PRACTICE



Single institutional experience with initial ultrasound followed by computed tomography or magnetic resonance imaging for acute appendicitis in adults

Priyanka Jha¹ · Nora Espinoza¹ · Emily Webb¹ · Marc Kohli¹ · Liina Poder¹ · Tara Morgan¹

Published online: 4 April 2019 © Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Purpose The objectives of this study was to assess the performance of ultrasound (US) for suspected appendicitis in adult patients and to evaluated the additive value of short-interval (within 1 week) computed tomography (CT) or Magnetic Resonance Imaging (MRI) after performing an initial US.

Methods In this IRB-approved, HIPAA-compliant, retrospective study, electronic medical records (EMRs) were queried for "US appendicitis" performed over a 2-year interval. EMR was reviewed for CT or MRI performed within 1 week of this exam, and if any new or additional information was available at subsequent exam. White count, patient disposition, and pathology, if surgery was performed, were also recorded.

Results 682 patients underwent US for appendicitis over a 2-year duration, age range from 18 to 92 years (average: 30.1 years, M:F=141:541). Findings showed 126/682 patients with normal appendix, 75/682 uncomplicated appendicitis, and 4/682 with complicated appendicitis. When performed, no additional findings were seen in these groups on short-interval CT or MRI. 2/682 patients had equivocal findings on US but eventually had normal appendix identified on CT. Four hundred and seventy-three patients had non-visualized appendix, of which only 14/473 (3.1%) eventually had appendicitis.

Conclusions Ultrasound is an effective initial modality for evaluating appendicitis even in adult patients. Once a normal appendix, uncomplicated or complicated appendicitis is identified on US, no further imaging is necessary. Very few patients with non-visualization of the appendix eventually have appendicitis. Hence, these patients can be managed with active clinical follow-up rather than immediate CT or MRI. Symptoms and clinical scoring systems can be used for triage of these patients.

 $\textbf{Keywords} ~~ Appendicitis \cdot Adults \cdot Ultrasound \cdot Follow-up \cdot Computed ~tomography \cdot Initial ~ultrasound ~~ Computed ~tomography \cdot Initial ~ultrasound ~~ Computed ~tomography ~ Computed ~ Computed ~tomography ~ Computed ~tomography ~ Computed ~tomography ~ Computed ~tomography ~ Computed ~$

Introduction

Appendicitis is the most common cause for right lower quadrant pain (RLQ) and surgical abdomen, most commonly presenting with fever and leukocytosis [1]. It is disease of children and young adults with an estimated annual incidence of 100 per 100,000 persons per year in Northern America, with an estimated 378,614 cases in 2015 [2]. In a study performed on emergency general surgery in the United Kingdom, appendectomy was the most common surgical

Priyanka Jha priyanka.jha@ucsf.edu

intervention required in the emergent setting, constituting 13.1% of all the surgeries performed [3].

Imaging is an important part of the work-up of acute appendicitis. Multiple modalities have been used in its diagnosis, including ultrasound (US), computed tomography (CT), and Magnetic Resonance Imaging (MRI). The latest ACR appropriateness criteria released in 2018 for imaging RLQ pain identify CT of the abdomen and pelvis with contrast as the primary exam modality ("usually appropriate") for work-up of suspected appendicitis, with US being categorized as a secondary modality ("may be appropriate") [1]. CT has been the conventional modality which has been shown to have an excellent sensitivity and specificity for diagnosing acute appendicitis with sensitivity ranging from 85.7 to 100%, and specificity ranging from 94.8 to 100% [4, 5]. MR imaging has been recently shown to have a comparable performance to CT [6]. Diagnostic

¹ Department of Radiology and Biomedical Imaging, University of California San Francisco, 505 Parnassus Avenue, Box 0628, San Francisco, CA 94131, USA

accuracy with ultrasound has been reportedly more variable. While ultrasound has been reported to have lower sensitivity compared to CT and MR, ranging from 76 to 83%, it has other advantages, particularly the lack of radiation [7–9]. In a study of patients aged 2–30 years, Imler et al. demonstrated that ultrasound is more inconclusive than rapid MRI, however is more time-efficient and less costly than rapid MRI, even considering some inconclusive studies after US imaging [10]. Despite the potentially higher incidence of inconclusive results with ultrasound compared with CT and MRI, its advantages are that it is the most widely available modality on a global scale and has been noted to have the quickest turnaround time, even in tertiary centers. Second-line imaging may become necessary in the event of inconclusive ultrasound results [1, 11]. Eng et al. recently conducted a meta-analysis, which showed US, CT, and MRI all have comparable and high accuracy in helping to diagnose appendicitis in children and adults, including pregnant women and suggested that any of the three modalities may be valid as second-line imaging in a clinical imaging pathway for diagnosis and management of appendicitis when necessary [11]. However, even in this meta-analysis, the number of studies evaluating ultrasounds in adults was small compared to pediatric studies [11].

At our institution, many adult patients undergo ultrasound of the appendix for the initial evaluation of suspected appendicitis. The usefulness of additional CT or MR imaging after initial ultrasound has not been well studied, and there is premise in the literature that this practice is relevant to emergency departments across the globe [11]. In this study, we attempted to assess the performance of ultrasound for suspected appendicitis in a population of adult patients. We evaluated the additive value of short-interval CT or MR for the diagnosis of appendicitis after performing an initial ultrasound. Specifically, we reviewed cases with an ultrasound result positive for appendicitis, cases with an ultrasound result negative for appendicitis, and cases with lack of visualization of the appendix with ultrasound. We expected that ultrasound may be a good initial screening test, when there is suspicion of acute appendicitis, even in an adult population.

Materials and methods

Patient selection

In this IRB-approved, HIPAA-compliant study, an archive of radiology reports was retrospectively queried for studies designated as "Ultrasound Appendix" over a 2-year period. Patients younger than 18 years of age were excluded. Informed consent was waived due to the retrospective nature of the study. Electronic medical records were queried to determine if second-line imaging with either CT or MRI was performed within 1 week of the initial ultrasound exam. Initially, the radiology reports were initially reviewed and sorted by a medical school student. US, CT, and MR imaging was subsequently reviewed by a radiologist with 5 years of abdominal imaging and ultrasound experience, who was blinded to the final diagnosis and outcome of the patients.

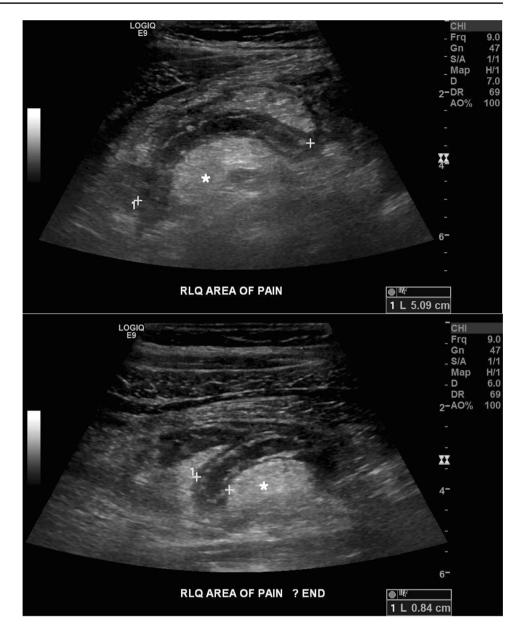
Ultrasound technique and imaging evaluation

At our institution, exams designated as "Ultrasound Appendix" are focused right lower quadrant ultrasounds performed with graded compression technique focused on the appendix. Curved 2-6 MHz and Linear 9 MHz probes are most commonly used to evaluate the patients based on body habitus. The sonographers scan the patient in a supine position, from the inferior liver margin to the pelvis and search the appendix. Identification of the ileocecal junction is also a useful landmark near the expected origin of the appendix. If the appendix is not identified in the supine position, left posterior oblique imaging is performed in the left lateral decubitus position and increases identification of retrocecal appendices. During the exam, patients are asked to point to the area of maximum pain and dedicated images at this location are recorded and annotated as the area of maximal tenderness. Routine endovaginal imaging is not performed as a part of the appendix protocol. At our institution, exams are performed by sonographers and are checked in real time by a radiologist before the patient is released from the department. Images are first obtained by sonographers, including dynamic cine clips and then reviewed by radiologists. Radiologists may choose to scan and obtain additional images, based on their discretion. Findings suspicious for acute appendicitis, which were evaluated on US included a transverse dimension measured from the serosa of more than 8 mm in diameter, wall thickening, non-compressibility of the appendix, focal sonographic tenderness, free fluid, echogenic peri-appendiceal fat, and appendiceal wall hyperemia on Doppler imaging. The most commonly accepted threshold for acute appendicitis in the literature is 8 mm, non-compressible appendix. Appendices measuring 6 mm or less are almost always normal [12, 13]. Our departmental protocols use the measurement of 8 mm and 6-8 mm as borderline dilated [12, 13]. Additional findings such as non-compressibility of the appendix, presence of appendicoliths, free fluid, echogenic peri-appendiceal fat, and specially tenderness over the appendix further substantiate the sonographic suspicion of appendicitis (Fig. 1).

Review of ultrasound imaging

The radiology reports available in PACS for these studies were reviewed and classified by one student as

Fig. 1 Twenty-nine-year-old woman with acute onset right lower quadrant (RLQ) pain. **a** and **b** Graded compression sonographic evaluation of the RLQ demonstrates a dilated (8 mm, calipers) blind ending structure, compatible with the appendix. The appendix was non-compressible on dynamic evaluation. Echogenic periappendiceal fat (asterisk) representing inflammatory changes in adjacent fat is also present



- 1. Normal appendix
- 2. Acute appendicitis without complications
- 3. Acute appendicitis with complications
- 4. Appendix identified with findings equivocal for appendicitis
- 5. Normal appendix visualized with alternate diagnosis identified on US
- 6. Non-visualization of the appendix with alternate diagnosis identified on US
- 7. Non-visualization of the appendix without alternate diagnosis identified on US.

CT and MRI technique and imaging evaluation

CT or MR imaging performed within 1 week of the initial ultrasound was included. Multidetector CT was performed with 64-detector row scanners (GE Healthcare). Intravenous contrast was administered to all patients who underwent CT and 150 mL of iohexol was injected via a power injector at a rate of 3 mL/s. Imaging was performed in the portal venous phase of enhancement (70 s delay) with anatomic coverage from the diaphragm through the pelvis. Images were reconstructed at 1.25 and 2.5 mm thickness. Coronal and sagittal reformats were performed at a 2 mm slice thickness. CT signs of appendicitis included thickened, hyperenhancing appendix, surrounding fat stranding, and/or free fluid. Our MR appendicitis protocol includes Multiplanar SSFSE sequences, axial and sagittal T1 non-fat saturated, T2-fat saturated, and diffusion-weighted images. On MR imaging, peri-appendiceal T2-hyperintensity was seen with around a fluid-filled appendix. Fat stranding is also be identified on T1-weighted images as T1-dark bands on the background of normal T1-hyperintense fat [6, 14].

Review of CT and MR imaging

CT and MR reports were reviewed by a single reader to assess whether the exam added value by providing additional information that affected management. This included instances of discordance between the initial US interpretation and a subsequent CT or MR interpretation. Additionally, cases where the appendix was not visualized at ultrasound or appeared equivocal were evaluated as to whether CT or MR provided a definitive diagnosis.

Clinical follow-up

Electronic Medical Records (EMRs) were also reviewed by a student to determine the patient's white blood cell (WBC) count at presentation, and their clinical disposition: (1) discharge home without additional treatment, (2) discharge with antibiotics, (3) inpatient admission without surgery, (4) inpatient admission with appendectomy (and surgical pathology), or (5) return to the emergency department within a week of discharge. When appendectomy was performed, surgical pathology results were also recorded.

Statistical analysis

Descriptive statistics were performed. Sensitivity, specificity, positive and negative predictive values were calculated for the scenarios where an appendix was visualized as well as for the entire cohort. For the statistical analysis involving the entire cohort, non-visualization of the appendix on US was treated as negative for sonographic evidence of appendicitis.

Results

A total of 682 patients underwent US evaluation for appendicitis over a 2-year duration. The ages of these patients ranged from 18 years to 92 years (median age: 28 years, average age: 30.1 years). There were 541 females in the cohort and 141 males. 23 of the women were pregnant (gestational age ranging from 5 weeks 3 days to 35 weeks 6 days) (Table 3).

The distribution of initial ultrasound results are reported in Table 1. The additive values of subsequent CT or MR are presented in Table 2.

- Normal appendix with no alternate diagnosis identified on US A total of 124/682 (18.2%) patients had a normal appendix at initial ultrasound imaging (Table 1). Of these, 99/124 (80%) had no additional imaging performed. 25/124 (20%) patients underwent a subsequent CT where a normal appendix was confirmed (Table 2) and no patients had a CT or MRI demonstrating acute appendicitis. Only one of these 124 patients returned to the ER within 1 week for additional similar complaints. The patient who returned to the ER was diagnosed with uncomplicated pyelonephritis.
- Normal appendix with alternate diagnosis identified on US 2 additional patients had an alternate diagnosis (enteritis) identified on US in addition to visualization of a normal appendix (Table 1). Both of these patients underwent subsequent CT, where enteritis was re-demonstrated (Table 2). They were treated with antibiotics and discharged home.
- Acute appendicitis without complications Ultrasound findings of uncomplicated appendicitis were identified in 74/682 (11%) patients (Table 1). Of these, 47/75 (64%) of patients did not have any additional imaging and went directly to surgery. Uncomplicated appendicitis was confirmed during surgery and at surgical pathology in all patients. None of these patients had additional findings during surgery and underwent uneventful appendectomy. 27/75 (36%) patients underwent subsequent CT, and one pregnant woman received subsequent MR imag-

Table 1Summary of initialultrasound findings in 682adults	Ultrasound findings	Adult patients $n = 682 (\%)$
	Normal appendix with no alternate diagnosis identified on US	124 (18.2)
	Normal appendix visualized with alternate diagnosis identified on US	4 (0.6)
	Acute appendicitis without complications	75 (11.0)
	Acute appendicitis with complications	4 (0.6)
	Appendix identified with equivocal findings for appendicitis	2 (0.3)
	Normal appendix not visualized with alternate diagnosis identified on US	14 (2.1)
	Non-visualization of the appendix without alternate diagnosis	459 (67.3)

Table 2	Distribution of	patients based	on US and C	T findings
---------	-----------------	----------------	-------------	------------

2361

Initial ultrasound findings	No sub- sequent imaging	CT/MR with normal appendix	CT/MR with appendicitis
Normal appendix $(n = 124)$	99	25	0
Uncomplicated Appendicitis $(n=75)$	47	3	25
Appendicitis with complications $(n=4)$	0	0	4
Appendix identified with equivocal findings for appendicitis $(n=2)$	0	2	0
Normal appendix visualized with alternate diagnosis identified on US $(n=4)$	0	4 (Alt. dx in 2/4)	0
Normal appendix not visualized with alternate diagnosis identified on US $(n = 14)$	6	8	0
Non-visualized appendix without alternate diagnosis on US $(n=459)$	290	155 (Alt. dx in 23/155)	14

 Table 3
 Appendix visualized at ultrasound: correlation between initial US diagnosis and eventual diagnosis based on surgical outcomes and clinical follow-up

	Normal appendix (%)	Appendicitis (%)
US positive $(n=79)$ or equivocal $(n=2)$ for appendicitis	5/81 (6)	76/81 (94)
US negative for appendi- citis (Normal appendix on US)	128/128 (100)	0/128 (0)
Appendix not identified at US	459/473 (97)	14/473 (3.0)

ing (1/75, 1%). The single patient who underwent subsequent MR had uncomplicated appendicitis confirmed. 24/27 patients who underwent subsequent CT had acute appendicitis confirmed. No additional findings of perforation or other complications were identified on CT. 2/27 patients were subsequently found to have normal appendices on CT without inflammatory changes, constituting false positive on US. (Table 2). Both the patients had normal white blood cell count. One patient had a dilated appendix measuring 8 mm in diameter at the midportion but with the normal measurement of the remaining segments. One patient with invasive cervical cancer had her appendix dilated to 8 mm but with no focal tenderness or hyperemia.

- Acute appendicitis with complications 4/682 (0.6%) patients had appendicitis with perforation identified on US (Table 1). The presence of perforation was confirmed by abscess in 2 cases and suggested by a large amount of adjacent free fluid on 2 other cases. All 4 of these patients had subsequent CTs, which confirmed the US findings (Table 2). Findings were subsequently confirmed at surgery and surgical pathology as well.
- Appendix identified with findings equivocal for acute appendicitis In 3/682 (0.4%) patients, the appendix was

identified on US but the findings were equivocal for acute appendicitis (Table 1). In two patients with focal right lower quadrant tenderness, the appendix was 6 mm but non-compressible and not hyperemic. In another patient, the appendix measured 10 mm but was compressible without focal tenderness in the right lower quadrant. All the three patients underwent subsequent CT demonstrating no evidence of acute appendicitis (Table 2). Additionally, the white blood cell count was normal in both patients.

- Non-visualized appendix with alternate diagnosis identified on US Although an appendix was not identified, other alternate etiologies for abdominal pain were identified on US in 14/682 (2%) patients (Table 1). These diagnoses included 2 hemorrhagic ovarian cysts, 1 ovarian torsion, 1 hydrosalpinx, 1 transverse colitis, 1 cecal diverticulitis, 1 sigmoid diverticulitis, 3 enteritis, 2 terminal ileitis, 1 cholelithiasis without cholecystitis, and 1 large RLQ mass. Eight of these patients underwent CT (Table 2) where the proposed sonographic diagnosis was confirmed (1 transverse colitis, 1 cecal diverticulitis, 1 sigmoid diverticulitis, 2 enteritis, 2 terminal ileitis and 1 large RLQ mass). Appendicitis was never seen on CT for these patients.
- Non-visualized appendix without alternate diagnosis identified on US The majority of our patients fell in this category with 459/682 (67.3%) patients having inconclusive results and non-visualized appendix at ultrasound. Of these, 290/459 (63.1%) had no further imaging work-up and no subsequent diagnosis of appendicitis (Table 1). 165/459 (35.9%) patients underwent subsequent CT and 4/459 (0.9%) pregnant patients underwent subsequent MR imaging. Overall, 14/459 (3.1%) patients with a non-visualized appendix and no clear alternate diagnosis at US were eventually diagnosed with appendicitis (Table 2). 169 patients who had subsequent CT or MR imaging and 14/169 (8.3%) had appendicitis subsequently diagnosed, compared to 155/169 (91.7%) patients

who had a normal appendix visualized (Table 2). Of the 14 patients with acute appendicitis, 8 had an elevated WBC count and 6 had a normal WBC count. An alternate diagnosis apart from appendicitis was identified on CT in 21/169 (13.6%) patients (5 sigmoid diverticulitis, 2 enterocolitis, 5 right pyelonephritis, 1 gastritis, 1 right renal abscess, 3 PID, 1 omental infarct, 2 epiploic appendagitis, and 1 necrotizing pneumonia). One MR in a non-pregnant woman showed endometritis. One/4 (25%) of the MRIs in a pregnant woman showed an alternate diagnosis of pyelonephritis. No MRIs showed concomitant appendicitis.

Overall, when the initial ultrasound result was positive or had equivocal findings for appendicitis, 76/81 (94%) of patients were confirmed to have appendicitis. When the initial ultrasound was negative for appendicitis, 0% of patients had a subsequent imaging or clinical diagnosis of appendicitis. In cases where the appendix could not be identified by ultrasound, only 3% (14/473) were eventually diagnosed with appendicitis (Table 3).

Based on our results, the overall sensitivity and specificity of ultrasound for appendicitis in an adult population was 84.4% (CI 75.3–91.2%), specificity 99.2% (CI 98.0–99.7%), positive predictive value 93.8% (CI 86.3–97.3%), and NPV of 97.7% (CI 96.3–98.5%). The accuracy was 97.2% (CI 95.7–98.3%).

When the appendix was visualized at ultrasound, the specificity was 98.7%, the positive predictive value was 93.8% (CI 86.6–97.3%), and NPV was 100%. The accuracy was 97.6% (CI 94.5–99.2%).

Special attention was paid to the subgroup of pregnant women (Table 4). In this group as well, most commonly the appendix was not visualized on US (12/23 patients). Four of these patients underwent MR imaging, where a normal appendix was identified in all cases. One showed an alternate diagnosis of pyelonephritis. In our cohort, none of the pregnant women who underwent MR imaging after an inconclusive US had evidence for appendicitis. When a normal appendix was identified, no further imaging was performed and the patients were discharged home and remained uneventful without return to ER over the next 3 days. In two patients, appendicitis was identified on US, of which one underwent MR imaging. Appendicitis was confirmed on the MR as well.

Discussion

Utilization of CT after initial US performed is a common practice in the emergency department both during daytime hours and after hours [15]. However, our results show that ultrasound is an effective modality for initial evaluation of acute appendicitis, even in adult patients. Importantly, a very small minority of acute appendicitis cases (3.1%) were missed due to a false-negative ultrasound. To the best of our knowledge, this is the largest study evaluating ultrasound for appendicitis, specifically in an adult population.

Our study suggests that once a normal appendix is identified on US, no further imaging with CT is necessary. Ultrasound was 100% accurate when a normal appendix was identified. When an ultrasound is positive for appendicitis, further imaging comparison with CT or MR imaging, may not be necessary. Avoidance of this additional imaging could increase efficiency of care and decrease health care costs. Our results are concordant with Koo et al. where initial sonography was determined to be as effective as CT in pediatric patients with suspected acute appendicitis when the results are definite. They suggested that supplementary CT should only be considered when sonography is inconclusive [16]. Ultrasound also performed as well as CT in identifying alternate causes of RLQ pain when appendicitis was absent.

Ultrasound identified all four cases of complicated appendicitis; however, the authors acknowledge that this is a very small number. There was a small false-positive rate for ultrasound diagnosis of uncomplicated appendicitis with 5/81 (6%) of cases, which were positive or equivocal at ultrasound and normal appendix at subsequent CT. Therefore, CT did confer some benefit in a small proportion of patients with positive ultrasound, particularly those with equivocally positive findings.

Our results also showed that once appendicitis was confirmed on US, no additional complications such as perforation or abscess were identified on CT. These results were confirmed surgically and pathologically. It is known that delays in care can lead to increased risk of complications,

Table 4Distribution ofpregnant patients based on USand CT findings

Ultrasound findings	MR not performed	MR performed with normal appendix	MR performed with appendi- citis
Normal appendix $(n=5)$	5	0	0
Appendicitis $(n=2)$	1	0	1
Non-visualized appendix without alternate diagnosis on US $(n = 17)$	12	4 Alt Dx-1 (pyelone- phritis)	0

which increases with the length of overall hospital stay and is potentially added to by unnecessary additional imaging [17]. A delay of 6–12 h increases the risk of surgical site infection and delays longer than 24 h can lead to higher odds of complicated appendicitis [17]. Our results are also supported by studies performed in children, where ultrasound was thought to be sufficient to diagnose complicated appendicitis [18].

As expected, a study performed by Pelin et al. in France has shown advanced age, high BMI, atypical appendix location, and complicated appendicitis to be associated with nonvisualized appendix and inconclusive ultrasounds [19]. In our study, when the appendix was non-visualized appendix at US, only 3.1% of patients were subsequently diagnosed with appendicitis. This is similar to the approximately 2% of patients who are eventually found to have appendicitis when the appendix cannot be visualized at CT [20-22]. Thus, we concur with Srinivasan et al. that non-visualization of the appendix on US does not equate to a non-diagnostic exam [23]. These results are discordant with Kelly et al. who showed that almost a half of pediatric patients have appendicitis in the setting of non-visualized appendix, and that CT or MR imaging may be subsequently indicated in this population [24]. Our results are also discordant with Williamson et al. who evaluated the outcomes of non-visualized appendix on ultrasound in pediatric patients and found that 11.9% of patients with non-visualized appendix eventually had appendicitis [25]. In our cohort, only 3.1% of adult patients with non-visualized appendix subsequently had appendicitis. This discrepancy could be explained by differences in ultrasound technique, differences in pre-test probability differences between the adult and pediatric patients undergoing US for appendicitis evaluation, as well as changes in ordering patterns in emergency departments, with a larger number of young adults getting US for initial evaluation. In a subgroup of our patients with non-visualized appendix and subsequent imaging performed, 8.3% (14/169) of patients were found to have appendicitis. These likely were patients where the clinician was sufficiently concerned and wanted to pursue additional imaging.

In the situation of a non-visualized appendix, our recommendations coincide with that of previous authors [19, 20], in that the patient should be managed with active clinical follow-up rather than immediate CT [26]. This was deemed appropriate in prior studies despite a higher percentage of patients with eventual diagnosis in their cohorts. Per Malia et al. when the appendix is not visualized on US, predictors for appendicitis include the presence of inflammatory changes in the RLQ, an elevated white count and C-reactive protein and abdominal pain < 3 days [27].

Compared to other studies, Koo et al. only included patients who had both US and CT within 12 h and our study extended the observation to one week for patients who did not have a CT after initial US [16]. Our study included all patients who had US for appendicitis and clinical followup was used for patients who did not have further imaging. Pelin et al. included only patients with acute appendicitis [19] and Kelley et al. included only patients who had appendectomies [24]. Our follow-up duration (1 week) was same as Williamson et al. [25] but lower than that of Stewart et al. (2 months) [26]. However in the latter study's cohort, the average duration between the US and subsequent CT was 3 h for patients found to have appendicitis and 4.4 h for those without appendicitis, with a range of 0.4 to 43.7 h [26]. Hence, our follow-up duration of one week should have captured most patients with acute appendicitis.

To decrease radiation exposure to young people, authors have recommended limited field of view CT imaging after an inconclusive US [28]. When reliable post-discharge follow-up is possible, clinical decision scores can be used to augment non-diagnostic or inconclusive ultrasound results to avoid second-line CT or MR imaging in the emergency department [29]. Our results differ from another study performed by the same group, where US underdiagnosed perforated appendicitis as simple non-complicated appendicitis [30]. A total of four cases of perforated appendicitis were noted in our cohort. Although the sample size is small, once complicated appendicitis was diagnosed, no further complications were noted either on short-interval CT or surgical correlation.

The additional value of assessing white blood cell count further augments the results from the ultrasound. Corkum et al. have proposed that an abnormally elevated white blood cell count can be used to determine the need for MR imaging in children, when US results are equivocal [31]. In our cohort, a normal white blood cell count was present in some patients with appendicitis, and hence when used alone, this was not a good predictor to guide the use of CT in patients with non-visualized appendix on ultrasound. Similar principles and additional clinical scoring systems such as the Alvarado score can be applied in adults to assess the need for CT or MR imaging after an inconclusive ultrasound study [23, 32].

Limitations of our study include the retrospective nature and variability in ultrasound technique as it was performed by different sonographers. However, the authors feel that this is closely reflective of the practice in community, where individuals with variable levels of expertise will be involved in the imaging of these patients. Studies have shown that sonographer expertise can be improved by education on secondary signs such as echogenic peri-appendiceal fat in addition to looking for the appendix itself [33]. The results could also be biased based on the ordering behavior of our emergency department physicians, again something that may be seen across multiple practices. Also, for reference standard, lack of appendicitis was based on clinical follow-up within 1 week based on review of our institutional Electronic Medical Records (EMRs). Our analysis would miss any patient, who would have been admitted elsewhere with appendicitis or presented more than a week later with appendicitis. However, as discussed above, 1-week follow-up is mostly reasonable based on results of prior studies, where patients were found to have appendicitis after a non-visualized appendix on ultrasound [26].

Hence, in conclusion once a sonographic diagnosis of normal appendix or uncomplicated or complicated appendicitis is diagnosed on ultrasound, further imaging for appendicitis does not change the diagnosis prior to surgery. If the appendix is not visualized, a very small percentage of patients may still have acute appendicitis. The majority of these patients too can be managed expectantly, and CT can be performed as warranted on an individual basis by patients' clinical symptoms and clinical scoring symptoms.

References

- Expert Panel on Gastrointestinal, I., et al., ACR Appropriateness Criteria((R)) Right Lower Quadrant Pain-Suspected Appendicitis. J Am Coll Radiol, 2018. 15(11S): p. S373–S387.
- Ferris, M., et al., *The Global Incidence of Appendicitis: A Systematic Review of Population-based Studies*. Ann Surg, 2017. 266(2): p. 237-241.
- Ramsay, G., J.M. Wohlgemut, and J.O. Jansen, *Emergency General Surgery in the United Kingdom: A lot of General, not many Emergencies, and not much Surgery.* J Trauma Acute Care Surg, 2018. Sep;85(3):500–506
- 4. Drake, F.T., et al., *Enteral contrast in the computed tomography diagnosis of appendicitis: comparative effectiveness in a prospective surgical cohort.* Ann Surg, 2014. **260**(2): p. 311-6.
- Chiu, Y.H., et al., Whether intravenous contrast is necessary for CT diagnosis of acute appendicitis in adult ED patients? Acad Radiol, 2013. 20(1): p. 73-8.
- Repplinger, M.D., et al., Prospective Comparison of the Diagnostic Accuracy of MR Imaging versus CT for Acute Appendicitis. Radiology, 2018. 288(2): p. 467-475.
- Balthazar, E.J., et al., Acute appendicitis: CT and US correlation in 100 patients. Radiology, 1994. 190(1): p. 31-5.
- Doria, A.S., et al., US or CT for Diagnosis of Appendicitis in Children and Adults? A Meta-Analysis. Radiology, 2006. 241(1): p. 83-94.
- Poortman, P., et al., Comparison of CT and sonography in the diagnosis of acute appendicitis: a blinded prospective study. AJR Am J Roentgenol, 2003. 181(5): p. 1355-9.
- Imler, D., et al., Magnetic Resonance Imaging Versus Ultrasound as the Initial Imaging Modality for Pediatric and Young Adult Patients With Suspected Appendicitis. Acad Emerg Med, 2017. 24(5): p. 569-577.
- Eng, K.A., et al., Acute Appendicitis: A Meta-Analysis of the Diagnostic Accuracy of US, CT, and MRI as Second-Line Imaging Tests after an Initial US. Radiology, 2018. 288(3): p. 717-727.
- Gaitini, D., et al., *Diagnosing acute appendicitis in adults: accuracy of color Doppler sonography and MDCT compared with surgery and clinical follow-up.* AJR Am J Roentgenol, 2008. **190**(5): p. 1300-6.

- Xu, Y., et al., Color Doppler Imaging of the Appendix: Criteria to Improve Specificity for Appendicitis in the Borderline-Size Appendix. J Ultrasound Med, 2016. 35(10): p. 2129-38.
- Knoepp, U.S., et al., MR Imaging of Pelvic Emergencies in Women. Magn Reson Imaging Clin N Am, 2017. 25(3): p. 503-519.
- Alzahrani, H., et al., Imaging Approach to the Diagnosis of Acute Appendicitis in a Group of Teaching Hospitals With 24/7 In-house Availability of Ultrasound Technologist: Effect of Timing of Request on Imaging Modality. Can Assoc Radiol J, 2018. Aug;69(3):311-315. https://doi.org/10.1016/j.carj.2018.03.002. Epub 2018 Jun 27.
- Koo, H.S., et al., Does computed tomography have any additional value after sonography in patients with suspected acute appendicitis? J Ultrasound Med, 2013. 32(8): p. 1397-403.
- Li, J., et al., Effect of Delay to Operation on Outcomes in Patients with Acute Appendicitis: a Systematic Review and Meta-analysis. J Gastrointest Surg, 2018. Jan;23(1):210-223. https://doi. org/10.1007/s11605-018-3866-y. Epub 2018 Jul 6.
- Gonzalez, D.O., et al., Can ultrasound reliably identify complicated appendicitis in children? J Surg Res, 2018. 229: p. 76-81.
- Pelin, M., et al., Acute appendicitis: Factors associated with inconclusive ultrasound study and the need for additional computed tomography. Diagn Interv Imaging, 2018. Dec;99(12):809-814. https://doi.org/10.1016/j.diii.2018.07.004. Epub 2018 Sep 7.
- Daly, C.P., et al., *Incidence of acute appendicitis in patients with equivocal CT findings*. AJR Am J Roentgenol, 2005. 184(6): p. 1813-20.
- Ganguli, S., et al., *Right lower quadrant pain: value of the non-visualized appendix in patients at multidetector CT.* Radiology, 2006. 241(1): p. 175-80.
- 22. Nikolaidis, P., et al., *The nonvisualized appendix: incidence of acute appendicitis when secondary inflammatory changes are absent.* AJR Am J Roentgenol, 2004. **183**(4): p. 889-92.
- 23. Srinivasan, A., et al., *Utility of CT after sonography for suspected appendicitis in children: integration of a clinical scoring system with a staged imaging protocol.* Emerg Radiol, 2015. **22**(1): p. 31-42.
- Kelly, B.S., et al., Improving diagnostic accuracy in clinically ambiguous paediatric appendicitis: a retrospective review of ultrasound and pathology findings with focus on the non-visualised appendix. Br J Radiol, 2018: Sep 12:20180585. https://doi. org/10.1259/bjr.20180585. [Epub ahead of print]
- Williamson, K., et al., Outcomes for Children With a Nonvisualized Appendix on Ultrasound. Pediatr Emerg Care, 2018. Nov 12. https://doi.org/10.1097/pec.00000000001672. [Epub ahead of print]
- Stewart, J.K., E.W. Olcott, and R.B. Jeffrey, Sonography for appendicitis: nonvisualization of the appendix is an indication for active clinical observation rather than direct referral for computed tomography. J Clin Ultrasound, 2012. 40(8): p. 455-61.
- Malia, L., et al., Diagnostic accuracy of laboratory and ultrasound findings in patients with a non-visualized appendix. Am J Emerg Med, 2018. Aug 7. pii: S0735-6757(18)30650-8. https:// doi.org/10.1016/j.ajem.2018.08.014. [Epub ahead of print]
- 28. O'Malley, M.E., et al., *CT following US for possible appendicitis: anatomic coverage*. Eur Radiol, 2016. **26**(2): p. 532-8.
- Leeuwenburgh, M.M., et al., A simple clinical decision rule to rule out appendicitis in patients with nondiagnostic ultrasound results. Acad Emerg Med, 2014. 21(5): p. 488-96.
- Leeuwenburgh, M.M., et al., Accuracy of MRI compared with ultrasound imaging and selective use of CT to discriminate simple from perforated appendicitis. Br J Surg, 2014. 101(1): p. e147-55.
- 31. Corkum, K.S., et al., Absolute neutrophil count as a diagnostic guide for the use of MRI in the workup of suspected appendicitis in children. J Pediatr Surg, 2018. Jun 22. pii:

S0022-3468(18)30397-X. https://doi.org/10.1016/j.jpeds urg.2018.06.021. [Epub ahead of print]

- 32. Jones, R.P., et al., Journal Club: the Alvarado score as a method for reducing the number of CT studies when appendiceal ultrasound fails to visualize the appendix in adults. AJR Am J Roentgenol, 2015. 204(3): p. 519-26.
- 33. Reddan, T., et al., Improving the value of ultrasound in children with suspected appendicitis: a prospective study

integrating secondary sonographic signs. Ultrasonography, 2019 Jan;38(1):67-75. doi: 10.14366/usg.17062. Epub 2018 May 7.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.