

Role of laboratory markers in identifying the severity of acute appendicitis in geriatric patients

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ABSTRACT

Objectives: Objectives: The main aim of our study is to investigate the effectiveness of laboratory markers in geriatric patients diagnosed with acute appendicitis in the emergency department.

Methods: A total of 73 cases aged over 65 who underwent appendectomy were reviewed retrospectively. Age, sex, laboratory values of leukocyte count, neutrophil and lymphocyte values, platelets, serum sodium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP) and serum total bilirubin levels and pathological findings were investigated. The patients were divided into two different groups according to the pathology reports of appendicitis: complicated appendicitis (gangrenous/perforated appendicitis) (Group 1) and simple (uncomplicated) appendicitis (catarrhal or phlegmonous appendicitis) (Group 2).

Results: A significant difference was found between Groups 1 and 2 concerning age, WBC, CRP, neutrophil, leukocyte, total bilirubin levels and neutrophil/lymphocyte ratio (NPR), and platelet/lymphocyte ratio.(PLR) No statistically significant differences were found for platelets, Na, AST and ALT levels.

Conclusions: Elderly patients with complicated appendicitis often presented with higher WBC, CRP, total bilirubin, neutrophil, NLR and PLR levels, and lower lymphocyte levels. Moreover, these parameters are adjunctive data with a lower cost, easily available, and rapid markers which can be obtained in the emergency department.

Keywords: Appendicitis, complicated, geriatric, laboratory markers

Acute appendicitis (AA) is the most common abdominal emergencies that require emergency surgery (appendectomy) and are encountered in emergency departments. While the incidence of AA in all age groups in the population is 7%, the incidence of perforation in patients with AA varies between 17-20%. The mortality rate in the general population is below 1%, but this rate approaches 50% in the geriatric age group (> 60 years) [1, 2].

Several scoring systems have been proposed for the diagnosis of AA, such as the Alvarado score. These scoring systems were created based on the patient's physical examination findings, clinical characteristics, and laboratory data. In some cases, the classic signs and symptoms of appendicitis may not be seen. This makes it difficult to make a definitive diagnosis of AA. Predictors of acute appendicitis severity are urgently needed, as delayed diagnosis and treatment of severe

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appendicitis is associated with perforation, abscess formation, postoperative morbidity, mortality, and prolonged hospital stay [3, 4].

For this reason, it is important to identify geriatric patients at risk of complicated appendicitis as early as possible, as it will determine the type of further examination and treatment. Recently, some authors have stated the predictive value of laboratory markers for inflammation such as White blood cell count (WBC), neutrophil/lymphocyte ratio (NLR), platelet count (PLT), platelet/lymphocyte ratio (PLR), serum total bilirubin level, C reactive protein (CRP) level, serum sodium (Na), aspartate aminotransferase (AST), alanine aminotransferase (ALT), which can be practical as a diagnostic-parameters in the peri-operative predictor of diagnosing AA. By the reason of the advantageous cost-effectiveness of these tests [5-8], we wanted to investigate the effectiveness of laboratory markers in diagnosis in geriatric patients diagnosed with AA in the emergency department.

METHODS

The medical records of 73 cases aged over 65 at a single institution who underwent an open or laparoscopic appendectomy in our clinic and had histo-pathological results reported as AA were analyzed retrospectively. For each patient; the age; sex, laboratory values of WBC, neutrophil and lymphocyte values, PLT, Na, AST, ALT, CRP, serum total bilirubin levels, NLR, PLR, and pathological findings were investigated.

The 73 patients were separated into 2 groups according to the pathological grade of AA: complicated AA (gangrenous/perforated) (Group 1) and simple (uncomplicated) AA (catarrhal/phlegmonous) (Group 2). We evaluated the pre-operative factors we identified between the groups and analyzed the risk parameters for complicated AA by multivariate analysis. Exclusion criteria were the presence of mortality, malignancy, the current course of oncological treatments, intra-operative diagnosis of other abdominal pathologies and presence of known liver or kidney diseases.

This study was approved by the Clinical Research Ethics Committee, informed consent was obtained from all patients and all procedures in this study involving human participants were performed in accor-

dance with the 1964 Helsinki Declaration and its later amendments.

Statistical Analysis

The conformity of continuous variables to the normal distribution was evaluated using the Shapiro-Wilk test. Continuous variables were expressed as mean \pm standard deviation if the data followed the normal distribution and median (25th percentage-75th percentage) values if the data did not follow the normal distribution. The Mann-Whitney-U test and independent samples t-test were used for continuous variables to compare groups. The chi-square test was used to compare the gender distribution between the groups. In order to estimate the sensitivity and specificity of the NLR ratio for predicting the presence of complicated appendicitis, receiver operator characteristic (ROC) curve analysis was performed. The SPSS program (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was used for statistical analysis, and the type I error rate was set at 5%.

RESULTS

A total of 73 patients who underwent appendectomies between January 2017-August 2021 were included. The median age was 74 years (25th percentage: 70 years – 75th percentage: 80 years) in Group 1 and 69.50 years (25th percentage: 66 years - 75th percentage: 73.25 years) in Group 2 (Table 1). The median age was found to be higher in Group 1 ($p = 0.020$). In Group 1; 48.70% ($n = 19$) of the participants were female and 51.30 ($n = 20$) were male. In Group 2; 32.40% ($n = 11$) were female and 67.60% ($n = 23$) were male. When compared in terms of gender, it was revealed that there was no significant difference between the groups. ($p = 0.156$) (Table 1).

Group 1 had a significantly higher median value in total bilirubin level compared to Group 2 ($p = 0.003$). Mean WBC and neutrophil levels were also found to be higher in Group 1 ($p = 0.003$ and $p = 0.006$), whereas the mean lymphocyte level was found to be higher in Group 2 ($p < 0.001$). The mean N/L level was significantly higher in Group 1 ($p < 0.001$). There was no difference between the groups according

Table 1. Comparison of the two groups

	Group 1 (n = 39)	Group 2 (n = 34)	p value
Age (years), median (IQR)	74 (70- 80)	69.5 (66-73.25)	0.020
Female, n (%)	19 (48.7%)	11 (32.4%)	0.156
Total Bilirubin (mg/dL)	1.22 (0.77-1.79)	0.81 (0.53-0.97)	0.003^a
WBC ($\times 10^3/\text{mm}^3$)	14.49 \pm 3.99	11.06 \pm 3.92	0.003^b
Neutrophil count ($\times 10^3/\text{mm}^3$)	11.73 \pm 4.03	9.05 \pm 4.06	0.006^b
Lymphocyte count ($\times 10^3/\text{mm}^3$)	1.20 \pm 0.41	1.84 \pm 0.66	< 0.001^b
Neutrophil / Lymphocyte ratio	10.16 (6.50-15.14)	5.17 (3.12-8.24)	< 0.001^a
PLT ($\times 10^9/\text{L}$)	241 (183-296)	238 (176-276)	0.682 ^a
Platelet/ Lymphocyte ratio	200 (153.96-266.25)	134.58 (95.10-181.25)	< 0.001^a
CRP (mg/dL)	101 (83-169)	35.40 (17.68-77.50)	< 0.001^a
Na (mEq/L)	137.39 \pm 4.14	137.79 \pm 5.04	0.704 ^b
AST (U/L)	22 (16-31)	20 (18-28.25)	0.553 ^a
ALT (U/L)	13 (11-21)	16.50 (12-21.25)	0.482 ^a

Data were presented as median (25th percentile – 75th percentile) and mean \pm standard deviation. WBC = White Blood Cell, PLT = platelet, CRP = C-reactive protein, Na = Sodium, AST = aspartate aminotransferase, ALT = alanine aminotransferase
^aMann-Whitney U Test, ^bIndependent Samples t-Test

to PLT level ($p = 0.682$), but PLR and CRP levels were higher in Group 1 ($p < 0.001$ and $p < 0.001$). There was no significant difference between the two groups in the median of Na, AST, and ALT levels ($p > 0.05$) (Table 1).

ROC curve analysis was performed to forecast the sensitivity and specificity of NLR for predicting the

presence of complicated appendicitis, and the cut-off point for NLR was determined as >5.85 . The area under the curve for NLR was 0.81 (sensitivity 84.60%, specificity 64.70%, $p < 0.001$), showing that a NLR > 5.85 was significantly related to an increased risk of the presence of complicated appendicitis (Fig. 1).

To determine the risk factors that may affect the

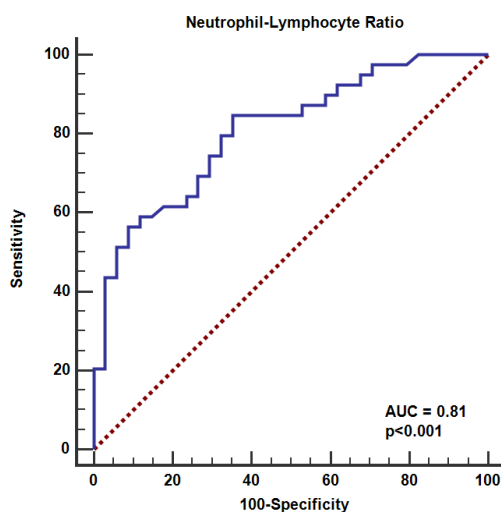


Fig. 1. Receiver-operator characteristic (ROC) curves for determining the presence of complicated appendicitis. The area under the curve (AUC) for Neutrophil to Lymphocyte Ratio (NLR) is 0.81 with $p < 0.001$

Table 2. Risk factors affecting of complicated appendicitis

	Wald	<i>p</i> -value	OR	95% CI	
				Lower	Upper
Total bilirubin	4.74	0.029	4.41	1.16	16.75
Lymphocyte	7.16	0.007	0.02	0.01	0.34
CRP	12.44	< 0.001	1.06	1.03	1.10

OR = Odds ratio, CI = Confidence Interval, CRP = C-reactive protein

Model Significance: $\chi^2 = 66.86$; $p < 0.001$, Hosmer & Lemeshow Test: $p = 0.809$

patients with complicated appendicitis, age, gender, and the variables given in Table 1 were first examined with univariate logistic regression analysis, and the variables were analyzed with multivariable logistic regression analysis. The forward selection approach was selected as the variable selection method in the analysis, and the final step's findings are given in Table 2.

When the results of the analysis were examined, it was found that the logistic regression model obtained in the final step was compatible with the data ($p = 0.809$) and the logistic regression model was also statistically significant ($p < 0.001$). As a result of the analysis, it is predicted that a one-unit increase in the total bilirubin level will increase the risk of complicated appendicitis 4.41 times. An increase of 1 unit in the lymphocyte level is predicted to reduce the risk of complicated appendicitis by 98%. On the other hand, CRP level was also determined as a risk factor that may affect the formation of complicated appendicitis, and it was determined that an increase of 1 unit in the CRP level would increase the risk of complicated appendicitis 1.03 times.

DISCUSSION

AA is one of the most prevalent causes of abdominal pain and emergency surgery. The mechanism of AA formation is in the form of inflammation of the vermiform appendix's lumen resulting from an obstruction. This obstruction can be caused by lymphoid hyperplasia (mostly in young patients), a fecalith, parasitic infection, or a tumor (carcinoid, adenocarcinoma or metastatic). Depending on its clinical forms, AA is divided into two groups: uncomplicated and compli-

cated. Uncomplicated (simple) appendicitis is characterized by the absence of perforation or abscess; complicated AA is the result of rupture of the appendix with or without abscess formation. Appendicitis can develop in patients of any age, but it is most commonly seen in patients between the ages of 10-30 [9]. Simple AA is most common in younger patients, but complicated AA is more common in very old and very young patients. Babies and young children often have a significant delay in evaluation, diagnosis, and treatment. The main reason is that they cannot specify pain symptoms like an adolescent/adult. Similar latency may occur for elderly patients because of cognitive deficits (such as dementia) or the reduced ability to sense and localize pain due to age-related changes in pain receptors [10]. Objective criteria, such as laboratory parameters, are needed to determine diagnostic parameters in geriatric AA patients. The main reason for this is that appendiceal perforation, formation of abscess, and pan-peritonitis are still common in elderly patients with AA. In this study, we investigated the value of several laboratory markers that are frequently used in the clinic and easily accessible in terms of their usability in the prediction of complicated AA in the elderly.

In acute appendicitis, the usual presentation involves leucocyte counts of between 10-18000 /mm³. Rarely, do they have moderate polymorphonuclear-Leucocytosis dominance (left shift). WBC in uncomplicated appendicitis cases is rarely greater than 18000. If they do reach this level, then appendicitis should be considered perforated or complicated [7]. The high mortality rate in the elderly due to AA is usually attributed to the delayed diagnosis and treatment of the condition and concomitant diseases. This is one

of the reasons why the mortality rate in the elderly is higher than in younger patients. Classical symptoms in geriatric patients may not be very clear. Physical examinations are generally not very obvious. Abdominal distension is usually seen. In about 30% of cases, appendiceal perforation can only be detected intraoperatively. Therefore, early surgical treatment is recommended in suspected cases of AA [11].

Previous studies have reported that levels of CRP were correlated with the severity of appendiceal inflammation and may be precise in predicting complicated appendicitis. On the other hand, various studies revealed that CRP levels and WBC counts are not sensitive and specific to describe between simple / complicated appendicitis [12, 13]. We evaluated in our study that both WBC counts and CRP levels were significantly higher in patients with complicated appendicitis compared with simple appendicitis.

The systemic inflammatory response may lead to lymphocytopenia or neutrophilia. This may lead to an increase in NLR and PLR, which are markers of inflammation in appendicitis. In addition, changes in platelet count are thought to be comprised of the inflammatory process. PLR, and NLR are inflammatory markers. Their advantageous features are that they can be easily calculated from the blood count, and they are simple, cost-effective, and non-invasive.

Ishizuka *et al.* [14] established a cut-off value of 8.0 for the NLR to distinguish gangrenous AA from catarrhal AA. Kahramanca *et al.* [15] reported a cut-off value of 5.74 to differentiate complicated appendicitis from simple appendicitis. In the present study, NLR cut-off value was 5.85 for differing complicated appendicitis from simple appendicitis. In these studies, patients in all age groups were calculated. Yavuz *et al.* [7] stated that NLR can be used to diagnose acute appendicitis in the geriatric patient group. In our study, we think that NLR is also effective in demonstrating complicated appendicitis in the geriatric age group. Despite conflicting recommendations regarding cut-off values, we believe that NLR is an important parameter in the diagnosis of acute appendicitis and in differentiating complicated cases. There was no significant difference in platelet count between patients with complicated and simple appendicitis, but higher PLR was reported in patients with complicated appendicitis.

Hyperbilirubinemia and cholestasis occur in sys-

temic infections caused by various diseases, diseases such as generalized peritonitis and sepsis. It has been previously established as a predictive factor for AA [16, 17]. Sevinc *et al.* [6] reported that hyper-bilirubinemia (> 1.0 mg/dL) was significantly associated with perforated appendicitis. Eren *et al.* [18] found that hyper-bilirubinemia (>1.2 mg/dL) was related to complicated AA. In our study, hyperbilirubinemia is significantly associated with complicated appendicitis.

We also analyzed and compared Na, ALT - AST levels between simple and complex groups. The results showed that these parameters did not differ significantly between the two groups.

Limitations

There were some limitations of our study. The most important of these are that our study was retrospective, the number of patients was limited and it was a single-center study.

CONCLUSION

Our study suggested that elderly patients with complicated appendicitis often presented with higher WBC, CRP, total bilirubin, neutrophil and PLR, NLR levels, and lower lymphocyte levels. It has been shown that there is currently no simple but perfect test for diagnosing and recognizing complicated appendicitis. However, an increase in NLR can be considered a highly reliable indicator for the diagnosis of complicated appendicitis in geriatric patients. Moreover, these parameters are adjunctive data with a lower cost, easily available, and rapid markers which can be obtained in the emergency department. We recommend that clinicians use these values with the results of physical examination and imaging studies to define high-risk geriatric appendicitis patients earlier.

Authors' Contribution

Study Conception: SA, MA; Study Design: SA, MFE; Supervision: MFE, NDT; Funding: SA, MA, SŞ; Materials: SŞ, MHB; Data Collection and/or Processing: MA, SŞ, MHB; Statistical Analysis and/or Data Interpretation: SA, MFE, MHB; Literature Review: SA, MA, NDT; Manuscript Preparation: SA, MA and Critical Review: MFE, NDT.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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