Appendicitis
Role of MRI

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Abstract: The diagnosis of pediatric appendicitis can be difficult, with a substantial proportion misdiagnosed based on clinical features and laboratory tests alone. Accordingly, advanced imaging with ultrasound (US), computed tomography (CT), and/or magnetic resonance imaging has become routine for most children undergoing diagnostic evaluation for appendicitis. There is increasing interest in the use of US as the primary imaging modality and reserving CT as a secondary diagnostic modality in equivocal cases. Magnetic resonance imaging, using a rapid protocol, without contrast or sedation, has been found to be highly sensitive and specific in the evaluation of children with acute right lower quadrant pain in a number of studies. Because magnetic resonance imaging has the advantage over CT of not using contrast or ionizing radiation, it may replace CT in many instances, whether after US as part of a stepwise imaging algorithm or as a primary imaging modality. Accessibility and cost, however, limit its more widespread use currently.

Key Words: abdominal pain, appendicitis, imaging, ultrasound, CT, MRI

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TARGET AUDIENCE

This CME activity is intended for clinicians who care for children with acute abdominal pain, including general pediatricians, emergency physicians, surgeons, and radiologists.

LEARNING OBJECTIVES

After completion of this article, the reader should be better able to:

1. Describe the role of ultrasound and CT in the diagnostic evaluation of children with suspected appendicitis.
2. Evaluate the role of MRI, both as a first line modality, and as a second-line modality after an equivocal ultrasound, in the diagnostic evaluation of children with suspected appendicitis.
3. Appraise the role of financial analysis in determining the appropriate advanced imaging modality for diagnostic evaluation of children with suspected appendicitis.

Abdominal pain is a common chief complaint accounting for 3.5% to 5% of all pediatric emergency department (ED) visits. Among these patients with abdominal pain and clinical features concerning for acute appendicitis, approximately one third are diagnosed with appendicitis, making it the most common surgical emergency in children.[1] Its incidence increases with age until adolescence, with approximately 60,000 to 80,000 cases diagnosed annually in North America. The diagnosis of pediatric appendicitis can be difficult, with a substantial proportion misdiagnosed based on clinical features and laboratory tests alone.[2] Missed appendicitis has been found to be the second most common diagnosis in malpractice claims in pediatric emergency medicine.[3]

The ideal diagnostic test for acute appendicitis must be safe, avoid exposure to ionizing radiation, inexpensive, widely available at teaching as well as community hospitals 24 hours a day, and effective in diagnosing appendicitis at an early stage to reduce the likelihood of perforation, with the resulting increase in morbidity and mortality. The test characteristics should have low interoperator variability, a high positive predictive value (PPV) to reduce the rate of negative appendectomy, and a high negative predictive value (NPV) to avoid cases of missed appendicitis.

Advanced imaging with ultrasound (US), computed tomography (CT), and/or magnetic resonance imaging (MRI) has become a routine for most children undergoing diagnostic evaluation for appendicitis, with some believing that appendectomy should not be undertaken without imaging to confirm the clinical suspicion.[4]

ULTRASOUND

There is increasing interest in the utilization of US for appendicitis but its use seems limited by concerns related to variable operator experience and overall performance. Secondary analysis of data from a prospective, 10-center study (N = 965) of children aged 3 to 18 years with acute abdominal pain concerning for appendicitis showed that US sensitivity and rate of visualization of the appendix varied across sites and seemed to improve with more frequent use.[5] It had a low overall sensitivity of 72% (95% confidence interval [CI] = 59–86) but high specificity of 97% (96–98) in diagnosing appendicitis.[5] Ultrasound had high specificity at all centers, supporting the clinical policy statement of American College of Emergency Physicians that across institutions, US is more useful to confirm acute appendicitis rather than exclude it.[6] Inability to visualize the appendix is the reason for the low sensitivity of US. This may happen because of multiple factors including obesity, pain, and tenderness in the right lower quadrant, which precludes a thorough examination, presence of overlying gas, which obstructs the penetration of the US beam, inflammation confined to the appendiceal tip with the proximal portion appearing normal, retrocecal location of appendix, gas-filled appendix, a markedly enlarged appendix mistaken for small bowel, or limited operator experience. As demonstrated in 1 multicenter study, when the appendix is clearly visualized on US (49% of 469 children), US has universally high sensitivity of 98% (95% CI = 95%–100%), specificity of 92% (95% CI = 87%–97%), NPV of 98% (95% CI = 94%–99%), and PPV of 92% (95% CI = 88%–95%).[5] This and other studies show that when, however, US does not identify the appendix clearly, clinicians need to consider other modalities before diagnosing or excluding appendicitis. These diagnostic modalities may include repeat clinical assessment, laboratory testing biomarkers (a developing field), admission for repeat clinical examinations, and/or US, CT, MRI, or discharge home with close follow-up.

Among patients with the final diagnosis of appendicitis, approximately a third present with abdominal pain of less than 12 hours, a third between 12 and 24 hours, and another third at

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more than 24 hours. The diagnostic accuracy of US varies with duration of abdominal pain, yielding more false-negative results in children in the initial stage of the disease.[7] The improvement in sensitivity of US with increasing duration of abdominal pain, however, raises the possibility of repeat US use in equivocal cases. Schuh et al[8] performed a prospective cohort study of children presenting to an ED with suspected appendicitis to determine the diagnostic accuracy of a serial US-clinical diagnostic pathway, which consisted of an initial US followed by clinical reassessment in all patients and interval US and surgical consultation in patients with equivocal initial US and persistent clinical concern about appendicitis. Children in whom this pathway did not rule in/rule out appendicitis underwent a CT scan. Cases with missed appendicitis, negative operations, and CT scans after the pathway were considered as being diagnostically inaccurate. The pathway had good sensitivity of 97% (95% CI = 94%–100%), but poor specificity of 91% (95% CI = 87%–95%) because of numerous cases of ovarian pathology mimicking appendicitis in girls who underwent negative operations.[8] This approach also requires time investment and associated costs. Another study of a second US, after an inconclusive first one, found the PPV and NPV to be 97% and 99%, respectively.[9]

COMPUTED TOMOGRAPHY WITH INTRAVENOUS CONTRAST

Computed tomography with intravenous (IV) contrast is widely available, has a sensitivity of more than 93%, and has a specificity of more than 92%, and the test characteristics are not influenced by the duration of symptoms.[6,7] It is, however, invasive, costly, requires IV contrast, and involves ionizing radiation with potential for increased cancer risk. Although dose reduction methods are often used in children, the effective dose of a CT scan of the abdomen/pelvis still remains high at approximately 6 mSv.[10] The lifetime cancer mortality risk attributable to CT correlates inversely with the patient's age. Radiation exposure from a single abdominal CT examination in a 1-year-old child has been estimated to lead to a lifetime cancer mortality risk of approximately 1 in 550.[11] These estimated risks are an order of magnitude higher than the risks for adults. Low-dose CT is another modality worth consideration. Callahan et al[12] have shown that the negative appendectomy rate and performance characteristics of the CT-based diagnosis of acute appendicitis in children were not affected by a 39% reduction in median absorbed radiation dose.

Despite its higher overall sensitivity in diagnosing appendicitis, investigators have noted a trend toward increased reliance on US and decreased utilization of CT for children with appendicitis among large US pediatric hospitals.[13] Computed tomography is being reserved as a secondary diagnostic modality in equivocal cases. Recently, Santillanes et al[14] published their results using such an approach and showed reduction in CT use to 42% of patients and, with a negative appendectomy rate of 1%, missed appendicitis rate of 2%, and perforation rate of 18%. The current American College of Radiology Appropriateness Criteria for Right Lower Quadrant Pain-Suspected Appendicitis, as well as the American College of Emergency Physicians advocate US as the preferred initial examination in children, followed by CT with IV contrast in equivocal cases.[6,15]

MAGNETIC RESONANCE IMAGING

If MRI can be shown to consistently perform as well as CT for diagnosing pediatric appendicitis, then the ALARA ("As Low As Reasonably Achievable") principle would suggest that it should ultimately replace CT in many instances, either following US as part of a stepwise imaging algorithm or as a primary imaging modality. This could be particularly relevant in community EDs, where pediatric patients are more likely to undergo CT for suspected appendicitis for want of access to pediatric ultrasonography.

Test Characteristics

Two recent systematic reviews of diagnostic performance of MRI for evaluation of acute appendicitis in children found excellent test characteristics: sensitivity of 96% (95% CI = 95%–97%), specificity of 96% (95% CI = 94%–98%), PPV of 92% (95% CI = 89%–94%), and NPV of 98% (95% CI = 97%–99%).[16,17] This is even true when MRI is used as a first-line test for patients presenting with abdominal pain of less than 24 hours duration versus those with more than 24 hours' duration. Sensitivity and specificity in patients with early abdominal pain were 98% (95% CI = 92%–99%) and 94% (95% CI= 89%–97%), respectively, versus 94% (95% CI = 84%–98%) and 97% (95% CI = 92%–99%) in those with longer duration abdominal pain (P = 0.36 and 0.35 for sensitivity and specificity, respectively).[18] This suggests that MRI is accurate for diagnosing acute appendicitis in children presenting with early abdominal pain and may be appropriate as the initial examination in children.

Magnetic resonance imaging for appendicitis, similar to CT, allows comprehensive evaluation and ability to pick up alternative diagnoses in patients found not to have appendicitis because most studies look at the entire abdomen and pelvis. Recent MRI studies found alternative diagnoses in approximately 20% patients, the commonest being adnexal pathology (including ovarian torsion, hemorrhagic cysts), enteritis-colitis, and mesenteric adenitis. Other rare diagnoses included pyelonephritis, obstructive urolithiasis, omental infarction, pneumonia, and malignancy.[19–21]

Technique

The variability in MRI imaging protocols, use of IV contrast, duration of scan, and diagnostic features used for acute appendicitis present a challenge in replicating study results. The other factor limiting the generalizability of these results to broader community practice settings is that almost all of the published studies are single-center studies emanating from academic hospitals with pediatric radiologists experienced in the use of MRI in children.

The features found to have the strongest association with appendicitis on MRI are diameter of greater than 7 mm, periappendiceal fat infiltration, and restricted diffusion of the appendiceal wall.[22] Studies conducted in the context of suspicion for acute appendicitis have reported identifying normal appendix in 60% to 80% of cases. The rate is higher when using 3-T magnets than with 1.5-T magnets and in those with higher body mass index.[20,21,23,24] The studies with nonvisualization of appendix are generally interpreted as negative similar to CT interpretation.

A recent systematic review found variability in the MRI technique used, although nearly all studies included a combination of multiplanar T2-weighted imaging.[16] Most studies used imaging both with and without fat suppression. Half of the studies used contrast.

Use of gadolinium-enhanced versus unenhanced MRI (P = 0.511) was not found to affect the diagnostic accuracy, sensitivity, or the false-positive rate for the identification of appendicitis.[16] Oral contrast material is generally not used in pediatric appendicitis MRI. Another review found half-acquisition single-shot fast spin-echo pulse sequences to be crucial, and balanced steady-state free precession sequences to be noncontributory.[17] They found that most centers used 4-sequence protocols, usually consisting of spectral adiabatic inversion recovery.

Limitations of conventional MRI in pediatric ED practice include the possibility of motion artifacts that occur in uncooperative patients (potentially reduced using short scans and distraction aids), potential need for sedation/anesthesia in children of preschool age and those with suboptimal cooperation (also reduced using short scans and distraction aids), higher costs compared with US or CT, and the feasibility of adding emergency cases in-between routinely booked MRI cases. Thus, for MRI to become a cost-effective and feasible diagnostic strategy, it needs to be of short duration, not require sedation, and must be accessible within an acceptable period. A number of recent studies have shown that all these objectives are achievable. Multiple groups have shown that MRI can be done successfully in most children 5 years and older without sedation, using short 4-sequence protocols with a median scan time of 6 to 15 minutes, to be available 24 hours a day, and the results available in a timely manner.[20,21,23,25–28]

Magnetic resonance imaging studies must also be read in a timely manner by on-call radiologists. A recent study found that although MR-nonexpert radiologists had good sensitivity (0.89) and specificity (0.83) in reading MRI in patients with suspected appendicitis, with good agreement with MR-expert reading (κ = 0.78), they were not at par with expert MR readers (sensitivity = 0.97, specificity = 0.93).[29] The same group has, however, shown that the diagnostic accuracy of inexperienced readers in the evaluation of abdominal MR images for acute appendicitis can be improved after training with direct feedback.[30]

Magnetic Resonance Imaging as First-Line Modality

Three recent studies have established the feasibility of using MRI as the first-line imaging modality for suspected appendicitis in children aged 5 years and older without using sedation or contrast (Table 1).[23,26,27] All showed quick turnaround times using rapid protocols and excellent test characteristics for diagnosing appendicitis.

Magnetic Resonance Imaging as Second-Line Modality as Part of US-MRI Pathway

Herliczek et al[31] examined 60 children who underwent MRI within 24 hours of inconclusive US for suspected appendicitis and found it to have sensitivity and specificity of 100% and 96%, respectively. Aspelund et al[25] showed that a diagnostic imaging pathway using US selectively, followed by MRI in equivocal cases, is feasible and comparable with CT in children with suspected acute appendicitis, with no difference in time to antibiotic administration, time to appendectomy, negative appendectomy rate, perforation rate, or length of stay. Epifanio et al[32] also published their experience with successful use of a diagnostic strategy using clinical findings followed by US and, in selected cases, MRI. Of the 166 patients in the cohort, 47% had acute appendicitis. The strategy under study had a sensitivity of 96%, specificity of 100%, PPV of 100%, NPV of 97%, and accuracy of 98%. In the 8 patients where clinical assessment and US findings were inconclusive, MRI was useful to detect normal and abnormal appendices and valuable to rule out other abdominal pathologies that mimic appendicitis.[32]

Dillman et al[21] published their experience comparing the performance of unenhanced MRI and contrast material-enhanced CT of the appendix, respectively, within 24 hours after an abdominal US examination with results equivocal for appendicitis. They found the diagnostic performance of the 2 strategies to be similar with respect to sensitivity and specificity for diagnosing appendicitis, for diagnosis of appendiceal perforation, as well as for identifying alternative diagnoses.[21]

These studies suggest that MRI may supplant CT as the secondary modality to follow inconclusive appendix sonography.

Financial Analysis

A comprehensive pediatric cost-effectiveness analysis that includes both direct and indirect costs is needed to establish the role of the multiple clinically effective potential imaging pathways—US followed by repeat US, CT with contrast, or MRI in equivocal cases, CT as the primary imaging modality, or MRI as the primary imaging modality. An ultra-fast MRI scan is likely to cost much less than a traditional MRI, and even CT scan, and may be used as second-line modality for cases with an equivocal diagnosis after US, or even as a first line study. The reduced time in the emergency department may make the cost of a pathway with MRI as the primary modality comparable with a 2-step pathway, which involves a wait of 6 to 8 hours to repeat an US.[20] This, and the better test characteristics of MRI as against US, would potentially reduce the expenditure associated with MRI and make it the preferred second-line test. Although the results of MRI and CT are comparable, and the test characteristics of both are independent of duration of abdominal pain, MRI has the advantage of not using contrast or ionizing radiation.

Cobben et al[33] prospectively studied 138 patients with suspected appendicitis (including 38 younger than 20 years) using a simple noncontrast MRI protocol. In addition to establishing the clinical value of MRI, they performed a financial analysis. The use of MRI yielded a calculated net savings of between €55,746 and €72,534 when the costs of unnecessary appendectomies and avoided admissions for observation were considered.[33] Imler et al[34] recently published findings of their study comparing

TABLE 1. Features of 3 Recent Studies Evaluating the Feasibility of Using MRI Without Sedation or Contrast as First-Line Modality in Evaluation of Suspected Appendicitis in Children

Study	Johnson et al, 2012[26]	Moore et al, 2012[27]	Kulaylat et al, 2015[23]
Equipment; technique	3-T; 4-sequence	1.5-T; 4-sequence	1.5/3-T; 4-sequence
No. subjects	42	208	510
Mean age	11.5 y	11.2 y	11.3 y
Median scan time	6 min	12 min	11 min
Median time from request to scan	NA	65 min	71 min
Median time from last sequence to report	NA	46 min	31 min
Sensitivity (95% CI)	100% (93%–100%)	98% (87%–100%)	97% (92%–99%)
Specificity (95% CI)	99% (95%–100%)	97% (93%–99%)	97% (95%–99%)
NPV (95% CI)	100% (97%–100%)	99% (97%–100%)	99% (97%–100%)
PPV (95% CI)	98% (89%–100%)	89% (76%–96%)	92% (86%–96%)

the 2 strategies of US followed by MRI for equivocal cases, versus rapid MRI as the first-line imaging modality. The rapid MRI compared with US group was associated with longer ED length of stay - mean difference 100 minutes (95% CI = 35–169), and increased ED charges - mean difference $4887 (95% CI = $1821–$8,513), showing that rapid MRI protocol needs to become more efficient and less expensive before it can take the role of first-line imaging modality in the diagnosis of appendicitis.[34]

Magnetic resonance imaging for evaluation of appendicitis offers great promise, but it must become more readily available before it will have significant impact. Recent studies have shown promise in using MRI without sedation for children 5 years and older, with quick turnaround times, and with excellent test characteristics. We need multicenter studies, however, to show that these good results can be sustained in real-life use outside academic environments with special interest in using MRI.

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