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REVIEW ARTICLE

Pediatric appendicitis: state of the art review

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Abstract Appendicitis is a common cause of abdominal pain in children. The diagnosis and treatment of the disease have undergone major changes in the past two decades, primarily as a result of the application of an evidence-based approach. Data from several randomized controlled trials, large database studies, and meta-analyses have fundamentally affected patient care. The best diagnostic approach is a standardized clinical pathway with a scoring system and selective imaging. Non-operative management of simple appendicitis is a reasonable option in selected cases, with the caveat that data in children remain limited. A minimally invasive (laparoscopic) appendectomy is the current standard in US and European children's hospitals. This article reviews the current 'state of the art' in the evaluation and management of pediatric appendicitis.

Keywords Appendicitis · Appendectomy · Scoring system · Laparoscopy · Abscess · Children · Pediatric · Non-operative management · Abdominal pain · Right lower quadrant

Abbreviations

AIR	Appendicitis inflammatory response
BMI	Body mass index
CI	Confidence interval
CRP	C-reactive protein
CT	Computed tomography
ED	Emergency department
GALT	Gut-associated lymphoid tissue
ICU	Intensive care unit
IR	Interventional Radiology
LOS	Length of stay
LR	Likelihood ratio
MRI	Magnetic resonance imaging
NPV	Negative predictive value
NSQIP	National Surgical Quality Improvement Program
PA	Perforated appendicitis
PAS	Pediatric Appendicitis Score
PHIS	Pediatric Health Information Systems
PPV	Positive predictive value
RCT	Randomized controlled trial
SSI	Surgical site infection
US	Ultrasound
WBC	White blood cell

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History

Appendiceal disease has a long and interesting history (Tables 1, 2) [1–4]. The first successful appendectomy was done nearly 300 years ago, and it became the accepted treatment for appendicitis at the beginning of the twentieth century.

Pathophysiology

The etiology of appendicitis is still largely unknown despite being such a common condition. Luminal obstruction from stool, appendicoliths, lymphoid hyperplasia, or neoplasm is a factor in about half the cases [5, 6], but it does not explain the increased incidence in summer [7, 8], or racial/geographic variations [9].

Table 1 History of appendicitis

Year	Event
1492	The appendix is depicted clearly in drawings by da Vinci
1521	Jacopo Berengario da Carpi first described the appendix
1711	Lorenz Heister describes perforated appendix with abscess
1735	The first successful appendectomy was performed by Claudius Amyand
1812	John Parkinson provided a description of fatal appendicitis
1800s	Surgeons began draining localized abscesses from appendicitis[a]
1880	Robert Lawson Tait made the first diagnosis of appendicitis and surgically removed the appendix
1886	Reginald Heber Fitz published a study on appendicitis and named the procedure an appendectomy. This was the first use of the term 'appendicitis' (Gr. suffix with Latin stem)
1893	McBurney proposed his original muscle splitting operation
1889	2500 articles or books dealing with the appendix had been published. By 1950, more than 13,000 articles or books dealing with the appendix had been published
1981	Kurt Semm performed the first laparoscopic appendectomy

[a] In the early 1800s, French physicians reported cases of perforated appendicitis and suggested surgical removal of the appendix. However, they were strongly opposed by the famous Baron Guillaume Dupuytren, who felt that the origin of *right lower* abdominal pain was the cecum, not the appendix. He was apparently a quarrelsome and difficult individual: "I have been mistaken, but I have been mistaken less than other surgeons [155]"

Table 2 Famous historical figures with appendicitis

Person	Year
Harvey Cushing (physician)[a]	1897
King Edward VII (Eng)[b]	1902
Walter Reed (physician)	1902
George Ryerson Fowler (surgeon, Fowler's position)	1906
Frederick Remington (artist)	1909

[a] Operated (successfully) by Halstead for appendicitis

[b] Edward delayed his coronation when told by Sir Frederick Treves (physician to the 'Elephant Man') that if he refused operation for his appendicitis and went anyway, "Then Sir, you will go as a corpse [156]." Notably, Treves' daughter also died of appendicitis many years later

Genetic, environmental, and infectious etiologies (bacterial, viral, fungal, and parasitic) have been implicated in appendicitis [10, 11]. A family history is associated with a nearly threefold increased appendicitis risk [9]. Genetic factors may account for 30 % of appendicitis risk [12]. Data from 23andMe were analyzed for genetic heritability of appendicitis. A GWAS (genome-wide association study) was done in 18,773 self-reported appendectomy cases and compared to 114,907 controls. One locus had genome-wide significance, and a candidate gene (PITX2) was identified which was associated with a protective effect for appendicitis [13].

Function

The appendix may serve as a 'safe house' for normal intestinal flora, potentially repopulating normal microbial balance after diarrheal illnesses [6, 14]. The appendix has the highest concentration of gut-associated lymphoid tissue (GALT) in the intestine. GALT's function is poorly understood. Appendectomy decreases the risk of ulcerative colitis, and increases the risk of recurrent *Clostridium difficile*-associated colitis [5, 6].

Epidemiology

Between 60,000 and 80,000 pediatric appendectomies are performed annually, with a mean cost of about $9000 [15]. The estimated lifetime risk of appendicitis is 7–9 % [16–18]. The U.S. incidence of appendicitis is $\sim$1 per 1000 [19] and is increasing [5, 16, 20]. The incidence is higher in South Korea [21] and lower in Africa [22]. The peak incidence occurs between 10 and 19 years of age [5, 16, 17], and mean age at diagnosis is increasing [19]. Appendicitis is less common in very young children; preschool-aged children account for 5 % of cases [23]. There is a male preponderance (55–60 %).

Appendicitis is increasing in Hispanics, Asians, and Native Americans, while the rates in Whites and African–Americans have declined [19, 24]. In large database analyses, African–American and Hispanic children presented with perforation more often than other racial groups [25] and had longer hospital stays and more complications, even after adjusting for perforation. African–American and low-income children had increased odds of PA, less imaging, more ICU admissions, and longer hospitalizations [26].

The percentage of appendicitis that is perforated varies widely from 15 to 50 % [16, 19, 24, 27–30]. The incidence of perforation also depends on age, gender, socioeconomic status, and ethnic/racial background [31, 32], as well as the definition of 'perforation.' The currently accepted definition is a hole in the appendix or an appendicolith in the abdomen [33].

Diagnosis

There are two aspects to the diagnosis of appendicitis: detecting the disease and identifying perforation. The advent of antibiotic-only treatment increases the importance of the latter distinction. There is significant variation in methods of diagnosis and treatment of appendicitis among hospitals [34]. However, negative appendectomy rates have decreased to under 5 % [30, 31, 35–37].

Symptoms and signs

An experienced clinician can achieve over 90 % accuracy in the diagnosis of appendicitis [38]. The most common presenting symptom is gradual onset of abdominal pain migrating from a periumbilical location to the right lower abdomen. Nausea, vomiting, anorexia, fever and diarrhea may follow. PA is uncommon in children ill for less than 24 h, and is usually present after 48 h of symptoms. Perforation may be initially accompanied by a slight decrease in pain, which then may become more diffuse unless the perforation is contained.

Common physical signs include tenderness in the right lower abdomen, rebound tenderness or guarding, abdominal distention, and fever. Rovsing's sign (right-sided pain from left lower abdominal palpation), obturator sign (pain with flexion and internal rotation of the right hip), psoas sign (pain with left side down right hip extension), Dunphy's sign (pain with coughing), or a positive Markle test (pain with heel-drop) may all be seen in acute appendicitis. A mass may be palpable in advanced disease, and the child may be febrile and ill-appearing, preferring to avoid movement.

Classic symptoms and signs are present in less than half of children [39, 40], and in very young children, the diagnosis can be particularly difficult. Over 80 % of children under 3 years of age present with PA [40].

Mid-abdominal pain migrating to the right lower quadrant had a likelihood ratio (LR) of 1.9–3.1 for appendicitis, and fever an LR of 3.4. Absence of fever lowered the likelihood of appendicitis by two-thirds [39]. The only physical finding correlated with an increased likelihood of appendicitis was rebound tenderness (LR 2.3–3.9). Absence of tenderness in the right lower quadrant resulted in a 50 % decrease in the likelihood of appendicitis [41–43].

Pediatric appendicitis risk scores

Scoring systems help to estimate the risk of appendicitis by combining the predictive value of clinical symptoms, physical exam findings, and laboratory data to maximize the diagnostic information considered individually [44]. In 1986, Alfredo Alvarado described a 10-point scoring system (Table 3) for acute appendicitis [45]. The Alvarado score differs from the PAS score (below) to include points given for leukocytosis and in the assessment of abdominal pain on physical exam. A meta-analysis of 42 studies found that a score <5 ruled out appendicitis with a pooled sensitivity of 99 % (95 % CI 97–99 %) and specificity of 43 % (CI 36–51 %) [17]. The overall sensitivity and specificity was slightly greater than 80 %, with inconsistency in children and over-estimation in women [17]. Other reports confirm the utility of the Alvarado score in eliminating the diagnosis in children with a score <5, and the lower accuracy in younger children [46, 47].

Table 3 Alvarado Score, also known as the MANTREL score (Migration of pain, Anorexia, Nausea, etc.—an acronym of the eight components of the scoring system)

Migration of pain	1
Anorexia	1
Nausea	1
Tenderness in RLQ	2
Rebound pain	1
Increase in temperature (>37 °C)	1
Leukocytosis (>10,000/μL)	2
Left shift in WBC count	1
Polymorphonuclear neutrophilia (>75 %)	
Total	10

Scores are categorized as: low probability of appendicitis (1–4 points); intermediate (5–6); or high (7–10)

In 2002, Samuel described the Pediatric Appendicitis Score, (Table 4) specifically designed for children aged 4–15 years, and based on 1170 children from Great Ormond Street [42]. The PAS is a ten-point score comprising eight elements which include symptoms, physical examination findings and WBC data (Table 4). Scores from 4 to 7 indicate a 'gray zone' where further testing/imaging is indicated. In the original study of the PAS score, the author reported a 100 % sensitivity and 92 % sensitivity for PAS in diagnosing appendicitis when using a scoring threshold of 6 points or higher [42]. The reported sensitivities and specificities are approximately 70–80 % [42, 48–52]. The authors' institution uses the PAS score as part of the emergency room workup to evaluate a patient with suspected appendicitis, in order to rely on the least amount of laboratory/subjective information.

The Appendicitis Inflammatory Response (AIR) score consists of eight variables based on weighted ordered logistic regression analysis [53, 54] (Table 5). The area under the receiver operating characteristic curve of the AIR score was 0.96 in 941 patients with suspected appendicitis, versus 0.82 for the Alvarado score. The AIR score may be preferable in young children since the Alvarado score requires children to identify nausea, anorexia, and migration of pain [54]. The Alvarado score compares more favorably to the AIR score in adolescents.

Scoring systems have been successfully used to differentiate simple acute appendicitis from PA, but the quality of data is poor and no particular system is widely accepted.

Table 4 Pediatric Appendicitis Score (PAS)

Parameter	Score
Migration of pain	2
Anorexia	1
Nausea/emesis	1
Tenderness in right lower quadrant cough/hopping/percussion	2
Cough/percussion tenderness	1
Fever	1
Leukocytosis (>10,000/µL)	1
Left shift of WBC count	1
Polymorphonuclear neutrophilia (>75 %)	
Total	10

Table 5 Appendicitis Inflammatory Response (AIR) score

Component	Score
Vomiting	1
RLQ Pain	1
Rebound or guarding, mild	1
Rebound or guarding, moderate	2
Rebound or guarding, severe	3
$T > 38.5$	1
WBC 10,000–14,900	1
WBC ≥15,000	2
CRP 10–49 g/L	1
CRP ≥ 50 g/L	2
Total	12

0–4 low probability. Outpatient follow-up if unaltered general condition, *5–8* indeterminate group. In-hospital active observation with re-scoring/imaging or diagnostic laparoscopy according to local traditions, *9–12* high probability. Surgical exploration is proposed

However, using clinical, laboratory, and radiographic (both CT and US were evaluated separately) scoring systems allowed differentiation of simple and PA with an NPV of 95 % (CT) and 97 % (US) in one recent study [55].

Appendicitis risk scores are neither sensitive nor specific enough to be effective diagnostic tools in isolation. Scoring is best used as a screening adjunct to identify moderate-to-high-risk patients for additional imaging or surgical consultation, as many children without appendicitis will meet the scoring threshold and potentially be at risk for a negative appendectomy.

Biomarkers

Biomarkers include laboratory studies such as WBC count and differential, C-reactive protein (CRP), bilirubin, procalcitonin and other measures. They can be used to: (1) diagnose acute appendicitis, (2) differentiate simple acute appendicitis from PA, (3) predict failure of attempted antibiotic-only management of acute appendicitis, and (4) predict postoperative complications.

Acute appendicitis

No single biomarker or combination of laboratory studies has adequate sensitivity or specificity for the diagnosis of appendicitis [39, 56–58]. However, in combination with clinical and radiographic factors, they are a part of every appendicitis scoring system. PPV and NPV were calculated from over 1000 patients with possible appendicitis in an international study. 580 (57 %) were eventually found to have appendicitis [59]. No combination of WBC count or CRP level resulted in an NPV of more than 90 % or a PPV of >80 %, regardless of the duration of symptoms. However, 1 % of the study group (WBC count >20,000 and symptoms >48 h) had a PPV of 100 %.

Antibiotic-only therapy

A recent use of biomarkers is monitoring patients managed with antibiotics-only, to identify those more likely to fail medical management [60]. In adult studies, WBC count >18,000 cells/uL or CRP >4 mg/dL have variously been reported as predictive of failure [15, 61–64].

Differentiation of simple versus complex appendicitis

WBC count, CRP, and procalcitonin have been used to differentiate simple from perforated appendicitis [59, 65–67]. Serum bilirubin, CA-125, and hyponatremia have also been reported to be markers of complex appendicitis [68, 69]. Better predictive models also include clinical and radiographic data [66].

Predictor of complications

Many pre-operative predictors of postoperative complications have been suggested: high CRP, high WBC, and appendiceal size [70, 71]. However, many of these markers may actually be differentiating simple and perforated appendicitis, the latter with a much higher complication profile [72].

Radiographic studies

The use of radiographic adjuncts in the diagnosis of appendicitis has evolved over the last few decades. Widespread use of CT scans for appendicitis in children peaked in the late 1990s to approximately 2010 [35, 44, 73].

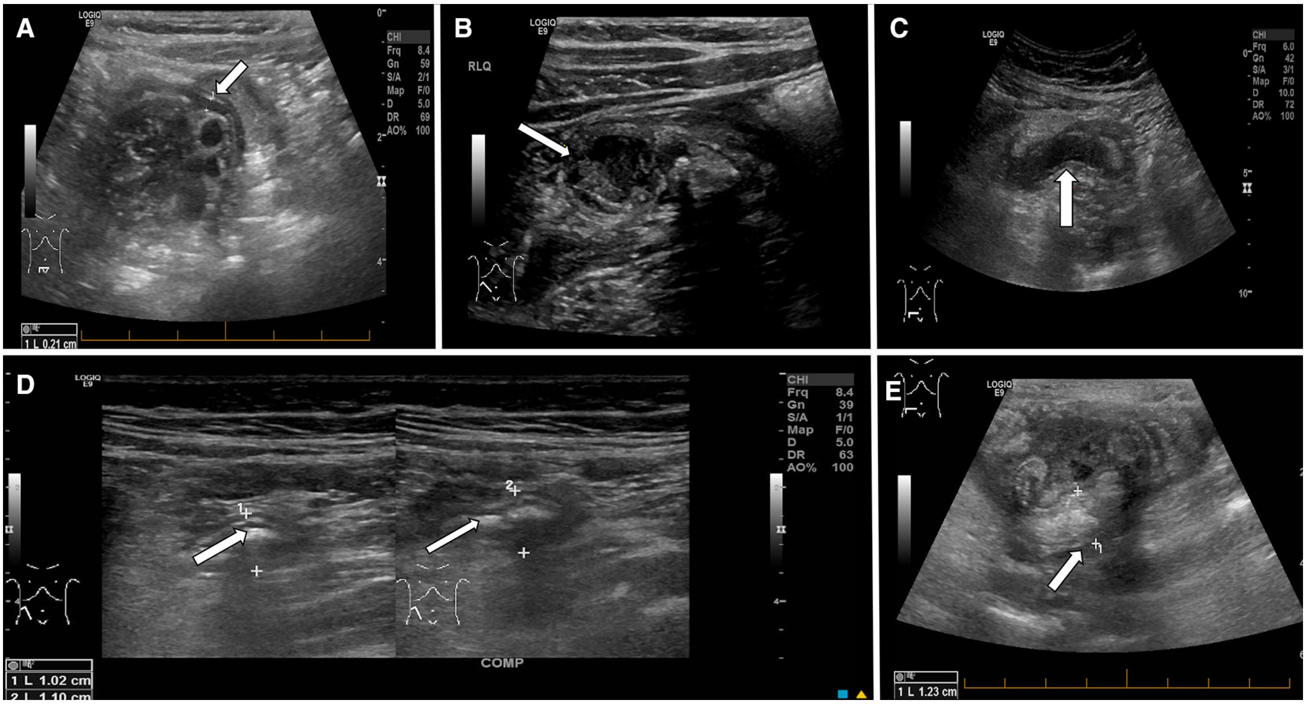

Fig. 1 Ultrasound imaging of the appendix. **a** Category 1 US (normal appendix without secondary findings). **b** Category 3 US (appendix non-visualized, but positive secondary findings with inflammatory changes). **c** Category 4 US, with a non-compressible, thickened appendix (*arrow*). **d** Category 4 US, with a non-compressible, thickened appendix and a shadowing appendicolith (*arrows*). **e** US demonstrating appendiceal perforation with hyperechoic enlarged appendix surrounded by heterogeneous fluid collection/abscess and surrounding inflammatory change

Recognition of the radiation risks led to a transition from CT scans to US. A 2015 review of more than 50,000 children with appendicitis found that about half did not have *either* a CT scan or US. 31 % had an US only, 16 % a CT scan only, and about 5 % had both [74]. There was a 46 % increase in the use of US alone and a 48 % decline in CT scans during the four-year study interval. Negative appendectomy rates decreased, while the proportion with PA and those with ED revisits did not change.

Ultrasound

Advantages of US include low cost, ready availability, rapidity, and avoidance of sedation, contrast agents, and radiation exposure. It is currently the imaging study of choice in children with an equivocal diagnosis. Standardized reporting protocols are very useful, particularly in indeterminate cases or those with appendiceal non-visualization [75, 76].

Sensitivity and specificity are approximately 88 and 94 % [77–80], but US is very operator-dependent and results are widely variable. Visualizing the appendix is difficult in obese individuals or those with low clinical suspicion. US sensitivity and specificity can be improved by increasing minimum appendix thickness for diagnosis from 6 to 7 mm, having dedicated sonographers, repeating questionable studies after several hours, and altering the study population (increased accuracy correlates with longer pain duration) [81–84].

US reports should have a description of the findings, and are usually categorized (Fig. 1a–e): Category 1: Appendix visualized, normal; Category 2: Non-visualized appendix, no secondary signs of appendicitis; Category 3: Non-visualized appendix with secondary signs; and Category 4: Clear appendicitis with or without abscess. The appendiceal non-visualization rate ranges from 25 to 60 % [76, 85]. The NPV for Category 1 and 2 studies is 95–99 %.

CT scan

CT scans are readily available, rapidly completed, and highly accurate (Fig. 2a–c). A meta-analysis of 2500 patients found a consistent sensitivity and specificity of approximately 95 % [78]. CT scans are more accurate when IV contrast is given, but GI contrast is unnecessary [86, 87]. Appendiceal non-visualization has a high (98.7 %) NPV [88]. CT is much less accurate in identifying perforation (sensitivity 62 %, specificity 82 %) [89].

The risk of future malignancy in children from ionizing radiation is increased but unknown. Population-based

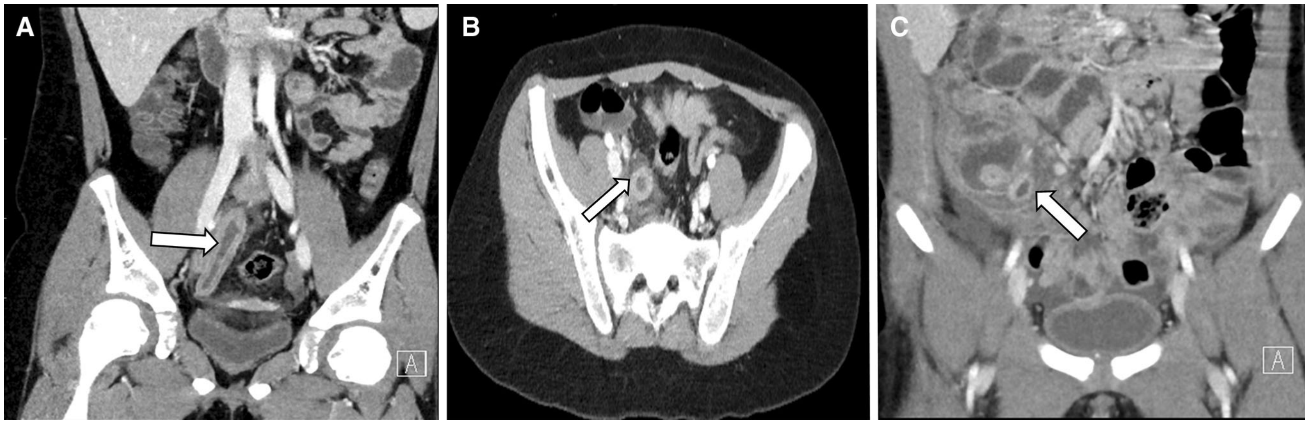

Fig. 2 CT scan of appendicitis. **a** CT scan, sagittal view, with an inflamed acute appendicitis (*arrow* demonstrates the appendix). **b** CT scan with acute appendicitis (*arrow* demonstrates appendix). **c** CT scan, sagittal view, with perforated appendicitis and phlegmon (*arrow*)

estimates are 13.1 to 14.8 malignancies per 10,000 abdominal CT scans for boys, and nearly double that for girls [90]. Strategies to diminish this risk include decreasing: (1) the use of CT scans in suspected appendicitis, (2) the radiation dosage used, and (3) the size of the exposed area (focused scans) and (4) the number of images [91].

There is significant institutional variation in the use of CT scans for suspected appendicitis. A review of 2538 children identified significantly higher odds of CT use in adult hospitals and lower rates of concordance [92]. More than 99 % of children in adult institutions had some form of pre-operative imaging. Radiation exposure per scan is also higher in adult hospitals. Lower tube kilovoltage and altered technique in pediatric abdominal CT for appendicitis resulted in a greater than 60 % reduction in radiation dose, while preserving diagnostic accuracy [93, 94]. Larger and older children required more radiation.

CT scan has a sensitivity of appendiceal perforation [95]. The accuracy of positive predictive value for detecting appendiceal perforation by CT scan was 67 % following review of 200 CT scans obtained for appendicitis [89]. The study concluded that the triage of patients based on pre-operative CT scans is imprudent.

Multiple studies have documented a reduction in both CT and US with a clinical pathway or scoring system while maintaining a low negative appendectomy rate [96–98].

MRI

MRI is infrequently obtained in suspected appendicitis, although its use is increasing. In a 2015 review of 52,275 children with appendicitis, only 0.2 % underwent MRI [81]. Nonetheless, the sensitivity, specificity, and accuracy are excellent [99–101]: the sensitivity was 96.8 %, specificity 97.4 %, PPV 92.4 %, NPV 98.9 %, and false-positive rate 3.1 % in a series of 510 children [102].

MRI availability, scan time, motion sensitivity, and cost are factors responsible for its lack of use. Improved MRI technology with faster imaging times, better resolution, lower cost, and increased availability makes it an increasingly attractive option [103].

Combining laboratory, clinical scores and ultrasound data

The combined predictive value of laboratory and ultrasound data for the diagnosis of appendicitis was retrospectively reviewed in 845 patients presenting for surgical consultation of possible appendicitis [56]. A high rate of equivocal ultrasounds with a lack of secondary signs of appendicitis was demonstrated (50 %). In this group, appendicitis was 18 % for those with an equivocal study but decreased to 3 % in the absence of leukocytosis (WBC <9000/uL and PMN <65 %) and increased to 48 % when leukocytosis was present [56]. The reverse, however, was found to be true as well in that US with secondary findings and leukocytosis were predictive of appendicitis approximately 79–97 % of the time. The authors concluded that they were not able to generate specific thresholds or cutoffs as these are institution-specific thresholds. However, by creating and combining US and laboratory data, high- and low-risk patients were identified where further imaging and observation is low yield, but also patients who are particularly at high risk for negative appendectomy [44, 56].

Clinical pathways

The goal of a clinical pathway is to standardize care, improve outcomes and reduce resource utilization in carrying out a diagnostic or treatment care plan [44]. A process of care and resource utilization efficiency can be streamlined by a clinical pathway. Using appendicitis risk scores, laboratory and selective imaging many clinical pathways for appendicitis have demonstrated improved diagnostic ability of appendicitis, decreased CT scan utilization (<6.6 %) and cost of hospital stay without negatively changing time to appendectomy or negative appendectomy rates [56, 104, 105].

Diagnosis: summary

A reasonable diagnostic approach is an initial history and physical examination by an experienced clinician and a WBC and differential. A standardized scoring system is useful. With an equivocal exam or score, US is the best initial imaging study. CT scan is a conditional alternative which may be useful when the clinical picture is confusing. We currently use the algorithm shown in Fig. 3.

Treatment

Laparoscopic appendectomy is currently the most common surgical approach, with open appendectomy markedly declining [106, 107]. Over the past 2–3 decades, length of hospital stay for both simple and PA has decreased. Appendectomy for simple acute appendicitis is now an outpatient procedure at many children's hospitals [20, 24] and the length of stay for PA averages 4–5 days.

Antibiotics-timing and choice

Antibiotics are initiated once the diagnosis of appendicitis has been made. For more than 30 years, pediatric surgeons used a triple-antibiotic regimen when dealing with appendicitis, consisting of ampicillin, gentamicin, and clindamycin [108]. With changes in adult antibiotic regimens, pediatric surgery has also changed to include simpler single-drug regimen, and has been demonstrated to be at least as efficacious [109]. In general, broad-spectrum coverage is recommended before operation. We prefer a single dose of Rocephin and Flagyl. We do not re-administer medication at the time of surgery as the patients are viewed as already on antibiotic prophylaxis for the operating room.

Non-operative management of appendicitis

A recent trend is non-operative management of children with acute uncomplicated appendicitis, prompted by: (1) successful management of diverticulitis, complications of Crohn's disease, gynecologic infections, and necrotizing enterocolitis with antibiotics alone, (2) antibiotic-only treatment of children with PA, (3) adult RCTs using antibiotic-only therapy for acute appendicitis with success rates of 70–85 [15], and (4) potential avoidance of postoperative complications and general anesthesia.

A meta-analysis of five adult trials (980 patients) concluded that non-operative management had fewer complications, better pain control, and shorter sick leave, but a high rate of recurrence compared to appendectomy [64, 110–113]. Antibiotic regimens varied, but most consisted of an initial 1–2 days of cefotaxime and metronidazole (or tinidazole), followed by either amoxicillin/clavulanic acid or ciprofloxacin with metronidazole (or tinidazole).

Other adult RCTs (NOTA, Non Operative Treatment for Acute Appendicitis from Italy in 2014 and the Finnish Appendicitis Acuta, APPAC) had a 13.8 % recurrence rate at 2 years, and a 27.3 % appendectomy rate at 1 year, respectively [61, 63].

The literature on the use of non-operative management of pediatric appendicitis is evolving (Table 6) [65, 114–122]. Most studies are very recent with only small numbers of patients. The long- and short-term failure rates in children are not well known. National and international multicenter RCTs of non-operative management for pediatric appendicitis are currently underway.

An appendicolith has been an adverse indicator for antibiotic-only treatment in many reports [122–124]. Abdominal pain for >48 h; WBC >18,000 and/or pronounced bandemia; CRP >4 mg/dL; and signs of bowel obstruction, abscess or phlegmon on imaging are also markers of non-operative failure [61–64, 111, 113, 125].

Parenteral and patient understanding of appendicitis may sharply differ from that of the clinician. It is a common misperception (82 % of 100 patients and caregivers) that delay in appendectomy is likely to lead to a ruptured appendix, with a high likelihood of major complications or death [126]. The authors pointed out that, in fact, death from a lightning strike is about 2.5 times more likely than from appendicitis.

Surgery

Incidental appendectomy

Incidental appendectomy is infrequent. More accurate diagnostic techniques for appendicitis, the advent of laparoscopy, and use of the appendix for urinary reconstruction or access for antegrade enemas have largely eliminated this procedure. However, Ladd's procedure for malrotation, Meckel's diverticulectomy, and surgical

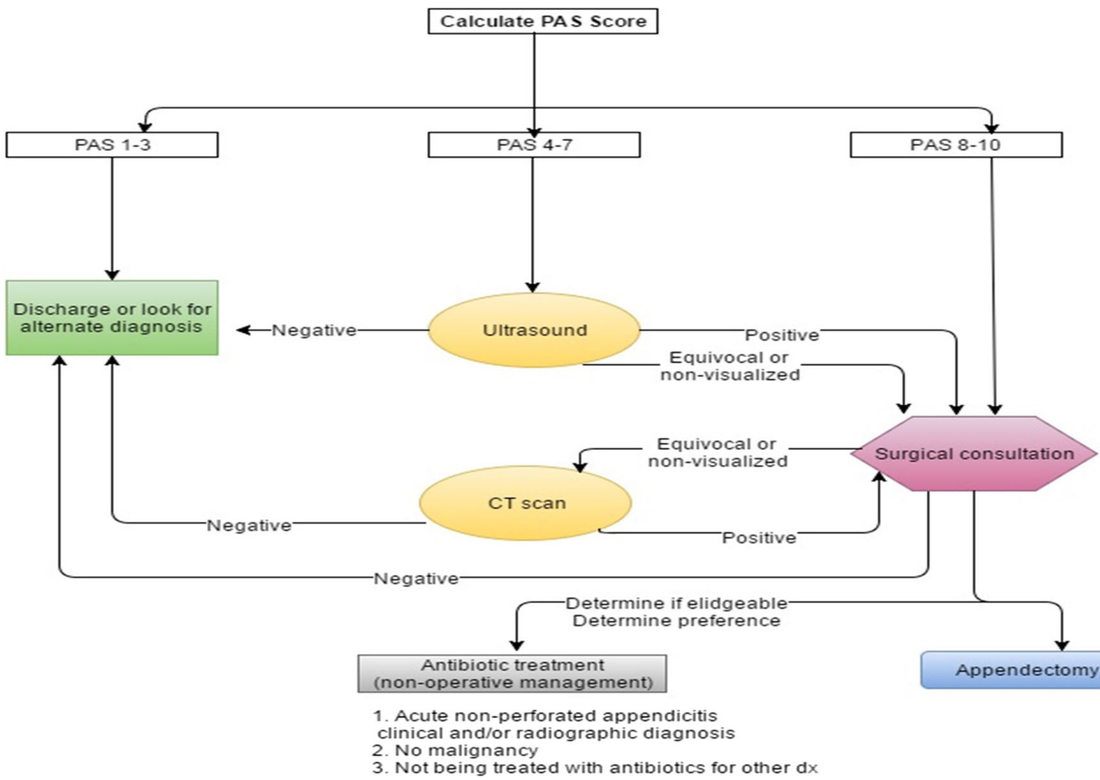

Fig. 3 Clinical pathway (algorithm) for the diagnosis of appendicitis

reduction of intussusception may still include incidental appendectomy. An estimated 36 incidental appendectomies are required to prevent one case of appendicitis [24].

Operative timing

Duration of symptoms is often hard to accurately quantitate, but a correlation with perforation is well accepted. The relationship between operative delay (time from ED arrival until operation) and outcome is unclear. An increased risk of SSI (surgical site infection) [127] or perforation [128] with longer delays was initially reported. However, most centers avoid middle-of the-night operations in favor of admission and surgery the next day [129]. A 2014 report studied 2510 patients with acute appendicitis and found that delays less than 24 h were not associated with increased rates of perforation, gangrene, or abscess [130]. A meta-analysis of 11 other non-randomized studies consisting of 8858 total patients concluded that a delay of 12–24 h did not increase the risk of PA. A recently published study evaluated a prospective cohort of 7548 adults undergoing appendectomy at hospitals across Washington State and related that overall, 63 % of patients presented between noon and midnight. Interestingly, they demonstrated that most patients with appendicitis presented in the afternoon/evening and that socioeconomic characteristics did not vary with time-of-presentation. Patients who presented during the workday were more often perforated [131]. Another recent review found no increased SSI risk after 16-h delay from ED presentation, or a 12-h delay from admission to appendectomy [132]. Since many children (70–85 %) with acute appendicitis can be successfully managed with antibiotics alone, it is logical to assume that the key interval is onset of symptoms to administration of IV antibiotics, not symptom onset to appendectomy.

Appendectomy for acute appendicitis

The patient is admitted after the diagnosis is made, and if otherwise healthy and the operative schedule permits ('daytime hours'), laparoscopic appendectomy is done electively that day with same-day discharge as the norm. Children who present 'after hours' are admitted overnight, hydrated, and given the same antibiotic regimen. At our institution, a single dose of ceftriaxone and metronidazole is administered IV after the diagnosis and prior to operation, and no further antibiotics are given unless a 24-h interval has passed (rare). Elective operation is done the next morning or early afternoon, and then, the child is discharged later that day. This general protocol is a very common approach in many children's hospitals. Currently, we have not analyzed or evaluated if there was a cost associated with an overnight stay prior or after to a

Table 6 Summary of studies of non-operative management of pediatric appendicitis

Year	Author	Origin	Study design	Comparison study	*N*	Success rate (%)	Length of FU (months)
2004	Kaneko [117]	Japan	Prospective cohort, NR	No	22	73	36
2007	Abes [114]	Turkey	Retrospective cohort	No	16	87	12
2014	Armstrong [115]	Canada	Retrospective cohort	Yes	12	75	6.5
2014	Koike [118]	Japan	Retrospective cohort, parent preference	No	130	81	30.6
2015	Gorter [65]	International	Prospective cohort, NR	Yes	25	92	2
2015	Hartwich [116]	USA	Prospective parent preference feasibility, NR	Yes	24	71	14
2015	Svensson [121]	International	Pilot RCT	Yes	24	63	12
2015	Steiner [120]	Israel	Prospective cohort, NR	No	45	83	14
2015	Tanaka [122]	Japan	Prospective cohort, parent preference	Yes	78	71	51.6
2016	Minneci [119]	USA	Prospective parent preference	Yes	37	76	12

Success rate did not require appendectomy, *Comparative* included a comparison group who underwent appendectomy, *NR* non-randomized

laparoscopic appendectomy for non-perforated appendicitis. As many hospitals continue to keep children overnight following surgery, we believe the cost to the family is included in the global operative cost.

Appendectomy for perforated appendicitis

Children with PA have two primary management options, early appendectomy (EA) after hydration/resuscitation and administration of antibiotics; or initial antibiotic-only treatment (with or without IR abscess drainage) followed by interval appendectomy (IA) in 6–10 weeks. IA advocates cite the difficulty of appendectomy in a hostile abdomen (abscess, phlegmon, and severe inflammation) [133]. In contrast, IA is usually an outpatient procedure. The need of IA in retrospective studies has shown that up to 80 % of children may not require appendectomy and that 3 % of patients suffer a complication secondary to IA [134]. More recent prospective studies have shown a recurrence rate of 8–43 % with an increased rate of reoccurrence among patients with appendicolith [135, 136]. EA proponents point to immediate one-step definitive treatment, and feel that the increased difficulty of the operation is rarely clinically significant. Initial abscess drainage also incurs significant cost and non-trivial risks of visceral perforation, bleeding, fistula, and soft tissue abscess [137]. A third option is initial non-operative management with elimination of the interval appendectomy. Surveys show that pediatric surgeons choose this option infrequently [138].

Distinguishing acute appendicitis from PA can be difficult. Laboratory studies are imprecise, and even CT scans predict perforation with poor accuracy [89]. Delaying surgery for false-positive ‘perforations’ may result in prolonged hospitalization, needless days of IV antibiotics, and IA for what could have been a 30-min operation with same-day discharge.

A 2016 meta-analysis of two pediatric RCTs comparing EA to IA found that EA reduced the odds of an adverse event, unplanned readmission, and total charges in children without a well-defined intra-abdominal abscess. There was no significant difference in outcomes for children with an abscess [137, 139, 140].

Surgical technique

Laparoscopic appendectomy can be performed with an umbilical camera via a 5- or 10-mm port, and two lower abdominal ports or stab incisions. Single-incision laparoscopy (SILS) is an alternative whereby instruments are also placed through the umbilical camera port with the appendix removed either intra- or extra-corporeally. Similar outcomes are obtained, and long-term cosmetic differences are minimal [141–143]. Many interventions once widely used in the treatment of appendicitis including intra-abdominal drains, prolonged nasogastric and Foley catheter drainage, wound packing, central lines and parenteral nutrition are all very rarely used nowadays.

Antibiotics after discharge

Home antibiotics are unnecessary after appendectomy for simple acute appendicitis. Administration of antibiotics after hospital discharge for PA has changed. Oral and IV administration are equivalent [144–147], and the duration of treatment has decreased. A prospective study of 540 children with PA found that those meeting discharge criteria with normal WBCs after 5 days of IV antibiotic therapy can be safely discharged without oral antibiotics [148].

Complications

The overall complication rate is approximately 10–15 % [149, 150]. A superficial SSI occurs in about 1–3 % of children after laparoscopic appendectomy [150]. The incidence of superficial SSI is lower in laparoscopic appendectomy compared to open; the rate of intra-abdominal abscess is similar [16, 151, 152]. The readmission rate is 5–10 %, most commonly for infection, followed by bowel obstruction or ileus and pain or malaise. Less than 1 % require reoperation (excluding IR abscess drainage) [150]. Mortality after appendectomy is quite rare (~0.1 % or less) [24, 150].

Postoperative intra-abdominal abscess develops in approximately 15–20 % of children with PA, and 1 % of non-perforated appendicitis [33, 34, 153]. Increasing age, weight and BMI correlate with the risk of a postoperative abscess, as does the presence of diarrhea at presentation. The only admission CT finding found to predict abscess was the presence of a high-grade obstruction [154].

The timing of abscess development is variable. There is a progressively increasing positive correlation between postoperative abscess and the maximum temperature each successive day, significant after the third day. Many centers wait until postoperative day seven to radiographically evaluate for abscess. Mildly delaying diagnostic evaluation results in fewer interventions (CT scans, IR drainage) without adverse outcomes [29].

Summary

The diagnosis and treatment of appendicitis have undergone substantial change in recent years. Clinical pathways, scoring systems, and selective imaging can maximize diagnostic accuracy while reducing costs, unnecessary imaging, and ionizing radiation exposure. US is the best imaging study, preferably with dedicated pediatric sonographers and standardized reports. Non-operative management for selected children with acute appendicitis is possible, but pediatric data are still limited and long-term outcomes are unknown. Semi-elective, non-emergent operation (laparoscopic) is safe and does not worsen outcomes. Same-day discharge without additional antibiotics is appropriate for simple acute appendicitis. PA without a distinct intra-abdominal abscess is best treated with early appendectomy. Abscess is the most common complication.

Compliance with ethical standards

Conflict of interest The authors have no disclosures or conflicts of interest.

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