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The Accuracy of Pre-Operative Radiological Assessment with Histopathological Correlation in Suspected Acute Appendicitis: Research in Saudi Arabia and Recommended Diagnostic Routine Approach

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Abstract

Background: Appendicitis is a common acute surgical condition. Despite the high frequency of acute appendicitis, its clinical diagnosis remains challenging. The most accurate radiological means of its diagnosis remains controversial. The most commonly used modalities are CT and US.

Objectives: The aim of this study is to compare the accuracy of CT and US as diagnostic modalities in suspected acute appendi-citis and to set a diagnostic routine to be followed in those cases.

Patients and Methods: A retrospective chart analysis was conducted at the surgery department in King Faisal Specialist Hospi-tal and Research Center, Al-Riyadh, KSA. The charts of all adult patients (age 14-99) with suspected acute appendicitis between 1 January 2010 and 30 May 2015 were reviewed. Included patients had at least one imaging study, went to the operating room, and had documented surgical pathology results. Patients were divided into 3 groups of different imaging routines to assess which one worked the best.

Results: The total number of patients reviewed in this study was 308, out of which 228 patients were included in the statistical analysis; the number of males was 119 (52.2%), and that of females was 109 (47.8%). The mean age of the included patients was 32 ± 15. Based on histopathology, CT had a sensitivity of 97.1% and specificity of 33.3%, while US showed sensitivity and speci-ficity of 62.5% and 66.7%, respectively, with equivocal results in 45% of the patients. The negative appendectomy rate in patients with positive CT is 7% and is 17% in patients with positive US. Both positive and negative predictive values of CT were higher than those of US; 95%, 45%, 83% and 40%, respectively. The diagnostic accuracy of CT was higher than that of US (92% vs 64%). The histopathology in patients who were clinically diagnosed with acute appendicitis (n=14) is positive in only 53.3%.

Conclusion: Clinical diagnosis alone can diagnose acute appendicitis in almost 50% of the patients with very high accuracy if the presentation is typical and the surgeon is an expert. In equivocal presentation, CT scan is the recommended imaging diagnostic modality. US showed no benefit in this study; thus, it's reserved to pediatric patients, and female patients who are either pregnant or have suspected gynecological problems.

Introduction

Acute appendicitis is the most common indication for emergency surgery worldwide, with incidence of 1.17 per 1000, and lifetime risk of 8.6% in men and 6.7% in women [1]. Despite the frequency of the disease, the clinical diagnosis of appendicitis remains a diagnostic challenge [2]. Early diagnosis, however, is very peremptory in preventing perforation and the consequent morbid-ity and mortality. Surgeons tolerate relatively high negative appendectomy rates in the range of 20%; however, such practice is

being opposed by others due to high hospital costs, estimated as $740 million per year. The most accurate means of its diagnosis remains a source of debate [3]. Over the past 2 decades, the use of dedicated Ultrasonographic (US) and Computed Tomographic (CT) techniques for the evaluation of patients clinically suspected of having acute appendicitis has led to improved diagnostic ac-curacy of 83%-98% [4-16]. CT has been shown to be superior in numerous studies [17-21]. CT scan reduces false-negative appen-dectomy rates up to 1.7% overall and 7% in women [22,23]. Find-ings such as appendiceal diameter >6 mm, wall thickening, en-hancement after contrast, periappendiceal inflammatory changes, including inflammatory fat stranding, phlegmon, free fluid, free air bubbles, abscess, and adenopathy, may indicate acute appendici-tis [24,25]. As CT imaging can still be equivocal, the RADPEER scoring system uses a peer-review process to grade the level of disagreement between two radiologists [26]. Despite its superior sensitivity, abdominal CT is expensive, not available in all medical centers, and subjects the patient to iatrogenic ionizing radiation, iodinated-contrast-media allergy or nephrotoxicity and prolonged hospital stay [27-32].

On the other hand, US is safer, and relatively inexpensive [30]. Outer appendiceal diameter of ⩾6 mm, periappendiceal find-ings of inflammatory fat changes, appendiceal perforation findings abscess, and circumferential loss of the submucosal layer are US findings that may indicate acute appendicitis [33-35]. The diagno-sis of acute appendicitis is confirmed only by the post-operative histopathology [36]. The presence of extra vascular polymorphs in the epithelium, lamina propria, and muscular layers is the main diagnostic feature of the acute inflammation [37]. Mucosa is largely destroyed with an extensive neutrophil infiltrate extending throughout the submucosa and into the muscularis externa [37]. In this study, we analyze the accuracy of CT and US as diagnostic modalities in acute appendicitis with histopathological findings at King Faisal Specialist Hospital, KSA.

Materials and Methods

A retrospective chart analysis was conducted at the surgery department of King Faisal Specialist Hospital and Research Center [KFSH&RC]. The Research Advisory Council (RAC) at KFSH&RC approved the study. The records of adult patients (age 14-99) with suspected diagnosis of acute appendicitis, between 1 January 2010 and 30 May 2015 were reviewed. Chosen patient should meet the inclusion criteria: (1) at least one imaging study;
(2) operative management; (3) documented surgical pathology results; and (4) complete chart information for data abstraction. Patients were excluded if they were younger than 14 or when the pathologists made a diagnosis of appendiceal tumor.

Ultrasound Examination

Color Doppler sonography of the abdomen and focused more on the right lower quadrant was performed using the graded compression technique with a Phillips HDT 5000 linear 1-5 MHz transducer, according to body size. Visualization of an incompressible blind-ended appendix measuring > 6 mm in diameter with additional positive findings, including hyperemic appendiceal walls, appendicolith, pericecal fluid, or abscess, was diagnostic of appendicitis. The US report was read as positive, negative, or Not Visualized (NV) for acute appendicitis.

Contrast-enhanced MDCT Examination

CT exams were performed using a multi-slice CT scanner (SOMATON Sensation and high Definition, GE Medical Solutions). The most common technique involved the use of triple contrast (oral, rectal, and IV). Patients were initially prepped with 1 l of oral and 200-500 ml of rectal contrast, followed by 145 cc of Isovue-300 IV contrast at a rate of 2-3 ml/sec just prior to the scan. Serial 3-mm axial images were obtained from the diaphragm through the perineum. Visualization of an appendix measuring > 6 mm in diameter with additional positive findings, including periappendicular fat stranding, cecal wall thickening, appendicolith, abscess, free air indicating perforation or phlegmon, was diagnostic for appendicitis. The CT report was read by the radiologist as positive or negative for appendicitis.

Radiology

CT scan was performed in the Department of Radiology by qualified technicians and read by consulted radiologisst. US was performed and read by trained ultrasonographers and reported by consultant radiologists in the Department of Radiology.

Statistical Analysis

In this retrospective study, the primary objective is to evalu-ate the accuracy of CT and US, adjusting for possible confounder such as age, and gender. Continuous variables are presented as means ± standard deviations. Categorical variables will be sum-marized as percentages. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and diagnostic ac-curacy of each imaging modality was calculated in their correla-tion with histopathology. When calculating sensitivity and speci-ficity, US for in which the appendix was not visualized were not considered in the calculations. Type I error rate was set at 5%, meaning that attest statistic has significant finding if the p-values falls below 5%.

1. Results

The study included 308 patients (Figure 1). We excluded 80 patients, 60 (19.5%) were admitted under pediatric surgery, 14 (4.5%) had no imaging prior to surgery, 3 (0.9%) were found to have other pathology, and 3 patients had insufficient information.

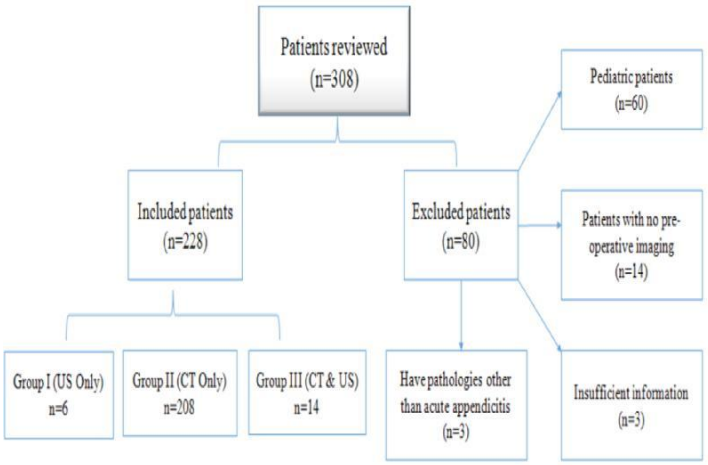

Figure 1: Showing patients reviewed in this study.

The 14 patients, who underwent appendectomy without preoperative imaging, had a mean age of 37 with males representing 50% of the patients. 53.3% had positive histopathology for acute appendicitis; however, in females the positive histopathology was only 57.1%. The statistical analysis included 228 patients. Their mean age was 32 ± 15 (minimum=14, maximum = 74). There were 119 (52.2%) males. Subsequently, we divided the patients into three groups: group I (n=6, 2.6%) patients who had pre-operative US, group II (n=208, 91.2%) included those who had abdominal CT scan imaging prior to the surgery, and group III (n=14, 6.15%) for those who had both abdominal CT scan imaging and US prior to surgery. Demographics of each group are listed in (Table 1).

Group	No. of patients	Mean age of patients
I	6	28 ±7
II	208	33 ± 15
III	14	25 ± 10

Table 1: Showing the demographics of each group.

CT scan imaging was reported as positive based on the following findings, namely: appendiceal wall thickness >6mm (n=170, 76.5%), fat stranding (n=158, 71.2%), free fluid (n=77, 34.7%), free air (n=14, 6.3%), and appendicolith (n= 39, 17.6%). In this study, appendiceal wall thickness (>6 mm) showed the highest sensitivity and diagnostic accuracy of 96% and 92%, respectively (see table 2).

Variables	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
Appendiceal wall thickness (>6mm)	96	43	92
Fat stranding	75	73	75
Appendicolith	19	100	24
Free air	6	87	12
Free fluid	33	50	35

Table 2: Showing the sensitivity, specificity and diagnostic accuracy of different CT findings.

In all patients who had pre-operative CT scan imaging (n=222, 97.3%), CT showed sensitivity of 97.1%, specificity of 33.3%, PPV US imaging was reported as positive based on the following variables, namely: appendiceal wall thickness >6mm (n=3, 15%), free fluid (n=2, 10%), and hyperemia (n=3, 15%). Considering that histopathology is the gold standard diagnostic modality for acute appendicitis, US in this study showed a sensitivity of 62.5% and specificity of 66.7%. Considering that histopathology is the gold standard diagnostic modality for acute appendicitis, group I showed that US, when done alone, has sensitivity and specificity of 100%. 4 patients (66.6%) out of 6 patients had positive histopathology for appendicitis.

Group II showed that CT, when done alone, has sensitivity of 97.9% and specificity of 25%, considering that histopathology is the gold standard diagnostic modality. 195 (93.8%) had positive histopathology for acute appendicitis. Group III showed that when both CT scan imaging and US were done preoperatively, they have sensitivity of 81.8% and 40%, respectively, and specificity of 66.7% and 0%, respectively. 11 patients (78.6%) had positive histopathology for acute appendicitis. This group assured that there is no significant difference between the positivity rate of both CT and US in one side and histopathology in the other side. (Table 3) summarizes the positive rates of imaging and histopathology in each group.

Group	# of patients with +ve CT	# of patients with +ve US	# of patients with +ve Histopathology	P value
I	0	3	4	1
II	199	0	195	0.267
III	10	3	11	1 for CT 0.625 for US

Table 3: Summarizing the positive rates of imaging and histopathology in each group.

(Figure 2) shows the significant difference between the 3 groups in terms of positive rate. Despite the insignificant difference between US and histopathology, in our study, the appendix was not visualized on US in 45% of patients. Although patients who had US in Group I showed 100% specificity and sensitivity and

in group III showed 0% specificity, these results don't reflect true values because of the small number of patients.

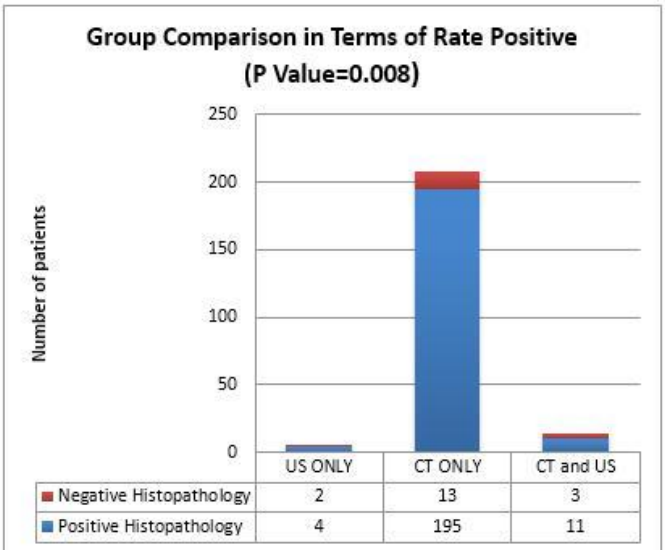

Figure 2: Comparing the positive rates in the three groups.

Discussion

Traditionally, the diagnosis of acute appendicitis has been a clinical diagnosis based on history, physical examination and laboratory investigations. An experienced examiner can make the correct diagnosis of acute appendicitis without imaging [38]. The diagnostic accuracy of the clinical examination has been approximately 80%, depending on the experience of the examining clinician, with Negative appendectomy rate (NAR) of 20% [39-51]. In this study, the accuracy of clinical diagnosis alone was only 57 %. Investigators in prior studies have reported that NAR varies by patient sex, with a range of 3%-16% in men and 11%-34% in women [39-42,52,53]. However, in the current study, clinical acumen alone resulted in an NAR of 43% in both men, and women, showing no difference. Many studies [4-15] showed that abdominal imaging has the potential to achieve higher diagnostic accuracy in acute appendicitis; thus, abdominal imaging is recommended in suspected cases. However, which imaging modality to use--either US or CT--remains a point of dispute [30]. In children, ultrasound is a viable and commonly used choice, though in adults, the choice is less clear [54]. CT has the risk of intravenous contrast side effects, exposure to ionizing radiation, and cost of more than $700 per examination in many institutions, which are all limiting factors [27-29,31-32,55,56]. Meanwhile, CT clearly has its advantages, with high sensitivity of 64%- 100% and the ability to perform the study in a way that is not operator dependent and in patients in which ultrasound is difficult to perform, such as those who are obese or with abdominal distention [54, 57]. Many studies [5, 57-59] assessed CT accuracy in diagnosing acute appendicitis (Table 4).

Source	No. of patients	Sensitivity (%)	Specificity (%)	Normal Appendix identified (%)	Accuracy (%)
Birbaum & Balthazar [57]	100	96	90	43	93
Malone, et al. [58]	211	87	97		
Rao, et al. [8]	100	100	95	100	98
Schuler, et al. [5]	97	98	91	68	96
Giuliano, et al. [59]	100	64	100		91
Present study (Glal M.A. et al)	222	97	33	2	92

Table 4: Diagnosis of Appendicitis by computed tomography.

In this study, CT has less NAR of 7.2%, when compared with NAR of clinical diagnosis alone (43%). Like most studies, CT has high sensitivity of 97% while the specificity was comparatively low (33%). This low specificity could be explained by misinterpretation by the radiologist or the fact that most patients presented with early acute appendicitis and minimal radiological findings.

On the other hand, US maintains the advantage of being quick, safe, easily accessible, not expensive and, most importantly, not using ionizing radiation [60-67]. Moreover, it has the ability to identify many alternative causes of acute Right Lower Quadrant (RLQ) symptoms such as ovarian cystic or ureteral stone disease [65]. However, US is highly operator dependent, mistakes a

diseased terminal ileum for an enlarged appendix, confuses any RLQ calcification for an appendicolith, and may overlook an inflamed appendix in obese patients and in those with appendiceal perforation, leading to false-negative interpretations [35,65-66]. Its diagnostic accuracy was reported to range from 71% to 99 % (Table 5) [15,67-70]. In this study, the diagnostic accuracy was equal to 64% which is less than the reported range with NAR of 17%. Many studies [15,67-74] reported that the sensitivity of US ranges between 44% and 98%, and its specificity ranges between 47% and 95% (Table 5). Similarly, in this study, the sensitivity and specificity of US were 62.5% and 66.7%, respectively. It's important however to mention that these results are not for all patients who had US as appendix wasn't visualized in 45% of the patients.

Source	No. of patients	Sensitivity (%)	Specificity (%)	Normal Appendix identified (%)	Accuracy (%)
Balthazar, et al. [15]	100	76	91	42	83
Schwerk, et al. [69]	532	88	98	74	96
Garcia Pena, et al. [72]	139	44	93	56	76
Pickuth, et al. [68]	120			16	84
Lee, et al. [70]	675	99	98	52	99
Present study (Glal M.A. et al)	20	63	67	10	64

Table 5: Diagnosis of Appendicitis by ultrasound.

From the literature review, the diagnostic accuracy of CT is superior over US (Table 6) but what diagnostic routine to be followed in acute appendicitis remains a rising question.

	CT (%)	US (%)
Sensitivity	64-100	44-98
Specificity	33-98	47-95
Accuracy	92-98	64-95
Normal Appendix seen	43-100	0-82

Table 6: Comparison between CT and US as reported in the literature review including this study.

Rao, et al. [65] stated that the decision to perform appen-diceal CT or US depends on a variety of factors, including the leading clinical impression, patient's age, gender and body habi-tus, relative availability of imaging modalities, and relative exper-tise of the consulted radiologist. Wilson et al. [75] suggested that all patients should undergo complete surgical evaluation before any radiographic studies where male patients suspected to have acute appendicitis are to be sent to operating room while females should have CT. In the same study, US was of no benefit. Nevertheless, Lameris, et al. [76], Toorenvliet, et al. [67], Gaitini, et al. [56], and Poortman, et al. [77] recommend routine imaging with US being the initial modality where the patient should go to surgery, if appendix is visualized and abnormal and if the appendix is not visualized, then the patient should have a CT. Randen et al, however, recommended CT as primary diagnostic modality in all patients with suspected acute appendicitis except in young, female, and slender patients, where graded compression US is the recommended primary diagnostic test.

Based on our results, the diagnosis of acute appendicitis is mainly determined by the clinical evaluation. Almost 50% of the patients can be diagnosed with high accuracy by clinical diagnosis alone if their presentation was typical and the surgeon was expert. On the other hand, in patients with equivocal signs, radiologi-cal imaging is highly recommended where CT is the modality of choice in suspected acute appendicitis. US is not recommended as it didn't show any benefit in this study (Figure 3). Yet it's the modality of choice in pediatric patients and female patients who are either pregnant or suspected to have gynecological complaints. Complimentary use of US is not recommended (Figure 4).

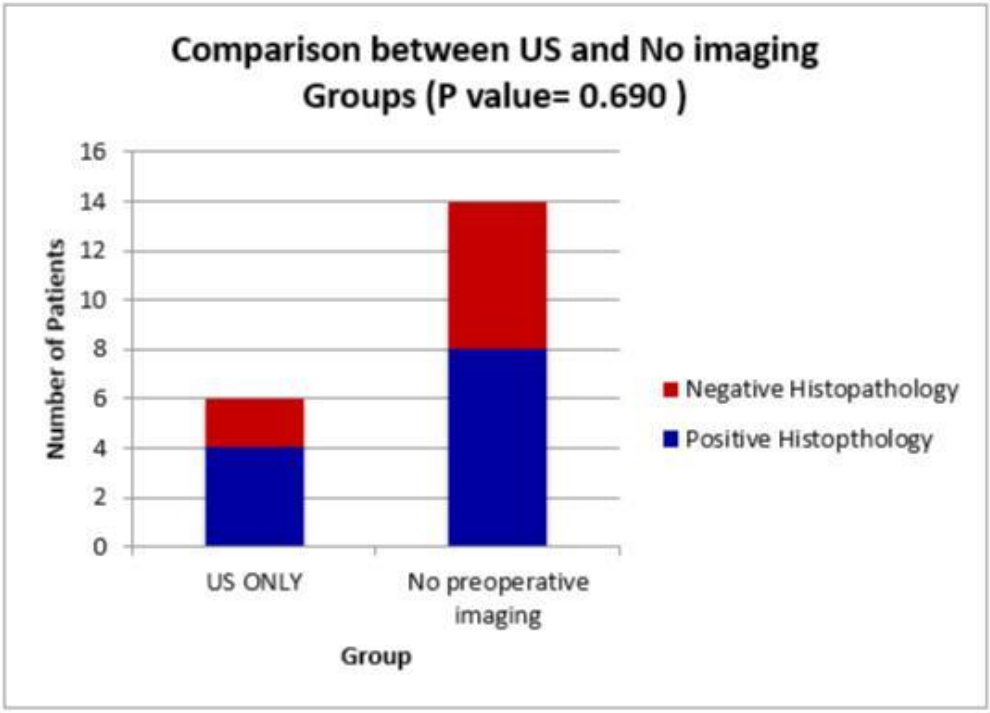

Figure 3: Showing the insignificant difference between clinical diagnosis alone and US only.

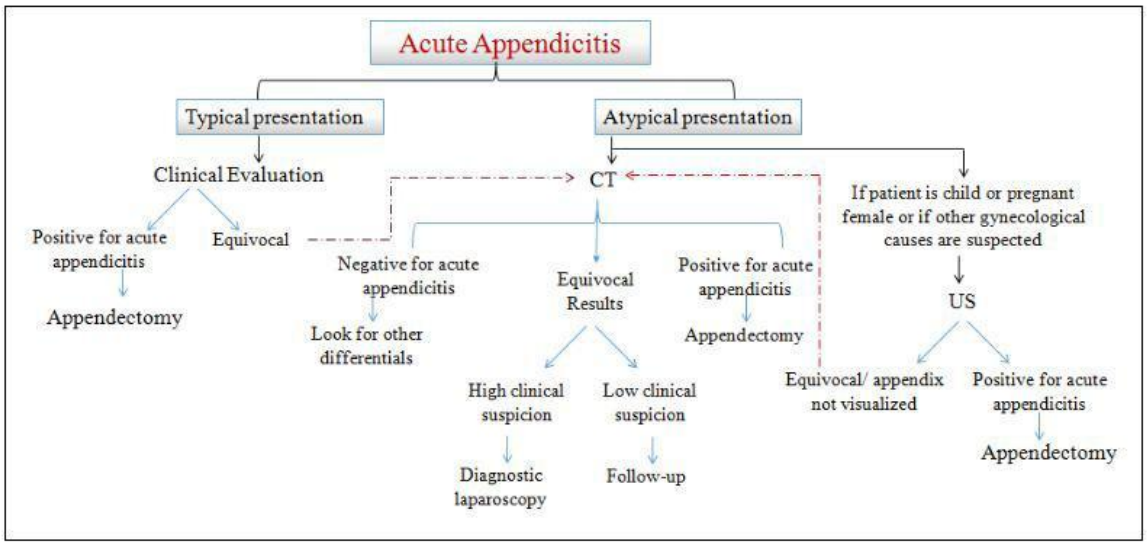

Figure 4: Showing the diagnostic routine of acute appendicitis.

Limitations

The number of patients who did US in this study is small, considering the fact that KFSH&RC is a tertiary care hospital; thus, further research may be done with larger number to verify the results. Moreover, this study doesn't address how clinical experience differences between resident surgeons and consultant surgeons affect the diagnostic accuracy of clinical diagnosis, which can be studied in further researches.

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