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Ultrasound in Emergency Medicine

THE POTENTIAL ROLE OF ULTRASOUND IN THE WORK-UP OF APPENDICITIS IN THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: Acute appendicitis is common in the adult emergency department (ED). Computed tomography (CT) scan is frequently used to diagnose this condition, but ultrasound (US)—commonly used in pediatric diagnosis—may also have a role. Objectives: Review the clinical utility and define the frequency and diagnostic accuracy of US to diagnose appendicitis in an adult population in the ED setting. Methods: Retrospective cohort study of patients who underwent appendiceal US in an academic, tertiary ED from July 2013–October 2015. Results: There were 174 patients included, of which 39 (22%) had pathology-confirmed appendicitis. There were 25 patients who had an US scan that was positive for appendicitis, 146 (84%) were indeterminate, and 3 (1.7%) were negative. Among patients with a positive US, 25/25 (100%, 95% confidence interval [CI] 84–100%) had appendicitis, 32/146 (22%, 95% CI 16–29%) with an indeterminate US had appendicitis, and 0/3 (0%, 95% CI 0–6.2%) with a negative US had appendicitis. In the 28 definitive cases, US had a sensitivity of 64%, specificity of 2%, positive predictive value of 100%, and negative predictive value of 100%. The likelihood ratio positive and negative were 173 and 0, respectively. Conclusion: Our initial data suggest that an US that shows appendicitis seems to be reliable; however, a high prevalence of indeterminate studies limits the diagnostic utility as a universal approach in adult patients in the ED setting. Larger studies are needed to identify which patient populations would benefit from US as the initial imaging modality, what factors contribute to the large numbers of indeterminate results, and if any interventions may reduce the number of indeterminate results.** © **2018 Elsevier Inc. All rights reserved.**

☐ **Keywords—acute appendicitis; emergency department; ultrasound**

INTRODUCTION

Acute appendicitis is a common diagnosis in the emergency department (ED), with more than 250,000 appendectomies performed in the United States each year (1). Diagnosis is made using the history, physical examination, laboratory tests, and imaging. Currently, three types of imaging are typically used to diagnose acute appendicitis: computed tomography (CT), ultrasound (US), and magnetic resonance imaging (MRI). Frequently, CT is the initial imaging modality used in the adult population. Although accurate, with sensitivities ranging from 90–96% and specificities ranging from 94–98%, there are limitations to this approach, including radiation exposure, risk of contrast administration, increased resource utilization, and cost (2,3).

An alternative diagnostic imaging approach is to incorporate US as part of the work-up of suspected appendicitis, and to reserve CT as a second diagnostic modality. US was

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first utilized in the 1980s to visualize the abnormal appendix; this was directly followed more recently using graded-compression US (4,5). US can often be performed more quickly and at a lower cost than CT or MRI. US is already used as the first imaging study of choice in the pediatric population, where there is increased concern for radiation exposure and the development of future malignancies (6). In one large, multicenter, prospective study of 2625 children presenting to the ED with abdominal pain and suspected acute appendicitis, US was 97.9% sensitive and 91.7% specific in identifying appendicitis when the appendix was visualized (7). In the adult population, a meta-analysis of 22 Korean studies found that, when the appendix was identified, US was 87% sensitive, with a range of 51–100%, and 90% specific with a range of 60% to 100% for appendicitis (8). This review demonstrated a negative appendectomy rate of 10.6%, which may be viewed as unacceptable in the United States. US is limited by operator experience and patient body habitus; however, its use is becoming more frequent in the ED as an initial diagnostic tool. CT still has a role for patients with high clinical suspicion for appendicitis, perforated appendicitis where the treatment is nonoperative, or if the appendix is not visualized.

In prior studies, US was demonstrated as sensitive and specific when the appendix was visualized; however, these studies were often performed by a single or small group of highly specialized, expert sonographers. We sought to study the clinical utility of US interpreted by attending radiologists in an academic ED. The objective of the study was to define the frequency of appendiceal visualization and diagnostic accuracy in an adult population in our academic ED setting.

METHODS

This was a retrospective, observational, cohort study conducted in the ED of a tertiary care teaching hospital with around 57,000 visits per year. The inclusion criteria were: 1) adult ED patients age 18 years or older; 2) an appendiceal US performed from July 2013 through October 2015 where the indication for the study included evaluation for appendicitis or if an attempt to visualize the appendix was specifically noted. Chart reviews were performed and included data information such as past medical history, height and weight, length of stay in the ED, radiological studies, operative report, patient disposition, and pathological reports. Patients were classified as having appendicitis based on pathologic diagnosis, if available. If no pathologic diagnosis was available, a final CT read was used to classify the patient. We also checked for return visits to our hospital for further evaluation to attempt to identify any false negative CT studies.

Transabdominal US was performed by certified registered diagnostic medical sonographers using a graded compression technique with a Philips IU22 linear 28-Hz probe (Philips Healthcare, Andover, MA) and with final interpretation by a board-certified attending radiologist. A study is typically classified as positive if there is visualization of a noncompressible appendix measuring more than 6 mm in diameter, as well as additional positive findings such as wall hyperemia, appendicolith, peri-appendiceal fluid, or peri-appendiceal inflammation. The radiologist determined if the study was positive, negative, or if the appendix was not visualized. The CT examinations were performed on a 64-slice multidetector CT GE LightSpeed VCT scanner (Light Speed; General Electric Medical Systems, Milwaukee, WI). The use of intravenous or oral contrast was administered at the discretion of the radiologist or treating physician. Serial 5-mm axial images were obtained through the abdomen and pelvis. Coronal and sagittal reformations were performed, and the images were interpreted by the radiologist.

Statistical Analysis

The primary goal of the study was to assess the operating characteristics of appendiceal US in an ED population. The results of the US were stratified as positive, negative, or indeterminate. An indeterminate test occurred when the diagnosis was unclear or the appendix was not confidently seen. We report the point estimates for rates of different US diagnoses. We also report the operating characteristics for a positive US scan, grouping indeterminate into the negative category. We report 95% confidence intervals along with point estimates, where appropriate. As many US studies were indeterminate, we calculated these statistics for US scans that were definitively positive and negative, excluding indeterminate studies.

We also calculated the positive and negative likelihood ratios for positive and negative US scans; because the positive likelihood ratio would result in division by zero, we substituted 0.5 (a small number within the confidence interval for the proportion) to allow for the calculation of a noninfinite number.

RESULTS

A total of 174 patients met the inclusion criteria and were included in the analysis (Figure 1). Table 1 demonstrates baseline demographic features, body mass index, historical features, disease course, and US findings in the populations of patients with positive, negative, and indeterminate US scans.

From this population, 3 patients (1.7%; 95% confidence interval [CI] 0.4–5.1%) had an US that demonstrated a normal appendix, and none of these patients

had appendicitis. A total of 25 patients (14.4%; 95% CI 9.9–20%) had a positive US for appendicitis; all these patients had appendicitis. There were 146 patients (84%; 95% CI 78–89%) who had an appendiceal US that was indeterminate. Most of these patients (n = 127) underwent CT, which confirmed 114 (78%; 95% CI 71–84%) negative studies. There were 11 (7.5%; 95% CI 4.1–13%) positive studies, and 2 (1.3%; 95% CI 0.06–5.1%) indeterminate studies; of these 13 patients, all went to the operating room and were diagnosed with appendicitis by pathology. One patient was diagnosed with clinical appendicitis but elected to be treated with antibiotics, but later returned to the ED after failure of antibiotic therapy and underwent appendectomy. Eighteen patients who were not candidates to undergo CT scan due to pregnancy or other contraindications underwent additional imaging with MRI, and all of these were negative studies. A single patient was taken to surgery without additional imaging, and appendicitis was found.

The diagnostic test characteristics for US are outlined in Figure 2. Overall, US was positive for appendicitis in 25/39 patients for a sensitivity of 64%, and a positive predictive value of 100% (25/25 patients). Interestingly, in our clinical practice, 60% of patients (15/25) went on to have another imaging test prior to being taken for surgery.

A total of 3 patients had a negative US, for a specificity of 2% and a negative predictive value of 100%. Among the 146 patients with an indeterminate US, 14/146 (10%) had appendicitis, and 132/146 (90%) did not have appendicitis.

Likelihood ratios were also calculated using the following formulas: positive likelihood ratio = (probability of positive US in those with appendicitis) / (probability of positive US in those without appendicitis); and negative likelihood ratio = (probability of negative US in those with appendicitis) / (probability of negative US in those without appendicitis). The positive likelihood ratio is 173 (when 0.5 is substituted for zero—otherwise it is infinite); the negative likelihood ratio is zero (Figure 2).

DISCUSSION

In this single-center study, we found that US had a poor sensitivity of 64% but a promising positive predictive value of 100%, as 25/25 patients with an US positive for appendicitis had appendicitis. There was a high rate of indeterminate scans (84%). In our academic practice environment, about half of the patients with a positive US scan underwent additional imaging prior to going to the operating room. Based on these preliminary data, there is a high prevalence that limits the utility of US as a first-choice imaging modality in adult patients; however, with further research, it may be possible to determine specific adult populations who will benefit from

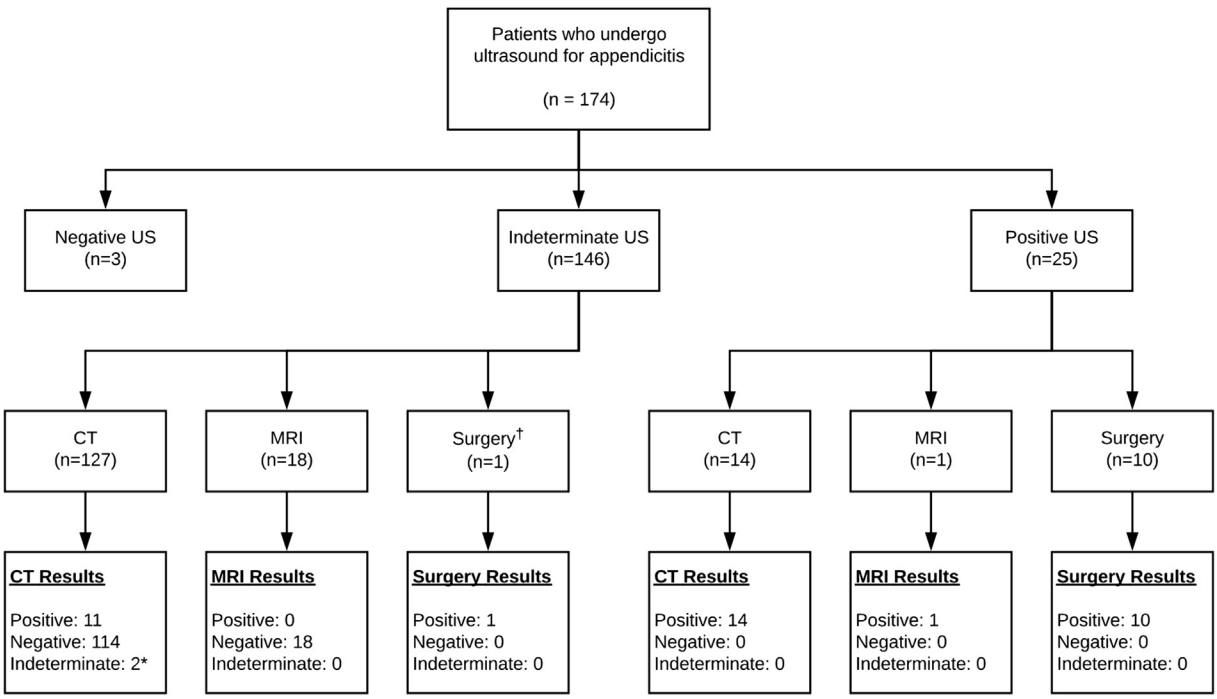

Figure 1. Flow diagram of patients who had appendiceal ultrasound performed in the emergency department. Positive = study read as having appendicitis, or appendicitis found at surgery. Negative = study read as negative, or appendicitis not found at surgery. CT = computed tomography; MRI = magnetic resonance imaging. *Indeterminate CT: both these patients were taken to the operating room and found to have appendicitis. †This patient was discharged and underwent surgery 2 weeks later after outpatient follow-up; found to have appendicitis.

Table 1. Baseline Population Characteristics*

Variable	Appendicitis Ultrasound Result		
	Negative (n = 3)	Positive (n = 25)	Indeterminate (n = 147)
Baseline demographics			
Age, y (95% CI)	36 (13–59)	27 (24–31)	28 (26–29)
Female gender, n (%)	3 (100)	16 (64)	129 (88)
BMI, mean (SD)*	16.6	24.6 (22.3–26.8)	26.0 (24.9–27.2)
History, n (%)			
Fever	0 (0)	7 (28)	29 (20)
Nausea	2 (66.7)	15 (60)	85 (58)
Diarrhea	1 (33.3)	0 (0)	15 (10)
Abdominal pain	3 (100)	25 (100)	145 (99)
Onset, n (%)			
< 24 h	2 (66.7)	15 (60)	62 (42)
24–48 h	1 (33.3)	3 (12)	24 (16)
48–72 h	0 (0)	3 (12)	10 (7)
> 72 h	0 (0)	3 (12)	47 (32)
Ultrasound findings, n (%)			
Enlarged appendix	0 (0)	25 (100)	4 (3)
Noncompressible appendix	0 (0)	22 (88)	1 (1)
Increased flow	0 (0)	16 (64)	0 (0)
Appendicolith	0 (0)	6 (24)	1 (1)
Stranding	0 (0)	6 (24)	0 (0)
Free fluid	0 (0)	5 (20)	0 (0)
Enlarged lymph nodes	0 (0)	0 (0)	0 (0)
Perforation	0 (0)	0 (0)	0 (0)
Wall thickening	0 (0)	0 (0)	0 (0)

CI = confidence interval; BMI = body mass index; SD = standard deviation.
* The characteristics are divided by ultrasound outcomes (positive, negative, or indeterminate). Note that only 1 patient in the negative ultrasound group had BMI data; in total, BMI data were available for only n = 117 patients.

appendicitis US, and to learn and adjust approaches with an aim to reduce indeterminate scans.

In a single, systematic literature review of 69 studies performed by Obermaier et al., the sensitivity and specificity of US for appendicitis in a single-center study were reported as 82% and 89%, respectively (9). What they demonstrated, however, was that improved results can be obtained if the US was limited to a few highly experienced operators. Similarly, a meta-analysis of 17 studies with a total of 3358 patients performed in the United States sought to review US test performance (10). This study was conducted using articles published since 1986, which included both adult and pediatric populations. Overall, the sensitivity was 84.7 (95% CI 81–87.8) and

		Gold Standard*		
		Positive	Negative	
Appendicitis Ultrasound	Positive	25	0	25
	Negative	0	3	3
	Indeterminate	14	132	146
		39	135	174

Sensitivity = 25/39 = 64%
Specificity = 3/135 = 2%
Positive predictive value = 25/25 = 100%
Negative predictive value = 3/3 = 100%

Likelihood ratio, positive† = P(positive US|+appendicitis) / P(positive US|-appendicitis)
= (25/39) / (0/135)
≈ (25/39) / (0.5/135)
≈ 173

Likelihood ratio, negative = P(negative US|+appendicitis) / P(negative US|-appendicitis)
= (0/39) / (3/135)
= 0

Figure 2. Appendicitis ultrasound (US) test characteristics. Positive, negative, and indeterminate results are included. *Gold standard includes computed tomography scan, magnetic resonance imaging, or operative exploration. †Because the positive likelihood ratio would result in division by zero, we substituted 0.5 (a small number within the confidence interval for the proportion) to allow for the calculation of a non-infinite number.

specificity was 92.1% (95% CI 88–95.2). Those patients with a high pretest probability and a positive US test demonstrated a positive predictive value of 97.6%, though a negative test could not exclude appendicitis. However, this analysis included mostly young adults and children in their studies possibly accounting for their higher sensitivity and specificity. Another meta-analysis study reviewed CT and US in adult and pediatric populations (11). There were 12 CT studies reviewed, with a total patient population of 1172. Three of the included studies were randomized controlled trials (n = 192) and the remainder were prospective cohort studies (n = 980). In addition, 14 US studies, all of which were prospective studies (n = 1516), were included in the meta-analysis. The demonstrated pooled sensitivities and specificities were 86% (95% CI 83–88) and 81% (95% CI 78–84), respectively, with a positive likelihood ratio of 5.8 (95% CI 3.5–9.5) and negative likelihood ratio of 0.19 (95% CI 0.13–0.27). As shown in our study, US is not recommended for patients with a low probability of appendicitis, as it cannot exclude patients with disease, given the low rate of negative US results.

There are a few useful insights from the data in our study that may inform practice and future research. The first is that positive US studies show promise as being able to reliably "rule in" appendicitis. The second insight is that there are many indeterminate studies. The reason these studies are indeterminate is unclear; possible contributors include patient body habitus, operator dependence of US (and perhaps, in adult sonographers' lack of comfort with this study), and radiologist comfort with reading a definitive result in adult populations. Future study might help determine what factors contribute to indeterminate studies, and to aim to reduce those on the hospital and provider side to improve the diagnostic utility of US.

Limitations

Limitations of this study include its size, retrospective design, and the fact that it was only performed at a single center. Furthermore, there may be a selection bias, as inclusion criteria were patients for whom the clinician ordered an US evaluated for appendicitis. These patients may have had a higher likelihood of a positive study. Our study population may not be representative of the broader group of patients presenting to the ED with suspected appendicitis. This study was not controlled for US operators and their varying operator experience. Rather, we sought to study the use of US in a typical academic setting. In this study, as in others, there is a high rate of nonvisualized appendices, which may be explained partly by the varying experience of the US technicians or by the body habitus of our adult patients. Further studies should be performed to investigate patient characteristics that would identify patients more likely to have an appendix that is identified by US.

CONCLUSIONS

In our population, US showed a high positive predictive value, and a positive US is sufficient to diagnose appendicitis; these patients likely do not require further imaging. However, the rate of indeterminate US scans was high. Conclusions cannot be drawn for patients with a negative study, due to small numbers. Future research should investigate patient populations in whom US may be most useful; it should also examine patient and hospital factors that may be modifiable to increase the number of definitive studies.

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ARTICLE SUMMARY

1. Why is this topic important?

Appendicitis is a frequently encountered diagnosis in the adult emergency department (ED). It is most often diagnosed by computed tomography (CT) scan; however, ultrasound has been successfully used in the pediatric population, and may be able to diagnose some adult patients more quickly and with less radiation and cost.

2. What does this study attempt to show?

This study attempts to define the test characteristics of ultrasound against a gold standard (CT, magnetic resonance imaging, or surgery) in the diagnosis of an adult population with appendicitis at a tertiary care ED.

3. What are the key findings?

Positive ultrasound had 100% positive predictive value in our study. However, there were few patients with negative ultrasounds in our study, and conclusions cannot be drawn about these patients. There were also many indeterminate scans.

4. How is patient care impacted?

Ultrasound may have a role in the diagnosis of appendicitis in adult patients in the ED. Patients with positive ultrasound likely do not need further imaging; patients with negative or indeterminate studies likely require CT for diagnosis.