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A New Diagnostic Tool for Acute Appendicitis: Clearmine Score

Abidin Aygün[1], Mustafa Burak Sayhan[2], Ömer Salt[3], Aykut Yucal[4], Eray Çeliktürk[2], Serhat Oğuz[5], Eylem Sezenler[6]

[1]*Hitit University, Erol Olçok Education And Research Hospital, Department of Radiology, Çorum, Türkiye*
[2]*Trakya University, Faculty of Medicine, Department of Emergency Medicine, Edirne, Türkiye*
[3]*Kayseri City Hospital, Department of Emergency Medicine, Kayseri, Türkiye*
[4]*Harakani State Hospital, Department of Emergency Medicine, Kars, Türkiye*
[5]*Bandırma Onyedi Eylül University, Faculty of Medicine, Department of General Surgery, Balıkesir, Türkiye*
[6]*Sultan 1. Murat State Hospital, Department of Emergency Medicine, Edirne, Türkiye*

Abstract

Objective: This study aimed to evaluate the diagnostic value of clinical, physical examination, and laboratory findings for acute appendicitis, to create a novel scale using the most meaningful parameters, and to compare it with current diagnostic scores.

Materials and Methods: This was a single-center, retrospective, observational study. Between July 2011 and January 2015, 172 patients aged ≥18 years who visited the emergency department and underwent surgery with a diagnosis of acute appendicitis were included in the study. Patients were divided into two groups, acute appendicitis and negative appendectomy, according to the histopathology reports. ROC analyses of age, sex, clinical characteristics, physical examination results, and laboratory findings were performed, and the areas under the curves were obtained according to the diagnostic groups. Clearmine (CRP, leukocyte, anorexia, rebound tenderness, migration of pain, neutrophil) scores and other scales were compared in terms of diagnostic value for acute appendicitis.

Results: A total of 110 patients were male. The mean age was 34.2±15.8 years. The negative appendectomy rate was 16.3%. Among the clinical presentations, migration of pain (AUC:0.78) and anorexia (AUC:0.75) had the highest diagnostic value. The parameters with the highest diagnostic value were rebound tenderness (AUC:0.68) among physical examination findings and neutrophil count (AUC:0.71), leukocyte count (AUC:0.70), and CRP (AUC:0.68) among laboratory findings. The Clearmine score reached the highest diagnostic value for acute appendicitis when the cutoff was ≥6 points (AUC:0.92). Other scales, including Alvarado, Andersson, Ohmann, and Tzanakis, had lower AUCs.

Conclusion: Compared with other acute appendicitis diagnostic scales currently used in the literature, the Clearmine score has greater diagnostic value; it is practical and useful for use in the emergency department.

Keywords: Acute appendicitis, Clearmine score, emergency medicine, missed appendicitis, negative appendectomy

Introduction

Approximately 10% of emergency department admissions are due to abdominal pain, and acute appendicitis remains the most common surgical cause [1-3]. Since the first appendectomy was performed, mortality rates have decreased dramatically from 67% to less than 1%, largely due to advances in surgical techniques, particularly laparoscopic surgery [4-7]. Despite improvements in treatment, diagnostic challenges persist. The clinical presentation of acute appendicitis can vary widely, and the decision to perform appendectomy is often finalized intraoperatively, contributing to reported negative appendectomy rates of up to 30% [2,8,9].

The diagnosis of acute appendicitis relies on a combination of clinical history, physical examination, laboratory findings, and imaging modalities. To integrate these components, several diagnostic scoring systems have been developed, including the Alvarado, Ohmann, Tzanakis, and Andersson scores [10-13]. Although advances in imaging have improved diagnostic accuracy, clinical scoring systems remain valuable, particularly in emergency

Address for Correspondence: Aykut Yucal, Department of Emergency Medicine, Harakani State Hospital, Yenişehir, Kars 36200, Türkiye
E-mail: dr.aykutyucal@gmail.com **ORCID-ID:** 0000-0001-5959-6855

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departments and resource-limited settings. Previous studies have shown that these scores can reduce negative appendectomy and complication rates; however, their overall diagnostic performance remains variable and sometimes limited [10-15].

On the other hand, although new approaches derived from commonly used inflammation markers, such as the neutrophil/lymphocyte ratio, are popular in this regard, studies have also shown their limited diagnostic accuracy [16].

Imaging methods are not always accessible everywhere, laboratory data alone cannot provide sufficient diagnostic power, and clinical scales continue to be valuable. However, the existing scoring systems in the literature led us to develop a new scale that could offer a more successful, practical, and rapid diagnostic evaluation for the emergency department. This is because some of them contain complex parameters that make practical application difficult, some include imaging parameters that may not always be accessible, and some have limited diagnostic success. In our study, we aimed to develop a new clinical scale that could solve all these problems and compare this scale with existing scales in terms of diagnostic value.

Materials and Methods

Study Settings and Design

This was a single-center, retrospective, observational study. The patients' clinical data were obtained by reviewing emergency department files, operative notes, epicrises, and the hospital information processing system database. We included patients aged 18 years and older who underwent appendectomy for acute appendicitis in the emergency department between July 2011 and January 2015. Pediatric patients, pregnant patients, and patients with incomplete clinical information were excluded from the study. There were 217 patients who were diagnosed with acute appendicitis and underwent appendectomy in the emergency department. Among these patients, 45 were excluded from the study because of missing information. A total of 172 patients who met the inclusion criteria were included in the study. Clinical findings, physical examination characteristics, laboratory data, and imaging results were recorded. Patients were divided into two groups according to the histopathological analysis of the excised appendix tissue. Patients with a confirmed diagnosis of acute appendicitis were classified into the "Acute Appendicitis (AA) Group," and patients with histopathological results incompatible with acute appendicitis were classified into the "Negative Appendectomy (NA) Group" (Figure 1).

The diagnostic value of a new scoring system that could be formed from clinical and physical examination findings and laboratory findings with the highest diagnostic value was investigated. ROC analyses were used to compare the scoring systems. In addition, false-positive (negative appendectomy) and false-negative (missed appendicitis) rates were compared.

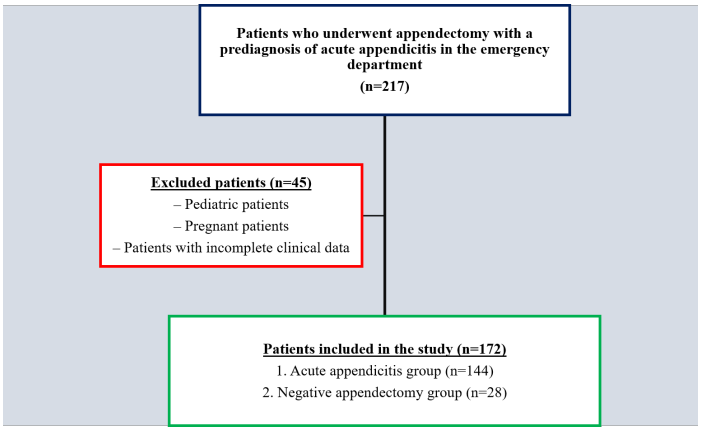

Figure 1. Flow chart of patient selection and study design.

Ethical Statement

The study was conducted with the approval of the Ethics Committee Presidency of Trakya University Faculty of Medicine (Protocol code: TUTF-GOBAEK 2015/112; May 27, 2015). The Declaration of Helsinki was fully complied with, and the data required to protect patient privacy were obtained from clinical records without any clinical intervention.

Examination of Laboratory Results

The diagnostic value of leukocyte count (WBC), neutrophil count (NEU#), neutrophil percentage (NEU%), and C-reactive protein (CRP) level for acute appendicitis was analyzed. The "Sysmex® pocH-100i Automated Hematology Analyzer, SN:F6797, Sysmex Corp., Kobe, Japan" was used for hemogram examination. The "Architect® c 16000 Clinical Chemistry and Immunoassay Test Analyzer, SN:C1600280, Abbott Laboratories, Illinois, USA" was used for CRP analysis.

Radiodiagnostic Examination

Diagnostic evaluation of the patients with USG was performed by radiologists at our hospital who had sufficient experience in the field; 3.5–7.5 MHz linear and convex probes of the "Mindray® UMT-150 (SN:PTA35003299, Shenzhen Biomedical Electronics Co. Ltd., Hamburg, Germany)" device were used.

Appendicitis Scoring Systems and Development of the Clearmine Score

For comparison, established appendicitis scoring systems were calculated for each patient according to their original definitions. The Alvarado score includes migration of pain to

the right lower quadrant, anorexia, nausea/vomiting, right lower quadrant tenderness, rebound tenderness, elevated body temperature, leukocytosis, and neutrophil left shift. The Andersson score consists of right lower quadrant pain, rebound tenderness or muscular defense, body temperature, leukocyte count, proportion of neutrophils, and C-reactive protein level. The Tzanakis score incorporates right lower quadrant tenderness, rebound tenderness, leukocytosis, and ultrasonographic findings. The Ohmann score includes right lower quadrant pain, rebound tenderness, abdominal rigidity, coughing pain, leukocyte count, and age- and sex-related variables. In addition, the Clearmine score developed in this study comprises the degree of pain migrating to the right lower quadrant, anorexia, rebound tenderness, leukocyte count, neutrophil count, and C-reactive protein level. All scoring systems were calculated retrospectively from recorded clinical, physical examination, laboratory, and imaging data.

A new diagnostic score, the Clearmine score, was developed using clinical and physical examination findings and laboratory parameters, which demonstrated the highest diagnostic performance on the basis of ROC curve analysis. Parameters were selected according to their AUC values and clinical applicability. Ultrasonography, despite its diagnostic value, was excluded to preserve simplicity and feasibility in emergency settings. Highly correlated variables were evaluated, and among correlated parameters, the one with the highest diagnostic performance was retained to avoid redundancy. Score weighting was assigned according to defined AUC categories to reflect the relative diagnostic contribution of each parameter. The cutoff values used for continuous variables, including WBC, neutrophil percentage, and CRP, were predefined on the basis of receiver operating characteristic (ROC) curve analysis and are presented in Table 2. The overall score was calculated by summing individual parameter points, and its diagnostic performance and optimal cutoff value were evaluated using ROC analysis. The detailed point allocation and diagnostic performance of the individual parameters are presented in the Results section.

Primary and Secondary Outcomes of the Study

The primary outcome of the study was the diagnostic accuracy of the Clearmine score for acute appendicitis, with histopathological findings used as the reference standard. The secondary outcomes included comparisons of the diagnostic performance of the Clearmine score with that of established appendicitis scoring systems and determination of the optimal cutoff value for clinical use.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 20.0 for Windows®, license no: 10240642, IBM Inc., Chicago, IL, USA. The distribution of continuous data was checked using the Kolmogorov–Smirnov test. Independent sample t-tests were used to compare the mean ages of the groups since they were normally distributed. The Pearson chi-square test was used to compare categorical data. Descriptive data are presented as means±standard deviations or numbers (percentages), as appropriate. While evaluating the diagnostic value of age, sex, clinical characteristics, physical examination and laboratory findings, imaging results, and clinical scales, receiver operating characteristic (ROC) curves were drawn, and areas under the curve (AUCs) were calculated. Additionally, cutoff values, sensitivity, and specificity ratios were calculated. Clearmine scores were analyzed using the DeLong test and compared with other important diagnostic parameters using receiver operating characteristic (ROC) curves.

For all statistical analyses, $p<0.05$ was chosen as the significance limit.

Results

Among the 172 patients included in the study, 83.7% (n=144) were in the acute appendicitis group, and 16.3% (n=28) were in the negative appendectomy group. A total of 64% (n=110) of all patients were male, 66.7% (n=96) were in the acute appendicitis group, and 50% (n=14) were in the negative appendectomy group. In the acute appendicitis group, there was no significant difference in sex rates compared with those in the general patient population (p=0.09); however, in the negative appendectomy group, the female rate was significantly greater (p<0.001). In addition, the rate of negative appendectomy was 22.6% in females and 12.7% in males, and there was a significant difference between the sex groups (p=0.01). The mean age of all patients was 34.2±15.8 years: 35.4±16.4 years in the acute appendicitis group and 27.8±10.2 years in the negative appendectomy group. This difference between the groups was statistically significant (p<0.001). A total of 55.8% (n=96) of the patients were under 30 years of age.

In the acute appendicitis group (n=144), according to histopathologic examinations, 31.9% (n=46) of the patients were reported as having simple inflammation, 18.8% (n=27) as having suppurative appendicitis, 16% (n=23) as having phlegmonous appendicitis, 1.4% (n=2) as having gangrenous appendicitis, 17.4% (n=25) as having perforated appendicitis, and 14.6% (n=21) as having plastron appendicitis. In the reports of the same group, only 47.9% (n=69) of patients had a known cause of luminal obstruction. Fecalith was the most common cause, with a rate of 73.9% (n=51). In 39.3% (n=11) of the patients in the negative appendectomy group, no histopathological findings were

detected, and cases were recorded as nonspecific abdominal pain. Descriptive data and histopathological results are given in detail in Table 1.

Receiver operating characteristic (ROC) analyses were performed to investigate the diagnostic value of clinical, physical, laboratory, and imaging data and acute appendicitis clinical scale scores in the detection of acute appendicitis. The areas under the curve in the ROC curves were compared. Sex, age, anorexia, nausea and vomiting, migration of pain to the right lower quadrant, absence of urinary complications, Rovsing's sign, persistence of abdominal pain, rebound tenderness, right lower quadrant pain, rigidity, pain intensity, leukocyte count, neutrophil count, neutrophil percentage, CRP, USG findings compatible with appendicitis, fever, and diagnostic scores of Alvarado, Ohmann, Andersson, Tzanakis, and Clearmine, a new scale created in our study, were evaluated (Figure 2).

Table 1. Descriptives and histopathological results

		Total (n=172)	Acute appendicitis (n=144)	Negative appendectomy (n=28)	p
Age (years)		34.2±15.8	35.4±16.4	27.8±10.2	<0.001*
Sex	Male	110 (64)	96 (66.7)	14 (50)	c) 0.01#c
	Female	62 (36)	48 (33.3)	14 (50)	
	p	-	0.09#a	b) <0.001#b	-
Causes that obstruct the lumen					
Cause			Total n (%)	Perforated appendicitis n (%)	Nonperforated appendicitis n (%)
No causative factor			75 (52.1)	7 (4.9)	68 (47.2)
Fecalith			51 (35.4)	12 (8.3)	39 (27.1)
Calculus			10 (6.9)	6 (4.2)	4 (2.8)
Carcinoid tumor			3 (2.1)	0 (0.0)	3 (2.1)
Appendiceal neuroma			2 (1.4)	0 (0.0)	2 (1.4)
Cecum tumor			2 (1.4)	0 (0.0)	2 (1.4)
Tubular adenoma			1 (0.7)	0 (0.0)	1 (0.7)
Total			144 (100)	25 (17.4)	119 (82.6)
Confirmed diagnosis in negative appendectomies					
Diagnosis			Total n (%)	Female n (%)	Male n (%)
Nonspecific abdominal pain			11(39.3)	4 (28.6)	7 (50.0)
Meseneteric lymphadenopathy			8 (28.6)	2 (14.3)	6 (42.9)
Ovarian cyst rupture			2 (7.1)	2 (14.3)	-
Typhlitis			1 (3.6)	1 (7.1)	0 (0.0)
Appendagitis			1 (3.6)	1 (7.1)	0 (0.0)
Pelvic inflammatory disease			1 (3.6)	1 (7.1)	-
Ileal perforation			1 (3.6)	0 (0.0)	1 (7.1)
Ectopic pregnancy			1 (3.6)	1 (7.1)	-
GALT lymphoma			1 (3.6)	1 (7.1)	0 (0.0)
Ileal ischemia			1 (3.6)	1 (7.1)	0 (0.0)
Total			28 (100)	14 (100)	14 (100)

GALT: gut-associated lymphoid tissue; *: independent sample t test; #: chi-square test; a: comparison of Acute Appendicitis group vs total; b: comparison of Negative Appendectomy group vs total; c: comparison of female vs male within Negative Appendectomy group. Note: Data in the table are expressed as means ± standard deviations or n(%) as applicable.

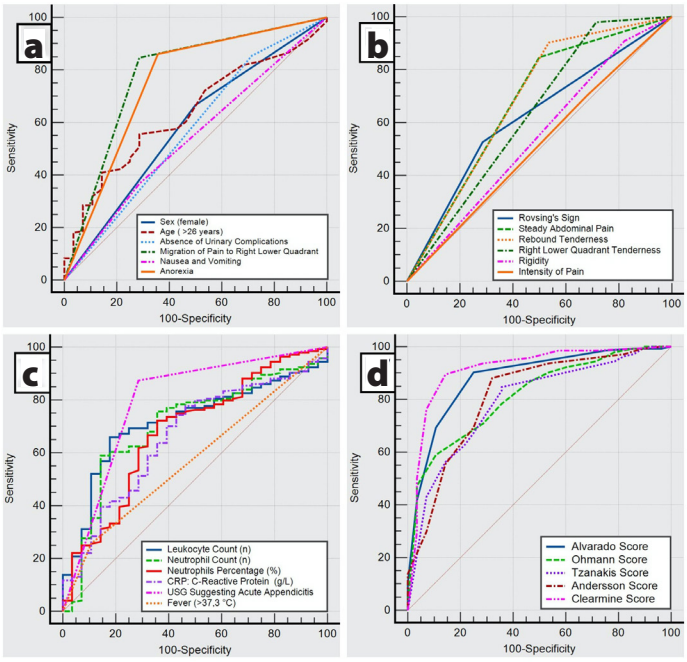

Figure 2. ROC analyses evaluating the predictive value of clinical and physical examinations, laboratory parameters and diagnostic scales for acute appendicitis. a: Comparison of anamnesis variables, b: Comparison of physical examination findings, c: Comparison of laboratory and vital measurements, d: Comparison of Clearmine and other scales.

The presence of pain in the right lower quadrant had the highest diagnostic value for acute appendicitis (AUC=0.78). Anorexia was the second highest complaint (AUC=0.75). Among the laboratory findings, leukocyte count and neutrophil count were found to have the highest diagnostic value (AUC=0.70 and AUC=0.71, respectively). Abdominal USG was also found to have a very high diagnostic value (AUC=0.79) (Table 2) .

Creation of the Clearmine score

On the basis of the data obtained, a new diagnostic scale was created from the parameters with the highest AUC values. Migration of pain to the right lower quadrant (AUC=0.78), anorexia (AUC=0.75), neutrophil count (AUC=0.71), leukocyte count (AUC=0.70), rebound tenderness (AUC=0.68), and CRP (AUC=0.68) were included in the scale. The acronym "CLeARMiNe," meaning "clear mine," was created using the first or first two letters of the parameters. Despite having high diagnostic value, the USG parameter was not included in the scale because it would require additional personnel, time, and experience for practical use of the scale. Neutrophil percentage also had high diagnostic value, but since it was highly correlated with neutrophil count, we included only neutrophil count, which had a relatively high AUC value. Thus, we tried to maintain the simplicity of the scale. The point coefficient was assigned according to the AUC values of the parameters in the scale. CRP, rebound tenderness, and leukocyte count, with AUC values between 0.65 and 0.70, were assigned 1 point; neutrophil count and anorexia, with AUC values between 0.70 and 0.75, were assigned 2 points; and pain migration to the right lower quadrant, with an AUC value above 0.75, was assigned 3 points. The diagnostic evaluation of the patients was performed on a total of 10 points. ROC analysis revealed that the cutoff value for the Clearmine score was 6 points and above. A score of 6 or above was found to have greater diagnostic value than other acute appendicitis diagnostic scales (AUC=0.92; sensitivity=91%; specificity=85.7%) (Table 2) .

According to the Clearmine score, 1.4% of acute appendicitis patients scored between 0 and 2 points, 7.9% scored between 3 and 5 points, and 90.6% scored 6 or above. Among negative appendectomy patients, 85.7% scored between 0 and 5. In negative appendectomy patients who scored 6 points or more, the prominent diagnoses were ovarian cyst rupture, nonspecific abdominal pain, mesenteric lymphadenopathy, and pelvic inflammatory disease. Among the scales used in the present study, the Clearmine score had the lowest rates of misdiagnosis, that is, the lowest rates of negative appendectomy diagnosis and missed appendicitis (Table 3) .

Discussion

Acute appendicitis is the most common cause of surgery in patients who present to the emergency department with abdominal pain. According to previous studies, acute appendicitis, which can occur in all age groups, is frequently observed between the first and third decades of life [2,17]. In our study, we found that most patients in the acute appendicitis group were younger than 30 years (55.8%). Additionally, in the literature, the frequency of acute appendicitis decreases with increasing age [18]. In our study, a similar change was observed in the patient group with increasing age.

Despite advances in diagnostic methods, false-positive diagnoses leading to negative appendectomy results remain an important problem in the management of suspected acute appendicitis. Contemporary evidence indicates that negative appendectomy rates remain clinically relevant, with recent systematic reviews reporting pooled rates of approximately 10–15%, despite the widespread use of imaging and laparoscopic surgery. Moreover, several recent studies have consistently demonstrated that negative appendectomy rates are significantly higher in females than in males. This difference has been largely attributed to the overlap between gynecologic conditions and appendicitis-like clinical presentations, which continues to complicate accurate diagnosis [9,19]. In line with these findings, the negative

Table 2. ROC analysis of important parameters for acute appendicitis diagnosis

Parameters	p*	AUC	CI 95%	Cutoff value	Sen (%)	Spe (%)	DeLong p values vs *Clearmine score*
Sex	0.16	0.58	0.47-0.70	-	33	50	-
Age (years)	0.02	0.64	0.54-0.74	≥27	56	71	<0.001
Absence of urinary symptoms	0.24	0.57	0.45-0.69	-	86	29	-
Migration of pain to the RLQ	<0.001	0.78	0.68-0.89	-	85	71	0.001
Nausea and vomiting	0.49	0.54	0.43-0.66	-	63	29	-
Intensity of pain	0.85	0.51	0.39-0.63	-	70	32	-
Anorexia	<0.001	0.75	0.64-0.86	-	86	64	<0.001
Fever	0.21	0.58	0.47-0.68	-	26	89	-
Steady abdominal pain	0.003	0.67	0.56-0.80	-	85	50	<0.001
Rovsing's sign	0.04	0.62	0.51-0.73	-	53	71	<0.001
Rebound tenderness	0.002	0.68	0.56-0.81	-	90	46	<0.001
Right lower quadrant tenderness	0.11	0.60	0.47-0.72	-	97	27	-
Rigidity	0.46	0.54	0.42-0.67	-	19	82	-
Leukocyte count (n)	0.001	0.70	0.60-0.80	>12500	66	82	<0.001
Neutrophils percentage (%)	0.002	0.69	0.57-0.80	76	71	64	<0.001
Neutrophil count (n)	0.001	0.71	0.61-0.82	>10000	59	86	<0.001
CRP	0.003	0.68	0.57-0.79	0.35	74	57	<0.001
USG suggesting acute appendicitis	<0.001	0.79	0.68-0.90	-	88	70	
Alvarado score	<0.001	0.88	0.81-0.95	≥7	90	75	0.04
Ohmann score	<0.001	0.81	0.73-0.89	≥12	81	61	0.01
Tzanakis score	<0.001	0.80	0.71-0.89	≥8	86	64	0.01
Anderson score	<0.001	0.82	0.73-0.91	≥9	89	68	0.01
Clearmine score	<0.001	0.92	0.85-0.98	≥6	91	86	-

RLQ: Right lower quadrant; *: ROC analysis; Sen: Sensitivity; Spe: Specificity; AUC: Area under the curve; CI: Confidence interval. Note: AUC values were compared using the DeLong method. Clearmine score was used as the reference model for ROC curve comparisons.

appendectomy rate in our study was 16.3%, and female patients had higher rates than male patients.

Recent evidence suggests that, among the clinical features of acute appendicitis, pain that initially arises periumbilically and subsequently migrates to the right lower quadrant remains one of the most valuable diagnostic indicators [20,21]. In our study, we similarly found that pain migration had the highest diagnostic value. On the basis of these results and the current literature, migration of pain to the right lower quadrant should be considered a typical finding of acute appendicitis and should be included in diagnostic algorithms.

Anorexia has been reported as an important presenting symptom in acute appendicitis and is included among the classic clinical features of the disease in contemporary literature. Recent systematic reviews and clinical overviews describe anorexia, often accompanying nausea and vomiting, among the characteristic symptoms that increase the likelihood of an appendicitis diagnosis when present [20]. Alvarado [10] reported that anorexia had a high diagnostic value for acute appendicitis and added it to the scale in his study, in which he defined the MANTRELS score. Similarly, anorexia was the symptom with the highest diagnostic value after pain migration for acute appendicitis and was included in our diagnostic scale.

Rebound tenderness has long been recognized as a key physical examination finding suggestive of peritoneal irritation and is frequently evaluated in suspected acute appendicitis [22]. We also determined the sensitivity of rebound tenderness as the

Table 3. Misdiagnosis rates of scales

Scales	Negative appendectomy (False positive) (%)	Missed appendicitis (False negative) (%)
Alvarado score	4.1	8.1
Ohmann score	6.4	15.7
Tzanakis score	6.0	12.0
Andersson score	5.4	9.0
Clearmine score	2.3	7.8

physical examination finding with the highest diagnostic value, at 90%, and thus decided to include rebound tenderness in the diagnostic scale.

Inflammatory parameters in routine laboratory tests remain essential for the diagnosis of acute appendicitis. Contemporary evidence shows that basic complete blood count parameters, particularly total leukocyte count, neutrophil count, and neutrophil percentage, are significantly elevated in patients with histopathologically confirmed acute appendicitis [10,23,24]. In addition to leukocyte count, neutrophil count was the laboratory parameter with the highest diagnostic value in our study. Neutrophil percentage ranked third after these two parameters. Thus, we decided to include leukocyte count and neutrophil count parameters in the Clearmine score that we created for acute appendicitis.

C-reactive protein (CRP) is a well-established acute-phase reactant whose level increases in response to inflammation, including in acute appendicitis. Recent clinical evidence indicates that CRP has moderate diagnostic value for suspected acute appendicitis [25,26]. In our study, the cutoff value of CRP was 0.35 mg/dL, and we included it in our scale. In this way, the high sensitivity of CRP can be utilized, and its low specificity can be compensated for when it is used in combination with other parameters.

Today, the diagnosis of acute appendicitis has become much easier with abdominal USG and abdominal CT/magnetic resonance imaging, but the need for extra devices/personnel or exposure to radiation/contrast material is a concern [17,27,28]. Therefore, diagnostic scales that are suitable for practical use are still important, especially in emergency departments. There are many scales, such as the Andersson, Tzanakis, Ohmann, and Alvarado scales, in the literature [10-13]. Despite many alternatives, some patients are still misdiagnosed or not clearly diagnosed with these scales. When we compared the diagnostic values, both the highest AUC value and the lowest rates of negative appendectomy or missed appendicitis were associated with the Clearmine score. On the basis of these results, we believe that our scale is suitable for use in the diagnosis of acute appendicitis and will minimize misdiagnosis.

Study Limitations

Our study is a single-center study with a relatively limited sample size. When multicenter studies with larger samples are conducted, the value of the Clearmine score for acute appendicitis will be more clearly understood. This study included only patients who underwent appendectomy and had a confirmed histopathological diagnosis. The exclusion of cases of suspected appendicitis that were managed conservatively or did not undergo surgery may have created a higher-risk cohort and led to an overestimation of diagnostic performance. The Clearmine score was developed and tested within the same dataset without external validation, which may introduce overfitting and optimistic performance estimates and limit generalizability.

Conclusion

The rate of negative appendectomy is higher in females, and gynecologic pathologies are the most common causes. Acute appendicitis is mostly observed in the 20–25-year age group. Simple inflammatory appendicitis is the most common form. The Clearmine score is a simple and rapidly applicable scale with high predictive value for the diagnosis of acute appendicitis, particularly in emergency departments. The Clearmine score was more effective than other scales that are currently in use for acute appendicitis. When these results are supported by multicenter studies with larger samples, the Clearmine score may become a preferred tool in routine diagnostic evaluation for acute appendicitis.

Ethics Committee Approval: The study was conducted with the approval of the Ethical Committee Presidency of Trakya University Faculty of Medicine (Protocol code: TUTF-GOBAEK 2015/112; May 27, 2015). The Declaration of Helsinki was fully complied with, and data required to protect patient privacy were obtained from clinical records without any clinical intervention.

Informed Consent: Informed consent was not required by the ethics committee in this study.

Authorship Contributions Surgical and Medical Practices: A.A., S.O., E.S., Concept: M.B.S., A.Y., S.O., Design: A.A., M.B.S., Ö.S., A.Y., E.Ç., Data Collection or Processing: A.A., E.Ç., E.S., Analysis or Interpretation: A.A., Ö.S., A.Y., E.Ç., Literature Search: A.A., M.B.S., S.O., E.S., Writing: A.A., M.B.S., Ö.S., A.Y.

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