

In the Diagnosis of Acute Appendicitis in Patients Referred to Shahid Faghihi Hospital, Shiraz

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Abstract

Background: Acute appendicitis is the major cause of abdominal pain which indicates urgent surgery. Commonly, it is diagnosed through clinical signs and symptoms and blood test. This study aimed to assess the accuracy of acute appendicitis diagnosis through signs and symptoms, Alvarado score system, and ultrasonography method.

Methods: This was a cross-sectional study. Medical profiles of 696 patients with abdominal pain suspected of acute appendicitis referred to Shahid Faghihi hospital were reviewed from June to October 2016. A checklist was used for data collection. The gold standard for diagnosis of acute appendicitis was patient's pathology report. For signs and symptoms, Alvarado score system and ultrasonography method sensitivity, specificity, positive and negative predictive value, and the Youden's index were calculated based on true positive and true negative values.

Results: Among 696 patients suspected of acute appendicitis, 371 (53.3%) were men and 325 (46.7%) women. The mean age for women and men was 30.14+11.49 and 30.53+11.61 years, respectively. Sensitivity and specificity for ultrasonography and Alvarado score system were 68.1% and 78.9%, 76.1%, and 59.9%, respectively. The areas under roc curve and the Youden's index for ultrasonography and Alvarado score system were 0.73, 0.47, and 0.71, 0.55, respectively.

Conclusion: The results showed that ultrasonography and Alvarado score system were effective pre-surgical diagnostic tests for patients suspected of acute appendicitis.

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Introduction

Acute appendicitis is the major cause of abdominal pain which indicates urgent surgery. Commonly, it is diagnosed through clinical signs and symptoms and blood test.^{1,3} Typical symptoms of acute appendicitis may not be always present, so atypical symptoms and other causes of abdominal pain overlap.⁴ Differential diagnosis in approximately 1/3 patients are: gastroenteritis, lymphadenitis, diseases of ovary and fallopian tubes, gastric ulcers and acute cholecystitis. Medical errors in the diagnosis of acute appendicitis account for 30-80%

of excision of normal appendix.⁵ Delayed detection of acute appendicitis leads to adverse complications such as perforation, abdominal abscesses, infection, infertility, and death.⁶ The proportion of negative appendectomy in child bearing age women is 35-45%, which is noticeably higher than men. It can be attributed to reproductive complications such as dysmenorrhea, ovarian cysts, and pregnancy complications.⁷⁻¹⁰

Diagnosis of acute appendicitis is made based on clinical signs and symptoms and laboratory tests. However, only 20-33% of symptomatic patients have positive lab tests. Therefore, radiology-based

diagnosis seems to be necessary. Early detection reduces the rate of acute appendicitis complications such as rupture and peritonitis.^{1-3, 11} The role of highly sensitive and specific pre-surgical test is essential to reduce the proportion of negative appendectomy.¹²

Before the introduction of ultrasonography as a diagnostic method, diagnosis of acute appendicitis was made using score systems based on medical history, physical exams and laboratory tests. Alvarado 10 score test is one of the best score systems. It is proved that ultrasonography method is the best diagnostic test for detecting the causes of abdominal pain, acute appendicitis or other causes, in the right lower quadrant region.¹³⁻¹⁸ This study was conducted to evaluate the accuracy of clinical symptoms, ultrasonography and Alvarado score system as diagnostic methods of acute appendicitis.

Methods and Materials

This is a cross-sectional study. Medical profiles of 696 patients suspected of acute appendicitis referred to Shahid Faghihi hospital, affiliated to Shiraz University of Medical Sciences, were reviewed from June to October 2016. According to the literature review, sensitivity and specificity (ultrasound scans) were considered 70% and 60%, respectively. Sample size was estimated using this formula in the level of 95% of confidence interval: $Z=1.96$, $d=0.07$.

According to this formula, 190 cases of negative appendectomy and 230 cases of positive appendectomy were needed. The prevalence of negative appendectomy was considered 0.28. To achieve an accurate estimation of sensitivity and specificity, we estimated final sample size to be 680.

Inclusion criteria:

1. At least 14 years of age
2. Patients diagnosed with acute appendicitis by a specialist in emergency medicine

Exclusion criteria:

Patients were excluded if they had a previous appendectomy or they had other abdominal inflammatory pathologies such as diverticulitis, adenitis mesenteric, adenocarcinoma cecum, ovarian cyst, etc.

Data were collected from the patients' medical profiles using a checklist consisting of the following information: Sex (male/female), and presence or absence of complications such as rebound tenderness, local tenderness, guarding, abdominal pain in the right lower quadrant region (RLQ pain), generalized abdominal pain, nausea/vomiting, diarrhea/constipation, anorexia, dysuria, shift pain, Leukocytosis (lower/higher than 10000 count per

mm^3), WBC urine (≤ 5 or $5 <$), fever (≤ 37 or $37 <$) and appendicitis based on pathology and sonography report.

In the Alvarado 10 score system, each clinical symptom is valued. Score 1 is attributed to each of the following symptoms: presence or absence of shifting pain, anorexia, nausea/vomit, left shift, rebound tenderness and fever higher than 37°C . Also, score 2 is attributed to leukocytosis (more than 10000 white blood cells per mm^3) and RLQ tenderness. Since left shifting is not evaluated routinely, modified Alvarado score system was used.^{19, 20} Low risk group consisted of patients with equal or lower than 7 score and high risk groups were patients with more than 7.²¹

Patient's pathology report was the golden diagnosis test of acute appendicitis. According to the pathology report, 2 study groups were defined: 1) positive cases, patients with acute appendicitis in the presence or absence of infection or complications such as gangrene or perforation.; 2) negative cases with no evidence of acute appendicitis. Suspected patients who had not undergone surgery were considered as negative cases. Based on the golden test, the sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio, and the Youden's index were calculated for clinical symptoms, laboratory test, and ultrasonography method.

STATA 11 statistical software was used for data analysis. Frequency indexes including mean and standard deviation were reported through descriptive analysis. Analytical statistics methods included chi-square test for qualitative variables and Student T-test for quantitative ones, in the significance level of $P < 0.05$.

Results

Descriptive Analysis

In this study, medical profiles of 696 patients suspected of acute appendicitis were reviewed. According to the pathology report, 4 distinct groups were defined: 376 (54%) patients with acute appendicitis, 190 (27.3%) patients with normal appendix, 68 (9.8%) patients with abdominal pathologies other than appendicitis, and 62 (8.9%) patients who had not undergone surgery. The third group was not included in the analysis. 371 (53.3%) patients were men and 325 (46.7%) were women. Their mean age was 30.14 ± 11.49 and 30.53 ± 11.61 years, respectively.

Based on the pathology report, 2 study groups were defined: patients diagnosed with acute appendicitis and those with normal appendix. Table 1 shows the distribution of signs and symptoms, results of laboratory tests, and ultrasonography reports.

Table 1: The frequency of clinical signs and symptoms, laboratory tests and ultrasonography report in patients suspected of acute appendicitis

Variable	Acute appendicitis N (%) 376(59.80)	Normal appendix N (%) 252(40.20)	Total N (%) 696(100)	P value
Nausea/vomiting				
Yes	300(88.00)	188(82.00)	488(85.60)	0.050
No	41(12.00)	41(18.00)	82 (14.4)	
Shift pain				
Yes	274(90.10)	82(57.80)	356(79.80)	0.001
No	30(9.90)	60(42.20)	90(20.20)	
Anorexia				
Yes	346(97.50)	185(75.20)	531(88.20)	0.001
No	9(2.50)	61(24.80)	70(11.80)	
Generalized abdominal pain				
Yes	78(65.00)	31(28.00)	109(47.20)	0.001
No	42(35.00)	80(72.00)	122(52.80)	
Pain around the navel				
Yes	209(90.10)	71(45.50)	280 (72.20)	0.001
No	23(9.90)	85(54.50)	108(27.80)	
Dysuria				
Yes	30(37.00)	4(3.00)	34(14.30)	0.001
No	51(63.00)	152(97.00)	203(85.70)	
Rebound tenderness				
Yes	357(96.70)	161(69.40)	518(86.20)	0.001
No	12(3.30)	71(30.60)	83(13.80)	
Local tenderness				
Yes	372(99.70)	182(76.10)	554(90.50)	0.001
No	1(0 .30)	57(23.90)	58(9.50)	
Guarding				
Yes	81(79.40)	22(17.00)	103(44.60)	0.001
No	21(20.60)	107(83.00)	128(55.40)	
Leukocytosis				
10000<	300(79.80)	137(54.60)	437(69.70)	0.001
<10000	76(20.20)	114(45.40)	190(30.30)	
WBC Urine				
5<	35(14.20)	45(27.00)	80(19.30)	0.001
<5	212(85.80)	122(73.00)	334(80.70)	
sonography				
Positive	182(68.20)	46 (21.10)	228(47.00)	0.001
Negative	85(31.80)	172(78.90)	257(53.00)	
Alvarado Score				
7<	234(90.00)	73(61.30)	307 (81.00)	0.001
<7	26(10.00)	46(38.70)	72(19.00)	

A significant difference was observed between the study groups regarding the signs and symptoms, except for nausea, vomit, diarrhea and cough signs. Also, regarding the laboratory tests, there was a statistically significant difference between the study groups in the level of white cells count (WBC) in the blood and urine, presence of bacteria, and red blood cell (RBC) in the urine sample. Ultrasonography was done for 435 patients. The sonography report was in favor of acute appendicitis in 182 (68.2%) patients with acute appendicitis and 35 (20.8%) patients with normal appendix.

Table 1 shows the frequency and distribution of signs and symptoms in patients suspected of acute appendicitis. Results showed that shift pain was present

in 90.1% of the patients with acute appendicitis and 57.8% of those with normal appendix. Also, anorexia was seen in 97.5% of patients with acute appendicitis and 75.2% of those with normal appendix; moreover, we found pain around the navel in 90.1% of patients with acute appendicitis and 45.5% of those with normal appendix. These differences were statistically significant ($P=0.001$). Rebound tenderness was present in 96.7% of patients with acute appendicitis and 69.4% of those with normal appendix. Also, local tenderness was present in 99.7% of patients with acute appendicitis and 76.1% of those with normal appendix; guarding was present in 79.4% of patients with acute appendicitis and 17% of those with normal appendix. These differences were statistically significant ($P=0.05$). Regarding the level of WBC,

leukocytosis was observed in 79.8% of patients with acute appendicitis and 54.6% of those with normal appendix ($P<0.05$). The ultrasonography report was in favor of acute appendicitis in 68.2% of patients with acute appendicitis and 21.1% of those with normal appendix. The Alvarado score was higher than 7 in 90% of patients with acute appendicitis and 61.3% of those with normal appendix. These differences were statistically significant ($P<0.05$).

Table 2 shows the predictors of acute appendicitis and sensitivity, specificity, predictive value, positive and negative likelihood ratio values. According to the results, the sensitivity and specificity were 90% and 54.4% for pain around the navel, 97.4% and 24.8% for anorexia, 96.7% and 30.6% for rebound tenderness, 99.7% and 23.8% for local tenderness, 79.4% and 82.9% for guarding, 68.1% and 78.9% for ultrasonography, and 76.1% and 59.9% for Alvarado score system. Also, the positive likelihood ratios for ultrasonography and Alvarado score system were 3.23 and 1.88, respectively.

The ROC curve was used to determine the diagnostic value of signs and symptoms, laboratory tests and ultrasonography. The highest area under ROC curve for signs and symptoms was attributed to guarding (0.81), pain around the navel (0.72), and shift pain (0.66). The Youden's index for guarding, pain

around the navel and shift pain were 0.62, 0.44 and 0.32, respectively. The area under ROC curve and the Youden's index for ultrasonography, Alvarado score system and leukocytosis were 0.73 and 0.47, 0.71 and 0.55, 0.63, and 0.28, respectively (Table 3, Figure 1).

Discussion

Acute appendicitis is a major cause of urgent surgery.²² Diagnosis of acute appendicitis is made based on clinical signs and symptoms and laboratory tests. Despite improvement in the diagnostic method used for patients suspected of acute appendicitis, such as radiography and antibiotic therapy, accurate diagnosis is still an issue.²³⁻²⁵ Regarding the low accessibility and cost-effectiveness of these developed methods, especially in less developed hospitals, surgeons agree on the use of simple laboratory diagnostic tests.²⁶ In order to reduce the proportion of unnecessary appendectomy, highly sensitive and specific pre-surgical tests seem to be crucial.²⁷

Regarding the clinical signs and symptoms, the highest sensitivity was attributed to local tenderness (99.7%), rebound tenderness (96.7%) and guarding (79.4%) with positive predictive values of 67.1%, 68.9% and 78.6%, respectively. In Khanal et al.'s study²⁸ the sensitivity, specificity, positive and negative predictive values for signs and symptoms were 59.2%, 100%,

Table 2: The area under Roc curve and the Youden's index for predictors of acute appendicitis

Variable	Youden's index	AUC	CI 95%	SE
Generalized abdominal pain	0.37	0.68	0.74-0.62	0.03
Pain around the navel	0.44	0.72	0.76-0.67	0.02
Shift pain	0.32	0.66	0.70-0.61	0.02
Nausea/vomiting	0.05	0.52	0.55-0.49	0.01
Anorexia	0.22	0.61	0.63-0.58	0.01
Guarding	0.62	0.81	0.86-0.76	0.02
Rebound tenderness	0.27	0.63	0.66 – 0.60	0.01
Local tenderness	0.23	0.61	0.64 – 0.59	0.01
Fever(37<)	0.02	0.46	0.49 – 0.42	0.01
Leukocytosis(10000<)	0.25	0.62	0.66 – 0.58	0.01
Sonography	0.47	0.73	0.77 – 0.69	0.01
Alvarado Score	0.55	0.71	0.76 – 0.65	0.02

Table 3: Sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratio of signs and symptoms, laboratory tests and ultrasonography

Variable	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Generalized abdominal pain	65.00	72.00	71.50	65.50	2.32	0.48
Pain around the navel	90.00	54.40	74.60	78.70	1.97	0.18
Shift pain	90.10	42.20	76.90	66.60	1.56	0.23
Nausea/vomiting	87.90	17.90	61.40	50.00	1.07	0.67
Anorexia	97.40	24.80	65.10	87.10	1.29	0.10
Guarding	79.40	82.90	78.60	83.50	4.65	0.24
Rebound tenderness	96.70	30.60	68.90	85.50	1.39	0.10
Local tenderness	99.70	23.80	67.10	98.20	1.30	0.01
Fever(37<)	74.10	28.20	57.90	31.60	0.90	1.41
Leukocytosis (10000<)	79.70	45.40	68.60	60.00	1.46	0.44
Sonography	68.10	78.90	79.80	66.90	3.23	0.4
Alvarado Score	76.10	59.90	72.10	46.40	1.88	0.39

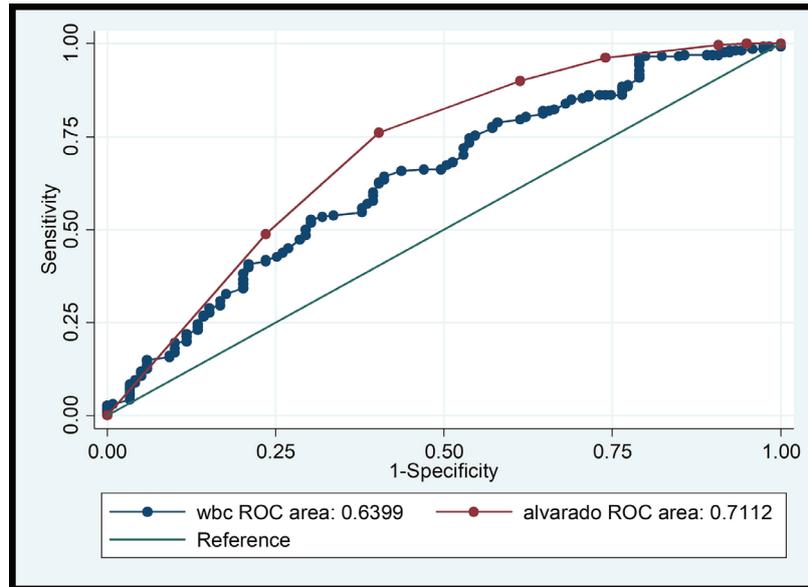


Figure 1: ROC curve analysis of the Alvarado score and WBC count

100% and 2.4%, respectively. Kwan et al.²⁹ indicated that diagnosis of acute appendicitis should be made based on accurate clinical signs and symptoms, and only suspected cases indicate the additional laboratory tests. However, negative appendectomy may lead to infections and lengthen the duration of hospitalization. Therefore, studies on the effectiveness of diagnostic tests are recommended to be conducted.

Leukocytosis can be considered as a diagnostic method of acute appendicitis. In this study, the sensitivity and specificity for WBC were 11950 mm³/l, 63.5% and 64.6%, respectively. Previous studies reported different sensitivity and specificity for WBC. In studies conducted by Sahbaz et al.,³⁰ Saaiq et al.,³¹ Anwar et al.,³² sensitivity and specificity were 67% and 36%; 81% and 43%; and 86% and 81%, respectively. In a study by Rafiq et al.,²⁶ sensitivity, specificity and cut off point for WBC were 88%, 92% and 11.9×10^3 respectively. In a study by Tanriqul et al.³³ sensitivity, specificity, positive and negative predictive values were 78%, 86%, 98% and 26%, respectively. Mesenteric adenitis, pelvic inflammatory diseases and other severe infections as well as acute appendicitis lead to leukocytosis, so leukocytosis is an unspecific diagnostic sign for acute appendicitis.³³ This study also showed that the higher cutoff points for the level of WBC can be attributed to leukocytosis which results from severe inflammation in patients with acute appendicitis.

In this study, the sensitivity, specificity, positive and negative predictive values for ultrasonography were 68.1%, 78.9%, 79.8%, and 66.9%, respectively. Regarding the ultrasonography method, in Piexoto et al.'s³⁵ study sensitivity, specificity, positive and negative predictive values were 64%, 72%, 92%, and 28%, respectively. Sensitivity, specificity, positive and

negative predictive values in Tanriqul et al.'s³³ study were 56%, 80%, 97%, and 14%, respectively. Also, in Nasiri et al.'s²⁰ study, sensitivity, specificity, positive and negative predictive values were 71%, 83%, 97%, and 25%, respectively. Sensitivity, specificity, positive and negative predictive values in Khanal et al.'s²⁸ study were reported 85%, 100%, 100%, and 7%. Sensitivity, specificity, positive and negative predictive values in Tauro et al.'s³⁶ research were 88%, 91%, 91%, and 88%, respectively. Results of this study were consistent with the findings of previous studies in which the sensitivity was reported 55-96% and specificity 85-98%.³⁷⁻³⁹ In Tatli et al.'s study, the sensitivity of US was 75.6% and specificity 72%. Positive predictive value (PPV) was 93%, negative predictive value (NPV) was 14.6%, and the accuracy of US value was 81.7%.⁴⁰ Also, Pedram et al showed that the sensitivity and specificity of ultrasound were 58% and 68%, respectively. Positive and negative predictive values were 77% and 46%, respectively. The area under curve (AUC) was 0.853 (CI 95% 0.788-0.917), indicating a test with moderate accuracy.⁴¹

According to the results of previous studies on the ultrasonography method, no single value for sensitivity was reported. It can be partially attributed to the study design, method and sample size. Low sensitivity of ultrasonography method results in a high proportion of false negative cases of acute appendicitis. It is clinically proved that a high proportion of false negative cases can be partially attributed to various pathologic sites of the appendix.^{42, 43} Thus, it can be concluded that negative report of ultrasonography method should not be the only criterion for decision on appendectomy in suspected cases, especially in the presence of leukocytosis.³¹ In addition, the accuracy of ultrasonography method in diagnosis of acute appendicitis depends on the technician's skill since expert technicians make more accurate diagnosis.⁴³

Results of this study showed that for the modified Alvarado scoring system sensitivity, specificity, positive and negative predictive values were 76.1%, 59.9%, 72.1% and 46.4%, respectively. With the score 7 as the cutoff point, the sensitivity and specificity of the modified Alvarado scoring system in Hooshmand et al.'s study were reported 74% and 68%.⁴⁴ In Tanriqul et al.'s study, sensitivity, specificity, positive and negative predictive values were 47%, 93%, 99% and 14%, respectively.³³ Nasiri et al. reported 65% sensitivity, 35% specificity, 89% positive predictive value, and 11% negative predictive value.²⁰ With the score 6 as the cutoff point, these values were 85%, 25%, 90% and 16%, respectively. The Alvarado score system should not be considered as the only diagnostic method. The use of Alvarado score equal or higher than 7 is valuable only in patients at risk of acute appendicitis who are candidate for surgery or radiography.²¹

In addition to all epidemiological studies on diagnostic tests, the results of this study are subject to two special biases. The first one is disease verification bias. In case the gold standard test is invasive, expensive or is not necessary for the process of treatment, some patients may not be detected and consequently excluded from the study. The second one is imperfect standard bias. This type of bias occurs when the researcher uses a simple diagnostic test instead of the gold standard to overcome the disease verification bias. Since all samples of appendectomy are verified through pathology tests, the results of this study were not affected by imperfect standard bias. However, randomized clinical trial is suggested for further analysis.^{45, 46}

Conclusion

According to the results of the current study, diagnosis of acute appendicitis with alvarado score and sonography are valuable and acceptable in our society, and we can use these two methods for diagnosis of acute appendicitis before surgery.

Strength and Limitations

The main strength of this study is its large sample size. Since data were collected from patient's medical profiles, this study may be subject to information bias due to lack of sufficient information, errors in information registration, and missing data.

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