Evaluating the risk of appendiceal perforation when using ultrasound as the initial diagnostic imaging modality in children with suspected appendicitis

Stephen Alerhand¹, James Meltzer² and Ee Tein Tay¹

Abstract

Background: Ultrasound scan has gained attention for diagnosing appendicitis due to its avoidance of ionizing radiation. However, studies show that ultrasound scan carries inferior sensitivity to computed tomography scan. A non-diagnostic ultrasound scan could increase the time to diagnosis and appendicectomy, particularly if follow-up computed tomography scan is needed. Some studies suggest that delaying appendicectomy increases the risk of perforation.

Objective: To investigate the risk of appendiceal perforation when using ultrasound scan as the initial diagnostic imaging modality in children with suspected appendicitis.

Methods: We retrospectively reviewed 1411 charts of children ≤ 17 years old diagnosed with appendicitis at two urban academic medical centers. Patients who underwent ultrasound scan first were compared to those who underwent computed tomography scan first. In the sub-group analysis, patients who only received ultrasound scan were compared to those who received initial ultrasound scan followed by computed tomography scan. Main outcome measures were appendiceal perforation rate and time from triage to appendicectomy.

Results: In 720 children eligible for analysis, there was no significant difference in perforation rate between those who had initial ultrasound scan and those who had initial computed tomography scan (7.3% vs. 8.9%, $p=0.44$), nor in those who had ultrasound scan only and those who had initial ultrasound scan followed by computed tomography scan (8.0% vs. 5.6%, $p=0.42$). Those patients who had ultrasound scan first had a shorter triage-to-incision time than those who had computed tomography scan first (9.2 (IQR: 5.9, 14.0) vs. 10.2 (IQR: 7.3, 14.3) hours, $p=0.03$), whereas those who had ultrasound scan followed by computed tomography scan took longer than those who had ultrasound scan only (7.8 (IQR: 5.3, 11.6) vs. 15.1 (IQR: 10.6, 20.6), $p<0.001$). Children < 12 years old receiving ultrasound scan first had lower perforation rate ($p=0.01$) and shorter triage-to-incision time ($p=0.003$).

Conclusion: Children with suspected appendicitis receiving ultrasound scan as the initial diagnostic imaging modality do not have increased risk of perforation compared to those receiving computed tomography scan first. We recommend that children < 12 years of age receive ultrasound scan first.

Keywords

Appendicitis, ultrasound, pediatrics, perforation, emergency

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Introduction

Over the past decade, the use of ultrasound scan (US) has gained attention as the initial diagnostic imaging modality in children with suspected appendicitis due

¹Icahn School of Medicine at Mount Sinai, NY, USA

²Albert Einstein College of Medicine, NY, USA

Corresponding author:

Stephen Alerhand, Icahn School of Medicine at Mount Sinai,
1 Gustave L. Levy Place, New York, NY 10029, USA.
Email: Stephen.Alerhand@gmail.com

to several advantages over computed tomography (CT). Ultrasonography avoids ionizing radiation exposure, the risks inherent with procedural sedation in young children, and the side effects associated with contrast administration. Moreover, the use of US as the primary imaging modality for these patients has been shown to decrease their overall length of stay in the emergency department (ED).¹

Abdominal US, however, has some inherent limitations. Several studies have shown that the sensitivity of US in the diagnosis of appendicitis is less than that of CT.^{1–5} A non-diagnostic or indeterminate US study could increase the time to the diagnosis of appendicitis and time to appendectomy in children, particularly if other confirmatory tests are needed. Some prior studies have suggested that a delay in appendectomy may increase the patient's risk of appendiceal perforation.^{6–8} The purpose of this study was to investigate the use of US as the initial diagnostic imaging modality in children with suspected appendicitis with regard to the risk of perforation.

Methods

Study setting

This was a planned secondary analysis of a larger retrospective study on a cohort of patients in which the following data were extracted by chart review: date of birth and gender, date and time of triage, white blood cell (WBC) count, CT scan report, pathology report, and date and time of the first surgical incision. For this secondary analysis, US reports were also collected from two participating urban academic hospitals. The Institutional Review Boards from both academic centers approved the study.

Study population

Children ≤ 17 years old diagnosed with appendicitis between 2003 and 2012 were identified using International Classification of Disease, Ninth Revision (ICD-9) codes (540.0, 540.1, 540.9, 541, or 542) and confirmed for eligibility using pathology reports. Patients were excluded from analysis if they met any of the following conditions: no US or CT scan was performed or either study revealed a perforated appendix, the pathology report showed a normal appendix, the patient was transferred from an outside hospital for suspected appendicitis, or the patient was not operated upon.

Exposure measures

Imaging results were collected from radiology reports. Patients who had an US as their initial imaging

modality (US-first) were compared to those who had a CT scan performed first (CT-first). For an US-first subgroup analysis, patients who had only an US performed (US-only) were compared to those who received both an US and a subsequent CT (US followed by CT).

Outcome measures

The main outcome measures were appendiceal perforation rate and the time from ED triage to surgical incision for appendectomy.

Data analysis

Normally distributed continuous variables were described using means and standard deviations (SD), and compared using t-tests. Non-normally distributed continuous variables were described using medians and interquartile ranges (IQR), and compared using Mann-Whitney tests. Normality was assessed using histograms. Categorical variables were described using frequencies and percentages, and compared using Chi-square or Fisher exact tests where appropriate. A Breslow-Day test of homogeneity was used to test for effect modification for the covariates age, gender, and WBC count based on a priori suspicion. Adjusted associations were calculated in the absence of significant effect modification using Mantel-Haenszel tests, and reported in strata, if the change in odds ratios was substantial ($\geq 15\%$). A p-value < 0.05 was considered significant for all analyses. All calculations were performed using SPSS Version 21 (IBM, Armonk, New York).

Results

Of the 1411 patient charts reviewed, 720 (51%) were eligible for analysis (Figure 1). Three hundred and ninety-seven (55%) were males and the median age was 12 years old (IQR: 9, 15).

Primary analysis: US-first vs. CT-first

Baseline characteristics of patients in the US-first group as compared to those of the CT-first group are presented in Table 1. In an unadjusted analysis, there was no significant difference in perforation rate between those patients in the US-first group and those in the CT-first group (OR: 0.8 (95% CI: 0.5–1.4)) (Table 2). However, age significantly modified the association of imaging modality and perforation ($p = 0.01$). For children younger than 12 years, the odds of perforation was significantly lower (OR: 0.4 (95% CI: 0.2–0.8)) if they received US-first, whereas there was no significant association between imaging modality and perforation

Figure 1. Study protocol flow chart.

Table 1. Primary analysis – Baseline clinical characteristics

	US-first, n = 395	CT-first, n = 325	Odds ratio	p
Characteristics				
Gender – male, n (%)	213 [53.9]	184 [56.6]	0.9	0.47
Age in years, median (IQR)	11.6 [8.4, 14.1]	13.2 [10.2, 16.0]		<0.001
WBC, $\times 10^9/L$, mean $\pm$ SD	14.6 $\pm$ 4.7	14.7 $\pm$ 5.0		0.70

Table 2. Primary analysis – Outcome measures by imaging modality

	US-first, n = 395	CT-first, n = 325	Odds ratio	p
Outcomes				
a. Perforation, n (%)				
Overall	29 [7.3]	29 [8.9]	0.8	0.44
<12 years old	18 [8.5]	23 [17.7]	0.4	0.01
≥ 12 years old	11 [6.0]	6 [3.1]	2.0	0.17
b. Triage-to-incision time in hours, median (IQR)				
Overall	9.2 [5.9, 14.0]	10.2 [7.3, 14.3]		0.03
<12 years old	8.9 [5.7, 13.5]	10.8 [8.1, 15.4]		0.003
≥ 12 years old	9.4 [6.5, 14.8]	9.8 [6.8, 13.3]		0.91

Table 3. Subgroup analysis – Baseline clinical characteristics

	US-only, n = 288	US followed by CT, n = 107	Odds ratio	p
Characteristics				
Gender – male, n (%)	168 (58.3)	45 (42.1)	1.9	0.004
Age in years, median (IQR)	11.2 (8.0, 13.8)	12.8 (9.8, 15.3)		0.004
WBC $\times 10^9/L$, mean $\pm$ SD	15.0 $\pm$ 4.8	13.5 $\pm$ 4.5		0.005

Table 4. Subgroup analysis – Outcome measures by imaging modality

	US-only, n = 288	US followed by CT, n = 107	Odds ratio	p
Outcomes				
Perforation, n (%)	23 (8.0)	6 (5.6)	1.5	0.42
Triage-to-incision time in hours, median (IQR)	7.8 (5.3, 11.6)	15.1 (10.6, 20.6)		<0.001

in children 12 years and older (OR: 2.0 (95% CI: 0.73–5.6)). In children younger than 12 years, there was no significant difference in mean ($\pm$ SD) WBC between those who received US-first (15.0 ± 4.9) vs. those who received CT-first (15.4 ± 5.4 , $p = 0.52$). Patients in the US-first group had a significantly shorter triage-to-incision time. After stratification by age, however, this association was significant only in the children less than 12 years old (Table 2).

US-first subgroup analysis: US-only vs. US followed by CT

Those in the US-followed-by-CT group were more likely to be female, older, and with a lower WBC count (Table 3). There was no significant difference in perforation rate between those patients in the US-only group and those in the US-followed-by-CT group (Table 4). There was no significant effect modification on this association due to gender, age, or WBC count. In addition, there was no significant difference in this association after adjusting for these potential confounders. Patients in the US-followed-by-CT group had a significantly longer triage-to-incision time. Stratification by gender, age, or WBC count also did not significantly affect this association.

Of the 395 patients who had US-first, 256 (64.8%) patients had an US demonstrating non-perforated appendicitis. Of these, 22 (8.6%) went on to have a CT scan despite the US findings. These patients did

not develop perforation significantly more often than the 234 who did not have the supplementary CT (1 of 22 (4.5%) vs. 15 of 234 (6.4%), $p = 0.99$).

Discussion

Abdominal US has become the primary imaging modality for children with suspected appendicitis due to its capacity to avoid radiation exposure from CT scans.^{1,3,4,9} Some clinicians may be concerned, however, that adopting an US-first policy would increase these children's risk of perforation since US, more often than CT, can be equivocal and sometimes prolong their work-up. In this large retrospective review from two institutions, US-first, as compared to CT-first, was not found to be associated with an increased risk of perforation nor did it prolong the overall time to surgical operation. In addition, for patients who underwent both an US and a subsequent CT, as compared to only US, we did not find an increased risk in perforation despite an increase in triage-to-incision time.

Our findings are supported by several recent studies. Bachur et al.⁹ examined a large cohort of children with appendicitis assembled over a four-year period using a database of children's hospitals across the United States. They observed that, while US use appeared to be increasing and CT use decreasing, the proportion of patients experiencing appendiceal perforation did not change substantially. Similarly, after implementation of a staged US-first pathway for pediatric patients

evaluated for appendicitis in a community, non-academic hospital, Chien et al.¹⁰ found a decrease in CT usage but no statistical difference in perforation rate between the 12 months pre- and post-intervention. Additionally, Aspelun et al.¹¹ retrospectively compared a CT pathway with an US-followed-by-MRI pathway in children with suspected appendicitis, each over a two-year period, and similarly found that there was no statistical difference in perforation rate.

One study by Hagendorf et al.¹² offered a different perspective on using US vs. CT to evaluate for suspected appendicitis. Using a large retrospective cohort, they created a decision analysis tree with the following management strategies as exposure variables: discharge, observation, CT, US, and appendectomy. The primary outcomes assessed were: length of stay, hospital charges, cost-effectiveness, and capacity to minimize perforation and avoid negative appendectomy (pathology findings of a normal appendix). The study found that although CT was more expensive, it was more cost-effective for preventing perforation than US and thus achieved a better risk-benefit profile. This study was different from others in that it examined clinical presentation (defined by a scale) to evaluate the benefit of imaging. A limitation to this study is that defining pre-test probability for imaging testing thresholds is difficult to standardize widely among physicians. Our study, conversely, only used WBC count as a means of potentially determining disease severity in the clinical presentation.

Although we did not find that children who had US-first were more likely to perforate, we found that younger children who received a CT-first were more likely to perforate. This likely occurred for several reasons. Performing a CT often takes longer than an US, particularly if the clinician needs to wait for oral contrast to reach the appendix. In addition, young children may require sedation to remain still to complete the CT examination, as well as encouragement to drink the oral contrast beforehand. Thus, these patients wait for a longer time with an infected appendix, which prior studies suggest may increase their likelihood of perforation.⁶⁻⁸ In our study, children younger than 12 years old who underwent CT first commonly had their appendectomy 2 hours later than those who had an US-first.

In our study, older patients were more likely to undergo a CT scan after the initial US, likely due to larger body habitus. This supports findings from prior studies correlating body mass index (BMI) with non-diagnostic US studies.¹³⁻¹⁵ Other factors associated with non-diagnostic US could have been operator experience. Additionally, 8.6% of patients diagnosed with appendicitis on US proceeded to have CT scan.

These patients may have appeared more clinically ill, another pathology was entertained, or perhaps it was performed at the surgeon's preference. It is also possible that there was a change in clinical examination in the interim period prior to planned appendectomy that warranted further imaging to evaluate for perforation.

Other studies have demonstrated additional benefits to an US-first imaging strategy. Hernandez et al.¹⁶ demonstrated that in a sample of children undergoing evaluation for appendicitis, a subset of patients receiving US-first had a negative appendectomy less than 3% of the time. Additionally, Ramarajan et al.¹⁷ retrospectively reviewed children with suspected appendicitis who were managed using an US-first pathway over a six-year period. The overall negative appendectomy rate was considered acceptable (7%) and the missed appendicitis rate was low (<0.5%). Moreover, Bachur et al.⁹ showed a decrease in negative appendectomy rate with its increasing use of US, whereas Chien et al.¹⁰ showed no difference in negative appendectomy or missed appendectomy rates.

Another benefit is that the US-first strategy in our study showed a shorter triage-to-incision time, in large part due to the children younger than 12 years old as mentioned previously. Other studies have shown similar results.^{18,19} For instance, in comparing a CT-only vs. US-first pathway in two separate tertiary care hospitals, Reich et al.¹⁸ found that the US-first pathway showed significant decreases in both median length of ED stay and the time from the ordering of imaging to its completion. Extrapolated calculations show that using US would have saved an average of 88.0 minutes per patient in the ED, while also avoiding CT in 65% of patients.

Limitations

This study carried some limitations that warrant mention. First, patients were not randomized to US or CT, but rather these decisions were based on a complex group of factors including time of day, availability of US technician, and clinician variability in evaluating for appendicitis, among others. This may have introduced bias into our results despite our efforts to adjust for several risk factors using stratification. Second, the data were obtained from two large urban academic hospital centers, and the results may not be applicable to other types of health-care facilities. Third, while this study did not investigate the effect of antibiotics on our patient population, patients receiving antibiotics may be less likely to have appendiceal perforation.^{20,21}

Fourth, given this study's retrospective design, subjective reports such as length of illness prior to presentation and degree of clinical severity were inherently more difficult to determine and would be subject to recall bias. For instance, perhaps the patients receiving CT first were clinically more ill-appearing in some way that we were unable to capture. The mean WBC count in both the US-first and CT-first groups was not significantly different, but this is an imperfect indicator of disease severity.

Fifth, by excluding patients whose appendices were normal on pathology and those who had no imaging, we introduced selection bias. However, these patients represent two ends of the spectrum of patients for whom imaging studies are not useful. The former group would be at low risk for perforation, while the latter may have had a classic clinical presentation for appendicitis for which imaging studies would not add much utility.

Moreover, if the appendix is difficult to diagnose by imaging, presumably this might be because the appendicitis is not as advanced, and therefore, at lower risk for perforation.

Conclusion

Adding to the growing body of literature supporting the US-first pathway, children with suspected appendicitis receiving US as the initial diagnostic imaging modality do not appear to be at an increased risk of appendiceal perforation compared to those receiving CT first. Given the shorter triage-to-incision time and decreased perforation rate in children under the age of 12 years old, we specifically recommend that this subgroup of patients undergo US as the first-line imaging modality in diagnosing appendicitis.

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Ethical approval

The Institutional Review Boards from both the Mount Sinai Medical Center and Jacobi Medical Center approved the study.

Guarantor

Ee Tein Tay MD

Contributors

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