

The Relationship Between Disease Severity and Hematologic Parameters in Geriatric Patients with Acute Pancreatitis

Erhan Önalın, Yusuf Gökalg

Firat University Medical Faculty Hospital, Department of Internal Medicine, Elazig, 23000, Turkey - Email: drakdeniz@msn.com

Summary. *Background:* Acute pancreatitis (AP) is an emergency disease within the field of internal diseases. Its prevalence in the older population has been increasing in parallel to the increase in the older population. *Objectives:* This study aims to demonstrate the relationship of the platelet/lymphocyte ratio (PLR) and the neutrophil/lymphocyte ratio (NLR), which were shown to be markers related to systemic inflammation, with Ranson criteria, which indicate the severity of acute pancreatitis at the time of admission, in geriatric (65 years and above) and non-geriatric (age < 65 years) patients. *Methods:* Data from patients with acute pancreatitis who presented to the Internal Medicine Polyclinic at Firat University Medical Faculty Hospital between March 2015- September 2018 were retrospectively evaluated. *Results:* Platelet/lymphocyte ratio and neutrophil/lymphocyteratio were determined to be positively correlated with CRP, BUN, and WBC among Ranson criteria at the time of admission (respectively; $P < 0.001$; $P < 0.001$; $P < 0.05$). Based on the results of linear regression analysis, we found that neutrophil/lymphocyteratio and platelet/lymphocyte ratio were independent predictors of acute pancreatitis severity. *Conclusion:* PLR and NLR, which indicate systemic inflammation, can be used as simple and reliable markers to determine acute pancreatitis severity, and can be used more specifically in the geriatric age group.

Keywords: Acute pancreatitis, Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, inflammatory marker.

Introduction

Acute pancreatitis is an important disease that can result in morbidity and mortality. Its yearly incidence varies between 13-45 in 100000. While its overall mortality rate is 2.5%, this rate can reach up to 10-30% in patients diagnosed with severe acute pancreatitis (1). The leading cause is determined as gallstones with a rate of 40%. Alcohol accounts for 38% of the cases as the second most common cause (2). The disease is associated with a wide spectrum of clinical manifestations ranging from self-limited mild forms to severe acute pancreatitis accompanied by local and systemic complications, multiorgan failure, and pancreatic necrosis (3, 4).

As the rate of the older population is increasing, determining AP prognosis in the geriatric population is of importance. There exist numerous scoring systems and laboratory parameters to determine the prognosis (5-8). Ranson Criteria, Modified Glasgow Score,

Acute Physiology and Chronic Health Evaluation II (APACHE II) are used commonly. These scoring systems are associated with certain limitations. Atlanta classification, which has been revised recently, is being used widely. Based on the Atlanta classification, AP patients are classified as mild, moderate, or severe AP (9). While older AP patients are thought to experience a less favorable clinical progression, only few studies have compared disease progression based on age. There are conflicting results with regard to the effect of AP on mortality in the geriatric population. Certain studies report unchanged mortality rates in geriatric patients, whereas others report higher mortality rates in geriatric patients (10, 11). As is known, acute pancreatitis is the inflammation of the pancreas gland and is an inflammatory process. Platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyteratio (NLR) were shown to be among parameters that indicate systemic inflammation alongside white blood cell (WBC),

sedimentation, and C-reactive protein (CRP) (12-16). Moreover, beyond a significant role in hemostasis and thrombosis, thrombocytes help support and modulate inflammatory reactions and immune response. In the literature, the relationship between PLR and acute pancreatitis has only been investigated in pregnant women, and no other studies on this subject could be identified (17). PLR and NLR are inexpensive parameters that can be tested and evaluated with ease.

This study aims to demonstrate the relationship of the platelet/lymphocyte ratio (PLR) and the neutrophil/lymphocyte ratio (NLR) with the Ranson criteria that indicate the severity of acute pancreatitis at the time of admission in geriatric (above 65-years) and non-geriatric (age < 65 years) patients.

Patients and Methods

Following an approval by the Firat University Clinical Research Ethics Committee (approval number: 2019/164), patients who presented to the Internal Diseases polyclinic at the Firat University Medical Faculty Hospital and got hospitalized with a diagnosis of acute pancreatitis were scanned retrospectively. A diagnosis of acute pancreatitis was made based on the presence of two of the three following properties: 1) characteristic abdominal pain; 2) increased amylase and lipase levels (>3 times the upper reference limit); 3) imaging results consistent with AP (18). A total of 346 patients were included in the study, of which 202 were female and 144 were male. Hemogram and biochemical parameters at the initial admission to the polyclinic, ages and sexes of the patients were recorded. The scores obtained by each patient at the time of admission based on Ranson criteria were calculated. Patients with a score < 3 and a score \geq 3 were accordingly grouped as mild and severe based on these scores. Patients with accompanying acute and chronic infections, rheumatismal diseases, acute coronary symptoms, chronic pancreatitis, acute and chronic hepatitis, and a diagnosis of malignancy were excluded from the study. The patients were divided into two groups; geriatric (65 years and above) and non-geriatric (< 65 years). The two groups were compared based on gender, AP etiology, laboratory parameters, Ranson criteria, and mortality rates.

All patients underwent abdominal imaging (ultrasonography and/or computed tomography based on severity). Etiology was defined as biliary in case of gallstones or sludge. Alcoholic AP was considered if the patient consumed more than 40 g ethanol per day (20 g for females) for a minimum of 5 years or consumed excessive amounts of alcohol prior to the appearance of the disease (10). A hyperlipidemic etiology was assumed in cases where other etiology were excluded and serum triglyceride levels were above 1000 mg/dl (10). Patients who manifested chronic pancreatitis with acute recurrence were excluded.

Criteria based on values obtained at the time of admission to the polyclinic included; Ranson criteria (4,19); Biliary pancreatitis: age > 70 years, WBC > 18000 K/mm³, glucose > 220 mg/dL, lactate dehydrogenase (LDH) > 400 U/L, aspartate aminotransferase (AST) > 250 U/L. Non-biliary pancreatitis: age > 55 years, BK > 16000 K/mm³, glucose > 200 mg/dL, LDH > 350 U/L, AST > 250 U/L.

Statistical analysis

All variables were tested with the Shapiro-Wilk and Kolmogorov-Smirnov tests for normality of distribution. Normally distributed variables were presented as mean + standard deviation (SD) and results from the student t-test used to evaluate differences. All continuous variables with a non-normal distribution were presented as median and interquartile ranges based on the non-parametric Kruskal-Wallis test used to evaluate differences. Statistical analyses were performed using SPSS 22 (SPSS, Chicago, IL, USA). A p-value < 0.05 was considered statistically significant.

Results

Of the 346 study patients, 202 were female and 144 male with a mean age of $62,25 \pm 22,1$ years. Most common etiological factors were respectively biliary stones and nonbiliary causes. The geriatric group included 187 patients and the non-geriatric group 169 patients. 274 (79.1%) patients had mild and 72 (20,8%) severe pancreatitis. 140 (88%) non-geriatric patients and 134 (71.6%) geriatric patients had mild

AP ($p < 0.05$). While 28.3% of geriatric patients had moderate-severe AP, 11.9% of non-geriatric patients had moderate-severe AP ($p < 0.001$). Mortality was higher in the geriatric group than in the non-geriatric group (respectively, 0.74% versus 0%) ($p < 0.001$). The

most prevalent etiological factors were biliary stone disease, hypertriglyceridemia, and alcohol. Demographics, etiological factors, laboratory parameters, results from scoring systems, and mortality rates of the patients have been presented in Table 1.

Table 1. Characteristics of patients with acute pancreatitis (geriatric and non-geriatric patients)

Parameter	All patients (n=346)	Non-geriatric (n=159)	Geriatric (n=187)	P value
Age (years)	62,2±15,1	41,7±13,5	79,8±8,8	<0.001
Gender:				
Female	202(58,3%)	96(60,3%)	106(56,6%)	
Male	144(41,6%)	63(39,6%)	81(43,3%)	
Etiology:				
Biliary	194	72	122	
Hypertriglyceridemia	32	18	14	
Alcohol	14	12	2	
Drugs	26	8	18	
Idiopathic	80	44	36	
Ranson score	1,43±1,1	1,06±1,2	1,74±1,2	<0.001
Ranson classification				
Mild	274(79,1%)	140 (88%)	134 (71,6%)	<0.05
Moderate and severe	72(20,8%)	19 (11,9%)	53 (28,3%)	<0.001
WBC (K/mm ³)		10748±4148	12356±4356	<0.05
Glucose (mg/dl)		127,3	136,2	>0.05
ALT(U/L)		237	219,4	>0.05
AST(U/L)		199,8	241,6	>0.05
Amylase		1514,9	1855,6	<0.05
PDW		45,3	46,6	>0.05
LDH		370,2	433,6	>0.05
CRP(mg/L)		39,2	28,9	<0.001
BUN(mg/dl)		13,4	22,6	<0.001
HTC(%)		41,4	40,3	>0.05
PLT(x10 ⁹ /L)		288462	263623	>0.05
NEUTROPHIL(x10 ⁹ /L)		8687	8446	>0.05
LYMPHOCYTE(x10 ⁹ /L)		1537	1203	>0.05
MONOCYTE(x10 ⁹ /L)		622	516	
RDW(%)		14,1	14,2	<0.05
NLR(%)		8,1	11,9	<0.001
PLR(%)		256,1	362,9	<0.001
Outcome:				
Discharge		159	173	
Exitus		0	14	< 0.001

WBC – white blood cells, Hb – hemoglobin, AST – aspartate aminotransferase, ALT – alanine aminotransferase, LDH – lactate dehydrogenase, CRP – C-reactive protein, PLR – platelet/lymphocyte ratio, NLR – neutrophil/lymphocyte ratio

The geriatric group involved 134 (71.6%) patients with mild AP, 53 (28.3%) with moderate and severe AP. The non-geriatric group involved 140 (88%) with mild AP, 19 (11.9%) patients with moderate and severe AP. The Ranson criteria was compared between the geriatric and non-geriatric groups and a statistically significant difference was detected ($p < 0.001$) (Table 1). Ranson scores were determined as $1,74 \pm 1,2$ for the geriatric group and $1,06 \pm 1,2$ for the non-geriatric group, with a statistically significant difference between the groups ($p < 0.001$). Mortality rates were 0.74% for the geriatric group and 0% for the non-geriatric group, with a statistically significant difference ($p < 0.001$) (Table 1). In the geriatric group, 12 patients with moderate and severe AP (85.7%) and 2 patients with mild AP (14.2%) died. Thrombocyte count, hematocrit count, lymphocyte, monocyte, neutrophil counts, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and glucose levels were not different across groups (Table 1). White blood cell counts, c-reactive protein levels, NLR, PLR, RDW levels were significantly different across groups.

Discussion

Acute pancreatitis refers to the acute inflammation of the pancreas. Digestive enzymes are activated in the pancreas interstitium and systemic circulation; resulting in autodigestion of the pancreatic tissue, increase in cytokine production, systemic inflammatory response syndrome (SIRS), and multiple organ failure (20). Determining the severity of the disease is very important for patient follow-up and to predict mortality. Certain scoring systems concerning this issue, such as the 1992 Atlanta classification, Ranson criteria, APACHE II scores (acute physiology and chronic health examination), BISAP (Bedside index of severity in acute pancreatitis), harmless acute pancreatitis score (HAPS), Imrie's score (modified Glasgow II scoring), and the computed tomography (CT) severity index (Balthazar score) have been developed, but none of these are yet perfect and sufficient (1, 3, 4, 21).

As is known, acute pancreatitis is an inflammatory process and a study focusing on the inflammatory marker CRP stated that CRP values > 190 ml/dL could signify the severity of acute pancreatitis (22). Another

study by Sternby et al. (23) mentioned that IL6 and CRP could be utilized in differentiating moderate and severe pancreatitis. Han et al. (24) found that the inflammatory marker NLR was positively correlated with Ranson criteria and proposed that NLR was an early predictor of acute pancreatitis severity. In the study Wang et al. (25) conducted on patients with acute pancreatitis induced by hypertriglyceridemia, NLR was found to be higher in severe acute pancreatitis compared to moderate and mild pancreatitis and it was described as an independent predictor of acute pancreatitis based on multivariate analysis. Li et al. investigated the basic prognostic markers of inflammation such as neutrophil/lymphocyteratio, prognostic nutritional index (PNI), RDW, and lymphocyte/monocyte ratio with regard to their prognostic value for acute pancreatitis severity and mortality in a retrospective cohort study (26). They determined NLR as the strongest marker predicting the prognosis in all survival times. Our study also identified PLR, similarly to NLR, as a marker that could be used as an early predictor of acute pancreatitis severity. Recent publications (12) have shown that PLR is among blood parameters that indicate systemic inflammation, exactly like NLR. Studies (14,16,27,28) have been conducted to investigate its relationship with disease prognosis and mortality. Our study investigated the relationship between Ranson criteria, which indicate the severity of acute pancreatitis, and PLR and NLR values. The patient group with a ≥ 3 Ranson criteria score was determined to have higher PLR and NLR. Platelet/lymphocyte ratio and neutrophil/lymphocyteratio can be used as clinically useful parameters in determining severe acute pancreatitis and can help in selecting the optimal treatment by allowing early determination of disease severity.

The older population is increasing across the world and accordingly incidences of disease encountered in the older population are also on the rise (29). Most studies report the mean age at first AP episode as 60, and AP incidence has increased in many western countries due to the increase in older population (30). AP incidence and related mortality increase in parallel to age, and studies report a correlation between age and mortality, with age as an independent parameter (18, 31). There are also studies that report no effects by

age on disease progression in AP patients. In a study by Kim et al. that included 85 (65 years and above) and 142 (<65 years) AP patients, age was found to have no significant effect on clinical results of AP (10).

The mortality rates in our study were 0.74% for geriatric patients and 0% for non-geriatric patients, with a statistically significant difference ($p < 0.001$). Moreover, only 19 non-geriatric patients (11.9%) in our study group had severe pancreatitis in accordance with studies demonstrating the effect of age on disease severity. Various scoring systems, imaging methods, laboratory parameters exist in order to determine the prognosis of AP. It is important in clinical practice to foresee disease severity, need for admission to the intensive care unit, hospitalization time, and prognosis.

Losurdo et al. reported higher Ranson scores in geriatric patients than in non-geriatric patients (in a study that involved 42 geriatric and 48 non-geriatric patients) (respectively, 2.52 ± 1.57 and 0.75 ± 0.73 in geriatric and non-geriatric patients) ($p < 0.0001$) (32). Xin et al. reported higher Ranson scores in geriatric patients than in non-geriatric patients (respectively, 3.4 ± 1.7 versus 2.8 ± 1.6 in geriatric and non-geriatric patients) ($p < 0.0069$) (33). In our study, Ranson scores were found as 1.74 ± 1.2 in the geriatric group and as 1.06 ± 1.2 in the non-geriatric group, with a statistically significant difference. Based on the Atlanta classification, Losurdo et al. reported mild pancreatitis in 39% and moderate-severe AP in 61% of their patients (32). In our study, 274 (79.1%) of the patients had mild AP (88% of non-geriatric and 71.6% of geriatric patients, $p < 0.05$). In the non-geriatric patient group, 19 (11.9%) had moderate-severe AP, whereas 53 (28.3%) of patients in the geriatric group had moderate or severe AP ($p < 0.001$).

Conclusion

In conclusion, this study has shown that PLR and NLR, which are non-specific inflammatory markers that can be tested easily and quickly, are independent predictors of disease severity in geriatric patients with acute pancreatitis. PLR and NLR may be used as parameters that aid the clinician in determining acute pancreatitis severity. Furthermore, geriatric patients manifested a more severe AP course compared

to the non-geriatric population. The geriatric population demonstrated a higher rate of mortality compared to the non-geriatric population. This finding needs to be inspected further with comprehensive prospective studies.

Limitations

This study has certain limitations. These include; its retrospective nature where the course of clinical follow-up was acquired entirely from patient records. Since cases with lacking records were not included in the study, the number of study patients were lower than desired. Secondly, the study includes a single center and a low number of patients. Thirdly, it did not include a comparison of Ranson criteria with parameters tested 48 hours later.

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Correspondence:

Erhan Önalın,
Fırat University Medical Faculty Hospital,
Department of Internal Medicine,
Elazığ, 23000, Turkey
Tel: +90-233-35-55/2437
E-mail: drakdeniz@msn.com