Sonography in the Evaluation of Acute Appendicitis

Are Negative Sonographic Findings Good Enough?

Preeyacha Pacharn, MD, Jun Ying, PhD, Leann E. Linam, MD, Alan S. Brody, MD, Diane S. Babcock, MD

Objective. The purpose of this study was to evaluate the negative predictive value (NPV) of sonography in the diagnosis of acute appendicitis. ***Methods.*** Right lower quadrant sonograms of 193 patients (158 female and 35 male; age range, 3–20 years) with suspected acute appendicitis over a 1-year period were retrospectively reviewed. Sonographic findings were graded on a 5-point scale, ranging from a normal appendix identified (grade 1) to frankly acute appendicitis (grade 5). Sonographic findings were compared with subsequent computed tomographic (CT), surgical, and pathologic findings. The diagnostic accuracy of sonography was assessed considering surgical findings and clinical follow-up as reference standards. ***Results.*** Forty-nine patients (25.4%) had appendicitis on sonography, and 144 (74.6%) had negative sonographic findings. Computed tomographic scans were obtained in 51 patients (26.4%) within 4 days after sonography. These included 39 patients with negative and 12 with positive sonographic findings. Computed tomography changed the sonographic diagnosis in 10 patients: from negative to positive in 3 cases and positive to negative in 7. Forty-three patients (22.2%) underwent surgery. The surgical findings were positive for appendicitis in 37 (86%) of the 43 patients who had surgery. Patients with negative sonographic findings who, to our knowledge, did not have subsequent CT scans or surgery were considered to have negative findings for appendicitis. Seven patients with negative sonographic findings underwent surgery and had appendicitis; therefore, 137 of 144 patients with negative sonographic findings did not have appendicitis. On the basis of these numbers, the NPV was 95.1%. ***Conclusions.*** Sonography has a high NPV and should be considered as a reasonable screening tool in the evaluation of acute appendicitis. Further imaging could be performed if clinical signs and symptoms worsen. ***Key words:*** appendicitis; children; sonography.

Abbreviations
CI, confidence interval; CT, computed tomography; NPV, negative predictive value; PPV, positive predictive value

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Address correspondence to Diane S. Babcock, MD, Department of Radiology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, MLC 5031, Cincinnati, OH 45229-3039 USA.

E-mail: diane.babcock@cchmc.org

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Acute abdominal pain is a common presentation of children seeking medical care. Suspected acute appendicitis is the most common condition requiring abdominal surgery in the pediatric population and must be differentiated from other conditions that may mimic its signs and symptoms.[1–3] A history of migrating abdominal pain, classically beginning in the periumbilical region and traveling to McBurney's point, combined with leukocytosis and other associated symptoms such as anorexia remains the best diagnostic clue.[4] However, diagnostic imaging plays an important adjunctive role in confirming the diagnosis when the clinical presentation is inconclusive.

Multiple studies have evaluated the use of sonography and computed tomography (CT) for the diagnosis of appendicitis.[1,5–14] In these studies, the sensitivity and specificity of sonography ranged from 67% to 88% and 78% to 100%, respectively, whereas the sensitivity and specificity of CT were 76% to 96% and 75% to 97%.[1,5,7,9,10,13] The purpose of our study was to evaluate the negative predictive value (NPV) of sonography and determine whether it can be used as a screening tool to exclude acute appendicitis.

Materials and Methods

The study was approved by the Institutional Review Board. An electronic medical record search at a large children's hospital for patients referred for right lower quadrant sonography to rule out appendicitis between August 1, 2006, and July 31, 2007, identified 230 patients. Thirty-seven of these patients were excluded because of incomplete follow up information. The remaining 193 patients (158 female and 35 male; age range, 3–20 years) were included in our study. One hundred six patients were referred by the emergency medicine department, 56 from pediatric primary care sites, and 31 were inpatients. Each sonogram was retrospectively reviewed by 2 radiologists: 1 pediatric radiologist with a Certificate of Added Qualification and 1 pediatric radiology fellow. Sonograms were reviewed without patient identification or clinical information. Interobserver reliability was assessed using κ statistics. Sonographic findings were compared with subsequent CT, surgical, and pathologic findings to determine the sensitivity and specificity of the sonographic examinations. The original reports were reviewed and graded by a certified pediatric radiologist.

Sonographic and CT Techniques and Interpretation

Sonographic examinations were performed by experienced sonographers using a linear array transducer (Acuson Sequoia; Siemens Medical Solutions, Mountain View, CA) and a standardized protocol involving graded compression longitudinal and transverse images of the right lower quadrant as well as right lower quadrant cine clips. Doppler images were reviewed in available cases. In questionable cases, additional images were acquired by a radiologist. Sonographic findings were retrospectively graded using a 5 point scale: 1 represented identification of a normal appendix; 2 indicated that the appendix was not seen, but no inflammatory changes or free fluid were evident; 3 indicated that the appendix was not seen, but secondary signs of appendicitis were present, such as a fecalith, pericecal fluid, or increased pericecal echogenicity consistent with infiltration of the mesenteric fat; 4 represented identification of an appendix of borderline enlarged size (5–6 mm); and 5 indicated acute appendicitis, defined as an enlarged noncompressible appendix with an outer diameter of greater than 6 mm. Findings graded 1 or 2 were classified as negative, and those graded 3 to 5 were classified as positive for acute appendicitis (Figure 1). Original reports were reviewed and graded using the same criteria.

Computed tomographic scans were performed on a multidetector CT scanner (LightSpeed; GE Healthcare, Milwaukee, WI) using a standard acute abdomen protocol involving 5-mm axial images, weight-based low tube current, and intravenous administration of 2-mL/kg iodinated contrast material. Oral contrast material was also given in cases in which the history of abdominal pain was 24 hours or longer. No rectal contrast material was used. Radiologic criteria for the diagnosis of acute appendicitis included an appendix diameter of greater than 6 mm, periappendiceal fat stranding or inflammatory changes, appendiceal wall thickening or enhancement, and periappendiceal abscesses. All CT studies were obtained within 4 days after the sonographic examinations.

Final Diagnoses

The final diagnoses were established on the basis of surgical and histopathologic findings for cases that underwent surgery (n = 43). For nonsurgically treated patients, medical records regarding postpresentation follow-up were reviewed to establish the diagnosis for use in this study. The hospital records for all study patients were reviewed for the 6-month period after their study entry sonograms. Because our institution is the only children's hospital with the only pediatric surgeons in our metropolitan area, few patients

would be admitted or taken to surgery outside our institution. Cases that did not involve surgery and for which follow-up medical records were not available were excluded.

Statistical Analysis

The diagnostic accuracy of sonography was examined using the NPV, positive predictive value (PPV), negative and positive likelihood

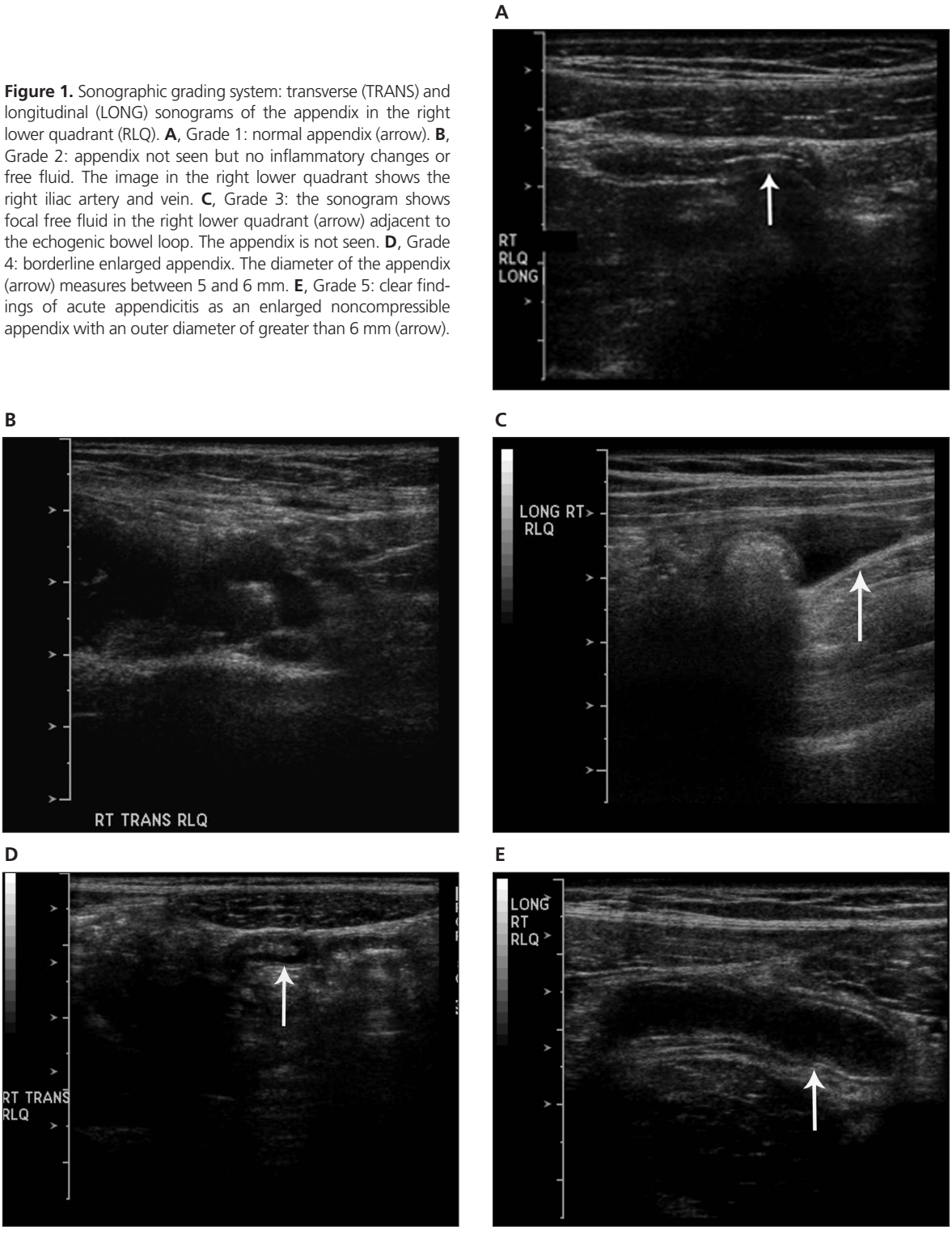


Figure 1. Sonographic grading system: transverse (TRANS) and longitudinal (LONG) sonograms of the appendix in the right lower quadrant (RLQ). **A**, Grade 1: normal appendix (arrow). **B**, Grade 2: appendix not seen but no inflammatory changes or free fluid. The image in the right lower quadrant shows the right iliac artery and vein. **C**, Grade 3: the sonogram shows focal free fluid in the right lower quadrant (arrow) adjacent to the echogenic bowel loop. The appendix is not seen. **D**, Grade 4: borderline enlarged appendix. The diameter of the appendix (arrow) measures between 5 and 6 mm. **E**, Grade 5: clear findings of acute appendicitis as an enlarged noncompressible appendix with an outer diameter of greater than 6 mm (arrow).

ratios, sensitivity, specificity, and their respective 95% confidence intervals (CIs). Frequency tables were generated using SAS version 9.1.3 software (SAS Inc, Cary, NC), and the 95% CIs were calculated using VassarStats.[15] The CIs were calculated using the efficient-score method (corrected for continuity).[16] Inter-reader reliability was verified using Cohen weighted κ and Kendall tau β coefficients. Values between 0.61 and 0.80 were considered good agreement. Values are reported as estimated values and 95% CIs.

Results

Among the 193 patients who underwent sonographic examination for clinically suspected acute appendicitis, the sonographic findings were negative in 144 (74.6%) and positive in 49 (25.4%). The Cohen weighted κ and Kendall tau β coefficients showed good inter-reader reliability between the 2 reviewers (Cohen κ = 0.764 [95% CI, 0.682–0.845]; Kendall tau β = 0.7048 [95% CI, 0.594–0.815]). Computed tomography was subsequently performed in 39 patients with negative and 12 with positive sonographic findings. Computed tomography changed the imaging diagnosis in 10 patients: from negative to positive in 3 cases and from positive to negative in 7 (Table 1).

Forty-three patients (22.2%) underwent surgery. The surgical findings were positive for appendicitis in 37 patients (86%). Seven patients with negative sonographic findings did have acute appendicitis according to surgical and pathologic findings (Table 2). On the basis of the final diagnosis, the sensitivity of sonography was 81.1% (30 of 37); specificity, 87.8% (137 of 156); PPV, 61.2% (30 of 49; 95% CI, 46.2%–74.4%); and NPV, 95.1% (137 of 144; 95% CI, 89.8%–97.8%; Table 3). Review of the original reports compared with the final diagnoses showed 147 patients with negative sonographic findings, of which 7 had appendicitis. The sensitivity was 81.1% (30 of 37); specificity, 89% (140 of 156); PPV, 65% (30 of 46; 95% CI, 49%–78%); and NPV, 95.2% (140 of 147; 95% CI, 90%–98%; Table 4).

Ovarian conditions were found in 13 patients, including 1 with a tubo-ovarian abscess and 12 with ovarian cysts; 3 patients had intrauterine pregnancy.

Table 1. Sonographic Diagnosis Compared With CT in Patients Who Underwent CT

	CT		
Sonography	Negative	Positive	Total
Positive	7	5	12
Negative	36	3	39
Total	43	8	51

Sensitivity, 0.62 (95% CI, 0.25–0.89); specificity, 0.83 (95% CI, 0.68–0.92); PPV, 0.41 (95% CI, 0.16–0.71); and NPV, 0.92 (95% CI, 0.78–0.97).

Table 2. Sonographic Diagnosis Compared With Surgical/Pathologic Findings in Patients Who Underwent Surgery

	Surgery		
Sonography	Negative	Positive	Total
Positive	2	30	32
Negative	4	7	11
Total	6	37	43

Sensitivity, 0.81 (95% CI, 0.64–0.91); specificity, 0.67 (95% CI, 0.24–0.94); PPV, 0.93 (95% CI, 0.78–0.99); and NPV, 0.36 (95% CI, 0.12–0.68).

Discussion

Suspected acute appendicitis is one of the most common diagnostic dilemmas encountered in clinical pediatric practice. Although the diagnosis is primarily based on clinical findings, the presentation can be confusing, and classic features may be subtle or difficult to elicit in children.[17] Moreover, clinical signs and symptoms may overlap with other conditions such as viral gastroenteritis, intussusception, and mesenteric adenitis. In female patients, ovarian conditions may also mimic appendicitis.

Imaging plays an important role in the modern evaluation of abdominal pain, although a definitive consensus on the appropriate imaging workup protocol remains elusive. The ideal imaging test would be readily available, fast, inexpensive, reproducible, safe, and accurate.[18] Radiographic findings are not specific, and as such, conventional radiographs are not considered cost-effective compared with CT.[19] A radiopaque appendicolith may suggest the specific diagnosis of appendicitis on conventional radiography, but this finding is present in less than 5% of cases of appendicitis.[20] Several studies

have reviewed the use of sonography and CT in the evaluation of acute appendicitis. Most studies to date have focused on the appendiceal visualization rate and the sensitivity and specificity of the study.[1,5–14]

Sonography is part of the diagnostic algorithm at our institution and is relatively inexpensive, safe, and readily available. Sonography can be performed at the bedside, involves a short acquisition time, does not use ionizing radiation, and may show evidence of other causes of abdominal pain such as ovarian cysts, tubo-ovarian abscesses, and mesenteric adenitis. It is particularly useful in evaluating young women, in whom the radiation dose to the reproductive organs should be minimized and for whom it is important to exclude ovarian and uterine conditions that might mimic appendicitis.[21] In our study, ovarian- and uterine-related findings were shown in 16 patients, and an alternative diagnosis was made by initial sonography.

The criteria for the diagnosis of acute appendicitis by sonography are well established and reliable.[22] The most specific sign is the identification of a noncompressible blind-ending structure in the right lower quadrant with an outer diameter of greater than 6 mm, consistent with an abnormal appendix. In our study, we also considered findings positive when the appendix was not identified but when secondary signs of appendicitis were present.

Prior studies have suggested that a normal appendix should be identified to exclude acute appendicitis.[20] Wiersma et al[23] reported identification of the normal appendix by sonography in 82% of asymptomatic children. In the evaluation of acute appendicitis, the visualization rate varies from institution to institution, from a high of 98% to a low of 22%.[18] This study sought rather to determine whether appendicitis could be excluded on the basis of negative sonographic findings. In our study, if an appendix was not visualized and there were no secondary signs to suggest appendicitis, the findings were considered negative. Using these criteria, the NPV was 95.1%, similar to results in prior studies.[10,24] Seven patients with acute appendicitis in our study had false-negative sonographic findings. These patients were 12 to 15 years old. Four were referred for CT because of continued clinical concern for appendicitis. Three went directly to surgery. Factors likely contributing to a false-negative diagnosis were identified in 4 of the 7 patients. A retrocecal appendix was identified in 2 of the 4 patients who had CT scans. One of these patients was also obese. Two of the 3 patients taken directly to surgery had a grossly normal appendix at surgery with a pathologic diagnosis of appendicitis.

Sonography can be limited by patient body habitus as well as the variable and at times inaccessible position of the appendix. Retrocecal and retroileal appendixes are difficult to visualize, whereas anterior appendixes are relatively easy to identify. In our study, 1 patient who had false-negative sonographic findings was obese, technically limiting the study. Subsequently, CT showed retrocecal appendicitis (Figure 2). Other indications for CT after sonography included nonvisualization of the appendix by sonography, an equivocal findings with secondary signs of appendicitis, and negative findings with clinical concern for appendicitis.

The PPV in our study was relatively low compared with other studies[10,24] and can be explained by the study design. Because our study focused mainly on the screening value of sonog-

Table 3. Sonographic Diagnosis Compared With Final Diagnosis (Surgery/Pathologic Examination)

	Appendicitis		
Sonography	No	Yes	Total
Positive	19	30	49
Negative	137	7	144
Total	156	37	193

Sensitivity, 0.81 (95% CI, 0.64–0.91); specificity, 0.88 (95% CI, 0.81–0.92); PPV, 0.61 (95% CI, 0.46–0.74); and NPV, 0.95 (95% CI, 0.90–0.98).

Table 4. Sonographic Diagnosis From Original Report Interpretation Compared With Final Diagnosis (Surgery/Pathologic Examination)

	Appendicitis		
Sonography	No	Yes	Total
Positive	16	30	46
Negative	140	7	147
Total	156	37	193

Sensitivity, 0.81 (95% CI, 0.64–0.91); specificity, 0.89 (95% CI, 0.83–0.93); PPV, 0.65 (95% CI, 0.49–0.78); and NPV, 0.95 (95% CI, 0.90–0.98).

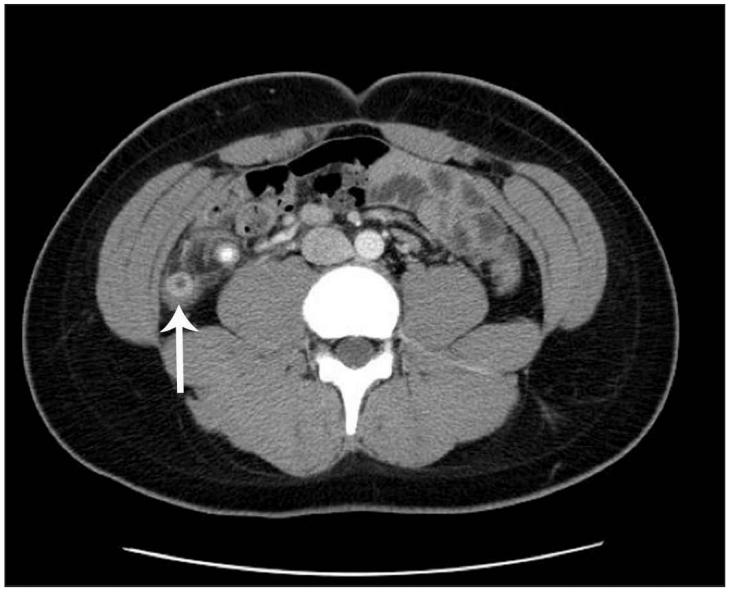
raphy, with the sonograms interpreted in a manner to avoid missing any cases with positive findings, subtle but nonspecific signs that might have indicated acute appendicitis, such as fluid in the right paracolic gutter, were interpreted as positive results (grade 3 sonographic findings). If we had interpreted grade 3 sonographic findings negative, the PPV would have increased to 79.4% (95% CI, 61.6%–90.7%; however, 3 more patients would have had false-negative sonographic findings. The pretest probability of disease in our population was likely relatively low, which could have contributed to our relatively low PPV. Our study was limited to pediatric patients, with 84% of the patients seen in the emergency department or a pediatrician's office. In addition, all patients referred for sonography to rule out appendicitis were included, with no requirement for a surgical evaluation or specific clinical or laboratory findings.

There were additional limitations in our study. Some patients who were highly suspicious for appendicitis from physical examination went directly to surgery. Some who were suspected to have complicated or perforated appendicitis might have gone directly to CT without sonography. This study was also limited by its retrospective design, which is particularly relevant to sonography because the examinations are highly operator dependent. However, our retrospective study was aided by the fact that a rigorous screening protocol for the exclusion of appendicitis has been in place at our institution, and the acquisition of detailed cine clips is part of this standardized protocol.

We have reviewed the original reports to compare with our retrospective interpretation. There were slight differences in the number of negative and positive results, but the NPV was similar (95%).

In conclusion, in our study, sonography was found to have a high NPV (95.1%) for the exclusion of acute appendicitis even if the appendix was not visualized. The role of sonography in screening algorithms for the evaluation of suspected acute appendicitis is supported, particularly in young female patients for whom the gonadal radiation dose should be kept to a minimum. However, further imaging could be performed if clinical signs and symptoms worsen or strongly suggest appendicitis.

Figure 2. Computed tomography (after administration of intravenous contrast material) through the lower abdomen in a patient with acute appendicitis. The sonographic findings were negative. Axial computed tomography shows retrocecal appendicitis (arrow). The patient also has thick subcutaneous tissue.



References

1. Kaiser S, Frenckner B, Jorulf HK. Suspected appendicitis in children: US and CT—a prospective randomized study. Radiology 2002; 223:633–638.
2. Sivit CJ, Siegel MJ, Applegate KE, Newman KD. When appendicitis is suspected in children. Radiographics 2001; 21:247–262, questionnaire 288–294.
3. van Breda Vriesman AC, Puylaert JB. Mimics of appendicitis: alternative nonsurgical diagnoses with sonography and CT. AJR Am J Roentgenol 2006; 186:1103–1112.
4. Lee SL, Ho HS. Acute appendicitis: is there a difference between children and adults? Am Surg 2006; 72:409–413.
5. Johansson EP, Rydh A, Riklund KA. Ultrasound, computed tomography, and laboratory findings in the diagnosis of appendicitis. Acta Radiol 2007; 48:267–273.
6. Gracey D, McClure MJ. The impact of ultrasound in suspected acute appendicitis. Clin Radiol 2007; 62:573–578.
7. Gamanagatti S, Vashisht S, Kapoor A, Chumber S, Bal S. Comparison of graded compression ultrasonography and unenhanced spiral computed tomography in the diagnosis of acute appendicitis. Singapore Med J 2007; 48:80–87.
8. Baldisserotto M, Peletti AB. Is colour Doppler sonography a good method to differentiate normal and abnormal appendices in children? Clin Radiol 2007; 62:365–369.

9. 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.

10. Assefa G, Meseret S, Nigussie Y. The role of ultrasound in diagnosing acute appendicictis. Ethiop Med J 2006; 44: 67–74.

11. Kaiser S, Jorulf H, Söderman E, Frenckner B. Impact of radiologic imaging on the surgical decision-making process in suspected appendicitis in children. Acad Radiol 2004; 11:971–979.

12. Incesu L, Yazicioglu AK, Selcuk MB, Ozen N. Contrast-enhanced power Doppler US in the diagnosis of acute appendicitis. Eur J Radiol 2004; 50:201–209.

13. Poortman P, Lohle PN, Schoemaker CM, et al. Comparison of CT and sonography in the diagnosis of acute appendicitis: a blinded prospective study. AJR Am J Roentgenol 2003; 181:1355–1359.

14. Lowe LH, Penney MW, Stein SM, et al. Unenhanced limited CT of the abdomen in the diagnosis of appendicitis in children: comparison with sonography. AJR Am J Roentgenol 2001; 176:31–35.

15. VassarStats. Utilities/convert to standard scores. VassarStats website. http://faculty.vassar.edu/lowry/VassarStats.html. Accessed November 2, 2009.

16. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Stat Med 1988; 17:857–872.

17. Rodriguez DP, Vargas S, Callahan MJ, Zurakowski D, Taylor GA. Appendicitis in young children: imaging experience and clinical outcomes. AJR Am J Roentgenol 2006; 186: 1158–1164.

18. Taylor GA. Suspected appendicitis in children: in search of the single best diagnostic test. Radiology 2004; 231:293–295.

19. Rao PM, Rhea JT, Rao JA, Conn AK. Plain abdominal radiography in clinically suspected appendicitis: diagnostic yield, resource use, and comparison with CT. Am J Emerg Med 1999; 17:325–328.

20. Old JL, Dusing RW, Yap W, Dirks J. Imaging for suspected appendicitis. Am Fam Physician 2005; 71:71–78.

21. Siegel MJ, Carel C, Surratt S. Ultrasound of acute abdominal pain in children. JAMA 1991; 266:1987–1989.

22. Puylaert JB. Acute appendicitis: US evaluation using graded compression. Radiology 1986; 158:355–360.

23. Wiersma F, Sramek A, Holscher HC. US features of the normal appendix and surrounding area in children. Radiology 2005; 235:1018–1022.

24. Chang YJ, Kong MS, Hsia SH, et al. Usefulness of ultrasonography in acute appendicitis in early childhood. J Pediatr Gastroenterol Nutr 2007; 44:592–595.