ORIGINAL ARTICLE

The role of neutrophil-to-lymphocyte ratio in predicting disease progression and emergency surgery indication in benign intestinal obstructions

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ABSTRACT

BACKGROUND: The physiological response of the immune system to various stress factors results in an increase in neutrophil count and a decrease in lymphocyte count. In the light of this information, some studies have suggested using the ratio of these two parameters as an infection marker. The aim of this study was to investigate the role of neutrophil-to-lymphocyte ratio (NLR) derived from complete blood count, a very cost-effective and rapidly measurable parameter, in predicting the urgency of the surgical indication and disease progression in intestinal obstructions secondary to benign causes.

METHODS: The data of patients who were admitted with the diagnosis of intestinal obstruction secondary to benign causes and underwent surgical intervention between January 2010 and January 2021 in Başkent University, Faculty of Medicine, Department of General Surgery, Konya Practice and Research Hospital were retrospectively analyzed. The data of 109 patients who met the study criteria and were included in the study were statistically analyzed. The correlation of admission NLR with factors indicating the severity of the disease such as intraoperatively detected ischemia, perforation, resection requirement, post-operative morbidity and mortality, and length of hospital stay was examined. Moreover, the diagnostic value of the NLR was compared with that of other infection markers (such as C-reactive protein [CRP] and leukocyte).

RESULTS: It was observed that the high NLR during admission to the hospital due to benign intestinal obstruction causes significantly increased the risk of ischemia, resection requirement, post-operative complications, and mortality during surgery ($p<0.05$). Furthermore, increased NLR was found to be associated with prolonged hospitalization. In correlation analysis, consistent with the literature, a positive correlation was found between NLR and hospitalization time ($p=0.03$), CRP value ($p<0.001$), ischemia ($p<0.001$), perforation ($p=0.007$), presence of post-operative complications ($p=0.009$), and mortality ($p=0.002$).

CONCLUSION: Our results show that the NLR has a very important role in predicting the course of the disease and surgical indication in benign intestinal obstructions.

Keywords: Intestinal obstruction; ischemia; mortality; neutrophil-to-lymphocyte ratio; resection.

INTRODUCTION

Intestinal obstructions may occur due to malignant causes as well as benign events. The benign causes of intestinal obstruction include inguinal, femoral, umbilical and incisional hernias, adhesion, invagination, internal herniation (post-operative or congenital), small and large bowel volvulus, and idiopathic intestinal pseudo-obstruction. If an intestinal obstruction is considered to be caused by the previous surgery in a patient diagnosed with intestinal obstruction, the patient's clinic can often be improved by conservative approaches. However, although rarely, there may be delays in surgical intervention due to conservative treatment. If surgical intervention is delayed after incarceration and probable strangulation of internal or external herniations, ischemia may develop within hours. [1] Similar conditions may also arise due to delayed surgical

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treatment of intestinal obstruction associated with other non-malignant causes such as invagination, small and large bowel volvulus, and idiopathic intestinal pseudo-obstruction.

The physiological response of the immune system to various stress factors results in an increase in neutrophil count and a decrease in lymphocyte count.[2] In the light of this information, some studies have suggested using the ratio of these two parameters as an infection marker.[3] A study by Wyllie et al.[4] reported that the neutrophil-to-lymphocyte ratio (NLR) was more valuable than C-reactive protein (CRP) or lymphocyte count in demonstrating the inflammatory process.

In intestinal obstructions secondary to benign causes, there may sometimes be delayed cases since there are no clear-cut limits about when to perform surgery. This leads to bowel resections, increased morbidity-mortality, and longer length of hospital stay due to ischemia and perforation. Numerous studies have shown that the NLR is a very important parameter in predicting the severity and progression of the current pathology in various malignancies, chronic diseases, inflammatory, and ischemic conditions. The aim of this study was to investigate the role of NLR derived from complete blood count, a very cost-effective and rapidly measurable parameter, in determining the urgency of the surgical indication and disease progression in intestinal obstructions secondary to benign causes.

MATERIALS AND METHODS

This study was approved by the Medical and Health Sciences Research Board of Başkent University (Project no: KA21/197) and supported by Başkent University Research Fund. The data of patients who were admitted with the diagnosis of intestinal obstruction secondary to benign causes and underwent surgical intervention between January 2010 and January 2021 in Başkent University, Faculty of Medicine, Department of General Surgery, Konya Practice and Research Hospital were retrospectively analyzed. Of these patients, those with benign diagnoses that may cause intestinal obstruction such as incarcerated inguinal, femoral, umbilical, incisional hernias, adhesion, invagination, internal herniation (post-operative or congenital), small and large bowel volvulus, and idiopathic intestinal pseudo-obstruction were included in the study. The definition of incarceration was used to describe irreducible hernias, while the definition of strangulation was used to describe irreducible hernias with concurrent ischemic findings. Patients with inflammatory pathologies that may cause ileus (inflammatory bowel diseases, diverticulitis, etc.), conditions that may cause paralytic and spastic ileus, malignancies, pathologies that may cause abnormal leukocyte, neutrophil, lymphocyte, and platelet count (patients with pulmonary, urinary, etc., infections, leukemia, and other hematological malignancies, patients with a history of splenectomy, chronic kidney/liver failure, and radiotherapy) were excluded from the study.

Demographic data, presenting complaints and onset of complaints, imaging and laboratory results at admission, etiological cause of intestinal obstruction, surgical findings, surgery type, post-operative complications, length of hospital stay, and mortality and morbidity data of patients were recorded and evaluated.

The data of 109 patients who met the study criteria and were included in the study were statistically analyzed. The correlation of admission NLR with factors indicating the severity of the disease such as intraoperatively detected ischemia, perforation, resection requirement, post-operative morbidity and mortality, and length of hospital stay was examined. Moreover, the diagnostic value of the NLR was compared with that of other infection markers (such as CRP and leukocyte).

Statistical Analysis

SPSS V21.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA) software package was used for the analyses of our study. The level of significance was set at $p<0.05$ for all analyses. The normality distribution of the data was evaluated by the Kolmogorov–Smirnov test. Categorical variables were presented as frequency tables, while numerical variables were presented as descriptive measures (mean±standard deviation or median (min–max) in non-parametric cases). One-way analysis of variance (ANOVA) was used for intergroup comparisons when parametric conditions were provided, while the Kruskal–Wallis ANOVA method was used in other cases. Post hoc, Tukey, Scheffe, and Tamhane tests were preferred for pairwise comparisons. The Student's t-test or Mann–Whitney U test was used for two-group comparisons. The Chi-square analysis was used to test whether categorical variables were correlated or not, and Pearson or Spearman correlation tests were used to determine the correlation between numerical variables. Performing receiver operating characteristic (ROC) analysis, cutoff values were calculated for age, leukocyte, neutrophil, lymphocyte counts, NLR, CRP, and the time from the onset of complaints to surgery. Logistic regression analysis was carried out to identify significant risk factors for the presence of ischemia, resection requirement, post-operative complications, secondary surgery requirement, and mortality.

RESULTS

Of the 109 patients included in the study, 58 (53.2%) were female and 51 (46.8%) were male, with a median age of 65 (range, 17–88) years. Seventy-nine (72.5%) patients had previously undergone abdominal surgery. While all of the patients had abdominal pain as a presenting complaint, 73 (67%) patients had nausea-vomiting, 34 (31.2%) patients had abdominal distention, 39 (35.8%) patients had gas and defecation problems, and 29 (26.6%) patients had painful swelling in the inguinal, abdominal regions, or surgical site. The median time from the onset of complaints to surgery was 4 (1–30) days.

A plain erect abdominal radiograph was preoperatively taken from 74 patients. Of these patients, 72 (97.3%) had air-fluid levels and 2 (2.7%) had free air on radiograph. Of the 22 patients, for whom an ultrasonographic examination was ordered, 17 (77.3%) had incarcerated hernia, 4 (18.2%) had dilated small intestine loops, and 1 (0.9%) had invagination. Seventy-six patients underwent computed abdominal tomography, which showed air-fluid levels in 54 (71.1%) patients, incarcerated hernia in 10 (13.2%) patients, free air in 7 (9.2%) patients, internal herniation in 3 (3.9%) patients, and an appearance of invagination in 2 (2.6%) patients.

During the surgery, intestinal obstruction secondary to adhesion was detected in 64 (58.7%) patients, incarcerated incisional hernia in 13 (11.9%) patients, incarcerated inguinal hernia in 10 (9.2%) patients, incarcerated umbilical hernia in 10 (9.2%) patients, internal herniation in 6 (5.5%) patients, invagination in 2 (1.8%) patients, incarcerated femoral hernia in 1 (0.9%) patient, pseudo-obstruction in 1 (0.9%) patient, and volvulus (one of the two patients operated for volvulus had sigmoid colon volvulus, while the other patient had small intestine volvulus) in 2 (1.8%) patients. Of these patients, 44 (40.4%) underwent resection and subsequently anastomosis on the detection of ischemic appearance and/or perforation in the small intestine, 31 (28.4%) underwent adhesiolysis, 25 (22.9%) underwent hernia repair (these patients were those who were operated for incarcerated hernia with no intraoperative ischemic appearance or normalized appearance after the bowel was released despite the presence of ischemia), 3 (2.8%) underwent laparotomy, 3 (2.8%) underwent primary repair of perforation, and 3 (2.8%) underwent small bowel resection and enterostomy. Regardless of the reason for undergoing surgery, 41 (37.6%) of the patients had ischemia and 10 (9.2%) of them had perforation during the operation.

The median length of hospital stay was 6 (range, 1–29) days. In the post-operative period, 15 (13.75%) of the patients developed complications. Of these, 4 (26.6%) had an anastomotic leak, 2 (13.3%) had evisceration-eventration at the wound site, 2 (13.3%) had wound infection, 1 (6.6%) had an intra-abdominal abscess, and 6 (40%) developed non-surgical complications. Ten (9.2%) patients required secondary surgery in the post-operative early period (before discharge) and 17 (15.6%) patients died.

The comparative demographic data and laboratory results of patients with/without ischemia during surgery and with/without resection requirement are summarized in Table 1, and the data of those with/without post-operative complications, with/without secondary surgery requirement, and with/without early mortality are summarized in Table 2. The comparison of the data of patients with and without ischemia revealed that the ischemia group had a longer length of hospital stay (p=0.07), while the time from the onset of complaints to surgery was similar in both groups (p=0.48). The analysis of laboratory values showed that the ischemia group had statistically significantly higher leukocyte (p<0.001), neutrophil (p<0.001), CRP (p<0.001), and NLR (p<0.001) values but a lower lymphocyte value (p<0.001). The evaluation for perforation showed similar leukocyte (p=0.46), neutrophil (p=0.34), and CRP (p=0.15) values in the groups with and without perforation. In contrast to these values, the perforation group had a significantly higher NLR (p=0.008) but a lower lymphocyte value (p=0.02). The data of patients who died in the early post-operative period and who survived were statistically analyzed. The time from the onset of complaints to surgery was similar between the two groups (p=0.87). The mortality group had a significantly longer length of hospital stay (p=0.003). Of the laboratory test studied at admission, the leukocyte (p=0.79),

Table 1. The comparative demographic data and laboratory results of patients with/without ischemia during surgery and with/without resection requirement

	Ischemia			Resection		
	No (n=68)	**Yes (n=41)**	**p**	**No (n=62)**	**Yes (n=47)**	**p**
Age (year)	64 (17–88)	65 (40–84)	0.26	64 (17–88)	66 (22–84)	0.66
Hospital stay (day)	5.5 (2–120)	7 (3–62)	0.007	5 (2–120)	7 (3–62)	<0.001
Time comp.-dia. (day)	3.5 (1–20)	4 (1–30)	0.48	3 (1–20)	5 (1–30)	0.02
Leukocyte ($\times10^3$/mm^3)	8.4 (2.7–29.7)	13.1 (1.8–27.4)	<0.001	9.2 (2.7–29.7)	9.9 (1.8–27.4)	0.56
Neutrophil ($\times10^3$/mm^3)	5.8 (1.3–15.3)	11.5 (1.6–23.2)	<0.001	7.0 (1.3–17.1)	7.7 (1.6–23.2)	0.47
Lymphocyte ($\times10^3$/mm^3)	1.5 (0.3–17.6)	0.8 (0.09–7.5)	<0.001	1.5 (0.3–17.6)	0.9 (0.09–7.5)	0.001
Thrombocyte ($\times10^4$/mm^3)	255 (2.8–870)	246 (85–508)	0.98	267 (2.8–870)	246 (85.1–508)	0.21
NLR	3.8 (0.6–10)	13.6 (0.9–62.5)	<0.001	5.2 (0.6–35.7)	7.7 (0.8–62.5)	0.007
CRP (mg/L)	20.3 (0.2–331)	60.9 (0.5–344)	<0.001	26.5 (0.4–331)	54.5 (0.2–344)	0.02
BUN (mg/dL)	17 (4–62)	29 (6–59)	0.005	17 (5–62)	24 (4–59)	0.17
Creatinine (mg/dL)	0.8 (0.4–3.5)	1 (0.5–6.1)	0.21	0.8 (0.4–3.55)	0.9 (0.5–6.1)	0.53

Time comp.-dia.: The time from the onset of complaints to diagnosis; NLR: Neutro-phil-to-lymphocyte ratio; CRP: C-reactive protein; BUN: Blood urea nitrogen.

Table 2. The comparative demographic data and laboratory results of patients with/without post-operative complications, with/without secondary surgery requirement, and with/without early mortality

	Complication			Secondary surgery			Mortality		
	No (n=94)	Yes (n=15)	p	No (n=99)	Yes (n=10)	p	No (n=92)	Yes (n=17)	p
Age (year)	64 (17–88)	69 (45–88)	0.16	65 (17–88)	59.5 (45–84)	0.75	64 (17–88)	68 (45–88)	0.16
Hospital stay (day)	6 (2–35)	25 (3–120)	<0.001	6 (2–120)	21.5 (3–62)	0.002	6 (2–35)	11 (3–120)	0.003
Time comp.-dia. (day)	3 (10–20)	10 (3–30)	0.001	3 (1–20)	10 (2–30)	0.004	3.5 (1.20)	4 (2–30)	0.08
Leukocyte (×10^3/mm^3)	9.3 (2.7–29.7)	11.2 (1.8–27.4)	0.42	9.5 (2.7–29.7)	9.7 (1.8–27.4)	0.93	9.4 (2.7–29.7)	9.9 (1.8–25.9)	0.79
Neutrophil (×10^3/mm^3)	7.1 (1.3–20.4)	9.3 (1.6–23.2)	0.26	7.4 (1.3–22.3)	8.3 (1.6–23.2)	0.91	7.1 (1.3–23.2)	9.1 (2.6–22.3)	0.72
Lymphocyte (×10^3/mm^3)	1.4 (0.3–17.6)	0.8 (0.09–2.1)	0.01	1.3 (0.3–17.6)	0.6 (0.09–2.1)	0.03	1.4 (0.3–17.6)	0.7 (0.09–2.1)	<0.001
Thrombo-cyte (×10^4/mm^3)	255 (2.8–870)	246 (88–439)	0.81	257 (2.8–870)	213 (88–439)	0.21	257 (2.8–870)	224 (85–374)	0.13
NLR	5.3 (0.6–35.7)	12.9 (0.9–62.5)	0.01	5.4 (0.6–35.7)	15.6 (0.9–62.5)	0.10	5.3 (0.6–35.7)	16.8 (0.9–62.5)	0.003
CRP (mg/L)	29.5 (0.2–344)	94.9 (2.7–342)	0.04	29.8 (0.2–344)	126.5 (20.1–279.3)	0.01	30.1 (0.2–344)	48 (2.7–342)	0.08
BUN (mg/dL)	19 (4–56)	27 (7–62)	0.07	19 (4–62)	20 (7–39)	0.71	18 (4–56)	29 (7–62)	0.02
Creatinine (mg/dL)	0.8 (0.4–3.5)	1 (0.5–6.1)	0.20	0.9 (0.4–6.1)	0.9 (0.5–3.2)	0.55	0.8 (0.4–3.5)	1 (0.5–6.1)	0.12

Time comp.-dia.: The time from the onset of complaints to diagnose; NLR: Neutrophil-to-lymphocyte ratio; CRP: C-reactive protein; BUN: Blood urea nitrogen.

neutrophil (p=0.72), platelet (p=0.13), and CRP (p=0.082) values were similar in both groups, but there were significant differences between the groups in terms of lymphocyte count (p<0.001) and NLR (p=0.003). While the mortality group had a significantly lower lymphocyte value (0.7 [range, 0.09–21]) compared to survivors (1.4 [range, 0.3–17.6]), they had a higher NLR (16.8 [range, 0.9–62.5] vs. 5.3 [range, 0.6–35.7]). Patients with the early post-operative complications had a longer length of hospital stay (p<0.001). The laboratory values of leukocyte (p=0.42) and neutrophil (p=0.26) counts were similar in patients with and without complications. Patients who developed complications had higher NLR (p=0.01) and CRP (p=0.04) values but a lower lymphocyte value (p=0.013). The analysis of the data of the groups with and without secondary surgery showed that the group with secondary surgery requirement had significantly longer time from the onset of complaints to surgery (p=0.004) and length of hospital stay (p=0.02). Those who underwent secondary operations were found to have a significantly lower lymphocyte value (p=0.031) and a higher CRP value (p=0.013). When the patients were grouped based on surgery types, the lymphocyte (p=0.001) and NLR (p=0.004) values were significantly different between the groups but the leukocyte (p=0.40), neutrophil (p=0.27), and CRP (p=0.10) values were similar. The NLR was significantly different especially between the laparotomy and resection + anastomosis, bridectomy and resection + anastomosis, hernia repair, and resection + anastomosis groups (p<0.05). When the patients were categorized for post-operative complications, the NLR (p<0.001) and leukocyte (p=0.007) values were different between the groups. The NLR was found to be higher in the group with wound infection and evisceration/eventration.

There was no correlation between the cause of intestinal obstruction and complications (p=0.99) and mortality (p=0.36), and between the type of surgical intervention and complications (p=0.77) and mortality (p=0.32). There was also no correlation between the cause of intestinal obstruction and the requirement for secondary surgery (p=0.06), ischemia (p=0.83), and perforation (p=0.44). The type of surgery was similar in patients with and without secondary operation requirement (p=0.055), patients with and without post-operative complications (p=0.11), and those with or without mortality (p=0.09). The analysis of variance showed that the development of ischemia and post-operative complications alone and together had an effect on the length of hospital stay (p<0.001). The correlation analysis showed a positive correlation between the length of hospital stay and the time from onset of complaints to surgery (p=0.007), neutrophil (p=0.049), NLR (p=0.003), and CRP (p<0.001) values, and a positive correlation between the length of hospital stay and lymphocyte value (p=0.005). In addition, there was a positive correlation between the NLR and the length of hospital

Table 3. The age, time from the onset of complaints to surgery, leukocyte, neutrophil, lymphocyte, neutrophil/lymphocyte ratio, and CRP cutoff values calculated by receiver operating characteristic analysis for state variables of ischemia, resection requirement, complication, secondary operation requirement, and mortality

Risk factor		AUC (95% CI)	Cutoff	p	Sensitivity (%)	Specificity (%)
Ischemia	Age	0.56 (0.45–0.67)	64.5	0.26	53.7	51.5
	Time comp.-dia	0.53 (0.42–0.65)	3.5	0.49	51.2	50
	Leukocyte	0.73 (0.63–0.84)	9.98	<0.001	73.2	70.6
	Neutrophil	0.76 (0.66–0.87)	8.06	<0.001	75.6	76.5
	Lymphocyte	0.81 (0.73–0.90)	1.20	<0.001	73.2	73.5
	NLR	0.86 (0.78–0.95)	6.56	<0.001	82.9	82.4
	CRP	0.70 (0.59–081)	40.35	<0.001	68.3	64.5
Resection	Age	0.52 (0.41–0.63)	64.5	0.66	53.2	51.6
	Time comp.-dia	0.63 (0.52–0.73)	4.50	0.02	55.3	61.3
	Leukocyte	0.53 (0.41–0.65)	9.75	0.56	53.2	54.8
	Neutrophil	0.54 (0.42–0.65)	7.56	0.47	53.2	53.2
	Lymphocyte	0.68 (0.57–0.78)	1.29	0.001	68.1	67.7
	NLR	0.65 (0.54–0.76)	6.61	0.007	59.6	72.6
	CRP	0.62 (0.51–0.74)	40.35	0.02	60.9	61.4
Complication	Age	0.61 (0.46–0.75)	68.5	0.16	53.3	61.7
	Time comp.-dia	0.76 (0.64–0.88)	4.50	0.001	66.7	57.4
	Leukocyte	0.56 (0.36–0.76)	9.86	0.42	60.0	54.3
	Neutrophil	0.59 (0.38–0.79)	9.12	0.26	60.0	68.1
	Lymphocyte	0.70 (0.56–0.84)	0.96	0.013	66.7	72.3
	NLR	0.71 (0.53–0.88)	8.87	0.01	66.7	75.5
	CRP	0.66 (0.53–0.79)	46.50	0.04	60.0	60.2
Sec. surg.	Age	0.47 (0.32–0.61)	62.5	0.75	40.0	43.4
	Time comp.-dia	0.77 (0.61–0.94)	9.0	0.004	60.0	87.9
	Leukocyte	0.49 (0.21–0.76)	13.25	0.93	50.0	80.8
	Neutrophil	0.51 (0.23–0.79)	11.95	0.91	50.0	83.8
	Lymphocyte	0.70 (0.51–0.90)	0.83	0.03	70.0	75.8
	NLR	0.65 (0.41–0.89)	12.69	0.10	60.0	83.8
	CRP	0.73 (0.60–0.87)	122.0	0.01	60.0	79.6
Mortality	Age	0.60 (0.47–0.73)	66.5	0.16	52.9	54.3
	Time comp.-dia	0.62 (0.47–0.78)	3.50	0.09	52.9	50.0
	Leukocyte	0.48 (0.29–0.66)	9.86	0.79	52.9	53.3
	Neutrophil	0.52 (0.34–0.71)	9.12	0.72	52.9	67.4
	Lymphocyte	0.80 (0.68–0.91)	0.90	<0.001	76.5	78.3
	NLR	0.73 (0.56–0.89)	7.48	0.003	70.6	69.6
	CRP	0.63 (0.50–0.75)	41.85	0.08	58.8	57.0

Time comp.-dia.: The time from the onset of complaints to diagnosis; NLR: Neutro-phil-to-lymphocyte ratio; CRP: C-reactive protein; Sec. surg.: Secondary surgery; CI: Confidence interval; AUC: Area under curve.

stay (p=0.03), CRP value (p<0.001), presence of ischemia (p<0.001), perforation (p=0.007), post-operative complications (p=0.009), and mortality (p=0.002).

The age, time from the onset of complaints to surgery, leukocyte, neutrophil, lymphocyte, NLR, and CRP cutoff values calculated by ROC analysis for ischemia, resection requirement, complication, secondary operation requirement, and mortality variables are summarized in Table 3 and Figures 1–5. The risk analysis performed with the Chi-square test showed that the detection of ischemia during surgery increased the risk of developing complications by 5.8-fold (p=0.03) and the

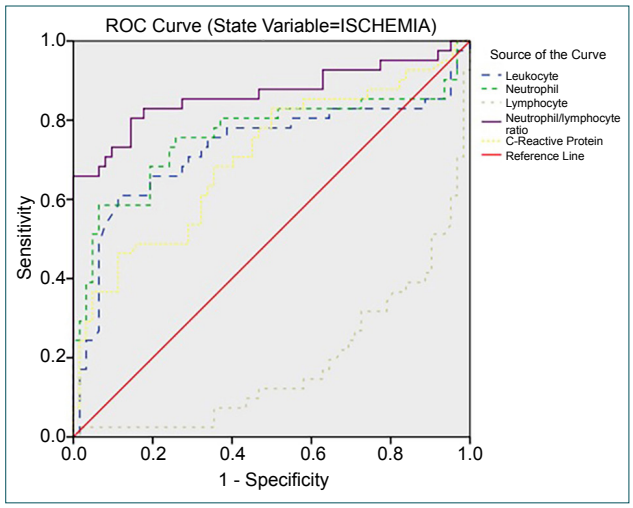

Figure 1. The receiver operating characteristic curve of laboratory findings for ischemia variable.

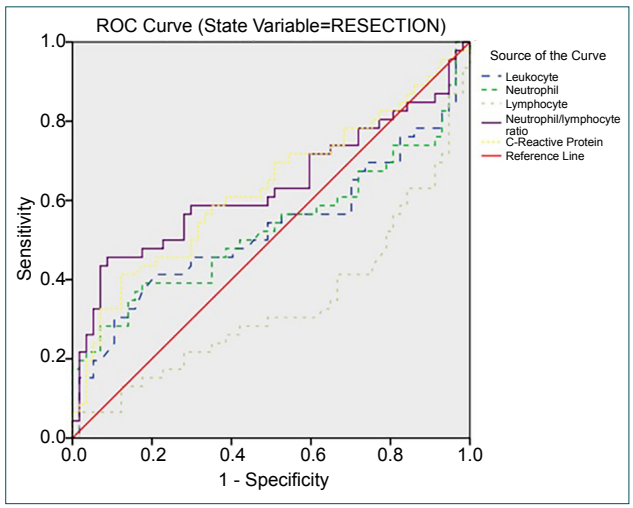

Figure 2. The receiver operating characteristic curve of laboratory findings for resection requirement variable.

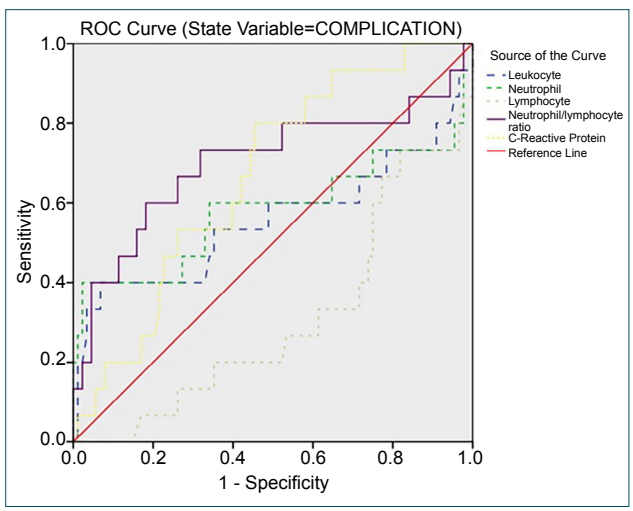

Figure 3. The receiver operating characteristic curve of laboratory findings for complication variable.

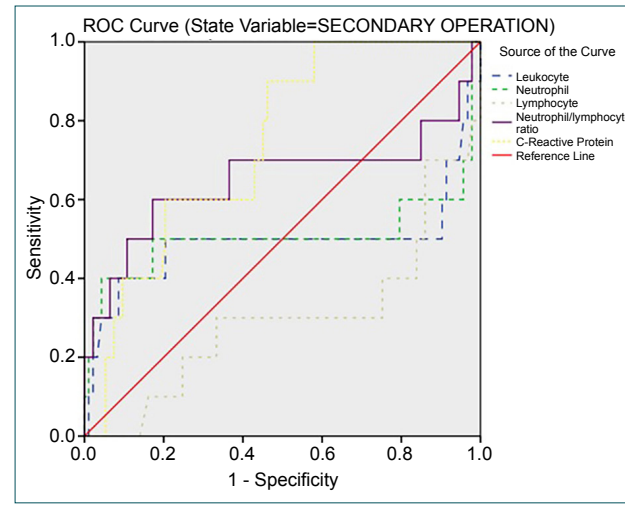

Figure 4. The receiver operating characteristic curve of laboratory findings for secondary surgery variable.

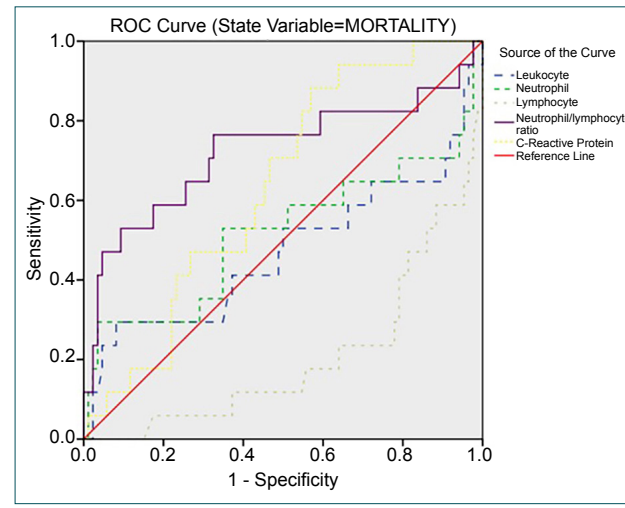

Figure 5. The receiver operating characteristic curve of laboratory findings for mortality variable.

mortality risk by 11.2-fold ($p<0.001$). Leukocyte, neutrophil, lymphocyte, NLR, and CRP values above the cutoff value increased the risk of developing ischemia by 6.54-, 10.07-, 7.57-, 22.66-, and 3.91-fold, respectively ($p<0.001$). The time from the onset of complaints to surgery was not found to have such an effect ($p>0.05$). A lymphocyte count below the cutoff value was found to cause a 7.5-fold increase in the risk of ischemia ($p<0.001$). While low lymphocyte count (odds ratio=5.9, $p=0.019$) and high NLR (odds ratio=6.3, $p=0.015$) were correlated with an increased risk of perforation, there was no such correlation for leukocyte, neutrophil, and CRP values ($p>0.05$). The evaluation for complication development showed that low lymphocyte count (odds ratio=5.23, $p=0.003$) and high NLR (odds ratio=6.17, $p=0.001$) were correlated with an increased risk of developing complications, while such a correlation could not be established for leukocyte, neutrophil, and CRP values. The time from the

onset of complaints to surgery (odds ratio=10.87, p<0.001), leukocyte (odds ratio=4.21, p=0.025), neutrophil (odds ratio=5.18, p=0.01), lymphocyte (odds ratio=7.29, p=0.002), NLR (odds ratio=7.78, p=0.001), and CRP value (odds ratio=5.84, p=0.006) were correlated with an increased risk of secondary surgery. Low lymphocyte count (odds ratio=11.76, p<0.001) and high NLR (odds ratio=5.48, p=0.002) were found to cause an increase in the risk of mortality, while the other mentioned parameters had no such correlation (p>0.05). The risk of resection requirement during surgery was also found to be correlated with low lymphocyte (odds ratio=4.48, p<0.001), high NLR (odds ratio=3.90, p=0.001), and high CRP values (odds ratio=2.43, p=0.02); however, it was not correlated with other parameters.

Table 4. Multivariate logistic regression analysis of risk factors associated with ischemia, resection requirement, development of complications, need for secondary surgery, and mortality in benign intestinal obstruction

Risk factor	Odds ratio	95% CI		p-value
		Lower	Upper	
Ischemia				
Time comp.-dia	1.093	0.980	1.220	0.111
Leukocyte	0.996	0.848	1.169	0.957
NLR	1.441	1.182	1.755	<0.001
CRP	1.006	0.998	1.014	0.139
Resection				
Time comp.-dia	1.109	1.011	1.216	0.029
Leukocyte	0.957	0.861	1.062	0.406
NLR	1.098	1.018	1.185	0.016
CRP	1.006	1.000	1.011	0.046
Complication				
Time comp.-dia	1.228	1.096	1.375	<0.001
Leukocyte	1.014	0.875	1.177	0.850
NLR	1.106	1.021	1.199	0.014
CRP	1.002	0.995	1.010	0.547
Sec. surg.				
Time comp.-dia	1.330	1.125	1.573	0.001
Leukocyte	0.863	0.682	1.092	0.221
NLR	1.162	1.029	1.311	0.015
CRP	1.011	1.001	1.022	0.032
Mortality				
Time comp.-dia	1.160	1.040	1.293	0.008
Leukocyte	0.828	0.689	0.995	0.044
NLR	1.191	1.079	1.316	0.001
CRP	1.003	0.996	1.010	0.354

Time comp.-dia.: The time from the onset of complaints to diagnosis; NLR: Neutrophil-to-lymphocyte ratio; CRP: C-reactive protein; Sec. surg.: Secondary surgery; CI: Confidence interval.

The linear regression analysis evaluating the parameters that may be correlated with the length of hospital stay showed that only the high NLR had an effect on the length of hospital stay (p=0.016). Univariate and multivariate logistic regression analysis was performed to identify significant factors that may be effective in determining the presence of ischemia, resection requirement, post-operative complications, secondary surgery requirement, and mortality. The time from the onset of complaints to surgery, leukocyte value, NLR, and CRP values that may affect these parameters were analyzed. According to the results of this analysis, the NLR alone was effective in determining ischemia; it was effective in determining the requirement for resection together with the time from the onset of complaints to surgery and CRP; it was effective in determining the development of complications together with the time from the onset of complaints to surgery; it was effective in determining the requirement for secondary surgery together with the time from the onset of complaints to surgery and CRP; it was effective in determining mortality together with the time from the onset of complaints to surgery and leukocyte count (p<0.05) (Table 4).

DISCUSSION

Systemic response to trauma, severe infection, ischemia-reperfusion injury, major surgery, shock, and burn are regulated by neuroendocrine and immune systems.[3] In individuals with a healthy immune system, monocyte, neutrophil, and lymphocyte values play a key role in systemic inflammatory response to severe infection, shock, multiple trauma, and injury.[3] Jilma et al.[5] demonstrated that the general response of the immune system to endotoxemia was in the form of an increase in circulating neutrophil count and a decrease in lymphocyte count. It is believed that lymphopenia arising in the aforementioned cases is caused by margination and redistribution of lymphocytes within the lymphatic system, and by the increase in apoptosis.[6] Neutrophilia, on the other hand, has been associated with the demargination of neutrophils, delayed neutrophil apoptosis, and stimulation of stem cells by growth factors.[3] These changes in lymphocyte and neutrophil counts during systemic inflammation are thought to be associated with increased cortisol levels.[7] Setting forth this basic information, clinical studies have shown that the NLR is an easily measurable laboratory parameter that can be used to predict the clinical condition of individuals with sepsis, systemic inflammation, and critical illness.[3] The NLR, which is considered an inflammatory marker, has been shown to be associated with circulatory, respiratory, gastrointestinal diseases, and tumors.[7]

Although there is no universally accepted reference value for the NLR, there are numerous studies on this subject. A study stated that this value could be considered normal when it is between 0.78 and 3.53 in healthy, non-geriatric adult individuals.[8] Similarly, a study conducted in the United States estimated the average value of NLR as 1.76 for non-Hispanic

Black citizens, 2.08 for non-Black Hispanic citizens, and 2.24 for non-Black non-Hispanic citizens.[9] A South Korean study on healthy individuals showed that this ratio was lower in the Asian population compared to other races, with mean values of 1.63 for men and 1.66 for women across all ages.[10] As is seen, the normal ranges of this value may differ by gender, age, and race. A study conducted by Aydın et al.[11] in our country attempted to determine the reference values of this ratio for citizens of different age groups and genders.

A study by Forget et al.[8] showed that the NLR measured at post-operative day 7 was significantly associated with complications after major abdominal surgery. A study evaluating the relationship between the post-operative NLR and complications following colorectal surgery concluded that this ratio may be a more useful parameter than leukocyte and CRP values.[12] Another study conducted to show the relationship between the length of hospital stay and the NLR in colorectal cancer surgery evaluated pre-operative albumin and NLRs. The results of the study showed that increased NLR and decreased albumin value were associated with prolonged length of hospital stay.[13] In our study, regression analysis evaluating the parameters that may be associated with the length of hospital stay showed that only the high NLR had an effect on the length of hospital stay (p=0.016). Different studies on septic patients have found that a high NLR at admission to the emergency department was associated with mortality during hospitalization, in the first 28 days, and in the first 6 months.[14,15] Moreover, most studies conducted on septic patients have shown that the NLR is a stronger marker than conventional parameters such as CRP, leukocyte, serum lactate level, neutrophilia, and lymphopenia.[16] In our study, the analysis of the data of patients with and without post-operative mortality showed similar leukocyte (p=0.79), neutrophil (p=0.72), platelet (p=0.13), and CRP (p=0.082) values in both groups but significantly different lymphocyte (p<0.001) and NLR (p=0.003) values. Lymphocyte count was significantly lower in the mortality group (0.7 [range, 0.09–21]) compared to survivors (1.4 [range, 0.3–17.6]), while the mortality group had a higher NLR (16.8 [range, 0.9–62.5] vs. 5.3 [range, 0.6–35.7]). The leukocyte (p=0.42) and neutrophil (p=0.26) values of patients with and without early complications were similar. On the other hand, the NLR (p=0.01) and CRP (p=0.04) values were higher but the lymphocyte value (p=0.013) was lower in patients with complications.

Considering the surgical option for the treatment of intestinal obstructions secondary to benign causes and the timing of surgery are very important. In intestinal obstructions caused by adhesions due to the previous surgery, the patient can be followed up with conservative treatment for a certain period of time if the clinical condition is suitable. Thus, unnecessary surgical interventions can be avoided. However, surgical intervention may be inevitable in patients who do not respond to conservative treatment. At this point, the timing of surgical intervention is of great importance. Possible delays can lead to ischemia and perforation of the intestines. As a result, this leads to the use of a more aggressive surgical technique, increased risk of morbidity and mortality, and prolonged length of hospital stay. In incarcerated hernias, emergency surgery is performed when the diagnosis is made. In these patients, it is often not possible to determine whether strangulation has developed in the pre-operative period, and if it has, how long it has been present, and to predict the patient's clinical course. In patients considered to have strangulation or ischemia secondary to adhesion, immediate surgical intervention is important in terms of the course of the disease. However, there is no objective criterion to demonstrate whether pre-operative ischemia has developed or not.[17] This leads to difficulties in deciding on surgical intervention or in determining its urgency for some patients. A study by Zhou et al.[17] on incarcerated hernias concluded that the pre-operative NLR could be an important marker for demonstrating whether incarceration developed and in determining the prognosis. A similar study analyzed the data of patients with and without resection requirement who were operated for an incarcerated hernia. The results of the study showed significantly higher leukocyte count, mean age, and NLR in the group requiring resection compared to the group not requiring resection.[1] In our study, the NLR was significantly higher in the resection group compared to the other groups (p<0.05). Similarly, a study by Wang et al.[7] on the significance of NLR in acute mesenteric embolism and thrombosis found that these rates were higher in ischemic cases. In addition, the high NLR was shown to be associated with poor prognosis in these patients. Likewise, a study by Karadeniz et al.[18] and another study by Aktimur et al.[19] suggested that high NLR, high thrombocyte/lymphocyte ratio, and low lymphocyte count could be used as diagnostic parameters in patients with a pre-diagnosis of acute mesenteric ischemia.

In line with the literature, the comparison of the data of our patients with and without ischemia during surgery showed statistically significantly higher leukocyte (p<0.001), neutrophil (p<0.001), CRP (p<0.001), and NLR (p<0.001) values but a lower lymphocyte value (p<0.001) in the ischemia group. The evaluation for perforation showed similar leukocyte (p=0.46), neutrophil (p=0.34), and CRP (p=0.15) values in the groups with and without perforation. Contrary to these values, the NLR (p=0.008) was significantly higher but the lymphocyte value (p=0.02) was lower in the perforation group. Likewise, in line with the literature, the result of our correlation analysis showed a positive correlation between NLR and length of hospital stay (p=0.03), CRP value (p<0.001), presence of ischemia (p<0.001), perforation (p=0.007), post-operative complications (p=0.009), and mortality (p=0.002). The Chi-square risk analysis revealed that leukocyte, neutrophil, NLR, and CRP values above the cutoff value increased the risk of ischemia by 6.54-, 10.07-, 7.57-, 22.66-, and 3.91-fold, respectively (p<0.001). Moreover, the high NLR increased the risk of perforation (odds ratio=6.3, p=0.015), complication development (odds ratio=6.17, p=0.001), secondary surgery (odds

ratio=7.78, p=0.001), mortality (odds ratio=5.48, p=0.002), and resection (odds ratio=3.9, p=0.001) more significantly compared to other infection markers.

Furthermore, our logistic regression analysis performed to identify significant factors that may be effective in determining the presence of ischemia, resection requirement, post-operative complications, secondary surgery, and mortality showed that the NLR was effective in predicting all of these parameters (p<0.05).

Limitations of the Study

The limitations of the study are collecting the data from patient records and operative reports and the absence of objective examination findings due to the retrospective nature of the study.

Conclusion

The results of this study demonstrated that the NLR has a pivotal role in predicting the prognosis in intestinal obstructions secondary to benign causes. We are of the opinion that the increased NLR in conservatively followed up patients for adhesion-related obstruction may be an important parameter in determining the surgical indication in combination with clinical findings. We believe that the NLR can be a valuable marker for predicting the development of strangulation, resection requirement during surgery, and disease progression in a patient presenting with an incarcerated hernia.

Ethics Committee Approval: This study was approved by the Başkent University Ethics Committee (Date: 13.04.2021, Decision No: KA21/197).

Peer-review: Internally peer-reviewed.

Conflict of Interest: None declared.

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REFERENCES

1. Xie X, Feng S, Tang Z, Chen L, Huang Y, Yang X. Neutrophil-to-lymphocyte ratio predicts the severity of ıncarcerated groin hernia. Med Sci Monit 2017;23:5558–63. [CrossRef]
2. De Jager CP, Van Wijk PT, Mathoera RB, Jongh-Leuvenink JD, Van der Poll T, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care 2010;14:R192. [CrossRef]
3. Zahorec R. Ratio of neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy 2001;102:5–14.
4. Wyllie DH, Bowler IC, Peto TE. Relation between lymphopenia and bacteraemia in UK adults with medical emergencies. J Clin Pathol 2004;57:950–5. [CrossRef]
5. Jilma B, Blann A, Pernerstorfer T, Stohlawetz P, Eichler HG, Vondrovec B, et al. Regulation of adhesion molecules during human endotoxemia. No acute effects of aspirin. Am J Respir Crit Care Med 1999;159:857–63.
6. Hotchkiss RS, Swanson PE, Freeman BD, Tinsley KW, Cobb JP, Matuschak GM, et al. Apoptotic cell death in patients with sepsis, shock, and multiple organ dysfunction. Crit Care Med 1999;27:1230–51. [CrossRef]
7. Wang S, Liu H, Wang Q, Cheng Z, Sun S, Zhang Y, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are effective predictors of prognosis in patients with acute mesenteric arterial embolism and thrombosis. Ann Vasc Surg 2018;49:115–22. [CrossRef]
8. Forget P, Dinant V, De Kock M. Is the neutrophil-to-lymphocyte ratio more correlated than c-reactive protein with postoperative complications after major abdominal surgery? PeerJ 2015;3:e713. [CrossRef]
9. Azab B, Camacho-Rivera M, Taioli E. Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. PLoS One 2014;9:e112361. [CrossRef]
10. Lee JS, Kim NY, Na SH, Youn YH, Shin CS. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. Medicine (Baltimore) 2018;97:e11138. [CrossRef]
11. Aydın İ, Ağıllı M, Aydın FN, Kurt YG, Çaycı T, Taş A, et al. Farklı yaş gruplarında nötrofil/lenfosit oranı referans aralıkları. Gülhane Tıp Derg 2015;57:414–8.
12. Cook EJ, Walsh SR, Farooq N, Alberts JC, Justin TA, Keeling NJ. Postoperative neutrophil-lymphocyte ratio predicts complications following colorectal surgery. Int J Surg 2007;5:27–30. [CrossRef]
13. Gohil R, Rishi M, Tan BH. Pre-operative serum albumin and neutrophil-lymphocyte ratio are associated with prolonged hospital stay following colorectal cancer surgery. Br J Med Med Res 2014;4:481–7. [CrossRef]
14. Hwang SY, Shin TG, Jo IJ, Jeon K, Suh GY, Lee TR, et al. Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med 2017;35:234–9. [CrossRef]
15. Akilli NB, Yortanlı M, Mutlu H, Günaydın YK, Koylu R, Akca HS, et al. Prognostic importance of neutrophil-lymphocyte ratio in critically ill patients: Short and long-term outcomes. Am J Emerg Med 2014;32:1476–80. [CrossRef]
16. Okashah AS, El-Sawy MM, Beshay BN, El-Raouf AA. Ratio of neutrophil to lymphocyte counts as a simple marker for sepsis and severe sepsis in intensive care unit. Res Opin Anesth Intensive Care 2014;2:39–45.
17. Zhou H, Ruan X, Shao X, Huang X, Fang G, Zheng X. Clinical value of the neutrophil/lymphocyte ratio in diagnosing adult strangulated inguinal hernia. Int J Surg 2016;36:76–80. [CrossRef]
18. Karadeniz E, Bayramoğlu A, Atamanalp SS. Sensitivity and specificity of the platelet-lymphocyte ratio and the neutrophil-lymphocyte ratio in diagnosing acute mesenteric ıschemia in patients operated on for the diagnosis of mesenteric ıschemia: A retrospective case-control study. J Invest Surg 2020;33:774–81. [CrossRef]
19. Aktimur R, Cetinkunar S, Yildirim K, Aktimur SH, Ugurlucan M, Ozlem N. Neutrophil-to-lymphocyte ratio as a diagnostic biomarker for the diagnosis of acute mesenteric ischemia. Eur J Trauma Emerg Surg 2016;42:363–8. [CrossRef]

ORİJİNAL ÇALIŞMA - *ÖZ*

Benign intestinal obstrüksiyonlarda nötrofil-lenfosit oranının hastalığın progresyonunu ve acil cerrahi endikasyonu belirlemedeki rolü

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AMAÇ: Çeşitli stres faktörlerine bağlı immün sistemin gösterdiği fizyolojik yanıt nötrofil sayısında artış, lenfosit sayısında ise azalma şeklinde olmaktadır. Bu bilginin ışığında bazı çalışmalar bu iki parametrenin oranını bir enfeksiyon belirteci olarak kullanmayı önermişlerdir. Yaptığımız bu çalışma ile maliyeti oldukça düşük ve hızlı bir şekilde çalışılabilen tam kan sayımı sonucu elde edilen nötrofil/lenfosit oranının benign sebeplere bağlı gelişmiş intestinal obstrüksiyonlarda cerrahi endikasyonun aciliyetini ve hastalığın progresyonunu belirlemedeki rolünün incelenmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Başkent Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Konya Uygulama ve Araştırma Hastanesinde Ocak 2010 ve Ocak 2021 tarihleri arasında, benign sebeplere bağlı intestinal obstrüksiyon tanısı ile yatırılmış ve cerrahi müdahale gerekliliği olmuş hastaların verileri geriye dönük olarak incelendi. Kriterlere uyan ve çalışmaya dahil edilen 109 hastanın verileri istatistiksel olarak analiz edildi. Başvuru anındaki nötrofil/lenfosit oranının ameliyatta saptanan iskemi, perforasyon, rezeksiyon gerekliliği, postoperatif morbidite ve mortalite, hastanede yatış süresi gibi hastalığın ciddiyetini gösteren faktörlerle ilişkisi incelendi. Ayrıca bu parametrenin diğer enfeksiyon belirteçlerine (CRP, lökosit gibi) bir üstünlüğünün olup olmadığına bakıldı.

BULGULAR: Benign sebeplere bağlı intestinal obstrüksiyon nedeni ile hastaneye başvuru esnasında bakılan nötrofil/lenfosit orandaki yüksekliğin ameliyat esnasında iskemi saptanması, rezeksiyon gerekliliği, postoperatif komplikasyon ve mortalite riskini anlamlı derecede artırdığı görüldü ($p<0.05$). Ayrıca artmış nötrofil/lenfosit oranı uzamış hastane yatışı ile ilişkili bulundu. Yapılan korelasyon analizlerinde de literatür ile uyumlu olarak nötrofil/lenfosit oranı ile hastane yatış süresi ($p=0.03$), CRP değeri ($p<0.001$), iskemi ($p<0.001$), perforasyon ($p=0.007$), postop komplikasyon varlığı ($p=0.009$) ve mortalite ($p=0.002$) arasında pozitif yönlü korelasyon olduğu saptandı.

TARTIŞMA: Bulgularımız nötrofil-lenfosit oranının benign sebeplere bağlı instestinal obstrüksiyonlarda hastalığın gidişatını öngörmede oldukça önemli role sahip olduğunu göstermiştir. Çalışmamızın verileri doğrultusunda benign sebeplere bağlı intestinal obstrüksiyonlarda nötrofil/lenfosit oranının hastalığın seyrini öngörmede ve bazı durumlarda cerrahi endikasyonu koymada önemli bir belirteç olabileceğini düşünmekteyiz.

Anahtar sözcükler: İntestinal obstrüksiyon; iskemi; mortalite; nötrofil-lenfosit oranı; rezeksiyon.

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