The value of hematological parameters in acute pancreatitis

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ABSTRACT

BACKGROUND: Acute pancreatitis (AP) is a common inflammatory disease in the emergency department (ED). This study aims to assess the role of CRP and hematologic parameters in mild/severe AP patients and biliary/nonbiliary AP at the time of admission to the ED.

METHODS: 168 patients who were diagnosed as AP in the ED, and as a control group, 100 patients were included in this study. At the time of application to the ED, the demographic information (age, sex) and the amylase, lipase, CRP, hematological parameters (WBC, MPV, RDW, PLT, NLR) of all patients and the control group were recorded and compared. According to the etiology of the patients, the patients were divided into biliary and nonbiliary AP groups and according to the severity, they were divided into mild and severe AP groups, then, the same parameters were evaluated.

RESULTS: Significant differences were found out between WBC, CRP, NLR, MPV and PLT values between patient and the control group (p<0.001). The length of hospitalization and the parameters were not significant between the biliary and the nonbiliary group. Ranson and APACHE II scores were correlated with WBC, CRP and NLR. There was a statistically significant difference between the mild and severe AP groups in terms of duration of the hospital stay, CRP, WBC and NLR values (p=0.003 for CRP, p<0.001 for the others). In severe AP, the cut-off value of NLR was found to be 8.05, sensitivity %93.48, specificity %86.89 and AUC 0.937 (p<0.001).

CONCLUSION: The use of parameters, such as WBC, CRP, and NLR, in combination with other diagnostic and prognostic tools in emergency service can provide convenience to clinicians at the time of admission and prognosis.

Keywords: Acute pancreatitis; mean platelet volume; neutrophil-to-lymphocyte ratio; platelet count; red cell distribution width.

INTRODUCTION

Acute pancreatitis (AP) is an important cause of abdominal pain, which is the most common complaint of emergency department (ED). Risk factors and the etiology of the disease affect the outcome of patients with AP.[1] Over 80% of the etiology of AP all over the world is gallstones and alcohol usage.[2] Some studies have reported that biliary AP is more severe and has higher mortality than alcoholic AP.[3] Diagnosis of AP was based on the presence of at least two of the following three criteria: (1) Continuous abdominal pain (2) serum amylase and/or serum lipase level at least three times higher than the normal upper limit and (3) Characteristic findings on abdominal imaging.[4–7]

Serum biomarkers, imaging studies and many scoring systems (Balthazar and early warning score (EWS), Atlanta, Ranson, APACHE score, Glasgow and Imrie scores) are widely used for the assessment of mortality and severity in acute pancreatitis.[4,8,9] Ranson score ≥3, APACHE II score ≥8, and Atlanta score
The majority of these scores are impractical for immediate use due to various reasons (such as follow-up, service intensities and need for further investigation). Investigations are underway for new rapid biomarkers to predict the seriousness of AP. Acute pancreatitis is an inflammatory disease that arises from inappropriate intrapancreatic activation of digestive enzymes, the infiltration of neutrophils and macrophages, and the necrosis of pancreatic tissue in its pathogenesis. Platelet count (PLT), mean platelet volume (MPV), neutrophil/lymphocyte ratio (NLR) and red cell distribution width (RDW) and other hematological parameters have been extensively studied in clinical settings, such as critical diseases, pneumonia, acute appendicitis, cerebrovascular and cardiovascular diseases, defined as prognostic factor. A complete blood count is a laboratory test with many parameters that can show the inflammatory state in the AP. The advantages of PLT, MPV, NLR, and RDW are that they are easily accessible, and they can be routinely performed in critical patients, including patients with severe AP. There are studies evaluating the prognosis and mortality of severe AP regarding white blood cell (WBC), C-reactive protein (CRP), PLT, NLR and RDW parameters. However, the correlation between CRP, WBC and NLR and Ranson and APACHE II score system is very rare in the literature. This study was conducted to investigate the possible associations of these hematological parameters in patients with biliary and non-biliary AP and the prognostic value of mild and severe AP.

**MATERIALS AND METHODS**

**Study Design**
A total of 168 patients who were diagnosed with AP in the ED between 01.01.2014–31.07.2016, and as a control group, 100 patients with inclusion and exclusion criteria were included in this study. This study was approved by the Mersin University Clinical Research Ethics Committee (Reference number: 2017/110, dated 14/04/2017). The medical records of 168 patients who applied to the emergency department for AP were obtained and analyzed using the “Nucleus and Enili Medical Information System.” All data were analyzed retrospectively. Demographic information (age, sex), amylase, lipase, CRP, hematological parameters (WBC, MPV, RDW, PLT, NLR) of the patient group and control group were recorded. The parameters of both groups were compared. Patients were divided into two groups according to pancreatitis etiology: biliary and non-biliary group. The ultrasonography (USG) findings of the patients were used to determine the etiology. Patients with acute cholecystitis, cholelithiasis and other biliary pathologies were accepted as biliary AP. The patient group with no evidence of stones in the gallbladder or biliary tract on ultrasonography was evaluated as normal and other causes of AP (e.g. hyperlipidemia, alcohol, idiopathic) were detected was defined as non-biliary AP. In addition, the distribution of diagnostic parameters according to the length of stay of AP patients was investigated.

All AP patients were divided into two types according to the severity of the disease: (1) mild AP and (2) severe AP. The severity of the illness was measured by Ranson, APACHE II and Atlanta scores at admission. Ranson score ≥3, APACHE II score ≥8, and Atlanta score ≥1 were categorized as severe AP. The patients with the values below these scores were accepted as mild AP.

**Laboratory Analysis**
The electrical impedance method was used in the analyzer (Beckman Coulter LH 780) after obtaining EDTA blood tube for hemoglobin (Hb), leukocyte count, platelet count, MPV and RDW assay. Serum CRP levels were measured by turbidimetric method (Roche Cobas C 501). The normal reference values of the parameters in our study were: Hemoglobin (11.7–16 g/dL), WBC (4.5–10 x10³/µL), neutrophil count (1.5–6.7 x10³/µL), lymphocyte count (1.5–4 x10³/µL), platelet count 150–400 x10³/µL, MPV (7.4–10.4 fL), RDW (11.6–14.8%) and serum CRP (0–5 mg/dL).

**Exclusion and Inclusion Criteria**
Exclusion criteria consisted of heart failure, hematologic disease, malignancy, chronic infection, liver disease, vascular disease, infectious disease other than infection or pancreatitis, failure to access file information, and history of drug use that could affect hematological parameters. For the control group, there was also an exclusion criterion for any other serious illness other than these diseases. Patients included in this study were adults over 18 years of age, patients diagnosed with AP between 01/01/2014 and 31/07/2016, patients without medications could cause low platelet count or platelet dysfunction by affecting platelet count and volume, no infection or inflammatory disease, and control group patients over 18 years of age.

**Statistical Analysis**
The Shapiro Wilks test was used for the correlation between the parameters and the corresponding normal scores in the biliary and non-biliary groups, that testing the normality of data. Normal distribution was not found to be appropriate for the subgroups. Median and percentage values were given as descriptive statistics of the parameters. The difference between the averages of the parameters was analyzed by Mann-Whitney U test. Receiver Operating Curve (ROC) analyses were performed to determine the cut-off points of continuous measurements. Cut-off, Area Under Curve (AUC) and p-values, sensitivity, selectivity, LR+ and LR- values are given as descriptive statistics. In addition, the separation power on the discrimination of a biliary and non-biliary group of related parameters was evaluated by ROC analysis. Statistical significance was taken as p<0.05.

**RESULTS**
In our study, the mean age of 168 patients diagnosed with pan-
The value of hematological parameters in AP was 48.13±13.28, while the mean age of the control group was 43.95±19.31. There was no statistically significant difference between two groups in the mean age (p=0.058).

Among 168 patients, 79 were male (47%) and 89 were female (53%). The number of women in the control group was 54 (54%), while the number of males was 46 (46%). There was no statistically significant difference regarding sex in both groups (p=0.871).

WBC, CRP, NLR, MPV, RDW and PLT parameters of the patient (AP) and control group were compared. There was a statistically significant difference between CRP, WBC, NLR, MPV and PLT levels (p<0.001 for others). There was no significant difference between the two groups in terms of RDW value (p=0.418), which is shown in Table 1. According to the results of ROC analysis in patients with AP, the cut-off value of CRP was 3, sensitivity was 73.81%, specificity was 58% and AUC was 0.687, p=0.001. The ROC curve and analysis of CRP and other hematological parameters are shown in Table 2 and Figure 1.
The amylase, lipase, WBC, CRP, NLR, MPV, RDW, PLT values and duration of hospital stay of the biliary and non-biliary AP group were compared. The median value of the amylase in the biliary group was 1300 [569–2670], while the median value of the lipase was 1200 [846–2180]. The median value of the amylase in the non-biliary group was 370 [168.5–683.5], while the median value of the lipase was 811 [441.5–1181.5]. There was a statistically significant difference between both groups of amylase and lipase values (p<0.001). There was no statistically significant difference between the biliary and non-biliary AP groups in duration of hospital stay and other parameters (WBC, CRP, NLR, MPV, RDW, PLT) (p>0.05).

The relation of hematological parameters with Ranson and APACHE II scores in patients with acute pancreatitis was investigated. Correlation of Ranson score with APACHE II score (r=0.424, p<0.001), WBC (r=0.421, p<0.001), CRP (r=0.200, p=0.009), NLR (r=0.628, p<0.001) and RDW (r=0.181, p=0.019) was determined. Correlation of the APACHE II score with the Ranson score (r=0.424, p<0.001), WBC (r=0.275, p<0.001) and NLR (r=0.412, p<0.001) was found (Table 3).

A total of 122 (72.6%) patients (57 males and 65 females) with a mean age of 47.45±12.46 were found to have mild AP diagnosis according to the severity scores performed at the time of emergency department admission. The remaining 46 (27.4%) patients (21 males and 25 females) were diagnosed with severe AP and their mean age was 50.39±15.71. Of the patients with mild AP, 26 (21.3%) were non-biliary AP and 96 (78.7%) were biliary AP. 11 of the severe AP patients (23.9%) were non-biliary AP and 35 (76.1%) were biliary AP. A statistically significant difference was found between the mild and severe AP groups for the duration of hospital stay, CRP, WBC, and NLR (Table 4).
WBC and NLR (p=0.003 for CRP, p<0.001 for others). No significant difference was found between the two groups for other parameters (p>0.05). This situation is shown in Table 4.

According to ROC analysis results in severe AP patients, the cut-off value of CRP was 6.63, sensitivity 80.43%, specificity 45.90% and AUC 0.647, p=0.0016. The cut-off value of WBC was 11.7, sensitivity was 76.09%, specificity was 67.21%, and AUC was 0.781, p<0.0001. The cut-off value of NLR was 8.05, sensitivity was 93.48%, sensitivity was 86.89%, and AUC was 0.937, p<0.001. The ROC curve and analysis of CRP, WBC, NLR and other hematological parameters are shown in Table 5 and Figure 2.

The median values of patients who were hospitalized for seven days and fewer than seven days were analyzed respectively. The median values were (19.5 [5.5–103.5] vs. 8 [3–26], p=0.033) for CRP (14.15 [11375–16850] vs. 10.5 [8400–13900], p<0.001) for WBC, (8 [4–14.75] vs. 5 [2–8], p=0.008) for NLR and (10 [9.25–11] vs. 9 [8–10] p=0.001) for MPV. However, there was no statistically significant difference between the amylase, lipase, RDW and PLT median values of the inpatients (p>0.05).

**DISCUSSION**

It is important that the diagnostic tests for diagnosing and in the clinical evaluation of the prognosis of acute pancreatitis should be fast and simple, inexpensive and potentially widely available. Hematological parameters (WBC, NLR, MPV, RDW, PLT) and especially CRP have been studied in many cases, such as stroke, heart failure, pneumonia, pancreatitis and rheumatologic diseases. The elevation of CRP, WBC, NLR and RDW in such diseases and low PLT and MPV values are considered as poor prognostic indicators.[5,7,10–13,16–18]

White blood cells, NLR, and CRP are usually prominent as indicators of acute inflammation.[8,19,20] High CRP value is often accepted as an important determinant of violence in AP. In particular, the CRP value measured within 48 hours from the onset of symptoms was found to be significant for the diagnosis of severe AP with 80–86% sensitivity and 61–84% specificity. CRP value within 48 hours from the onset of symptoms was found to be significant for necrotizing pancreatitis with specificity over 80%.[21] In a study by Khanna et al.,[9] CRP value was found to be 100% sensitive and 81.4% specific for the detection of pancreatic necrosis. The disadvantage of CRP as a marker is the late peaking (48–72 h) and non-specificity as an inflammatory marker. Similarly, the number of WBCs (12.2x103/L) at the time of admission in mild AP patients was significantly higher than that of healthy subjects (6.3x103/L).[14] In our study, CRP and WBC values were found higher in AP patients than the control group. In other studies, NLR was found to be higher in AP patients. In a study conducted in our country, the cut-off value for NLR in patients aged 16.2 years was defined as 92.9% and specificity as 41.4%.[17] In our study, NLR was found to be high in AP patients (Cut-off value >2, sensitivity 76.79%, specificity 47% and AUC 0.654). NLR is significantly higher in cases with more severe cases,

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<td>CRP</td>
<td>&gt;6.63</td>
<td>0.647 [0.57–0.72]</td>
<td>0.0016</td>
<td>80.43 [66.1–90.6]</td>
<td>45.90 [36.8–55.2]</td>
<td>1.49 [1.2–1.8]</td>
<td>0.43 [0.2–0.8]</td>
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<td>WBC</td>
<td>&gt;11700</td>
<td>0.781 [0.711–0.841]</td>
<td>&lt;0.0001</td>
<td>76.09 [61.2–87.4]</td>
<td>67.21 [58.1–75.4]</td>
<td>2.32 [1.7–3.1]</td>
<td>0.36 [0.2–0.6]</td>
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<td>NLR</td>
<td>&gt;8.05</td>
<td>0.937 [0.89–0.97]</td>
<td>&lt;0.0001</td>
<td>93.48 [82.1–98.6]</td>
<td>86.89 [79.6–92.3]</td>
<td>7.13 [4.5–1.3]</td>
<td>0.075 [0.03–0.2]</td>
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<td>PLT</td>
<td>&gt;253000</td>
<td>0.532 [0.454–0.61]</td>
<td>0.5330</td>
<td>63.04 [47.5–76.8]</td>
<td>51.64 [42.4–60.8]</td>
<td>1.3 [1.0–1.7]</td>
<td>0.72 [0.5–1.1]</td>
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<td>RDW</td>
<td>&gt;14.7</td>
<td>0.584 [0.506–0.660]</td>
<td>0.0905</td>
<td>39.13 [25.1–54.6]</td>
<td>79.51 [71.3–86.3]</td>
<td>1.91 [1.2–3.2]</td>
<td>0.77 [0.6–1.0]</td>
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<td>MPV</td>
<td>&gt;9.4</td>
<td>0.592 [0.52–0.67]</td>
<td>0.0667</td>
<td>71.74 [56.5–84]</td>
<td>49.18 [40.0–58.4]</td>
<td>1.41 [1.1–1.8]</td>
<td>0.57 [0.4–0.9]</td>
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ROC: Receiver operating curve; AP: Acute pancreatitis; CI: Confidence interval; AUC: Area under the curve; WBC: White blood cell count; CRP: C-reactive protein; MPV: Mean platelet volume; NLR: Neutrophil lymphocyte ratio; RDW: Red cell distribution width; PLT: Platelet count.
especially in gastrointestinal cases (appendicitis and chole-
cystitis). Azab et al.\[8\] reported that NLR was better than
WBC, without anticipating the undesirable consequences of
AP. This study also showed that 44.7 NLR cut-off value was
determined as a simple indicator of AP severity. However,
Binnetoğlu et al.\[23\] concluded that NLR was a controversial
issue in determining the prognosis of AP, although the study
reported that the NLR reported an increase in AP, especially
in the first 48 hours. In a study of 146 patients by Suppiah et
al.,\[25\] similar to our data, there was no significant difference
in the first three days than in the other patients. This study
concluded that NLR elevation was significantly as-
associated with severe AP for the first 48 hours after admission
and was an independent negative prognostic marker in AP. In
this study, sensitivity was 63–90% and specificity was 5–57%.

A direct correlation of Ranson and APACHE II score with
WBC, CRP and NLR was determined in our study. CRP, WBC
and NLR values were higher in severe AP. Especially in severe
AP, the sensitivity of NLR was 93.48%, specificity was 86.89%
and AUC was 0.937 and cut-off value was 8. The most widely
used clinical prognostic scores include Ranson criteria and
APACHE II classification system. The two scoring systems are
commonly used to identify patients with severe pancreatitis
who have an increased risk of complications: Ranson’s criteria
and APACHE II. A Ranson score ≥3, or an APACHE II score
≥8 indicates severe pancreatitis.\[8,10,11\] Limitations of Ranson’s
criteria include a 48-hour time requirement for score de-
termination and a lack of ability to reassess severity at later
points during the hospitalization. The APACHE II scoring sys-
tem allows determination of severity on admission and at any
point during the hospital course; however, the complexity of
scoring may limit its use. Therefore, it may be possible to
predict AP prognosis much more easily with WBC, CRP,
and NLR in patients with AP clinical, laboratory, and imaging
findings. Some studies on acute pancreatitis have reported
that the height of RDW is proportional to the severity of
inflammation, and patients with high RDW values may have
higher mortality. It has been reported that RDW can be used
in evaluating acute pancreatitis severity with other scoring
systems.\[7,24\] In another study, the RDW value (12.6±0.59) at
admission in mild AP patients was significantly lower than that
of healthy subjects (13.4±2.085). However, in the same study,
RDW (14.4±1.06) was significantly higher in patients with se-
vere AP than in healthy subjects.\[14\] In the study of Akbal et
al.,\[22\] similar to our data, there was no significant difference
between the healthy and the patient group and between the
mild and severe AP for the RDW value. The RDW value was
not meaningful in our work because it was only measured on
admission to the hospital.

A study examining the condition of the platelets and remission
of the disease showed that platelets were directly involved in
the systemic inflammatory process and contributed to the
formation of AP.\[30\] Median and mean platelet counts were
significantly lower in patients with severe AP and in patients
who died of AP. Generally, patients without thrombocytopenia
showed good prognosis. Meanwhile, with the treatment of
AP, platelet counts increased within just a few days.\[11\] In a
case report, serious thrombocytosis, as well as thrombocy-
topenia, may be seen in AP.\[27\] On the contrary, another study
found out that PLT and RDW were not effective in determin-
ing the mortality of AP cases within the first 48 hours.\[18\] In
several studies, there were no significant differences between
patients with AP and healthy groups in terms of PLT numbers
at the time of admission.\[16,17\] The increase in MPV showing
platelet activation has been described as an independent risk
factor for different clinical situations in the literature.\[28–30\] In
a study of AP, no difference was found between baseline and
remission MPV levels in 24 AP patients. Compared with the
healthy group, the MPV value at the time of admission was
higher in the patient group.\[23\] Similarly, in another study, the
number of MPV in AP patients was found to be significantly
higher than in healthy individuals.\[14\] In all these studies, the
findings suggest that the severity of systemic inflammation is
related to platelet volume. In our study, the number of PLT
and MPV values in the AP at the time of admission was higher
than the control group, even though it was in the normal
reference interval. There was no difference between the mild
and severe AP groups regarding PLT number and MPV value.
Biliary causes (64–70%) take place on the top and idiopathic
causes (24–31%) are in the second place in some studies
which were conducted in Turkey.\[31,32\] When the etiologies
of these patients were examined in detail, gallstones were
determined as 40%, idiopathic causes 25.6%, alcohol 22% and
post-ERCP 3.9%.\[2\] In our study, 77.9% of the 168 patients
with AP were classified as biliary AP, while 22.1% were classi-
fied as non-biliary AP. 23.9% of severe AP patients were non-
biliary AP and 76.1% were biliary AP. The data obtained in
our study are consistent with the literature in this regard. In
our study, no significant difference was found between CRP
and hematological parameters (WBC, NLR, MPV, RDW, PLT)
between biliary and non-biliary AP groups. In our country,
Turkey, related to AP, Kara et al.\[20\] reported that the WBC
levels measured during admission did not show a signif-
icant difference between alcohol-dependent AP and biliary
AP groups.\[5\] In the same study, levels of serum amylase and
lipase were significantly higher in the biliary AP group than in
the alcoholic AP group.\[7\] Similar to our study, Okuturlar et
al.'s\[5\] study showed that the amylase and lipase values in the
biliary AP group were higher than the nonbiliary AP group.

The average length of stay in the hospital for acute pancre-
atitis patients was reported to be 4–14 days.\[2,7,14\] Thus, we
admitted an average length of stay in hospital is 7-day in our
study, and the relationship between CRP and hematologic pa-
rameters was evaluated. CRP, WBC, NLR and MPV values
were higher in patients with a stay over seven days, amylase, lipase, RDW, and PLT mean values were not statistically significant. CRP value was found to be 19.5 mg/dL on average in hospitalized patients over seven days. Cetin et al.[33] found out that 7th day CRP was associated with necrotizing pancreatitis with a sensitivity of 71% and specificity of 74% when the cut-off value was accepted as 10 mg/dL. In the study of Azab et al.[8] the NLR level was significantly longer than in the hospital (average duration of stay 6.2 days). High WBC, CRP, NLR and MPV values in AP patients with a longer hospital length of stay (more than seven days) may be associated with the severity of inflammation in pancreatitis. Patients with severe AP in our study had a longer stay in the hospital and WBC, CRP, and NLR values of these severe AP patients were also higher.

In conclusion, our study aimed to evaluate the value of parameters, such as CRP, WBC, NLR, MPV and PLT, in AP patients at the time of admission. Parameters, such as CRP, WBC, NLR, MPV and PLT, found significant in AP. The same parameters were not found to discriminate between the biliary and non-biliary AP groups. Amylase and lipase values were higher in biliary AP. WBC, CRP, NLR and MPV were higher in long-term hospitalised patients. The high level of these parameters can provide clues to that AP patients may stay longer in the hospital. This study revealed that the correlation between Ranson and APACHE II prognostic scoring systems and WBC, CRP, NLR values is new and important information. Sensitivity, specificity and AUC value of NLR are better, especially when predicting the severity of the disease. It may be possible to predict AP prognosis much more easily with WBC, CRP, and NLR in patients with AP clinical, laboratory, and imaging findings.

Limitations
The most important limitations of our study are retrospective study and small sample sizes. However, long-term outcomes, complications, and mortality have not been studied. We should note that only one measurement of the evaluated parameters has been taken into account. In addition, acute changes in haematological parameters due to technical reasons, such as haemolysis and possible changes over time, have not been evaluated. Although close attention has been paid to time constraint between the first blood sampling and laboratory analysis when selecting patient groups, this issue may not be fully standardized given that this study is retrospective.

Conflict of interest: None declared.

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Akut pankreatitte hematolojik parametrelerin değeri

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AMAC: Akut pankreatit (AP), acil serviste sık görülen bir enfiamatuar hastalıktır. Bu çalışmanın amacı, acil serviste başvurular ve biliyer ve non-biliyer AP’li hastalarda C-reactif protein (CRP) ve hematolojik parametrelerin rolünü değerlendirmektir.

GEREC VE YONTEM: Kontrol grubu olarak 100 hasta ve acil serviste AP tanısı alan 168 hasta çalışmaya dahil edildi. Kontrol grubunun ve AP hastalarını demografik bilgileri (yaş, cinsiyet), amilaz, lipaz, CRP, hematolojik parametreler (veyaz kan hücreleri değişkeni [MPV], kirmızı hücre dağılım genişliği [RDW], trombosit sayımı [PLT], nötrofil-lenfosit oranı [NLR]) kaydedildi ve karşılaştırıldı. Hastalar, AP etyolojisine göre biliyer ve nonbiliyer grub olarak ayrıldı. Hastaların şiddetine göre, haffı ve şiddetli AP olarak iki grup oluşturuldu, aynı parametreler değerlendirildi.

BULGULAR: Hasta ve kontrol grubuna WBC, CRP, NLR, MPV ve PLT değerleri arasında anlamli bir fark bulundu (p<0.001). Ransons ve APECHİ leveleaması WBC, CRP ve NLR ile korele ida. Haffı ve şiddetli AP grupları arasında, hastanede yatsısı süresi, CRP, WBC ve NLR değerleri arasında istatistiksel olarak anlamli bir fark vardi (CRP için p=0.003, diğerleri için p<0.001). Ciddi AP'de NLR’nin kestirim değeri 8.05, sensitivite %93.48, spesifite %86.89 ve AUC: 0.937 olarak bulundu (p<0.001).

TARTIŞMA: Beyaz kan hücreleri değişkeni, nötrofil-lenfosit oranı, ortamalı trombosit hacmi ve trombosit sayısı.