

Role of hematological parameters in the selection of acute appendicitis treatment

Comparison of hematological parameters of patients with acute appendicitis

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Abstract

Aim: The aim of this study was to compare hematological parameters of patients hospitalized and undertaken operative and non-operative antibiotherapy due to acute appendicitis (AA) in the emergency unit, and to investigate its effect on decision-making for the treatment.

Materials and Methods: Files of the patients hospitalized in the emergency unit due to AA within two years were obtained from electronic records and were retrospectively evaluated. Patients were grouped according to their treatments as non-operative antibiotherapy and surgical treatment. Hematological parameters of the groups on admission to the emergency unit were compared.

Results: Among the 94 patients hospitalized in the emergency unit due to AA and undertaken surgical treatment, 40.4% (n=38) were females and 59.6% (n=56) were males. Among the 108 patients undertaken medical treatment, 38.9% (n=42) were female and 61.2% (n=66) were male. The mean age was 33.4±14.8 which was similar between groups. Among the hematological parameters compared between antibiotherapy (AT) and surgical treatment (ST) groups, white blood cell (WBC) count (p<0.001), neutrophil count (p<0.01), monocyte count (p=0.010) and neutrophil/lymphocyte ratio (p=0.005) were found to be significantly increased in the surgery group. According to ROC analysis, sensitivity, specificity, positive predictive value (PPV) and negative predictive (NPV) values for WBC count at a cut-off level of >13,3 were 58,51, 65,74, 59,78, and 64,55, respectively.

Discussion: WBC, neutrophil and monocyte count, and neutrophil/lymphocyte ratio parameters significantly differed between patients receiving surgical or medical therapy.

Conclusion: Hematological parameters may be helpful for the clinician in the selection of the treatment in combination in acute appendicitis, however, they are insufficient alone.

Keywords

Acute Appendicitis; WBC; Neutrophil Count; Monocyte; Neutrophil/Lymphocyte Ratio

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Introduction

Appendicitis, which is one of the common causes of acute abdominal pain in emergency units, is a clinically urgent situation. Although several factors such as infections have a role in the development of appendicitis, the most important cause is the obstruction of appendiceal lumen. Abdominal pain typically begins in the periumbilical area and subsequently localizes in the lower right quadrant, which is the major symptom, and may be accompanied by loss of appetite, nausea, and vomiting [1]. The most specific findings in physical examination are rebound tenderness, pain on percussion, rigidity and guarding. Tenderness of the lower right quadrant is observed in 96% of the patients, but is a non-specific finding. Methods such as ultrasonography, computed abdominal tomography, laparoscopy and scoring systems are used for the diagnosis of AA [2,3]. Computed tomography has 100% specificity and 97% sensitivity, ultrasonography has 90% specificity and 76% sensitivity [4]. Although appendectomy is preferred as the standard treatment approach in order to avoid complications of acute appendicitis, Coldrey has reported a case series defining non-surgical approach to acute appendicitis, with recovery in most of the cases without surgery [5,6]. Parallel to the advances in imaging technologies, perforations in cases with AA could be determined easily, and non-operative antibiotherapy (AT) is preferred in cases with especially non-perforated acute appendicitis [7,9]. Although non-surgical, antibiotics mediated medical therapy has been preferred in cases at risk for uncomplicated surgery such as those with advanced age, cardiologic or respiratory diseases, or obese patients, there is no standardization for the selection of antibiotherapy. In most of the studies, selection of surgical therapy or antibiotherapy has been made upon randomization, and comparisons such as complications or duration of hospital stay have been made [7, 10, 11]. Studies on hematological parameters in patients with acute appendicitis are generally related to the diagnosis of appendicitis. However, studies on the selection between surgical treatment or antibiotherapy, or hematological parameters on admission to the emergency unit are insufficient [12].

In our study, we aimed to compare the hematological parameters of patients treated surgically and non-surgically using antibiotherapy, who were hospitalized in the emergency unit due to acute appendicitis, and to determine the effect of these parameters on the decision of the treatment.

Material and Methods

The study was started upon approval of the local ethical committee of the university. Patients hospitalized due to AA within the recent 24 months, subsequent to clinical, examinational and imaging methods, were included in the study. Demographic characteristics, imaging technique reports and treatment methods of the patients obtained from the electronic records were recorded into the prepared standard data forms. Patients were grouped according to their treatments as AT and ST. The diagnosis of non-complicated AA in the AT group was confirmed using abdominal tomography and abdominal ultrasonography combination. Antibiotherapy was started as 1 g IV ceftriaxone twice daily and 500 mg metronidazole IV three

times daily for 2 days, and was followed by oral ampicillin/sulbactam (750 mg twice daily) and oral metronidazole (500 mg three times daily) for 10 days. Ciprofloxacin was used for the patients with penicillin allergy. Ciprofloxacin was used for patients with penicillin allergy.

Patients with a history of cardiac failure, peripheral vascular disease, acute or chronic infection, hematological disease, cancer or hepatic disease, those using anticoagulants, nonsteroidal anti-inflammatory drugs or oral contraceptives, those who were not histopathologically confirmed to have appendicitis following surgery, and those who were diagnosed to have a disease other than appendicitis following hospitalization were excluded. The study included patients over 18 years of age.

Hematological parameters including WBC count (range 3.8–8.6 $10^3/\text{micL}$), hemoglobin (HGB) level (range: 11.1–17.1 g/dL), hematocrit (HCT) level (range: 33–57%), mean corpuscular volume (MCV) (range: 76–100 fL), red cell distribution width (RDW) (range: 12–15%), red blood cell (RBC) (range: 4.1–6.0 $10^6/\text{micL}$), platelet (PLT) (range: 140–360 $10^3/\text{micL}$), mean platelet volume (MPV) (range: 7–9 fL), neutrophil count (range: 2.1–6.1 $10^3/\text{micL}$), lymphocyte count (range: 1.3–3.5 $10^6/\text{micL}$) and neutrophil/lymphocyte ratio (NLR) were measured using Advia 2120i (Siemens, Germany) automated analyzer.

Statistical Analysis

Data obtained in the study were analyzed using SPSS 21.0 (IBM Corporation, Armonk, NY, USA) and MedCalc (Version 10.1.6.0) program packages. The Kolmogorov-Smirnov normality test and distribution of continuous variables were performed. Comparison of normally distributed continuous variables between two groups was analyzed via the Student t-test. Numeric variables were expressed as mean \pm standard deviation, and qualitative data were expressed as percentages. Outcomes of ROC Curve analysis were expressed as specificity % and sensitivity % [Area under the ROC curve (AUC), p, 95% Confidence Interval (CI)]. A p-value <0.05 was accepted as statistically significant.

Results

Among the 94 patients hospitalized in the emergency unit due to AA and undertaken ST, 40.4% (n=38) were females (F) and 59.6% (n=56) were males (M). Among the 108 patients undertaken medical treatment, 38.9% (n=42) were females and 61.2% (n=66) were males. M/F ratio was 1.52, the mean age was 33.4 ± 14.8 (range: 18–94). The mean age was similar between groups (Table 1).

Among the hematological parameters compared between AT and ST groups, WBC count ($p < 0.001$), neutrophil count ($p < 0.01$), monocyte count ($p = 0.010$) and neutrophil/lymphocyte ratio ($p = 0.005$) were found to be significantly increased in the surgery group. No significant difference was observed between groups with regard to the remaining parameters (Table 1).

According to ROC analysis, sensitivity, specificity, PPV and NPV values for WBC count at a cut-off level of >13.3 were 58,51, 65,74, 59,78, and 64,55, respectively. ROC analysis outcomes of other hematological parameters are presented in Table 2.

Table 1. Comparison of demographic and hematological parameters of the patients.

	Medical treatment (AT)	Surgical treatment (ST)	P
n (M/F)	108 (66/42)	94 (56/38)	0.824
Age	33,287± 15,685	33,532±13,8414	0,906
WBC (Mean± SD)	12,035±3,569	14,19±4,2803	<0,001
RBC (Mean± SD)	4,73±0,536	4,841±0,537	0,143
HGB (Mean± SD)	13,793±1,686	14,214±1,8333	0,091
HCT (Mean± SD)	41,531±4,486	42,685±5,1083	0,089
MCV (Mean± SD)	88,244±7,611	88,413±6,2337	0,865
RDW (Mean± SD)	15,262±2,203	14,85±1,6885	0,142
PLT (Mean± SD)	250,83±60,684	255,51±72,4699	0,618
MPV (Mean± SD)	8,666±0,862	8,65±0,8984	0,899
PDW (Mean± SD)	15,545±2,245	15,65±2,025	0,730
Lymphocyte (Mean± SD)	1,955±0,760	1,803±0,7818	0,163
Neutrophil (Mean± SD)	9,011±3,548	11,178±4,3761	0,000
Monocyte (Mean± SD)	0,827±0,319	0,955±0,3858	0,010
Eosinophil (Mean± SD)	0,201±0,159	0,171±0,1424	0,160
Basophil (Mean± SD)	0,0455±0,039	0,0452±0,04452	0,966
NLR (Mean± SD)	5,852±4,688	8,195±6,8989	0,005

WBC: white blood cell, RBC: red blood cell, HGB: hemoglobin, HCT: hematocrit, MCV: mean corpuscular volume, RDW: red cell distribution width, PLT: platelet, MPV: mean platelet volume PDW: Platelet Distribution Width, NLR: Neutrophil/lymphocyte ratio

Discussion

Acute appendicitis is an emergency surgical situation that may have complications such as perforation, abscess or peritonitis. However, surgical complications such as intestinal infection, intraabdominal abscess or ileus increase attention to non-surgical alternative treatments [13].

Hematological parameters are generally measured for the diagnosis of AA, and the results are found to be variable. The first hematological parameter is WBC count. Many studies have reported that increased WBC count was generally an early indicator of the inflammation in the appendix, increased leukocyte count was observed in most of the patient as well [14, 15]. In various studies, WBC sensitivity has been recorded as 85.8%, 97.8%, 67%, and 76%; specificity as 31.9%, 55.6%, 80%, and 56%; and PPV as 89.2% in AA diagnosis. Xharra et al. [16] in a prospective, double-blind study, specificity and sensitivity of WBC count for the diagnosis of AA were found to be 85.1% and 68%, respectively; the positive predictive value was found to be 94%. WBC count was found to be normal in 8 patients with histopathologically confirmed AA, and as increased in the remaining. WBC count was reported to be increased in

Table 2. ROC analysis outcomes.

	Cutt-off	AUC	95% CI	P	Sensitivity	Specificity	PPV	NPV
WBC	>13,3	0,646	0,575- 0,711	0,0002	58,51	65,74	59,78	64,55
Neutrophil	>11,2	0,649	0,579- 0,714	0,0001	52,13	75,93	65,3	64,6
Monocyte	>0,64	0,590	0,519- 0,658	0,0249	84,04	38,89	54,5	73,7
NLR	>5,86	0,636	0,565 -0,702	0,0006	57,45	67,59	60,7	64,6

WBC : white blood cell, NLR: Neutrophil/lymphocyte ratio, AUC: Area under the ROC curve, PPV: Positive predictive value, NPV: Negative predictive value

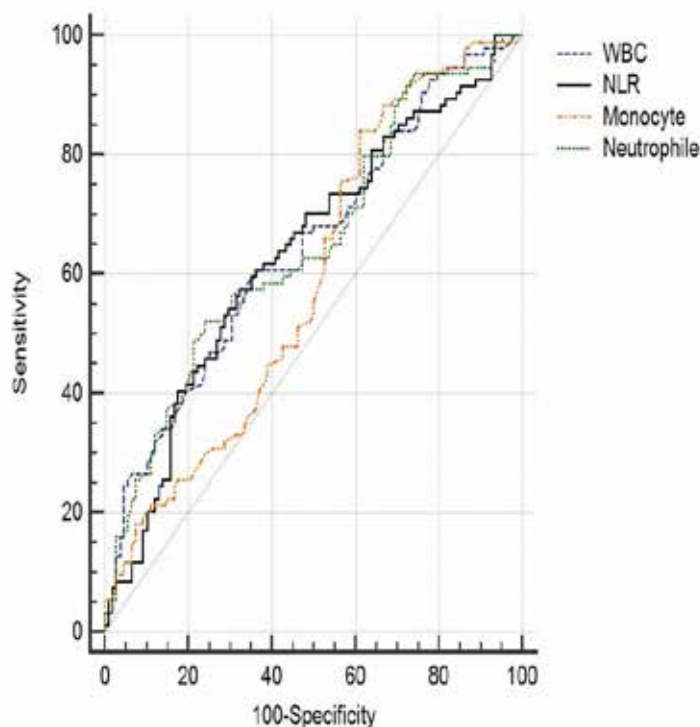


Figure 1. ROC analysis plot.

cases with AA in the presence of complications. In the study of Kaya et al. [17], WBC count was found to be significantly increased in cases with perforated appendicitis than those with phlegmonous appendicitis. A total of 126 patients were included in the study of Yardeni et al. [12], among those, 38 were operated within 6 hours and 88 were operated within 24 hours; no difference was found between the WBC count measure at the emergency unit. Likewise, in the prospective study of Malik AA et al. [11] including 80 patients 40 of whom were undertaken surgical treatment and the remaining were undertaken medical therapy, treatment method was performed in a randomized manner and it was observed that WBC count showed a rapid decrease in the antibiotherapy group. In the study of Hansson et al. on 369 patients with AA, medical and surgical treatments were compared, where treatment method was performed in a randomized manner as well. Patients undertaken surgery demonstrated a higher level of WBC, higher body temperature and peritonitis risk compared to patients undertaken antibiotherapy [8]. Kirkil et al. [18] have reported that WBC count had no effect in predicting recurrence in patients undertaken non-operative antibiotherapy. In our study,

we observed that WBC count on admission to the emergency unit was significantly higher in the surgical treatment group. However, sensitivity, specificity, PPV, and NPV values were found to be 60%. We believe that WBC count, which is an increased marker in patients with AA, may be effective for the decision of the treatment between surgery and antibiotherapy, and that WBC count alone may not be a sufficiently effective parameter. Neutrophil count or neutrophil percentage which are known to increase in inflammatory situations, have been shown to increase in AA as well [19, 20]. Albayrak et al. [21] have reported that neutrophil percentage was significantly increased in patients with AA compared to the healthy control group and the sensitivity, specificity, PPV and NPV values were 68.6%, 86.4%, 84.7% and 71.5, respectively. Bilici et al. [22] have reported significantly increased neutrophil percentage in pediatric patients with a specificity and sensitivity level of 90% and 93%, respectively. Lin et al. [23] have reported that the duration of symptoms, peritoneal signs and increased CRP were predictors of a rupture in patients with acute appendicitis, but leukocyte count did not differ between patients with or without rupture. In our study, neutrophil count on admission to the emergency unit was found to be significantly increased in the surgery group with a sensitivity and specificity of 52.13% and 75.93%, respectively.

Left shift of neutrophilia and hemogram in acute appendicitis is generally associated with lymphopenia and was reported to be presented by monocytosis, which is a characteristic finding of acute infections [14, 24]. In our study, no difference was observed between patients undertaken surgical treatment or antibiotherapy with regard to lymphocyte count, however, monocyte count was found to be higher in the surgery group. A monocyte count >0.64 had a sensitivity and specificity of 84% and 38.8%, respectively.

Neutrophil-to-lymphocyte ratio and mean platelet volume (MPV) are hematological parameters that have been shown to have a relationship with inflammatory conditions. Many studies have reported increased neutrophil count and decreased lymphocyte count in acute appendicitis, and related increase in neutrophil/lymphocyte ratio (NLR) was found to have a high sensitivity for the diagnosis of the disease. In the study of Markar et al. investigating 1117 patients undertaken appendectomy, NLR was reported to have significantly higher diagnostic sensitivity compared to leukocyte count and CRP.

Another hematological parameter investigated for the diagnosis of AA is RDW, which has demonstrated different results. Narci et al. [29] have retrospectively evaluated the data of 590 patients operated due to AA for 3 years and compared the outcomes of these patients to those of healthy controls (n=121). They have detected significantly lower RDW in patients with AA, and the sensitivity and specificity levels were found to be 47 and 67% respectively, when the cutoff value was accepted as 15.6%. In the study of Tanrikulu et al., no significant difference was observed between RDW of patients with AA and individuals in the control group. In our study, no difference was observed between RDW values of patients planned to undergo surgical treatment and those planned to receive medical therapy.

Albayrak et al. [21] have reported significantly reduced MPV in patients with AA compared to healthy controls as well. The

best MPV level cutoff point for AA was 7.6 fL, with a sensitivity of 73% and a specificity of 84%. Bilici et al. have reported significantly reduced MPV in pediatric patients with AA as well, with a specificity of 60% and a sensitivity of 87%. In our study, no significant difference was observed between MPV values of the patients planned to undergo surgical treatment and those planned to receive medical therapy.

Treatment decision for patients with AA is made upon factors such as the clinical situation and imaging outcomes of the patient, and response to therapy. Hematological parameters may be used for the diagnosis of AA, and may help the clinician in the selection of the treatment. However, we believe that this alone is not sufficient for decision making compared to hematological parameters, and other factors should carefully be considered as well.

Limitations of the study

This study had the following limitations: it was designed on the blood samples collected in the emergency unit on admission, no standardization was performed for the patients undertaken surgical treatment or antibiotherapy, the design was retrospective, decision of surgery was left completely to the choice of the surgeon, no histopathological discrimination of perforation, abscess or inflammation was performed, the diagnosis was made upon physical examination, patient history, clinical, laboratory and imaging findings for especially patients undertaken antibiotherapy, which are not 100% diagnostic, and no histopathological data were present for precise diagnosis of these patients.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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