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ORIGINAL RESEARCH

Usage of the Ranson criteria and neutrophil-lymphocyte ratio measured on presentation to the emergency department in the prediction of mortality in acute pancreatitis

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Abstract

The aim of this study is to examine the usefulness of the Ranson criteria and neutrophil-to-lymphocyte ratio (NLR) on admission to the emergency department (ED) in regard to the prediction of mortality for patients diagnosed with acute pancreatitis (AP) and compare the predictive ability of these two parameters. All patients information aged over 18 years who presented to ED and were diagnosed with AP in the three-year study period were analyzed retrospectively. The data were provided from the electronic-based hospital information system. To assess the cut-off value of each variable in discriminating between the survivor and non-survivor groups, the receiver operating characteristic (ROC) analysis and the area under the curve (AUC) were used. This study included 318 adult patients (47.5% male) with a mean age of 58.6 $\pm$ 17.6 years. As a result of the ROC analysis of the Ranson criteria for mortality prediction, the AUC value was calculated as 0.65 (95% confidence interval (CI): 0.57–0.70), the Youden index as 0.28, and the p value as 0.002, while the ROC analysis of NLR revealed an AUC value of 0.58 (95% CI: 0.52–0.64), Youden index of 0.29, and p value of 0.08. The Ranson criteria can provide a clinical guide in the prediction of the prognosis of AP patients. However, according to the results of this study, NLR recorded at the time of admission was found to be ineffective on predicting the prognosis of AP patients.

Keywords

Acute pancreatitis; Neutrophil-lymphocyte ratio; Ranson criteria; Mortality

1. Introduction

Acute pancreatitis (AP) is a digestive enzyme-related disorder, which are normally inactive in the pancreas, being activated by any etiological factor and digesting the pancreatic tissue and surrounding tissues, and the consequent development of widespread inflammation [1]. In 80% of patients, pancreatitis is of the acute edematous type, which has a self-limiting mild course, rarely causes local and systemic complications, and can be resolved with supportive treatment. In the remaining 20% of cases, clinical manifestation is acute necrotizing pancreatitis with severe organ failure and high morbidity and mortality [2, 3].

Recent studies have shown that the worldwide prevalence of AP varies between 4.9 and 73.4 per 100,000 [4]. While the overall mortality rate in acute pancreatitis is 10% for all patients, this rate also varies according to the severity of the disease, reaching 35% in patients with infected necrotizing pancreatitis [5]. AP can cause cardiovascular, pulmonary and renal failure in the early stage and septic problems during the later stage. AP—related mortality depends on the development of pancreatic necrosis, infection, and associated multiple organ failure and local complications [6].

The prediction of disease severity can help identify high-risk patients and facilitate early and implementation of appropriate diagnosis and therapeutic interventions, including early transfer to the intensive care unit (ICU). The prognostic classification of the disease and determination of its severity are extremely important in predicting mortality or possible complications that may develop. Various scoring systems are used to determine clinical severity and prognosis in AP. The Ranson criteria, which is a scoring system specific to AP, are based on the evaluation of some clinical and laboratory findings at the admission time and at the 48th hour [7].

The neutrophil-to-lymphocyte ratio (NLR), referring to the ratio of neutrophil and lymphocyte counts to each other, is used to react quickly to the severity of the inflammatory process and regarded as a useful predictive biomarker to determine the severity of AP [8–10].

The objective of the present study is to examine the usefulness of the Ranson criteria and neutrophil-to-lymphocyte ratio (NLR) on admission to the emergency department (ED)

in prediction of mortality for patients diagnosed with AP and compare the predictive ability of these two parameters.

2. Methods

From 1 January 2018 to 1 January 2021, a single-center, retrospective, observational study was conducted in the ED of a tertiary care education hospital. The study protocol was approved by local ethics committee of University of Health Science Haydarpasa Numune Education and Research Hospital, and a waiver of permission was issued (ethical committee ruling number: 2021/KK/290, date: 15 November 2021). The patients aged over 18 years who were admitted to the ED and were diagnosed with AP during the study period were included in the study. The presence of at least two of the following three criteria was used to diagnose AP: typical abdominal pain, elevated serum amylase and/or lipase levels greater than three times the upper limit of the normal range, and abdominal imaging abnormalities consistent with AP [11]. Age, gender, AP etiology (biliary/non-biliary), laboratory parameters at the time of admission to ED, and abdominal imaging findings were screened from the hospital-based electronic record system and registered in an Excel file (Microsoft Inc., Richmond, WA, USA). The Ranson scores of the patients at the admission time were calculated considering the biliary and non-biliary etiologies [7]. The NLR was determined using the following formula: absolute number of neutrophils/absolute number of lymphocytes. Patients who were younger than 18 years of age, pregnant women, patients transferred from another hospital, those with unavailable or missing data, and those with hematological malignancies were excluded from the study. The main endpoint of the study was mortality of the patients, and the survival follow-up was assessed 28 days after admission.

IBM SPSS Statistics version 26.0 (SPSS Inc., Chicago, IL, USA) and MedCalc Statistical Software version 19.0.6 (MedCalc Software bvba, Ostend, Belgium) were used for statistical analysis. Descriptive criteria were presented as median, minimum-maximum and percentage distributions. The conformity of the data to the normal distribution was checked with the Kolmogorov-Smirnov test. The receiver operating characteristic (ROC) analysis was performed to determine the cut-off values of the Ranson criteria and NLR in predicting mortality. The ROC analysis was conducted with the DeLong method [12]. To assess the effectiveness of NLR and the Ranson criteria in predicting 28-day mortality, the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Youden J index were determined. p 0.05 was used as the significant level.

3. Results

The study was completed with a total of 318 patients after applying the study's inclusion and exclusion criteria. The study population's demographic and clinical features, as well as test results, are presented in Table 1. The average age of the patients in the study was 58.6 $\pm$ 17.6 years, and 47.5% of the patients were male.

Statistical analysis revealed that mean age of the non-survivor group was significantly higher than that of the survivors ($p < 0.001$). The non-survivor group's mean Ranson score was statistically significantly higher than the survivor group's ($p = 0.005$).

According to the ROC analysis of the Ranson criteria for mortality prediction, the AUC value was calculated as 0.65 (95% confidence interval (CI): 0.57–0.70), the Youden index as 0.28, and the p value as 0.002. The statistical analysis revealed that the accuracy of the Ranson criteria in predicting mortality was statistically significant ($p = 0.002$). At a cut-off value of >1, the Ranson criteria had 92.9% sensitivity, 35.6% specificity, 13.8% PPV, and 97.8% NPV in the prediction of mortality (Table 2, Fig. 1). When NLR is combined with Ranson criteria, it had 78.6% sensitivity, 56.1% specificity, 15.1% PPV, and 96.4% NPV in the prediction of mortality.

As a result of the ROC analysis of NLR at admission in the prediction of mortality, the AUC value was determined as 0.58 (95% CI: 0.52–0.64), the Youden index as 0.29, and the p value as 0.08. According to the results of the statistical analysis, NLR evaluated at admission was not statistically significant in predicting mortality ($p = 0.08$) (Table 2, Fig. 1). As a result of the statistical analysis, when the areas under the curve of both scores were compared, no statistically significant difference was found ($p = 0.20$) (Table 2).

4. Discussion

In the present study, the efficacy of the Ranson criteria and NLR value evaluated at the time of admission to ED was investigated in the prediction of mortality in patients with AP. According to the results of the study, while the Ranson criteria were successful in estimating mortality, NLR was found to be of no use.

AP is an inflammatory disease frequently seen among diseases related to the gastrointestinal system. It can resolve spontaneously and have a mild course or result in life-threatening severe conditions, organ failure, and even death [13, 14]. In many nations, AP is still one of the most prevalent reasons for hospitalization. While alcohol consumption is the most common cause of AP in Western countries, gallstones are the main etiological factor in Turkey [15]. Gallstones larger than 5 mm can induce AP by obstructing the main channel, resulting in increased pressure in the pancreatic duct or bile reflux into the pancreatic duct. Gallstones are detected in 35–40% of patients with AP, while AP develops in only 3–7% of patients with gallstones [16]. In the current study, gallstones were the etiological factor of AP in 51.4% the patients.

In AP cases, the diagnosis and resolution of the severity of the disease at an early stage play a very important role in both initiating supportive treatment and reducing hospitalization, as well as complications, morbidity, and mortality. Among various risk scoring systems developed for this purpose, the most well-known is the Ranson criteria, which were established in 1976. These criteria are determined based on blood count analysis, biochemistry test, and evaluation of clinical data at the time of admission and at the 48th hour. The Ranson criteria are still widely used in predicting mortality of AP patients. In the Ranson scoring system, five parameters are evaluated at the time of admission and six parameters are evaluated at the 48th

TABLE 1. General characteristics of the study population.

	Survivors		Non-survivors		Total	*p* value
	Number	Percentage	Number	Percentage		
	Mean	Standard deviation	Mean	Standard deviation	n	
	Median	Min-Max	Median	Min-Max		
Age*	56.9	17.3	72.9	15.2	318	0.001
Gender**						
Male	125	49.4	14	50	318	0.99
Female	128	50.6	14	50		
Biliary**	163	51.4	13	46.4	318	0.69
Non-biliary	155	48.6	15	53.6		
Neutrophil count (10^3/uL)***	8.6	4.4	8.5	3.4	318	0.69
	7.9	2.3–27.0	7.5	4.1–14.1		
Glucose (mg/dL)***	141.4	65.2	159.7	92.8	318	0.27
	135	55–437	119	79–322		
AST (U/L)***	194.8	256.9	168	205.6	312	0.82
	87	6–1507	50.5	13–487		
ALT (U/L)***	191.2	241.1	111.3	115.6	312	0.2
	77	7–1292	58.5	8–314		
Lymphocyte count (10^3/mm^3)*	1.6	0.8	1.3	0.6	317	0.08
	1.5	0.02–3.92	1.4	0.76–1.74		
LDH (U/L)***	275.9	182.2	290.3	152.3	234	0.72
	231	105–919	241	152–663		
HCT (%)*	38.7	5.5	35.7	4.7	318	0.005
Urea (mg/dL)***	17.7	13.9	27.2	21.2	318	0.001
	15	5.0–125.0	20.5	9.0–110.0		
Calcium (mg/dL)*	8.9	0.8	8.6	0.7	314	0.07
Ranson score at admission***	2.3	1.5	3.2	1.6	318	0.005
	3	0–7	2.5	1–4		
NLR value at admission***	7.9	8.2	8.6	8.1	318	0.58
	5.7	0.9–53.5	5.1	2.6–18.6		

**Student's t-test, **Chi-square test, ***Mann-Whitney U test.*
HCT: hematocrit, ALT: Alanine amino transferase, AST: aspartate amino transferase, LDH: lactate dehydrogenase.

TABLE 2. Accuracy of NLR and Ranson criteria in predicting mortality in patients with acute pancreatitis.

	AUC (95% CI)	Cut-Off	Sensitivity	Specificity	+LR	−LR	PPV	NPV	Youden Index	*p* value
Ranson score	0.65 (0.57–0.70)	>1	92.9	35.6	1.4	0.2	13.8	97.8	0.28	0.2
NLR	0.58 (0.52–0.64)	>4.4	82.1	46.4	1.5	0.4	14.6	95.8	0.29	

NLR = neutrophil-to-lymphocyte ratio; AUC = area under the curve; PPV = positive predictive value; NPV = negative predictive value; LR = likelihood ratio; CI = confidence interval.

hour, and each variable was scored as 0 or 1 point. Therefore, the mildest case is scored 0 point while the most severe case is scored 11 points. In cases scored 0–2 points, mortality has been determined as 1–2% and the complication rate as 3–7%, and this group is classified as mild pancreatitis, while the mortality rate can reach 62% in cases with a Ranson score of 3 or higher [7]. In a study by Papachristou *et al.* [17], the Ranson scoring system was found to have the highest sensitivity and specificity in detecting severe AP and predicting mortality when compared to the Bedside Index for Severity in Acute Pancreatitis (BISAP), Ranson, Acute Physiology and Chronic Health Evaluation II (APACHE II), and computed tomography (CT) severity index (CTSI) scores used in the prediction of organ failure, complications, and mortality in AP cases. In 2014, Zhang *et al.* [18] compared BISAP, APACHE-II, and Ranson, which are scores used in the assessment of acute

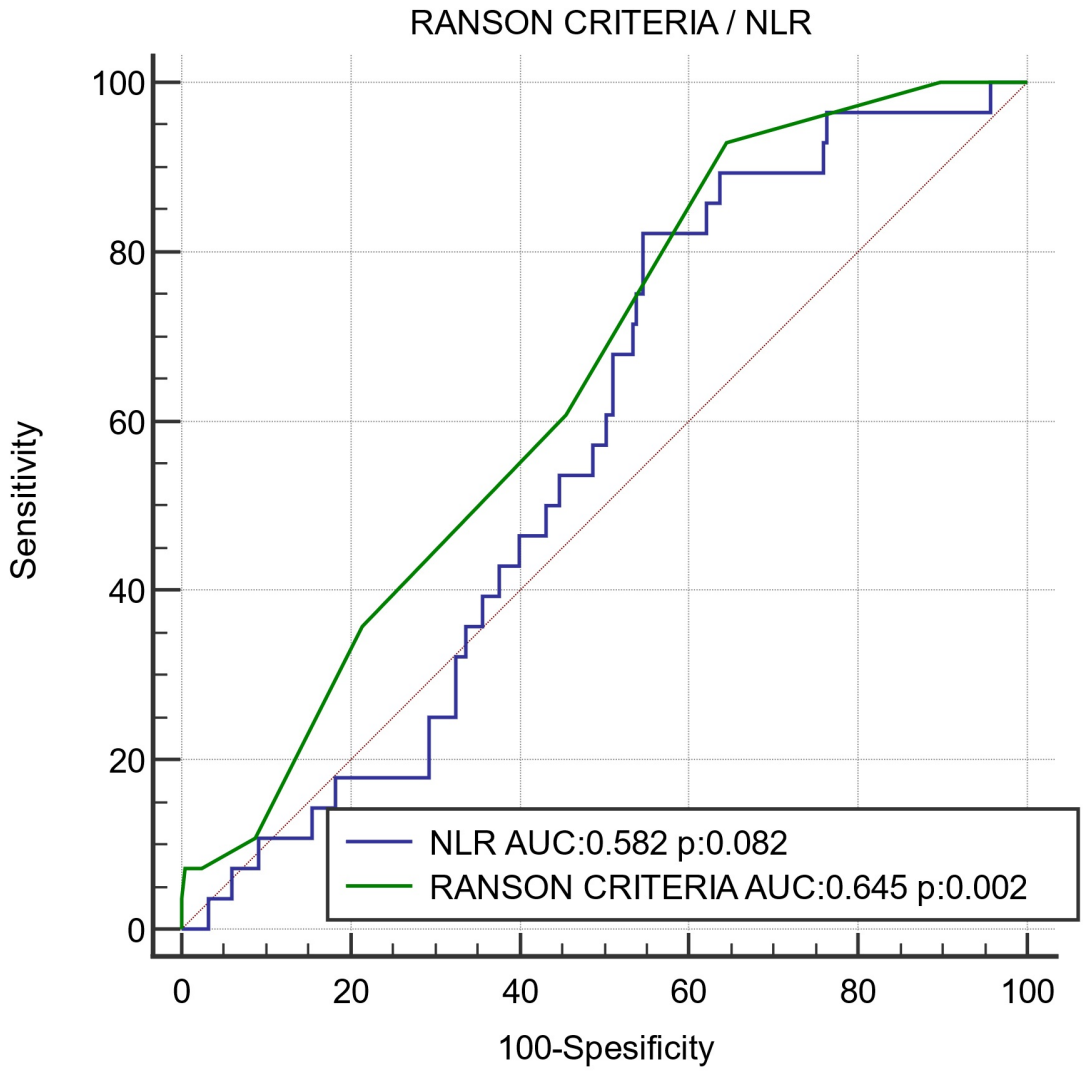

FIGURE 1. Neutrophil-to-lymphocyte ratio (NLR) and Ranson criteria as predictors of mortality in patients with acute pancreatitis.

pancreatitis severity in China, in terms of their ability to predict the severity of AP and development of pancreatic necrosis and mortality. The authors evaluated 155 patients and reported that Ranson was superior to other scoring systems with an AUC of 0.904 (95% CI: 0.829–0.979) in the prediction of mortality. In the current study, the Ranson criteria had 92.9% sensitivity and 35.6% specificity at a cut-off value of >1 in the prediction of mortality. 0.65 was found to be the AUC value (95 percent CI: 0.57–0.70).

NLR is a simple measure that is calculated by dividing the neutrophil-to-lymphocyte ratio. Research suggests that NLR is a good indicator of inflammation [19]. An increase in neutrophils indicates acute inflammation, while a decrease in lymphocytes indicates physiological stress. There are many studies examining the relationship between NLR and AP. In a study conducted with 328 patients with AP, Han *et al.* [20] reported that NLR and fluid sequestration could be as effective as the Ranson criteria in determining the severity of the disease. Similarly, Azab *et al.* [21] suggested that NLR could be used to predict admission to the ICU and length of hospital stay among patients with AP. Other researchers focused on the potential of hematological markers such NLR, red cell distribution width, and lymphocyte-to-monocyte ratio to predict mortality in patients with AP, and NLR was found to be superior to the other two [22]. However, in the current study, surprisingly, NLR did not provide a satisfactory result in predicting mortality in patients with AP, with its AUC value being calculated as 0.58 (95% CI: 0.52–0.64). This finding can be related to use of NLR recorded on admission to the ED, unlike previous studies in the literature.

The present study has certain limitations, such as its single-center and retrospective design. Furthermore, both the Ranson criteria and NLR were evaluated using only data obtained at admission, which may have limited the power of the tests. Finally, the small number of patients in the sample can be regarded as a limitation.

5. Conclusions

Expedient diagnosis and treatment of patients with AP are of critical importance. The Ranson criteria, with which many clinicians are already familiar, provide an effective clinical guide in the prediction of the prognosis of AP patients. Accord-

ing to the results of this study, NLR evaluated on presentation to the ED was useless in predicting the outcomes of patients with AP.

AUTHOR CONTRIBUTIONS

DT—Concept, design, supervision, materials, data; DT, MK—Analysis, literature search, writing, critical revision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by local ethics committee of University of Health Science Haydarpaşa Numune Education and Research Hospital, and a waiver of permission was issued (ethical committee ruling number: 2021/KK/290, date: 15 November 2021).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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