
NAVIGATING THE DIAGNOSTIC PUZZLE: APPENDICITIS IN PATIENTS WITH NORMAL WHITE BLOOD CELL COUNT

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Abstract

Aim: This study aims to examine the clinical, imaging, and laboratory findings associated with the diagnosis of acute appendicitis (AA) specifically in patients who have a normal white blood cell count (WBCC).

Study Design: Over the course of twelve months, a captivating retrospective cross-sectional investigation took place within the emergency surgery department of King Hussein Hospital. The aim was to investigate the diagnostic factors associated with AA specifically in patients who exhibited a normal WBCC. To achieve this, the medical records of eligible patients were thoroughly assessed for demographic and clinical variables, along with patient outcomes.

Findings: The study included a total of 105 patients who underwent appendectomy and were found to have a normal WBCC. Among these patients, 53 (50.5%) were male and 52 (49.5%) were female. The average age of the patients was 34.2 ± 12.3 years (minimum 14 years, maximum 78 years). The rate of negative exploration, indicating cases where the appendix was found to be normal during surgery, was determined to be 19%. In the multivariate analysis, only the diameter of the appendix demonstrated statistical significance ($p = 0.002$). Receiver Operating Characteristic (ROC) analysis established the optimal appendiceal diameter cut-off point to be 8 mm.

Conclusion: Our findings suggest that in patients with suspected AA and an appendiceal diameter of 8 mm or larger determined by imaging, we recommend surgical intervention, even in cases where the WBCC and neutrophil count appear normal.

Introduction

Acute appendicitis (AA) stands as the prevailing urgent surgical condition affecting the abdomen. Studies of the epidemiology surrounding this condition reveal that approximately 10% of individuals with AA experience abdominal pain [1].

In different series, it has been observed that approximately 10% of cases involving patients diagnosed with AA result in negative appendectomies [2]. Causes leading to these negative appendectomies encompass conditions such as constipation, gastroenteritis, mesenteric lymphadenectomy, pelvic inflammatory disease, and instances of ovarian torsion or rupture [3].

When it comes to diagnosing AA, the white blood cell count (WBCC) lacks both sensitivity and specificity. This is due to the fact that WBCC levels are increased in nearly 70% of cases involving various causes that lead to right lower abdominal pain [4].

The use of imaging techniques has reduced the occurrence of negative appendectomies, but it is widely acknowledged that relying solely on WBCC is insufficient [5]. While computed tomography (CT) and ultrasonography (US) are frequently employed in diagnosing AA, medical history, physical examination, and laboratory analyses remain the primary approaches for this purpose [6]. Nevertheless, it is widely recognized that the sensitivities of various findings and symptoms associated with AA, such as nausea, right lower quadrant pain, and loss of appetite, are relatively low [7].

The assessment of signs and symptoms pertaining to AA is conducted using the Alvarado score as a tool to aid in the diagnostic process [8]. A prompt and accurate diagnosis holds utmost significance as any delay in treatment could lead to appendicitis perforation, resulting in longer recovery time and extended hospitalization. Furthermore, recent studies have indicated that a normal WBCC serves as an independent predictive factor for negative appendectomy [9].

The objective of this study was to examine the clinical, imaging, and laboratory characteristics of patients previously diagnosed with AA in order to assess the potential of their WBCC in aiding clinicians with future diagnoses.

Methods

Study Sample

The study comprised a total of 648 patients who underwent surgical procedures for AA at our emergency surgery department in King Hussein Hospital from January 2022 to December 2022. Only patients with complete medical records containing the necessary information were included, while those with incomplete clinical data were excluded. The study received approval from the Ethics Committee of the Jordanian Royal Medical Services.

Study Protocol

Patient complaints and physical examination findings were extracted from their electronic medical records. Patients with elevated white blood cell count (WBCC), hematologic disease, immunosuppression, or malignancy were excluded from the study. Furthermore, patient complaints, physical examination findings, and laboratory results (including WBCC, neutrophil count, amylase, direct bilirubin, and RDW) were retrospectively documented by evaluating the parameters that constitute the Alvarado score (pain migration, anorexia, nausea, tenderness in the right lower quadrant, rebound pain, elevated temperature ($>37.3^{\circ}\text{C}$), WBCC $>10,000/\text{mm}^3$, neutrophilia $>75\%$). These data were collected by reviewing the corresponding patient files and hospital records. Additionally, the appendiceal diameters of patients with normal WBCC were measured based on preoperative ultrasound images. Pathology specimens were categorized as either a normal appendix or appendicitis (see Figure 1).

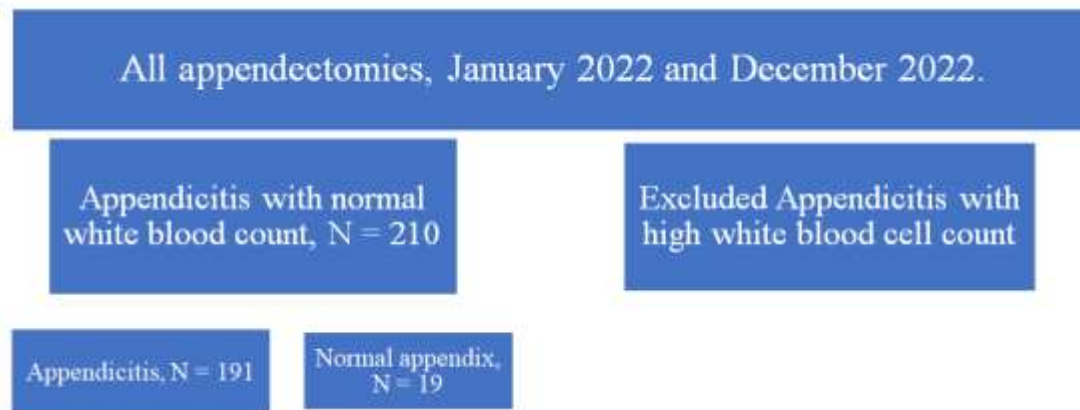


Figure 1: Study flowchart

Statistical Analysis

The data collected for statistical analysis in this study were processed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 24.0 for Windows. Descriptive statistical methods, such as mean and standard deviation, were employed. For normally distributed quantitative data, intergroup comparisons were conducted using Student's t-test, while the Mann-Whitney U-test was utilized for non-normally distributed parameters. Correlation analysis was performed to examine relationships between numerical data. The Chi-square test was employed to compare qualitative data. Significant factors identified in the univariate analysis were included in the multivariate analysis. A multivariable logistic regression model was constructed using stepwise regression modeling based on the results of the univariate model with a level of inclusion set at $p < 0.2$. The findings were evaluated within a 95% confidence interval, and statistical significance was defined as a p-value less than 0.05.

Results

The study included a total of 210 patients who underwent appendectomy and were found to have a normal white blood cell count (WBCC). Among these patients, 106 (50.5%) were male and 104 (49.5%) were female, as shown in Table 1. The average age of the patients was 33.0 ± 11.3 years (ranging from 10 to 70 years). Based on the pathology reports, 191 patients were diagnosed with acute appendicitis (AA), while 19 had a normal appendix. The rate of negative exploration was found to be 9.1%, and all cases were attributed to pathological end-stage lymphoid hyperplasia.

Table 1: 105 acute appendicitis patients with normal white blood cell counts: demographic, clinical, radiological, and pathological features.

Variable	Value
Number of patients	210
Age (years)	33.0 ± 11.3
Gender M/F	
Men (%)	106 (50.5%)
Women (%)	104 (49.5%)
Median Alvarado score	4
Appendicitis diagnosis in pathology	
Appendicitis	191 (90.9%)
Normal appendix	19 (9.1%)

Table 2: Laboratory and pathological results in 105 acute appendicitis patients with normal white blood cell counts.

	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 prediction 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

In the univariate analysis (as shown in Table 2), statistically significant factors included the neutrophil count, appendix diameter, and Alvarado score ($p < 0.05$). However, in the multivariate analysis (refer to Table 3), only the diameter of the appendix remained statistically significant ($p = 0.002$). Among the 105 patients, those with an appendix diameter greater than 8 mm based on preoperative ultrasound had a 90.9% likelihood of having acute appendicitis, while 9.1% had a normal appendix upon pathological examination. Conversely, among patients with an appendix diameter less than 8 mm, 30% were diagnosed with acute appendicitis, while the remaining 70% had a normal appendix. The receiver operating characteristic (ROC) analysis yielded an area under the curve of 0.721 at a 95% confidence interval ($p = 0.002$), with the cut-off appendix diameter identified as 8 mm (see Figure 2).

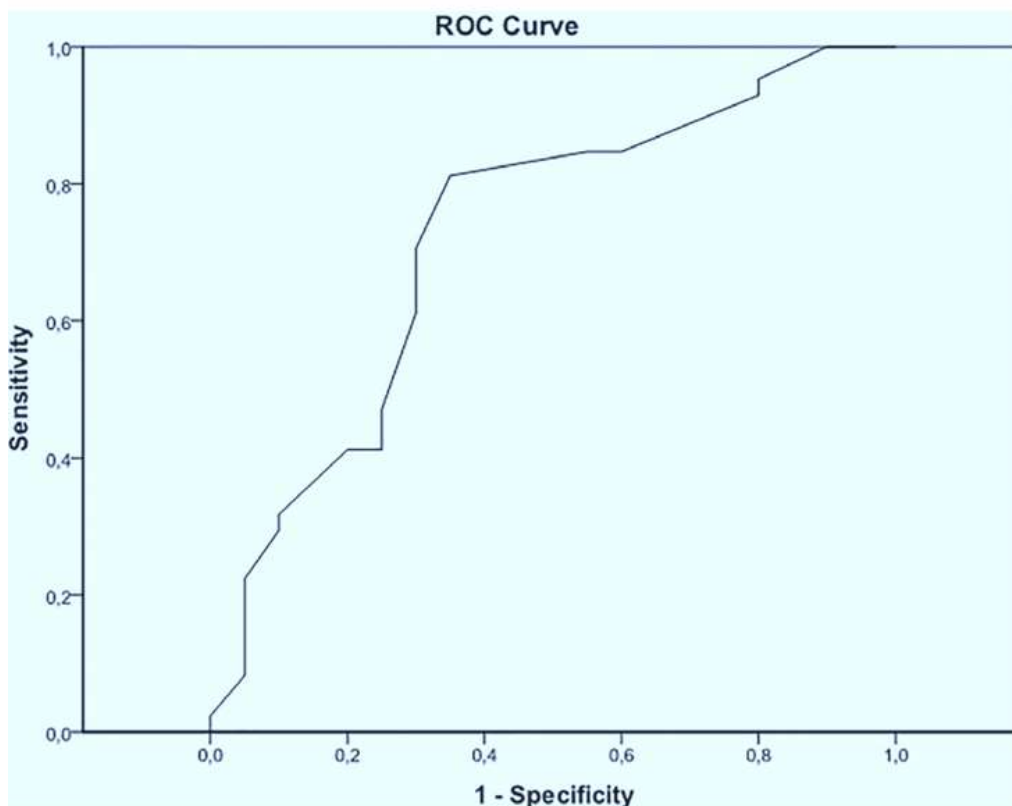


Figure 2: ROC curve. AUC: 0.721 at 95% CI ($p=0.002$); cut-off appendix diameter: 8 mm

Discussion

Acute appendicitis represents the prevailing surgical emergency within the abdominal cavity. The diagnosis of AA poses challenges in elderly individuals, children, and pregnant patients, as it can escalate to a more complex condition and potentially lead to sepsis [10]. The utilization of imaging techniques aids in the diagnosis of acute

appendicitis (AA) and reduces the occurrence of negative appendectomies. Several studies have indicated that the implementation of radiological imaging can significantly decrease the rate of negative appendectomy, decreasing it from 20% to a range of 2-14% [11]. An increased WBCC complements the physical examination when diagnosing AA, but the absence of an elevated WBCC does not rule out the possibility of AA. Patients with a normal WBCC may be admitted for observation; however, several studies have emphasized the importance of an elevated WBCC in the diagnosis of AA [12].

In the present study, statistically significant findings were observed in patients with a normal WBCC, including the neutrophil count, appendix diameter, and Alvarado score. US is the preferred supplementary diagnostic imaging technique for AA, particularly in pregnant patients and women of reproductive age, due to its ability to reduce the rate of negative appendectomy. Ultrasound diagnostic indicators for AA comprise an appendix diameter exceeding 6 mm, an appendix that is not compressed or peristaltic, the presence of free effusion, peri appendicular and bowel wall edema or thickened appendicolith, as well as the existence of peri appendicular abscesses [13]. In our study, we determined that 8 mm serves as the threshold for differentiating a condition with a normal WBCC.

In a study conducted by Nalin et al., it was discovered that among 281 patients with a normal white blood cell count (WBCC), an Alvarado score of 4 was observed [14]. The results of our study validate the conclusions drawn by these authors. Nonetheless, it is important to acknowledge that an Alvarado score below 4 does not exclude the possibility of AA. In an analysis conducted by Bhangu et al., a scoring system was introduced as a component of the diagnostic flowchart for patients suspected of having appendicitis. According to the authors, the newly proposed Angioedema Activity Score demonstrated better performance compared to the validation results of the Alvarado score and Appendicitis Inflammatory Response Score [15].

Within the confines of this investigation, a fascinating exploration revealed that an overwhelming 81% of patients possessing a WBCC within the normal range were diagnosed with AA. Surprisingly, the remaining 19% exhibited a healthy appendix, indicating a negative appendectomy rate that aligns with the upper bounds documented in the literature, specifically ranging from 5% to 15%. In clinical practice, when a patient exhibits an elevated WBCC and presents with suspicious findings during physical examination and laboratory analysis upon arrival, a preliminary diagnosis of AA is made. In particular, for female patients and cases where physical examination is inconclusive and WBCC is normal, US is recommended. If a definitive diagnosis cannot be established, it is advisable to repeat physical examination, laboratory analysis, or US. In cases where these findings present conflicting results, abdominal tomography may be necessary. It is worth noting that this study has certain limitations, including its retrospective design and the involvement of a single center. However, a normal WBCC and an Alvarado score below 4 decrease the likelihood of AA.

Conclusion

An appendiceal diameter exceeding 8 mm in imaging studies (such as ultrasound or computed tomography) demonstrated a 90.9% correlation with AA in histopathological analysis. Based on our findings, we suggest performing appendectomy for patients with a normal WBCC but an appendiceal diameter greater than 8 mm. It is important to note that this study follows a retrospective cohort design, and therefore, the acquisition of informed consent from the patients was not pursued.

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