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Review Article

Evidence-based Practice in Pediatric Appendicitis

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Abstract **Management of acute appendicitis is one of the most challenging topics in pediatric surgery. Recent researches have focused on systematic approaches in diagnosis and minimally invasive surgical techniques. In order to avoid morbidity caused by delayed management, clinical scoring systems and imaging modalities have been undergoing continuing modifications with an attempt to find the optimal diagnostic algorithm. Although an appendectomy is the mainstay treatment, some recent studies have reported successes with initial non-operative management in selected cases of uncomplicated appendicitis. In cases with an appendiceal mass, evidences have suggested that conservative management is preferable in the pediatric age group. Interval appendectomy for a subsided appendiceal mass is no longer mandatory. As minimally invasive surgery has gained its popularity among pediatric surgeons, laparoscopic appendectomy is an attractive procedure with proven advantage in enhancing recovery and reducing post-operative wound complications, especially in complicated appendicitis.**

Keywords: **pediatric appendicitis, appendectomy**

Introduction and Epidemiology

Appendicitis is the most common pediatric abdominal surgical emergency, diagnosed in up to 7-10% of children evaluated for urgent abdominal pain[1-3] and comprises 50-60% of emergency abdominal operations in this age group[4]. The global incidence rate of appendicitis was recently estimated at 10 per 10,000 population-year[5]. In Thailand, a survey in the North-Eastern reported an incidence of appendicitis at 3.2-3.7 per 10,000 population-year[6]. The highest frequency is reported in the second decade of life, the adolescent age group, which is the period in which the lymphoid follicles reach their maximal size and potentially cause luminal obstruction of the vermiform appendix[7]. Although the incidence in neonates and younger children (age < 5years) is lower, there are also more reports of perforations and higher mortality in these groups. Perforation rates as high as 90% have been reported in neonatesand infants and as high as 31% in young children (age 5-9 years)[8-9], compared to less than 25% in adolescents and adults[3,7,10]. Delayed diagnosis may contribute to these figures and the problem is usually a result of non-specific clinical signs and symptoms and limited clinical data caused by the inability of young children to explain their symptoms or cooperate with a physical examination. Furthermore, non-surgical conditions such as acute gastroenteritis, mesenteric adenitis and even constipation may cause symptoms that mimic appendicitis[11]. These and other factors make pediatric appendicitis a challenging problem in terms of balancing between making a timely and accurate diagnosis and avoiding unnecessary appendectomies. Interestingly, although modern imaging technologies have been employed more widely

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in the past few years, the perforation rate remained unchanged[7]. In addition to the diagnostic issues, minimally invasive surgical procedures and non-operative strategies have been extensively studied in childhood appendicitis. This review aimed to examine for recent studies regarding diagnosis and management of acute appendicitis in the pediatric age group with a main focus on clinical prediction guidelines and alternative management options.

Clinical Manifestation

Clinical data is always regarded as the fundamental clue that brings a child to more specific diagnostic evaluation. Although the classic description of appendicitis in adults includes periumbilical pain, anorexia and nausea, right upper quadrant pain, and later, vomiting and fever, some of these symptoms can be difficult for practitioners to assess, and also may have different diagnostic value in infants and young children[8]. Clinical presentations may vary with age group.

Neonatal appendicitis

In neonates, appendicitis is a rare condition, but one with high mortality[12]. Factors that explain the low incidence include a funnel-shaped appendix, soft and easily digestible diet, recumbent posture and infrequent gastrointestinal and respiratory tract infections[13]. Acute appendicitis is often misdiagnosed as necrotizing enterocolitis (NEC) and other causes of intestinal perforation. In neonates with suspected NEC whose abdominal radiographs show no obvious signs of NEC, e.g. pneumatosis intestinalis, an abdominal ultrasound is then suggested to rule out appendicitis. In one systematic review of clinical features in 33 cases of neonatal appendicitis, the most prominent clinical finding was abdominal distension, followed by vomiting, anorexia, abdominal tenderness and temperature instability[12]. A significant number of patients had associated prematurity (60%) and co-morbidities such as Hirschsprung's disease, cardiac anomalies and cystic fibrosis. An inflamed appendix may protrude into a hernia sac in the right groin, also known as Amyand's hernia, following its first description by an English surgeon, Claudius Amyand[14-16].

Preschool age or young children

In preschool age children, early differentiation between other causes of abdominal pain and acute appendicitis is often challenging. Common presentations include abdominal pain (94%), nausea and vomiting (86%), and fever (75%)[9]. Fever was identified as the single most useful symptom as its positive predictive value was exceptionally high (27%) and the negative predictive value was low (3.4% calculated when the pretest probability was at 10%)[10].

Older children and adolescents

Appendicitis is much more frequent in children aged from 5-6 years to adolescents compared to younger children. The clinical features in this age group are quite similar to those found in adulthood and include the classical findings of anorexia, periumbilical pain that migrates to the right lower quadrant and vomiting. One study documented the clinical presentations

Table 1 Accuracy of symptoms associated with acute appendicitis in childhood(modified from Bundy DG 2007[10]) LR; likelihood ratio, 95% CI; 95% confidence interval

Symptom	Sensitivity (%)	Specificity (%)	Positive LR (95% CI)	Negative LR (95% CI)
Pain symptom duration < 24 h	44-50	40-46	0.83 (0.55-1.2)	1.3 (0.82-1.9)
Right lower quadrant pain	62-96	5-63	1.2 (1.0-1.5)	0.56 (0.43-0.73)
Migratory pain	45-68	76-78	3.1 (1.8-5.3)	0.41 (0.30-0.57)
Fever	75	78	3.4 (2.4-4.8)	0.32 (0.16-0.64)
Vomiting	79	64	2.2 (1.7-2.9)	0.33 (0.15-0.71)
Diarrhea	33	87	0.83 (0.59-1.1)	1.0(0.97-1.1)
Anorexia	21	73	0.77 (0.34-1.7)	1.1 (0.87-1.35)
Nausea	29	79	1.4 (0.70-2.7)	0.90 (0.69-1.2)

significantly associated with histologically proven appendicitis were history of migratory pain (74%), right lower quadrant pain (39%) and nausea (79%)[17]. Another study correlated the accuracy of diagnosis related to the major symptoms (Table 1). Note that in this study, right lower quadrant pain in children had a lower likelihood ratio compared to adults and although migratory pain had a high specificity, its sensitivity was relatively low. A history of diarrhea provided only a low diagnostic value in both ruling in and ruling out appendicitis in children.

A girl who has reached adolescence has become sexually mature and information regarding menstruation can be helpful in distinguishing gynecologic conditions, including ovulation pain, ovarian cyst, ectopic pregnancy or pelvic inflammatory disease. Acute sharp right-sided pelvic pain without significant gastrointestinal tract symptoms is more likely to be caused by a ruptured ovarian follicle or twist of the right ovary.

The accuracy of clinical signs in diagnosing acute appendicitis are summarized in Table 2. Traditional teaching recommends a digital rectal examination (DRE) as a mandatory part of evaluating a child suspected to have appendicitis. Tenderness at the right side of the rectum suggests pelvic type appendicitis while a finding of hard feces can be a sign of constipation. A recent meta-analysis found that rectal tenderness gave a likelihood ratio of having appendicitis at 2.3 (95%CI 1.3-4.1) and a negative likelihood ratio of 0.7 (95% CI 0.56-0.87)[10]. Another study found that although a DRE alone gave an accuracy at up to 75% in the diagnosis of appendicitis in children, this is no more accurate than diagnostic accuracy based on clinical history and abdominal examination[18,19]. Taken together with its relatively low sensitivity and specificity as compared to the adult age group[19] and the potential psychological impact, DRE might be omitted in an uncooperative child[20].

Laboratory studies

As limitations exist in obtaining clinical data, laboratory tests have been used with an aim to increase the accuracy of the clinical diagnosis. Certain standard tests are widely employed in evaluating a child suspected to have appendicitis.

White blood cell (WBC) count

Although WBC is elevated in up to 90% of children with appendicitis[21], it may also be elevated in other infectious conditions. The estimated sensitivity (19-88%) and specificity of leukocytosis (53-100%) in the diagnosis of appendicitis have varied widely in studies examining this[8]. Moreover, the cut-off point of significant leukocytosis in this condition also varies. Bundy DG and colleagues showed that a WBC greater than 10,000/μL gave the best positive likelihood ratio[10]. To improve the accuracy, age-specific upper limits for WBC count or a left-shift (> 80% of neutrophils (PMN) plus band) were considered for pediatric age group[1,10]. When clinical presentations were atypical, WBC and absolute neutrophil count became the strongest negative predictors (negative likelihood ratios of 0.18 and 0.35, respectively)[22]. A retrospective study of 847 appendectomies, in which the incidence of normal appendixes following histological examination was 2.6%, demonstrated that if the cut-off value of leukocytosis was reset at 9,000 cells/microliter, the

Table 2 Accuracy of clinical signs in diagnosing acute appendicitis in children older than the neonate group[summarized from Bundy DG 2007[10], Colvin JM 2007[17], Kessler C 2012[20]] LR; likelihood ratios presented with 95% confidence interval

Sign	Sensitivity (%)	Specificity (%)	Positive LR	Negative LR
Right lower quadrant tenderness	80-97	5-52	1.3 (1.1-1.4)	0.45 (0.35-0.59)
Rebound tenderness	53-88	46-86	3.0 (2.3-3.9)	0.28 (0.14-0.55)
Guarding	62-86	63-67	1.6 (1.4-2.0)	0.61 (0.49-0.76)
Decreased bowel sound	33	87	2.5 (1.6-3.7)	0.77 (0.68-0.88)
Pain on percussion, hopping, cough	78	62	2.0 (1.7-2.4)	0.36 (0.26-0.50)
Psoas sign	26-36	87	2.5 (1.7-3.7)	0.75 (0.66-0.86)
Digital rectal examination	44-55	44-75	2.3 (1.3-4.1)	0.70 (0.56-0.87)

negative appendectomy rate would have been reduced to 0.6%[23].

C-reactive protein

The C-reactive protein, CRP, is a nonspecific inflammatory mediator. An elevation of CRP (> 6 to 10 mg/L) has been reported in children with appendicitis. A recent meta-analysis showed a sensitivity for acute appendicitis of elevated CRP of 57% and specificity of 87%, values which are more specific but less sensitive than leukocytosis alone[24]. Because CRP has not had time to develop in patients symptomatic less than 12 hours[8], some studies have suggested that elevated CRP is more helpful in identifying complicated appendicitis (gangrenous or perforated), and is also more accurate if combined with an elevated serum bilirubin level[25].

Urine analysis (UA)

A UA and urine pregnancy test may be indicated when a urinary tract infection or nephrolithiasis is suspected or to exclude some gynecologic conditions in post-menarche females. However, pyuria and/or hematuria have been documented in 30% children with histologically confirmed appendicitis[8]. In addition, a systematic review found that the test is less efficient in the pediatric age group in terms of poor sensitivity and there is no significant correlation between the results and the presence of acute appendicitis[10].

Other laboratory tests

Other biological markers that may have value in diagnosing acute appendicitis include serum procalcitonin, bilirubin and fibrinogen, although most of these studies were conducted in adults[25-27]. Hyperbilirubinaemia (serum bilirubin > 20 μmol/L or 1.7 mg/dl) was reported to have an association with acute appendicitis with an odds ratio of 3.25-9.53[26,28]. The marker can be more specific in diagnosing perforated appendicitis[28]. Hyperbilirubinemia may be explained by the intrahepatic cholestasis process caused by bacterial translocation[26].

A recent prospective study in 466 children found that hyperfibrinogenemia (serum fibrinogen > 5 g/L) had a high specificity in the diagnosis of acute appendicitis. Consistent with serum bilirubin, higher fibrinogen levels had value in the diagnosis of appendiceal perforation[27].

Clinical scoring systems

Symptoms and signs of a pediatric patient with acute appendicitis vary with age and the majority of cases present one or more atypical features such as no migration of pain (50%), no fever (83%), no guarding and/or rebound tenderness (50%)[22]. Clinical scoring systems were developed in order to increase the objectivity of decision-making. The logic of clinical scoring is to put together multiple parameters from both clinical and laboratory findings into one equation. Each parameter is weighted differently according to its association with confirmed appendicitis. Currently available scoring systems to assess pediatric appendicitis share the same objective of distinguishing between children with a higher likelihood to have appendicitis from those who are less likely to need a specific treatment. One recent study found that an appendicitis scoring system helped increase diagnostic accuracy,

Table 3 Accuracy of laboratory tests in diagnosing acute appendicitis (summarized from references 1, 10, 25 and 27).LR: likelihood ratio presented with 95% confidence interval; *: no available data on 95% confidence interval

Sign	Sensitivity (%)	Specificity (%)	Positive LR	Negative LR
WBC > 10,000 /μL	80-98	29-76	2.0 (1.3-2.9)	0.22 (0.17-0.30)
WBC with age specific cut-off	70	79	3.4 (1.9-6.3)	0.37 (0.24-0.56)
WBC with left shift	59	94	9.8*	0.44*
CRP > 10 ng/L	64-85	33-82	3.6 (2.1-6.2)	0.44 (0.33-0.59)
UA (RBC > 3 cells/HPF)	5	90	0.48 (0.1-2.3)	1.10 (0.94-1.2)
Serum bilirubin (> 20 μmol/L)	70	82	0.47 (0.32-.58)	0.93 (0.87-0.96)
Serum fibrinogen (> 5 g/L)	74	82	0.72*	0.84*

and significantly reduced unnecessary appendectomy rate in children assessed by general surgeons, from 29% to 17%[29]. The diagnostic scoring system was especially helpful when the clinical data were contradictory.

Clinical scores generally categorize patients into 3 groups: those with low-risk (less than 5% likelihood), moderate-risk and high-risk (greater than or equal to 80% likelihood) of having appendicitis[30]. Patients are then managed through a risk-based approach. Low-risk patients do not need to be exposed to any risk from radiological investigations and can be discharged with careful advice or hospitalized only in a short-stay observation unit. Moderate-risk patients are recommended to have further diagnostic evaluation in order to avoid treatment delay, while patients in the high-risk group are recommended for immediate treatment as any delay caused by waiting for unnecessary investigations could lead to perforation and the associated problems.

Although many scoring systems have been developed, the most validated scoring systems are the Alvarado Score and the Pediatric Appendicitis Score (PAS) or Samuel score (Table 4)[31,32]. Other scoring systems such as the Kharbanda[33] and van den Broek[34], systems, although showing good predictive power on their derivation studies, have had no validation studies. The main differences between the 2 most validated systems are that the PAS scores provocation pain on the right lower quadrant (2 points) instead of 'rebound tenderness (1 points)' in the Alvorado score and the PAS gives less weight to leukocytosis than the Alvorado system[35].

The Alvarado score has been found in various studies to have sensitivities of 72-93% and specificities of 80-82%, compared to the PAS, which has been found to have sensitivities of 82-100% and specificities of 65-92%[10]. The accuracies varied depending on the lower and upper cutoff values and on the pretest probability to have appendicitis in an individual patient in the study. According to a recent systematic review, at pretest probability of 60%, an Alvorado score of 9 was associated with 85% or higher probability of appendicitis and a score lower than 4 was associated with a probability of appendicitis of less than 3%. Given the same conditions, a PAS of 8 or higher was associated with an 89% or higher probability of appendicitis[36].

The efficiency of the PAS and the Alvorado scores were reported at indistinguishable statistics. However, one meta-analysis reported that, the PAS had poorer results in terms of being able to rule out appendicitis (negative likelihood ratio of the scores less than 4 was 0.13 compared to 0.02 in the Alvarado system)[36]. Another study has reported that the Alvarado Score had a lower rate of misdiagnosis when compared to the PAS[37]. On the other hand, another meta-analysis reported a 35% over-diagnosis rate in PAS and 32% in the Alvorado score[11].

Table 4 Scoring systems of the Alvarado and Pediatric Appendicitis Score with suggested actions (summarized from references 31, 32 and 35); RLQ: Right lower quadrant

Alvarado Scores			Pediatric Appendicitis Scores		
Feature		**Point**	**Feature**		**Point**
Migration of pain		1	Migration of pain		1
Anorexia		1	Anorexia		1
Nausea		1	Nausea		1
RLQ tenderness		2	RLQ tenderness		2
Rebound pain		1	Cough/hopping/percussion tenderness in RLQ		2
Fever		1	Fever		1
Leukocytosis (10,000/µL)		2	Leukocytosis (10,000/µL)		1
Shift to the left		1	Shift to the left		1
Points	**Scoring system**	**Action**	**Points**	**Scoring system**	**Action**
5-6	Less probable	Observe	≤ 5	Not appendicitis	Observe
7-8	Probable	Imaging	≥ 6	Appendicitis	Surgery
9-10	Very probable	Surgery			

Imaging modality

Current imaging modalities have also became an integral part of the diagnosis of pediatric appendicitis. The most widely used imaging studies are ultrasonography (USG) and computed tomography (CT) (Figure 1). In addition, the use of magnetic resonance imaging (MRI) has also been reported.

USG provides a sensitivity of 88-93% and specificity of 96-97% in diagnosing acute appendicitis, and is recommended by the American College of Radiology and the American College of Emergency Physicians as the initial imaging modality for suspected appendicitis in children[38,39]. The disadvantages of USG are its operator dependency and limited accuracy in obese patients. One study found that the rates of vermiform appendix visualization on USG differed among work shifts as the appendix was clearly depicted at a higher frequency during working hours compared to after-hours. The same study showed that the appendix was not visualized in any patients with a weight in kilograms to age ratio > 6[40]. In another study, Ross and colleagues reported that 15% of children with non-visualized appendices on USG had pathologically confirmed appendicitis[41]. However, another study suggested that appendicitis can be safely ruled out in cases with a non-visualized appendix but concurrent low-risk score on the Alvorado scoring system. The most common causes of false-negative results from USG are problems of measurement, especially in a focal appendicitis when the normal part was measured and the inflamed portion, especially at its base, was overlooked[42].

The CT has been considered as the gold standard for a diagnosis of appendicitis with high sensitivity (94-100%) and specificity (93-98%). The advantages of CT include less operator dependency, easier visualization of a retrocecal type appendix, and less influence from bowel gas or obesity. The cost and radiation exposure are the main disadvantages. The use of CT as the first imaging modality is generally avoided. Srinivasan and colleagues suggested that CT was likely to affect patient management when the clinical scoring system and the USG result were discordant[40]. One study found that a positive predictive value of a subsequent CT was 100% when used in a clinical high-risk group whose USG reported negative. On the other hand, when CTs were used in low-risk group, the sensitivity decreased to 25%[40]. For these reasons, CT might not be a good diagnostic tool for early appendicitis, but may be more effective in detecting perforations(usually associated with a high score when a scoring system is used). Moreover, another study found that although the number of CT studies had increased; the perforation rate (30%) had not been reduced[43]. In addition, studies have reported that CT scan in childhood significantly increased the risk of malignancy later in life, as high as 1:1,000 cases, especially leukemia and brain tumors[44,45].

An MRI may also be used as an abdominal imaging study in a child with suspected appendicitis, with the advantage that there is no radiation exposure. A recent study that analyzed 662 patients with suspected appendicitis in whom MRI was used in combination with ultrasonography found that the MRI had high sensitivity and specificity, comparable with the ultrasonography results, although its negative appendectomy or perforation rates were not assessed[46].

Summary of a systematic approach to a child suspected to have appendicitis

According to recent observational studies, up to 50% of children with appendicitis may undergo surgery solely by clinical diagnosis without diagnostic imaging. Negative appendectomy rates around 12% to 15% were considered acceptable when the diagnosis was based largely on clinical and laboratory evaluations[36,47]. In recent years, in an attempt to decrease the number of negative appendectomies, some institutions have begun the more frequent use of diagnostic imaging. The fact that the USG-only approach gave high negative appendectomy rates suggested that the CT was an unavoidable tool with superior accuracy in selected situations[48]. On the other hand, of course, making a CT before an appendectomy created the risk from radiation exposure, thus it was necessary to be able to recommend the CT only when it was likely to be useful. The optimal algorithm seems to be a staged approach with clinical data and USG first, followed by considering a CT only if there was a significant probability of appendicitis as defined by scoring systems. By this method, the overall negative appendectomy rate was reduced to less than 5%[48]. One of the largest pediatric databases concerning the association between the use of diagnostic imaging and the rate of negative appendectomies reported that increased use of diagnostic imaging only affected the negative appendectomy rate in children younger than five

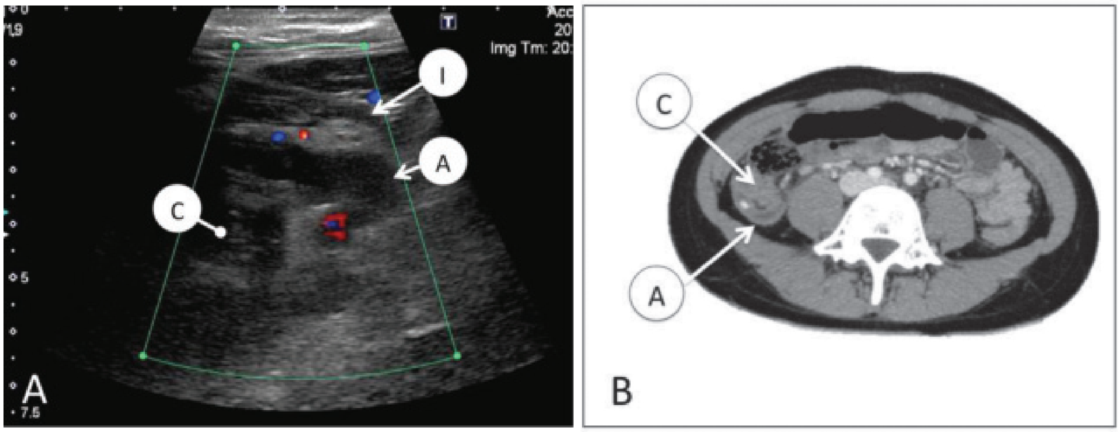

Figure 1 Imaging studies commonly used in the diagnosis of pediatric appendicitis A) Abdominal ultrasonography A: inflamed appendix; I: ileum; C: cecum, B) Computerized tomography A: retrocecal appendix containing an appendicolith at its base; C: cecum (courtesy of the Department of Radiology, Faculty of Medicine, Prince of Songkla University)

years, while having no meaningful impact on other groups[48]. Regarding the concern that awaiting for an imaging study may cause a potentially harmful delay in surgical management, one study found that if the imaging study was performed within 12 hours of symptom and the patient received appropriate antibiotics during the waiting time, the perforation rate and operative-waiting time did not significantly increased[49]. Based on those evidences, our recommended approach for a patient with suspected appendicitis is shown in Figure 2.

Treatment

Early appendicitis

Early appendicitis is defined as appendicitis without evidence of perforation or gangrene. Appendectomy is the mainstay treatment for this

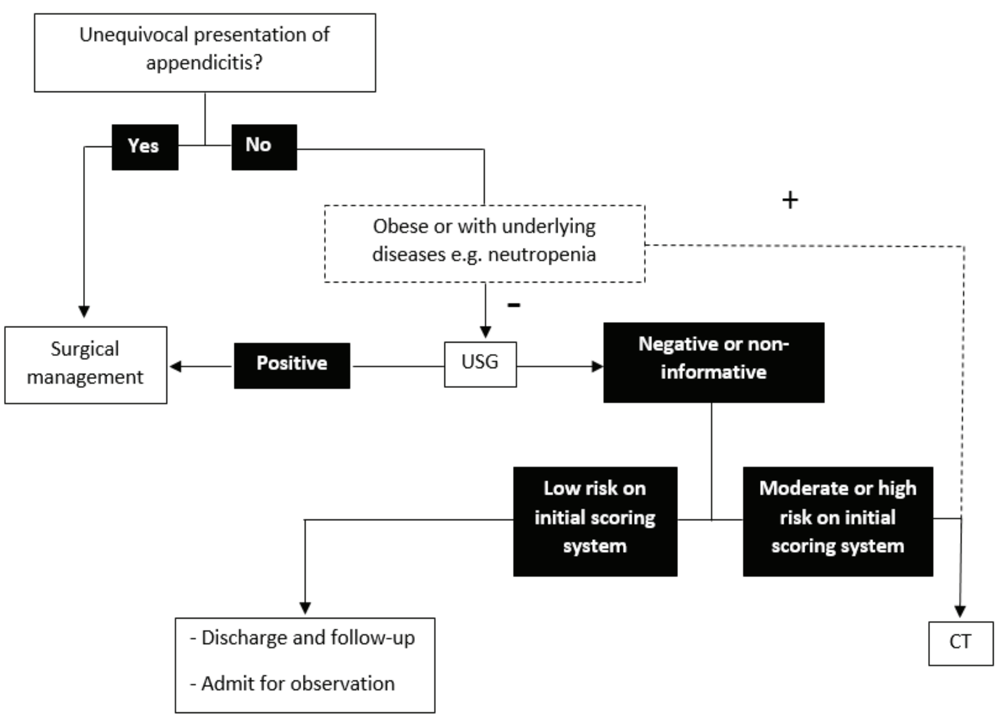

Figure 2 Algorithm in approaching to a child with suspected appendicitis[29,36,40-42,48] USG: ultrasonography; CT: computerized tomography

condition. However, a debatable question has been raised as to whether an emergent appendectomy is required in all patients with early appendicitis. A study that included 126 patients with early appendicitis reported that treatment in this group of patients could be securely begun with antibiotics for 6 to 12 hours prior to an appendectomy without significant increase in perforation or complication rates[49]. This may be akin to the current treatment of acute cholecystitis in which the operation may be delayed until the disease process has been "cooled down" with antibiotics. Based on this concept, recent studies have reported successful non-operative management of early appendicitis with or without a subsequent appendectomy. A retrospective review that included 24 patients in which 12 patients were managed non-operatively reported an overall success rate of 75% with 2 early failures, one failing to improve in the hospital and the other developing recurrent abdominal pain at 6 weeks after the initial treatment[50]. The series had a 10% recurrence rate and a 25% appendectomy rate at the follow-up period of 6 months. The patient selection and management algorithm in that study are summarized in Figure 3. The report should be interpreted with an awareness of its small size and relatively short follow-up period. Another study demonstrated an initial success rate of 94% with a 13% recurrence rate and a 20% overall appendectomy rate at a one-year follow-up[51]. To date, although there is not enough data from randomized trial that support delayed appendectomy in childhood non-perforated appendicitis, growing data suggests that early appendicitis might not always require an emergency surgery. A study that focused on intraabdominal abscesses after an appendectomy reported that an short overnight regimen of antibiotics and resuscitation prior to an appendectomy led to a significantly lower risk of intraabdominal abscess[52]. Recently, Svensson and colleagues reported a pilot randomized control trial of 50 children with acute non-perforated appendicitis and suggested that non-operative therapeutic approach was feasible and safe[53,54]. A well-designed, large randomized trial is needed to investigate these issues further.

Advanced appendicitis

Appendicitis is considered advanced when perforation or gangrene has already developed. Traditionally, advanced appendicitis is promptly treated with an appendectomy. A randomized trial of 131 children with a clinical presentation suggestive of perforated appendicitis without any detectable appendiceal phlegmon or abscess compared an early appendectomy (EA) with initial non-operative management followed by an interval appendectomy

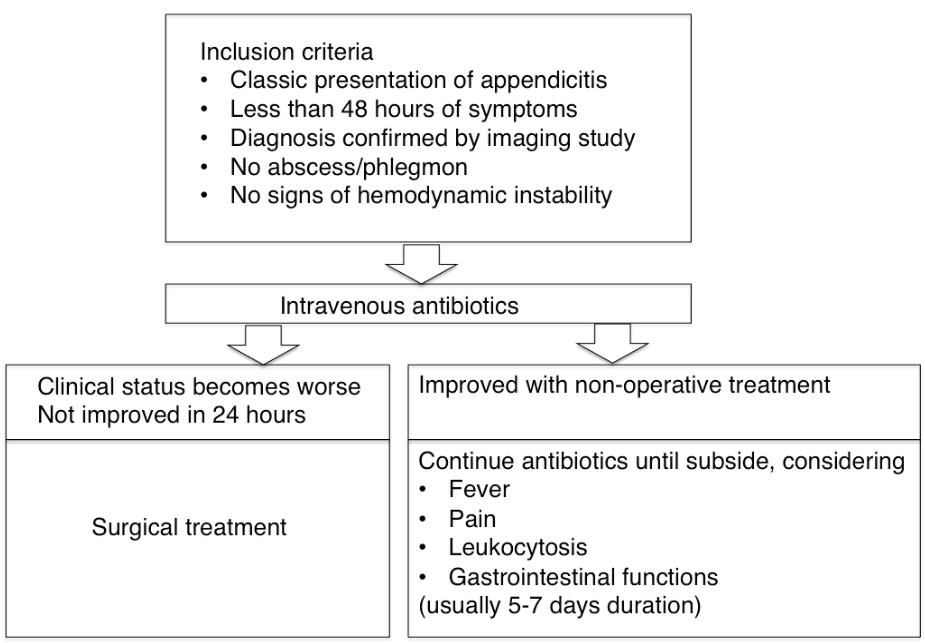

Figure 3 Clinical scheme for non-operative management of early appendicitis (derived from references 50 and 55)

(IA)[56,57]. The study found that the EA group had significantly less time away from normal activities and the overall complication rate was lower[56]. A subsequent study by the same group found that after the first trial, changes in practice patterns in their hospital significantly improved the outcomes, especially in terms of wound infection rate from 14% to 2%[57].

Appendiceal mass or phlegmon

When an appendiceal mass is demonstrated without signs of generalized peritonitis, treatment is usually begun with non-operative management which means intravenous antibiotics until the infection is subsided, followed by an interval appendectomy with an aim to prevent recurrence. An image-guided percutaneous drainage is recommended for an abscess larger than 3 to 4 cm in diameter. A systematic review in adults supported the practice of non-surgical management by the evidence that an immediate surgery was associated with a higher complication rate compared with nonsurgical treatment (odds ratio, 3.3; CI: 1.9-5.6). In addition, after successful nonsurgical treatment, malignant diseases were detected in 1.2% of cases[58]. In the pediatric age group, a recent study reported a success rate of non-operative management in this setting at 96% and suggested that the presence of an appendicolith was not a contraindication to continue with the non-operative approach[59].

SURGICAL APPROACHES IN PEDIATRIC APPENDECTOMY

The choice for a surgical approach is either a laparoscopic or open appendectomy. There is a scarcity of Level I evidence that clearly supports each technique. Most studies have been retrospective in nature and the difference in outcomes between the two techniques has been minimal, and is related to the patient's condition and surgeon's experience. Compared to open surgery, the laparoscopic procedure is associated with a significantly decreased hospital length of stay (mean difference 0.5 days), wound infection (1-2.2% versus 3.7-6%) and risk of small bowel obstruction (0.4% versus 1.5%)[60-62]. However, evidence that supports laparoscopy in the areas of decreased postoperative pain and an earlier return to normal activities is not clear. Although adult studies have shown that the incidence of intraabdominal abscess was significantly higher in the laparoscopic surgery group[61], there is no evidence that this would be the case in children with appendicitis[62-64]. Moreover, an RCT that evaluates the practice of peritoneal irrigation during laparoscopic appendectomies in pediatric perforated appendicitis cases found that peritoneal irrigation provided no additional benefit when compared to suction alone[75]. In the authors' experience, a laparoscopic appendectomy is likely to provide comparative advantages in obese children and in cases with uncertain diagnosis of abdominal pain, especially in teenage girls.

The conventional laparoscopic technique uses 3 (3-5 mm) ports for an appendectomy (Figure 3). With recent advances in surgical technology, a single-port technique has been attempted with the primary aim of improving the cosmetic outcome[63,66]. A systematic review showed that 8% of these procedures failed to complete the appendectomy by a single port and needed an additional port[63]. A recent meta-analysis further found that the single port procedure required a longer operative time, although the patient in successful procedures benefited from a shorter time to return to normal activities and a better cosmetic result at an early period[66-69]. A single-port appendectomy in children has been described both intracorporeally and extracorporeally[70]. In the latter technique, the appendix is exteriorized through the umbilical port to be removed.

On open appendectomy, a stump burying in a purse-string fashion is traditionally practiced although there is no concrete evidence that supports the procedure. Some researchers have argued that stump burying unnecessarily prolongs operative time and increases the risk of bowel wall hematoma/necrosis without any proven benefit. Routine peritoneal irrigation and drainage are not recommended in pediatric cases of perforated appendicitis[70-72]. A drain is helpful in cases in which the stump cannot be securely controlled. Removal of an appendix that appears grossly normal is generally recommended. According to one study, 29% of appendices thought to be normal on their macroscopic appearance were found to be inflamed on subsequent histological examination[73].

Interval appendectomy

Because of the awareness of recurrence of disease, an interval appendectomy is often performed at 8 to 20 weeks after initial non-operative management.

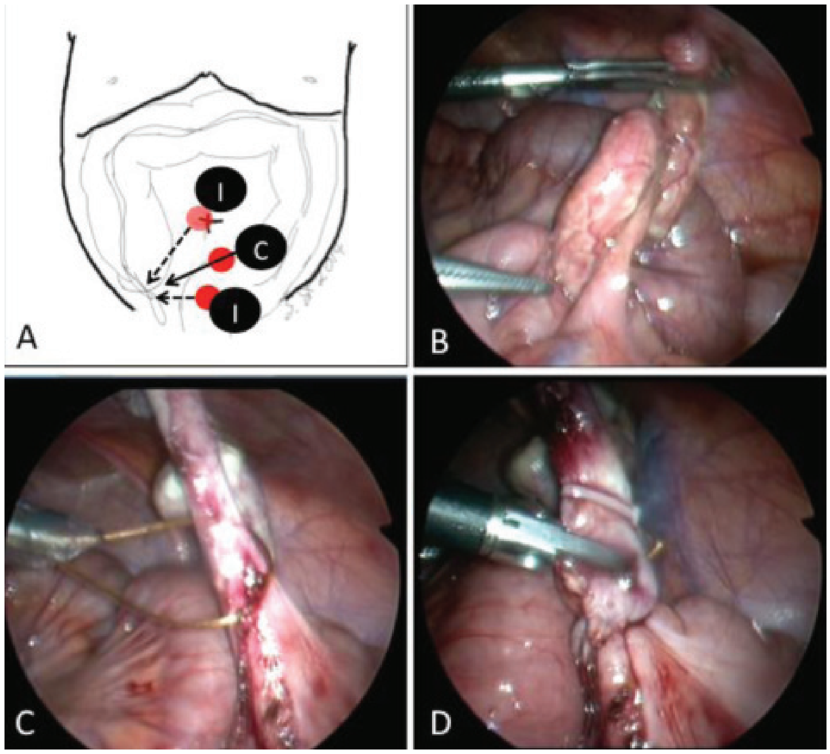

Figure 4 A schematic representation of a standard laparoscopic appendectomy A) Port position in a 3-port technique composed of 2 instrument ports (I) and a camera port (C) B) After identification of the appendix, the mesoappendix is controlled. C) Ligation of the appendiceal base using chromic catgut loops D) Transection of the appendix between proximal and distal controls

Table 5 Selected results from recent large studies that compared open (OA) and laparoscopic (LA) appendectomies in pediatric patients. UA: uncomplicated appendicitis, CA: complicated appendicitis

Outcomes studied	OA	LA	*p*-value
Mean length of hospital stay (LOH)			
Andersson RE 2014 (n; 169,896)	3.20 days	2.83 days	< 0.001
Wound infection rate (%)			
Markar SR 2012 (UA-n;73,150)	1.0	0.8	0.13
Markar SR 2012 (CA-n;34,474)	4.1	3.3	< 0.05
Other surgical complications rate (%)			
Andersson RE 2014	8.2	7.2	0.005
Andersson RE 2014	5.3	4.1	0.033
Markar SR 2012-UA	0.4	0.6	0.97
Markar SR 2012-CA	2.6	3.7	< 0.05
Re-admission rate (%)			
Andersson RE 2014	5.8	6.9	< 0.001
Markar SR 2012-UA	1.2	1.2	0.30
Markar SR 2012-CA	4.1	3.9	0.27

However, recent studies have challenged the traditional practice of routine IA in the pediatric age group. The potential benefit of this total non-operative treatment, notably an avoidance of any risk from surgery and anesthesia, has to be weighed against the risk of recurrence and the risk of a missed diagnosis of other pathologies.

According to published pediatric studies, the recurrence rate of appendicitis at 6 months is 10% and at 1 year is 13% in after an initial non-operative treatment[50,51]. One study with a mean follow-up period at 2.4 years found the recurrence rate in cases that presented with phlegmon or abscess in a series was at 14% with higher rate in patients with appendicolith[59]. The same study also reported that, without surgical treatment, 81% of appendicolith disappeared during the follow-up period and these patients had a significantly lower incidence of recurrent appendicitis compared to those whose appendicolith remained[59]. More than 95% of the disappearance occurred with the first month[59]. Relative to adults, unexpected pathology in pediatric cases who presented with appendicitis is lower. A recent study reported that emergency appendectomy in cases of relapse appendicitis did not increase morbidity when compared to IA[75]. Taken together those evidences, IA should be reserved for patients with appendiceal mass with persistent appendicolith after a few months of follow-up.

Antibiotic uses in pediatric appendicitis

The guideline for antibiotic use is based on an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. The guideline suggested that in cases of non-perforated appendicitis, the child should receive a single preoperative prophylactic dose of a broad-spectrum antibiotic when surgical treatment is decided on. The effectiveness of such an antibiotic compared to a placebo in decreased wound infection (odds ratio 0.31) and abscess formation (odd ratio 0.46) has been demonstrated, with no evidence to support the use of any further doses of antibiotic in the postoperative period if the appendectomy is uncomplicated[55].

Traditionally, a patient with perforated appendicitis has been given a triple antibiotic to cover gram positive, gram negative and anaerobic bacteria. But, several studies have found that a broad-spectrum combination, with single or double agents (i.e. piperacillin, tazobactram or ceftriaxone and metronidazole), is as effective as triple therapy. Considering no significant differences in efficacy, a combination therapy using ceftriaxone and metronidazole is suggested by the committee[55].

The duration of intravenous antibiotic administration for perforated appendicitis is usually based on clinical criteria, primarily fever, pain, return of bowel function and white blood cell count. Although a standard recommendation suggests that antibiotics can be discontinued when these parameters return to normal values[55], most surgeons preferred a 7-10 day course of antibiotics, either totally parenteral or initially parenteral followed by a switch to an oral form when the clinical parameters begin to improve. A study by Fraser JD and colleagues found that a 5-day course of an intravenous antibiotic followed by an oral regimen up to a total duration of 7 days provided no significantly different outcomes compared to a 5-day course of totally intravenous antibiotics, in terms of postoperative abscess rate (20% versus 19%)[76]. In non-operative management of perforated appendicitis, antibiotic duration should be based on clinical response. Acceptable antibiotic choices are shown in Table 6.

Table 6 Recommended choices of antibiotics for pediatric appendicitis according to a systematic review of the American Pediatric Surgical Association Outcomes and Clinical Trials Committee[55].

Cefoxitin
Piperacillintazobactam
Ceftriaxone and metronidazole
Cefotetan
Gentamicin and either clindamycin or metronidazole

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