Original Research

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Low diagnostic values of ultrasonography and negative appendectomy: still a major problem in university hospitals

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Abstract

Background: Misdiagnosis of the acute appendicitis may increase the rate of negative appendectomies, which involve a huge waste of resources and are sometimes associated with severe complications. Furthermore, false negative result of ultrasonography (US) could lead to perforation of appendix. Since ultrasonography is still the most common imaging technique used in Iranian appendicitis patients, the study focused on evaluate the accuracy of ultrasonograghy in an educational hospital in Iran.

Methods: We retrospectively reviewed the results of ultrasonograghy in 270 patients who referred to Rasoul-e-Akram hospital in Tehran, Iran, between April 2002 and October 2004 with acute abdominal symptoms suggestive of appendicitis. The results of ultrasonography were compared with the histopathologic reports of biopsies as a gold standard. In data analysis Chi-square, independent t-test and Mann-Whitney U-test were performed.

Results: The accuracy of ultrasonograghy in acute appendicitis was 60.4% and the rate of negative appendectomy was 17.4%. Diagnostic values of US were calculated as the sensitivity of 55.4% [95% confidence interval (CI)=48.6-62], specificity of 72.3% (95%CI=57.1-83.9), positive predictable value (PPV) of 90.4% (95%CI= 83.9-94.6) and negative predictable value (NPV) 25.6% (95%CI=18.6-34).

Conclusion: Although the results of our study implied that the diagnostic values of ultrasonography were not considerable, but it is still the only imaging techniques available for patients in Iran. In reference to the low NPV, using an alternative technique such as abdominal CT scan is recommended. More attention must be paid on the signs and symptoms related to acute appendicitis in such patients especially in teaching hospitals.

Keywords: Acute appendicitis, ultrasonography, diagnostic value, accuracy.

Introduction

Appendicitis is known as luminal obstruction of appendiceal orifice [1] and as one of the most common causes of abdominal pain worldwide which needs surgical interventions [2]. More than 70000 appendectomies performed in United States yearly [3,4]. Despite the fact that appendicitis is one of the most common causes of emergency abdominal surgery [5,6], the diagnostic methods have not changed drastically over the past few decades [7,8]. Diagnostic approaches such as history, physical examination, and routine laboratory tests are not always ac-

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curate [2,9] and appendicitis is not always easy to diagnose. Appendectomy is performed after false positive diagnosis in 20% of patients [10]. Some studies have reported even more than 40% false negative rates [11-13]. These negative rates are accepted to avoid perforation consequences [14-16]. However, misdiagnosis and unnecessary appendectomy could result in morbidity and mortality in healthy patients and substantial costs in any surgery unit [17-25].

Although us is an easy method for evaluating patients without having ionizing radiation and high expense, it requires some experience and expertise [16,22,26-29]. If the operator is experienced enough, the sensitivity and specificity of US will reach 76-90% and 86-100%, respectively [30-32].

Despite our knowledge about the roles of high experience of US performance and CT scanning to increase diagnostic value of appendicitis, it seems that the real condition in university hospital settings of developing countries may be completely different. On one hand, CT scan modalities are not available for suspected appendicitis; on the other hand, most emergency US are performed by residents of radiology instead of highly expertise radiologists. In addition, the excessive dependency to the results of US rather than physical examination and patient's history may also raise question and must be evaluated.

With this in our mind, we performed this study to evaluate the accuracy and other diagnostic values of US in individuals with suspected appendicitis in our educational hospital setting in comparison with the histopathology results as a gold standard. Furthermore, the diagnostic values of various signs and symptoms were also assessed and compared with US.

Methods

Patients' Recruitment: Between April 2002 and October 2004, 270 patients with acute abdominal pain, and highly suggestive of acute appendicitis referred to Rasoul-e-Akram Hospital (affiliated to Iran University of Medical Sciences), Tehran, Iran for this study. In this retrospective study we reviewed all the archived transcription reports of patients with impression of acute appendicitis during these 2 years. All the patients' symptoms and results of their laboratory tests, ultrasonography and pathology findings were recorded. The patients with incomplete medical records were not eligible to enroll in this study. It was noted that all patients undertook ultrasonography as the diagnostic test and biopsy followed by surgery as a standard procedure.

Assessments: All the patients underwent imaging study by US after taking their history and physical examinations. It was noted that normally CT scan was not used principally for appendicitis work-up in this hospital. Radiologic examinations were performed with 3.5-5.5 MHz linear-array transducer (ADARA sonoline; Siemens, Erlangen, Germany) by radiology residents of the hospital with experience ranging from 1 to 4 years. Criteria for diagnosis of acute appendicitis were consisted of noncompressible, fluid-filled, blind-ended tubule with more than 6 mm diameter of the appendix.

The results of imaging study were categorized in to 4 groups: early acute, acute suppurative, gangrenous and negative result. After the performance of US, each patient was undergone appendectomy by a surgeon with their biopsy samples sent to pathology laboratory. Pathologist classified all specimens into 9 different groups consist of: acute suppurative, acute appendicitis, acute gangrenous, early suppurative appendicitis, early acute appendicitis, vermicular appendicitis, congested appendicitis and no pathologic changes.

Moreover, in order to extract the 2×2 table to calculate diagnostic values, early acute, acute suppurative and gangrenous appendicitis were considered as positive US results; while, in pathologic reports, acute, acute suppurative, acute gangrenous, early suppurative and early

Table 1. Comparison of the results of ultrasonography with pathological reports.

		Pathological results		
		positive	negative	total
Ultrasonography	positive	123	13	136
	negative	100	34	133
	total	223	47	270

acute appendicitis were defined as positive findings. On the other hand, the patients with congested appendicitis, vermicular appendix or no pathologic changes in their pathologic reports were considered as negative appendectomized cases.

Statistical analysis: All information taken from patients were analyzed by SPSS v.16 (Chicago, IL, USA) and Chi-square, independent T-test and Mann-Whitney U-test. Nonetheless EPI info.6 software was used to calculate diagnostic values indices including sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV). In addition, the 95% confidence interval of each index was also reported.

The NAR (negative appendectomy rate) was obtained by dividing the number of patients with negative result of pathology to the total number of all recruited patients. The accuracy of ultrasonography was calculated using the proportion of the number of patients that was diagnosed correctly to the total number of all recruited cases. All p-values were two-tailed and $p<0.05$ considered statistically significant.

Results

Of 270 patients with suspected appendicitis, 137 (50.7%) were female and 133 (49.3%) were male with the mean age of 26.4(SD=13.2) ranges between 5-83 year. According to US study, 134 (49.6%) patients had negative and 136(50.4%) positive results. Based on pathology data 47(17.4%) patients (17 male and 30 female) had negative result of pathology and appendicitis was pathologically confirmed in 223(82.6%) consist of 120 male and 103 female. Data obtained from US results and pathology reports demonstrated that the accuracy of ultrasonography was 60.4% and the negative appendectomy rate 17.4% which in 27.7% (13 out of 47) a false positive result of US recorded. Also there was a statistically significant association between negative appendectomy rate (NAR) and gender (p=0.028) in a manner that NAR was higher in females (22.6% vs. 12.4%), while the accuracy rate of US was not significantly different between males and females (60.6% vs. 55.6%, p=0.410). Moreover, there was not a significant association between US results and gender (p=0.809).

Based on Table 1, sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of US were calculated and thereafter compared with diagnostic value indices of patients' symptoms (Table 2). According to data in Table 2 the right upper quadrant pain, epigastric pain, preumbilical pain and US had the greatest sensitivity, specificity, PPV and NPV, respectively.

The overall results of US and patients' gender are presented in Table 3. As it is shown, early acute condition was the most frequent positive findings of US.

Among the types of pathology in our data (Table 4), the most frequent diagnosis was acute suppurative in 123 patients (45.6%). The pathologic type could not be specified in 6 patients. Finally, 47 specimens had negative pathology result including 21 patients with no pathologic change, 20 with vermicular and 6 with congested appendix. Furthermore, diagnostic accuracy of US was significantly higher

Table 2. Diagnostic values of different clinical findings and ultrasonography in patients with acute abdominal symptoms suggestive of appendicitis.

	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
Sonography	55.4% (48.6-62)	72.3% (57.1-83.9)	90.4% (83.9-94.6)	25.6% (18.6-34)
Anorexia	82.7% (76.6-87.6)	15% (6.2-30.5)	82.7% (76.6-87.6)	15% (6.2-30.5)
Nausea	77.8% (71.5-83.1)	17.8% (8.5-32.6)	81.7% (75.5-86.6)	14.5% (6.9-27.2)
Vomiting	62.1% (55.1-68.7)	34.8% (21.8-50.3)	81% (73.8-86.6)	17% (10.3-26.5)
Fever	24.3% (15.4-35.9)	50% (22.3-77.7)	75% (52.9-89.4)	9.7% (4-20.5)
Chill	16.9% (9.1-28.7)	60% (27.4-86.3)	73.3% (44.8-91.1)	10% (4.1-21.2)
RLQ pain	87.7% (82.5-91.6)	6.4% (1.7-18.6)	81.4% (75.8-86.1)	10% (2.6-27.7)
Periumblical pain	38.6% (32.2-45.4)	87.2% (73.6-94.7)	93.4% (85.7-97.3)	23.3% (17.4-30.4)
Epigastric Pain	15.1% (10.7-20.8)	91.5% (78.7-97.2)	88.9% (73-96.4)	19.3% (14.4-25.2)

in normal individuals than patients with positive diagnosis of appendicitis (72.3% vs. 55.2%, p=0.030).

Diameter of loops was measured only in 87 patients with minimum of 4.50 mm and maximum of 25 mm with the mean size of 8.80 (SD=3.20).

According to what is illustrated in Fig. 1, there was a significant increase in the mean number of serum WBC with increased the severity in appendicitis ($p<0.001$).

Discussion

The preoperative evaluation and diagnosis of acute appendicitis has been previously established according to the clinical presentation and laboratory findings. However, these presentations overlap with gastrointestinal and genitourinary system symptoms and may distract physicians from correct diagnosis which could leads into perforation of the appendix. Moreover, the overall clinical accuracy for diagnosis of appendicitis has been approximately 80% [11,16, 33-36].

In recent decades, new methods such as CT scan and US have provided more reliable information for in evaluating patients with symptoms suggestive of acute appendicitis especially in atypical patients [24,36,37]. Imaging studies can facilitate establishing the diagnosis earlier, resulting less costs and complications and early treatment for the patients [6,9,10,17-25, 38-42]. But the question which remain in this field is when we can rely on the result of imaging study particularly US, and also who benefits most from preoperative imaging evaluations.

The US is an easy and inexpensive method for investigation of acute appendicitis in patients. The diagnosis of appendicitis was based on detection of a non-compressible distended

Table 3. Comparison the results of Ultrasonography and gender.

	Final results of ultrasonography				
	Negative	Early acute	Acute superlative	Gangrenous	Total
Female	67 (50.3%)	49 (36.8)	12 (9%)	5 (3.7%)	133
Male	67 (48.9%)	55 (40.1%)	15(10.9%)	0	137
Total	134 (49.6%)	104 (38.5%)	27 (10%)	5 (1.8%)	270

(6 mm in anteroposterior dimension) appendix [26]. Since pathologic evaluation of resected appendix is considered the gold standard of acute appendicitis diagnosis [43] and surgery could lead into different complications and consequences in patients who do not have acute appendicitis [17-25]. Imaging studies through US could be used along with taking history, conducting physical exam and checking laboratory tests for primary assessment of patients and to decrease the rate of negative appendectomy.

The result of our study suggested that diagnostic accuracy of US in appendicitis was lower in comparison with other countries. However, it was noted that even developed countries have accepted NAR of 20% in their settings [11, 16, 33-36]. Similar to our study, previous researches [11,16,33,34,41,44] have reported that NAR varies in males and females, with a range of 5%–16% and 11%–34% respectively. In accordance with their findings, we found 22.6% NAR in females and 12.4% in males. These differences reveal that the diagnosis of appendicitis in females is extremely difficult due to similarity of presentations in both appendicitis and gynecological diseases [45].

At our hospital almost every patient with acute abdominal pain and other symptoms suggestive of appendicitis have undergone US. Negative result may causes delay in diagnosis and lead to perforated appendix. As it has been proved that appendectomy in patients with perforated appendix has unavoidable morbidity and mortality. Hence further investigations are necessary before perforation in these patients. Therefore it is important to do our bests in evaluating patients before taking them to any surgery unit [15]. However, imaging evaluation is performed by residents of radiology in our university hospital setting.

Orr et al [46], reported from their meta-analysis of all the pediatric studies performed between 1986 and 1994 an overall sensitivity of 85% and specificity of 92% for US in the diagnosis of appendicitis in children. Sivit et al [47] reported a sensitivity of 78%, a specificity of 93%, and an accuracy of 89%. In a more recent study by Shirazi et al [48] in 2010 in Iran, 110 patients suspected of having appendicitis by US were evaluated. Their results show that US had 92.7% sensitivity, 94.5% specificity, 93% accuracy, 94.4% positive predictive value and 92.5% negative predictive value. In a similar

Table 4. Comparison the results of ultrasonography and types of pathology.

	types of pathology results								Total
	Acute supporative	Acute appendicitis	Acute gangrenous	Early supporative appendicitis	Early acute appendicitis	No pathologic change	Vermicular appendicitis	Congested appendicitis	
Neg US	49	19	12	1	11	17	12	9	130
Pos US	74	19	19	1	8	4	8	1	134
Total	123	38	31	2	19	21	20	10	264

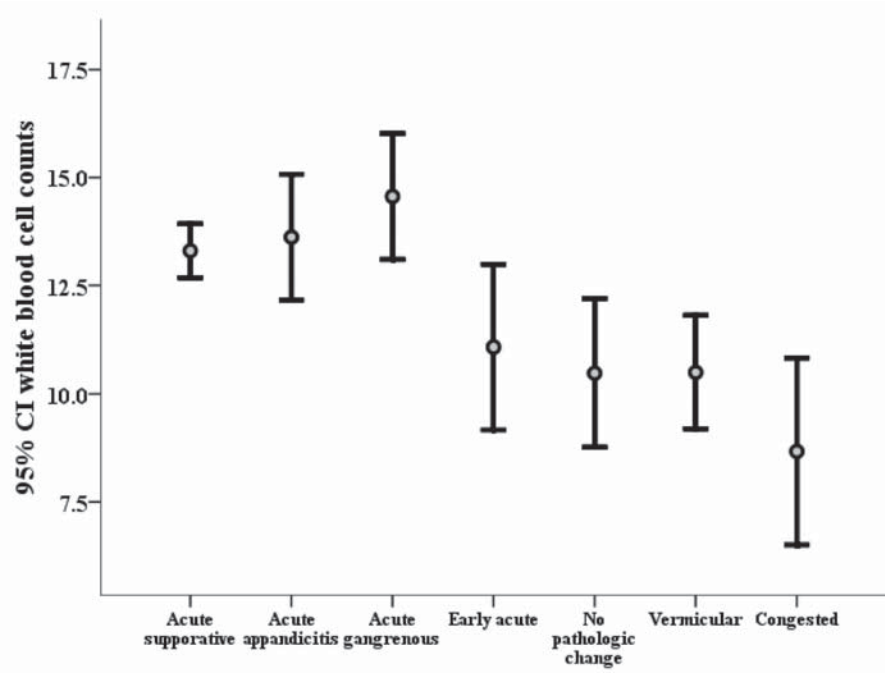

Fig. 1. Mean of WBC counts in the serum of patients with suspected appendicitis and different histopathologic findings.

study [49] performed in a university hospital in Saudi Arabia, negative appendectomy rate was 27.2%; whereas, the accuracy rate of appendicitis with Alvarado scale was 67.7%, US 57.9%, and CT 66.7%. These findings more emphasized that clinical findings and experience remain to be major factor in appendicitis-diagnosis.

Despite the low NPV, our findings revealed a considerable high PPV of more than 90% for US in diagnosis of acute appendicitis. These results suggested more reliable US finding when it is positive. In other words, a negative ultrasound result must be re-evaluated and checked with other findings and more accurate modalities such as CT scanning should be excuted if possible.

The limitations of our study included those factors related to retrospective designing. Also, inter-observer bias could affect the histopathologic result of acute appendicitis depending on pathologist experience. Furthermore, this assessment was a single center study. It must be also considered that, like other studies with invasive reference standard such as surgical biopsy, only patients with highly suspicion of acute appendicitis who underwent surgery regardless of US results were enrolled in this study. However, this fact was unavoidable because both modalities of test and reference must be performed for all of the potential enrolled cases in order to evaluate the diagnostic values of the test. Thus, the NPV of such diagnostic tests like US could wrongly be underestimated.

Since our hospital setting is an educational one, and imaging study is performed by residents who do not have enough experienced for this job, therefore this may explain the low diagnostic value of this modality in the educational setting. Hence there more attention should be paid to patients who are admitted to the hospital with impression of acute appendicitis. After a complete evaluation of their clinical presentation, it is expected to conduct primarily a simple imaging study such as US for them. Sometimes clinical presentations of our cases led us in approaches to our patients. Moreover, in our study we found some clinical

presentations were more specific and sensitive than US. This emphasized more on the importance of history taking and physical examination in these patients.

Conclusion

Conclusively, if there is a high clinical suspicious of acute appendicitis it is recommended to perform computed tomography for complicated and atypical cases before taking them to surgery unit for appendectomy. However, we believe that it costs more in comparison with US for patients and basically, there is an insufficient number of CT scan modality in our setting which is the most important limitation that causes patients with more serious diseases have the priority to undergo CT scan first. On the other hand, regarding the high diagnostic values of the findings of physical examinations, more consideration must be made on the signs and symptoms proposing acute appendicitis in such patients especially in teaching hospitals.

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