Non-operative Management of Uncomplicated Appendicitis

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Case Example
A 13-year-old boy presents with a 1 day history of abdominal pain that localized to the right lower quadrant. On physical exam he has signs and symptoms consistent with acute appendicitis. His laboratories reveal a white blood cell count of 12,000 per cubic millimeter of blood. He has an ultrasound performed which does not show any evidence of perforation, and no fecalith is visualized. The family asks whether there is an alternative to surgical appendectomy.

Introduction

Appendicitis remains the most common surgical emergency in children with a lifetime risk of 7–8% and a peak incidence in the teenage years [1]. In the United States, the standard of care for children diagnosed with acute appendicitis is to perform a laparoscopic appendectomy. Approximately 60,000 and 80,000 pediatric appendectomies are performed each year, with an average cost of approximately $9000 [2]. The morbidity rate varies from 5% to 30%, with higher rates reported in cases of perforated appendicitis [3–6], defined as either a hole in the appendix or a fecalith in the abdomen during the operation [7]. Major complications associated with an appendectomy include surgical site and organ-space surgical site infections, adhesive small bowel obstruction, hospital readmissions, and reoperation. Minor complications include superficial surgical site infections, urinary retention, and urinary tract infections. Efforts to avoid both major and minor complications associated with appendectomy include the use of antibiotics to manage children with uncomplicated appendicitis. There has been growing evidence regarding the use of

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non-operative management (NOM) for both adults and children with uncomplicated appendicitis. In this chapter, we will review the current evidence for NOM in children.

Discussion

Managing children diagnosed with uncomplicated appendicitis without an appendectomy is a treatment option that has gained significant traction in the past few years among both providers and patient families. Despite the relatively low-risk implications of performing an appendectomy, it requires general anesthesia and is an abdominal operation with inherent risks. Complications related to surgery or anesthesia occur in more than 10% of children within 30 days of appendectomy [8]. Even with current imaging methods, 6.3% of children in Canada and 4.3% in the United States undergoing appendectomy are subsequently found to have a normal appendix [9].

Several adult trials demonstrate the benefit of using NOM for non-perforated appendicitis [10–16]. These trials show the early success rate of NOM to be approximately 90%. However, this falls to approximately 70% at 1 year, with the risk thereafter unknown [17]. These studies demonstrate similar rates of perforation and fewer complications when compared to patients undergoing an appendectomy. Furthermore, patients undergoing NOM exhibit improved pain control, shorter sick leave, but increased recurrence rates when compared to initial appendectomy [17, 18]. A recent systematic review and meta-analysis found a longer hospitalization stay with antibiotic treatment but also found an incidental malignancy rate of 0.6% [17]. While this is a lower concern in children, it still exists as we have documented an unsuspected carcinoid in 0.2% of appendectomy specimens in children [19]. The adult literature has identified several predictors for failure of NOM. These include the presence of an appendicolith, a phlegmon or abscess on imaging, an elevated white blood cell (WBC) count >18,000 or CRP >4 mg/dl, and abdominal pain for more than 48 hours [10–16]. Adult patients wishing to undergo NOM for acute appendicitis with any of these predictors should be counseled on the increased failure rate.

In children with appendicitis, the literature is a little less mature for NOM (Table 7.1) [20–29]. A pilot randomized trial performed in Sweden included 26 operative patients and 24 non-operative patients and showed a success rate of 92% at discharge and 62% at 1 year [27]. Furthermore, at 1 year follow-up, there was no increased risk of complications and similar costs among children managed non-operatively. A second trial published from Japan was a patient choice trial from 2007 to 2013 in which 78 patients chose NOM and 86 patients elected to undergo surgery [28]. With a median follow-up of 4.3 years, the success rate for NOM was 99% at discharge and 71% at median follow-up. However, 29% of patients electing for NOM had a recurrence at 1 year. There was no difference in the operative time or rates of postoperative complications between the two groups. In a feasibility study, 24 patients between the ages of 5 and 18 years old with less than 48 hours of symptoms were enrolled and compared to 50 controls [23]. At an average follow-up of 14 months, 3 of the 24 patients failed on NOM, and 2 of 21 patients returned with

Table 7.1 Existing literature for non-operative management of acute uncomplicated appendicitis in children

Study	Year of publication	Study design	Children enrolled in non-operative management
Minneci et al.	2016	Prospective parent preference-based trial	30
Hartwich et al.	2016	Prospective parent preference-based feasibility trial	24
Tanaka et al.	2015	Non-randomized retrospective cohort	78
Steiner et al.	2015	Non-randomized prospective cohort	45
Svensson et al.	2015	Pilot randomized control trial	24
Gorter et al.	2015	Non-randomized prospective cohort	25
Koike et al.	2014	Retrospective cohort	130
Armstrong et al.	2014	Non-randomized retrospective cohort	12
Abes et al.	2007	Retrospective cohort	16
Kaneko et al.	2004	Prospective cohort	22

recurrent appendicitis at 43 and 52 days, respectively. Furthermore, two patients elected to undergo an interval appendectomy despite the absence of symptoms. The appendectomy-free rate at 1 year was 71% with no patient developing perforation or other complications. The hospital costs from this study decreased from $4130 to $2771 [23].

Finally, a prospective single-institution patient choice trial was performed in the United States that enrolled 102 children who met specific clinical inclusion criteria [26, 30]. These criteria were 7–18 years of age, less than 48 hours of abdominal pain, WBC less than 18,000 cells per microliter, and US or computed tomography (CT) scan identifying an appendix less than 1.2 cm in diameter without an appendicolith, abscess, or phlegmon. If a patient decides to undergo surgery, they receive an urgent laparoscopic appendectomy. Patients who chose non-operative management were hospitalized for at least 24 hours to receive intravenous antibiotics. They were given a diet after 12 hours; if at 24 hours they had no clinical improvement, they underwent laparoscopic appendectomy. Of the 102 enrolled patients, 65 elected for surgery, and 37 elected for NOM with antibiotics alone. The success rate for NOM was 93% at hospital discharge, 90% at 30-day follow-up, and 76% at 1 year [30]. In analyzing quality-of-life scores at 30 days, patients treated with NOM reported higher scores and fewer disability days. Furthermore, the authors demonstrated lower overall costs, no treatment-related complications, or rates of complicated appendicitis at 1 year for patients electing for NOM. The patient preference design has been expanded through the Midwest Pediatric Surgery Consortium to enroll 1000 patients in a funded trial.

Based on the previously described studies [27, 30], there is currently an international, multicenter, randomized trial to evaluate NOM for children with acute appendicitis (Fig. 7.1). This ongoing trial across 12 children's hospital in the United States, Canada, and Europe will be the largest randomized study to evaluate antibiotic treatment of acute appendicitis in children. In this trial, the inclusion criteria are age 5–16 years old, clinical and/or radiological diagnosis (US and/or CT scan) of

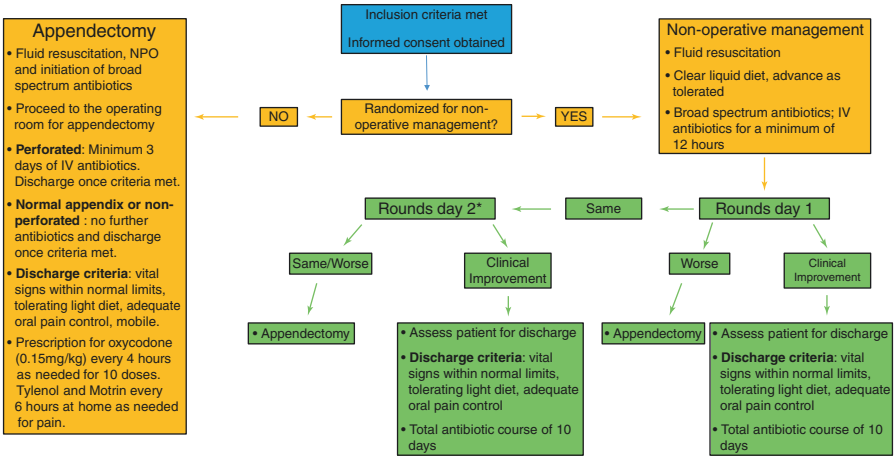

Fig. 7.1 Clinical flowchart for the current international, multicenter, randomized trial to evaluate the non-operative management for children with acute appendicitis

acute non-perforated appendicitis, and written informed parental consent. Exclusion criteria include presentation with an appendiceal mass or phlegmon (on physical examination and/or imaging), suspicion of perforated appendicitis, NOM (two or more doses of IV antibiotics) initiated at an outside institution, previous episode of appendicitis treated non-operatively, positive pregnancy test, diagnosis of cystic fibrosis, and current treatment for malignancy.

The ability to establish risk factors for failure of NOM remains essential for appropriate patient selection. Published reports in the literature suggest that an appendicolith is an adverse indicator for successful NOM [31, 32]. A prospective study evaluating the utility of NOM in children with acute appendicitis identified 47% (9/19) of patients with an appendicolith failing NOM compared to 24% (14/59) of patients without an appendicolith ($p = 0.05$) [28]. Furthermore, a small prospective, nonrandomized trial in children aged 7–17 years old was terminated early because 60% (3/5) of patients with an appendicolith failed NOM at a median follow-up of 5 months [32]. These findings indicate that parents or caregivers considering NOM for their child with an appendicolith should be educated on the reported failure rates. The available data does suggest that antibiotics alone for children found with an appendicolith on imaging may not be effective for treating acute appendicitis.

Misconceptions from both parents and caregivers that a delay in performing an appendectomy leads to a greater likelihood of developing perforated appendicitis have challenged the framework for NOM [33]. However, it has been shown that delaying appendectomy doesn't increase the risk of complications [34]. Furthermore, the increased public awareness of NOM for children with acute appendicitis is slowly improving, and we expect this treatment modality to gain significant traction as more studies show its benefit.

A second challenge for NOM in children with acute appendicitis relates to parents and caregivers developing a clear understanding of the disease process in order to make an informed management decision. A published feasibility study which included 100 participants highlighted the knowledge gap regarding the perception of appendicitis. Caregivers and patients greater than 15 years of age were questioned before and after an education session about their understanding of appendicitis. Eighty-two percent of participants thought it was likely or very likely that the appendix would rupture if the operation was delayed. In addition, the participants also acknowledged that a rupture of the appendix would lead to severe complications and even death. This study highlights the importance of patient and caregiver education which will improve the capacity to make decisions on alternative treatments for acute appendicitis [33].

The major limitation of the data on NOM is the inadequate long-term follow-up for children, making it difficult to fully assess the failure rate. Furthermore, many of the studies evaluating NOM for children with acute appendicitis have a variable duration of antibiotic therapy and length of hospital stay. To counteract these limitations, future cohort studies and prospective clinical trials need to establish core parameters during the study period so that clinical outcomes can be universally measured for comparison.

Conclusion

Based on the current body of literature utilizing the non-operative approach for children with acute uncomplicated appendicitis, the use of antibiotics is a reasonable treatment alternative to surgery in well-selected patients. Parents and caregivers should be educated on the potential benefits and risks for this approach. In addition, providers should be fully aware of the risk factors that increase the failure rate for NOM.

Clinical Pearls

- NOM of uncomplicated appendicitis appears to be a reasonable alternative to surgery in select patients.
- The presence of a fecalith or elevated laboratories is associated with a lower likelihood of successful NOM.
- Caregiver and patient family education regarding the pathophysiology of appendicitis are crucial prior to recommending NOM.

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