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Relationship Between Platelet Indices and Prolonged Hospitalization in Patients with Acute Pancreatitis: A Retrospective Observational Study

Akut Pankreatit Hastalarında Trombosit İndeksleri ile Uzamış Yatış Arasındaki İlişki: Retrospektif Gözlemsel Bir Çalışma

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Abstract

Aim: To investigate relationship between platelet count, platelet mass index, mean platelet volume, platelet distribution width and plateletcrit and prolonged hospitalization in patients with acute pancreatitis.

Material and Method: This study was conducted as a retrospective cohort study of all patients with acute pancreatitis from a tertiary level, academic emergency department between June 2017 and July 2021. Demographics, comorbidities, laboratory parameters, length of stay in the hospital and 30-day mortality information of the patients were recorded using computer-based data system of the hospital. Hospitalizations lasting longer than 7 days were considered as prolonged hospitalization.

Results: 752 patients with a median of age of 58 years (25th-75th percentiles: 43.5-75) were included in the study. The median length of hospital stay of the enrolled patients was 4 days (25th-75th percentiles: 3-7). The hospitalization of 166 patients was prolonged, and the prolonged hospitalization rate was 22.1%. The univariate analysis for platelet indices showed that there was no statistically significant difference [Platelet count (p=0.543), mean platelet volume (p=0.656), plateletcrit (p=0.427), platelet distribution width (p=0.497), and platelet mass index (p=0.484)].

Conclusion: There is no clear relationship between platelet indices and prolonged hospitalization and they could not be predictors of prolonged hospitalization in patients with acute pancreatitis.

Keywords: Platelet count, mean platelet volume, acute pancreatitis, prolonged hospitalization, platelet mass index

Öz

Amaç: Akut pankreatitli hastalarda uzamış yatış ile trombosit sayısı, ortalama trombosit hacmi, trombosit kitle indeksi, platelet dağılımı ve plateletkrit değerleri arasındaki ilişkinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Bu çalışma, Haziran 2017 ile Temmuz 2021 tarihleri arasında üçüncü basamak akademik acil serviste akut pankreatit tanısı alan tüm hastaların retrospektif bir kohort çalışması olarak yürütüldü. Hastalar, hastanenin bilgisayar tabanlı veri sistemi kullanılarak kayıt altına alındı. Yedi günden uzun süren yatışlar uzamış yatış olarak kabul edildi.

Bulgular: Ortanca yaşı 58 olan (25-75 persentil: 43,5-75) 752 hasta çalışmaya dahil edildi. Kaydedilen hastaların ortanca hastanede kalış süresi 4 gündü (25-75. persentil: 3-7). 166 hastanın yatış süresi uzamış yatış olarak değerlendirildi ve uzamış yatış oranı %22.1 idi. Trombosit indeksleri için univariant analizde istatistiksel olarak anlamlı bir fark olmadığını gösterildi [Platelet sayısı (p=0,543), ortalama trombosit hacmi (p=0,656), trombositkrit (p=0,427), trombosit dağılım genişliği (p=0,497) ve trombosit kitle indeksi (p=0,484)].

Sonuç: Trombosit indeksleri ile hastanede yatış süresinin uzaması arasında net bir ilişki yoktur ve akut pankreatitli hastalarda hastanede yatış süresinin uzamasını öngöremezler.

Anahtar Kelimeler: Trombosit sayısı, ortalama trombosit hacmi, akut pankreatit, uzamış yatış, trombosit kitle indeksi

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INTRODUCTION

Acute pancreatitis is a potentially fatal inflammatory disease characterized by inflammation and destruction of the pancreatic tissue by the activation of lytic enzymes stored in pancreatic acinar cells, triggered by various factors such as gallbladder stones, alcohol, hypertriglyceridemia, hypercalcemia, drugs, genetics, and autoimmune diseases. Although there are various causes in the etiology, local necrosis and systemic inflammation are generally effective in the pathogenesis of the disease [1]. Platelets are nucleated cells originating from megakaryocytes. In addition to its important role in the coagulation cascade, it also has an important role in the formation of inflammation through the cytokines it secretes [2]. IL-1β is the main molecule released from platelets and plays a role in inflammation. IL-1β triggers the release of other major inflammatory cytokines and plays a key role in the inflammatory reactions that can progress to cytokine storm [2, 3]. However, thrombocytopenia may be seen in cases where the inflammatory process is dominant, such as sepsis. Thrombocytopenia has been associated with poor outcome in patients with systemic inflammatory response syndrome [4].

The relationship between platelet indices and severity of pancreatitis and mortality in intensive care unit admissions has been demonstrated in the literature [5, 6]. In this study, we aimed to investigate the relationship between platelet indices and prolonged hospitalization of the patients with acute pancreatitis.

MATERIAL AND METHODS

This study was conducted as a retrospective cohort study of all adult patients with acute pancreatitis from a tertiary level, academic emergency department between June 2017 and July 2021, which has 1,316,136 presentations during this period. The electronic health data was queried for ICD-10-CM Diagnosis Code K.85 for acute pancreatitis. The researchers evaluated the patient files containing the K.85 ICD code. The presence of two of the triad of acute pancreatitis criteria [high lipase, acute pancreatitis-related symptom, and acute pancreatitis-related radiological finding (ultrasonography or computed tomography)] was considered as an indication for acute pancreatitis [7]. Demographics, comorbidities, laboratory parameters, length of stay in the hospital and 30-day mortality information of the patients were recorded. Patients with missing data and not meeting at least two of the three criteria were excluded from the study. Patients who were referred to another hospital due to lack of clinical or intensive care beds were excluded from the study. Comorbidities were noted as hypertension, active malignity, diabetes mellitus, hyperlipidemia, Alzheimer disease, COPD, ischemic heart disease, asthma, heart failure, chronic renal failure, and cerebrovascular disease. The recorded biochemical parameters were alanine transaminase, albumin, amylase, aspartate transaminase, C-reactive protein, glucose, blood urea nitrogen, creatinine, lipase, potassium, and sodium. The recorded hematological parameters were leukocyte count, neutrophil count, platelet count, hemoglobin, mean platelet volume (MPV), plateletcrit, platelet mass index and platelet distribution width (PDW). The platelet mass index was calculated by multiplying the platelet count with the MPV [8]. Length of hospital stay was defined as the number of days of hospitalization from admission to discharge. Length of hospital stay more than 7 days was considered as prolonged hospitalization.

The primary outcome of this study was prolonged hospitalization. The secondary outcome of this study was short-term mortality after emergency department admission.

The free up-to-date 2022 version of the Jamovi program was used for statistical analysis. Categorical data were expressed as percentages and continuous data as numbers. In continuous data, interquartile range or standard deviation was used where necessary. The conformity of the data to the normal distribution was tested with the Shapiro Wilk test. Patients were grouped as expected and prolonged hospitalization. Chi-square test was used to compare categorical data and Mann Whitney U test was used to compare continuous data between groups. Receiver operating characteristic (ROC) analysis was used to test the predictability of platelet indices. ROC analysis results were presented with the area under the curve (AUC), 95% confidence interval (95% CI), and p values. A p value < 0.05 was considered statistically significant and an AUC value > 0.7 was considered as significant [9]. The accuracy, AUC, sensitivity, and specificity were calculated for the prolonged hospitalization prediction of the model.

Ethics

The study was carried out with the permission of Ümraniye Training and Research Hospital Clinical Research Ethics Committee (Date: 08/26/2021, Decision No: 17856). Due to the retrospective design of the study and the absence of personal information, consent was not obtained from the patients whose data were included in the study, within the knowledge of the approved ethics committee.

RESULTS

Patient Characteristics

A final analysis of 752 patients was performed after applying the inclusion and exclusion criteria as shown in **Figure 1**. 435 (57.8%) patients were female. The median age of the enrolled patients was 58 years (25th-75th percentiles: 43.5-75). A total of 43 patients died, and the mortality rate was 5.7%. The baseline characteristics of the enrolled patients and the comparison of the characteristics between the expected and prolonged hospitalization groups are

shown in **Table 1**. The median length of hospital stay of the enrolled patients was 4 days (25th-75th percentiles: 3-7). The hospitalization of 166 patients was prolonged, and the prolonged hospitalization rate was 22.1%.

Laboratory Values and Outcomes

There were significant differences between the expected and prolonged hospitalization groups in the following laboratory parameters: Neutrophil count [8.25 (6.16 – 11.19) versus 9.13 (6.40-13.10) 103/μL, p=0.035], Lymphocyte count [1.49 (0.95-2.19) versus 1.24 (0.86-1.78) 103/μL, p=0.009], Hemoglobin [13.3 (12-14.4) versus 12.85 (11.3-14.2) g/dL, p=0.019]. neutrophil / lymphocyte ratio [5.67 (3.32-9.99) versus 7.20 (3.91-14.24), p=0.007], Blood urea nitrogen [32.10 (23.54-44.94) versus 38.52 (27.82-66.34) mg/dL, p=<0.001], creatinine [0.81 (0.71-1) versus 0.91 (0.74-1.31) mg/dL, p=<0.001], albumin [41.1 (37.6-44) versus 39.9 (36-42) mg/dL, p=<0.001], glucose [121 (101-154) versus 131.5 (107-174) mg/dL, p=0.021], and sodium [139 (137-140) versus 138 (136-140) mEq/L, p=0.007].

Table 1. Baseline characteristics and laboratory parameters of the enrolled patients and their comparison between the expected and prolonged hospitalization groups

Variables	Total n=752 n (%)/Median (25th-75th percentiles)	Expected Hospitalization n=586 (77.9%) n (%)/Median (25th-75th percentiles)	Prolonged Hospitalization n=166 (22.1%) n (%)/Median (25th-75th percentiles)	P
Age	58 (43.5-75)	57 (43-71)	64.5 (49-79)	<0.001
<65 years	459 (61.0%)	376 (81.9%)	83 (18.1%)	<0.001
≥65 years	293 (39.0%)	210 (71.7%)	83 (28.3%)	
Gender				
Female	435 (57.8%)	348 (80.0%)	87 (20.0%)	0.108
Male	317 (42.2%)	238 (75.1%)	79 (24.9%)	
Comorbidities				
Chronic obstructive pulmonary disease	63 (8.4%)	43 (68.3%)	20 (31.7%)	0.053
Hypertension	352 (46.8%)	256 (72.7%)	96 (27.3%)	<0.001
Diabetes mellitus	175 (23.3%)	125 (71.4%)	50 (28.6%)	0.018
Coronary artery disease	152 (20.2%)	111 (73.0%)	41 (27.0%)	0.103
Congestive heart failure	50 (6.6%)	35 (70.0%)	15 (30.0%)	0.162
Asthma	81 (10.8%)	56 (69.1%)	25 (30.9%)	0.043
Active malignancy	64 (8.5%)	36 (56.3%)	28 (43.8%)	<0.001
Cerebrovascular disease	51 (6.8%)	38 (74.5%)	13 (25.5%)	0.542
Chronic renal failure	48 (6.4%)	28 (58.3%)	20 (41.7%)	<0.001
Hyperlipidemia	208 (27.7%)	152 (73.1%)	56 (26.9%)	0.047
Alzheimer disease	28 (3.7%)	18 (64.3%)	10 (35.7%)	0.076
Laboratory parameters				
White blood cell count (103/μL)	10.81 (8.49-14.13)	10.79 (8.48-13.66)	11.29 (8.60-15.35)	0.137
Neutrophil count (103/μL)	8.51 (6.20-11.67)	8.25 (6.16-11.19)	9.13 (6.40-13.10)	0.035
Lymphocyte count (103/μL)	1.43 (0.93-2.08)	1.49 (0.95-2.19)	1.24 (0.86-1.78)	0.009
Hemoglobin (g/dL)	13.2 (11.9-14.3)	13.3 (12-14.4)	12.85 (11.3-14.2)	0.019
Platelet count (103/μL)	249 (200.5-306)	250 (202-307)	245.5 (196-302)	0.543
Mean platelet volume (fL)	9.40 (8.55-10.20)	9.40 (8.58-10.2)	9.30 (8.5-10.2)	0.656
Plateletcrit (%)	0.23 (0.19-0.29)	0.23 (0.19-0.29)	0.23 (0.18-0.29)	0.427
Platelet distribution width	16.2 (15.9-16.6)	16.2 (15.9-16.6)	16.3 (16-16.7)	0.497
Platelet mass index	2316.6 (1879.75-2861.35)	2313.3 (1882.5-2861.2)	2326.15 (1786.02-2861.5)	0.484
Neutrophil / Lymphocyte Ratio	5.85 (3.45-10.90)	5.67 (3.32-9.99)	7.20 (3.91-14.24)	0.007
Blood urea nitrogen (mg/dL)	32.10 (25.68-47.08)	32.10 (23.54-44.94)	38.52 (27.82-66.34)	<0.001
Creatinine (mg/dL)	0.82 (0.72-1.07)	0.81 (0.71-1)	0.91 (0.74-1.31)	<0.001
C-reactive protein (mg/dL)	9.16 (2.94-39.5)	8.1 (3-33)	13.50 (2.47-61)	0.102
Albumin (g/dL)	41 (37-43.85)	41.1 (37.6-44)	39.9 (36-42)	<0.001
Glucose (mg/dL)	123.5 (102-157)	121 (101-154)	131.5 (107-174)	0.021
Amylase (mg/dL)	806.5 (321-1926)	806.5 (335-1915)	818 (281-2001)	0.994
Lipase (mg/dL)	1722.50 (574.50-4616.50)	1.829.50 (590.00-4.348.00)	1466 (478.8-5283)	0.518
Potassium (mEq/L)	4.3 (4.0-4.6)	4.3 (4.0-4.6)	4.22 (4.0-4.7)	0.983
Sodium (mEq/L)	139 (136-140)	139 (137- 140)	138 (136-140)	0.007
Aspartate transaminase (U/L)	123 (34-284)	123 (34-280)	124 (33- 302)	0.824
Alanine transaminase (U/L)	100 (27-297)	102 (27- 297)	98 (25-297)	0.562
Length of hospital stay (days)	4 (3 – 7)	3 (2 – 5)	11 (9 – 15)	<0.001

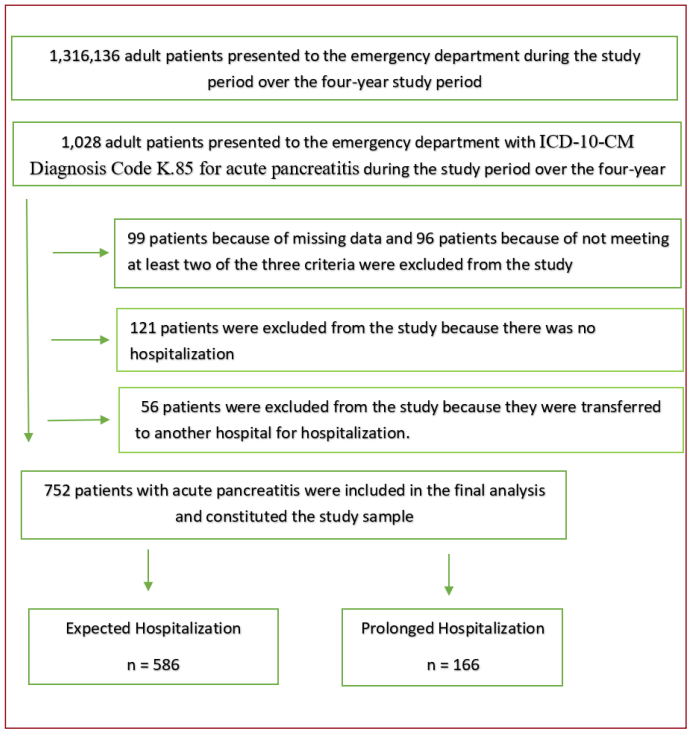

Figure 1. Flowchart of the study

As a result of the univariate analysis for platelet indices, it was found that there was no statistically significant difference between expected and prolonged hospitalizations: Platelet count [250 (202-307) versus 245.5 (196-302) 103/µL, p=0.543], Mean platelet volume [9.40 (8.58-10.2) versus 9.30 (8.5-10.2) fL, p=0.656], Plateletcrit [0.23 (0.19-0.29) versus 0.23 (0.18-0.29) %, p=0.427], Platelet distribution width, [16.2 (15.9-16.6) versus 16.3 (16-16.7) %, p=0.497], and Platelet mass index [2313.3 (1882.5-2861.2) versus 2326.15 (1786.02-2861.5), p=0.484].

Demographics and laboratory parameters of the enrolled patients and their comparison between survivor and non-survivor groups are shown in **Table 2**.

According to ROC analysis, AUC values of platelet count, MPV, plateletcrit, PDW, and platelet mass index for prolonged hospitalization were determined as 0.515 (95% CI:0.464-0.567, p=0.553), 0.511 (95% CI: 0.461-0.561, p=0.658), 0.520 (95% CI:0.469-0.572, p=0.443), 0.483 (95%CI: 0.433-0.533, p=0.501), and 0.518 (95% CI:0.466-0.569, p=0.499), respectively.

In the ROC curve constructed to determine the accuracy of the regression model to predict prolonged hospitalization, the accuracy, AUC, sensitivity, and specificity value was 0.795, 0.725, 0.96, and 0.18, respectively (**Figure 2**).

Table 2. Demographics and laboratory parameters of the enrolled patients and their comparison between survivor and non-survivor groups.

Variables	Survivor n=709 (94.3%) n (%)/Median (25th-75th percentiles)	Non-Survivor n=43 (5.7%) n (%)/Median (25th-75th percentiles)	P
Age	58 (44-72)	78 (61-85)	<0.001
<65 years	446 (97.2%)	13 (2.8%)	<0.001
≥65 years	263 (89.8%)	30 (10.2%)	
Gender			
Female	410 (94.3%)	25 (5.7%)	0.968
Male	299 (94.3%)	18 (5.7%)	
Laboratory parameters			
White blood cell count (103/µL)	10.81 (8.50-14.00)	10.59 (8.50-14.92)	0.944
Neutrophil count (103/µL)	8.50 (6.20-11.58)	9.47 (6.59-13.48)	0.322
Lymphocyte count (103/µL)	1.47 (0.96-2.14)	0.87 (0.58-1.32)	<0.001
Hemoglobin (g/dL)	13.3 (12.0-14.4)	11.0 (9.6-13.2)	<0.001
Platelet count (103/µL)	250 (202-307)	232 (160.5-288.5)	0.049
Mean platelet volume (fL)	9.40 (8.60-10.20)	9.10 (8.05-10.35)	0.408
Plateletcrit (%)	0.23 (0.19-0.29)	0.20 (0.16-0.25)	0.024
Platelet distribution width	16.2 (15.9-16.6)	16.20 (15.85-16.60)	0.486
Platelet mass index	2331.8 (1886.8-2868.4)	2041.60 (1528.34-2473.90)	0.024
Neutrophil / Lymphocyte Ratio	5.75 (3.40-10.22)	11.73 (5.45-20.75)	<0.001
Blood urea nitrogen (mg/dL)	32.10 (23.54-44.94)	59.92 (38.52-140.61)	<0.001
Creatinine (mg/dL)	0.81 (0.72-1.02)	1.28 (0.73-2.75)	<0.001
C-reactive protein (mg/dL)	8.12 (2.26-33.00)	55 (25-100.5)	<0.001
Albumin (g/dL)	41.00 (37.85-44.00)	34.40 (31.0-36.67)	<0.001
Glucose (mg/dL)	124 (103-157)	121 (90-170.50)	0.329
Amylase (mg/dL)	898 (350-1976)	289 (182.5-561.50)	<0.001
Lipase (mg/dL)	1945 (610-4722)	502 (343-1037.30)	<0.001
Potassium (mEq/L)	4.30 (4-4.6)	4.50 (4.19-4.80)	0.018
Sodium (mEq/L)	139 (137-140)	136 (132.85-138)	<0.001
Aspartate transaminase (U/L)	110 (28-30)	49 (19-159)	0.266
Alanine transaminase (U/L)	128 (36-28)	73 (27.5-271)	0.014
Length of hospital stay (days)	4 (3 – 7)	5 (2 – 10.5)	0.626

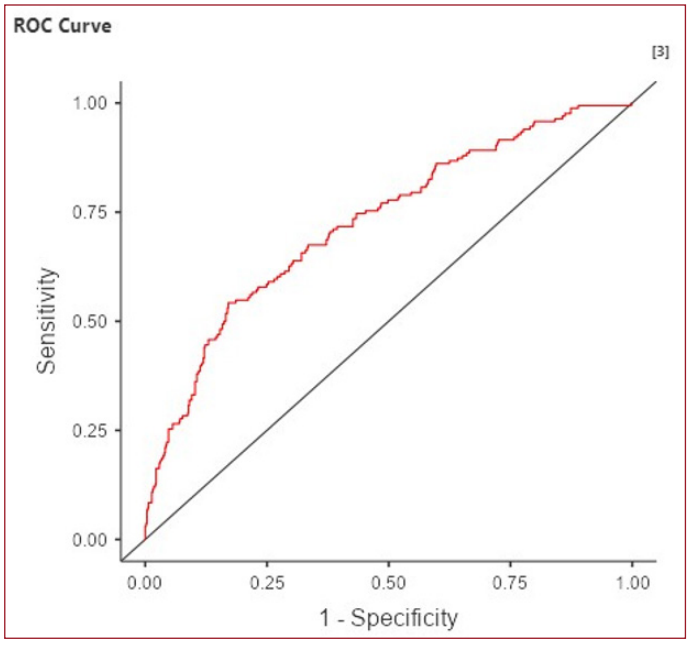

Figure 2. The receiver operating characteristic curve of the multivariate logistic regression model for predicting prolonged hospitalization

DISCUSSION

In this study, we investigated relationship between platelet count, platelet mass index, MPV, PDW and plateletcrit and prolonged hospitalization in patients with acute pancreatitis. Results of current study demonstrated that there is no clear relationship between platelet indices and prolonged hospitalization, and they could not be predictors of prolonged hospitalization in patients with acute pancreatitis. To the best of our knowledge, this study is first study that evaluates the role of platelet mass index in acute pancreatitis. More importantly, the regression model generated was able to predict the probability of prolonged hospitalization with high accuracy as 0.795 [10]. In addition, platelet count, plateletcrit and platelet mass index were found to be statistically significantly lower in the non-survivor group.

Acute pancreatitis is a process dominated by inflammatory processes. Based on the hypothesis that platelets play a role in inflammation, researchers suggested that platelet changes might occur in acute pancreatitis [11-14]. In the retrospective study conducted by Yarkaç et al., on 168 patients with acute pancreatitis in the emergency department, they found increased platelet count and MPV in the acute pancreatitis group compared to the control group [12]. On the other hand, they reported that there was no significant difference in platelet count and MPV between severe and mild acute pancreatitis cases. In conclusion, in the study of Yarkaç et al., it was stated that platelet count and MPV value are poor prognostic indicators in severe acute pancreatitis. With a similar methodology, Beyazıt et al investigated the ability of platelet indices to predict severe disease as determined by the Modified Glasgow Prognostic Score (mGPS) and computed tomography severity index (CTSI) in patients with acute pancreatitis [13]. They reported statistically significant decrease in MPV levels in patients with acute pancreatitis compared with healthy controls. The results of the aforementioned study showed that MPV could be a predictor of severity classification according to mGPS. However, they found that it was an unsuccessful predictor in severity classification according to CTSI. In addition, they showed that platelet count and PDW were insufficient to predict disease and its severity. Bilgiç et al. showed that there is a statistically significant correlation between classical prognostic scores such as APACHE-II and platelet indices including PDW and MPV in patients with mild acute pancreatitis [14]. On the other hand, they found that there was no statistically significant correlation between classical prognostic scores and platelet and plateletcrit in patients with mild acute pancreatitis. Moreover, they reported that there was no powerful correlation between classical prognostic scores and platelet and plateletcrit in patients with severe acute pancreatitis. Methodological differences between studies may have been effective in reporting conflicting results.

The platelet mass index indicates the platelet mass per unit volume. It can be calculated by multiplying the platelet count by the MPV. Platelet mass index is a newly studied biomarker that is thought to be effective in urological infections, neonatal infections and inflammatory processes [15-18]. According to the results of our study, the platelet mass index is not an adequate predictor of the disease in predicting prolonged hospitalization in patients with acute pancreatitis. A logical explanation for this might be that the predictive ability of the platelet count and MPV, which was used in the calculation of the platelet mass index, was not sufficient in our cohort. In addition, platelet mass index was significantly lower in non-survivor group than survivor group. A plausible explanation for this might be that platelet count was significantly lower in non-survivor group than survivor group.

The most important limitation of the current study is its retrospective design. Secondly, the severity scores of acute pancreatitis cases could not be recorded. However, recording the mortality rate and length of hospital stay can give an idea about the severity of the patients in the sample. In a sample that included nearly two thousand patients and only included severe acute pancreatitis cases, the mean hospital stay was 22 days, and the mortality rate was 11.8% [19]. According to the results of this study, we think that our sample consisted of relatively mild acute pancreatitis cases. A third limitation of our study is that the etiology could not be recorded. As the last limitation, the single-center nature of our study limits its generalizability. We recommend that our results be validated with multi-center studies.

CONCLUSION

In this retrospective study, there is no clear relationship between platelet count, platelet mass index, MPV, PDW and plateletcrit and prolonged hospitalization in acute pancreatitis. According to our results, platelet indices could not be predictors of prolonged hospitalization in acute pancreatitis.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ümraniye Training and Research Hospital Clinical Research Ethics Committee (Date: 08/26/2021, Decision No: 17856).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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