

# The Prognostic Role of Systemic Inflammatory Parameters and Severity Scores in Patients with Acute Pancreatitis

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## Abstract

**Objective:** To investigate the predictive power of the neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/eosinophil ratio (MER), and C-reactive protein (CRP) levels, as well as the harmless acute pancreatitis score (HAPS) and modified computed tomography severity index (mCTSI) score, in patients with acute pancreatitis (AP).

**Materials and Methods:** This retrospective study included adult patients hospitalized for AP. Patients were classified according to disease severity using HAPS and mCTSI. Systemic inflammatory parameters and demographic data were compared among patients to identify factors associated with disease severity.

**Results:** A total of 442 patients, 199 males (45%) and 243 females (55%), were enrolled in the study. Patients with severe disease had significantly higher mean NLR, PLR, MER, and CRP values than those with mild or moderate disease according to HAPS and mCTSI classifications. Positive correlations were observed between serum NLR, PLR, MER, CRP, and mCTSI. HAPS was correlated with NLR, MER, and CRP. Elevated NLR, MER, and CRP levels were independent predictors of disease severity in patients with AP according to HAPS and mCTSI.

**Conclusion:** NLR, MER, and CRP levels, but not PLR, in conjunction with HAPS or mCTSI may be useful for clinical decision-making regarding AP severity.

**Keywords:** Acute pancreatitis, systemic inflammatory parameters, harmless acute pancreatitis score, modified CT severity index

## Introduction

Immediate pancreatic tissue inflammation is referred to as acute pancreatitis (AP). The condition can cause significant morbidity and mortality in severe cases, especially when accompanied by pancreatic necrosis [1]. Rapid evaluation and determination of disease severity in patients presenting to the emergency department (ED) with AP are crucial for improving prognosis and treatment success [2].

Numerous biological markers and inflammatory mediators can be used to diagnose and assess the severity of AP. During the initial examination, amylase and lipase levels, complete blood count, metabolic panel (levels of urea, creatinine, glucose,

calcium, etc.), triglyceride level, urinalysis, and arterial blood gas are diagnostically valuable [3]. Moreover, scoring systems such as the Ranson's criteria, Glasgow-Imrie criteria, acute physiology and chronic health evaluation II scale, computed tomography severity index (CTSI), harmless acute pancreatitis score (HAPS), and prognostic nutritional index can be used to assess AP severity [4]. However, most scoring systems used to evaluate AP severity require at least 48 hours of patient monitoring. As a result, scoring systems have limited utility in patients with AP [5].

HAPS facilitates an early diagnosis of mild, non-intensive care unit (ICU) AP cases [6]. HAPS can be assessed during the first 30



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minutes of a patient's visit to the clinic based on the absence of rebound pain or guarding, normal hematocrit levels, and normal serum creatinine levels [7]. HAPS accurately predicted benign prognosis in 98% of 394 patients [6]. The CTSI, as defined by Balthazar et al. [8], revealed a highly significant association of mortality and morbidity with the presence of necrosis >30% of the pancreatic gland on abdominal CT. In addition, a retrospective analysis of 268 patients with AP showed that individuals with a CTSI >5 had an eightfold increased mortality rate [9].

The systemic inflammatory indicators neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/eosinophil (MER) ratio, and C-reactive protein (CRP) level are associated with disease severity and clinical outcomes in critical illness [10]. Azab et al. [11] showed that an elevated NLR in patients with AP was associated with an increased rate of ICU admission and length of stay. In the same study, the NLR was significantly higher in deceased patients than in survivors [11]. Larvin [12] found that CRP levels >15 mg/dL within the first 48 hours could distinguish severe and moderate AP. A study of 168 patients with AP showed the utility of systemic inflammatory parameters such as leukocyte count, CRP level, and NLR in addition to other diagnostic and prognostic tools [13].

We evaluated the ability of the NLR, PLR, MER, and CRP levels, as well as the HAPS and CTSI, to predict the severity of AP during clinical follow-up.

## Materials and Methods

### Ethics Committee Approval and Patient Consent

This study was conducted in accordance with the 1989 Declaration of Helsinki and was approved by the University of Health Sciences Türkiye, Istanbul Haseki Training and Research Hospital's Ethics Committee (decision number: 127-2021, date: 09.02.2022). The institutional review board did not require patient consent to access the medical records because there were no potentially identifiable markers or patient identifiers in the photographs or text.

### Study Design and Setting

This retrospective, cross-sectional, observational, single-center study included 442 consecutive adult patients aged  $\geq 18$  years diagnosed with pancreatitis in the ED and hospitalized between January 1, 2016 and January 1, 2021.

Data were collected by searching for the K85 and K86 international classification of disease codes in the hospital's record systems and archives. We assessed the patients' demographics (age and sex), laboratory parameters [leukocyte (normal level [N]: 4.5-10.0  $10^3/\mu\text{L}$ ), neutrophil (N: 1.5-8.0  $10^3/\mu\text{L}$ ), lymphocyte (N: 0.8-5.0  $10^3/\mu\text{L}$ ), eosinophil (N: 0.01-0.40

$10^3/\mu\text{L}$ ), and platelet counts (N: 150-450  $10^3/\mu\text{L}$ ) and monocyte (N: 4.2-11.8%), neutrophil (N: 42.9-74.3%), eosinophil (N: 0.2-5.3%), and lymphocyte (N: 18.3-45.7%) percentages, NLR, PLR, MER, and CRP (N: <5 mg/dL)] values measured on admission, and radiological findings.

Initially, patients were divided into two groups based on clinical outcome (ward vs. ICU admission). The groups were compared according to age, sex, etiology, HAPS, CTSI, modified CTSI (mCTSI), NLR, PLR, MER, and CRP. Patients were separated into three groups based on AP severity defined by the HAPS: mild, moderate, and severe AP. Finally, the CTSI and mCTSI were used to categorize AP as mild, moderate, or severe. We investigated differences in age, sex, and inflammatory parameters among the groups.

### Scoring Systems for Severity in AP

The HAPS is a clinical scoring system that identifies patients with their first episode of AP who do not require intensive care. HAPS is generally determined within 30 minutes of admission and is based on a lack of rebound tenderness or guarding, normal hematocrit level, and normal serum creatinine level [6].

The CTSI was created by Balthazar et al. [8] to assess the severity of AP. The grades of pancreatitis (normal pancreas: 0; pancreatic enlargement: 1; inflammatory changes in the pancreas and peripancreatic fat: 2; poorly defined single peripancreatic fluid collection: 3; two or more poorly defined peripancreatic fluid collections: 4) and the extent of pancreatic necrosis (none: 0;  $\leq 30\%$ : 2; >30-50%: 4; >50%: 6) are components of the CTSI. The maximum score was 10 [14].

The mCTSI has a stronger relationship with patient outcomes, including hospitalization duration and the incidence of organ failure. The score (maximum 10) was based on estimated pancreatic inflammation and necrosis. Three factors were considered in the mCTSI: pancreatic inflammation (normal pancreas: 0, intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat: 2, pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis: 4), pancreatic necrosis (none: 0;  $\leq 30\%$ : 2; >30%: 4), and extra-pancreatic consequences (one or more pleural effusions, ascites, vascular complications, parenchymal complications, and/or gastrointestinal involvement: 2) [15].

### Study Population and Sampling

To reduce selection bias, all patients meeting the eligibility criteria during the study period were included. We enrolled 2,360 consecutive adult patients diagnosed with AP in the ED who were hospitalized during the study period. Of these patients, the following were excluded: 220 due to unavailable data, 4 due to pregnancy, 1,152 due to a diagnosis of chronic pancreatitis, 150 due to a history of hematological disease,

and 392 due to an additional inflammatory disease, other than pancreatitis, including cholangitis, or a history of medication usage (anti-inflammatory drugs, antibiotics, statins, etc.) during the previous week, which can affect the serum NLR, PLR, MER, and CRP levels. Finally, 442 patients were included in the analysis.

### Statistical Analysis

Before data collection, the sample size was determined by power analysis using data from previous studies. With a power of 95% and alpha error of 5%, it was anticipated that at least 334 patients would be required to detect significant differences in disease severity among groups.

Data analysis was conducted using SPSS statistical software (version 15.0 for Windows; SPSS Inc., Chicago, IL). Categorical variables (sex and age) are expressed as numbers of patients (n) expressed as percentages (%). Numerical data are expressed as means with standard deviations. Intergroup comparisons were conducted using the Mann-Whitney U test for non-normally distributed data (e.g., NLR, PLR, MER, CRP, HAPS, CTSI, and mCTSI). One-Way ANOVA was used to compare numerical variables among more than two groups for normally distributed variables (e.g., age and sex), and the Kruskal-Wallis test was used for non-normally distributed variables (e.g., NLR, PLR, MER, CRP, HAPS, CTSI, and mCTSI). Non-parametric subgroup analyses were conducted using the Mann-Whitney U test and interpreted using Bonferroni correction. Spearman's correlation analysis was used to analyze the relationship between numerical variables when the parametric test condition was

not satisfied. Independent variables were analyzed using multivariate logistic regression analysis. All potential predictor variables were included in the initial model using the enter method. Significance assessments via the likelihood ratio test led to the retention of statistically significant variables in the final model. Non-significant variables were removed to achieve a more parsimonious model. The alpha significance level was set to  $p < 0.05$ .

### Results

The study included 442 patients, including 199 (45.0%) males and 243 (55.0%) females. The mean age of the patients was  $54.5 \pm 18.2$  years (minimum 18, maximum 97 years). Biliary pancreatitis accounted for 50.7% (n=224) and nonbiliary pancreatitis for 49.3% (n=218) of the cases. Regarding clinical outcomes, 419 patients (94.8%) were followed up in the ward, whereas 23 (5.2%) were followed up in the ICU. There were no fatalities.

There were no significant differences in age or sex between the ward and ICU patients ( $p=0.110$  and  $p=0.149$ , respectively). When the participants were categorized according to HAPS, a significant difference was observed between the ward and ICU patients ( $p < 0.001$ ). In addition, the CTSI and mCTSI were significantly higher in the ICU than ward patients ( $p < 0.001$ , for both comparisons). There were significant differences in the NLR and MER between the ward and ICU patients ( $p=0.002$  and  $p < 0.001$ , respectively). However, the PLR and CRP levels did not differ between the two groups ( $p=0.232$  and  $p=0.064$ , respectively) (Table 1).

**Table 1. Clinical outcomes**

		ICU	Ward	p*
Age (years), mean $\pm$ SD		60.20 $\pm$ 18.20	54.20 $\pm$ 18.10	0.110
Sex, n (%)	Male	7 (30.4%)	192 (45.8%)	0.149
	Female	16 (69.6%)	227 (54.2%)	
Etiology, n (%)	Biliary	11 (47.8%)	213(50.8%)	0.779
	Nonbiliary	12 (52.2%)	206 (49.2%)	
HAPS	Mild	0 (0.0%)	281 (67.1%)	<0.001
	Moderate	8 (34.8%)	108 (25.8%)	
	Severe	15 (65.2%)	30 (7.2%)	
		<b>Mean <math>\pm</math> SD</b>	<b>Mean <math>\pm</math> SD</b>	
CTSI		4.20 $\pm$ 1.30	1.80 $\pm$ 1.40	<0.001
Modified CTSI		6.00 $\pm$ 1.90	2.10 $\pm$ 1.90	<0.001
NLR		12.79 $\pm$ 10.16	7.71 $\pm$ 8.43	0.002
PLR		246.10 $\pm$ 216.6	191.70 $\pm$ 159.30	0.232
MER		59.00 $\pm$ 37.40	28.30 $\pm$ 27.60	<0.001
CRP		82.80 $\pm$ 71.30	55.8 $\pm$ 6.69	0.064

Data are expressed as numbers (n) and percentages (%), means, and standard deviations (SD)

\*Intragroup analyses (ICU vs. ward) were conducted using chi-squared and the Mann-Whitney U tests, as appropriate

ICU: Intensive care unit, HAPS: Harmless acute pancreatitis score, CTSI: Computed tomography severity index, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MER: Monocyte/eosinophil ratio, CRP: C-reactive protein

Age was positively correlated with NLR ( $\rho = 0.227$  and  $p < 0.001$ ), PLR ( $\rho = 0.113$  and  $p = 0.017$ ), and CRP level ( $\rho = 0.166$  and  $p < 0.001$ ). However, no significant correlation was observed between age and MER ( $p = 0.512$ ). HAPS was positively correlated with NLR ( $\rho = 0.165$  and  $p < 0.001$ ), MER ( $\rho = 0.190$  and  $p < 0.001$ ), and CRP level ( $\rho = 0.196$ ). Similarly, the CTSI and mCTSI were positively correlated with NLR, PLR, MER, and CRP levels (Table 2).

Based on HAPS, 281 (63.6%) patients were classified as mild AP, 116 (26.2%) as moderate AP, and 45 (10.2%) as severe AP. Neither age nor sex was significantly different according to AP severity ( $p = 0.187$  and  $p = 0.086$ , respectively). However, the NLR, PLR,

MER, and CRP levels differed significantly according to HAPS ( $p = 0.001$  for all comparisons) (Table 3). Multivariate logistic regression analysis identified MER [odds ratio (OR): 1.014, confidence interval (CI): 1.006-1.021;  $p < 0.001$ ], CRP level (OR: 1.005, 95% CI: 1.002-1.008;  $p = 0.002$ ), and NLR (OR: 1.046, 95% CI: 1.002-1.089;  $p = 0.031$ ) as independent predictors of severe AP according to HAPS (Table 4).

For identifying severe AP according to the HAPS, a MER  $\geq 21.2$  had 57.1% sensitivity and 56.6% specificity [area under the curve (AUC): 0.604, 95% CI: 0.548-0.660,  $p < 0.001$ ]. A CRP level  $\geq 29.5$  mg/L indicated severe AP with 57.8% sensitivity and 56.3% specificity (AUC: 0.599, 95% CI: 0.544-0.655,  $p = 0.001$ ).

**Table 2. Correlations of the mean serum NLR, PLR, MER, and CRP level with demographic and clinical characteristics**

Characteristic	NLR		PLR		MER		CRP	
	r	p	r	p	r	p	r	p
Age	0.227	<0.001	0.113	0.017	0.031	0.512	0.166	<0.001
HAPS	0.165	<0.001	0.013	0.790	0.190	<0.001	0.196	<0.001
Length of stay in hospital	0.155	0.001	0.067	0.159	0.043	0.364	0.297	<0.001
ICU length of stay	0.146	0.002	0.057	0.228	0.190	<0.001	0.086	0.070
CTSI	0.248	<0.001	0.133	0.005	0.348	<0.001	0.258	<0.001
Modified CTSI	0.259	<0.001	0.144	0.002	0.365	<0.001	0.281	<0.001

NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MER: Monocyte/eosinophil ratio, CRP: C-reactive protein, HAPS: Harmless acute pancreatitis score, CTSI: Computed tomography severity index, ICU: Intensive care unit

**Table 3. Demographic characteristics and systemic inflammatory parameters according to AP severity based on severity scores**

Characteristic	Parameter	Mild	Moderate	Severe	p*
		mean $\pm$ SD	mean $\pm$ SD	mean $\pm$ SD	
HAPS	NLR	7.30 $\pm$ 8.60	7.60 $\pm$ 6.20	13.10 $\pm$ 11.70	<0.001
	PLR	193.80 $\pm$ 161.50	161.50 $\pm$ 100.40	284.40 $\pm$ 250.30	0.001
	MER	25.30 $\pm$ 25.40	34.10 $\pm$ 30.70	47.60 $\pm$ 36.30	<0.001
	CRP	47.00 $\pm$ 54.90	61.10 $\pm$ 70.50	111.00 $\pm$ 98.00	<0.001
CTSI	Non-severe mean $\pm$ SD		Severe mean $\pm$ SD		p*
	NLR	7.90 $\pm$ 8.50	14.10 $\pm$ 12.70	0.131	
	PLR	192.80 $\pm$ 162.90	279.30 $\pm$ 145.40	0.449	
	MER	29.60 $\pm$ 28.70	44.00 $\pm$ 37.60	0.265	
	CRP	56.50 $\pm$ 67.10	88.90 $\pm$ 74.30	0.585	
Modified CTSI	Mild mean $\pm$ SD		Moderate mean $\pm$ SD		p*
	NLR	6.70 $\pm$ 6.20	9.90 $\pm$ 11.60	15.80 $\pm$ 11.90	
	PLR	175.00 $\pm$ 117.40	225.20 $\pm$ 218.00	302.40 $\pm$ 264.50	0.031
	MER	21.20 $\pm$ 22.30	46.20 $\pm$ 31.40	56.60 $\pm$ 40.70	<0.001
	CRP	43.70 $\pm$ 51.60	81.60 $\pm$ 85.00	107.10 $\pm$ 86.00	<0.001

Data are expressed as numbers (n) and percentages (%), means, and standard deviations (SD)  
 \*Intragroup analyses (eg, non-severe or severe) were conducted using chi-squared, One-Way ANOVA test (eg, mild, moderate, or severe), and the Kruskal-Wallis tests, as appropriate  
 AP: Acute pancreatitis, HAPS: Harmless acute pancreatitis score, CTSI: Computed tomography severity index, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MER: Monocyte/eosinophil ratio, CRP: C-reactive protein

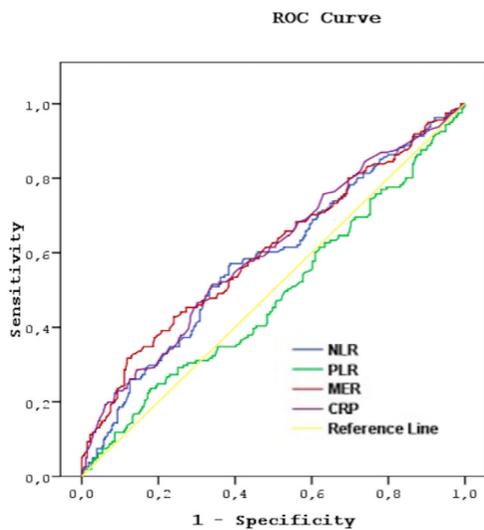
Finally, an NLR  $\geq 5.59$  was identified as the cut-off value for detecting severe AP, with 58.4% sensitivity and 57.7% specificity (AUC: 0.583, 95% CI: 0.527-0.638,  $p=0.004$ ) (Figure 1).

Based on the CTSI, 433 patients (97.9%) had non-severe AP and 9 severe AP. There were no significant differences in age or sex ( $p=0.195$  and  $p=0.840$ , respectively) between the non-severe and severe AP groups. Moreover, the NLR, PLR, MER, and CRP values did not differ between the groups ( $p=0.131$ ,  $p=0.449$ ,  $p=0.265$ , and  $p=0.585$ , respectively) (Table 3).

There were 296 (67%) individuals with mild AP, 129 (29.2%) with moderate AP, and 17 (3.8%) with severe AP based on the mCTSI. Age and sex did not differ significantly according to AP severity ( $p=0.090$  and  $p=0.168$ , respectively). However, the NLR, PLR, MER, and CRP levels differed significantly according to AP severity ( $p<0.001$ ,  $p=0.031$ ,  $p<0.001$ , and  $p<0.001$ , respectively) (Table 3). Multivariate logistic regression analysis

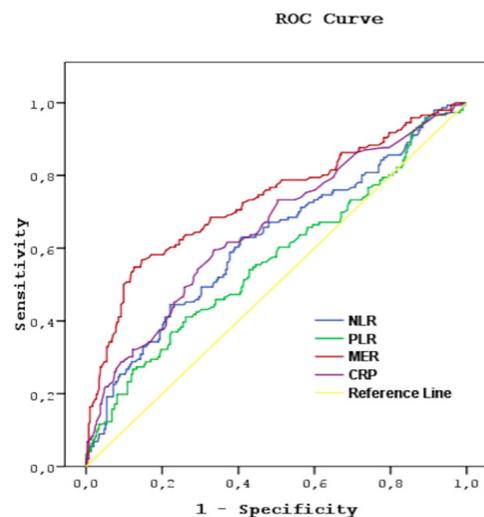
identified NLR (OR: 1.046, 95% CI: 1.014-1.079;  $p=0.005$ ), MER (OR: 1.034, 95% CI: 1.026-1.043;  $p<0.001$ ), and CRP level (OR: 1.008, 95% CI: 1.004-1.011;  $p<0.001$ ) as independent predictors of severe AP according to the mCTSI (Table 4).

An MER  $\geq 23.45$  was identified as the cut-off value for detecting severe AP according to the mCTSI, with 68.5% sensitivity and 67.3% specificity (AUC: 0.731, 95% CI: 0.678-0.784,  $p<0.001$ ). A CRP level  $\geq 35.5$  mg/dL had 61.6% sensitivity and 62.9% specificity for the detection of severe AP (AUC: 0.654, 95% CI: 0.598-0.709,  $p<0.001$ ). An NLR  $\geq 5.93$  was identified as the cut-off value for predicting severe AP, with a sensitivity of 60.3% and specificity of 60.9% (AUC: 0.621, 95% CI: 0.564-0.678,  $p<0.001$ ). Finally, a PLR  $\geq 152.1$  was identified as the cut-off value for detecting severe AP, with 55.5% sensitivity and 55.4% specificity (AUC: 0.570, 95% CI: 0.511-0.628,  $p=0.017$ ) (Figure 2).



**Figure 1.** Specificity and sensitivity of the NLR, PLR, MER, and CRP level for determining the severity of AP according to the HAPS using ROC curves

ROC: Receiver operating characteristics, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MER: Monocyte/eosinophil ratio, CRP: C-reactive protein



**Figure 2.** Specificity and sensitivity of the NLR, PLR, MER, and CRP level for determining the severity of AP according to the modified CTSI using ROC curves

ROC: Receiver operating characteristics, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MER: Monocyte/eosinophil ratio, CRP: C-reactive protein

Table 4. Multivariate logistic regression analysis to determine disease severity					
		p	OR	95% CI	
HAPS	NLR	0.031	1.046	1.004	1.089
	PLR	0.050	0.998	0.996	1.000
	MER	<0.001	1.014	1.006	1.021
	CRP	0.002	1.005	1.002	1.008
Modified CTSI	NLR	0.005	1.046	1.014	1.079
	MER	<0.001	1.034	1.026	1.043
	CRP	<0.001	1.008	1.004	1.011

OR: Odds ratio, CI: Confidence interval, HAPS: Harmless acute pancreatitis score, CTSI: Computed tomography severity index, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MER: Monocyte/eosinophil ratio, CRP: C-reactive protein

## Discussion

The clinical manifestations of AP range from transient abdominal discomfort to death [16]. Given the significant mortality and morbidity rates, early assessment of clinical characteristics and treatment initiation are crucial. We assessed the predictive power of systemic inflammatory markers and HAPS and mCTSI in patients with AP.

The key findings are as follows. The HAPS, CTSI, and mCTSI were significantly higher in the ICU than ward patients. Additionally, NLR and MER differed significantly between the groups. HAPS was significantly and positively correlated with NLR, MER, and CRP levels. The CTSI and mCTSI were positively correlated with NLR, PLR, MER, and CRP levels. Patients with severe AP, according to the HAPS, had significantly higher NLR, PLR, and CRP values than those with mild and moderate AP patients. According to the mCTSI, patients with severe AP had increased NLR, PLR, MER, and CRP values. Moreover, NLR, MER, and CRP levels were independent predictors of severe AP based on HAPS and mCTSI. According to HAPS, an MER  $\geq 21.2$ , CRP level  $\geq 29.5$  mg/dL, and NLR  $\geq 5.59$  were identified as the cut-offs for predicting severe AP. Based on the mCTSI, an MER  $\geq 23.45$ , CRP level  $\geq 35.5$  mg/dL, NLR  $\geq 5.93$ , and PLR  $\geq 152.1$  predicted severe AP.

None of the AP scoring systems are completely reliable [17,18]. Typically, scoring systems require 48 hours to obtain results, which may not be feasible in the ED. The HAPS can be calculated quickly using only three simple parameters [6]. In a cohort trial involving 394 patients, Lankisch et al. [6] reported that HAPS reliably identified mild AP. In a study of 322 patients with AP, Gülen et al. [19] found that HAPS was not predictive of poor prognosis. In the same study, logistic regression analysis of the CTSI, HAPS, red blood cell distribution width, NLR, age, diabetes mellitus, and systolic blood pressure revealed that only the CTSI was independently associated with mortality. We found that HAPS and CTSI were significantly higher in ICU patients than in hospitalized adults. Furthermore, the NLR, PLR, and CRP levels were positively correlated with HAPS. Moreover, the CTSI was significantly and positively correlated with the NLR, PLR, MER, and CRP levels.

Systemic inflammatory parameters such as NLR, PLR, MER, and CRP levels are indicative of disease severity and poor clinical outcomes in various conditions [20-22]. NLR and CRP levels are inexpensive, reproducible, rapid, and easily accessible markers of inflammatory status. Song et al. [23] showed that initial NLR was associated with the prognosis of infection-related diseases. Additionally, Jeon and Park [10] reported that NLR was associated with organ failure and disease severity in patients with AP. Larvin [12] showed that CRP  $>15$  mg/dL within the first 48 hours differentiated severe from moderate AP. Similarly, Stirling et al. [24] revealed that a CRP level of  $>190$  mg/dL indicates severe AP. Yarkaç et al. [13] found a statistically significant difference between mild and severe

AP in terms of hospitalization duration, CRP level, leukocyte count, and NLR among 168 patients with AP. In a comparison of the predictive values of inflammatory markers for AP severity and mortality, NLR had the greatest predictive power, regardless of age [25]. Kaya et al. [26] reported that the PLR could predict AP severity early. In this study, ICU patients had higher NLR and MER values than ward patients. However, PLR and CRP levels did not significantly differ between the groups. According to the HAPS, patients with severe AP had higher NLR, PLR, and CRP values than those with mild or moderate AP patients. Regression analysis showed that MER, CRP level, and NLR were predictive of severe AP.

Ward and ICU AP patients had significantly different CTSI values. However, the NLR, PLR, MER, and CRP levels did not differ between severe and non-severe AP patients according to the CTSI. The NLR, PLR, MER, and CRP levels significantly differed among patients with mild, moderate, and severe AP, as defined by the mCTSI. In addition, NLR, MER, and CRP levels were independent predictors of severe AP. No previous study has compared the CTSI and mCTSI. Our results showed that the mCTSI was more predictive of morbidity than the CTSI. HAPS and mCTSI were positively correlated with NLR, PLR, MER, and CRP levels. In patients presenting to the ED with AP, HAPS or mCTSI in conjunction with inflammatory markers can potentially differentiate serious diseases in patients with AP.

Azab et al. [11] recommended an NLR  $>4.7$  as a predictor of severe AP. Suppiah et al. [27] reported that the optimal cut-off value determined from a receiver operating characteristic curve was  $>4.8$ , with 90.9% sensitivity and 22.5% specificity. In this study, NLR values  $\geq 5.59$  and  $\geq 5.93$  were considered predictive of severe AP based on HAPS and mCTSI, respectively. Furthermore, HAPS defines severe AP as an MER  $\geq 21.2$  and CRP level  $\geq 29.5$  mg/dL. Finally, an MER  $\geq 23.45$ , CRP level  $\geq 35.5$  mg/dL, and PLR  $\geq 152.1$  were identified as cut-offs for detecting severe AP according to the mCTSI.

## Study Limitations

This study had several limitations, most of which were its retrospective, single-center design and inclusion of only 442 patients. The rate of unavailable data was quite high, potentially affecting our results. Missing data can introduce bias and reduce study precision. In addition, single measurements of serum NLR, PLR, MER, and CRP levels were performed upon admission to the ED. Hence, these parameters, which can affect long-term outcomes, were not assessed in the AP patients following hospitalization. These issues should be considered in future studies.

## Conclusion

Our findings revealed that systemic inflammatory parameters, including the mean serum NLR, MER, and CRP levels, but not the PLR, upon admission to the ED when evaluated in combination with HAPS or mCTSI, may be useful biomarkers

for predicting disease severity in patients with AP. However, randomized controlled studies with more cases are needed to validate the use of NLR, MER, and CRP as biomarkers and for clinical decision-making regarding AP severity.

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### Ethics

**Ethics Committee Approval:** This study was conducted in accordance with the 1989 Declaration of Helsinki and was approved by the University of Health Sciences Türkiye, İstanbul Haseki Training and Research Hospital's Ethics Committee (decision number: 127-2021, date: 09.02.2022).

**Informed Consent:** The institutional review board did not require patient consent to access the medical records because there were no potentially identifiable markers or patient identifiers in the photographs or text.

### Authorship Contributions

Concept: T.A., A.A., Ö.S., Design: T.A., Ö.S., T.A., Data Collection or Processing: T.A., T.A., T.S.C., Analysis or Interpretation: T.A., T.S.C., Literature Search: T.A., A.A., Writing: T.A., A.A., Ö.S.

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

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### References

- van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology*. 2011;141:1254-63.
- Flasar MH, Goldberg E. Acute abdominal pain. *Med Clin North Am*. 2006;90:481-503.
- Shah AP, Mourad MM, Bramhall SR. Acute pancreatitis: current perspectives on diagnosis and management. *J Inflamm Res*. 2018;11:77-85.
- Carroll JK, Herrick B, Gipson T, Lee SP. Acute pancreatitis: diagnosis, prognosis, and treatment. *Am Fam Physician*. 2007;75:1513-20.
- Jain D, Bhaduri G, Jain P. Different scoring systems in acute alcoholic pancreatitis: which one to follow? an ongoing dilemma. *Arq Gastroenterol*. 2019;56:280-5.
- Lankisch PG, Weber-Dany B, Hebel K, Maisonneuve P, Lowenfels AB. The harmless acute pancreatitis score: a clinical algorithm for rapid initial stratification of nonsevere disease. *Clin Gastroenterol Hepatol*. 2009;7:702-5.
- Talukdar R, Sharma M, Deka A, Teslima S, Goswami AD, Goswami A, et al. Utility of the "harmless acute pancreatitis score" in predicting a non-severe course of acute pancreatitis: a pilot study in an Indian cohort. *Indian J Gastroenterol*. 2014;33:316-21.
- Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. *Radiology*. 1990;174:331-6.
- Simchuk EJ, Traverso LW, Nukui Y, Kozarek RA. Computed tomography severity index is a predictor of outcomes for severe pancreatitis. *Am J Surg*. 2000;179:352-5.
- Jeon TJ, Park JY. Clinical significance of the neutrophil-lymphocyte ratio as an early predictive marker for adverse outcomes in patients with acute pancreatitis. *World J Gastroenterol*. 2017;23:3883-9.
- Azab B, Jaglall N, Atallah JP, Lamet A, Raja-Surya V, Farah B, et al. Neutrophil-lymphocyte ratio as a predictor of adverse outcomes of acute pancreatitis. *Pancreatol*. 2011;11:445-52.
- Larvin M. Assessment of severity and prognosis in acute pancreatitis. *Eur J Gastroenterol Hepatol*. 1997;9:122-30.
- Yarkaç A, Kose A, Bozkurt Babuş S, Ates F, Orekiçi Temel G, Ölmez A. The value of hematological parameters in acute pancreatitis. *Ulus Travma Acil Cerrahi Derg*. 2019;25:453-60.
- Vriens PW, van de Linde P, Slotema ET, Warmerdam PE, Breslau PJ. Computed tomography severity index is an early prognostic tool for acute pancreatitis. *J Am Coll Surg*. 2005;201:497-502.
- Konur S, Ozkahraman A, Surmeli N, Gunduz I, Iliklerden UH, Dertli R, et al. The Severity of Acute Pancreatitis According to Modified Balthazar Classification in Patients With Pancreatic Cancer. *Tumori*. 2020;106:356-61.
- Otsuki M, Takeda K, Matsuno S, Kihara Y, Koizumi M, Hirota M, et al. Criteria for the diagnosis and severity stratification of acute pancreatitis. *World J Gastroenterol*. 2013;19:5798-805.
- Mounzer R, Langmead CJ, Wu BU, Evans AC, Bishehsari F, Muddana V, et al. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis. *Gastroenterology*. 2012;142:1476-82.
- Wang X, Xu Y, Qiao Y, Pang X, Hong L, Fu J, et al. An evidence-based proposal for predicting organ failure in severe acute pancreatitis. *Pancreas*. 2013;42:1255-61.
- Gülen B, Sonmez E, Yaylaci S, Serinken M, Eken C, Dur A, et al. Effect of harmless acute pancreatitis score, red cell distribution width and neutrophil/lymphocyte ratio on the mortality of patients with nontraumatic acute pancreatitis at the emergency department. *World J Emerg Med*. 2015;6:29-33.
- Ayça B, Akin F, Celik O, Sahin I, Yildiz SS, Avci II, et al. Neutrophil to Lymphocyte Ratio is Related to Stent Thrombosis and High Mortality in Patients With Acute Myocardial Infarction. *Angiology*. 2015;66:545-52.
- Xue J, Huang W, Chen X, Li Q, Cai Z, Yu T, et al. Neutrophil-to-Lymphocyte Ratio Is a Prognostic Marker in Acute Ischemic Stroke. *J Stroke Cerebrovasc Dis*. 2017;26:650-7.
- Oh J, Kim SH, Park KN, Oh SH, Kim YM, Kim HJ, et al. High-sensitivity C-reactive protein/albumin ratio as a predictor of in-hospital mortality in older adults admitted to the emergency department. *Clin Exp Emerg Med*. 2017;4:19-24.
- Song H, Kim HJ, Park KN, Kim SH, Oh SH, Youn CS. Neutrophil to lymphocyte ratio is associated with in-hospital mortality in older adults admitted to the emergency department. *Am J Emerg Med*. 2021;40:133-7.
- Stirling AD, Moran NR, Kelly ME, Ridgway PF, Conlon KC. The predictive value of C-reactive protein (CRP) in acute pancreatitis-is interval change in CRP an additional indicator of severity? *HPB (Oxford)*. 2017;19:874-80.
- Li Y, Zhao Y, Feng L, Guo R. Comparison of the prognostic values of inflammation markers in patients with acute pancreatitis: a retrospective cohort study. *BMJ Open*. 2017;7:e013206.
- Kaya Y, Düğeroğlu H, Çınar H. Akut Pankreatitin Şiddeti ile Platelet Lenfosit Oranı Arasındaki İlişki. *F.Ü.Sağ.Bil.Tıp.Derg*. 2017;31:137-41.
- Suppiah A, Malde D, Arab T, Hamed M, Allgar V, Smith AM, et al. The prognostic value of the neutrophil-lymphocyte ratio (NLR) in acute pancreatitis: identification of an optimal NLR. *J Gastrointest Surg*. 2013;17:675-81.