



Diagnosis of Appendicitis in Patients with a Normal White Blood Cell Count; A Cross-Sectional Study

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ABSTRACT

Objective: To investigate the clinical, imaging and laboratory findings for diagnosis of acute appendicitis (AA) in patients with a normal white blood cell count (WBCC).

Methods: This retrospective cross-sectional study was conducted in Ankara Numune Training and Research Hospital, Ankara, Turkey, during a 1-year period. To determine diagnostic factors in AA in patients with normal WBCC, medical records of eligible patients were reviewed for demographic and clinical variables, as well as patient outcome.

Results: A total of 105 patients that had undergone appendectomy and were found to have a normal WBCC were included in the study. Of these patients, 53 (50.5%) were men and 52 (49.5%) were women. The mean age of the patients was 34.2±12.3 (min 14, max 78). The negative exploration rate was identified as 19%. In the multivariate analysis, only the diameter of appendix was statistically significant ($p=0.002$). ROC analysis revealed the cut off appendiceal diameter as 8 mm.

Conclusion: In patients suspected of AA due to ≥ 8 mm appendiceal diameter determined by imaging, we recommend surgical treatment even if WBCC and neutrophil count are normal.

Keywords: Acute appendicitis; White blood cell count; Diagnosis; Appendix diameter.

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Introduction

Acute appendicitis (AA) is the most common abdominal surgical emergency. Epidemiological studies have reported that 10% of AA patients have abdominal pain [1, 2]. Negative appendectomies

in patients with a preoperative diagnosis of AA comprise 10% of all cases in various series [3, 4]. The etiologies for these negative appendectomies include constipation, gastroenteritis, mesenteric lymphadenectomy, pelvic inflammatory disease, and ovarian torsion or rupture [4]. In the diagnosis

of AA, white blood cell count (WBCC) is neither sensitive nor specific. This is secondary to the fact that WBCC is elevated in almost 70% of etiologies causing right lower abdominal pain [5]. Utilization of imaging techniques has decreased the rate of negative appendectomies; however, it is accepted that WBCC alone is not adequate [5-7]. Although computed tomography (CT) and ultrasonography (US) are more commonly used for the diagnosis of AA, medical history, physical examination and laboratory analyses are still the mainstream for this purpose [8, 9]. However, it is well known that sensitivities of findings and symptoms, such as nausea, right lower quadrant pain, and loss of appetite are low [10]. The signs and symptoms related to AA are evaluated based on the Alvarado score to assist in the diagnostic process [11]. A timely diagnosis is of critical importance since delayed treatment may cause perforation of appendicitis, increasing recovery time and prolonging hospital stay. Also, recent studies demonstrated that normal WBCC was found to be independent predictive factor for negative appendectomy[12].

In this study, we aimed to investigate the clinical, imaging and laboratory findings of patients that had been diagnosed with AA to determine whether their WBCC can assist clinicians in the diagnosis of future cases.

Materials and Methods

Study Population

This study included 648 patients who had surgery due to AA diagnosis in our emergency surgery clinic between January 2016 and December 2016. Patients whose medical files had the required information were included. We excluded the patients who with incomplete clinical information. The study was approved by Ankara Numune Education and Research Hospital Ethics Committee in June 2017(E-17-1220).

Study Protocol

The complaints and physical examination findings of the patients were obtained from their medical files. Patients with a high WBCC, hematologic disease, immunosuppression and malignancy were excluded from the study. In addition, patient complaints, physical examination findings and laboratory findings (WBCC, neutrophil, amylase, direct bilirubin, RDW) were recorded retrospectively by assessing the parameters constituting the Alvarado score [migration of pain, anorexia, nausea, tenderness in right lower quadrant, rebound pain, elevated temperature ($>37.3^{\circ}\text{C}$), $\text{WBCC}>10.000/\text{mm}^3$, neutrophilia $>75\%$], as well as examining the related patient files and hospital records. The appendiceal diameters of the patients with a normal WBCC were also recorded. These diameters had been calculated in diameters based on the US images taken before

the operation. Whole blood samples were collected in 4 mL K2EDTA tubes and leukocyte counts were made with optical method by using Sysmex XT-1800 i automated hematology analyzer. Pathology specimens were grouped as normal appendix and appendicitis (Figure 1).

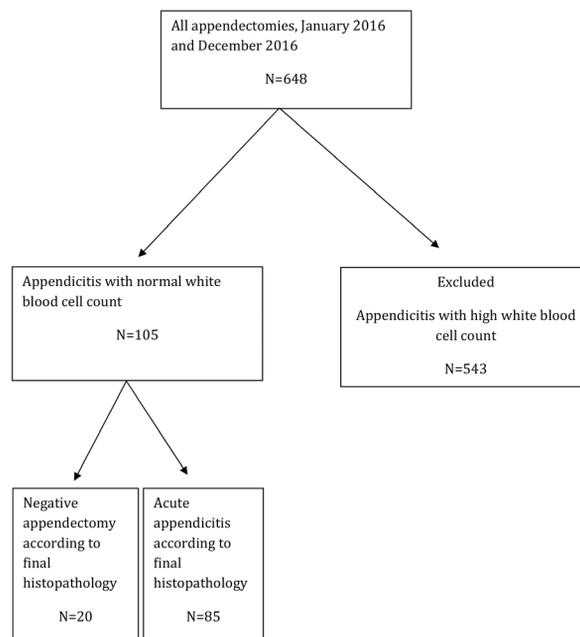


Fig. 1. The flow-diagram of the study.

Statistical Analyses

The Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 16.0 for Windows was used for the statistical analyses of the data. As well as descriptive statistical methods (mean, standard deviation), intergroup comparison of normally distributed parameters of the quantitative data was undertaken using the Student's t-test whereas the Mann-Whitney U-test was used for the parameters that were not normally distributed. Relationships between numeric data were analyzed through a correlation analysis. Qualitative data was compared using the Chi-square test. Factors which were significant in univariate analysis were included in multivariate analysis. From the results of the univariate model with level of inclusion of $p<0.2$, a multivariable logistic regression model was planned using stepwise regression modeling. The results were evaluated within 95% confidence interval and at a p level less than 0.05 was considered statistically significant.

Results

A total of 105 patients that had undergone appendectomy and were found to have a normal WBCC were included in the study. Of these patients, 53 (50.5%) were male and 52 (49.5%) were female (Table 1). The mean age of the patients was 34.2 ± 12.3 (min 14, max 78) years. According to the pathology reports, 85 patients had AA and 20 had

Table 1. Demographic, clinical, imaging and pathological features of 105 patients with acute appendicitis and normal white blood cell count.

Variable	Value
Number of patients	105
Age (years)	34.2±12.3
Gender M/F	
Men (%)	53 (50.5%)
Women (%)	52 (49.5%)
Median Alvarado score	4
Appendicitis diagnosis in pathology	
≥8 mm appendix diameter	77 (90.9%)
<8 mm appendix diameter	8 (30%)
Surgery type	
Laparoscopy (%)	93 (88.5%)
Open (%)	12 (11.5%)

a normal appendix. The negative exploration rate was identified as 19%, with all being reported as pathologically end-stage lymphoid hyperplasia. In the univariate analysis, neutrophil count, appendix diameter and Alvarado score were found to be statistically significant ($p<0.05$) (Table 2) whereas in the multivariate analysis, only the diameter of appendix was statistically significant ($p=0.002$) (Table 3). Of the 105 patients, 90.9% with an appendix diameter of greater than 8 mm based on preoperative US had AA while 9.1% had a normal appendix on pathological examination. Thirty percent of those with an appendix diameter of less than 8 mm had been diagnosed with AA while the remaining 70% had a normal appendix. In the ROC analysis, the area under the curve was 0.721 at the 95% confidence interval ($p=0.002$), and the cut-off appendix diameter was 8 mm (Figure 2).

Discussion

AA is the most common surgical emergency of the abdominal cavity. Diagnosis of AA is especially

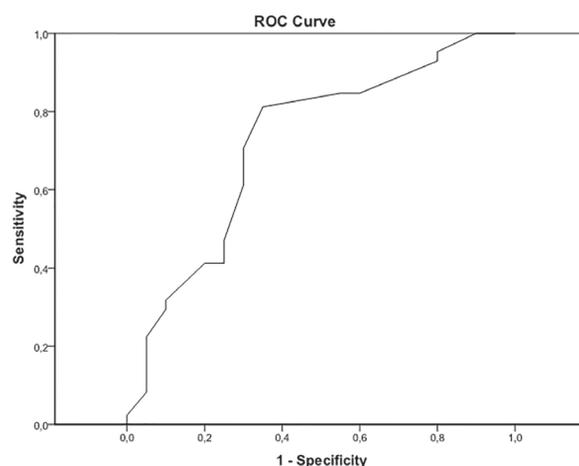
Table 2. Comparison of laboratory variables with respect to the pathology results in 105 patients with primary impression of acute appendicitis and normal white blood cell count.

	Acute appendicitis (N=85)	Normal appendix (N=20)	p value
WBCC^a	8.26±1.822	8.44±1.701	0.648
Neutrophil	68.32±10.240	62.59±6.862	0.012
Amylase	54.69±19.664	56.00±20.178	0.166
Direct Bilirubin	0.16±0.098	0.13±0.046	0.778
RDW^b	13.72±1.684	13.68±1.441	0.594
Appendix Diameter	9.80±2.599	8.02±2.281	0.002
Alvarado Score	4.64±0.94	4.10±0.45	0.015

^aWBCC: White Blood Cell Count; ^bRDW: Red Cell Distribution Width

Table 3. Multivariate logistic regression analysis of the predicting factors of pathologically diagnosed acute appendicitis in patients with normal white blood cell count.

	Odds Ratio	95% Confidence interval	p value
Neutrophil count	1.015	0.943 – 1.091	0.367
Alvarado Score	4.646	0.410 – 52.611	0.582
Appendix Diameter	1.369	1.006 – 1.864	0.046

**Fig. 2.** Results of receiver-operative characteristic (ROC) curve analysis. Area under the curve (AUC): 0.721 at 95% confidence interval ($p=0.002$); the cut-off appendix diameter: 8 mm

intriguing in elderly, children and pregnant patients as it can progress to a more complicated state and even sepsis [3]. Imaging techniques can support the diagnosis of AA and decrease negative appendectomies. Various studies have reported that radiological examination can decrease the negative appendectomy rate from 20% to 2-14% [13]. Elevated WBCC supports physical examination in the diagnosis of AA but a normal WBCC does not preclude AA. Patients with a normal WBCC can be admitted for observation but several studies have pointed out that elevated WBCC could be crucial for AA diagnosis [14]. Adam *et al.*, [15] showed that appendiceal mucosa can ulcerate secondary to viral infections, and non-complicated viral appendicitis cases can subside without antibiotics [16]. Jeon *et al.* [12] showed that normal WBCC was an independent predictor for negative appendectomy in patients with equivocal AA. Ortega-Deballon *et al.* [17] suggested that patients with a normal WBCC should not undergo appendectomy. Similarly, Atema *et al.*

[18] showed that WBCC and C-reactive protein were important parameters to rule out AA.

In the current study, neutrophil count, appendix diameter and Alvarado score in patients with a normal WBCC were found statistically significant. US is the first-choice adjunctive diagnostic imaging method for AA, especially in pregnant patients and women of reproductive age as it decreases the negative appendectomy rate. It is known that imaging can decrease this rate to the 3-10% range [19, 20]. In US, diagnostic findings for AA include an appendix diameter of >6 mm, a non-compressed or non-peristaltic appendix, free effusion, periappendicular and bowel wall edema or thickened appendicolith and presence of periappendicular abscesses.

The cut-off value for appendiceal diameter in AA was found as 6 mm in previous studies [21] but we identified 8 mm as the cut-off in our study, which can be attributed to an illness presenting with a normal WBCC.

Nalin *et al.* [22] found an Alvarado score of 4 in 281 patients who had a normal WBCC. Our study confirms the findings of these authors. However, it should be noted that an Alvarado score of lower than 4 does not rule out AA. On the other hand, in a recent analysis by Bhangu *et al.*, scoring was proposed as a step in the diagnostic flowchart of patients with suspected appendicitis. The authors reported that the new Angioedema Activity Score was superior to the validation results of Alvarado and Appendicitis Inflammatory Response Score [23].

In the current study, 81% of the patients with a normal WBCC had AA while 19% had a normal appendix. The latter percentage represents the negative appendectomy rate, which is close to the upper range in the literature (i.e., 5-15%). In clinical practice, if the patient has an elevated WBCC and suspicious findings according to the physical examination and laboratory analysis at the time of arrival, we make a pre-diagnosis of AA. Especially in female patients and cases of silent physical examination and normal WBCC, US should be undertaken. If a definitive diagnosis cannot be made, physical examination and laboratory analysis or US should be repeated. If any of these findings are contradictory, abdominal tomography may be required. An important limitation of this study was the use of a retrospective design and involvement of a single center. A normal WBCC and an Alvarado score of less than 4 decrease the possibility of AA.

In conclusion, an appendiceal diameter larger than 8 mm in imaging (US or CT) predicted AA in histopathological analysis by 90.9%. We recommend appendectomy for patients with a normal WBCC, with an appendiceal diameter of greater than 8 mm.

This is a retrospective cohort study; thus, informed consent of the patients was not sought.

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Conflicts of Interest: None declared.

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