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Diagnostic Value of Basic Laboratory Parameters in the Diagnosis of Complicated Appendicitis

Komplike Apandisitin Belirlenmesinde Temel Laboratuvar Parametrelerinin Tanısal Değeri

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ABSTRACT

In this investigation, we sought to examine the efficacy of laboratory parameters in predicting complicated appendicitis in patients who had surgery for acute appendicitis. 153 patients who underwent appendectomy were included and whose pathological results showed acute appendicitis. The patients were divided into two groups based on pathology findings and surgical findings: simple and complicated appendicitis groups. The patients' age, gender, preoperative leukocyte count, neutrophil count, neutrophil percentage, neutrophil–lymphocyte ratio, erythrocyte distribution width, mean platelet volume, and C-reactive protein levels were recorded. The simple and complicated appendicitis groups comprised 97 and 56 patients, respectively. Patients with complicated appendicitis were older on average than those with simple appendicitis (p=0.007). In the complicated appendicitis group, leukocyte count (p<0.001), neutrophil count (p=0.007), neutrophil percentage (p<0.001), neutrophil–lymphocyte ratio (p<0.001), and C-reactive protein levels (p<0.001) were significantly higher than in the simple appendicitis group. In terms of erythrocyte distribution width and mean platelet volume, there were no statistically significant differences between the groups. The cut-off values for age, leukocyte count, neutrophil count, neutrophil percentage, neutrophil–lymphocyte ratio, and C-reactive protein levels were 24.5/years, 12.500/µL, 9.950/µL, 78.15%, 4.98, and 0.29 mg/dL, respectively. Logistic regression analysis showed that age (OR: 1.036), neutrophil count (OR: 14.934), and C-reactive protein levels (OR: 4.225) are independent risk factors for the diagnosis of complicated appendicitis. Thus, age, neutrophil count, and C-reactive protein levels may be used as auxiliary parameters to differentiate between simple and complicated appendicitis.

Keywords: Abdominal pain, Acute appendicitis, Complicated, C-reactive protein

ÖZET

Bu çalışmanın amacı akut apandisit nedeni ile opere edilen hastalarda laboratuvar parametrelerinin komplike apandisit öngörülmesindeki etkinliğini araştırmaktır. Appendektomi uygulanmış ve patoloji sonucu akut apandisit olarak bildirilen 153 hasta çalışmaya dahil edildi. Hastalar patoloji sonuçları ve operasyon bulgularına göre basit ve komplike apandisit olarak iki gruba ayrıldı. Hastalara ait yaş, cinsiyet, operasyon öncesi lökosit sayısı, nötrofil sayısı, nötrofil yüzdesi, nötrofil-lenfosit oranı, eritrosit dağılım genişliği, ortalama trombosit hacmi ve C-reaktif protein değerleri kaydedildi. Basit apandisit grubunda 97, komplike apandisit grubunda 56 hasta mevcuttu. Her iki grupta da erkek cinsiyet ön planda idi. Komplike apandisit gubunda yaş daha ileri idi (p=0.007). Lökosit sayısı (p<0.001), nötrofil sayısı (p=0.007), nötrofil yüzdesi (p<0.001), nötrofil-lenfosit oranı (p<0.001) ve C-reaktif protein (p<0.001) komplike apandisit grubunda istatistiksel olarak anlamlı fark oluşturacak şekilde yüksek tespit edildi. Eritrosit dağılım genişliği ve ortalama trombosit hacmi için gruplar arasında anlamlı fark yoktu. Kesim değerleri yaş için 24.5/yıl, lökosit sayısı için 12500/µL, nötrofil sayısı için 9950/µL, nötrofil yüzdesi için % 78.15, nötrofil-lenfosit oranı için 4.98 ve C-reaktif protein için 0.29 mg/dl olarak hesaplandı. Lojistik regresyon analizinde yaş (OR:1.036) nötrofil sayısı (OR: 14.934) ve C-reaktif protein (OR: 4.225) komplike apandisit tanısı için bağımsız risk faktörleri olarak tespit edildi. Yaş, nötrofil sayısı ve C-reaktif protein basit-komplike apandisit ayrımında yardımcı parametreler olarak kullanılabilir.

Anahtar Kelimeler: Akut apandisit, C-reaktif protein, Karın ağrısı, Komplike

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INTRODUCTION

The most frequent cause of acute abdomen that necessitates surgical intervention is acute appendicitis (AA).[1] Approximately 7%–8% of the population is diagnosed with AA throughout their life.[2,3] Physical examination, laboratory values, and imaging methods such as ultrasonography (USG), and computed tomography (CT) are effective in the diagnosis of AA.[4] Although the most effective treatment is appendectomy, there are studies on the effectiveness of antibiotic therapy in specific patients.[5-7]

Imaging methods such as USG and CT are commonly used; therefore, the diagnosis of AA can usually be made more easily.[8,9] However, there are patients who have been treated for AA and found to have a normal appendix or who developed complications such as perforation and abscess due to the late diagnosis of AA.[10] In addition, there are cases wherein access to imaging methods is not always available.[11] For all such reasons, there has always been a search for cheap and practical biochemical markers that are easily accessible for the diagnosis of AA. In this regard, leukocyte count (WBC), neutrophil count, neutrophil percentage, lymphocyte count, neutrophil–lymphocyte ratio (NLR), platelet count, other platelet-related parameters, and C-reactive protein (CRP) levels, which are easily accessible by routine hemogram tests, have frequently been studied.[2,12] In this study, we sought to assess the diagnostic value of WBC, neutrophil count, neutrophil percentage, NLR, erythrocyte distribution width (RDW), mean platelet volume (MPV), and CRP levels in differentiating simple appendicitis (SA) and complicated appendicitis (CA) as well as to investigate their effectiveness in predicting CA in patients who were operated for AA.

METHODS

In this single-center retrospective study, we included patients who underwent appendectomy in the İdil State Hospital between November 6, 2018 and December 31, 2019. The patients' written consent could not be taken due to the retrospective design of the study and the anonymity of data. The patient files were scanned using the hospital information system and the demographic characteristics, laboratory values (WBC, neutrophil count, neutrophil percentage, NLR, RDW, MPV, and CRP levels), surgical findings, and pathological results were recorded. The diagnosis of AA was made based on the patient history, physical examination, laboratory values, and imaging methods. We included patients who underwent appendectomy and whose pathological results showed AA. We excluded the following patients: 1) who underwent appendectomy but were reported to have normal appendix based on the pathological results; 2) who were diagnosed with autoimmune disease, chronic inflammatory disease, hematological disease, or cancer; 3) who were pregnant and operated for AA; and 4) who received steroid and anticoagulant treatment. We finally included a total of 153 patients who were seperated into two groups based on the pathological reports and surgical findings. Patients who were reported to have severe adhesion with peripheral tissues during surgery, those who had inflammation or perforation, or whose pathological results showed gangrene, necrosis, or phlegmon were included in the CA group and the others were included in the SA group.

SPSS 18.0 program was used to interpret the statistical results. Chi-square test was used for analyzing the correlation between categorical variables and outputs as well as for descriptive statistics such as median, range, and percentage. The Kolmogorov–Smirnov test was used to decide if the research data distribution was natural. The distribution of all variables was analyzed one by one. Non-parametric tests were performed because the parameters were not normally distributed. The non-normally distributed findings were interpreted using the Mann–U Whitney test. Multiple logistic regression analyses were performed to determine the effect of independent variables showing significant correlation with dependent variables in single analysis on the dependent variables. Hosmer–Lemeshow test was used for model adaptation. To evaluate diagnostic precision, the receiver operating characteristic (ROC) curve analysis was used. The cut-off values for parameters were determined with an area under the curve (AUC) of >0.600. In addition, the sensitivity and specificity values were calculated. The conditions with a type-1 error level of <5% were deemed statistically significant.

RESULTS

We included a total of 153 patients; 97 (63.4%) and 56 (36.6%) in the CA and SA groups, respectively. The proportion of male patients was higher in both the groups. The median age was 24 (17.5-33.5) years; 22 (16-30) and 29 (20.25-38.75) years in the SA and CA groups, respectively. In terms of age, there was a significant difference between the groups (p=0.007; Table 1).

Table 1. Patients' age, gender, WBC, neutrophil count, neutrophil percentage, NLR, RDW, MPV, CRP levels, and distribution by groups

Parameters	All of the patients	Simple appendicitis	Complicated appendicitis	P value
Number of cases	153	97 (63.4%)	56 (36.6%)	-
Age †	24 (17.5-33.5)	22 (16-30)	29 (20.25-38.75)	**0.007**
Gender ‡				
Male	90 (58.8%)	53 (58.9%)	37 (41.1%)	0.166
Female	63 (41.2%)	44 (69.9%)	19 (30.1%)	
WBC*10^3/µL †	11.9 (7.9-15)	10 (7-12.9)	14 (11.9-15.8)	**<0.001**
Neutrophil count*10^3/µL†	9.4 (5.5-12.1)	7.2 (4.2-10.6)	11.3 (9.4-12.9)	**0.007**
Neutrophil percentage (%) †	77.5 (67.3-84.2)	73.2 (60.5-81.25)	81.7 (76.7-85.6)	**<0.001**
NLR †	4.83 (2.92-8.5)	3.85 (1.89-6.75)	6.51 (4.62-9.75)	**<0.001**
RDW (%) †	12.7 (12.4-13.2)	12.7 (12.3-13.2)	12.8 (12.5-13.2)	0.062
MPV (fL) †	8.1 (7.5-8.75)	8,1 (7.5-8.75)	8.05 (7.4-8.7)	0.921
CRP (mg/dL) †	0,2 (0.2-1.1)	0,2 (0.2-0.6)	0.89 (0.2-4.3)	**<0.001**

†: median (IQR), ‡: n (%); WBC: leukocyte count; NLR: neutrophil–lymphocyte ratio; RDW: erythrocyte distribution width MPV; mean platelet volume; CRP: C-reactive protein.

Table 2. ROC analysis results and cut-off values

	Cut-off value	Sensitivity (%)	Spesifity (%)	AUC	95% CI (min-max)	P value
Age (years)	24.5	57.1	57.7	0.631	0.541-0.722	**0.007**
WBC	12.5*10^3/µL	64.3	71.1	0.716	0.634-0.799	**<0.001**
Neutrophil count	9.95*10^3/µL	69.6	70.1	0.732	0.652-0.812	**<0.001**
Neutrophil percentage	78.15	62.5	62.9	0.709	0.628-0.790	**<0.001**
NLR	4.98	62.5	62.9	0.721	0.642-0.801	**<0.001**
CRP (mg/dL)	0.29	67.9	66	0.706	0.619-0.794	**<0.001**

AUC: area under the curve; CI: Confidence interval; WBC: leukocyte count; NLR: neutrophil–lymphocyte ratio; CRP: C-reactive protein.

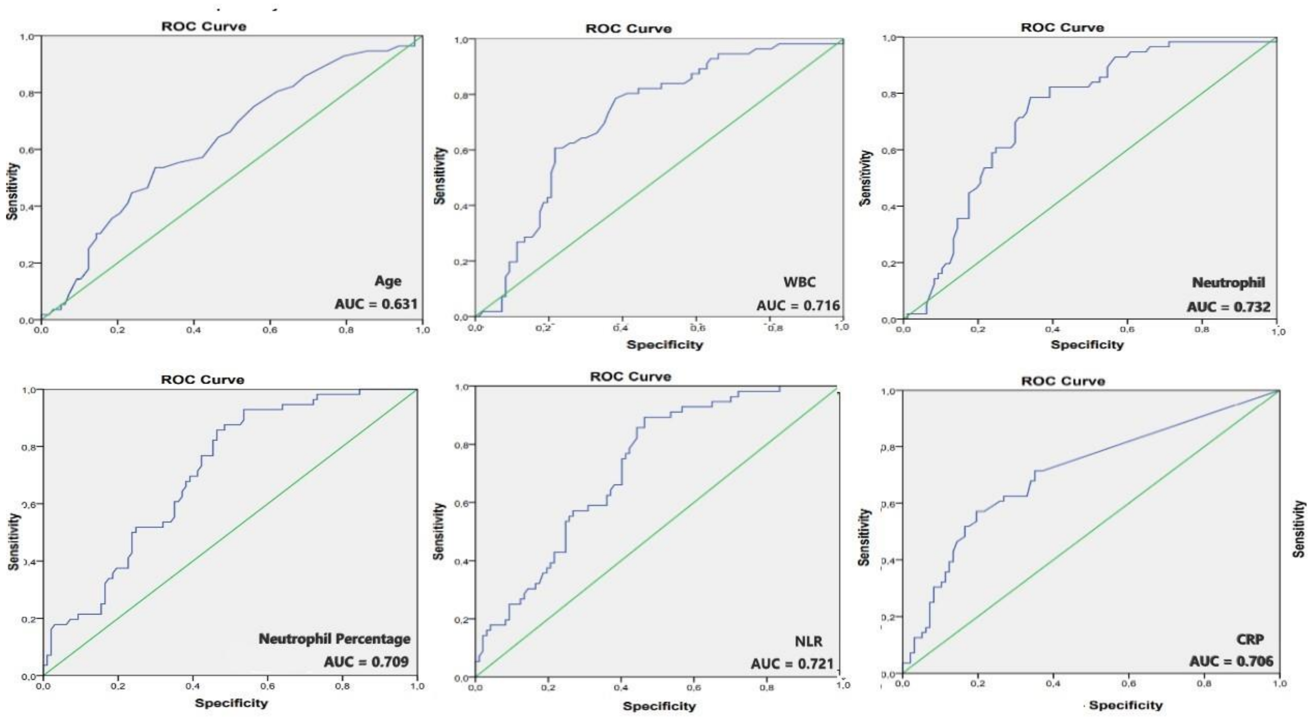

Figure 1. ROC curves for age, WBC, neutrophil count, neutrophil percentage, NLR and CRP

Table 3. Logistic regression analysis results involving age, WBC, neutrophil count, neutrophil percentage, NLR, and CRP parameters

	OR	95% CI (min-max)	P value
Age	1.036	1.002-1.072	**0.038**
WBC	0.503	0.115-2.197	0.361
Neutrophil count	14.934	2.559-87.140	**0.003**
Neutrophil percentage	1.072	0.065-17.668	0.961
NLR	0.671	0.041-11.074	0.781
CRP	4.225	1.851-9.643	**0.001**

OR: Odds ratio; CI: Confidence interval; WBC: leukocyte count; NLR: neutrophil–lymphocyte ratio; CRP: C-reactive protein.

WBC, neutrophil count, neutrophil percentage, NLR, RDW, MPV, and CRP levels are represented in Table 1. WBC (p<0.001), neutrophil count (p=0.007), neutrophil percentage (p<0.001), NLR (p<0.001), and CRP level (p<0.001) were significantly higher in the CA group than in the SA group. Further, RDW was higher in the CA group, but with no significant difference (p=0.062). In addition, the MPV values were similar in both the groups (p=0.921).

The ROC analysis was performed on the parameters found to be significantly different between the groups, and the parameters that were successful in predicting CA were determined. Those with an AUC of >0.6 in the ROC curve were considered to be successful. AUC values for age, WBC, neutrophil count, neutrophil percentage, NLR, and CRP levels were 0.631, 0.716, 0.732, 0.709, 0.721, and 0.706, respectively. The cut-off values for these parameters were estimated by considering the optimum sensitivity and specificity values. In the ROC analysis, the cut-off values were determined for age (24.5/year, sensitivity: 57.1%, specificity: 55.7%), WBC (12.500/µL sensitivity: 64.3%, specificity: 71.1%), neutrophil count (9.950/µL, sensitivity: 69.6%, specificity: 70.1%), neutrophil percentage (78.15%, sensitivity: 62.5%, specificity: 62.9%), NLR (4.98, sensitivity: 62.5% specificity: 62.9%), and CRP level (0.29 mg/dL, sensitivity: 67.9%, specificity: 66%). The ROC analysis results are provided in Table 2 and the ROC curves are presented in Figure 1.

Logistic regression analysis was performed for age, WBC, neutrophil count, neutrophil percentage, NLR, and CRP levels. Age (OR: 1.036, 95% CI: 1.002-1.072, p=0.038), neutrophil count (OR: 14.934; 95% CI: 2.559-87.140, p=0.003), and CRP level (OR: 4.225, 95% CI: 1.851-9.643, p=0.001) were independent risk factors for the diagnosis of CA. Additionally, WBC, neutrophil percentage, and NLR were found to be insignificant in the logistic regression analysis (Table 3). Hosmer–Lemeshow test used for model adaptation revealed that the predictive value of the model was high (p=0.635).

DISCUSSION

Acute appendicitis is a common condition encountered by surgeons.[1,13] Patients who are reported to have severe adhesion with peripheral tissues during the surgery, who have inflammation or perforation, or whose pathological results show gangrene, necrosis, or phlegmon are considered to have CA.[1,14] It is rare in patients with CA; however, complications such as abscess, peritonitis, ileus, or wound site infection may develop.[13,15,16] In the present study, we aimed to determine the basic and distinctive characteristics of SA and CA in terms of basic laboratory parameters in patients who are operated for AA.

In our study, the majority of patients in the SA and CA groups were male. In addition, the patients were significantly older in the CA group. In contrast, previous studies have reported that appendicitis generally is common in both genders, regardless of its severity, and there is no correlation between gender and appendicitis severity [14,16,17,18]; however, there are some exceptions.[4] Regarding age and severity of appendicitis, studies have reported that age is higher in CA groups.[14,15] In some studies, the correlation between advanced age and CA has also been statistically proven.[10,19,20] There are also studies reporting that age is lower in CA groups.[11]

Generally, WBC is significantly higher in CA group than in SA groups.[11,14,18,20] In some studies, WBC failed to differentiate between SA and CA.[21,22] In our study, WBC was higher in the CA group (p<0.001). Regression analysis revealed that WBC was not successful (p=0.361). The cut-off value for WBC in CA in the literature varies between 12.500 and 14.870/µL.[4,13,23] In these studies, the sensitivity and specificity values varied between 66.7%–86.1% and 41.6%–68.1%, respectively.[4,13,23] In the present study, the cut-off value was 12.500, sensitivity was 64.3% and specificity was 71.1%, which is consistent with the literature.

Neutrophil count and neutrophil percentage are generally increased in AA. There is no such consensus in the studies on CA. Ishizuka et al. reported that neutrophil count was not successful in predicting gangrenous appendicitis.[19] Another study performed to differentiate between gangrenous appendicitis and AA reported that neutrophil percentage is not significantly different between the groups.[24] In another study on the diagnosis of AA and differentiation of CA, neutrophil percentage was a significant parameter in the diagnosis of AA, and no significant difference was found between complicated and SA groups in terms of neutrophil percentage.[14] In contrast, there are studies reporting that neutrophil count [11,25] and neutrophil percentage [1,10,11] are significantly higher in CA groups. In our study, both neutrophil count and neutrophil percentage were significantly higher in the CA group. Logistic regression analysis revealed that neutrophil count is an independent risk factor for CA, but the same did not apply to neutrophil percentage. Al-gaithy et al. reported that the cut-off value for neutrophil count in differentiating between CA and inflammatory appendicitis is 7.540/µL (sensitivity: 81.2%, specificity: 65.5%).[25] In a study comparing patients with acute gangrenous appendicitis and healthy controls, the cut-off value for neutrophil percentage was 69.5% (sensitivity: 92.5%, specificity: 96.9%).[1] In another study comparing patients with pediatric SA and CA, the cut-off value for neutrophil percentage was 76% (sensitivity: 97.2%, specificity: 32.2%).[13] In our study, the cut-off value for neutrophil count was 9.950/µL (sensitivity: 70.1%, specificity: 73.2%; AUC=0.732) and neutrophil percentage was 78.15% (sensitivity: 62.5%, specificity: 62.9%). Although the sensitivity and specificity values for WBC, neutrophil count, and neutrophil percentage are high in some studies, they are so low in most of them; thus, they are not considered as excellent independent variables in differentiating between SA and CA.

In inflammatory events, neutrophil count is increased, but lymphocyte count is decreased, leading to increased NLR. NLR is a variable that can be simply calculating from the complete blood count. There are several studies have reported that NLR is a successful parameter in the diagnosis of AA and differentiation of CA.[2,18,19,26-28] The cut-off value for NLR in the diagnosis of CA varies between 5.47 and 6.94.[4,11,23,26] In these studies, the sensitivity and specificity values varied between 61.1%–78.42% and 48.5%-70.33%.[4,11,23,26] In a study comparing patients with pediatric SA and CA, NLR was 10.4 (sensitivity: 73.2%, specificity: 61.1%).[13] In our study, NLR was significantly higher in the CA group than in the SA group, which is consistent with the literature. NLR was not significant in logistic regression analysis. The cut-off value for NLR was 4.98 (sensitivity: 62.5%, specificity: 62.9%). Despite different cut-off values in many studies, NLR is a significant parameter in differentiating between SA and CA. It should be noted that NLR may increase in many inflammatory events and its sensitivity and specificity are insufficient to differentiate between acute and CA. There are limited studies reporting the negative results for NLR. According to one study, NLR is a significant variable in the AA diagnosis; however, there was no statistically important variation in the differentiation of CA.[15] Aktimur et al. compared AA and normal appendicitis groups and reported that NLR is higher in the AA group, but statistically significant.[29] RDW is routinely studied in complete blood count, and it expresses how much the volume of circulating erythrocytes varies. RDW is an inflammatory parameter and RDW levels vary in many inflammatory events.[4,30,31] RDW was not successful in differentiating between SA and CA in three studies.[4,13,22] Gunay et el. reported that the RDW value is significantly higher in the CA group than in the appendicitis group, and it has an independent diagnostic value in CA.[11] In our study, RDW was higher in the CA group, but there was no significant difference between the groups, which is consistent with the literature. MPV is a parameter obtained from routine blood count. MPV decreases in acute inflammatory events and increases in chronic inflammatory events.[1,18,29] Literature review has also shown different results in terms of MPV in CA. In two different studies, MPV was significantly lower in CA.[1,12] Aydogan et al. reported that MPV is significantly higher in perforated appendicitis than in non-perforated appendicitis.[20] Similarly, there was no significant difference between patients with SA and CA in terms of MPV in various studies, which is consistent with our study.[11,13,15] CRP is an acute phase protein and CRP levels increase in many inflammatory events.[10] The use of CRP along with other inflammatory parameters and the physical examination findings in the diagnosis of AA and CA increase the success rates.[10]

A study comparing patients with perforated and non-perforated AA showed that WBC, CRP, and bilirubin levels are significantly higher in the perforation group and are the strongest parameters in terms of the determination of perforation.[32] In another study, although there was no statistical difference in terms of CRP levels in differentiating between AA and normal appendicitis, increased CRP level was an independent factor in predicting complications in patients with AA. The cut-off value for CRP has been found to be 25.5 mg/dL (sensitivity: 63.8%, specificity: 58.2%).[4] In another study comparing patients with CA and SA, the cut-off value for CRP was 10.5 mg/dL (sensitivity: 65.2%, specificity: 70.59%).[23] Ayrik et al. found the cut-off value for CRP to be 4.59 mg/dL (sensitivity: 66%, specificity: 69.6%).[21] Although CRP level is generally successful in differentiating CA, there are studies reporting opposite results.[15,22] In our study, CRP was significantly higher in the CA group, which is consistent with the literature. The cut-off value for the differentiation between CA and SA (0.29) was lower than that reported in the literature. However, the sensitivity and specificity values were consistent with the literature. In regression analysis, we found CRP to be an independent risk factor for CA. In logistic regression analysis, all significant variables were included in the model and all variables associated with each other, which eliminates the possibility of random significance. Logistic regression analysis performed in our study for age, WBC, neutrophil count, neutrophil percentage, NLR, and CRP levels revealed that only age, neutrophil count, and CRP levels are successful in predicting CA. Our study's key drawbacks are its retrospective existence and the small number of patients. In addition, information such as the duration of admission and the onset of symptoms are not available. However, it is considered that our study contains useful information about the diagnostic accuracy of basic laboratory parameters in terms of differentiating between CA and SA. Averaging consecutive values instead of a single value in the laboratory values may yield more beneficial results. In addition, the time of tests before operations results in change in some results; if it is possible to standardize them, more valuable results may be obtained.

CONCLUSION

Physical examination, laboratory values, and imaging methods are helpful in the diagnosis of AA and the determination of its severity. The biochemical markers analyzed in our study can assist surgeons make more precise decisions in the following uncommon situations: 1) that imaging methods can only be accessed partially or at specific times for technical reasons; 2) patient suitability for conservative treatment for surgeons who prefer conservative treatment in AA; and 3) limited use of radiological imaging methods for pregnant, pediatric, and patients with additional problems. Presently, there is no excellent laboratory value that can be used alone in the detection of AA and the distinction of CA without the need for imaging methods. In addition, age, neutrophil count, and CRP levels may be a guide for differentiating between SA and CA.

Authorship contribution statement

Consept and desing: MU, AU, ST.

Acquisition of data: MU, AU.

Analysis and interpretation of data: MU, AU, ST.

Drafting of the manuscript: MU, ST.

Critical revision of the manuscript for important Intellectual content: MU, AU, ST.

Statistical analysis: MU, AU.

Supervision: MU, ST.

Declaration of competing interest

None of the authors have potential conflicts of interest to be disclosed.

Ethical approval

Ethics committee approval was received for this study from Ethical Committee for Clinical Studies, Karadeniz Technical University, Faculty of Medicine, 2020/163 (2020/163).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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