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ARAŞTIRMA/RESEARCH

Diagnostic value of neutrophil-to-lymphocyte ratio in emergency department patients diagnosed with acute pancreatitis

Acil serviste akut pankreatit tanısı alan hastalarda nötrofil lenfosit oranının tanısal değeri

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Abstract

Purpose: Decreased lymphocyte count and increased neutrophil count may be associated with severe sepsis, bacteremia, and surgical stress. The neutrophil-to-lymphocyte ratio (NLR) may be used to assess inflammatory conditions and surgery. We evaluated whether NLR may be useful in the differentiation between biliary and nonbiliary acute pancreatitis.

Material and Methods: Data from patients aged > 18 years who were diagnosed with acute pancreatitis between January 2011 and July 2014 were evaluated retrospectively. Patients were grouped as having biliary or nonbiliary pancreatitis. The white blood cell, neutrophil, and lymphocyte counts and NLR were evaluated and compared between the 2 groups.

Results: In the 225 patients with acute pancreatitis (mean age, 59±18 y; 81 male patients [36%]), most patients had biliary pancreatitis (biliary, 144 patients [64%]; nonbiliary, 81 patients [36%]). Frequency of hypertension and mean arterial pressure were lower in patients who had biliary than nonbiliary pancreatitis. The mean white blood cell, neutrophil, and platelet counts were greater in patients who had nonbiliary than biliary pancreatitis.

Conclusions: Although the NLR was increased in acute pancreatitis, there were no differences in NLR between patients who had biliary or nonbiliary acute pancreatitis. Therefore, the NLR is not useful in differentiating biliary from nonbiliary acute pancreatitis.

Key words: Gastroenterology, acute abdomen, pancreas, white blood cell, hematology.

Öz

Amaç: Artmış nötrofil sayısı ile birlikte azalmış lenfosit sayısı ağır sepsis, bakteremi ve cerrahi stres ile bağlantılıdır. Beyaz kan hücrelerinin bu farklı iki kompanentinin birbirine oranıyla bulunan nötrofil-lenfosit oranı (NLR), cerrahi ve inflamasyon durumlarını değerlendirmede kullanılmaktadır. Biz bu çalışmada akut pankreatit hastalarda, biliyer ve non-biliyer pankreatitli hastaların ayrımında NLR'nin prognostik değerini araştırmayı amaçladık.

Gereç ve Yöntem: Ocak 2011 ve Temmuz 2014 tarihleri arasında akut pankreatit tanısı almış 18 yaşından büyük hastalar geriye dönük olarak değerlendirmeye alınmıştır. Hastalar etyolojik olarak biliyerpankreatit ve non-biliyerpankreatit olarak ikiye ayrıldı.

Bulgular: Çalışmaya 255 akut pankreatitli hastanın yaş ortalaması 59±18 yıl olup, 81 tanesi (%36) erkekti. Etiyolojik faktörlere bakıldığında biliyer pankreatitli hasta sayısı 144 (%64) non-biliyer pankreatitli hasta sayısı 81 (%36) idi. Hastaların fizik muayene ve laboratuar bulguları, pankreatit etyolojisine göre karşılaştırıldığında Beyaz kan hücreleri ve nötrofil değerlerinin non-biliyer pankreatit grubunda anlamlı olarak yüksek olduğu görüldü.

Sonuç: Bulgularımıza göre NLR akut pankreatitte yüksek bulunmasına rağmen non-biliyer ve biliyer pankreatit arasında NLR değerinde istatiksel olarak anlamlı bir değişme olmamıştır.

Anahtar kelimeler: Gastroenteroloji, akut batın, pankreas, beyaz kan hücresi, hematoloji

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INTRODUCTION

Acute pancreatitis is an inflammatory condition of the pancreas that may cause local tissue and systemic complications. This condition may have a varied clinical course, from mild self-limiting pancreatic inflammation to life-threatening organ system failure and death within several days. The patient may have spontaneous recovery or may develop abdominal pain, hypotension, fluid sequestration, metabolic disorders, severe hemorrhagic gangrene, and sepsis[1]. The incidence of the disease is increasing throughout the world, especially in developed countries. The etiology can be determined in most patients, and most commonly includes alcohol use and gallstones. Other causes of acute pancreatitis include invasive procedures such as endoscopic retrograde cholangiopancreatography, surgery, medications, infections, hyperlipidemia, hypercalcemia, biliary system anomalies, and idiopathic causes[2,3].

The early diagnosis of acute pancreatitis may be difficult and is established by a combination of the patient history, physical examination, serologic biomarkers, and imaging findings. In addition, various scoring systems such as the Ranson criteria, Acute Physiology And Chronic Health Evaluation [APACHE] II score, and Imrie score are employed to triage patients based on severity of disease, need for intensive care, and aggressiveness of treatment required[4,5]. However, these scores are limited in clinical practice because of low sensitivity and complexity of the calculations.

Serum amylase and lipase levels are useful serologic biomarkers because the diagnosis of acute pancreatitis is likely when these enzyme levels are 3-fold greater than normal[6]. Serum amylase levels are sensitive for the diagnosis of acute pancreatitis but less specific than other pancreatic enzymes. The serum amylase level may increase rapidly at the onset of acute pancreatitis and decrease faster than other enzymes. Serum lipase is more sensitive than serum amylase. Even when serum amylase level is normal, a high serum lipase level may be highly suggestive of the diagnosis of acute pancreatitis[7].

Various inflammatory markers may be evaluated to determine the severity of acute pancreatitis. The white blood cell (WBC) count is determined routinely as part of the complete blood count and is used in all scoring systems for acute pancreatitis and emergency surgery. The total WBCs include neutrophils and lymphocytes, and both types of white blood cells can be used as markers of inflammation. Decreased lymphocyte count and increased neutrophil count may be associated with severe sepsis, bacteremia, and surgical stress. The neutrophil-to-lymphocyte ratio (NLR) is better than the WBC count in evaluating severe inflammatory states in various clinical situations[8].

We hypothesized that inflammation, WBC count, neutrophil count, and NLR may be higher in nonbiliary than biliary acute pancreatitis. The purpose of this study was to evaluate the diagnostic value of NLR in the differentiation between biliary and nonbiliary acute pancreatitis.

MATERIAL AND METHODS

Materials

This retrospective study was performed with patients who were admitted consecutively to the Emergency Medicine Clinic and General Surgery Clinic of Selcuk Faculty of Medicine, and General Surgery Clinic of Konya Education and Research Hospital between January 2011 and July 2014. Patients were included in the study when they (1) were aged > 18 years, (2) presented for evaluation within 24 hours after the onset of symptoms, and (3) were diagnosed with acute pancreatitis in their first evaluation with medical history and physical examination, confirmed with laboratory and imaging studies. Patients who had the diagnosis of acute pancreatitis were excluded from the study when they had comorbid conditions, were pregnant, or underwent cardiopulmonary resuscitation. After exclusions, there were 225 patients included in the study. The study was approved by the Ethics Committee for Nondrug Clinical Studies, Medical Faculty, Selcuk University (No. 2014/229).

Procedure

The archived electronic hospital records were reviewed retrospectively for information including temperature, heart rate, and mean arterial pressure. Laboratory data were recorded including complete blood count (WBC, neutrophil, lymphocyte, and platelet counts, hematocrit, and hemoglobin level) and biochemical tests such as levels of glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, urea, sodium, potassium, amylase, lipase, alkaline phosphatase,

gamma-glutamyl transpeptidase (GGT), and calcium. On the basis of clinical diagnosis made by taking into account all possible factors including past medical history results of radiological studies such as ultrasonography, intravenous contrast-enhanced abdominal computed tomography, magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography, and laboratory data, the remaining 225 patients of them were included in this study, and divided into two groups: gallstone induced pancreatitis group (biliary pancreatitis group) and non-biliary pancreatitis group.

Table 1. Demographic, Clinical, and Laboratory Characteristics of Patients with Acute Pancreatitis*

Characteristic	Biliary	Nonbiliary	Total	P ≤ †
No. of patients	144 (64)	81 (36)	225 (100)	---
Age (y)	59 ± 18	58 ± 17	59 ± 18	NS
Sex, male	47 (21)	34 (15)	81 (36)	NS
Comorbidities				
Hypertension	13 (6)	17 (8)	30 (13)	.01
Diabetes mellitus	17 (8)	7 (3)	24 (11)	NS
Acute coronary syndrome	7 (3)	5 (2)	12 (5)	NS
Stroke	1 (0.4)	0 (0)	1 (0.4)	NS
Mean arterial pressure (mm Hg)	87 ± 8	91 ± 7	88 ± 8	.001
Heart rate (beats/min)	76 ± 5	76 ± 6	76 ± 5	NS
Temperature (°C)	36.9 ± 0.2	36.9 ± 0.2	36.9 ± 0.2	NS
Laboratory tests				
White blood cell count (×109/L)	12 ± 5	14 ± 6	13 ± 5	.02
Neutrophil count (×109/L)	10 ± 5	11 ± 6	10 ± 5	.03
Lymphocyte count (×109/L)	1.6 ± 0.8	1.6 ± 0.9	1.6 ± 0.9	NS
Neutrophil-lymphocyte ratio (NLR)	8 ± 6	9 ± 6	9 ± 6	NS
Hematocrit (%)	41 ± 5	40 ± 5	41 ± 5	NS
Platelet count	250 ± 72	272 ± 84	14 ± 2	.04
Glucose	143 ± 54	147 ± 66	144 ± 59	NS
Alanine aminotransferase (ALT)	318 ± 366	153 ± 208	258 ± 328	.001
Aspartate aminotransferase (AST)	291 ± 237	184 ± 257	253 ± 249	.002
Amylase	1595 ± 1201	1394 ± 1264	1523 ± 1225	NS
Lipase	3578 ± 3206	2821 ± 2869	3306 ± 3104	NS
Alkaline phosphatase	172 ± 96	136 ± 86	159 ± 94	.007
Gamma-glutamyl transpeptidase (GGT)	360 ± 261	258 ± 294	323 ± 277	.008

* Data reported as number (%) or mean ± SD; †Comparison between biliary and nonbiliary acute pancreatitis. NS, not significant (P > .05).

Statistical analysis

Data analysis was performed with statistical software (SPSS, Version 18.0, SPSS Inc., Chicago, IL, USA). The NLR for all patients was determined by dividing the neutrophil by lymphocyte counts. Average values were expressed as mean ± standard deviation. Differences between groups were evaluated using 1-way analysis of variance. Differences between the biliary and nonbiliary acute pancreatitis groups were evaluated using cross tabulation and χ^2 test (chi-square test). The cutoff values of WBC, neutrophil, and lymphocyte counts and NLR to differentiate the 2 groups were determined using receiver operating characteristic (ROC) curve analysis, and area under the curve (AUC) was determined for each variable. Sensitivity and specificity values were calculated using different cutoff values. Statistical significance was defined by P ≤ .05.

RESULTS

There were 225 patients with acute pancreatitis, mostly biliary pancreatitis (Table 1). The age, sex, heart rate, and temperature were similar between the biliary and nonbiliary pancreatitis groups (Table 1). Frequency of hypertension and mean arterial pressure were lower in patients who had biliary than nonbiliary pancreatitis (Table 1). The mean WBC, neutrophil, and platelet counts were greater in patients who had nonbiliary than biliary pancreatitis.

The mean ALT, AST, alkaline phosphatase, and GGT levels were significantly greater in patients who had biliary than nonbiliary pancreatitis (Table 1). However, mean lymphocyte count and NLR were similar between the groups (Table 1).

DISCUSSION

The present study showed that there were no differences in NLR between patients who had biliary or nonbiliary acute pancreatitis. Therefore, the NLR is not useful in differentiating biliary from nonbiliary acute pancreatitis.

In patients who have acute pancreatitis, neutrophils are the main host cells responsible for nonspecific inflammation, and neutrophils initiate tissue destruction by causing the release of mediators such as myeloperoxidase, elastase, interleukin 1, and interleukin 6. Although trypsinogen and pancreatic proteases are important in the systemic response to acute pancreatitis, trypsinogen is employed in nonserologic markers rarely used in clinical practice such as peptide activating trypsinogen, C-reactive protein, procalcitonin, and phospholipase A2[8,9].

In the present study, there were no significant differences in serum amylase or lipase levels between patients who had biliary or nonbiliary pancreatitis (Table 1). Therefore, although elevated amylase and lipase levels may be useful in the diagnosis of acute pancreatitis, they cannot be used to distinguish biliary from nonbiliary pancreatitis.

The WBC count is part of the common scoring systems used for acute pancreatitis and is routinely measured before emergency surgery. The WBC count can be determined quickly and is easily accessible and less costly than other biomarkers of pancreatitis. The significant difference observed in mean WBC count between patients who had biliary or nonbiliary acute pancreatitis suggests that the WBC count may be useful as an inflammatory marker to distinguish between the 2 groups in our study, but sensitivity and specificity were low (Table 1 and 2).

Table 2. Results of receiver operating characteristic curve analysis for patients with acute pancreatitis

Parameter	Area Under Curve	(95% Confidence Interval)	Cutoff Value	Sensitivity (%)	Specificity (%)
White blood cell (WBC) count	0.576	(0.497-0.656)	11.9 ×109/L	57	57
Neutrophil count	0.576	(0.497-0.655)	9.9 ×109/L	57	57
Lymphocyte count	0.502	(0.423-0.580)	1.36 ×109/L	50	50
Neutrophil-lymphocyte ratio (NLR)	0.547	(0.469-0.625)	7.1	55	56

Neutrophils spread inflammation and tissue damage in acute pancreatitis by activating inflammatory cytokines, proteolytic enzymes, and free oxygen radicals. Lymphocyte count increase following the initial stress and mediate the subsequent inflammatory response. The traditional view is that neutrophilia is the primary cause of an elevated NLR, systemic inflammatory response syndrome, and poor prognosis, while lymphocyte count remains static[10].

It was established in previous studies that lymphocytopenia is an independent factor in predicting the severity of inflammation and poor clinical outcomes[11]. In the present study, the mean neutrophil count was significantly different between patients who had biliary or nonbiliary pancreatitis, but the lymphocyte count was similar between the groups (Table 1).

The NLR is a sensitive inflammatory and prognostic marker in various clinical conditions including sepsis, cardiac diseases, stroke, and acute appendicitis[12]. Increased NLR may predict hospital death caused by acute coronary syndrome and mortality after coronary artery bypass graft surgery[13]. In patients with acute ischemic stroke, increased NLR may predict infarct volume and severity, regardless of cause[14].

The NLR may be more valuable than other markers of infection in predicting the severity of community-acquired pneumonia at the first admission to the emergency department[15]. The NLR values are useful in determining the severity of acute exacerbations in patients with chronic obstructive pulmonary disease[16]. Increased NLR in patients with an acute abdomen such as acute appendicitis may vary in differentiating normal and inflamed appendix and

may be associated with gangrenous appendicitis17. Increased NLR also may be useful in predicting cancer recurrence in colorectal cancer, survival after liver resection for colorectal liver metastasis, and poor prognosis for survival after liver transplant18. In the present study, NLR did not differentiate between patients who had biliary or nonbiliary acute pancreatitis (Table 1 and 2).

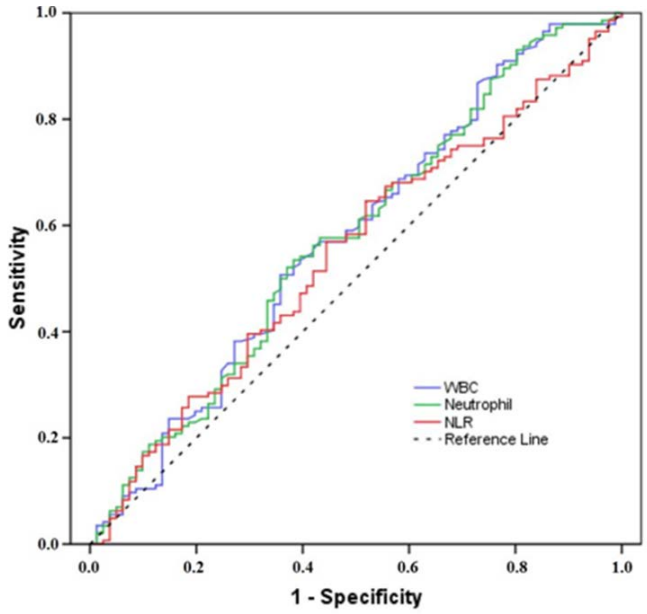

Figure 1. Receiver Operating Characteristic (ROC) Curves of White Blood Cell (WBC) Count, Neutrophil Count, and Neutrophil-to-Lymphocyte Ratio (NLR) For Differentiating Biliary From Nonbiliary Acute Pancreatitis.

The ROC curve analysis showed comparable AUC values for WBC, neutrophil, and lymphocyte counts and NLR (Table 2 and Figure 1). For the cutoff values of these 4 variables determined from the ROC curve analysis, sensitivity and specificity ranged from 50% to 57% (Table 2). Compared with the NLR cutoff 7.1, using a lower NLR cutoff 4.7 caused lower sensitivity (39%) and higher specificity (70%); using a higher NLR cutoff 11.1 caused higher sensitivity (75%) and lower specificity (31%).

The NLR may differentiate between patients who have moderate or severe acute pancreatitis. In addition, NLR may decrease to normal levels in uncomplicated cases, but may remain high in complicated cases of acute pancreatitis8. The NLR values may reflect Sequential Organ Failure Assessment (SOFA) and APACHE II scores used to predict the severity of acute pancreatitis in intensive care patients19.

The NLR may be better than the WBC count in predicting mortality of patients who have acute pancreatitis in intensive care units20. Although there were significantly greater WBC and neutrophil counts in patients who had nonbiliary than biliary pancreatitis, the NLR was similar between two groups (Table 1). Literature search showed no previous studies that compared NLR between patients with biliary and nonbiliary pancreatitis. In a previous study in which NLR was used as an inflammatory marker in benign events and cancer surgery, the cutoff value of NLR was > 518. In another study in which the severity of pancreatitis was assessed, the cutoff of NLR was > 4.7 because of 90% sensitivity and 22% specificity8. In the present study, the sensitivity and specificity for different cutoff values of NLR showed that it was not feasible to use NLR as a marker to distinguish biliary and nonbiliary acute pancreatitis.

Limitations of the present study include the small number of patients and availability of only 1 measurement of NLR. We could not evaluate variations in NLR with time. In addition, NLR was

determined at 3 clinics in 2 centers, and NLR may vary in different populations.

The NLR may be useful because it may be determined from a complete blood count, is simple to use, can be repeated, and does not require arterial blood or extended biochemistry evaluation. In this study, the inexpensive and widely applicable NLR test was a useful hematologic parameter in the diagnosis of acute pancreatitis. However, the NLR had low sensitivity and specificity and cannot be used as a marker for the definitive diagnosis of acute pancreatitis or distinguishing between biliary and nonbiliary acute pancreatitis. The NLR was not better than the total WBC count in predicting acute pancreatitis. Further studies are required to investigate the relation between hematologic parameters and acute pancreatitis.

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