Seminars in Pediatric Surgery 25 (2016) 198–203

Contents lists available at ScienceDirect

Seminars in Pediatric Surgery

journal homepage: www.elsevier.com/locate/sempedsurg

Overview and diagnosis of acute appendicitis in children

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ARTICLE INFO

Keywords:
Appendicitis
Diagnosis and management
Clinical pathway

ABSTRACT

Appendicitis represents the most common abdominal surgical emergency in the pediatric age group. Despite being a relatively common condition, the diagnosis of appendicitis in children can prove to be challenging in many cases. The goal of this article is to review the predictive utility for presenting signs and symptoms, laboratory tests, and imaging studies in the diagnostic work-up of appendicitis. Furthermore, we sought to explore the predictive utility of composite measures based on multiple sources of diagnostic information, as well as the utility of clinical pathways as a means to streamline the diagnostic process.

Introduction

Abdominal pain is one of the most common chief complaints of children seen in the emergency department, and appendicitis represents the most common abdominal surgical emergency in the pediatric population. Appendicitis occurs in approximately 70,000 children in the United States per year and accounts for approximately one-third of childhood admissions for abdominal pain and nearly 30% of the cumulative cost of all pediatric general surgical conditions combined.[1–4] Despite being a relatively common condition, diagnosis of appendicitis in children can prove challenging in many cases. In a retrospective cohort study of 13,328 patients, Rice-Townsend et al.[5] characterized wide variation in the diagnostic approach to suspected appendicitis among children's hospitals, including a 3.5-fold variation in preoperative imaging and a 5-fold variation in laboratory utilization. According to data from the American College of Surgeon's Pediatric National Quality Improvement Program, 65% of children who underwent appendectomy for suspected appendicitis received a preoperative ultrasound and 42% underwent a computed tomography (CT) scan.[6] Several factors may underlie this practice variation, including differences among hospitals with available resources and in the perceived value of different diagnostic adjuncts used individually and in combination. The goals of this article are to review the available evidence surrounding the predictive value of presenting signs and symptoms, laboratory tests and imaging studies for diagnosing appendicitis. Furthermore, we sought to explore the predictive utility of composite measures based on multiple sources of diagnostic information, as well as the utility of clinical pathways as a means to streamline the diagnostic process.

Diagnosis

Clinical presentation

The classic presentation of appendicitis has been well described, and includes fever, anorexia, nausea, guarding, and migration of pain from the umbilical region to the right lower quadrant.[7] However, the predictive value of these signs and symptoms for appendicitis has been found to be relatively weak in many studies. In one of the largest such studies which included 755 children presenting to the emergency department (ED) with abdominal pain, Becker et al. found that many of these “classic” symptoms were absent in children with pathologically proven appendicitis, including 40% who presented without anorexia, 29% without nausea or a history of vomiting, 50% without pain migration, and 50% without rebound tenderness. Furthermore, the investigators found that these “classic” symptoms were present in many children without appendicitis, including 47% who presented with anorexia, 56% with nausea, 42% with right lower quadrant guarding, and 28% with a history of pain migration.[8] Such “classic” signs and symptoms may have even less predictive utility in younger children due to their limited ability to effectively communicate their symptoms to parents and providers. It is well described that younger children are more likely to present with complicated disease, and this may be in large part related to the difficulty in differentiating early appendicitis from non-surgical causes of pain such as gastroenteritis and viral syndromes.[9]

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http://dx.doi.org/10.1053/j.sempedsurg.2016.05.001
1055-8586/

Laboratory data

White blood cell count and absolute neutrophil count

The utility of white blood cell counts (WBC) and absolute neutrophil counts (ANC) in the diagnosis of appendicitis has been well studied. Elevated WBC and ANC counts can be found in several conditions associated with abdominal pain in children, and up to 20% of patients with pathology-proven appendicitis may present without a leukocytosis.[10] It is therefore not surprising that the reported sensitivity and specificity for WBC in the diagnosis of appendicitis varies widely among studies, ranging from 70% to 80% and 60% to 68%, respectively.[11–15] Similarly, the reported sensitivity and specificity for ANC in diagnosing appendicitis has also varied widely, ranging from 59% to 97% and 51% to 90%, respectively.[1,11,15] The wide range in reported predictive value for these laboratory tests likely reflects the wide variation in pre-test probability among hospitals where these tests were performed. In this regard, the predictive value of WBC for diagnosing appendicitis is likely to be very different for all children evaluated in the ED vs. those where the WBC is only obtained after a surgeon evaluates a child with RLQ pain and feels that the likelihood for appendicitis is high.

C-reactive protein

The reported sensitivity and specificity for C-reactive protein (CRP) in the diagnosis of appendicitis ranges between 58% and 93% and 28% and 82%, respectively.[1,15,16] A total of 2 studies have reported an association between disease severity and CRP level. In a prospective study of 78 patients, Chung et al.[17] reported that patients with perforated appendicitis had a significantly higher mean CRP compared to patients without perforated appendicitis (92 vs. 31 mg/L). In a retrospective study of 200 patients, Grönroos et al.[10] reported that higher levels of CRP were associated with perforated appendicitis and abscess formation. While CRP may be helpful in identifying patients who may have complicated disease (and those who may benefit from additional cross-sectional imaging), its predictive value for appendicitis is limited as a sole diagnostic test. Furthermore, studies have not demonstrated any additional predictive value when obtaining a CRP in addition to a WBC count compared with obtaining a WBC count alone.[18]

Imaging studies

Ultrasound

Due to the relatively poor predictive value associated with clinical and laboratory data, imaging tests are often employed as a diagnostic adjunct for children with suspected appendicitis. In this regard, abdominal ultrasound is relatively inexpensive in comparison to CT and magnetic resonance imaging (MRI), and requires no sedation, ionizing radiation, or contrast agents.[19–21] In a meta-analysis of 26 studies including 7448 patients, Doria et al. reported a pooled sensitivity and specificity for ultrasound of 88% and 94%, respectively. However, a wide range of sensitivities and specificities were found across the 26 component studies, ranging from 44% to 88% and 90% to 97%, respectively, suggesting that the pooled results may not necessarily be generalizable to individual hospitals (Table 1).[22–26]

Despite the benefits of US, the diagnostic utility of the modality may be greatly limited by operator experience and lack of availability at many hospitals during nights, weekends and holidays.[22,27] Several studies have attempted to explore patient-related factors that may contribute to the high variability in diagnostic accuracy for US reported in the literature. In a prospective study of 263 patients, Schuh et al.[28] reported that obesity and low clinical suspicion were independent predictors for a non-diagnostic ultrasound in children with abdominal pain. In a prospective study of 1810 children evaluated with abdominal pain in the emergency department (ED), Bachur et al.[29] reported that the sensitivity of US increased with the duration of abdominal pain, from 81% in patients presenting with less than 12 h of pain to 96% in children with greater than 48 h of pain. The evolution of pain (and therefore inflammatory change which may be visualized on US) may underlie the reported efficacy of serial abdominal US as a strategy to increase its diagnostic accuracy.[30] In a prospective study of 294 children, Schuh et al. reported that interval ultrasound in patients with an equivocal initial study and ongoing clinical suspicion was associated with a sensitivity and specificity of 97% and 91%, respectively, compared to 80% and 39%, respectively, for the initial ultrasound. The authors reported a negative appendectomy rate of 4.8% and a mean time from the initial ultrasound to the interval study of 9.2 h.[30]

Other studies have attempted to explore operator-dependent factors associated with improved diagnostic accuracy. In a retrospective study of 1009 patients, Trout et al.[31] reported that dedicated pediatric sonographers were able to identify the appendix at a significantly higher rate compared to sonographers who imaged both pediatric and adult patients (39% vs. 19%). In a prospective multi-center study of 2625 patients, Mittal et al. reported a pooled sensitivity and specificity for ultrasound of 72.5% and 97%, respectively. When the investigators examined ultrasound performance at the level of individual hospitals, they found that sensitivity was higher at hospitals with more frequent utilization (78% at hospitals that used ultrasound in $\geq$ 89% of cases of suspected appendicitis vs. 35% at hospitals that used US in less than 10% of cases), suggesting that increased utilization may be important for negotiating the "learning curve" associated with effective US utilization. In contrast, specificity was relatively high across all hospitals (96–99%), suggesting improvement with experience was most important for the ability to diagnose appendicitis when present, rather than avoiding a false positive (and operating on such findings) in the absence of appendicitis.[26] In a prospective cohort study of 2337 patients, Nielsen et al.[32] reported that the sensitivity and specificity of ultrasound examinations for suspected appendicitis increased from 67% to 92% and 97% to 98%, respectively, following implementation of a standardized ultrasound reporting template.

Table 1
Reported sensitivities and specificities associated with the use of abdominal ultrasound in the diagnosis of appendicitis in children.

Study	Patients (*n*)	Study design	Sensitivity (95% CI)	Specificity (95%)
Garcia Peña et al.[23]	139	Retrospective cohort	0.44 (0.29–0.59)	0.93 (0.89–0.99)
Doria et al.[22,a]	7448	Meta-analysis	0.88 (0.86–0.90)	0.94 (0.92–0.95)
Mittal et al.[26]	2625	Prospective cohort	0.73 (0.59–0.86)	0.97 (0.96–0.98)
Yu et al.[24]	2643	Meta-analysis	0.87 (0.86–0.88)	0.90 (0.89–0.91)
Weston et al.[25]	5060	Meta-analysis	0.88 (0.87–0.90)	0.92 (0.91–0.93)
Orth et al.[44]	81	Prospective cohort	0.90 (0.74–0.94)	0.86 (0.74–0.94)

[a] Meta-analysis.