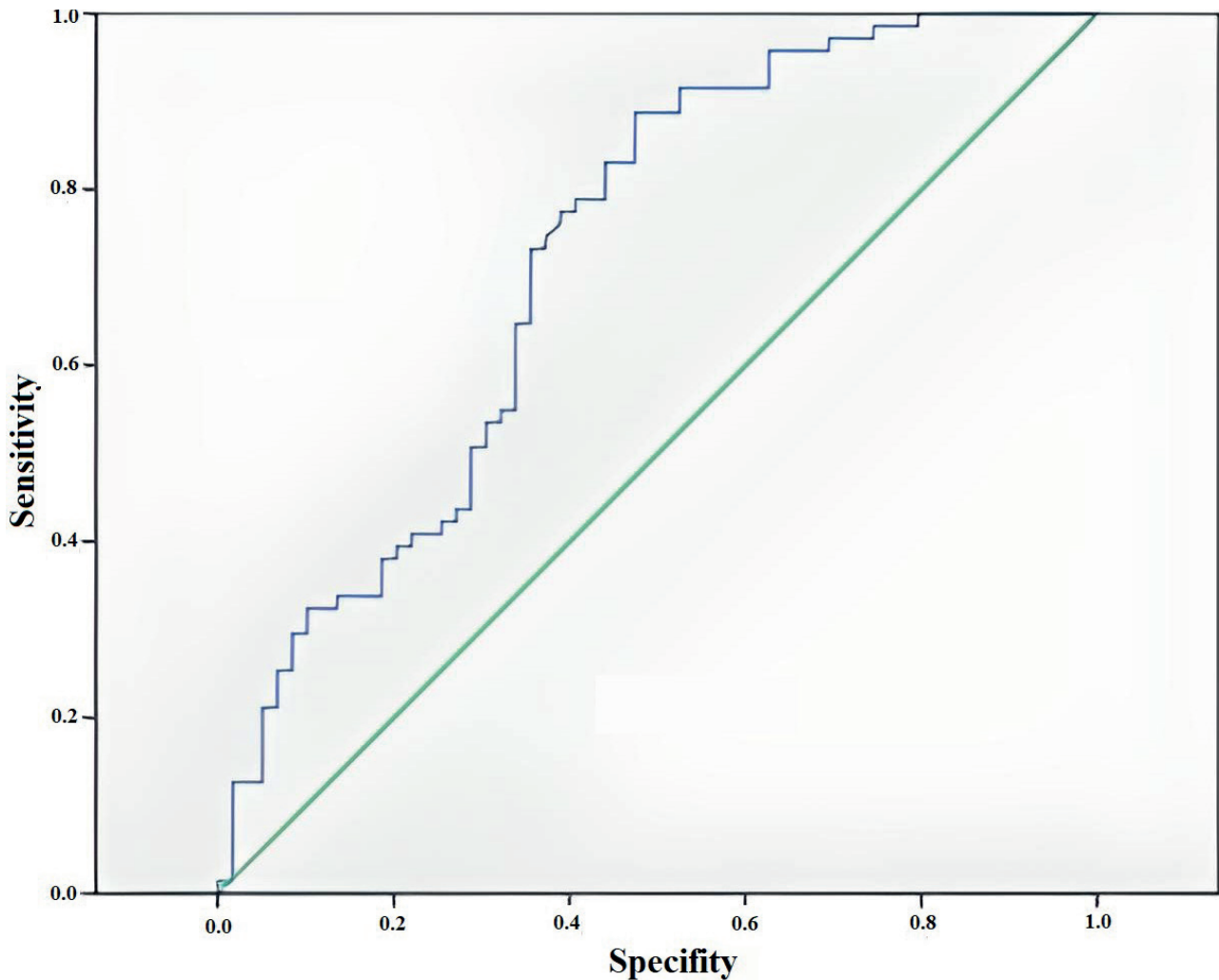


Figure 1: Fibrinogen/albumin ratio (FAR) in receiver operating characteristic (ROC) analysis in the pulmonary embolism (PE) patient group.

there was no statistical difference between the two groups ($P = 0.144$). PE was detected in 71 (54%) of the patients. Of those, 7 (9.9%) were subsegmental, 50 (70.4%) were segmental, and 14 (19.7%) were massive pulmonary. The neutrophil/lymphocyte ratio, D-dimer level, and mean platelet volume (MPV) of the PE patients were 5.6 (3.6–12.7), 3962.4 ± 1385.6 ng/mL FEU, and 10.3 ± 1.8 fL, respectively. In the control group, these values were 4.7 (2.9–8.0), 2633.3 ± 1441.3 ng/mL FEU, and 9.6 ± 1.2 fL, respectively. Demographic characteristics and laboratory results of the groups are given in Table 1.

The albumin values of the subjects in the control group were 3.2 ± 0.7 g/dL, and the albumin values of the patients in the PE group were 3.1 ± 0.6 g/dL. In the statistical evaluation between the groups, no significant difference was found in terms of albumin levels ($P = 0.302$). Fibrinogen levels were significantly higher in the PE group (520.6 ± 191 mg/dL) than in the control group (379.5 ± 187.6 mg/dL; $P < 0.001$). The FAR of the subjects in the control group was 99.1 (75.2–167.9), whereas the FAR in the PE group was 151 (125.1–220.5), significantly higher than the control value ($P < 0.001$). When ROC analysis was performed in the PE group, the FAR was found to be a significant predictive factor (AUC: 0.724; 95% CI = 0.635–0.814; $P < 0.001$). When the FAR was 119.3, the sensitivity was

77.5%, and specificity was 61.0% (Figure 1).

Twenty-seven patients (38%) were followed-up in the service and Forty-four patients (62%) were placed in the intensive care unit (ICU). Nine patients died in the first 3 days of treatment, 11 patients died within 7 days, and 14 patients died within 30 days. Six patients were referred to a different hospital because there was no intensive care unit, and their outcomes are unknown. Mortality rate with known outcomes in the PE group was 21%.

DISCUSSION

It should be noted that this study is the first to evaluate FAR in patients with PE. The most important step in the diagnosis of PE is emergent diagnosis. The gold standard for diagnosis is CTPA. CTPA is expensive, exposes the patient to radiation, and can also cause complications due to the use of contrast agents. The PERC rule (7), Wells and Geneva score (8,9), and D-dimer test are used to prevent unnecessary pulmonary CT angiography. Although the negative predictive value of the D-dimer test is high, there is unfortunately no test that can diagnose PE (10). Therefore, new laboratory tests and new biomarkers are needed.

Increased levels of fibrinogen increase coagulation, and reductions in albumin also increase platelet aggregation and facilitate thrombus formation. In a study by Karahan

et al., fibrinogen levels and FAR were evaluated in 68 patients with ST-elevation myocardial infarction (STEMI). Significantly higher fibrinogen and FAR were detected in STEMI patients (11).

In a study by Demir et al, the FAR was significantly higher in the patient group whose Syntax Score was moderate-high compared to the group with low Syntax Score (12).

In a study Kuyumcu et al., the FAR levels were significantly lower in normal ascending aortic diameter group compared with ascending aortic aneurysm group ($p < 0.001$) (13).

Qiaodong et al. evaluated the FAR in 151 hepatocellular carcinoma patients. Patients underwent liver resection and were followed to evaluate survival. Patients with a high FAR had poorer survival and a higher recurrence rate (14). In a study conducted by Sun et al., the FAR was

compared between 455 control patients and 455 patients newly diagnosed with colorectal cancer. The FAR was significantly higher in patients with colorectal cancer (15). In a study by Wei-Ming et al., 160 patients with rheumatoid arthritis and 159 control patients were enrolled. The FAR was compared between groups, and was found to be significantly higher in rheumatoid arthritis patients (16). In terms of fibrinogen levels, when patients with and without PE were evaluated, a significant difference ($P < 0.001$) and a significant difference in FAR ($P < 0.001$) were found. No statistical correlation was found between the size of PE and FAR.

CONCLUSION

The FAR can be helpful in the diagnosis of PE. Based on the FAR value, physicians may recommend treatment for PE or referral to an ICU.

Limitations: The study had limitations: These were limited time and conducting single center.

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

Ethics: This study was approved by the Adnan Menderes University Ethics Committee (Meeting Decision No. 2018/1434).

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