The Effect of Abdominal Pain Duration on the Accuracy of Diagnostic Imaging for Pediatric Appendicitis

Richard G. Bachur, MD, Peter S. Dayan, MD, MSc, Lalit Bajaj, MD, Charles G. Macias, MD, Manoj K. Mittal, MD, Michelle D. Stevenson, MD, Nanette C. Dudley, MD, Kelly Sinclair, MD, Jonathan Bennett, MD, Michael C. Monuteaux, ScD, Anupam B. Kharbanda, MD, MSc, for the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics

From the Division of Emergency Medicine, Children's Hospital Boston, Harvard Medical School, Boston, MA (Bachur, Monuteaux); the Department of Pediatrics, Columbia University College of Physicians and Surgeons, New York, NY (Dayan, Kharbanda); the Department of Pediatrics, Children's Hospital Colorado, University of Colorado School of Medicine, Denver, CO (Bajaj); the Department of Pediatrics, Baylor College of Medicine, Houston, TX (Macias); the Department of Pediatrics, The Children's Hospital of Philadelphia and Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Mittal); the Department of Pediatrics, University of Louisville, Louisville, KY (Stevenson); the Department of Pediatrics, University of Utah School of Medicine, Salt Lake City, UT (Dudley); the Department of Pediatrics, The Children's Mercy Hospital, University of Missouri, Kansas City, MO (Sinclair); the Department of Pediatrics, Alfred I. duPont Hospital for Children, Wilmington, DE (Bennett); and the Department of Pediatrics, University of Minnesota, Minneapolis, MN (Kharbanda).

Study objective: Advanced imaging with computed tomography (CT) or ultrasonography is frequently used to evaluate for appendicitis. The duration of the abdominal pain may be related to the stage of disease and therefore the interpretability of radiologic studies. Here, we investigate the influence of the duration of pain on the diagnostic accuracy of advanced imaging in children being evaluated for acute appendicitis.

Methods: A secondary analysis of a prospective multicenter observational cohort of children aged 3 to 18 years with suspected appendicitis who underwent CT or ultrasonography was studied. Outcome was based on histopathology or telephone follow-up. Treating physicians recorded the duration of pain. Imaging was coded as positive, negative, or equivocal according to an attending radiologist's interpretation.

Results: A total of 1,810 children were analyzed (49% boys, mean age 10.9 years [SD 3.8 years]); 1,216 (68%) were assessed by CT and 832 (46%) by ultrasonography (238 [13%] had both). The sensitivity of ultrasonography increased linearly with increasing pain duration (test for trend: odds ratio=1.39; 95% confidence interval 1.14 to 1.71). There was no association between the sensitivity of CT or specificity of either modality with pain duration. The proportion of equivocal CT readings significantly decreased with increasing pain duration (test for trend: odds ratio=0.76; 95% confidence interval 0.65 to 0.90).

Conclusion: The sensitivity of ultrasonography for appendicitis improves with a longer duration of abdominal pain, whereas CT demonstrated high sensitivity regardless of pain duration. Additionally, CT results (but not ultrasonographic results) were less likely to be equivocal with longer duration of abdominal pain. [Ann Emerg Med. 2012;60:582-590.]

Please see page 583 for the Editor's Capsule Summary of this article.

A **feedback** survey is available with each research article published on the Web at www.annemergmed.com.
A **podcast** for this article is available at www.annemergmed.com.

0196-0644/$-see front matter

http://dx.doi.org/10.1016/j.annemergmed.2012.05.034

SEE EDITORIAL, P. 603.

INTRODUCTION

Background

Computed tomography (CT) and ultrasonography are commonly used in the diagnostic evaluation for appendicitis. Both imaging modalities were originally purported to improve outcomes related to pediatric appendicitis.[1-8] CT and ultrasonography have decreased the incidence of negative appendectomy results; however, there has not been a measureable reduction in appendiceal perforation rate.[9-12]

CT has greater diagnostic accuracy over ultrasonography for diagnosing acute appendicitis.[13] However, because of increasing concern over long-term cancer risk, routine use of CT is being reappraised.[14-17] Recently, a trend of increased reliance on ultrasonography and decreased use of CT for children with appendicitis was observed among large US pediatric hospitals.[18]

To our knowledge, no previous investigations have assessed the performance of CT and ultrasonography according to the duration of abdominal pain. Although not completely predictable, the duration of abdominal pain is associated with the severity of disease, with the risk of appendiceal perforation

Editor's Capsule Summary

What is already known on this topic

The role of computed tomography (CT) and ultrasonography in children with suspected appendicitis is controversial.

What question this study addressed

In children with suspected appendicitis, does the duration of previous abdominal pain affect the diagnostic accuracy of ultrasonography or CT?

What this study adds to our knowledge

In this multicenter analysis of 1,810 children, there was an enhancement of ultrasonographic sensitivity (but not specificity) with a longer duration of symptoms but no such time-related variance with CT.

How this is relevant to clinical practice

In children with suspected appendicitis, CT is highly sensitive regardless of symptom duration, whereas ultrasonography is less sensitive with less than 48 hours of pain.

generally occurring after 24 to 48 hours' duration of symptoms.[19,20]

Importance

Theoretically, advanced imaging performed at the earliest stages of disease, when the disease might be less "macroscopic," could lead to false-negative results. The relatively easy access to emergency care for most US children may lead to children presenting early in the course of disease. Under these conditions, we postulate that the performance of diagnostic imaging may be diminished. If the accuracy of diagnostic imaging varies by the duration of symptoms, clinicians should determine the optimal timing of advanced imaging for children with equivocal clinical findings for appendicitis and no signs of peritonitis or ill appearance.

Goals of This Investigation

We investigated the test performance characteristics of CT and ultrasonography according to the duration of abdominal pain in children being assessed for appendicitis.

MATERIALS AND METHODS

Study Design and Setting

We conducted a secondary analysis of a prospective multicenter observational study whose aim was to validate and refine a clinical prediction rule for appendicitis.[21] The parent study enrolled children with suspected appendicitis at 9 pediatric emergency departments (EDs) that were members of the Pediatric Emergency Medicine Clinical Research Committee of the American Academy of Pediatrics. Subjects were enrolled from March 2009 through April 2010. The study was approved by each site's institutional review board. Six boards granted a waiver of written consent or assent, and we obtained verbal consent. At the 3 remaining sites, we obtained written consent from the guardians and assent from children aged 7 years and older.

Selection of Participants

ED patients who were aged 3 to 18 years and presented with acute abdominal pain (<96 hours' duration of symptoms) and possible appendicitis were enrolled. We defined "possible appendicitis" for patients whose treating physician obtained blood tests, radiologic studies (CT or ultrasonography), or a surgical consultation for the purpose of diagnosing appendicitis. Radiologic studies or surgical consultations were obtained at the discretion of the treating physician. Each site followed internal protocols for its imaging standards. We excluded patients with any of the following conditions: pregnancy, previous abdominal surgery, chronic gastrointestinal condition, or severe developmental delay (that might interfere with an accurate clinical assessment). We also excluded patients who had radiologic studies (CT or ultrasonography) performed before ED arrival. For this secondary analysis, we included only those patients who had abdominal pain for less than 72 hours and had an abdominal CT or ultrasonography.

Data Collection and Processing

Site primary investigators received a manual of operations and were instructed on proper completion of case report forms. They subsequently conducted instructional sessions with clinicians. A pediatric emergency physician (attending or fellow) completed a standardized case report form that included the duration of abdominal pain coded categorically in hours as less than 12, 13 to 24, 25 to 36, 37 to 48, or 49 to 72. A resident physician, nurse practitioner, or physician assistant was allowed to complete the ED assessment form, with attending physician oversight. Each clinician completed case report forms before knowledge of CT or ultrasonographic results (and needed to attest to that on the form). For 31% of children enrolled in the parent study, a second physician completed a form; the κ statistic for duration of abdominal pain was 0.73 (95% confidence interval [CI] 0.67 to 0.78).[22] The time of the examination and completion of survey was recorded, and a decision was made to exclude all cases in which the time between the questionnaire completion and imaging was greater than 8 hours to avoid misclassification of cases by the duration of symptoms.

Research assistants entered data for electronic transfer to a central data management warehouse. Quality assurance practices at the data warehouse included checks for missing and duplicate data. The timing and results of the imaging studies were collected from the medical record by research assistants using

abstraction rules. The research assistants were not blind to the outcomes.

For coding of the radiology reports, the following abstraction rules were used:

- CT:
  - Normal: appendix visualized and no evidence of appendicitis; or no visualization of appendix plus no secondary signs of appendicitis (periappendiceal fat stranding, presence of an appendicolith, free fluid collection or abscess in the right lower quadrant/pelvis, focal thickening of the cecal wall [>2 mm]).
  - Positive: findings "consistent with" or "positive for" appendicitis; notations such as "likely" or "probable" appendicitis were also considered positive. Indications of perforated appendicitis were coded as appendicitis.
  - Equivocal: findings "unclear," "unsure," "not conclusive," or "equivocal" for appendicitis.
- Ultrasonography:
  - Normal: appendix was visualized and no evidence of appendicitis, or appendix was not visualized but no secondary signs of appendicitis (increased echogenicity of the mesenteric fat, fluid collection in the right lower quadrant, local dilatation of small bowel loop).
  - Positive: report explicitly stated "appendicitis" or "consistent with appendicitis" or the radiologist used the words "likely" or "possible" appendicitis. If no formal impression, the report was coded positive for appendicitis when the appendix was visualized and text indicated a dilated, noncompressible tubular structure or appendix dilated with a wall diameter greater than 6 mm.
  - Equivocal: report indicated that the appendix was not visualized but secondary signs of appendicitis were present or final impression stated "unclear," "unsure," "uncertain," or "not conclusive," or the findings were "equivocal" for appendicitis.

Outcome Measures

The primary outcome was the presence or absence of appendicitis. For those patients who underwent an operation, we determined the presence of appendicitis from the attending pathologist's written report. Presence or absence of perforation was determined from the attending surgeon's operative report.

For patients discharged without an operation, we conducted telephone follow-up between 1 and 2 weeks postvisit to determine the resolution of signs and symptoms, visits to other sites of care, and need for any surgery. If we were unable to contact the guardian, research coordinators reviewed the medical record for the 90 days after the ED visit to determine whether the patient underwent an operation at the index facility.

Primary Data Analysis

Descriptive analyses were performed to characterize the study population. We calculated standard test performance characteristics of CT and ultrasonography within subgroups according to the duration of pain. We conducted a subanalysis for cases with appendiceal perforation (as determined by the surgeon's operative note). CIs were calculated for proportions with Stata (version 12.0; StataCorp, College Station, TX). Tests of trend were performed across the ordinal scale for duration of abdominal pain, using logistic regression models. We analyzed patients with equivocal imaging results in 2 ways: (1) equivocal imaging cases excluded; or (2) equivocal imaging treated as a positive result to provide the maximal estimates of sensitivity, assuming that children with equivocal imaging results would be managed operatively, have further imaging (especially if ultrasonography was the initial study), or be hospitalized for observation. To account for the potential correlation in imaging practices and results among patients within a given hospital, we used robust standard error estimates clustered on hospital, which allow intrahospital correlation, relaxing the assumption that observations from the same hospital are independent.

RESULTS

Characteristics of Study Subjects

We enrolled 2,349 children in the parent study. Of these, 80% (n=1,884) underwent an imaging study (CT only n=1,016; ultrasonography only n=586; both CT and ultrasonography n=282). Among this subsample, the duration of time from the physical examination to the imaging studies varied (CT median 2.8 hours, interquartile range 1.7, 4.5; ultrasonography median 1.7 hours, interquartile range 0.9, 2.8; see Figure E1 in Appendix E1, available online at http://www.annemergmed.com). A small proportion (5%; n=89) of patients waited an extended period for an imaging study (>8 hours) and were excluded. Thus, the final subsample for the current analysis consisted of the patients who reported an abdominal pain duration of less than 72 hours, underwent CT or ultrasonography, and waited less than 8 hours from the time of their clinical examination to their imaging study (n=1,810; n=1,216 and 832 for CT and ultrasonography, respectively; Figure 1).

The demographic and clinical characteristics of our study population by imaging modality are displayed in Table 1. Thirty-eight percent (n=680) had appendicitis, including 26% (174/680) with perforated appendicitis. The most frequent abdominal pain duration reported across all 3 subgroups was the 12- to 23-hour category, followed by less than 12 hours and 24 to 35 hours.

Final outcomes for the study patients included operative care in 40.2% of patients (n=728; 670 with appendicitis and 58 with negative appendectomy). Of those who did not undergo surgery (n=1,082), follow-up telephone calls were conducted for 957 patients (88.6%); the remainder who could not be reached by telephone were subjected to chart review (n=123; 11.4%; data on the method of follow-up was missing for 2 patients). The choice of imaging modality, as well as final patient outcomes, is displayed in Figure 2.

First, we assessed imaging performance as a function of abdominal pain duration, with equivocal-imaging cases

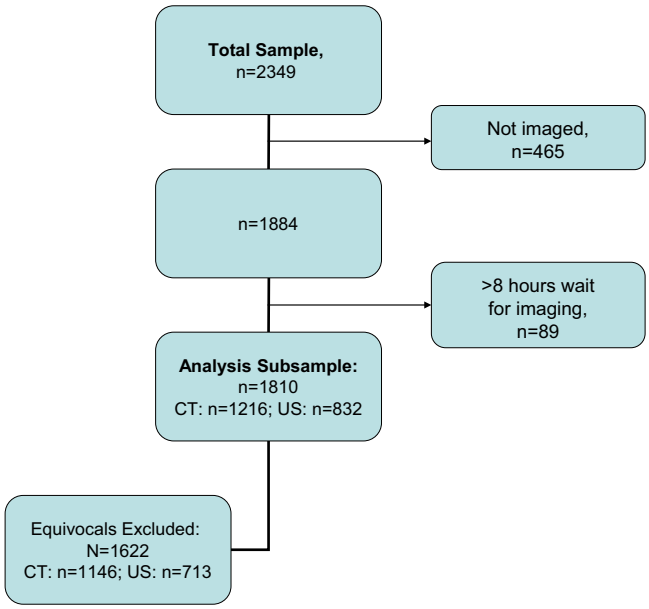


Figure 1. Pediatric patients included in the analysis subsample. US, ultrasound.

excluded (Table 2). The duration of abdominal pain was not associated with the sensitivity or specificity of CT to diagnose appendicitis. However, we detected an increasing sensitivity and negative predictive value for ultrasonography with longer duration of abdominal pain (Table 2, Figure 3). No association was found for the specificity of ultrasonography and pain duration. A subanalysis by sex yielded similar results. Next, we repeated the analysis but included cases that had equivocal imaging results (treated as a positive result); the findings were similar to those of the first analysis (Table 2). For the subsample of patients who had both a CT and ultrasonography, the results were also similar (Table 3). When we repeated these analyses while including patients who waited greater than 8 hours for an imaging study, the results did not change.

The equivocal CT rate decreased with increasing pain duration (test for trend: odds ratio=0.76, 95% CI 0.65 to 0.90; Figure 4). There was no association between pain duration and the proportion of equivocal ultrasonography.

We investigated the association between imaging, abdominal pain duration, and the presence of perforated appendicitis. Overall, 174 (9.7%) of the study sample received a diagnosis of perforated appendicitis. The risk for perforated appendicitis increased significantly with increasing abdominal pain duration, with rates of 3.0%, 7.6%, 13.0%, 15.2%, and 23.3% from the shortest to the longest pain duration categories (test for trend: odds ratio=1.65; 95% CI 1.50 to 1.82). Among cases with perforation, there was no association between the duration of abdominal pain and the sensitivity of CT (n=133; $P>.05$; odds ratio=1.03; 95% CI 0.61 to 1.75). However, there was a statistically significant association between the duration of abdominal pain and the sensitivity of ultrasonography (n=61; $P<.001$; test for trend: odds ratio=2.08; 95% CI 1.44 to 3.01). For patients with perforated appendicitis, the sensitivities of ultrasonography (by category of duration; <12, 13 to 24, 25 to 36, 37 to 48, and 49 to 71 hours) for appendicitis were 83%, 80%, 85%, 100%, and 100%, respectively.

LIMITATIONS

The major challenge in studying diagnostic imaging for appendicitis is the varying thresholds of emergency physicians or surgeons to rely on imaging for the evaluation of abdominal pain; this study did not try to define clinical thresholds for imaging or account for other diagnoses being considered. Because of this, the test characteristics reported reflect a population for whom imaging was believed to be indicated. Additionally, for the final outcome of appendicitis, we were able to reach only 88.6% of patients without operative care; this raises the possibility of misclassifying patients with false-negative imaging results if they ultimately received a diagnosis of appendicitis at another institution. The analysis is also limited by the use of large time intervals rather than time as a continuous variable; time intervals are practical for most patients who cannot recall the exact onset of their pain but tend to lessen the power of analysis for a study focused on elapsed time. This analysis is limited further by a time increment between the completion of the case report form and the radiologic study. We tried to minimize the effect of long delays by removing patients who had intervals greater than 8 hours between completion of the case report form and CT or ultrasonography; the analysis was repeated without excluding these patients and appears in Appendix E1 as supplementary Tables E1 and E2 (available online at http://www.annemergmed.com). Additionally, not all the centers had similar experience with ultrasonography; operator skill and experience are known to affect test performance for ultrasonography. Each site followed its own standard protocols for image acquisition, which were not studied but likely varied between sites.

DISCUSSION

Appendicitis is the most common pediatric surgical emergency, accounts for 5% of urgent pediatric outpatient visits for abdominal pain,[23] and carries a lifetime risk of 8.6% for boys and 6.7% for girls.[24] Because appendicitis is so common, clinicians are familiar with its typical presentation, but many patients present with atypical findings.[25] Given these circumstances of a common disease but often a difficult diagnosis, previous research has focused on the development of clinical decision rules and scoring systems to guide the management of patients with suspected appendicitis. Despite considerable efforts to develop and validate clinical scoring systems and decision rules, their performance is inadequate for clinical management.[26-29] Thus, cross-sectional imaging with CT and ultrasonography has been studied and commonly used to improve the diagnostic evaluation of children with possible appendicitis.[2,3,5,30-35] Although not the intent of the developers of the clinical scoring systems, recent adaptations recommend

Table 1. Demographic and clinical characteristics of pediatric patients with suspected appendicitis evaluated with advanced imaging in the ED.*

Demographic and Clinical Characteristics	CT or Ultrasonography, n=1,810	CT, n=1,216	Ultrasonography, n=832
Age, median (IQR), y	10.8 (8.0,13.9)	10.9 (8.1,14.0)	11.1 (8.1,13.9)
Sex, male	879 (49)	597 (49)	379 (46)
Focal pain, right lower quadrant	1417 (78)	950 (78)	654 (79)
Final diagnosis of appendicitis	680 (38)	454 (37)	297 (36)
Perforated appendicitis†	174 (10)	133 (11)	61 (7)
Equivocal imaging findings	185 (10)	70 (6)	119 (14)
Duration of abdominal pain, h			
<12	528 (29)	344 (28)	252 (30)
12–23	592 (33)	401 (33)	272 (33)
24–35	330 (18)	220 (18)	153 (18)
36–47	171 (9)	122 (10)	72 (9)
48–71	189 (10)	129 (11)	83 (10)

IQR, Interquartile range.
*Data are presented as No. (%) unless indicated otherwise.
†Perforation defined by the surgeon's operative note.

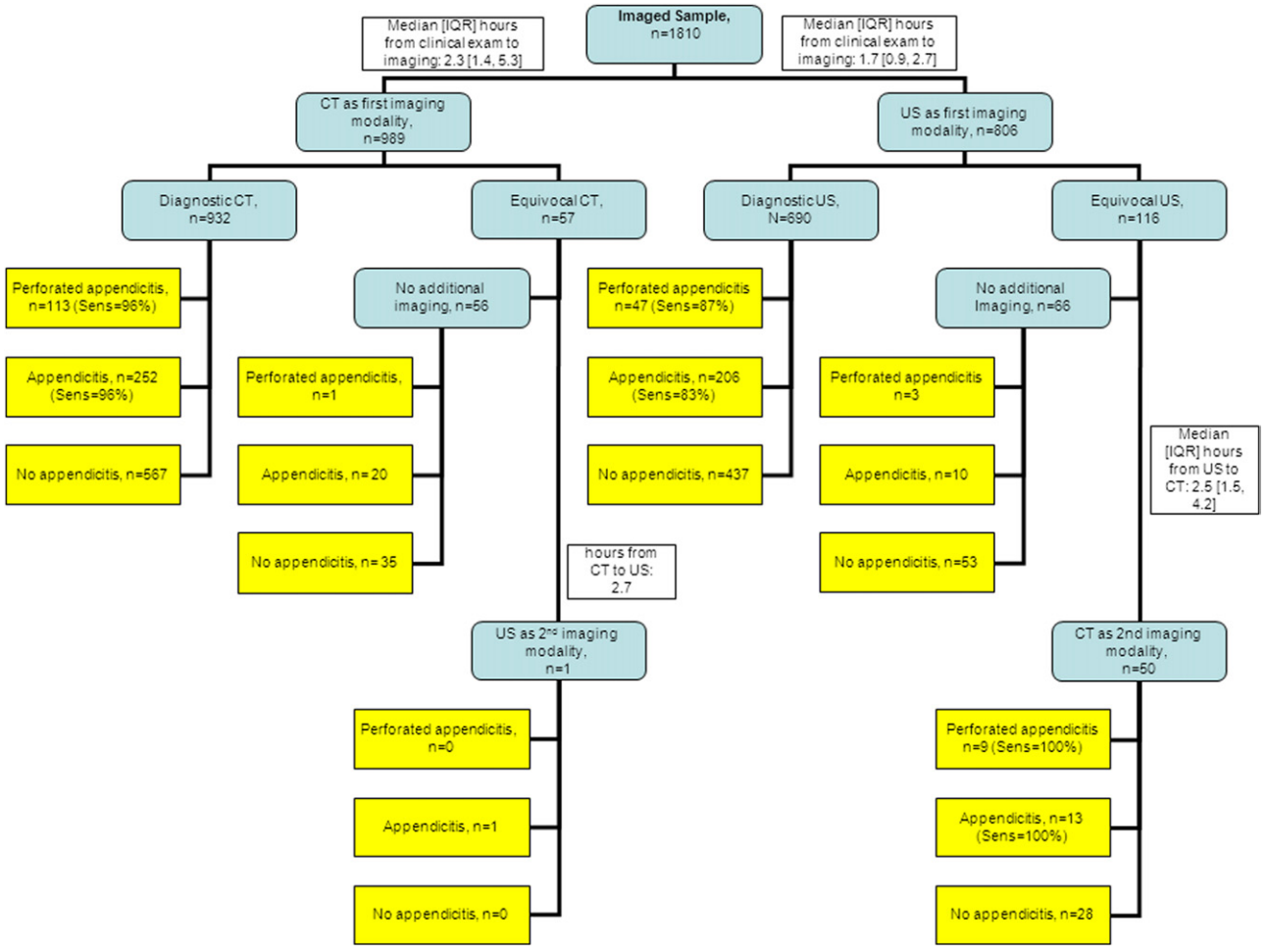


Figure 2. Flow diagram to indicate the number of patients who had each imaging modality, the results of the imaging, and the final outcomes (rectangles). Fifteen patients who had both imaging modalities are not shown in Figure 2 because there is conflicting data regarding the order of the 2 studies.

Table 2. Sensitivity and specificity of CT and ultrasonography for the diagnosis of appendicitis among pediatric patients in the ED, with and without the inclusion of equivocal cases.

Test Characteristics	Duration of Abdominal Pain, Hours					Test for Trend: Odds Ratio (95% CI)
Equivocal cases removed						
CT (n=1,146)	<12	12–23	24–35	36–47	48–71	
Sensitivity	0.98	0.94	0.98	0.96	0.96	0.98 (0.74–1.31)
Specificity	0.97	0.97	0.96	0.97	0.96	0.91 (0.67–1.25)
PPV	0.94	0.95	0.94	0.96	0.94	1.02 (0.76–1.38)
NPV	0.99	0.96	0.98	0.97	0.97	0.88 (0.64–1.22)
Ultrasonography (n=713)						
Sensitivity	0.79	0.79	0.85	0.89	0.96	1.40 (1.14–1.73)
Specificity	0.96	0.97	0.99	0.95	0.98	1.15 (0.80–1.66)
PPV	0.90	0.93	0.98	0.89	0.96	1.26 (0.92–1.72)
NPV	0.90	0.89	0.89	0.95	0.98	1.26 (1.02–1.54)
Equivocal cases included as positive						
CT (n=1,216)						
Sensitivity	0.98	0.94	0.98	0.96	0.96	0.96 (0.72–1.28)
Specificity	0.92	0.91	0.90	0.90	0.96	1.07 (0.89–1.27)
PPV	0.85	0.86	0.87	0.87	0.94	1.19 (0.96–1.46)
NPV	0.99	0.96	0.98	0.97	0.97	0.88 (0.64–1.22)
Ultrasonography (n=832)						
Sensitivity	0.81	0.81	0.87	0.92	0.96	1.39 (1.14–1.71)
Specificity	0.81	0.80	0.86	0.85	0.84	1.10 (0.96–1.25)
PPV	0.67	0.68	0.83	0.77	0.74	1.19 (0.94–1.50)
NPV	0.90	0.89	0.89	0.95	0.98	1.26 (1.02–1.54)

PPV, Positive predictive value; *NPV*, negative predictive value.
Equivocal results treated as a positive test result (see text). Statistical analyses adjusted for clustering on hospital.

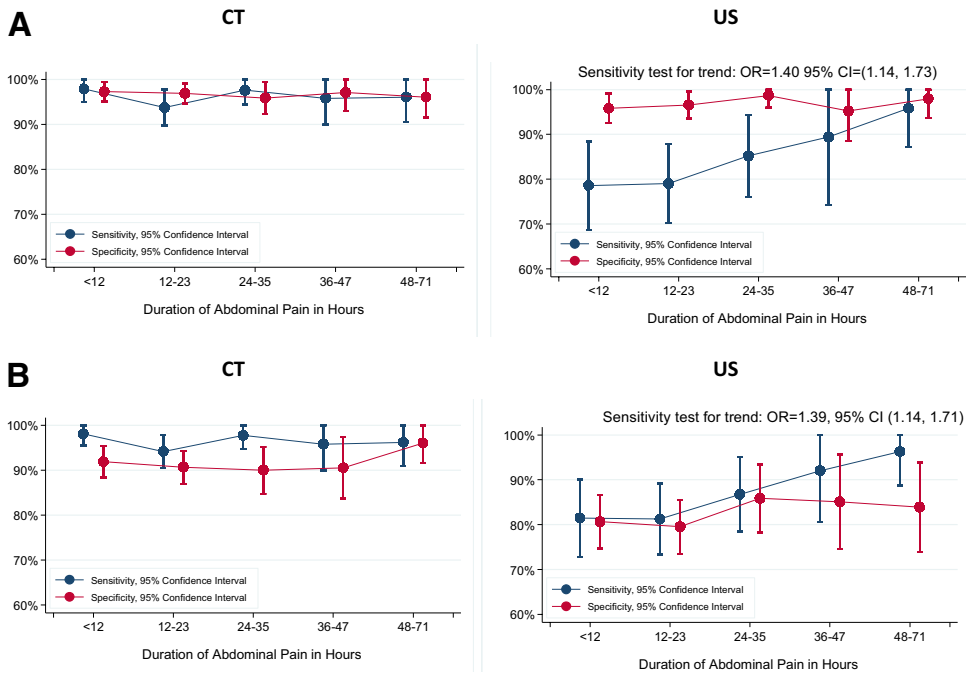


Figure 3. *A*, Sensitivity and specificity of CT and ultrasonography to detect appendicitis, excluding equivocal cases. *B*, Sensitivity and specificity of CT and ultrasonography to detect appendicitis, including equivocal cases.

adjunctive imaging for indeterminate scores,[26-28,36] and one decision rule was specifically created to limit CT use in low-risk patients.[37]

Cross-sectional imaging has improved the negative appendectomy result rate, yet advanced imaging has not been reliably shown to reduce the rate of perforation.[10,12,32,38-46] CT has much higher accuracy than ultrasonography, as reported in a 2006 meta-analysis by Doria et al,[13] with pooled estimates of sensitivity (CT 94%, 95% CI 92% to 97%; ultrasonography 88%, 95% CI 86% to 90%) and specificity (CT 95%, 95% CI

Table 3. Sensitivity and specificity of CT and ultrasonography for the diagnosis of appendicitis among pediatric patients in the ED who were imaged with both modalities (n=238).*

Test Characteristics	Duration of Abdominal Pain, Hours					Test for Trend: Odds Ratio (95% CI)
Equivocal cases included as positive						
CT	<12	12–23	24–35	36–47	48–71	
Sensitivity	0.95	0.96	1.00	1.00	1.00	2.62 (0.82–8.34)
Specificity	0.92	0.91	0.87	0.93	1.00	1.17 (0.78–1.76)
PPV	0.82	0.82	0.76	0.89	1.00	1.26 (0.70–2.27)
NPV	0.98	0.98	1.00	1.00	1.00	2.37 (0.68–8.26)
Ultrasonography						
Sensitivity	0.47	0.46	0.54	0.75	0.86	1.52 (1.22–1.89)
Specificity	0.82	0.79	0.83	0.93	0.69	0.96 (0.66–1.40)
PPV	0.50	0.48	0.58	0.86	0.54	1.18 (0.68–2.04)
NPV	0.80	0.78	0.81	0.88	0.92	1.20 (0.94–1.53)

*Statistical analyses adjusted for clustering on hospital.

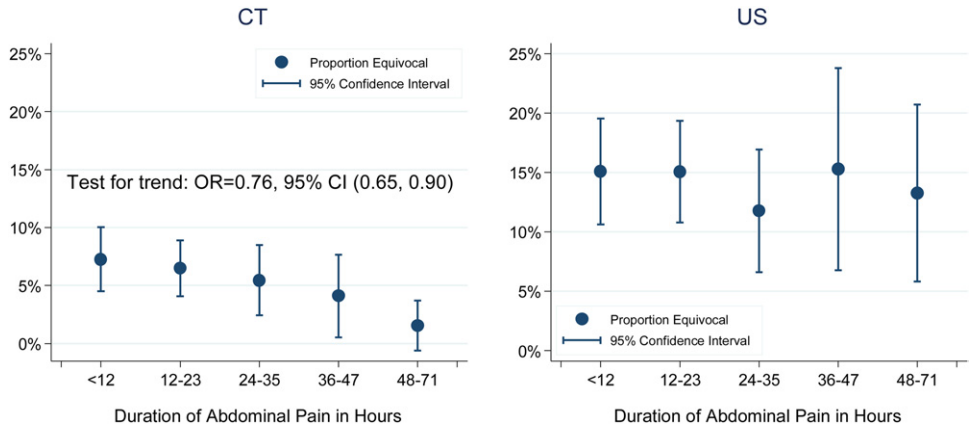


Figure 4. The proportion of pediatric patients with equivocal CT and ultrasonographic findings across subgroups of patients stratified by abdominal pain duration.

94% to 97%; ultrasonography 94%, 95% CI 92% to 95%). Recently, there have been increasing concerns about exposure to ionizing radiation from medical diagnostics, especially for children. Consequently, recent efforts have tried to minimize the use of CT in favor of increased reliance on ultrasonography.[13,17,47-54]

For patients with a "textbook" presentation of acute appendicitis, the decision to proceed with operative care without advanced imaging can be straightforward. Additionally, for patients with prolonged symptoms and findings concerning for appendiceal perforation with abscess, imaging is often used to guide management. However, when the child presents acutely with equivocal clinical findings but a concern for appendicitis, diagnostic imaging is often used. Among US children with appendicitis and presenting to a major US pediatric hospital in 2009, the CT and ultrasonographic use was 29% and 24%, respectively.[18] The major outcomes for ED care of children with suspected appendicitis relate to timely and accurate diagnosis: minimize missed appendicitis, avoid misdiagnosis leading to negative appendectomy results, and proper identification of appendicitis before perforation. For each of these outcomes, diagnostic imaging serves a key role when there is clinical uncertainty. Logically, more advanced disease should be more visible by CT or ultrasonography, yet the test characteristics of CT and ultrasonography have not been previously studied according to the duration of pain.

In this study, we evaluated the diagnostic performance of ultrasonography and CT according to the duration of abdominal pain. Most important, we showed that ultrasonographic sensitivity increases from 81% in the first 12 hours of pain to 96% after 48 hours of pain. Similarly, the negative predictive value increased with the duration of pain, with a marked improvement after 36 hours. Overall, the sensitivity of ultrasonography in the subgroup of patients with perforated appendicitis was even higher than for nonperforated appendicitis and increased with the duration of pain. The sensitivity of CT is not similarly affected by the duration of pain, but the frequency of equivocal readings is highest in the first 12 hours of pain and decreases over time. The specificity of ultrasonography and CT was not affected by duration of pain.

With these findings, clinicians should not rely on ultrasonography early in the course of illness. When an ultrasonographic result is obtained and negative, clinicians

might choose a period of observation, potentially followed by repeated ultrasonography (or CT) if clinical suspicion remains. The improved performance of ultrasonography over time indicates that this strategy of repeated ultrasonography should be considered as an option rather than performance of a CT subsequent to an inconclusive ultrasonographic result. For patients with mild focal right lower quadrant pain for less than 24 hours but an otherwise well appearance, another option would be to forgo imaging and monitor the patient with repeated examinations to avoid multiple imaging studies or overreliance on CT. In practice, other diagnoses besides appendicitis (eg, ovarian torsion) might be under consideration and driving the urgency of diagnostic imaging. Likewise, when complicated appendicitis (perforation or abscess) is suspected, there should be no purposeful delay in imaging even if the duration of pain is relatively short.

The performance of CT and ultrasonography for accurately identifying appendicitis is influenced by the duration of abdominal pain. Specifically, the sensitivity and negative predictive value of ultrasonography increase with the duration of pain, and CT is less likely to be indeterminate with a longer duration of pain. Clinicians should incorporate this time-dependent accuracy of imaging when deciding to obtain imaging for suspected appendicitis.

Supervising editors: David M. Jaffe, MD; Steven M. Green, MD

Author contributions: ABK was the principal investigator for the original multicenter study proposal and was responsible for oversight over the parent study protocol, data collection, data security, and multicenter coordination. ABK approved the secondary analysis. PSD, LB, CGM, MKM, MDS, NCD, KS, JB, MCM, and AKB provided critical review of the article. PSD was the senior investigator for the original multicenter study. RGB and MCM were responsible for drafting the article. RGB conceived of this secondary study and was responsible for primary data analysis. LB, CGM, MKM, MDS, NCD, KS, and JB contributed as site principal investigators under the parent protocol. MCM provided statistical expertise. RGB takes responsibility for the paper as a whole.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Publication dates: Received for publication January 31, 2012. Revisions received April 6, 2012, and May 15, 2012. Accepted for publication May 25, 2012. Available online July 27, 2012.

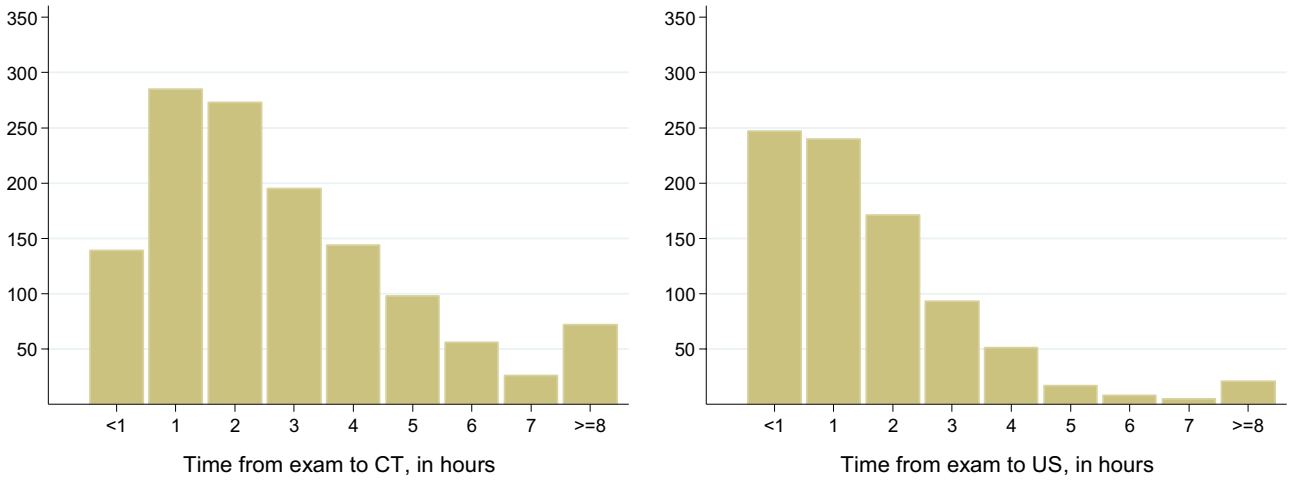
Presented at the Pediatric Academic Societies meeting, April and May 2012, Boston, MA.

Address for correspondence: Richard G. Bachur, MD, E-mail richard.bachur@childrens.harvard.edu.

REFERENCES

1. Pena BM, Taylor GA, Fishman SJ, et al. Costs and effectiveness of ultrasonography and limited computed tomography for diagnosing appendicitis in children. *Pediatrics*. 2000;106:672-676.
2. Garcia Pena BM, Mandl KD, Kraus SJ, et al. Ultrasonography and limited computed tomography in the diagnosis and management of appendicitis in children. *JAMA*. 1999;282:1041-1046.
3. Roosevelt GE, Reynolds SL. Does the use of ultrasonography improve the outcome of children with appendicitis? *Acad Emerg Med*. 1998;5:1071-1075.
4. Ooms HW, Koumans RK, Ho Kang You PJ, et al. Ultrasonography in the diagnosis of acute appendicitis. *Br J Surg*. 1991;78:315-318.
5. Sivit CJ. Imaging children with acute right lower quadrant pain. *Pediatr Clin North Am*. 1997;44:575-589.
6. Hahn HB, Hoepner FU, Kalle T, et al. Sonography of acute appendicitis in children: 7 years experience. *Pediatr Radiol*. 1998; 28:147-151.
7. Frush D, Beam C, Effmann EL. Acute appendicitis in children: an evaluation with ultrasound. *Invest Radiol*. 1992;27:489-490.
8. Rao PM, Rhea JT, Novelline RA, et al. Effect of computed tomography of the appendix on treatment of patients and use of hospital resources. *N Engl J Med*. 1998;338:141-146.
9. Raja AS, Wright C, Sodickson AD, et al. Negative appendectomy rate in the era of CT: an 18-year perspective. *Radiology*. 2010; 256:460-465.
10. Cuschieri J, Florence M, Flum DR, et al. Negative appendectomy and imaging accuracy in the Washington State Surgical Care and Outcomes Assessment Program. *Ann Surg*. 2008;248:557-563.
11. Kaiser S, Jorulf H, Soderman E, et al. Impact of radiologic imaging on the surgical decision-making process in suspected appendicitis in children. *Acad Radiol*. 2004;11:971-979.
12. Pena BM, Taylor GA, Fishman SJ, et al. Effect of an imaging protocol on clinical outcomes among pediatric patients with appendicitis. *Pediatrics*. 2002;110:1088-1093.
13. Doria AS, Moineddin R, Kellenberger CJ, et al. US or CT for diagnosis of appendicitis in children and adults? a meta-analysis. *Radiology*. 2006;241:83-94.
14. Brenner D, Elliston C, Hall E, et al. Estimated risks of radiation-induced fatal cancer from pediatric CT. *AJR Am J Roentgenol*. 2001;176:289-296.
15. Mettler FA Jr, Thomadsen BR, Bhargavan M, et al. Medical radiation exposure in the US in 2006: preliminary results. *Health Phys*. 2008;95:502-507.
16. Macias CG, Sahouria JJ. The appropriate use of CT: quality improvement and clinical decision-making in pediatric emergency medicine. *Pediatr Radiol*. 2011;41(suppl 2):498-504.
17. Schuh S, Man C, Cheng A, et al. Predictors of non-diagnostic ultrasound scanning in children with suspected appendicitis. *J Pediatr*. 2011;158:123-129.
18. Bachur RG, Hennelly K, Callahan MJ, et al. Advanced radiologic imaging for pediatric appendicitis, 2005-2009: trends and outcomes. *J Pediatr*. 2012;160:1034-1038.
19. Narsule CK, Kahle EJ, Kim DS, et al. Effect of delay in presentation on rate of perforation in children with appendicitis. *Am J Emerg Med*. 2011;29:890-893.
20. Rothrock SG, Pagane J. Acute appendicitis in children: emergency department diagnosis and management. *Ann Emerg Med*. 2000; 36:39-51.
21. Kharbanda AB, Dudley N, Bajaj L, et al. Validation of a prediction rule to identify children at low risk of appendicitis. Paper

presented at: Pediatric Academic Societies and Asian Society of Pediatric Research Joint Meeting; April 30-May 3, 2011; Denver, CO.
22. Kharbanda AB, Stevenson MD, Macias CG, et al. Interrater reliability of clinical findings in children with possible appendicitis. *Pediatrics*. 2012;129:695-700.
23. Scholer SJ, Pituch K, Orr DP, et al. Clinical outcomes of children with acute abdominal pain. *Pediatrics*. 1996;98(4 pt 1):680-685.
24. Addiss DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol*. 1990;132:910-925.
25. Becker T, Kharbanda A, Bachur R. Atypical clinical features of pediatric appendicitis. *Acad Emerg Med*. 2007;14:124-129.
26. Mandeville K, Pottker T, Bulloch B, et al. Using appendicitis scores in the pediatric ED. *Am J Emerg Med*. 2011;29:972-977.
27. Bhatt M, Joseph L, Ducharme FM, et al. Prospective validation of the pediatric appendicitis score in a Canadian pediatric emergency department. *Acad Emerg Med*. 2009;16:591-596.
28. Goldman RD, Carter S, Stephens D, et al. Prospective validation of the pediatric appendicitis score. *J Pediatr*. 2008;153:278-282.
29. Schneider C, Kharbanda A, Bachur R. Evaluating appendicitis scoring systems using a prospective pediatric cohort. *Ann Emerg Med*. 2007;49:778-784, 784.e1.
30. Sivit CJ, Applegate KE, Berlin SC, et al. Evaluation of suspected appendicitis in children and young adults: helical CT. *Radiology*. 2000;216:430-433.
31. Garcia-Aguayo FJ, Gil P. Sonography in acute appendicitis: diagnostic utility and influence upon management and outcome. *Eur Radiol*. 2000;10:1886-1893.
32. Rao PM, Rhea JT, Rattner DW, et al. Introduction of appendiceal CT: impact on negative appendectomy and appendiceal perforation rates. *Ann Surg*. 1999;229:344-349.
33. Rao PM, Boland GW. Imaging of acute right lower abdominal quadrant pain. *Clin Radiol*. 1998;53:639-649.
34. Rao PM, Rhea JT, Novelline RA, et al. Helical CT technique for the diagnosis of appendicitis: prospective evaluation of a focused appendix CT examination. *Radiology*. 1997;202:139-144.
35. Bundy DG, Byerley JS, Liles EA, et al. Does this child have appendicitis? *JAMA*. 2007;298:438-451.
36. Rezak A, Abbas HM, Ajemian MS, et al. Decreased use of computed tomography with a modified clinical scoring system in diagnosis of pediatric acute appendicitis. *Arch Surg*. 2011;146:64-67.
37. Kharbanda AB, Taylor GA, Fishman SJ, et al. A clinical decision rule to identify children at low risk for appendicitis. *Pediatrics*. 2005;116:709-716.
38. Coursey CA, Nelson RC, Patel MB, et al. Making the diagnosis of acute appendicitis: do more preoperative CT scans mean fewer negative appendectomies? a 10-year study. *Radiology*. 2010;254:460-468.
39. Holscher HC, Heij HA. Imaging of acute appendicitis in children: EU versus US . . . or US versus CT? a European perspective. *Pediatr Radiol*. 2009;39:497-499.
40. Kaiser S, Frenckner B, Jorulf HK. Suspected appendicitis in children: US and CT—a prospective randomized study. *Radiology*. 2002;223:633-638.
41. Kaiser S, Mesas-Burgos C, Soderman E, et al. Appendicitis in children—impact of US and CT on the negative appendectomy rate. *Eur J Pediatr Surg*. 2004;14:260-264.
42. Karakas SP, Guelfguat M, Leonidas JC, et al. Acute appendicitis in children: comparison of clinical diagnosis with ultrasound and CT imaging. *Pediatr Radiol*. 2000;30:94-98.
43. Oyetunji TA, Ong'uti SK, Bolorunduro OB, et al. Pediatric negative appendectomy rate: trend, predictors, and differentials. *J Surg Res*. 2011.
44. van Breda Vriesman AC, Kole BJ, Puylaert JB. Effect of ultrasonography and optional computed tomography on the outcome of appendectomy. *Eur Radiol*. 2003;13:2278-2282.
45. Rhea JT, Halpern EF, Ptak T, et al. The status of appendiceal CT in an urban medical center 5 years after its introduction: experience with 753 patients. *AJR Am J Roentgenol*. 2005;184:1802-1808.
46. Chooi WK, Brown JA, Zetler P, et al. Imaging of acute appendicitis and its impact on negative appendectomy and perforation rates: the St. Paul's experience. *Can Assoc Radiol J*. 2007;58:220-224.
47. van Randen A, Bipat S, Zwinderman AH, et al. Acute appendicitis: meta-analysis of diagnostic performance of CT and graded compression US related to prevalence of disease. *Radiology*. 2008;249:97-106.
48. Tsze DS, Asnis LM, Merchant RC, et al. Increasing computed tomography use for patients with appendicitis and discrepancies in pain management between adults and children: an analysis of the NHAMCS. *Ann Emerg Med*. 2011.
49. Newman B. Ultrasound body applications in children. *Pediatr Radiol*. 2011;41(suppl 2):555-561.
50. Krishnamoorthi R, Ramarajan N, Wang NE, et al. Effectiveness of a staged US and CT protocol for the diagnosis of pediatric appendicitis: reducing radiation exposure in the age of ALARA. *Radiology*. 2011.
51. Goldin AB, Khanna P, Thapa M, et al. Revised ultrasound criteria for appendicitis in children improve diagnostic accuracy. *Pediatr Radiol*. 2011;41:993-999.
52. Hricak H, Brenner DJ, Adelstein SJ, et al. Managing radiation use in medical imaging: a multifaceted challenge. *Radiology*. 2010.
53. Ramarajan N, Krishnamoorthi R, Barth R, et al. An interdisciplinary initiative to reduce radiation exposure: evaluation of appendicitis in a pediatric emergency department with clinical assessment supported by a staged ultrasound and computed tomography pathway. *Acad Emerg Med*. 2009;16:1258-1265.
54. Howell JM, Eddy OL, Lukens TW, et al. Clinical policy: critical issues in the evaluation and management of emergency department patients with suspected appendicitis. *Ann Emerg Med*. 2010;55:71-116.



Supplementary Figure 1 Time from clinical exam to imaging study among pediatric patients assessed in the ED for appendicitis.

Appendix E1. Pain and Diagnostic Abdominal Imaging

Appendix. Detailed methodology and results of logistic regression models[2]

Analytical Approach	Test Characteristic Assessed	Subsample Analyzed	Dependent Variable	Trend Estimate for Duration of Abdominal Pain[1]	Model Goodness of Fit (χ^2 (df), p value)
Equivocal cases removed	Sensitivity of CT	Appendicitis cases	CT result	0.98 (0.74, 1.31)	χ^2 (3)=3.4, p=0.33
Equivocal cases removed	Specificity of CT	Patients without appendicitis	CT result	0.91 (0.67, 1.25)	χ^2 (3)=0.3, p=0.95
Equivocal cases removed	PPV of CT	Patients with positive CT	Appendicitis status	1.02 (0.76, 1.38)	χ^2 (3)=0.3, p=0.96
Equivocal cases removed	NPV of CT	Patients with negative CT	Appendicitis status	0.88 (0.64, 1.22)	χ^2 (3)=4.6, p=0.21
Equivocal cases removed	Sensitivity of US	Appendicitis cases	US result	1.40 (1.14, 1.73)	χ^2 (3)=1.1, p=0.79
Equivocal cases removed	Specificity of US	Patients without appendicitis	US result	1.15 (0.80, 1.66)	χ^2 (3)=1.5, p=0.69
Equivocal cases removed	PPV of US	Patients with positive US	Appendicitis status	1.26 (0.92, 1.72)	χ^2 (3)=3.1, p=0.37
Equivocal cases removed	NPV of US	Patients with negative US	Appendicitis status	1.26 (1.02, 1.54)	χ^2 (3)=3.4, p=0.34
Equivocal Imaging Results	Equivocal rate of CT	Patients who received a CT	Equivocal CT result	0.76 (0.65, 0.90)	χ^2 (3)=1.3, p=0.72
Equivocal Imaging Results	Equivocal rate of US	Patients who received a US	Equivocal US result	0.96 (.084, 1.09)	χ^2 (3)=0.9, p=0.82
Equivocal cases included as positive	Sensitivity of CT	Appendicitis cases	CT result	0.96 (0.72, 1.28)	χ^2 (3)=3.6, p=0.32
Equivocal cases included as positive	Specificity of CT	Patients without appendicitis	CT result	1.07 (0.89, 1.27)	χ^2 (3)=2.6, p=0.45
Equivocal cases included as positive	PPV of CT	Patients with positive CT	Appendicitis status	1.19 (0.96, 1.46)	χ^2 (3)=1.4, p=0.71
Equivocal cases included as positive	NPV of CT	Patients with negative CT	Appendicitis status	0.88 (0.64, 1.22)	χ^2 (3)=4.6, p=0.21
Equivocal cases included as positive	Sensitivity of US	Appendicitis cases	US result	1.39 (1.14, 1.71)	χ^2 (3)=1.3, p=0.73
Equivocal cases included as positive	Specificity of US	Patients without appendicitis	US result	1.10 (0.96, 1.25)	χ^2 (3)=1.2, p=0.76
Equivocal cases included as positive	PPV of US	Patients with positive US	Appendicitis status	1.19 (0.94, 1.50)	χ^2 (3)=4.1, p=0.26
Equivocal cases included as positive	NPV of US	Patients with negative US	Appendicitis status	1.26 (1.02, 1.54)	χ^2 (3)=3.4, p=0.34
Appendiceal Perforation Results	Perforation rate	All patients	Perforation status	1.65 (1.50, 1.82)	χ^2 (3)=4.7, p=0.20
Appendiceal Perforation Results	Sensitivity of CT	Patients with perforated appendix	CT result	1.03 (0.61, 1.75)	χ^2 (3)=1.2, p=0.75
Appendiceal Perforation Results	Sensitivity of US	Patients with perforated appendix	US result	2.08 (1.44, 3.01)	χ^2 (3)=2.0, p=0.58

PPV, positive predictive value; *NPV*, negative predictive value.
All models estimated with robust standard errors to account for non-independence of observations from the same hospital.
[1]For all models, the independent variable was the ordinal *duration of abdominal pain* measure <12, 13-24, 25-36, 37-48, and 49-71 hours). Trend estimate expressed as *odds ratio (95% confidence interval)*.
[2]Pearson goodness-of-fit test.

Supplementary Table 1. Demographic and clinical characteristics of pediatric patients with suspected appendicitis evaluated with advanced imaging in the emergency department. Analysis is the same as Table 1 in article but includes all patients regardless of time between exam and imaging study. Numbers in parentheses represent percentages.

Demographic and Clinical Characteristics	CT and/or US, n=1862	CT, n=1284	US, n=851
Age in years {median, IQR}	11.0 (8.0, 13.9)	11.0 (8.1, 14.0)	11.1 (8.1, 13.9)
Sex, male	905 (49)	622 (48)	388 (46)
Focal pain, right lower quadrant	1455 (78)	1001 (78)	667 (78)
Final diagnosis of appendicitis	696 (37)	479 (37)	300 (35)
Perforated appendicitis*	177 (10)	138 (11)	62 (7)
Equivocal imaging findings	188 (10)	73 (6)	120 (14)
Duration of abdominal pain	n/a		
<12 hours		374 (29)	260 (31)
12–23 hours		424 (33)	277 (33)
24–35 hours		227 (18)	157 (18)
36–47 hours		127 (10)	73 (9)
48–71 hours		132 (10)	84 (10)

CT, computed tomography; *US*, ultrasound; *IQR*, interquartile range.
*Perforation defined by the surgeon's operative note.

Supplementary Table 2. Sensitivity and specificity of CT and US for the diagnosis of appendicitis among pediatric patients in the emergency department, with and without the inclusion of equivocal cases. Analysis is the same as Table 2 in article but includes all patients regardless of time between exam and imaging study.

Test Characteristics	Duration of Abdominal Pain in Hours					Test for Trend: Odds Ratio (95% CI)
Equivocal cases removed						
CT (n=1211)	<12	12-23	24-35	36-47	48-71	
Sensitivity	.98	.94	.97	.96	.96	0.98 (0.75, 1.29)
Specificity	.97	.97	.96	.97	.96	0.94 (0.68, 1.29)
PPV	.94	.95	.95	.96	.94	1.04 (0.77, 1.41)
NPV	.99	.96	.98	.97	.98	0.89 (0.66, 1.21)
US (n=731)						
Sensitivity	.79	.78	.87	.85	.96	**1.38 (1.14, 1.66)**
Specificity	.96	.97	.99	.96	.98	1.18 (0.82, 1.69)
PPV	.90	.93	.98	.89	.96	1.26 (0.92, 1.72)
NPV	.90	.88	.91	.93	.98	**1.27 (1.03, 1.57)**
Equivocal cases included as positive						
CT (n=1284)						
Sensitivity	.98	.95	.97	.96	.96	0.96 (0.73, 1.25)
Specificity	.92	.91	.90	.91	.96	1.08 (0.91, 1.28)
PPV	.85	.87	.86	.88	.95	1.19 (0.98, 1.44)
NPV	.99	.96	.98	.97	.98	0.89 (0.66, 1.21)
US (n=851)						
Sensitivity	.81	.80	.88	.88	.96	**1.379 (1.14, 1.64)**
Specificity	.80	.80	.87	.84	.85	1.11 (0.95, 1.30)
PPV	.67	.69	.83	.74	.74	1.17 (0.91, 1.51)
NPV	.90	.88	.91	.93	.98	**1.27 (1.03, 1.57)**

CT, computed tomography; *US*, ultrasound; *PPV*, positive predictive value; *NPV*, negative predictive value; *CI*, confidence interval.
Statistical analyses adjusted for clustering on hospital.