Neutrophil to C-reactive protein ratio and lymphocyte to C-reactive protein ratio can be a predictor for severity of acute appendicitis

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Background
Acute appendicitis (AA) is one of the most common causes of acute abdomen. Mortality and morbidity rates increase in patients with AA from the simple group to the complicated group. In this study, the authors wanted to show the effectiveness of lymphocyte to C-reactive protein (CRP) ratio (LCR) and neutrophil to CRP ratio (NCR) in detecting complications in patients with AA.
Patients and methods
The study population was selected from patients who were admitted to the emergency department with abdominal pain between June 2019 and June 2021, and who were operated in the general surgery clinic with a preliminary diagnosis of AA. Demographic data such as age, sex, and laboratory results were recorded. The patients were histopathologically divided into two groups as simple appendicitis (SA) and complicated appendicitis (CA).
Results
A total of 778 patients met the inclusion criteria. The LCR and NCR levels of the patients were found to be significantly lower in the CA group compared with the SA group (0.11 ± 0.31 vs. 0.44 ± 1.07; 0.65 ± 1.65 vs. 2.44 ± 5.54, $P<0.001$, respectively). In regression analysis, LCR (odds ratio [OR] 0.380, 95% confidence interval [CI] 0.156–0.929, $P=0.034$) and NCR (OR 0.539, 95% CI 0.295–0.985, $P=0.044$) were independent predictors of complication.
Conclusions
Low LCR and NCR levels at the time of admission to the emergency department are a biomarker that can predict complications in patients with AA.

Keywords:
acute appendicitis, complication, lymphocyte to C-reactive protein ratio, neutrophil to C-reactive protein ratio

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Introduction

Acute appendicitis (AA) is one of the most common causes of acute abdomen in patients with abdominal pain presenting to the emergency department and is seen with a high incidence in both developed and developing countries [1]. AA is divided into two groups as simple appendicitis (SA) and complicated appendicitis (CA), and CA can be seen in ~5%–28% of cases [2,3]. Mortality and morbidity rates increase in patients with AA from the simple group to the complicated group, and early detection of complications such as perforation is important in terms of appropriate medical treatment and timing of the operation [4,5].

The diagnosis of AA can be made with a detailed anamnesis, physical examination, laboratory tests, and appropriate imaging methods [6]. Although many scoring systems have been used recently for diagnostics, a clear consensus has not been achieved yet [7–9]. Although many methods can be used as imaging methods, different and affordable inflammatory parameters are worth examining because of the need for special equipment and personnel, the need for experienced radiologist, and the increase in treatment costs [10]. Previous studies have shown the effectiveness of inflammatory markers such as C-reactive protein (CRP), immature granulocyte, neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio in diagnosing AA and its complications [6,11]. Lymphocyte to CRP ratio (LCR) and neutrophil to CRP ratio (NCR), obtained by the

ratio of these parameters to each other, have recently been used as a systemic inflammation response, especially in malignant patients [12]. To the best of our knowledge, there are few studies in the literature showing the efficacy of NCR and LCR in patients with AA, without complications. Therefore, in this study, we wanted to show the effectiveness of NCR and LCR in detecting complications in patients with AA.

Patients and methods

Study design and setting

Our study was designed as a single-center retrospective and the study population was selected from patients who were admitted to our tertiary emergency department with abdominal pain between June 2019 and June 2021, and who were hospitalized and operated in the general surgery clinic with a preliminary diagnosis of AA. All patients 18 and over who were operated for AA were included in our study. Exclusion criteria in our study were those who did not accept the operation or had elective surgery, patients <18 years of age, pregnant, those with known rheumatological, hematological and oncological diseases, those with an acute cardiovascular disease, patients with known kidney and liver failure, and patients with missing data.

The diagnosis of AA was made by clinical, physical examination, laboratory parameters, and imaging findings. Demographic data such as age, sex, white blood count (WBC), neutrophil count, lymphocyte count, and CRP values of patients who met the inclusion criteria were recorded. Whole blood analyzes were performed within the first hour as a routine hospital procedure. LCR and NCR were calculated separately by the ratio of neutrophil counts and lymphocyte counts to CRP. The patients were histopathologically divided into two groups as SA (phlegmonous or suppurative appendicitis) and CA (gangrenous and perforated appendicitis with or without intra-abdominal abscess). The groups were compared in terms of parameters.

Statistical analysis

Statistical analysis of all variables SPSS 23.0 evaluated using continuous variables were used as mean±SD for the analysis of data in our study, and frequency and percentage (%) were used to define categorical data. Student's *t*-test was used for the normal distribution variables and Mann–Whitney *U* test was used for the non-normally distributed variables in the comparison of simple and complicated patients with AA in terms of groups. Receiver operating characteristic (ROC) analysis was performed to determine the success of LCR and NCR parameters in indicating severity in AA patients. A *P* value below 0.05 was considered statistically significant.

Results

Our study included 778 patients who met the inclusion criteria. Of them, 713 (91.6%) patients were in the SA group and 65 (8.4%) were in the CA group. While the mean age of the patients was 35.33 ± 13.52 in the SA group, it was 46.80 ± 18.20 in those with CA. The mean age of the patients was found to be significantly higher in the CA group (P<0.001). While 442 (62%) of these patients were male in the SA group, 44 (67.7) of the complicated patients were male. The mean CRP and NLR levels of the patients were significantly higher in the CA group than in the SA group; lymphocyte, LCR and NCR levels were found to be significantly lower. The mean CRP levels of the patients were found to be significantly higher in the CA group than in the SA group (79.5 (160) vs. 17.6 (49); P<0.001). Significantly higher NLR levels were observed in the CA group compared with the SA group (8.61 ± 5.29 vs. 6.97 ± 5.51; P<0.001). Significantly lower lymphocyte levels were found in the CA group compared with the SA group (1.62 ± 0.67 vs. 2.02 ± 0.81; P<0.001). In addition, the LCR and NCR levels of the patients were found to be significantly lower in the CA group compared with the SA group (0.11 ± 0.31 vs. 0.44 ± 1.07; 0.65 ± 1.65 vs. 2.44 ± 5.54, P<0.001, respectively) Table 1.

In multivariate logistic regression analysis, age (odds ratio [OR] 1.037, 95% confidence interval [CI] 1.020–1.054, P<0.001), LCR (OR 0.380, 95% CI 0.156–0.929, P=0.034), NCR (OR 0.539, 95% CI 0.295–0.985, P=0.044), NLR (OR 1.949, 95% CI 1.045–3.636, P=0.036) were independent predictors of complication Table 2. In addition, in the ROC curve analysis, the LCR was 0.17 cutoff value with 52% sensitivity and 88.2% specificity; NCR has been shown to predict complications with a sensitivity of 61.5% and specificity of 70% at a cutoff value of 0.21 (area under the curve: 0.756 (0.690–0.822); 0.708 (0.642–0.773), P<0.001, respectively) (Fig. 1 and Table 3).

Discussion

Early diagnosis of AA is not always easy in emergency departments, especially in those with a large patient population [11,13]. Until the diagnosis is clarified by surgeons, undesirable complications such as perforation and peritonitis may develop in patients with AA, and sometimes early operation may lead to negative appendectomy [14,15]. Although complication rates decrease with advanced imaging methods, such imaging methods may not always be available, especially in small centers. accessible and inexpensive parameters still remain important [6,16]. In this study, we showed that decreased LCR and NCR can be a parameter that can predict complications in patients with AA.

Table 1 Demographic characteristics and laboratory parameters in the differentiation of SA and CA

Variables	Simple appendicitis (*n*=713)	Complicated appendicitis (*n*=65)	*P*
Age (years)	35.33±13.52	46.80±18.20	<0.001
Male sex *n* (%)	442 (62)	44 (67.7)	0.364
Laboratory blood values			
White blood cell count	14.23±4.52	14.32±4.41	0.747
Neutrophil	11.10±4.51	11.52±4.13	0.339
Lymphocyte	2.02±0.81	1.62±0.67	<0.001
C-reactive protein (IQR)	17.6 (49)	79.5 (160)	<0.001
LCR	0.44±1.07	0.11±0.31	<0.001
NCR	2.44±5.54	0.65±1.65	<0.001
NLR	6.97±5.51	8.61±5.29	0.001

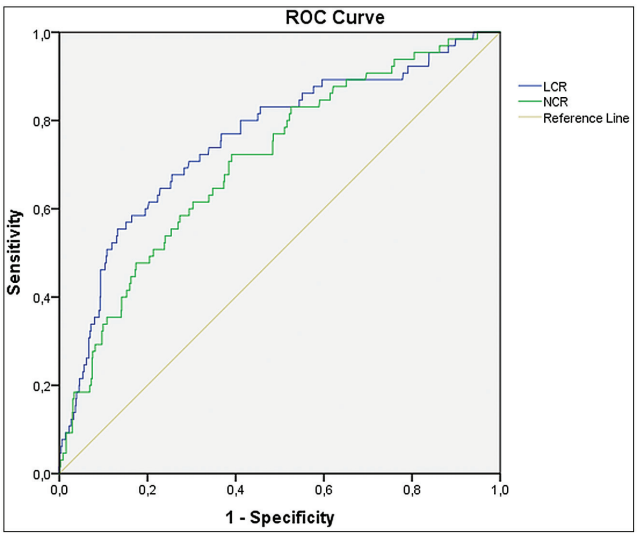
CA, complicated appendicitis; IQR, XXX; LCR, lymphocyte-to-C-reactive protein ratio; NCR, neutrophil-to-C-reactive protein ratio; NLR, neutrophil-to-lymphocyte ratio; SA, simple appendicitis.

Table 2 Logistic regression analysis of the independent predictors of simple and complicated appendicitis patients

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	1.048 (1.032–1.065)	<0.001	1.037 (1.020–1.054)	<0.001
Sex	1.285 (0.748–2.208)	0.365		
LCR	0.195 (0.88–0.432)	<0.001	0.380 (0.156–0.929)	0.034
NCR	0.297 (0.177–0.498)	<0.001	0.539 (0.295–0.985)	0.044
NLR	2.111 (1.167–3.845)	0.014	1.949 (1.045–3.636)	0.036

CI, confidence interval; LCR, lymphocyte-to-C-reactive protein ratio; NCR, neutrophil-to-C-reactive protein ratio; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio.

Figure 1



Receiver operating characteristic curves for lymphocyte-to-C-reactive protein ratio and neutrophil-to-C-reactive protein ratio values in complication prediction.

Table 3 The receiver operating characteristic curves for prediction of complication

	Cutoff	AUC (95% CI)	Sensitivity (%)	Specificity (%)	*P*
LCR	0.17	0.756 (0.690–0.822)	52	88.2	<0.001
NCR	0.21	0.708 (0.642–0.773)	61.5	70	<0.001

AUC, area under the curve; CI, confidence interval; LCR, lymphocyte-to-C-reactive protein ratio; NCR, neutrophil-to-C-reactive protein ratio.

A complication that may develop in patients with AA is associated with high mortality and morbidity and should be considered by physicians [17]. Conditions such as intra-abdominal abscess, perforation, and peritonitis that develop in AA patients should be detected early and treated quickly. Advanced imaging methods, ultrasonography, and tomography have been used to detect such conditions early, and they still maintain their importance. However, these viewing methods may not always be accessible [18]. In addition, ultrasonography has disadvantages such as being practitioner dependent and having lower sensitivity and specificity than tomography. Tomography should be used with caution due to exposure to contrast and radiation [19]. Therefore, in recent years, various inflammatory markers have been used to predict complications in patients with AA.

Many articles have been published on simple and easily accessible biochemical parameters, among which WBC, CRP, NLR, hyperbilirubinemia, and sedimentation are the main ones [20]. One study showed that an NLR above 8 was significantly associated with complication in patients with AA [21]. In another study, it was emphasized that NLR values of 7.5 and above could indicate complications in patients with AA with low specificity and high sensitivity [22]. In another recent study, it was shown that CRP above 35 mg/dl may be a marker of complication in AA [23]. Similar to the literature, in our study, a significant difference was

observed between SA and CA groups with increased NLR and CRP values.

Although LCR has been used as a new inflammatory marker to predict the prognosis of oncological diseases in recent years, as far as we know, there is no study in the literature showing the use of NCR as an inflammatory marker [24]. Okugawa *et al.* [25] showed that LCR may be an auxiliary parameter for postoperative treatment strategies in rectal cancer patients undergoing chemoradiotherapy. Yildirim *et al.* [26] reported that a low preoperative LCR level in incarcerated hernias can be used as a bioindicator to help predict intestinal ischemia. Ullah *et al.* [27] in a study conducted on patients with COVID-19 reported that low LCR values were an indicator of mortality in these patients. In our study, we examined LCR and NCR as an inflammatory marker to predict complications in patients with AA. As far as we know, there is no study about NCR predicting complications in patients with AA. Based on our findings, we observed that low LCR and NCR levels are a marker that can distinguish complications in patients with AA.

Our study had some limitations. First of all, our study was designed retrospectively, but the high number of patients compared with other similar studies increases the reliability of our results. Another limitation is that physical examination findings and symptoms could not be clearly identified due to the design of our study, and the time from symptom onset to sampling could not be examined. Multicenter and prospective studies are required to demonstrate the accuracy of the results in our study.

Conclusion

Low LCR and NCR levels at the time of admission to the emergency department are a biomarker that can predict complications in patients with AA (Tables 1–3).

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Conflicts of interest

There are no conflicts of interest.

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