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A Retrospective Study of Patients with Diverticulitis: Does Neutrophil-to-Lymphocyte Ratio Predict Chronic Diverticulitis Disease Progression?

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ABSTRACT

Introduction: Diverticular disease is defined as the presence of an asymptomatic diverticulum in the colon, and an infected diverticulum is called diverticulitis. Among patients with diverticular disease, 10-25% experience diverticulitis at some stage in their lives. This study aimed to evaluate the neutrophil-to-lymphocyte ratio (NLR) determined by dividing the neutrophil value by the lymphocyte value by comparing the stages of the patients according to the Hinchey classification who presented to the emergency department and were diagnosed with acute diverticulitis and to make a decision whether the patient should be treated by hospitalization or in the outpatient clinic.

Methods: Patients who were admitted to the İstanbul Training and Research Hospital, between 2015 and 2019 and were diagnosed with acute diverticulitis by abdominal computed tomography were included in the study. Patients aged ≤18 years, pregnant patients, and patients with Crohn's disease, ulcerative colitis, colorectal, and/or anal cancer were excluded from the study.

Results: Age, white blood cell count, hemoglobin, hematocrit, platelet, monocyte, granulocyte, neutrophil, NLR, C-reactive protein, and procalcitonin values were compared according to their stage. The neutrophil and NLR values were lower in patients with stage 1 than in those with stages 3 and 4. Moreover, the neutrophil and NLR values were lower in stage 2 than in stage 3.

Conclusion: In our study, patients with acute diverticulum with higher NLR levels are more likely to develop complications. The combined use of NLR with physical examination, imaging, and other laboratory tests facilitates the diagnosis of complicated acute diverticulitis. However, further studies should be performed to confirm the utility of the NLR value in clinical practice.

Keywords: Diverticulitis, neutrophil/lymphocyte ratio, hynchey classification

Introduction

Diverticular disease, once rarely diagnosed, is now one of the most frequent gastrointestinal disorders among inpatients and outpatients (1-3). Painter and Burkitt first demonstrated a large increase in the prevalence of diverticular disease that began during the industrial revolution and documented differences in prevalence between Western and Eastern countries. In the last two decades, interest in diverticular disease has increased once again. Widespread use of modern imaging techniques like computed tomography (CT) (Figure 1) and colonoscopy and accurate diagnosis of diverticulitis and asymptomatic diverticular disease allow understanding their epidemiology (2).

Asymptomatic diverticular disease is often noticed during another imaging method. There is no consensus on the treatment and follow-up of the disease, as there is no clinical finding in patients without symptoms (4).

Diverticular disease is defined as the presence of an asymptomatic diverticulum in the colon, and the infection of these diverticula is called diverticulitis. Of the entire population with diverticular disease, 10-25% experience diverticulitis at some stage in their lives (4).

An inflammation of a colonic diverticulum is also considered diverticulitis. This process could be either acute or chronic (5). In its pathophysiology, the diverticulum orifice is obstructed by a plug such as fecalith. This condition may lead to variable clinical manifestations ranging from simple diverticulitis to complicated diverticulitis, such as colonic obstruction (6). Diverticulitis can be clinically classified as complicated and non-complicated. Complicated diverticulitis usually presents with abscess formation, fistula, obstruction, or perforation (6).

The decision of whether to hospitalize the patient is an important consideration in the management of diverticulitis. The American Society for Colon and Rectal Surgery stated that several factors influence

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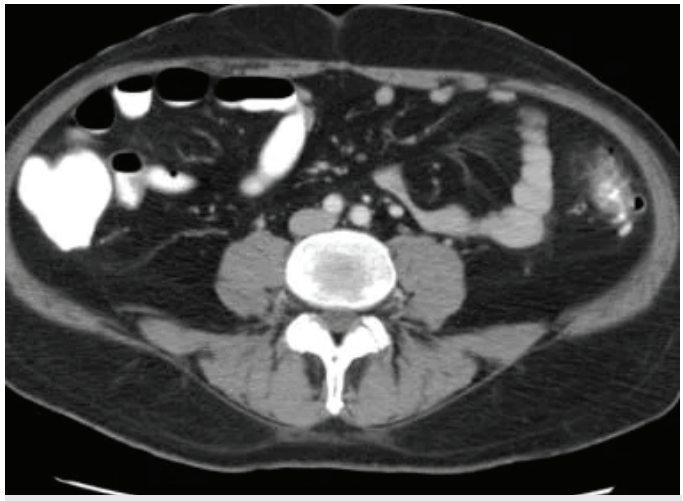

Figure 1. Diverticulitis on computed tomography

this decision, including oral intake intolerance, pain level, general comorbidities, and social support at home (7).

In recent years, its prevalence has been increasing worldwide, especially in Western countries, probably due to lifestyle changes. Although the left-sided colonic diverticular disease is more common among elderly patients, a dramatic increase has been observed in its incidence in younger age groups in recent years. Studies have shown that the lifetime risk of developing acute left-sided colonic diverticulitis in patients with diverticulosis is approximately 4%. Data from Western societies indicate that one-fifth of the patients with acute diverticulitis are under the age of 50 (8,9).

Patients with acute or chronic exacerbation of diverticulitis present with different clinical manifestations. The most common are left lower quadrant pain, nausea, vomiting, fever, and impaired oral intake. Leukocytosis, neutrophilia, and increased C-reactive protein (CRP) are observed in laboratory findings frequently. Although some patients with diverticulitis require hospitalization as has been stated above, the identification of patients who are likely to progress to complicated diverticulitis would help the clinician.

In this study, we aimed to evaluate the neutrophil-to-lymphocyte ratio (NLR), determined through dividing the neutrophil value by the lymphocyte value, by comparing the stages of the patients according to the Hinchey classification who presented to the emergency department and were diagnosed with acute diverticulitis and to make a decision whether the patient should be treated by hospitalization or in the outpatient clinic.

Methods

The patients who were admitted to the University of Health Sciences Turkey, İstanbul Training and Research Hospital, between 2015 and 2019 and were diagnosed with acute diverticulitis by abdominal CT were included in the study. Patients aged <18 years, pregnant patients, and patients with Crohn's disease, ulcerative colitis, colorectal, and/or anal cancer were excluded from the study.

The approval form the University of Health Sciences Turkey, İstanbul Training and Research Hospital Local Ethics Committee was obtained (approval number: 2421, date: 12.06.2020). Informed consent was obtained from each patient.

Statistical Analysis

Data were statistically analyzed using SPSS version 17.0. Histogram plots and the Kolmogorov-Smirnov test were employed to examine the conformity of the variables to the normal distribution. The descriptive analysis was presented using mean, standard deviation, median, and 25-75 percentile values. Categorical variables were compared by the Pearson chi-square test. The Kruskal-Wallis test was utilized to evaluate the differences between the stages in non-normally distributed (non-parametric) variables, and p-values <0.05 were regarded as significant. A total of 217 patients, including 122 men and 95 women, participated in the study.

Results

All patients were grouped according to the Hinchey classification based on tomographic imaging (Table 1). The examination of the Hinchey stages revealed that 176 patients were in stage 1, 22 in stage 2, 16 in stage 3, and 3 in stage 4. Moreover, 19 patients underwent surgery, 4 had drainage, 106 were hospitalized for >5 days, and 7 died (Table 2).

The mean age of the patients was 58.77±14.50 years. White blood cell count (WBC), hemoglobin (Hb), hematocrit (HCT), platelet (PLT), monocyte, granulocyte, neutrophil, NLR, CRP, and procalcitonin values are given in Table 3.

Patients were compared according to their Hinchey stages in terms of gender, surgery, drainage, hospitalization, and mortality rates (Table 4). The surgery rate was lower in patients at stage 1 than in those at stage 3. The rate of undergoing surgery was higher in stage 4 than in other stages. The drainage rate was lower in stage 1 than in stage 3. The rate of hospitalization for >5 days in stage 1 was lower than that in other

Table 1. Hinchey classification

Hinchey classification
I. Pericolic abscess or phlegmon
II. Pelvic, intraabdominal, or retroperitoneal abscess
III. Generalized purulent peritonitis
IV. Generalized fecal peritonitis

Table 2. Clinical data of the patients

	n	%
Male	122	(56.22)
Female	95	(43.78)
Stage 1	176	(81.11)
Stage 2	22	(10.14)
Stage 3	16	(7.37)
Stage 4	3	(1.38)
Operation	19	(8.76)
Drainage	4	(1.84)
>5-day hospitalization	106	(48.85)
Mortality	7	(3.23)

groups. The mortality rate was significantly lower in stage 1 than in stage 4.

Age, WBC, Hb, HCT, PLT, monocyte, granulocyte, neutrophil, NLR, CRP, and procalcitonin values of the patients were compared according to their stage (Table 5). The WBC count of patients at stage 3 was higher than those of patients at stages 1 and 2. The neutrophil and NLR values were lower in stage 1 than in stages 3 and 4. Moreover, the neutrophil and NLR values were lower in stage 2 than in stage 3. Procalcitonin levels were lower in stage 1 than in stage 3. Although a significant relationship was found between the groups in terms of Hb, PLT, and CRP values, no significant differences were found in pairwise comparisons according to the post-hoc analysis.

Table 3. Complete blood count values of the patients

	Mean	Median	P25	P75
WBC	10.79	10.40	8.10	13.27
Hb	13.07	13.30	11.80	14.40
HCT	39.03	39.90	36.30	42.50
PLT	271.85	263.00	209.00	313.00
Monocytes	0.80	0.76	0.56	1.02
Granulocyte	2.22	2.17	1.64	2.77
Neutrophil	7.56	6.90	4.79	9.44
NLR	4.33	3.04	2.12	4.80
CRP	18.30	6.00	2.60	21.00
Procalcitonin	1.68	0.50	0.01	1.60

WBC: White blood cells, Hb: hemoglobin, HCT: hematocrit, PLT: platelet, NLR: neutrophil-to-lymphocyte ratio, CRP: C-reactive protein

Discussion

In acute diverticulitis, clinical manifestations range from mild abdominal pain to hemodynamic instability and peritonitis, depending on disease severity. The most common presenting symptom is left lower quadrant pain, which typically begins 1 or 2 days earlier. As most diverticulitis occurs in the sigmoid or descending colon, the pain is in the left lower quadrant. However, diverticulitis is predominantly right-sided in Asian populations; thus, the pain is felt more on the right side (10).

Among gastrointestinal diseases, acute appendicitis, acute cholecystitis, intestinal obstruction, colon malignancy, inflammatory bowel disease, acute pancreatitis, constipation, acute gastroenteritis, and inguinal hernia are included in the differential diagnosis of diverticulitis (11).

Table 4. Gender, surgery, drainage, and mortality rates were compared according to the stage of the patients

n		Stage 1		Stage 2		Stage 3		Stage 4	
		%	n	%	n	%	n	%	
Gender	Male	99	(56.25)	12	(54.55)	8	(50.00)	3	(100.00)
	Female	77	(43.75)	10	(45.45)	8	(50.00)	0	(0.00)
Operation	No	169	(96.02)	19	(86.36)	10	(62.50)	0	(0.00)
	Yes	7	(3.98)	3	(13.64)	6	(37.50)	3	(100.00)
Drainage	No	176	(100.00)	20	(90.91)	14	(87.50)	3	(100.00)
	Yes	0	(0.00)	2	(9.09)	2	(12.50)	0	(0.00)
Hospitalization	>5 days	103	(58.52)	7	(31.82)	1	(6.25)	0	(0.00)
	<5 days	73	(41.48)	15	(68.18)	15	(93.75)	3	(100.00)
Mortality	No	173	(98.30)	21	(95.45)	14	(87.50)	2	(66.67)
	Yes	3	(1.70)	1	(4.55)	2	(12.50)	1	(33.33)

Table 5. Complete blood count values, NLR, procalcitonin, and CRP values were compared according to the stage of the patients

	Stage 1	Stage 2	Stage 3	Stage 4	p
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
	58.13±13.66	65.14±18.51	57.88±15.79	54.33±19.86	0.392
WBC	10.34±3.63	10.69±3.16	14.57±3.93	18.23±5.51	**0.000**
Hb	13.25±1.89	12.26±1.81	12.40±1.88	12.13±1.79	**0.043**
HCT	39.42±4.95	36.92±4.63	37.86±4.76	37.90±2.91	0.061
PLT	262.93±79.88	299.50±75.42	312.87±149.64	373.67±110.14	**0.006**
Monocytes	0.79±0.33	0.89±0.37	0.84±0.36	0.96±0.64	0.604
Granulocyte	2.25±0.82	2.25±0.80	1.99±1.03	1.30±0.70	0.178
Neutrophil	7.06±3.26	7.35±3.03	11.81±3.99	15.85±5.94	**0.000**
NLR	3.84±3.91	3.88±2.71	8.33±7.64	14.94±8.63	**0.000**
CRP	14.31±20.37	19.74±21.12	45.31±66.63	97.67±130.20	**0.013**
Procalcitonin	1.40±2.63	2.03±3.45	4.04±6.07	2.87±1.58	**0.001**

Kruskal-Wallis test. WBC: White blood cells, Hb: hemoglobin, HCT: hematocrit, PLT: platelet, NLR: neutrophil-to-lymphocyte ratio, CRP: C-reactive protein, SD: standard deviation

In general, WBC counts, procalcitonin, and CRP levels are elevated in patients with diverticulitis. In one study, the combination of high WBC count and CRP value was associated with a four-fold increased likelihood of diverticulitis compared with other causes of abdominal pain (12).

Diagnosing diverticulitis by clinical examination may be difficult for patients without a previous history of diverticulitis. Previous studies have indicated that the clinical diagnosis was incorrect in 40-60% of the patients with suspected diverticulitis. Thus, various auxiliary diagnostic tests should be implemented (13).

It may be difficult to diagnose diverticulitis based solely on clinical findings. Besides, complications of diverticulitis such as abscess cannot be confirmed without imaging examination. Differentiating the complicated diverticulitis from the uncomplicated one is very important to determine the need for antibiotics, percutaneous abscess drainage, and surgery (14).

Abdominal tomography is the most preferred imaging method in the diagnosis of diverticulitis, with a sensitivity of 96% and a specificity of 95%. Abdominal ultrasonography, with sensitivity and specificity of approximately 90%, can be used in the evaluation of patients with suspected diverticulitis. Ultrasonography does not require contrast, radiation is not applied, and it can be performed at the bedside. The sensitivity and specificity of magnetic resonance imaging are also high. Plain abdominal radiography may help in the evaluation of pneumoperitoneum and exclude other diagnoses such as intestinal obstruction, but it cannot be used to confirm the diagnosis of diverticulitis or abscess (15).

In a study of 177 patients with acute cholecystitis in which NLR was used as a biomarker, as in our study, NLR values were determined to be effective in the diagnosis and determination of disease severity (16). In another study of 600 patients with acute cholecystitis, NLR was successful in the diagnosis and determination of disease severity (17).

High NLR values were reported to be associated with severe abdominal infections and worse outcomes; thus, it was used as a predictor of outcomes in patients who underwent surgery (18).

Currently, the debate on the usefulness of NLR as a predictor of complications in acute diverticulitis remains open, especially concerning disease severity, clinical impact, and the need for minimally invasive or emergency surgical procedures (19).

If the CRP value in patients with diverticulitis is >150, it is always necessary to perform CT; if <150, performing CT is decided according to the clinical condition of the patient (20).

The peripheral blood NLR has been widely reported to be associated with an inflammatory response and indicates the inflammatory state of many diseases. NLR is more significant as a biomarker than PLT and CRP, especially in advanced-stage acute diverticulitis.

Study Limitations

Patients aged <18 years, pregnant patients, and patients with Crohn's disease, ulcerative colitis, colorectal, and/or anal cancer were excluded from the study.

Conclusion

In this study, patients with acute diverticulitis with higher NLR levels are more likely to develop complications. The combined use of NLR with physical examination, imaging, and other laboratory tests facilitates the diagnosis of complicated acute diverticulitis. To confirm the utility of the NLR value in clinical practice, further studies and meta-analysis are needed.

Ethics Committee Approval: The approval form the University of Health Sciences Turkey, İstanbul Training and Research Hospital Local Ethics Committee was obtained (approval number: 2421, date: 12.06.2020). Informed consent was obtained from each patient.

Informed Consent: Informed consent was obtained from each patient.

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