



Role of non-operative management in pediatric appendicitis



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ABSTRACT

Appendectomy is currently considered the standard of care for children with acute appendicitis. Although commonly performed and considered a safe procedure, appendectomy is not without complications. Non-operative management has a role in the treatment of both uncomplicated and complicated appendicitis. In uncomplicated appendicitis, initial non-operative management appears to be safe, with an approximate 1-year success rate of 75%. Compared to surgery, non-operative management is associated with less disability and lower costs, with no increase in the rate of complicated appendicitis. In patients with complicated appendicitis, initial non-operative management with interval appendectomy has been shown to be safe with reported success rates between 66% and 95%. Several studies suggest that initial non-operative management with interval appendectomy may be beneficial in patients with perforated appendicitis with a well-formed abscess or inflammatory mass. Recent data suggest that interval appendectomy may not be necessary after initial non-operative management of complicated appendicitis.

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Introduction

In the United States, appendectomy is currently considered the standard of care for children with acute appendicitis. Between 60,000 and 80,000 pediatric appendectomies are performed annually, with a mean cost of about \$9000.¹ Although appendectomy is considered safe and effective, it is not without short- and long-term complications. The overall morbidity rate varies from 5% up to 30%, with higher rates reported in cases of complicated appendicitis.^{2–6} Minor complications include urinary retention, urinary tract infection, and superficial and/or deep surgical site infection (SSI). Major complications include bleeding, organ space SSI, adhesive bowel obstruction, readmission, and reoperation. In an effort to minimize complications and improve care, surgeons have managed selected patients with appendicitis non-operatively. Over the past 2 decades, several studies have reported the results of trials investigating non-operative management of appendicitis in different subsets of patients with appendicitis. In this article, we

will review the role of non-operative management in both uncomplicated and complicated pediatric appendicitis.

Evolution of non-operative management of appendicitis

Non-operative management of appendicitis is not new, with multiple reported case series of successful treatment of soldiers during wartime or submariners during long missions.⁷ Recently, there has been a renewed interest in managing patients with appendicitis non-operatively. Several factors that have contributed to the rationale for non-operative management of appendicitis include improved imaging capabilities, development of interventional radiology (IR) drainage techniques, and the availability of oral broad-spectrum antibiotics. Our diagnostic accuracy has improved as a result of better imaging.^{8–10} Early and uncomplicated appendicitis can be reliably distinguished from perforated appendicitis on imaging studies.^{11,12} As a result, we are able to select eligible patients for non-operative management. In addition to improved diagnostic accuracy, symptomatic or large intra-abdominal collections or abscesses can now be drained using IR-placed catheters, rather than surgical drainage.^{13,14} Finally, the development of oral broad-spectrum antibiotics with excellent bioavailability allows for patients to complete their antibiotic course on an outpatient basis. Once tolerating a diet, patients can be transitioned to oral antibiotics and discharged from the

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hospital. This has allowed for shorter hospitalizations and obviates the need for a peripherally inserted central catheter for IV antibiotics at home.^{15–17}

Several intra-abdominal infectious processes, including diverticulitis, abscesses resulting from Crohn's disease, and tubo-ovarian abscesses are now treated with antibiotics alone, with surgery reserved for failures of medical management.^{18,19} These practices have evolved because the majority of these patients can be managed successfully without surgery, with minimal harm occurring in patients who subsequently undergo surgery after failed medical management. To be a reasonable treatment alternative to urgent appendectomy, non-operative management of appendicitis must have a clinically acceptable success rate with minimal harm in patients who fail and subsequently undergo appendectomy.²⁰

Role of non-operative management in uncomplicated appendicitis

Non-operative management of uncomplicated appendicitis has been studied in several international adult trials.^{21–28} Overall, these trials demonstrated successful non-operative management of acute appendicitis in 70–85% of cases at 1-year follow-up. These studies demonstrated no increase in the rate of perforated appendicitis and fewer treatment-related complications in patients initially managed non-operatively with antibiotics alone, compared to appendectomy. The adult literature on non-operative management of acute appendicitis identified several risk factors for failure, including abdominal pain for more than 48 h, the presence of an appendicolith, phlegmon, or abscess on imaging, and elevated laboratory measures; specifically, a white blood cell (WBC) count > 18,000 cells/ μ L or a C-reactive protein > 4 mg/dL.^{21–28}

The literature on the role of non-operative management of uncomplicated appendicitis in children is more limited. There are three retrospective studies that included selected children with uncomplicated appendicitis.^{29–31} In these studies, the success rate of non-operative management of uncomplicated appendicitis ranged between 75% and 81%, with no reported increase in the rates of perforated appendicitis in patients who were initially managed non-operatively.

Recently, three prospective pediatric trials have been published. Svensson et al.³² published their experience in Sweden in a pilot randomized controlled trial (RCT) that included 24 non-operative and 26 operative patients. In this trial, non-operative management consisted of a minimum of 48 h of intravenous antibiotics and was associated with a success rate of 92% at discharge and 62% at 1 year. There was no increase in the rate of complicated appendicitis in the non-operative group and no differences in complications or cost at 1 year. The second trial, published by Tanaka et al.³³ from Japan, was a patient choice trial in which 78 patients chose non-operative management and 86 chose surgery. In this trial, non-operative management had a success rate of 99% at discharge and 71% at a median follow-up of 4.3 years. There was no difference in the operative time or rate of post-operative complications between patients who underwent appendectomy after failed non-operative management and those who underwent appendectomy as their initial treatment. Of note, in this study, non-operatively managed patients received intravenous antibiotics for at least 48 h, and the mean length of stay was 6.5 days in each group.

The third study was a prospective single-institution patient choice trial in the United States that enrolled patients who met specific clinical inclusion criteria.^{34,35} Patients were included if they were age 7–18 years with less than 48 h of abdominal pain, a

WBC count < 18,000 cells/ μ L, and an ultrasound or computed tomography (CT) scan demonstrating an appendix less than 1.2 cm in diameter with no evidence of an abscess, appendicolith, or phlegmon. If patients chose to undergo surgery, they received an urgent laparoscopic appendectomy with routine post-operative care. Patients who chose non-operative management were hospitalized for at least 24 h to receive intravenous antibiotics and for serial monitoring. They were kept nil per os (NPO) for at least 12 h, and diet was advanced if symptomatic improvement was achieved. Those patients who improved clinically were transitioned to oral antibiotics and discharged home. If at 24 h the patient demonstrated no clinical improvement, or if at any point during the hospitalization, a patient's clinical status deteriorated, they underwent appendectomy. This trial enrolled 102 patients, with 65 choosing surgery and 37 choosing non-operative management with antibiotics alone. Non-operative management had an in-hospital success rate of 94%, a 30-day success rate of 89%, and a 1-year success rate of 76%.^{34,35} Compared to the surgery group, patients managed non-operatively reported higher quality of life scores at 30 days and had significantly fewer disability days and lower costs, with no differences in the rates of complicated appendicitis or treatment-related complications at 1 year of follow-up.^{34,35} Results from additional trials are necessary to confirm the consistency of the success rate of non-operative management across other institutions in the United States. Currently, there is an ongoing multi-institutional trial investigating non-operative management of uncomplicated appendicitis in children across 10 pediatric hospitals in the United States.

Identifying risk factors for failure of non-operative management will allow for improved patient selection and minimize harm. A previous retrospective adult study identified an appendicolith as an independent predictor of failure of non-operative treatment.²⁸ Available pediatric data suggests that an appendicolith identified on imaging studies is a risk factor for failure of non-operative management in children with acute appendicitis. In the Tanaka trial, 47% (9/19) of patients with an appendicolith failed non-operative management compared to 24% (14/59) without an appendicolith ($p = 0.05$).³³ In the Svensson trial, 60% (3/5) of children with an appendicolith initially managed non-operatively underwent appendectomy.³² Finally, a prospective single center trial in the United States investigating non-operative management in children with uncomplicated appendicitis with an appendicolith on imaging was terminated early due to a high failure rate of non-operative management (60%, or 3 of 5, at a median follow-up of 4.7 months).³⁶ The failure rate of non-operative management in children with an appendicolith across these three pediatric trials was consistent, with an overall failure rate of 52%. Taken together, the available data suggests that non-operative management of children with acute appendicitis with an appendicolith may not be effective.³⁶

With the growing body of evidence, non-operative management of uncomplicated appendicitis appears to be a safe initial management strategy for select patients. As results from additional trials become available, non-operative management of uncomplicated appendicitis may be more widely offered as a treatment alternative in clinical practice.

Role of non-operative management in complicated appendicitis

Approximately, 30% of cases of appendicitis present as perforated appendicitis.³⁷ For the purposes of this article, we will interchangeably refer to perforated appendicitis, with or without a well-formed abscess, as complicated appendicitis. It should be noted, however, that the definition of complicated appendicitis

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