Research Article / Araştırma Makalesi
doi: 10.18678/dtfd.684148

Duzce Med J, 2020;22(2):79-83
Düzce Tıp Fak Derg, 2020;22(2):79-83

Can Hematological Parameters Predict the Severity of Acute Pancreatitis?

Hematolojik Parametreler Akut Pankreatitin Şiddetini Öngörebiliyor mu?

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Received / Geliş Tarihi : 04.02.2020
Accepted / Kabul Tarihi : 04.05.2020
Available Online / Çevrimiçi Yayın Tarihi : 25.08.2020

ABSTRACT

Aim: Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), mean platelet volume (MPV) and erythrocyte distribution width (RDW) are considered to be associated with systemic inflammation. In this study, it was aimed to evaluate NLR, PLR, MPV and RDW as prognostic factors in acute pancreatitis (AP).

Material and Methods: A total of 315 patients admitted to Health Sciences University Gazi Yaşargil Training and Research Hospital between May 2016 and May 2019 and diagnosed with AP were included in the study. Data of the patients were analyzed retrospectively. Laboratory values of the patients at the time of admission to the hospital were recorded and the Ranson score was calculated. Patients were divided into two groups as Ranson score <3 (mild AP) and ≥3 (severe AP). NLR, PLR, MPV and RDW parameters were compared between these groups.

Results: Of the patients, 103 (32.7%) were males and 212 (67.3%) were females, and mean age was 57.2±19.5. According to the Ranson criteria, number of patients with a score below 3 was 274 (87.0%), and number of patients with a score of 3 or above was 41 (13.0%). In the severe AP group, NLR and PLR were significantly higher than in the mild AP group (16.2±14.3 vs. 8.2±7.7, p<0.001 and 283.7±223.0 vs. 195.5±139.3, p=0.004 respectively), but there was no statistically significant difference in terms of RDW-CV and MPV (13.7±1.0 vs. 13.9±1.9, p=0.849 and 9.7±1.3 vs. 9.5±1.1, p=0.201, respectively).

Conclusion: NLR and PLR are simple and safe tests that can be used to determine the severity of AP.

Keywords: Acute pancreatitis severity; Ranson criteria; neutrophil to lymphocyte ratio; platelet to lymphocyte ratio; erythrocyte distribution width; mean platelet volume.

ÖZ

Amaç: Nötrofil-lenfosit oranı (NLO), trombosit-lenfosit oranı (TLO), ortalama trombosit hacmi (MPV) ve eritrosit dağılım genişliğinin (RDW) sistemik inflamasyon ile ilişkili olduğu kabul edilir. Bu çalışmada, akut pankreatitte (AP) prognostik faktörler olarak NLO, TLO, MPV ve RDW değerlerinin incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: Mayıs 2016 ile Mayıs 2019 tarihleri arasında Sağlık Bilimleri Üniversitesi Gazi Yaşargil Eğitim ve Araştırma Hastanesine başvuran ve AP tanısı konulan toplam 315 hasta çalışmaya dahil edildi. Hasta verileri retrospektif olarak analiz edildi. Hastaların hastaneye başvuru zamanındaki laboratuvar değerleri kaydedildi ve Ranson skoru hesaplandı. Hastalar, Ranson skoru <3 (hafif AP) ve ≥3 (şiddetli AP) olanlar şeklinde iki gruba ayrıldı. Bu gruplar arasında NLO, TLO, MPV ve RDW parametreleri karşılaştırıldı.

Bulgular: Hastaların 103'ü (%32,7) erkek ve 212'si (%67,3) kadın olup yaş ortalaması 57,2±19,5 idi. Ranson kriterlerine göre skoru 3'ün altında olan hasta sayısı 274 (%87,0), skoru 3 ve üstünde olan hasta sayısı ise 41 (%13,0) olarak saptandı. Şiddetli AP grubunda NLO ve PLO, hafif AP grubuna göre anlamlı derecede yüksekti (sırasıyla 16,2±14,3'e karşı 8,2±7,7; p<0,001 ve 283,7±223,0 karşı 195,5±139,3; p=0,004), ancak RDW-CV ve MPV açısından istatistiksel olarak anlamlı bir farklılık yoktu (sırasıyla 13,7±1,0'e karşılık 13,9±1,9; p=0,849 ve 9,7±1,3'e karşı 9,5±1,1; p=0,201).

Sonuç: NLO ve PLO, AP şiddetini belirlemek için kullanabilecek olan basit ve güvenli testlerdir.

Anahtar kelimeler: Akut pankreatit şiddeti; Ranson kriterleri; nötrofil-lenfosit oranı; trombosit-lenfosit oranı; eritrosit dağılım genişliği; ortalama trombosit hacmi.

INTRODUCTION

Acute pancreatitis (AP) is an inflammatory disease of the pancreas, which is characterized by abdominal pain and increased pancreatic enzymes and can cause local and systemic complications. It is one of the most common hospitalization reasons among gastroenterological diseases. It may course in a wide clinical range from mild pancreatitis with a mortality rate of 1.5% to severe pancreatitis with a mortality rate of 17%. The overall mortality rate is 5% (1). Therefore, determining the severity of the disease is very important in order to predict its prognosis. Many scoring systems, serum biomarkers and imaging methods are used in determining the severity and mortality of AP. Systemic Inflammatory Response Syndrome (SIRS), Ranson criteria, Bedside Index of Severity In Acute Pancreatitis(BISAP), Acute Physiology and Chronic Health Examination (APACHE) II, Harmless Acute Pancreatitis Score (HAPS), Glasgow score and BT severity indices are the scoring systems used (2-5). The fact that some of these scoring systems require at least 48 hours to complete, some scoring systems are complex and contain many parameters, and none of them have high precision in determining the severity of AP in a certain patient limit their usage. Among these scoring systems, APACHE II is recommended for the evaluation of AP and its use in patients other than intensive care patients is not very practical (6). Due to the insufficiency of these scoring systems, new biomarker searches have emerged that going to determine the severity and prognosis of AP. For this purpose, studies with platelet-lymphocyte ratio (PLR), mean platelet volume (MPV), neutrophil-lymphocyte ratio (NLR), red blood cell distribution width (RDW) and procalcitonin level have been performed in the literature. Severe pancreatitis with organ failure is thought to be caused by an uncontrolled systemic inflammatory response. The number of white cells, including neutrophil and lymphocyte count, is one of SIRS criteria and is a hematological test found in most AP scoring systems. While neutrophils advance SIRS and the inflammatory cascade in AP, lymphocyte reduction occurs in severe sepsis and is associated with poor results (7,8). The NLR may be more valuable than total White Blood Cell (WBC) or per se neutrophil and lymphocyte counts in predicting the course of inflammatory disease. PLR, RDW and MPV, which are also whole blood parameters, are associated with inflammatory diseases. In this study, we aimed to investigate the relationship of NLR, PLR, RDW and MPV with disease severity in patients diagnosed with AP.

MATERIAL AND METHODS

The data of patients who were admitted to Health Sciences University Gazi Yaşargil Training and Research Hospital between May 2016 and May 2019 and diagnosed with AP were retrospectively analyzed. Ethics committee approval was obtained from the ethics committee of Health Sciences University Gazi Yaşargil Training and Research Hospital with the number of 379 and dated 29.11.2019. Diagnosis of AP was made in the presence of two criteria among abdominal pain, an increase in amylase and/or lipase and imaging methods supporting the diagnosis. Patients aged sixteen and over were included in the study. Patients with concomitant cholangitis, cholecystitis, with an infection focus such as abscess, with chronic pancreatitis, pancreatic cancer history, hematological disease, who were receiving anti-inflammatory medication, antiviral medication, immunosuppressive medication, and who were not hospitalized while having diagnosed with AP in the emergency room, were not included in the study. The discharge reports, laboratory values and imaging tests of the patients were reached through the hospital information system. Whole blood, biochemistry parameters, and C-reactive protein (CRP) values at the time of appeal to the hospital of the patients were recorded. Patients' referral Ranson score [Biliary pancreatitis: WBC >18000 mm^3, age >70 years, lactate dehydrogenase (LDH) >400 U/L, glucose >220 mg/dL, aspartate aminotransferase (AST) >250 U/L; Non-biliary pancreatitis: WBC >16000 mm^3, age >55 years, glucose >200 mg/dL, AST >250 U/L, LDH >350 U/L] were calculated. Those with a Ranson score of <3 were considered as mild and those with ≥3 were considered as severe pancreatitis. NLR, PLR, RDW and MPV parameters were compared between these groups.

Statistical Analysis

Statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program. In the evaluation of the data, as well as the descriptive statistics (mean, standard deviation, median, minimum, maximum, frequency and percentage), the distribution of variables were examined by Kolmogrov-Smirnov normality test, and Independent samples t-test was used for comparison of two groups of variables with normal distribution, and Mann Whitney U test was used for comparison of two groups of variables without normal distribution. Chi-square test was used for comparison of qualitative data, and Pearson and Spearman correlation tests were used as the correlation analysis. The results were evaluated at $p<0.05$ significance level.

RESULTS

A total of 315 patients diagnosed with AP were included in this study. Of these patients, 103 (32.7%) were male and 212 (67.3%) were female. The mean age of all patients was determined as 57.2±19.46 (range, 16-97) years. The etiological factors determined in this study are given in Table 1. A total of 4 patients (1.3%) died due to the disease, and the mean age of these patients was 75.7±5.5 years. In the mild AP group, the number of cases was 274 (87.0%, 184 female and 90 male) and the mean age was 54.8±19.0 years. In the severe AP group, the number of

Table 1. Distribution of the patients according to etiology of acute pancreatitis, n=315

Etiology	n	%
Gallstone	247	78.4
Idiopathic	53	16.8
PostERCP	6	1.9
Hyperlipidemia	3	1.0
Azathioprine	1	0.3
Fasiola Hepatica	1	0.3
Hypercalcemia	1	0.3
Ketoacidosis	1	0.3
Drug dependent	1	0.3
Weil's Disease	1	0.3

cases was 41 (13.0%, 28 female and 13 male) and the mean age was 72.4±14.2 years. In the severe AP group, the mean age was statistically significantly higher (p<0.001). In the mild AP group, necrosis was found in 7 cases and mortality was found in 3 cases. Mortality was detected in 1 patient in the severe AP group, whereas necrosis was not detected. There was no significant difference in necrosis and mortality between the two groups (p=0.301 vs p=0.473, respectively). Initial laboratory findings of mild and severe AP patients are summarized in Table 2. WBC (p=0.001), neutrophil (p<0.001), glucose (p<0.001), ALT (p<0.001), AST (p<0.001), LDH (p<0.001), bilirubin (p=0.008), NLR (p<0.001) and PLR (p=0.004) were significantly higher in the severe AP group than in the mild AP group. CRP1 (p=0.687), CRP2 (p=0.932), CRP3 (p=0.932), Hct(%) (p=0.693), Hgb (p=0.119), MCV (p=0.171), MPV (p=0.201), urea (p=0.619), creatinine (p=0.070), albumine (p=0.068), PLT (p=0.673) and RDW-CV (p=0.849) did not differ significantly between the groups. Lymphocyte was significantly higher in the mild AP group than in the severe AP group (p=0.001). Correlation analysis was performed between NLR, PLR, RDW, MPV and Ranson score (Table 3). While positive correlation was found between NLR and PLR and the Ranson score (r=0.236, p<0.001, and r=0.163, p=0.004, respectively), no correlation was found between MPV and RDW and the Ranson score (r=0.720, p=0.201 and r=-0.010, p=0.855, respectively).

DISCUSSION

Early detection of the severity of the AP and early therapeutic interventions to decrease morbidity and mortality rates are extremely important. Estimating the severity of AP is still difficult, especially at an early stage and poses a challenge for clinicians. It has been stated that there is a 4-fold increase in the risk of death in patients with a 24-hour delay in admission (9). Due to the stated causes, and deficiencies of existing scoring systems, new biomarker searches that going to determine the severity and prognosis of AP have emerged. In our study, AP severity and age, WBC, lymphocyte count, neutrophil count, NLR, PLR, glucose, AST, ALT and LDH levels were found to be associated. As is known, age, glucose, WBC, AST and LDH are the parameters used in Ranson scoring.

It has been shown in various studies that NLR which is obtained by dividing the number of neutrophils by the number of lymphocytes, increases in many diseases that have a course with inflammation and is effective in predicting the prognosis (7,8,10-14). In the study of Zahorec et al. (8), it has been reported that NLR is an inflammatory and stress parameter which is simple, fast, cheap and can be used routinely in critical patients. There are studies in the literature investigating the relationship between NLR and AP. In a performed study, it has been suggested that NLR is superior to total WBC in predicting the negative results of AP, and the value of NLR >4.7 should be used in determining the severity of the disease (15). In another study, it has been stated that the increase of NLR in patients appealed with AP can effectively distinguish between mild and severe AP. It also has been reported in this study that NLR represents a dynamic process, returns to normal in those whose clinic is stabilized, however, the highness continues in patients with complicated AP (16). In another study, NLR in the severe AP group was found to be significantly higher than in the mild AP group (17). In our study, we compared with the Ranson score of NLR and found that NLR was significantly higher in the severe disease group. Our conclusion supports the literature.

Platelets have an important role in coordinating inflammation and immune response. They affect inflammation by releasing cytokines, changing leukocyte and endothelial responses (18). PLR has been studied in various diseases (19-21). In some cancers, PLR has been shown to be a superior predictive factor compared to NLR (22). The predictive effect of PLR in AP has been less studied compared to NLR. In one study, it has been stated that PLR significantly increased in severe pancreatitis (23), while in another study, PLR rate in biliary pancreatitis has only been detected to show disease severity (24). In our study, regardless of etiology, we found PLR to be significantly higher in the severe pancreatitis group. However, there was no alcohol in etiology of the patients included in the study.

Another biomarker studied in AP is MPV. There are contradictory results in the literature regarding the place of MPV in AP. In some studies, MPV has been found to be significantly lower in patients with AP (25,26), while in another study they have reported that MPV was significantly higher in patients with acute edematous pancreatitis than in controls (27). However, in our study, the values of patients with AP were measured at the time of admission, and the control values were not examined. But, no significant difference in MPV level between mild and severe pancreatitis groups was detected.

One of the whole blood parameters investigated in AP is RDW. There are studies that provide opposing views regarding RDW. There are some studies stating that RDW is a biomarker associated with mortality and morbidity in AP (28), while in others it was found as unrelated (29). In our study, there was no significant difference found in RDW levels.

The facts that the study was retrospective, single-centered, and the Ranson score was not calculated after 48 hours by only taking the Ranson criteria as the basis, were the limitations of our study.

As a result, we determined that NLR and PLR are independent predictive parameters in determining the severity of AP. Also, we found that MPV and RDW could not determine the severity of the disease. We believe that NLR and PLR, which can be examined daily due to being easy, fast and having low cost and that obtained from the proportion of whole blood parameters, are acceptable for the clinician to use in determining the severity of AP.

Table 3. Correlation of parameters with Ranson score

	r	p
NLR	0.236	**<0.001**†
PLR	0.163	**0,004**†
MPV (fL)	0.720	0.201††
RDW-SD (%)	-0.039	0.496††
RDW-CV (%)	-0.010	0.855††

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, MPV: Mean platelet volume, RDW: Erythrocyte distribution width, †: Spearman correlation, ††: Pearson correlation

Table 2. Comparison of patient groups according to acute pancreatitis severity

	Group	n	Mean±SD	Median	Q1-Q3	Min-Max	p
Age (years)	Mild AP	274	54.9±19.1	55.0	40-69	16-94	<0.001*
	Severe AP	41	72.4±14.2	75	67-81.5	32-92	
CRP 1st day (mg/L)	Mild AP	258	34.5±51.9	11.3	5.4-50.7	0.5-385.4	0.687†
	Severe AP	40	49.8±88.7	11.9	5.4-53.9	1-385.4	
CRP 2nd day (mg/L)	Mild AP	215	70.9±83.4	38.2	13.3-99.9	1.3-406.3	0.932†
	Severe AP	30	81.7±111.6	27.7	12.7-92.4	3.1-406.3	
CRP 3rd day (mg/L)	Mild AP	165	110.2±101.8	85.1	25.6-168.9	0.9-445	0.932†
	Severe AP	25	121.1±103.2	93.5	42-185.5	11.6-383.5	
WBC (10^3/uL)	Mild AP	274	12.6±5.1	11.5	9.2-15.0	3.2-45.4	0.001*
	Severe AP	41	15.5±5.1	14.5	10.8-19.9	7.6-27.9	
Htc (%)	Mild AP	274	42.0±5.3	41.5	38.5-45.5	22.2-61.1	0.693*
	Severe AP	41	42.3±5.6	43	38.8-46.8	26.8-50.1	
Hgb (g/dL)	Mild AP	274	13.6±1.9	13.4	12.3-14.9	7-19.3	0.119*
	Severe AP	41	14.1±2.7	13.7	12.7-15.3	10-26.8	
Neu (10^3/uL)	Mild AP	274	10.1±4.9	9	6.6-12.9	2.4-37.7	<0.001†
	Severe AP	41	13.5±5.2	13	8.7-17.7	6.3-25.8	
Lym (10^3/uL)	Mild AP	274	1.8±1.2	1.6	1.1-2.3	0.3-10.3	0.001†
	Severe AP	41	1.3±0.8	1	0.7-1.8	0.3-4.5	
MCV (fL)	Mild AP	274	88.2±7.1	88.8	84.7-92.3	60.2-128.6	0.171*
	Severe AP	41	89.8±4.4	89.3	87.2-92.5	78.6-98.6	
MPV (fL)	Mild AP	274	9.5±1.1	9.4	8.6-10.2	7.2-13	0.201*
	Severe AP	41	9.7±1.3	9.4	8.8-10.9	7.5-12.5	
PLT (10^3/uL)	Mild AP	274	265.1±75.9	256	207-314	101-563	0.673*
	Severe AP	41	258±73.8	255	203-288.5	127-492	
RDW-SD (%)	Mild AP	274	41.8±4.0	41.2	39.4-43.5	33.7-73.3	0.497*
	Severe AP	41	41.4±3.2	40.8	39.5-42.1	36.9-52.8	
RDW-CV (%)	Mild AP	274	13.9±1.9	13.6	13.1-14.5	11.9-21	0.849*
	Severe AP	41	13.7±1.0	13.4	13.2-14.1	12.1-17	
Glucose (mg/dl)	Mild AP	257	138.6±62.5	127	106-156	67-441	<0.001†
	Severe AP	39	197.3±101.1	146	125-221	100-532	
Urea (mg/dL)	Mild AP	257	38.9±37.5	31	24-41	11-207	0.619†
	Severe AP	40	40.1±27.1	32	25-43.8	19-160	
Creatinine (mg/dL)	Mild AP	258	0.9±0.5	0.8	0.7-1	0.1-3.7	0.070†
	Severe AP	40	1.1±0.7	0.8	0.7-1	0.6-3.7	
ALT (GPT) U/L	Mild AP	257	203.9±216.6	129	43-287	2-1503	<0.001†
	Severe AP	40	346.1±257.7	305.5	177.3-463.8	5-1177	
AST (GOT) U/L	Mild AP	257	200.6±199.3	151	57-274.5	2-1542	<0.001†
	Severe AP	40	430.4±283.8	378	291.3-517.3	1-1300	
LDH (U/L)	Mild AP	253	366.5±295.6	300	244-388	11-3129	<0.001†
	Severe AP	40	550.2±200.9	508.5	439-653.8	11-1056	
Albumine (g/L)	Mild AP	102	3.9±0.6	3.8	3.5-4.2	2.6-5.7	0.068†
	Severe AP	16	4.2±0.6	4	3.7-4.6	3.4-5.7	
Bilirubin (mg/dL)	Mild AP	262	1.7±1.8	1	0.6-2.2	0.2-15.5	0.008†
	Severe AP	39	2.0±1.5	1.81	0.9-2.7	0.3-6.5	
NLR	Mild AP	274	8.2±7.7	5.4	3.4-10.1	0.6-51.0	<0.001†
	Severe AP	41	16.2±14.3	10.8	5.7-25.5	2.7-63	
PLR	Mild AP	274	195.5±139.3	163.7	108.1-238.2	22.4-958.1	0.004†
	Severe AP	41	283.7±223.0	204.7	142.3-388.3	57.8-1142.9	

AP: acute pancreatitis, SD: Standard deviation, Q1: 1st Quartile, Q3: 3rd Quartile, Min: Minimum, Max: Maximum, *: Independent samples t-test, †: Mann Whitney U test, CRP: C-Reactive Protein, WBC: White blood cell, Htc: Hematocrit, Hgb: Hemoglobin, Neu: Neutrophil, Lym: Lymphocyte, MCV: Mean platelet volume, PLT: Platelet, RDW: Erythrocyte distribution width, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

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