

## A NEW MARKER TO DETERMINE PROGNOSIS OF ACUTE PANCREATITIS: PLR AND NLR COMBINATION

NOVI MARKER ZA PROGNOZU AKUTNOG PANKREATITISA: KOMBINACIJA PLR I NLR

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### Summary

**Background:** We aimed to investigate the prognostic importance of platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) combination for patients diagnosed with acute pancreatitis and its relationship with mortality.

**Methods:** This retrospective study was included 142 patients diagnosed with acute pancreatitis. Ranson, Atlanta and BISAP 0h, 24h and 48h scores of the patients were calculated by examining their patient files. The patients were divided into three groups as low-risk, medium-risk and high-risk patients according to their PLR and NLR levels.

**Results:** The number of patients with acute pancreatitis complications such as necrotizing pancreatitis, acute renal failure, sepsis and cholangitis was significantly higher in the high-risk group compared to other groups. Mortality rate was found to be 90% in the high-risk group, 16% in the medium-risk group, and 1.9% in the low-risk group. The number of patients with a Ranson score of 5 and 6, a severe Atlanta score, a BISAP 0h score of 3 and 4, a BISAP 24h and 48h score of 4 and 5 was higher in the high-risk group compared to other groups. PLR-NLR combination, Atlanta and Ranson scores, and C-reactive protein level were determined to be independent risk factors predicting mortality in stepwise regression model. PLR-NLR combination had the highest area under curve value in terms of predicting acute

### Kratak sadržaj

**Uvod:** Svrha ovog istraživanja je da se utvrdi značajnost kombinacije trombocitno-limfocitnog odnosa (PLR) i neutrofilno-limfocitnog odnosa (NLR) za dijagnostikovanje akutnog pankreatitisa kao i u odnosu na mortalitet.

**Metode:** Retrospektivno izučavanje obuhvatilo je 142 pacijenta sa dijagnozom akutnog pankreatitisa. Ranson, Atlanta i BISAP 0h, 24h i 48h skorovi kod pacijenata računati su uvidom u istorije bolesti pacijenata. Pacijenti su podeljeni u tri grupe i to niskog, srednjeg i visokog rizika prema nivoima njihovih PLR i NLR.

**Rezultati:** Broj pacijenata sa akutnim pankreasnim komplikacijama kao što su nekrotizirajući pankreatitis, akutni renalni poremećaj, sepsa i holangitis bili su značajno viši u grupi sa visokim rizikom u odnosu na druge grupe. Nađeno je da je kod visoko rizične grupe mortalitet iznosio 90%, 16% kod grupe sa srednjim rizikom i 1,9% kod grupe niskog rizika. Broj pacijenata sa Ranson skorom 5 i 6, teškim Atlanta skorom, i BISAP 0h skorom 3 i 4, i BISAP 24h i 48h skorom 4 i 5 je bio viši u grupi sa visokim rizikom u odnosu na druge grupe. Utvrđeno je da su PLR-NLR kombinacija, Atlanta i Ranson skorovi, i nivo C-reaktivnog proteina bili nezavisni faktori rizika u predviđanju mortaliteta u regresionom modelu. PLR-NLR kombinacija je imala najveću površinu ispod vrednosti krive u predviđanju prognoze akutnog pankreatitisa i sličnu dijagnostičku diskriminaciju sa drugim skor sistemima.

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pancreatitis prognosis and had a similar diagnostic discrimination with other scoring systems.

**Conclusions:** In our study it was found that PLR-NLR combination had a similar prognostic importance with other scoring systems used to determine acute pancreatitis prognosis.

**Keywords:** Atlanta classification, BISAP score, necrotizing pancreatitis, Ranson score

## Introduction

Acute pancreatitis is the sudden onset severe inflammation of pancreas and the most common cause of gastrointestinal hospitalization in the United States (1). The most common symptoms are epigastric pain, nausea, vomiting, loss of appetite, fever and hemodynamic instability in severe cases. The two most important causes in its etiology are alcohol and gallstones, whereas hereditary causes, hypertriglyceridemia, hypercalcemia, malnutrition and complications associated with endoscopic retrograde cholangiopancreatography (ERCP) are among other common causes (2).

In spite of treatments, acute pancreatitis leads to high morbidity, mortality and complications. Hence, determination of its prognosis is of vital importance. Several scoring systems such as Ranson score (3), Atlanta classification (4), acute physiology and chronic health evaluation (APACHE)-2 (5), the bedside index for severity in acute pancreatitis (BISAP) (6), and laboratory parameters such as C-reactive protein (CRP) are used for this purpose. In spite of all these scoring systems and laboratory parameters, it may still be difficult to determine its prognosis. Practical, quantifiable and easy-to-use markers are particularly required.

Changes in peripheral blood components are used to show the prognosis of many diseases. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are new markers used to this end, on which there are several studies available in the literature (7). These markers are especially thought to show inflammation response (8). Lately, it has been suggested that PLR-NLR combination could be used to predict disease prognosis (9, 10).

Although we have found studies in the literature suggesting that NLR and PLR could be used to predict prognosis of acute pancreatitis (11), there is not a study that compares the combination of these markers with CRP and scores commonly used for pancreatitis prognosis such as Ranson, Atlanta, and BISAP. Hence, in this study, we aimed to investigate the prognostic importance of PLR-NLR combination for patients diagnosed with acute pancreatitis and its relationship with mortality.

**Zaključak:** U našem izučavanju nađeno je da PLR-NLR kombinacija ima sličan prognostički značaj sa drugim skor sistemima koji se koriste za utvrđivanje prognoze akutnog pankreatitisa.

**Ključne reči:** Atlanta klasifikacija, BISAP skor, nekrotizirajući pankreatitis, Ranson skor

## Methods

### Study Population

This study was carried out by examining patient files of acute pancreatitis patients in Gastroenterology Clinic of Türkiye Yüksek İhtisas Education and Research Hospital between May 2012 and June 2015. The study was designed as a retrospective cohort study. Of the 300 patients hospitalized with acute pancreatitis diagnosis, 158 were excluded from the study due to absence of patient files or lack of neutrophil and lymphocyte values. The final study population consisted of 142 patients.

Acute pancreatitis diagnosis was made using clinical, laboratory and radiological findings. Patients who had admitted to emergency room with upper abdominal pain, high amylase-lipase levels in the laboratory and pancreatic inflammation in ultrasonography or tomography were included in the study (12). Ranson score, Atlanta score and BISAP 0h, 24h and 48h scores of the patients were calculated by examining their patient files. In order to evaluate necrosis status, patients who had abdominal CT on the day of admission or on the 7th day of hospitalization in cases of long-term hospitalization were included in the study.

For laboratory measurement, blood was collected and used for routine blood tests and biochemical tests. Laboratory values of the patients were retrieved from their patient files. Patients with known renal and liver failure or malignancy diagnosis and patients who suffered severe infectious attack within the last month were excluded from the study.

Receiver operating characteristic (ROC) curve analysis was used to determine prediction points of PLR and NLR levels for mortality. The threshold value of NLR level was found to be  $>13.64$  with 73.0% sensitivity and 82.7% specificity ( $AUC \pm SE = 0.788 \pm 0.071$ ,  $p < 0.001$ ), whereas the threshold value of PLR level was found to be  $>342.31$  with 73.3% sensitivity and 99.2% specificity ( $AUC \pm SE = 0.863 \pm 0.077$ ,  $p < 0.001$ ). For patient with both NLR and PLR values, those with both values greater than the determined thresholds were classified as high risk ( $PLR > 342.31$  and  $NLR > 13.6$ ), those with either NLR or PLR value greater than the threshold were clas-

sified as moderate risk (PLR>342.31 or NLR>13.6), and those with both values smaller than the threshold were classified as low risk (PLR 342.31 and NLR 13.6).

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Local Ethics Research Committee.

### Statistical analysis

Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, USA) and Medcalc 11.4.2 (MedCalc Software, Mariakerke, Belgium) softwares were used for statistical assessments. The normal distribution of the data was evaluated with the Shapiro-Wilk test. Values with normal distribution were presented as mean±standard deviation and values without normal distribution were presented as median [interquartile range (IQR)]. Categorical variables were presented as numbers and percentages. ROC Curve analysis was used to determine prediction points of PLR and NLR levels for mortality. In comparison of 3 risk groups obtained from the combination of these levels, the ANOVA test was used for parametrically distributed data and the Kruskal-Wallis H test was used for non-parametrically distributed data. The Bonferroni correction was applied to paired comparisons. Student T test or Mann Whitney U test were used to compare groups. Chi-square test and Fisher's exact Chi-square test were used in comparison of categorical data. In order to determine the effects of potential prognostic factors on mortality, independent predictors were obtained from stepwise multivariate cox regression analysis. The Kaplan-Meier analysis was used to show the relationship of risk factors with mortality throughout the follow-up period. The diagnostic discrimination of scoring systems and PLR-NLR combination in prognosis of acute pancreatitis was examined with ROC Curve analysis, area under the curve (AUC). In statistical analysis,  $p<0.05$  with 95% confidence interval and 5% margin of error was considered to be statistically significant.

## Results

### Entire Population Findings

The research population consisted of 142 patients in total, 84 female (59.2%) and 58 male (40.8%). The mean age of the patients was  $61.6\pm 17.4$  years. In terms of pancreatitis etiology, the most common cause was gallstones ( $n:117$ ). Alcohol use (2.8%), hypertriglyceridemia (2.1%), hereditary reasons (8.5%), ERCP complication (1.4%) were the other causes. In terms of pancreatitis-associated complications, 4.9% of the patients had acute renal failure (ARF) ( $n:7$ ), 3.5% had abscess ( $n:5$ ), 2.8% had sepsis ( $n:4$ ), 4.9% had pseudocyst ( $n:7$ ), 1.4%

had ascites ( $n:2$ ), 1.4% had hematoma ( $n:2$ ), 1.4% had cholangitis ( $n:2$ ), and 9.2% other pancreatitis complications. 14.8% of the patients had necrotizing pancreatitis ( $n:21$ ) and 85.2% had edematous pancreatitis ( $n:121$ ). Exitus occurred in 10.6% of the patients ( $n:15$ ). The median duration of hospitalization was 8.5 (IQR:9) days.

60.6% had a Ranson score of 0-2 ( $n:86$ ), 28.2% had a Ranson score of 3-4 ( $n:40$ ), and 11.3% had a Ranson score of 5-6 ( $n:16$ ). 73.2% of the patients had a »mild« Atlanta score ( $n:104$ ), 17.6% had a »moderately severe« Atlanta score ( $n:25$ ), and 9.2% had a »severe« Atlanta score ( $n:13$ ). In terms of BISAP 0 scores, 21.1% of the patients had a score of »0« ( $n:30$ ), 34.5% had a score of »1« ( $n:49$ ), 29.9% had a score of »2« ( $n:41$ ), 12.7% had a score of »3« ( $n:18$ ), and 2.8% had a score of »4« ( $n:4$ ). In terms of BISAP 24h scores, 31% of the patients had a score of »0« ( $n:44$ ), 44.4% had a score of »1« ( $n:63$ ), 17.6% had a score of »2« ( $n:25$ ), 4.9% of the patients had a score of »3« ( $n:7$ ), 1.4% had a score of »4« ( $n:2$ ), and 0.7% had a score of »5« ( $n:1$ ). In terms of BISAP 48h scores, 34.5% of the patients had a score of »0« ( $n:49$ ), 46.5% had a score of »1« ( $n:66$ ), 8.5% had a score of »2« ( $n:12$ ), 7% of the patients had a score of »3« ( $n:7$ ), 2.8% had a score of »4« ( $n:2$ ), and 0.7% had a score of »5« ( $n:1$ ).

### Distribution by Combination Groups

Table I summarizes demographic characteristics and clinical findings of risk groups. The number of patients with necrotizing pancreatitis was higher and the number of patients with edematous pancreatitis was lower in the high-risk group compared to other groups. While exitus occurred in 90% of the high-risk group patients, the exitus rate was 16% in the medium-risk group, and 1.9% in the low-risk group.

The distribution of laboratory findings by risk groups is given in Table II in detail.

Values of prognostic scoring systems by risk groups are shown in Table III in detail. The number of patients with a Ranson score of »5-6« was found to be higher in the high-risk group compared to other groups. 40% mortality score was found in 70% of the high-risk group, 20% of the medium-risk group, and 3.7% of the low-risk group. The number of patients classified as severe according to Atlanta classification was higher in the high-risk group compared to other groups (60% vs 8% vs 4.7%, respectively;  $p<0.001$ ). The number of patients with a BISAP 0 score of »3« and »4«, a BISAP 24h score of »3«, »4«, and »5« and a BISAP 48h score of »4« and »5« was found to be higher in the high-risk group compared to other groups.

Correlation analysis results related to PLR and NLR are given in Table IV in detail.

**Table 1** Demographic characteristics and clinical findings of study population.

Variables	Low Risk	Intermediate Risk	High Risk	<i>p</i>
	<i>n</i> =107	<i>n</i> =25	<i>n</i> =10	
Age (year)	59±16	69±16	68±24	0.013*
Gender, <i>n</i> (%)				
Male	44(41.1)	11(44)	3(30)	0.795
Stomachache	102(95.3)	25(100)	10(100)	0.710
Jaundice	7(6.5)	2(8)	2(20)	0.302
Fever	13(12.1)	1(4)	4(40)	0.027*
Nausea	12(11.2)	5(20)	4(40)	0.045*
Asymptomatic	1(0.9)	0(0)	0(0)	0.999
The etiology of pancreatitis				
Stone	90(84.1)	21(84)	6(60)	0.039*
Alcohol	4(3.7)	0(0)	0(0)	
Hypertriglyceridemia	3(2.8)	0(0)	0(0)	
Hereditary	8(7.5)	2(8)	3(30)	
Post ERCP	2(1.9)	0(0)	0(0)	
Others	0(0)	2(8)	2(20)	
ERCP	65(60.7)	22(88)	7(70)	0.020*
Complications of pancreatitis				
ARF	2(1.9)	0(0)	5(50)	<0.001*
Abscess	1(0.9)	3(12)	1(10)	0.015*
Sepsis	0(0)	0(0)	4(40)	<0.001*
Cholangitis	0(0)	1(4)	1(10)	0.028*
Pseudocyst	6(5.6)	1(4)	0(0)	0.999
Ascites	1(0.9)	1(4)	0(0)	0.434
Hematoma	0(0)	2(8)	0(0)	0.054
Pancreatitis type				
Necrotizing	10(9.3)	6(24)	5(50)	<0.001*
Edematous	97(90.7)	19(76)	5(50)	
Mortality				
Alive	105(98.1)	21(84)	1(10)	<0.001*
Exitus	2(1.9)	4(16)	9(90)	
Hospitalization time	8(8)	10(11)	11(19)	0.182
Follow-up time	31(34)	33(37)	12(32)	0.120

\**p* < 0.05 is accepted as statistical significance level.

Abbreviations: ERCP: endoscopic retrograde cholangiopancreatography, ARF: acute renal failure

**Table II** Distribution of Laboratory Findings by Risk Groups.

Variables	Low Risk n=107	Intermediate Risk n=25	High Risk n=10	p
FBG (mmol/L)	6.3825	7.881	6.549	0.072
Urea (mmol/L)	11.424	13.209	17.85	0.033*
Creatinine (mmol/L)	70.72	88.4	85.748	0.143
AST (U/L)	125	123	62	0.874
ALT (U/L)	140	120	32	0.244
GGT (U/L)	238	240	74	0.064
ALP (IU/L)	166	146	94	0.315
Amylase (U/L)	840	1256	1085	0.208
Lipase (U/L)	1200	1500	1371	0.518
LDH (U/L)	372	474	392	0.060
Calcium (mmol/L)	2.2±0.2	2.1±0.3	1.8±0.3	0.001*
ESR (mm/h)	35	36	63.5	0.459
CRP (mg/L)	52	90	147.5	0.012*
WBC (μL)	9800	15200	13100(	<0.001*
Platelet (μL)	239000	185000	248000	<0.001*
Neutrophile (μL)	7300	12630	11600	<0.001*
Lymphocyte (μL)	1400	700	595	<0.001*
PLR	172.67	276	418.08	<0.001*
NLR	5.39	16.56	20.37	<0.001*

\* $p < 0.05$  is accepted as statistical significance level.

Abbreviations: FBG: fasting blood glucose, AST: aspartate aminotransferase, ALT: alanine aminotransferase, GGT: gamma glutamyl transferase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, INR: international normalized ratio, WBC: white blood cell, PLR: platelet to lymphocyte ratio, NLR: neutrophile to lymphocyte ratio

According to regression model; PLR-NLR combination, Atlanta and Ranson score, and CRP level were found to be independent risk factors for predicting mortality (Table V).

Survival chart of the high-risk group is given in Figure 1. Accordingly, the survival rate was lower in the high-risk group patients ( $p < 0.001$ ). In addition, PLR-NLR combination and CRP predictors were com-

pared to Ranson score, Atlanta score, and BISAP 0, BISAP 24h, BISAP 48 scores in terms of diagnostic discrimination by using the ROC curve analysis. Accordingly, PLR-NLR combination had the highest AUC value in terms of predicting acute pancreatitis prognosis and had a similar diagnostic discrimination with other scoring systems. PLR-NLR combination and scoring systems had better diagnostic discrimination value compared to the CRP variable.

**Table III** Distribution of Prognostic Scores by Risk Groups.

Variables	Low Risk n=107	Intermediate Risk n=25	High Risk n=10	p
Total ranson score	2(2)	3(2)	5(2)	<0.001*
0	20(18.7)	1(4)	1(10)	
1	28(26.2)	1(4)	0(0)	
2	30(28)	5(20)	0(0)	
3	16(15)	7(28)	2(20)	<0.001*
4	9(8.4)	6(24)	0(0)	
5	2(1.9)	4(16)	6(60)	
6	2(1.9)	1(4)	1(10)	
Mortality score				
2% mortality	78(72.9)	7(28)	1(10)	
15% mortality	25(23.4)	13(52)	2(20)	<0.001*
40% mortality	4(3.7)	5(20)	7(70)	
100% mortality	0(0)	0(0)	0(0)	
Atlanta				
Mild	88(82.2)	14(56)	2(20)	
Moderate	14(13.1)	9(36)	2(20)	<0.001*
Severe	5(4.7)	2(8)	6(60)	
Bisap 0 score	1(2)	2(1.5)	3(0.75)	<0.001*
0	29(27.1)	1(4)	0(0)	
1	40(37.4)	7(28)	2(20)	
2	30(28)	11(44)	0(0)	<0.001*
3	8(7.5)	4(16)	6(60)	
4	0(0)	2(8)	2(20)	
Bisap 24 score	1(1)	1(1)	2(1.5)	<0.001*
0	41(38.3)	2(8)	1(10)	
1	49(45.8)	13(52)	1(10)	
2	14(13.1)	7(28)	4(40)	<0.001*
3	3(2.8)	2(8)	2(20)	
4	0(0)	1(4)	1(10)	
5	0(0)	0(0)	1(10)	<0.001*
Bisap 48 score	1(1)	1(1)	2(3)	
0	46(43)	2(8)	1(10)	
1	50(46.7)	14(56)	2(20)	
2	5(4.7)	4(16)	3(30)	<0.001*
3	6(5.6)	3(12)	1(10)	
4	0(0)	2(8)	2(20)	
5	0(0)	0(0)	1(10)	

\*p &lt; 0.05 is accepted as statistical significance level.

**Table IV** Findings related to PLR and NLR obtained as a result of correlation analysis.

Variables	PLR		NLR	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Age	0.215	0.010	0.374	<0.001*
FBG	0.159	0.058	0.217	0.010
Ürea	0.367	<0.001*	0.514	<0.001*
Creatinine	0.099	0.240	0.223	0.008*
AST	0.098	0.244	0.071	0.404
ALT	0.020	0.816	-0.028	0.742
GGT	0.033	0.699	-0.070	0.410
ALP	0.114	0.178	-0.114	0.176
Amylase	0.062	0.463	0.203	0.021*
Lipase	0.061	0.474	0.180	0.032
LDH	0.185	0.057	0.247	0.003*
Total bilirubin	0.116	0.170	0.139	0.099
Direct bilirubin	0.112	0.185	0.088	0.299
Calcium	-0.159	0.058	-0.232	0.005*
ESR	0.286	0.001*	0.272	0.001*
CRP	0.295	<0.001*	0.518	<0.001*
WBC	0.157	0.061	0.622	<0.001*
Total Ranson	0.367	<0.001*	0.514	<0.001*
Mortality score	0.354	<0.001*	0.465	<0.001*
Atlanta	0.249	0.003*	0.202	0.016*
Bisap 0	0.269	0.001	0.449	<0.001*
Bisap 24	0.344	<0.001*	0.418	<0.001*
Bisap 48	0.360	<0.001*	0.385	<0.001*

\* $p < 0.05$  is accepted as statistical significance level.

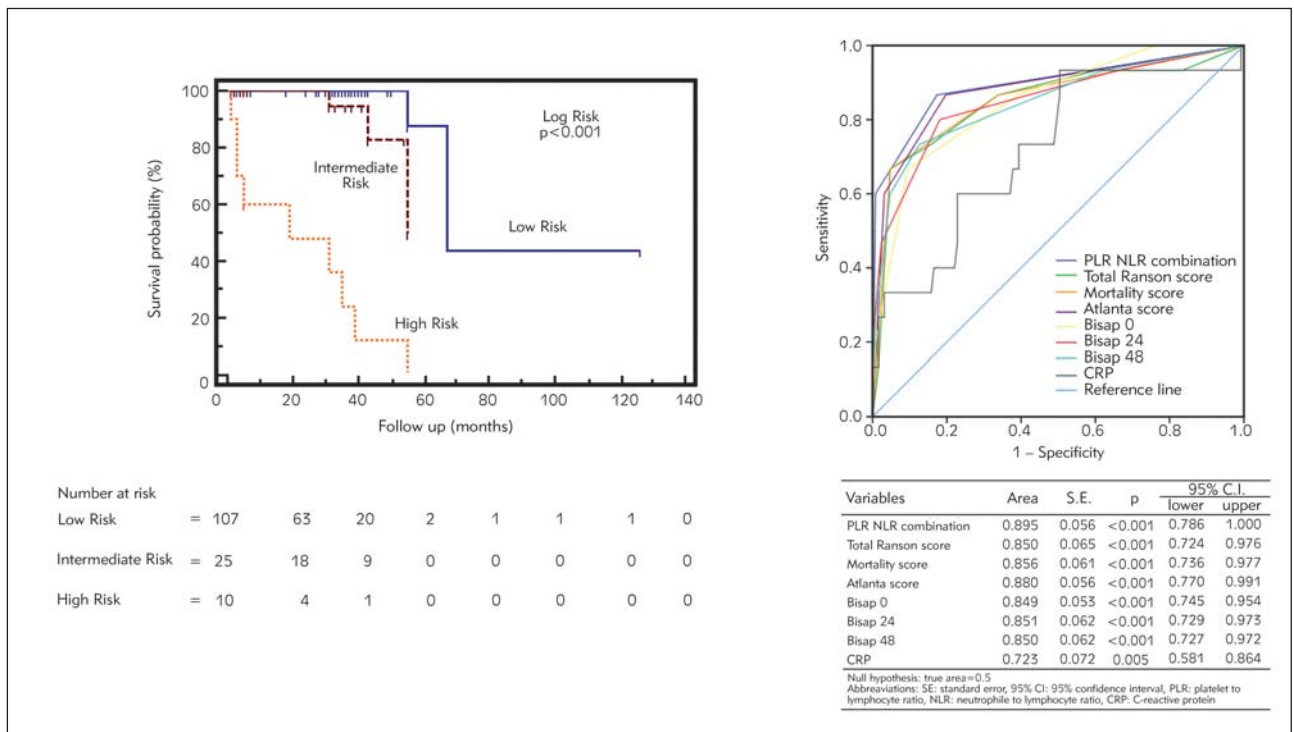
Abbreviations: PLR: platelet to lymphocyte ratio, NLR: neutrophile to lymphocyte ratio, FBG: fasting blood glucose, AST: aspartate aminotransferase, ALT: alanine aminotransferase, GGT: gama glutamyl transferase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, ESR: erythrocyte sedimentation rate, CRP: c-reactive protein, INR: international normalized ratio, WBC: white blood cell

**Table V** Independent Predictors of Mortality Risk.

Variables	HR	95% C.I.		<i>p</i>
		lower	upper	
PLR/NLR Combination (ref: Low risk)				
Intermediate Risk	10.667	1.183	96.199	0.035*
High Risk	99.490	12.566	787.686	<0.001*
Total Ranson	2.012	1.388	2.916	<0.001*
Atlanta (ref:Low)				
Intermediate	8.865	1.102	71.337	0.040*
Severe	16.443	1.190	227.119	0.037*
CRP	5.719	1.239	26.399	0.025*

\* $p < 0.05$  is accepted as statistical significance level. All demographic characteristics, admission complaints, clinical findings, laboratory findings, and scoring systems were included in the backward stepwise regression model.

Abbreviations: HR: Hazar Ratio; CI: Confidence intervals PLR: platelet to lymphocyte ratio, NLR: neutrophile to lymphocyte ratio, CRP: C-reactive protein



**Figure 1** PLR-NLR combination's survival graphic for risk groups and its diagnostic discrimination against scores.

**Discussion**

It was found in this study that PLR-NLR combination had a similar prognostic importance with other scoring systems used to determine acute pancreatitis prognosis. In risk groups according to PLR-NLR levels, it was found that mortality and acute pancreatitis complications such as ARF, sepsis and cholangitis increased in proportion to risk. The number of patients with a Ranson score of 5 and 6, a severe Atlanta score, a BISAP 0h score of 3 and 4, a BISAP 24h and 48h score of 4 and 5 was found to be higher in the high-risk group compared to other groups.

Acute pancreatitis is one of the most common gastrointestinal emergencies. While mortality rate is around 1% in all acute pancreatitis cases, this rate can reach up to 20–30% in severe acute pancreatitis cases (13). Currently, no single prognostic index is available for evaluating the severity of acute pancreatitis in the clinic. Disease occurrence and mortality is often predicted by combined use of clinical data, imaging, and biochemical analysis. However, approximately 20–30% of severe acute pancreatitis is misdiagnosed (14). There is a need for economical, objective, repeatable, non-invasive, specific, sensitive, simple laboratory parameters that do not require additional examination to diagnose the disease in early stages and determine severe cases. For this reason, we investigated whether PLR-NLR combination, which can be easily obtained in complete blood

count, could be used to determine the disease prognosis in patients diagnosed with acute pancreatitis.

Inflammatory markers are known to be usable for prognostic purposes in many diseases including cancer (15, 16). NLR and PLR are new markers used for this purpose. In our literature review, we have found a small number of studies investigating the relationship between NLR and acute pancreatitis (17, 18). In a study conducted by Azab et al. (18) it was reported that NLR was superior to total white blood cell count in terms of predicting adverse outcomes such as intensive care admission and longer hospital stay and a cut-off value about >4.7 could suggest severe disease. It was found in a study conducted by Suppiah et al. (19) that NLR was significantly higher in the severe pancreatitis group determined according to the Atlanta classification. Similar to above mentioned studies, a positive correlation was found in our study as a result of the correlation analysis between NLR and Ranson, Atlanta, BISAP scores and laboratory findings such as urea, creatinine, ESR, CRP. A cut-off value about NLR >13.64 was found to show disease severity with 73.0% sensitivity and 82.7% specificity. The fact that, unlike above mentioned studies, we obtained significant results with scoring systems and laboratory findings most commonly used for disease activity supports the idea that NLR is an effective parameters to show disease severity.

There is only a single study investigating the relationship between PLR and prognosis of acute



pancreatitis (11). Although a relationship was found between NLR and acute pancreatitis severity similar to above mentioned studies, Ilhan et al. could not find such a relationship between PLR and acute pancreatitis severity. In contrast to the study conducted by Ilhan et al. we found a relationship between PLR and acute pancreatitis severity in our study. A positive correlation was found as a result of the correlation analysis between PLR and Ranson, Atlanta, BISAP scores and laboratory findings such as urea, creatinine, ESR, CRP and a cut-off value about PLR  $>342.31$  was found to show disease severity with 73.3% sensitivity and 99.2% specificity. Only the Ranson criteria were used to show disease activity in the study conducted by Ilhan et al. and the study was performed on pregnant patients, which might be the reason why they obtained different results from us. However, comprehensive population of our study and the use of other popular scoring systems other than the Ranson score are superior aspects of our study.

Although there are a small number of studies investigating the relationship of NLR and PLR with acute pancreatitis, there is not a study investigating the PLR-NLR combination in acute pancreatitis. There are a number of studies reporting that the PLR-NLR combination could be used in prognosis of other diseases other than acute pancreatitis, particularly cancer (17–20). Similar to our study, patients were classified as 0-1-2 (low-medium-high risk) according to certain cut off levels in a study conducted by Feng et al. and the PLR-NLR combination was found to be associated with tumor progression in patients who underwent surgery due to esophageal cancer (20). The fact that, similar to above mentioned study, mortality was found to be around 90% in the high-risk group in our study suggests that the PLR-NLR combination is an effective marker to determine the course to mortality in acute pancreatitis.

It was shown in our study that high-risk group patients were mostly in advanced age group and more often had complications such as ARF, cholangitis, sepsis, abscess, and necrosis. High occurrence of complications directly associated with mortality in the high-risk group shows the prognostic importance of the PLR-NLR combination. Similar to our study, it was reported in studies available in the literature that advanced age ( $>70$  years) and acute pancreatitis complications were directly related with mortality (21, 22).

There are several studies in the literature comparing prognostic scores used for acute pancreatitis. In a study conducted by Surco et al. (23) it was found that BISAP score was similar to Atlanta score in terms of showing disease severity and both were superior to

Ranson score. Koziel et al. (24) found APACHE II had the highest predictive value in terms of showing disease severity and mortality; however, a similar sensitivity was observed using the BISAP score. Zhang et al. (25) found BISAP score and Ranson score to be similar in terms of showing mortality. On the other hand, it was determined in our study that medium- and high-risk PLR-NLR, moderately severe and severe Atlanta scores and Ranson score were found to be among independent predictors of mortality. It was found that BISAP 0, 24h, and 48h were not independent predictors of mortality.

The major limitations of our study are its retrospective design and low number of patients. Another limitation is the low number of pancreatitis cases due to ethylism and other causes in our hospital, which is an ERCP center.

In spite of all the studies on prognostic markers of acute pancreatitis, it is still uncertain which scoring system or laboratory finding is the most reliable in terms of determination of prognosis and mortality. In addition, each scoring system has its advantages disadvantages. Although the Ranson score presents a great advantage to assess disease severity, it is a disadvantage that it requires 48h data. Similarly, although it is very easy to use, the Atlanta classification is unable to differentiate between moderately acute pancreatitis and severe acute pancreatitis before 48 h after onset. Although BISAP provides quick data, it is complicated, cumbersome, and insufficiently sensitive. The PLR-NLR combination has advantages over other scoring systems such as being easy-to-use, simple, highly sensitive and specific and providing information regarding mortality and prognosis without requiring 48 hours of assessment time.

In conclusion, the PLR-NLR combination was found to have the highest AUC value in the ROC curve analysis in terms of survival and shown to have superior diagnostic discrimination compared to Ranson, Atlanta and BISAP scoring systems in terms of predicting mortality. In addition, the fact that the high-risk group had a mortality rate of approximately 99.5 times higher than the low-risk group and a Hazard Ratio (HR) higher than other risk factors shows that the PLR-NLR combination is an important marker in determination of prognosis.

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### **Conflict of interest statement**

The authors declare that they have no conflicts of interest for this work.

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