EVIDENCE-BASED CASE REVIEWS

Abdominal pain in children and the diagnosis of appendicitis

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A 5-year-old girl presents to the emergency department (ED) because of vomiting, abdominal pain, and fever for the past 36 hours. The pain is periumbilical and cramping in nature, and its location has not changed since onset. The child does not have diarrhea, rash, dysuria, sore throat, or upper respiratory tract symptoms. Her temperature is 38.7°C (101.7°F), and abdominal examination reveals diffuse tenderness to deep palpation with notable rebound tenderness. There is guarding, and the pain does not decrease when the patient is distracted. The findings of the examination are otherwise normal. Plain abdominal radiographs show no abnormalities. The white blood cell (WBC) count is 16.9×10^9/L (16,900/μL) with 0.88 (88%) neutrophils. The patient is unable to provide a urine specimen. You are concerned that this child might have acute appendicitis and question the value of the history, examination, and preliminary investigations in confirming this diagnosis.

Summary points

- Pain duration by history should not influence the decision to operate on a patient with abdominal pain, but pain present for a short (<7 hours) or a long duration (>48 hours) is unlikely to be due to appendicitis
- In isolation, a history of vomiting does not help make the diagnosis of appendicitis. However, in combination with historical and physical findings (such as right lower quadrant pain or abdominal tenderness or guarding), vomiting may help predict appendicitis
- Rebound tenderness on physical examination may be a useful predictor of appendicitis in a child with a high probability of having acute appendicitis. Furthermore, in a patient with few other findings that suggest appendicitis, a lack of guarding on physical examination may indicate that observation, rather than operation, would be prudent
- Appendicitis is unlikely to be present when the white blood cell count is low, unless the pretest probability of appendicitis is high. A high white blood cell count for age increases suspicion for acute appendicitis, although whether there is an upper limit is unclear
- Ultrasonography is most helpful for ruling in appendicitis, primarily in patients with equivocal clinical findings
- Computed tomography is most helpful in patients who have a nonconclusive ultrasonogram and in whom there is still concern about the diagnosis of appendicitis. No studies have shown it to be clearly superior to ultrasonography

Appendicitis is among the most serious causes of acute abdominal pain and is the most common indication for emergency abdominal surgery in children. Its incidence varies with age, sex, and clinical setting in which patients are evaluated. The prevalence of abdominal pain among pediatric ED or outpatient clinic patients is 3.0% to 5.1% for pain of less than 3 days' duration and 8.1% for pain of any duration. Appendicitis explains 1% of abdominal pain episodes, and the incidence peaks in older children and adolescents, with an estimated rate of 23.3 per 10,000 population per year in persons aged 10 to 19 years. The male-to-female ratio is 1.4:1.[1,2]

Of children undergoing appendectomy for presumed appendicitis, 10% to 40% have a normal appendix and usually a nonsurgical explanation for their abdominal pain.[3-10] In 15% to 40% of those undergoing appendectomy who do have appendicitis, it will have progressed to perforation[3,5,7,9,10]; this proportion is even higher (71%-100%) in children younger than 6 years.[10,11] Perforation rates are higher in boys. Negative appendectomies occur more commonly in postpubertal girls—the threshold for surgery is lower in girls because of the risk of infertility associated with untreated peritonitis.[3,6] Mortality has declined since the recognition of appendicitis in the 1800s; currently it is a cause of death in 0.02% to 0.8% of general populations studied.[5,12] In one US community, death from undetected appendicitis in early childhood occurred in 4.5 per million children at risk per year.[13] Prompt and accurate diagnosis of appendicitis remains the key to reducing morbidity and mortality.

You wish to use an evidence-based approach to answer your questions about the diagnosis of appendicitis in children with abdominal pain. You start by looking for high-quality evidence syntheses and evidence-based guidelines to answer your questions but are unable to find any systematic reviews of the diagnostic issues in question. Thus, you look for primary studies that compare findings with the standard for the diagnosis: histologically confirmed

Search strategy by which to pursue answers to clinical scenario-generated questions

Question	Search strategy*
Will historical details (ie, duration of pain, vomiting) help in the diagnosis of acute appendicitis?	Appendicitis: diagnosis AND (exp: abdomen OR exp: pain) AND duration AND time factors Appendicitis: diagnosis AND (vomiting or nausea)
Will specific physical findings (ie, pain location, rebound tenderness) help in the diagnosis of acute appendicitis?	Appendicitis: diagnosis AND exp: pain; limit children
Will laboratory measures of inflammation (eg, leukocyte count) help in the diagnosis of acute appendicitis?	Appendicitis: diagnosis AND exp: leukocyte count
Will radiographic studies (ie, ultrasonography, computed tomographic scanning) help in the diagnosis of acute appendicitis?	Appendicitis: diagnosis AND ultrasonography Appendicitis: diagnosis AND computed tomography

*Limit to English-language journals, human subjects, and prospective studies for each. exp = explode/expand

appendicitis. The Table summarizes your questions and search strategies.

HISTORICAL FINDINGS

O'Shea and colleagues prospectively studied 246 patients aged between 3 and 18 years who had abdominal pain for less than 1 week.[9] The standard for a diagnosis of appendicitis was the pathologic appearance of the appendix or patient status 1 week after the ED visit. The likelihood ratio (LR) for appendicitis for pain less than 12 hours versus greater than 12 hours was 0.64; for pain less than versus greater than 24 hours, the LR was 0.83.

Andersson and colleagues prospectively evaluated 502 patients (aged 10-86 years) admitted to the hospital with abdominal pain and possible appendicitis for duration of pain and vomiting, dividing the pain duration into 6-hour increments up to 72 hours.[14] The greatest LR was 1.7 at a pain duration of 7 to 12 hours (95% confidence interval [CI], 1.1-2.6). The LR for appendicitis in a patient with vomiting compared with no vomiting was 1.8 (95% CI, 1.4-2.4). If pain migrated to the right lower quadrant, the LR for appendicitis was 1.45 (95% CI, 1.07-1.99). If the pain did not migrate to the right lower quadrant, the LR was 0.74 (95% CI, 0.55-0.95).

Reynolds and Jaffe prospectively studied 377 children (aged 2-16 years) seen in an ED with abdominal pain.[15] In this study, the presence of two of four findings—vomiting, right lower quadrant pain, abdominal tenderness, and abdominal guarding—had a sensitivity of 0.96 and a specificity of 0.72, which produces an LR of 3.4 for two or more of four predictors and an LR of 0.08 for having less than two of these four findings. Therefore, a patient with only one or none of these predictors is unlikely to have appendicitis.

PHYSICAL FINDINGS

Golledge and colleagues prospectively evaluated 100 patients (aged 4-81 years) who had right lower quadrant pain and possible appendicitis.[16] The only findings with an LR of greater than 3.0 were rebound tenderness (LR, 7.4) and percussion tenderness (LR, 4.1) in the right lower quadrant. Alshehri and associates found less impressive results in 130 patients with suspected appendicitis (LR, 1.2) because 80% of their patients who did not have appendicitis also had rebound tenderness (20% specificity).[17] They found similar LRs for guarding (1.2), Rovsing's sign (1.5), and rigidity (1.7). The high sensitivities of these peritoneal signs (ie, probability of being present in patients who have appendicitis) mean that the absence of these signs may be more useful in ruling out the diagnosis of acute appendicitis. The lack of rebound tenderness gives a negative LR of 0.3 and lack of guarding, 0.06.

The physical examination findings in the studies by O'Shea and colleagues and Reynolds and Jaffe provide insufficient information to influence your clinical practice and decision making.[11,15] You conclude that rebound tenderness may be a useful predictor of appendicitis, but a lack of guarding on physical examination may sway you to observe, rather than operate on, a patient with few other findings that suggest appendicitis.

Appendicitis explains 1% of abdominal pain episodes in young children

Laboratory findings

Andersson and colleagues also studied the WBC count and found an LR for appendicitis of 0.16 for a total WBC count of less than 8.0×10^9/L (<8,000/μL).[14] The LR increased with rising WBC counts, to a maximum of 7.0 for a WBC count of 15.0×10^9/L (15,000/μL) or more. The likelihood ratios and 95% confidence intervals for different levels of total WBC counts demonstrate that only at the extremes of the WBC count is this test clinically useful.

Dueholm and associates reported the findings of a blind, prospective study that evaluated the usefulness of WBC count, neutrophil count, and C-reactive protein level in 237 patients (aged 15-45 years) with possible appendicitis.[18] Using single cutoff values rather than stratified values of WBC means that information from individual strata are pooled, which results in smaller LRs. Izbicki and colleagues conducted a retrospective evaluation of 536 patients followed by a prospective evaluation of 150 patients with the presumed diagnosis of appendicitis.[7,19] They also used single cutoff values, none of which are as useful as the stratified values evaluated by Andersson and co-workers. However, all of the available studies give consistent results and suggest that the diagnosis of appendicitis is unlikely when the WBC count is low, unless there is a high pretest probability.

Abdominal ultrasonography

A properly performed systematic review by Orr and colleagues summarized 17 studies that assessed the role of ultrasonography in 3,358 adults and children suspected of having appendicitis (37% had the disease).[20] The LR for acute appendicitis with a positive scan was 10.7, and the LR with a negative scan was 0.17, based on pooled sensitivity and specificity of 85% (95% CI, 81.0%-87.8%) and 92% (95% CI, 88.0%-95.2%). This suggests that patients with equivocal clinical findings will benefit from ultrasonography, but for those in whom the diagnosis is either very unlikely or very likely, the change in probability of disease after ultrasonography is not likely to change clinical management.

Five studies specifically addressed the use of ultrasonography in children.[21-25] You exclude two for methodologic reasons, the first because it included only patients with clinical evidence supporting operative intervention regardless of ultrasonographic findings. This population's pretest probability of having appendicitis is 95%, resulting in LRs closer to 1.0 than a test used in the population of interest, children in whom the diagnosis is uncertain.[21] You exclude the second because you are concerned that the availability of a second confirmatory test (the computed tomographic [CT] scan) may have biased ultrasonographic readings and led to a misclassification bias.[25] Considering the remaining three studies, you conclude that the most accurate estimate of LRs ranges from 8.5 to 30 for positive findings to 0.10 to 0.07 for negative findings.[22-24]

Sources of bias in these studies include the use of different types of ultrasound machines, the skill levels of the radiologists performing the examination (some including radiology residents and surgeons), and the criteria used for defining appendicitis by ultrasonography. Few studies clearly state how patients with inconclusive results or findings consistent with an alternative diagnosis were handled. Variation in the patient populations and in the follow-up routines also may have introduced bias. Given these caveats, it can be concluded that patients with strong clinical evidence of appendicitis should be referred to a surgeon without an ultrasonogram, given the large number of false-negative results when this is used as a diagnostic test. Patients with a low probability of appendicitis on clinical grounds should not undergo ultrasonography, given the large number of false-positive results obtained. The ultrasonogram is most useful in patients in whom the diagnosis is uncertain, but it still does not definitively rule the disease in or out.

Douglas and colleagues conducted a randomized controlled trial of ultrasonography in diagnosing appendicitis.[26] They compared clinical diagnosis with ultrasonographic diagnosis of appendicitis in patients with an intermediate probability of appendicitis based on the Alvarado score (10-point clinical scoring system). The authors concluded that ultrasonography is an accurate procedure that reduces time to operation, but there were no differences in the important outcomes of mean hospital stay or adverse outcomes, including the proportion of patients undergoing a nontherapeutic operation or delayed treatment in association with perforation. Unfortunately, you recall reading articles that reported higher diagnostic accuracy of clinical examination over the Alvarado scoring system in children. Thus, it is unclear if the failure to find improved outcomes using ultrasonography is a failure of the ultrasonogram or the selection criteria for the patient population receiving the ultrasonogram.

CT scanning

Most studies that evaluate the diagnostic accuracy of CT in diagnosing appendicitis have been conducted in adult patients. Sources of bias are similar to those identified for ultrasonography, in addition to different types of contrast being used. The range of LRs found was 5.5 to infinity for positive findings and 0.1 to less than 0.001 for negative findings.

The study by Pena and associates focused on children and has results consistent with those of adult studies. Scanning with CT identified appendicitis in 28 of the 29 patients with appendicitis; 74 patients without appendicitis had normal (negative) CT results.[25] The authors conservatively treated patients with equivocal CT results as false-positives (if they did not have appendicitis) and false-negatives (if they did have appendicitis), for a total of 1 false-negative result and 5 false-positive results. Thus, you derive a positive LR of 16.2 and a negative LR of 0.03. The study's objective was to determine the diagnostic value of a protocol involving ultrasonography followed by CT scanning in the diagnosis of appendicitis; thus you cannot directly compare the accuracy of CT scanning with that of ultrasonography. Although the study authors conclude that a CT scan following ultrasonography is highly accurate in diagnosing appendicitis in children, concern remains that this additional test may involve delays in diagnosis, radiation exposure, hazards and discomfort from rectal contrast, and possibly an adverse event related to sedation.

About 1% of children evaluated in the ED for abdominal pain have appendicitis. Vomiting and abdominal tenderness represent two of the four predictors from the Reynolds and Jaffe study (LR, 3.4), modifying this patient's likelihood of appendicitis to about 3.4%[14]; the finding of rebound tenderness (LR, 7.0) modifies the risk to about 20%. Additional information from the WBC count (LR, 7.0) increases this risk to about 65%. This is likely an overestimation because these findings are not independent; however, there is no suggestion of an alternative diagnosis. You are unwilling to send the child to the operating room without further information, so you arrange an abdominal ultrasonogram. This reveals a dilated tubular structure in the right lower quadrant, consistent with acute appendicitis. The likelihood of appendicitis is now greater than 94%. This exceeds your threshold for surgical intervention, so you do not request a CT scan. The consulting surgeon takes the child to the operating room, where a nonperforated, thickened, inflamed appendix is removed. The patient recovers without complication.

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