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C-reactive protein/albumin ratio greater than 7.1 is a good candidate to be used as an inflammation biomarker to predict perforation in appendicitis

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Abstract. – OBJECTIVE: We aimed at identifying novel biomarkers to predict perforation in patients with acute appendicitis.

PATIENTS AND METHODS: Medical records of patients who underwent appendectomy due to acute appendicitis were reviewed. Complete blood count and biochemistry panel results of these patients were analyzed. This study included 58 patients, 42 (72.4%) male and 16 (27.6%) female. The mean age of the patients was 33.8±14.1 years (range: 18-75). 49 (84.5%) patients had non-perforated acute appendicitis. Perforated acute appendicitis was observed in 9 (15.5%) patients.

RESULTS: Patients with perforated appendicitis had higher appendiceal diameter, C-reactive protein (CRP) level, CRP/albumin and monocyte/lymphocyte (M/L) compared to patients with non-perforated appendicitis. Moreover, patients with perforated appendicitis had lower lymphocyte count than those with no perforation. Sensitivity rates of appendiceal diameter, CRP level, CRP/Albumin and M/L for perforated appendicitis were similar (89%). However, the most specific biomarker for perforation was CRP/albumin (87.8%), followed by CRP (85.7%), M/L (63.3%) and appendiceal diameter (57.1%). Patients with CRP/albumin>7.1, CRP>32.7 mg/L, M/L>0.44 and appendiceal diameter>9.8 mm were most likely to have appendiceal perforation.

CONCLUSIONS: We suggest that CRP/albumin, CRP, M/L, appendiceal diameter and lymphocyte count can be used to predict perforation in patients with acute appendicitis. However, the most specific inflammation biomarker indicating perforated acute appendicitis is CRP/Albumin>7.1.

Key Words:
Appendicitis, Biomarker, Blood count, Inflammation, Perforation.

Introduction

Acute appendicitis is the most common abdominal emergency with a lifetime risk of 8.6% in men and 6.7% in women[1,2]. Appendicitis is the inflammation of the appendix, which usually occurs as a result of luminal obstruction. The exact cause of acute appendicitis remains unclear. The most important complication of acute appendicitis is perforation since it may result in abscess, peritonitis and sepsis. Perforation has been reported in up to 32% of the patients with acute appendicitis[1].

Appendicitis is generally treated with appendectomy. However, the use of antibiotics has been reported to be effective in the management of uncomplicated appendicitis[3]. Antibiotic treatment was found to be successful in 91% of patients with appendicitis and 71% of them did not require surgery within a year. Moreover, acute uncomplicated appendicitis can be treated by a novel technique called endoscopic retrograde appendicitis therapy in which pus can be discharged and narrowing of the appendiceal cavity can be reversed by fecalith removal[3,4].

Nonsurgical management of uncomplicated acute appendicitis has become increasingly popular[5]. However, delay in surgery increases the risk of perforation[3]. Acute appendicitis remains as a major reason of morbidity and mortality, especially in elderly patients[6]. Perforated appendicitis which requires a meticulous management can be misdiagnosed in spite of various diagnostic methods[7]. Certain laboratory tests have been proposed to be used to predict perforation as early as possible and to identify patients who are appropriate for conservative treatment[8]. For

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instance, high levels of white blood cell count (WBC), neutrophil percentage, C-reactive protein (CRP) and procalcitonin have been associated with perforation[7,9]. Moreover, it has been suggested that serum bilirubin levels above 1.0 mg/dl and neutrophil/lymphocyte ratio higher than 4.8 might indicate perforation in acute appendicitis[10]. Higher platelet/lymphocyte ratio has also been reported in patients with perforated appendicitis compared to patients with appendicitis at early stages[11]. However, no certain laboratory test has been reported to differentiate complicated appendicitis from non-complicated appendicitis prior to surgery.

Within this study, we evaluated inflammation biomarkers and diameter of appendix in patients with acute appendicitis who underwent appendectomy in order to identify the most specific biomarker to predict the risk of perforation in acute appendicitis.

Patients and Methods

This study was performed between September 2017 and March 2019 at Aksaray University School of Medicine. The study was performed in accordance with the Declaration of Helsinki. The Aksaray University Ethics Committee approved the study (Approval number: 2019/03-29). Each patient who was admitted to Aksaray University School of Medicine Hospital gave written informed consent about the usage of their medical information for academic research purposes. Medical records of patients who underwent appendectomy due to acute appendicitis were reviewed. Patients who had acute appendicitis diagnosis confirmed with both abdominal computerized tomography (CT) and histopathological evaluation were included within this study. Patients whose appendices were not visible during the CT scan, patients younger than 18-year-old, patients who had other infectious diseases, malignancy, liver disease, kidney disease, chronic inflammatory disorders and hematological disorders were excluded from this study. Patients with complete blood count and biochemistry panel results which included CRP, CRP/albumin, WBC, absolute neutrophil and lymphocyte counts, percentage of neutrophils and lymphocytes, mean corpuscular volume (MCV), mean platelet volume (MPV), red cell distribution width (RDW-SD), platelet count (PLT) and platelet distribution width (PDW) were evaluated.

Moreover, the neutrophil/lymphocyte (N/L), monocyte/lymphocyte (M/L), platelet/lymphocyte (PLT/L), mean platelet volume/platelet count (MPV/PLT), derived neutrophil/lymphocyte ratio [neutrophils/(white blood cells-neutrophils)] (DNLR), (neutrophil×monocyte)/lymphocyte (NM/L), and (neutrophil×monocyte×platelet)/lymphocyte (NMP/L) ratios were analyzed[12,13].

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Data were represented as mean±standard deviation or median, interquartile range for quantitative variables, counts and percentage for categorical variables. Continuous variables were investigated with analytical methods (Shapiro-Wilk's test) to determine whether they were normally distributed. Differences between two groups were evaluated with Mann-Whitney U test for continuous variables and Chi-square test as appropriate for categorical variables. While investigating the associations between non-normally distributed variables, the correlation coefficients and their significance were calculated using the Spearman test. CRP, CRP/albumin, diameter of appendix and M/L values to predict the presence of appendiceal perforation were analyzed using ROC (Receiver Operating Characteristics) curve analysis. When a significant cut off value was observed, the sensitivity, specificity, positive and negative predictive values, positive likelihood ratios, negative likelihood ratios and accuracy were presented. While evaluating the area under the curve, a 5% type-I error level was used to accept a statistically significant predictive value of the test variables. $p<0.05$ was considered statistically significant.

Results

This study included 58 patients, 42 (72.4%) male and 16 (27.6%) female. The mean age of the patients was 33.8±14.1 years (range: 18-75). 49 (84.5%) patients had non-perforated acute appendicitis. Perforated acute appendicitis was observed in 9 (15.5%) patients (Table I).

The mean CRP level was 37.4±60.6 mg/dL (min-max: 0.3-267.9 mg/L). CRP level was increased in 43 (74.1%) patients, whereas 15 (25.9%) patients had CRP levels within normal limits (reference range: 0-5 mg/L). The mean CRP/albumin level was 9±15.7 (min-

Table I. Characteristics and laboratory findings of the patients with non-perforated and perforated appendicitis.

	Non-perforated (n=49)	Perforated (n=9)	
	Mean±SD Median (IQR)	Mean±SD Median (IQR)	*p*-value
Male n (%)	37 (75.5)	5 (55.6)	0.243*
Female n (%)	12 (24.5)	4 (44.5)	
Age (year)	31.9±11.6 29 (23-36)	44.4±21.4 35 (25.5-65.5)	0.127
Diameter (mm)	9.5±1.8 9 (8-10)	11.5±2.2 11 (10-14)	<0.001
CRP (mg/L)	25.6±49.8 11.9 (4.1-23.1)	101.6±75.9 103.9 (33.3-158.5)	<0.001
WBC (x10^9/L)	14.1±4.2 13.8 (10.7-17.1)	13.7±3.7 12.1 (11.0-16.4)	0.707
Neutrophil count (x10^9/L)	10.9±4.1 10.5 (8.0-13.7)	10.9±3.6 8.9 (8.6-13.6)	0.855
Neutrophil (%)	76.4±8.8 78.5 (72.9-81.5)	79.0±5.5 79.1 (74.5-84.9)	0.652
Lymphocyte count (x10^9/L)	2.1±0.7 2 (1.5-2.6)	1.6±0.5 1.5 (1.1-2.0)	0.042
Lymphocyte (%)	15.9±7.1 14.3 (10.7-19.8)	12.3±4.4 13.4 (7.5-15.9)	0.242
MCV (fl)	86.6±14.3 84.6 (82.2-87.3)	84.3±4.5 84.7 (80.1-88.4)	0.872
RDW (fl)	39.2±3.0 39 (37.3-40.5)	39.7±2.4 39.3 (37.6-41.7)	0.452
PLT (x10^9/L)	265.7±62.6 256 (214-316.5)	255.2±67.4 229 (207.5-306)	0.499
MPV (fl)	10.1±0.8 10 (9.5-10.6)	9.9±1.2 9.4 (9.1-10.9)	0.426
PDW (fL)	11.6±1.5 11.6 (10.6-12.4)	11.4±2.5 10.6 (9.1-13.5)	0.526
CRP/albumin	6.3±13.9 2.5 (0.8-4.8)	23.6±17.6 22.7 (8.0-37.3)	<0.001
N/L	6.2±3.4 5.6 (3.7-8.1)	8.4±4.2 6 (5-12.6)	0.160
M/L	0.5±0.2 0.4 (0.3-0.6)	0.7±0.4 0.6 (0.5-1.1)	0.010
P/L	135.8±57.4 123.7 (104.1-165.9)	183.8±79.8 155.5 (118.1-248.7)	0.105
MPV/PLT	0.04±0.05 0.03 (0.03-0.04)	0.04±0.01 0.03 (0.03-0.05)	0.710
DNLR	3.8±1.8 3.6 (2.7-4.4)	4.7±1.6 5.1 (3.1-6.3)	0.160
NM/L	5.5±4.1 4.0 (3.0-7.2)	9.7±7.9 5.7 (4.3-15.9)	0.082
NMP/L	1,463.8±1,162 1,151.9 (657.3-1962.2)	2,596.6±2,342.6 1,685.4 (911.0-4509.5)	0.125

Mann-Whitney U Test, SD: Standard Deviation, IQR: Interquartile Range, *Fisher's Exact Test. CRP: C-reactive protein, MCV: Mean corpuscular volume, MPV: Mean platelet volume, PDW: Platelet distribution width, PLT: Platelet count, RDW: Red cell distribution width, WBC: White blood cell count, DNLR: Derived Neutrophil/Lymphocyte Ratio, M/L: Monocyte/Lymphocyte count, MPV/PLT: Mean platelet volume/Platelet count, N/L: Neutrophil/Lymphocyte count, P/L: Platelet/Lymphocyte count, NM/L: (Neutrophil×Monocyte)/lymphocyte, NMP/L: (Neutrophil×Monocyte×Platelet)/Lymphocyte). In patients with perforated appendicitis, appendiceal diameter, CRP level, CRP/Albumin, M/L were higher and lymphocyte count was lower than those with no perforation.

max: 0.05-69.7). The mean WBC count was 14.0±4.1x10^9/L (min-max: 6.4-24.6). WBC count was increased in 52 (89.7%) patients and 6 (10.3%) patients had normal WBC levels (reference range: 4-10x10^9/L). The mean absolute neutrophil count was 10.9±3.9x10^9/L (min-max: 3.7-21.8). Absolute neutrophil count was increased in 53 (91.4%) patients and 5 (8.6%) patients had normal neutrophil count level (reference range: 1.56-6.13x10^9/L). The percentage of blood neutrophils was increased in 49 (84.5%) patients and it was normal in 9 (15.5%) patients (reference range: 34-70%). The mean absolute lymphocyte count was 1.9±0.7x10^9/L (min-max: 0.4-3.5). Absolute lymphocyte count was normal in 51 (87.9%) patients and it was decreased in 7 (12.1%) patients (reference range: 1.18-3.74x10^9/L). The percentage of blood lymphocytes was decreased in 47 (81%) patients and it was normal in 11 (19%) patients (reference range: 20-51%).

The mean MCV level was 86.2±13.3 fl (min-max: 75.9-181.4). The mean MPV level was 10.1±0.8 fl (min-max: 8.3-12.1). MCV and MPV were normal in 53 (91.4%) patients and decreased in 5 (8.6%) patients (reference range: MCV: 79-94.8 fl, MPV: 9-12.4 fl). The mean RDW-SD level was 39.3±2.9 fl (min-max: 34-48.6). RDW-SD was 53 normal in (91.4%) patients, decreased in 4 (6.9%) patients and increased in 1 (1.7%) patient (reference range: 35.1-46.3 fl). The mean PLT count was 264.1±62.8x10^9/L (min-max: 108-413). Platelet count was normal in 55 (94.8%) patients, increased in 2 (3.4%) patients and decreased in 1 (1.7%) patient (reference range: 100-400x10^9/L). The mean PDW level was 11.6±1.7 fL (min-max: 8.6-16). PDW was normal in 56 (96.6%) patients and decreased in 2 (3.4%) patients (reference range: 9-17 fL).

Patients with high CRP values had both high CRP/albumin (Mean±SD: 11.9±17.2) and MPV/PLT (Mean±SD: 0.04±0.05) values compared to patients with normal CRP values (Mean±SD levels of CRP/albumin and MPV/PLT were 0.4±0.3 and 0.03±0.01, $p<0.001$, $p=0.03$, respectively. SD: standard deviation). A moderate positive correlation was found between the CRP level and age, M/L level and a very strong positive correlation with the CRP/albumin level (correlation coefficient: 0.407, 0.439, 0.997, respectively). As age increased, the level of CRP increased ($p=0.002$). As CRP level increased, M/L and CRP/albumin level increased ($p=0.001$, $p<0.001$, respectively). A moderate negative correlation was found between the CRP level and the lymphocyte count (correlation coefficient: -0.371). As CRP level increased, the lymphocyte count decreased ($p<0.004$). In addition, a moderate positive correlation was found between the diameter of the appendix, CRP and CRP/albumin levels (correlation coefficient: 0.307, 0.310, respectively). As the appendix diameter increased, CRP and CRP/albumin levels increased ($p=0.019$, $p<0.001$, respectively).

A very strong positive correlation was detected between WBC and neutrophil counts (correlation coefficient: 0.754, $p<0.001$); a positively strong correlation between WBC count with the percentage of neutrophil (correlation coefficient: 0.518, $p<0.001$), and a moderate positive correlation between WBC count and MCV, PLT, M/L, DNLR (correlation coefficient: 0.278, 0.349, 0.303, 0.468, $p=0.034$, $p=0.007$, $p=0.021$, $p<0.001$, respectively). A strong negative correlation was detected between WBC count and the percentage of lymphocytes (correlation coefficient -0.523) and a moderate negative correlation was detected between WBC count and MPV/PLT level (correlation coefficient: -0.316). As WBC count increased, the lymphocyte percentage and MPV/PLT level decreased ($p<0.001$, $p=0.016$).

Appendiceal diameter, CRP level, CRP/Albumin and M/L were higher in patients with perforated appendicitis compared to those with non-perforated appendicitis. On the contrary, lower lymphocyte count was detected in patients with perforated appendicitis compared to patients with non-perforated appendicitis (Figures 1 and 2). Sensitivity rates of appendiceal diameter, CRP level, CRP/albumin and M/L for perforated appendicitis were all 89%. However, the most specific biomarker for perforation was CRP/albumin (87.8%), followed by CRP (85.7%), M/L (63.3%) and appendiceal diameter (57.1%). Moreover, patients with CRP/albumin>7.1, CRP>32.7 mg/L, M/L>0.44 and appendiceal diameter>9.8 mm were most likely to have perforated acute appendicitis (Tables II and III).

Discussion

Definitive diagnosis of acute appendicitis may be troublesome, thus unnecessary surgery has been reported in up to 20% of the patients[14]. Radiological investigations, such as ultrasonography and CT, are successfully used in the differ-

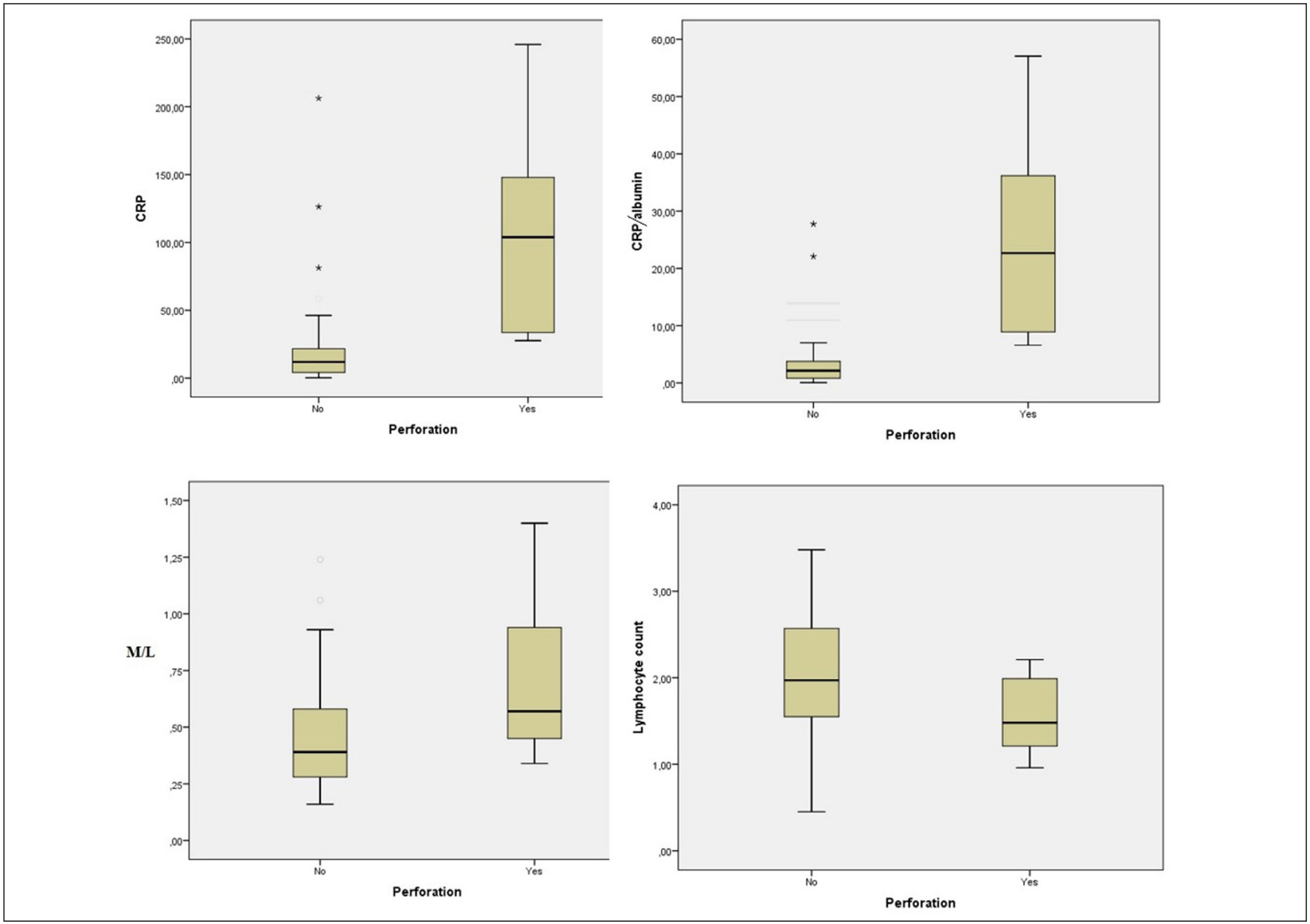

Figure 1. Laboratory findings associated with appendiceal perforation. Increased CRP, CRP/albumin and M/L values were positively correlated, whereas lymphocyte count was negatively correlated with appendiceal perforation.

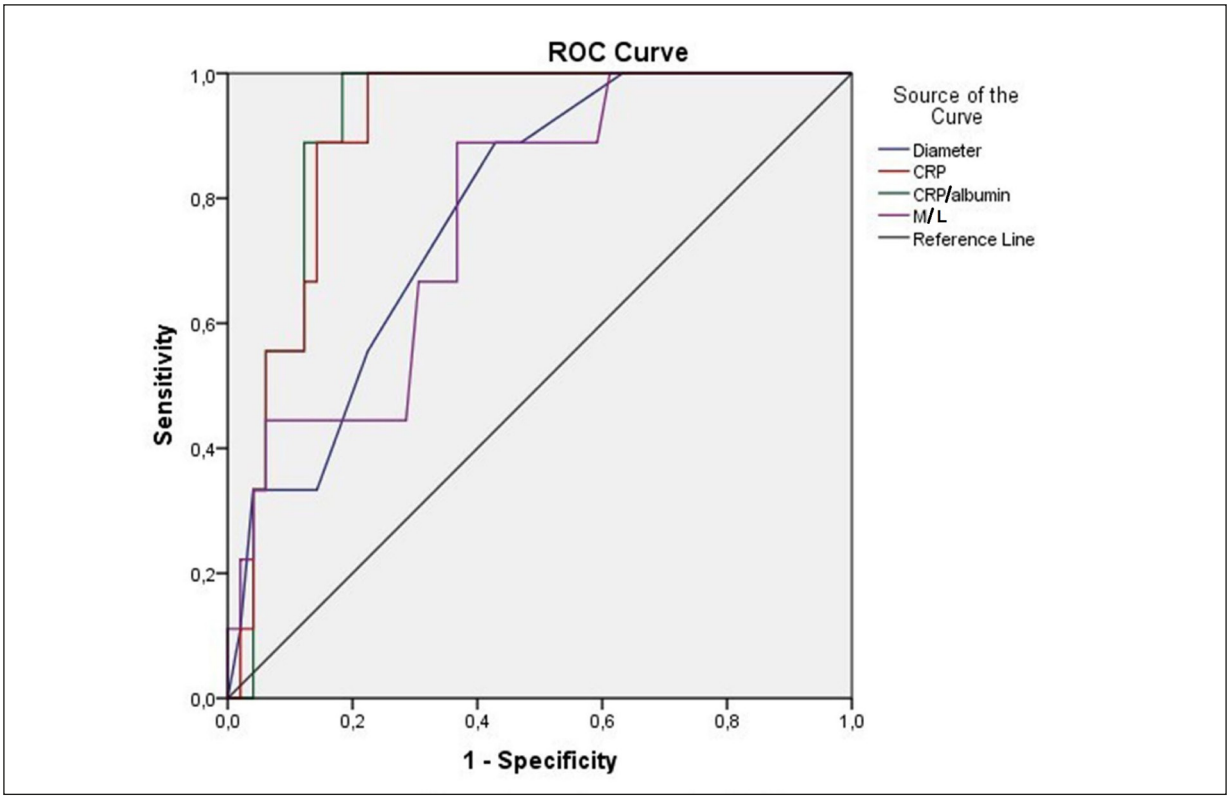

Figure 2. ROC curve for the diameter of appendix, CRP, CRP/albumin, M/L values in predicting appendiceal perforation. Diagonal segments are produced by ties. ROC: Receiver operating characteristic curve. The curves of CRP/albumin, CRP, appendiceal diameter, M/L values are visibly higher than the reference line, and thus they have diagnostic value in terms of the presence of perforation in patients with appendicitis. This finding is also statistically supported in the area under the curve table (Table II). CRP/albumin, CRP, appendiceal diameter and M/L are valuable variables and form a significantly better curve than the area under the reference line (gray line) (p <0.05).

ential diagnosis of acute appendicitis. However, appendix may not be clearly detected in about half of the patients by ultrasonography. Furthermore, CT is not cost effective and causes radiation exposure[14]. Therefore, novel biomarkers are needed both to diagnose acute appendicitis rapidly and to predict the severity of the disease. Novel biomarkers may faciliate the further evaluation of patients in order to choose the most appropriate treatment option for the management of acute appendicitis. White blood cell count, CRP, bilirubin, procalcitonin, interleukin-6 (IL-6) and urinary serotonin have been suggested as biomarkers for the detection of acute appendicitis with different sensitivity and specificity rates[14]. The rates for the prediction of perforation have been reported as 69%, 78%, 71%, 83% and 84% for WBC, CRP, bilirubin, procalcitonin and IL-6, respectively[14].

The MPV, platelet count, PDW and red blood cell distribution width have also been used to identify acute appendicitis[15]. However, none of these biomarkers have been universally accepted as ideal for the diagnosis of acute appendicitis and for the prediction of appendiceal perforation[14]. For instance, normal serum levels of WBC and CRP have been reported in 39.8% of the patients with acute appendicitis[16]. Boshnak et al[17] suggested that coexistence of high PDW level, high WBC and neutrophil counts indicated acute appendicitis whereas no correlation was found between acute appendicitis, MPV and RDW. Divergent results have been observed in studies[16] about the use of increased inflammatory biomarkers in acute appendicitis. Liu et al[15] suggested that platelet/lymphocyte count (P/L) was a good indicator of acute appendicitis and thus it might be used in patients before appendectomy, especially during pregnancy. However, no association was detected between P/L and perforation. Moreover, Pehlivanli and Aydin[18]

Table II. Area under the curve.

Variable	n	Area	SE	95% CI	*p*-value
Diameter of appendix	58	0.781	0.071	0.642-0.920	0.008
CRP	58	0.905	0.040	0.827-0.982	<0.001
CRP/ Albumin	58	0.912	0.038	0.837-0.986	<0.001
M/L	58	0.772	0.076	0.622-0.922	0.010

SE: Standard Error, CI: Confidence Interval. ROC analysis was performed to determine the cut-off points according to CRP/albumin, CRP, appendiceal diameter and M/L values for the diagnosis of perforation in patients with appendicitis. The area under the curve in the ROC analysis were 0.912, 0.905, 0.781, 0.772, respectively, which were statistically significant ($p<0.05$).

reported that P/L and N/L were notable biomarkers to differentiate acute appendicitis from perforated appendicitis. Similarly, Hajibandeh et al[19] suggested that N/L>8.8 could indicate complicated appendicitis and thus it could be used in pregnant patients and children both to avoid CT and to select patients for surgical or conservative treatment. Furthermore, Beecher et al[20] reported that N/L>5.47 was an accurate marker to detect complicated acute appendicitis. Although not widely used, pentraxin-3, IL-6, IL-8 and TNF-α levels have also been associated with perforated appendicitis[21,22]. In addition, Eun et al[23] reported that neutrophil-to-lymphocyte ratio had a moderate predictive power for acute appendicitis to decide whether an imaging testing should be used when the physical examination findings were vague in pediatric patients.

Within this study, inflammatory markers, which were routinely examined when acute appendicitis was suspected, such as CRP and WBC were within normal limits in 15 (25.9%) patients and 6 (10.3%) patients with acute appendicitis, respectively. In addition, MPV, RDW-SD and PDW were recommended to be used for the diagnosis of acute appendicitis. However, within this study, MPV and RDW-SD were normal in 53 (91.4%) patients and also PDW was normal in 56 (96.6%) patients with acute appendicitis.

Our results revealed that patients with perforated appendicitis had higher appendiceal diameter, CRP level, CRP/albumin and M/L compared to patients with non-perforated appendicitis. Moreover, patients with perforated appendicitis had lower lymphocyte count than those with no perforation. Therefore, we suggest that appendiceal diameter, CRP level, CRP/albumin, M/L and lymphocyte count can be used to predict perforation in patients with acute appendicitis. Especially patients with CRP/albumin>7.1, CRP>32.7 mg/L, M/L>0.44 and appendiceal diameter>9.8 mm were most likely to have perforated acute appendicitis.

Limitations

A limitation of the study was the lack of blood samples from a homogeneous patient group. A homogenous patient group with acute appendicitis should be reevaluated with CRP/albumin, CRP, M/L, appendiceal diameter and lymphocyte count to predict perforation. Furthermore, a prospective multi-center study with a larger sample size would provide more information about the applicability of these formulas related to the prediction of appendiceal perforation.

Conclusions

We suggest that the most specific inflammation biomarker indicating perforated acute appendicitis is CRP/albumin. A CT scan may not be suitable for all cases such as patients who are pregnant and for those who have radiocontrast allergy. Furthermore, CT may not be available in all hospitals and it may not be cost-effective to perform CT scan in all patients with the suspicion of acute perforated appendicitis. Therefore, CRP/albumin can be a good candidate to be used as an indicator of perforation in these circumstances. Immediate surgical intervention should be the preferred treatment option in patients with acute appendicitis particularly with CRP/albumin>7.1, which would point out the increased risk of appendiceal perforation.

These results will hopefully contribute to the medical literature about the biomarkers which can be performed easily and provide results rapidly, in order to prevent complications due to prolonged

Table III. CRP/albumin, CRP, appendiceal diameter and M/L cut off values to predict the presence of perforation in patients with appendicitis.

Variables	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Positive Likelihood Ratio	Negative Likelihood Ratio	Accuracy (%)
CRP/albumin							
6.5	100	81.6	47.4	100	5.4	0	82.7
6.6	89.0	81.6	47.1	97.6	4.8	0.1	82.7
6.7	89.0	83.7	50.0	97.6	5.5	0.1	84.5
6.9	89.0	85.7	53.3	97.7	6.2	0.1	86.2
7.1	**89.0**	**87.8**	**57.1**	**97.7**	**7.3**	**0.1**	**87.9**
8.0	77.8	87.8	53.8	95.6	6.4	0.1	86.2
CRP							
26.1	100	77.6	45.0	100	4.5	0	81.0
27.9	89.0	77.6	42.1	97.4	4.0	0.1	79.3
28.3	89.0	79.6	44.4	97.5	4.4	0.1	81.0
30.3	89.0	81.6	47.1	97.6	4.8	0.1	82.7
32.3	89.0	83.7	50.0	97.6	5.5	0.1	84.5
32.7	**89.0**	**85.7**	**53.3**	**97.7**	**6.2**	**0.1**	**86.2**
33.3	77.8	85.7	50.0	95.5	5.4	0.3	84.5
Diameter							
8.8	100	36.7	22.5	100	1.6	0	46.6
9.3	89.0	53.1	25.8	96.3	1.9	0.2	58.6
9.8	**89.0**	**57.1**	**27.6**	**96.6**	**2.1**	**0.2**	**62.1**
10.5	55.6	77.6	31.2	90.5	2.5	0.6	74.1
M/L							
0.33	100	38.8	22.5	100	1.6	0	46.5
0.34	89.0	40.8	23.1	100	1.5	0.2	48.2
0.36	89.0	44.9	22.9	95.7	1.6	0.2	51.7
0.38	89.0	47.1	22.9	95.7	1.7	0.2	51.7
0.39	89.0	55.1	23.5	95.8	1.9	0.1	53.4
0.40	89.0	57.1	26.7	96.4	2.1	0.1	60.3
0.41	89.0	59.2	27.6	96.6	2.2	0.1	62.0
0.43	89.0	61.2	29.6	96.8	2.3	0.1	65.5
0.44	**89.0**	**63.3**	**29.6**	**96.8**	**2.4**	**0.1**	**65.5**
0.48	66.7	63.3	25.0	91.2	1.4	0.5	63.7

As a result of the evaluation performed by ROC analysis, it was revealed that CRP/albumin, CRP, appendiceal diameter and M/L values had diagnostic value in predicting perforation in patients with appendicitis. Recommended cut-off values to predict appendiceal perforation are stated in Table III ($p<0.05$).

hospital stay of patients with acute appendicitis during the evaluation process.

Conflict of Interest

The authors declare that they have no conflict of interest.

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The authors declare no financial support.

Informed Consent

Informed consent was obtained from all participants included in the study.

Ethics Approval

This study was approved by the Aksaray University Ethics Committee (Approval number: 2019/03-29).

Authors' Contributions

Mehmet Eren Yuksel: Conception/design of the work, acquisition of data, drafting and reviewing the work. Namik Ozkan: Conception/design of the work, acquisition of data, drafting and reviewing the work. Emine Avci: Conception/design of the work, analysis of data, drafting and reviewing the work All the authors approved the submitted version of the manuscript.

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References

1) Snyder MJ, Guthrie M, Cagle S. Acute appendicitis: efficient diagnosis and management. Am Fam Physician 2018; 98: 25-33.
2) Tatsuta K, Miyazaki S, Ogiku M, Harada T, Yoshiro N. Defining treatment strategy for uncomplicated appendicitis based on patient satisfaction feedback: a cross-sectional study. Asian J Surg 2022; 45: 167-171.
3) Krzyzak M, Mulrooney SM. Acute Appendicitis review: background, epidemiology, diagnosis, and treatment. Cureus 2020; 12: 8562.
4) Ding W, Du Z, Zhou X. Endoscopic retrograde appendicitis therapy for management of acute appendicitis. Surg Endosc 2022; 36: 2480-2487.
5) Wagner M, Tubre DJ, Asensio JA. Evolution and current trends in the management of acute appendicitis. Surg Clin North Am 2018; 98: 1005-1023.
6) Iamarino APM, Juliano Y, Rosa OM, Novo NF, Favaro MDL, Ribeiro MAF. Risk factors associated with complications of acute appendicitis. Rev Col Bras Cir 2017; 44: 560-566.
7) Yang J, Liu C, He Y, Cai Z. Laboratory markers in the prediction of acute perforated appendicitis in children. Emerg Med Int 2019; 2019: 4608053.
8) McGowan DR, Sims HM, Zia K, Uheba M, Shaikh IA. The value of biochemical markers in predicting a perforation in acute appendicitis. ANZ J Surg 2013; 83: 79-83.
9) Orellana-Henriquez J, Robalino-Rodriguez I, Sanchez-Alban H, Franco-Orellana J, Oleas R, Baquerizo-Burgos J, Patiño-Aquin M, Torres-Herrera C, Puga-Tejada M. Predictive biomarkers for complicated acute appendicitis: A prospective Ecuadorian study. Cir Cir 2020; 88: 599-607.
10) Sevinç MM, Kınacı E, Çakar E, Bayrak S, Özakay A, Aren A, Sarı S. Diagnostic value of basic laboratory parameters for simple and perforated acute appendicitis: an analysis of 3392 cases. Ulus Travma Acil Cerrahi Derg 2016; 22: 155-162.
11) Ozkan A, Gokce AH, Gokce FS. The importance of laboratory tests and Body Mass Index in the diagnosis of acute appendicitis. Pol Przegl Chir 2020; 92: 7-11.
12) Djordjevic D, Rondovic G, Surbatovic M, Stanojevic I, Udovicic I, Andjelic T, Zeba S, Milosavljevic S, Stankovic N, Abazovic D, Jevdjic J, Vojvodic D. Neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume-to-platelet count ratio as biomarkers in critically ill and injured patients: which ratio to choose to predict outcome and nature of bacteremia? Mediators Inflamm 2018; 2018: 3758068.
13) Pinna A, Porcu T, D'Amico-Ricci G, Dore S, Boscia F, Paliogiannis P, Carru C, Zinellu A. Complete blood cell count-derived inflammation biomarkers in men with age-related macular degeneration. Ocul Immunol Inflamm 2019; 27: 932-936.
14) Acharya A, Markar SR, Ni M, Hanna GB. Biomarkers of acute appendicitis: systematic review and cost-benefit trade-off analysis. Surg Endosc 2017; 31: 1022-1031.
15) Liu L, Shao Z, Yu H, Zhang W, Wang H, Mei Z. Is the platelet to lymphocyte ratio a promising biomarker to distinguish acute appendicitis? Evidence from a systematic review with meta-analysis. PLoS One 2020; 15: 0233470.
16) Kim JJY, Dobson BH, Ng CLH, Thong DW, Arthur T, Parker D. Can normal inflammatory markers rule out acute appendicitis? The reliability of biochemical investigations in diagnosis. ANZ J Surg 2020; 90: 1970-1974.
17) Boshnak N, Boshnaq M, Elgohary H. Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. J Invest Surg 2018; 31: 121-129.
18) Pehlivanlı F, Aydin O. Role of platelet to lymphocyte ratio as a biomedical marker for the pre-operative diagnosis of acute appendicitis. Surg Infect Larchmt 2019; 20: 631-636.
19) Hajibandeh S, Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: A systematic review and meta-analysis. Am J Surg 2020; 219: 154-163.
20) Beecher SM, Hogan J, O"Leary DP, McLaughlin R. An appraisal of inflammatory markers in distinguishing acute uncomplicated and complicated appendicitis. Dig Surg 2016; 33: 177-181.
21) Gul VO, Destek S. Using pentraxin-3 for diagnosing acute appendicitis and predicting perforation: A prospective comparative methodological study. Ulus Travma Acil Cerrahi Derg 2020; 26: 21-29.
22) Peeters T, Martens S, D'Onofrio V, Stappers MHT, Hilst JCH, Houben B, Achten R, Joosten LAB, Gyssens IC. An observational study of innate immune responses in patients with acute appendicitis. Sci Rep 2020; 10: 17352.
23) Eun S, Ho IG, Bae GE, Kim H, Koo CM, Kim MK, Yoon SH. Neutrophil-to-lymphocyte ratio for the diagnosis of pediatric acute appendicitis: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 2021; 25: 7097-7107.