

Review

Is Appendicectomy Outdated in the Management of Paediatric Appendicitis?

Katherine Lehovsky¹, Nigel J Hall^{1,*}¹University Surgical Unit, Faculty of Medicine, University of Southampton, SO16 6YD Southampton, UK*Correspondence: n.j.hall@soton.ac.uk (Nigel J Hall)

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Abstract

Appendicitis is the most common emergency surgical presentation and is particularly prevalent in the paediatric population. At present, the majority of children are managed with surgical removal of the inflamed appendix, a procedure that was established centuries ago, before the widespread availability of antibiotics. There are anecdotal historical cases of non-operative management of appendicitis, particularly in geographically remote areas. In recent decades, there has been increasing interest in the potential to manage appendicitis non-operatively. This review explores the relative merits of non-operative and surgical management of appendicitis and their current role across the spectrum of disease in clinical practice in the UK. It concludes that both operative and non-operative management are safe and effective treatments in appropriately selected patients. However, the results of further large-scale studies are needed to help refine our application of these treatments in clinical practice. The current evidence supports discussion of both operative and non-operative management as part of informed consent and the shared decision-making process.

Keywords: appendicitis; paediatric; appendicectomy; antibiotics; surgical; non-operative treatment

1. Introduction

Appendicitis is one of the most common causes of acute abdominal pain, with rates of 5.7–50 patients per 100,000 of the population per year. There is a peak in the incidence between the ages of 10 and 30, which makes this pathology highly relevant to the paediatric population [1]. The peak in adolescence is attributed to increased lymphoid follicular hyperplasia in this age group [2]. The management of appendicitis has been based on the dogma that surgery, namely appendicectomy, is the mainstay of treatment. The earliest appendicectomy is thought to have been performed by Amyand in 1735 [3]. Further reports by Fitz in 1886 described and named the condition ‘appendicitis’, advocating for surgical management with appendicectomy [4]. Widespread availability of antibiotics did not emerge until decades after this publication. Reflecting on the historical evolution of appendicitis management, perhaps provides a rationale for the emphasis on operative management, which persists to the present day. Surgery and early anaesthesia techniques were available prior to the discovery and ubiquitous introduction of antibiotics.

Non-operative management refers to the use of antibiotics as a primary therapy for appendicitis in conjunction with close monitoring for complications or progression of disease. Early reports of non-operative management of appendicitis date back to 1959 and have since been explored in the adult and paediatric populations [5]. This review explores non-operative management of paediatric appendicitis in several clinical settings to reflect on the ongoing role of appendicectomy. The aim is to provide clinicians with

insight into the varied management approaches to appendicitis and to introduce the concept of non-operative management as a safe and effective alternative to appendicectomy. Importantly, however, we do not propose that appendicitis should become a ‘non-surgical’ disease and argue that both diagnosis and management should remain under the care of a surgeon. Rather, we hope our review may contribute to primary and secondary care non-surgical clinicians being better informed and able to refine their communication with patients ahead of surgical referral, for example, by not portraying appendicectomy as the sole management of appendicitis, which may be misleading.

2. The Spectrum of Disease

Acute appendicitis represents a spectrum of disease from uncomplicated (also sometimes referred to as simple) to complicated. These are distinguished based on clinical and radiological characteristics. In fact, some have gone as far as to suggest that two disease entities exist for acute appendicitis. The first is a form of mild inflammation that can spontaneously settle, and the second is more severe inflammation with risk of progression to perforation and gangrene [6]. Uncomplicated acute appendicitis refers to acute appendicitis without perforation, peri-appendicular abscess or appendix mass [7]. This cohort of patients has been identified as being potentially suitable for non-operative management with antibiotics. However, safe and effective implementation will require refined patient stratification to correctly identify those who are suitable candidates. In contrast, complicated disease refers to appendicitis with perfo-



ration, the presence of a peri-appendicular abscess or peritonitis [8]. It also encompasses the pathology termed an appendix mass, which refers to an inflammatory mass of bowel and omentum that surrounds and adheres to an inflamed appendix [9]. Minimising progression of disease to complicated appendicitis is central to clinical practice as complicated appendicitis is associated with higher morbidity and healthcare costs [10].

3. Operative Management of Appendicitis

Operative management of appendicitis involves the removal of the acutely inflamed appendix. Appendectomy is a well-established surgical procedure that dates back as far as 1735 [3]. In the UK, it is estimated that approximately 12,000 emergency appendectomies are performed annually in children under the age of 18, with only 20% managed in specialist paediatric surgical units [11]. There is a widespread perception that appendectomy is the default treatment amongst members of the public and many clinicians who are unfamiliar with evolving research in the field. Appendectomy is perceived as a simple and safe procedure which is routinely carried out by general surgeons and paediatric surgeons. Whilst this is true, it requires a general anaesthetic and intraperitoneal abdominal entry via either a laparoscopic or open approach, with the associated risks. The National Appendectomy Audit reported the 30-day adverse rate (a composite of readmission, re-intervention, pelvic collection and wound infection) as 15.3%, highlighting that the risk of morbidity following appendectomy is not innocuous [12].

There has been a paradigm shift over the past 30 years within surgery towards minimally invasive surgery, such that the majority of paediatric appendectomies in developed countries are now performed laparoscopically. A recent Cochrane review addressed the relative merits of laparoscopic and open approaches, considering 10 paediatric trials. They found no difference in pain intensity on day 1, incidence of intra-abdominal abscess or time to return to normal activities. In contrast, laparoscopic appendectomy was associated with less wound infections and a shorter length of hospital stay by 0.8 days. Quality of life was not reported in any of the included studies, although in the adult population, patients had better quality of life scores in the first 6 months post-operatively after laparoscopic compared with open appendectomy [13].

Complicated appendicitis is known to be a resource-intensive condition with longer hospital stays and a higher risk of complications and readmission than uncomplicated cases [1]. There is an ongoing debate about the optimal timing of appendectomy, with inconclusive evidence about whether a longer time to appendectomy increases the risk of complicated appendicitis. In a large multicentre retrospective cohort study, increasing time to appendectomy within 24 hours of presentation was not associated with increased risk of complicated disease. The median time to ap-

pendectomy was reported as 7.4 hours. This implies that appendectomy can be managed as an urgent rather than an emergency procedure, provided it is performed within a reasonable time frame. Timing of surgery is a multifactorial decision; however, this data dispels disease progression as a justification for mandatory out-of-hours operating [14].

Paediatric appendicitis places a significant logistical and economic burden on our healthcare system, with an estimated cost exceeding 21 million pounds per year in England [15]. As previously discussed, the timing of surgery is a composite decision which must also take into account its impact on the length of hospital stay. The average length of hospital stay with uncomplicated appendicitis has been reported as 1 day [16]. There is evidence to support same-day discharge after appendectomy for acute, non-perforated appendicitis [17]. A large retrospective cohort study in the USA found no difference in the odds of 30-day readmission for patients with same-day discharge compared with those discharged within 2 days. Shorter admission length could alleviate the financial burden of paediatric appendicitis, improve efficiency of care and bed availability [17].

Another consideration of operative management is the potential for overdiagnosis and arguably unnecessary surgery. Ultimately, the diagnosis of appendicitis can be made on clinical grounds alone. In the context of diagnostic uncertainty, despite clinical examination findings and even radiological imaging, performing a diagnostic laparoscopy may be an appropriate course of action. The negative appendectomy rate refers to the absence of an inflammatory process or other significant pathology of the appendix on histological examination [18]. This retrospective assessment is used as a metric for unnecessary appendectomies. The UK National Appendectomy Audit (2012) reported a negative appendectomy rate of 19.2%. Of note, the negative appendectomy rate was only 10.3% in specialist paediatric centres. Therefore, two-thirds of children undergoing appendectomy in the UK are being exposed to a higher risk of having a normal appendectomy based on where they present [12]. The more recent Right Iliac Fossa Pain Treatment (RIFT) study demonstrated some improvement with a negative appendectomy rate of 15.9% [19]. Appendectomies are associated with complications, and preventing children from being exposed to these unnecessarily is essential.

4. Non-Operative Management of Uncomplicated Appendicitis

Non-operative management of appendicitis is not a new concept despite the fact that most children globally with acute appendicitis continue to be managed with surgical intervention. There are anecdotal historical reports of successful non-operative management of appendicitis with conservative treatment dating back for centuries. One early large case series in 1959 treated 471 patients with intravenous antibiotics; there was one mortality, and nine pa-

tients required drainage of an abscess acutely. Recurrence rates were reported at 10% [5]. Non-operative management of uncomplicated appendicitis as a primary therapy has been more formally explored in adults since the mid-1990s, and more recently in children. Several large-scale randomised controlled trials have compared antibiotic therapy with appendectomy in adults. The Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) trial took place in 25 USA centres and demonstrated non-inferiority of antibiotics based on 30-day health status determined from a quality-of-life questionnaire. However, the failure rate was high, with 29% of those treated with antibiotics having undergone an appendectomy by 90 days. The risk of failure was higher in those with an appendicolith (41% vs. 25%) [20]. A previous trial, Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis (APPAC), showed a lower incidence of appendectomy in the antibiotics group, with 16% at 90 days and only 39% at 5 years. This lower incidence could be explained by differences in inclusion criteria, as the APPAC trial excluded patients with faecoliths, which are associated with a higher rate of complicated appendicitis [21]. Trial data in the adult population provides a clear rationale for the exploration of non-operative management in children.

One early large-scale prospective multicentre non-randomised study in 1068 children with uncomplicated appendicitis showed positive results, with 67.1% of children who received initial non-operative management not requiring an appendectomy by 1 year. Of note, this study allowed the patient/parents to choose which treatment they received, as it was felt that strong preferences would preclude randomisation. Non-operative management was associated with significantly fewer patient disability days at 1 year (6.6 days vs. 10.9 days) [22]. Subsequently, the Coronavirus Disease 2019 (COVID-19) pandemic provided a unique opportunity to observe the application of non-operative management of appendicitis in the real-world setting—its use had previously been restricted to observational cohort studies and a single feasibility randomised controlled trial. The Children with Appendicitis during the Coronavirus pandemic (CASCADE) study was a prospective multicentre observational study which showed a success rate of 63.1% for non-operative management at 1 year in a cohort of paediatric patients treated during the pandemic in the UK. Non-operative treatment was associated with fewer complications when compared with surgery (odds ratio 5.9, 1.3% vs. 7.3%) [23]. However, the translation of this study is limited by its observational nature. A parallel international retrospective multicentre study undertaken in 23 countries found that only 12.8% of paediatric patients managed non-operatively for simple appendicitis required an appendectomy within one month [24].

Prospective randomised controlled trials have the potential to provide more rigorous and robust results. Until recently, only three small randomised controlled trials had

published data with heterogeneous appendectomy rates after non-operative management ranging from 7% to 59% [25–27]. The results of the first adequately powered multicentre non-inferiority randomised controlled trial were recently published [28]. A total of 222 children were recruited and randomised to either operative or non-operative management. Non-inferiority was not demonstrated at either 30 days or 12 months, with 46% of patients managed non-operatively subsequently undergoing an unplanned operation. Study design may have contributed to treatment failure, as there was a low threshold for conversion to appendectomy if children were not ready for discharge at 48 hours, although their symptoms may have improved if given more time. In these cases, there was a 20% negative appendectomy rate, which was higher than the baseline at these centres. Another factor that may have compounded the failure of non-operative management was inadvertent recruitment of cases of complicated appendicitis, as there was no requirement for diagnostic imaging. Reassuringly, non-operative management was found to be safe with no difference in adverse outcomes. Children who underwent non-operative management required less narcotic analgesia and were found to return to school and their usual activities significantly sooner, although they had a slightly longer initial hospital stay and significantly higher rates of representation and readmission [28].

One of the challenges faced when refining the non-operative management of appendicitis is selecting suitable candidates. To date, there has been a significant variety in the inclusion criteria for studies comparing operative and non-operative management. Some have mandated stringent inclusion criteria, for example in the Midwest Paediatric Surgery Consortium study patients were only offered non-operative management if they had radiological confirmation of uncomplicated appendicitis (ultrasound/computed tomography/magnetic resonance imaging), an appendix diameter <1.1 cm, no faecolith or phlegmon, white cell count within a specified range and abdominal pain for less than 48 hours duration [22]. These strict criteria may limit the generalisability of the study's findings. Conversely, the APPY (appendectomy versus antibiotics for acute uncomplicated appendicitis in children) trial is more pragmatic and included all children between 5 and 16 years diagnosed with non-perforated appendicitis, based on clinical or radiological grounds [29]. This highlights the absence of a ubiquitous standard for diagnosing uncomplicated appendicitis in the trial setting. There are clear advantages in the applicability of the more pragmatic approach in terms of its ability to translate into routine clinical practice, where there is significant variation in the use of diagnostic tests for uncomplicated appendicitis.

The APPY trial, an international, multicentre, non-inferiority trial comparing appendectomy and antibiotics for acute uncomplicated appendicitis, recently published the results of their 936 patients [29]. The primary outcome

Table 1. Potential benefits and disadvantages of non-operative treatment when compared to appendicectomy for uncomplicated appendicitis in children.

Benefits	Disadvantages
Safe alternative to surgery [28,29]	Small chance of not responding to initial treatment course [28,29]
Avoids general anaesthesia and invasive surgery [22–24]	Risk of recurrent appendicitis [29]
Lower analgesia requirements [28,29]	May require longer initial hospital stay [28,29]
Shorter convalescence and return to full activities [22,28,29]	Higher rate of readmission [28]
Fewer complications [23]	
Fewer days away from school [28,29]	

in the APPY trial was treatment failure, defined as the need for appendicectomy within 1 year in the antibiotic group or a negative appendicectomy or complication requiring general anaesthesia within 1 year in the operatively managed group. At 12-month follow-up, treatment failure had occurred in 34% of patients in the antibiotic group versus 7% in the appendicectomy group (26.7% difference). In the antibiotic group, 16% experienced failure of initial antibiotic therapy, whilst 18% had a recurrence that necessitated an appendicectomy. In the appendicectomy group, 27 out of 28 treatment failures were negative appendicectomies. Reassuringly, there were no deaths or serious adverse events reported in either group. However, there were cases of misdiagnosis and inclusion of perforated appendicitis within the study. Of those assigned to the appendicectomy group, 6% had a histopathological diagnosis of perforated disease, and in patients who experienced early failure of non-operative management, 35% had perforated disease at the time of operative management. The results of this study are in line with those of Adams *et al.* [28], with patients managed non-operatively having a marginally longer initial hospital stay (1.25 vs. 1.0 days) but a faster return to school (2 vs. 3 days) and normal activities (1 vs. 4 days), and lower analgesia requirements (0 vs. 3 days). This trial concludes that, based on a 20% non-inferiority margin, antibiotic management was inferior to appendicectomy. However, non-operative management appears to represent a safe treatment option in those wishing to avoid surgery with the added benefits of rapid return to normalcy [29].

Non-operative management appears to be a safe treatment option in an appropriately stratified patient cohort. The challenge remains to determine which health, social and economic outcomes are most important to consider when defining the role of non-operative management in clinical practice (Table 1, Ref. [22–24,28,29]). Future research should be centred on providing comparative data derived from homogenous patient groups that are allocated by unbiased randomisation. Furthermore, focus should be placed on outcomes that are considered important by patients and their parents, not just medical professionals, to facilitate more nuanced shared decision making (Table 1). Parents have shown interest in non-operative management of appendicitis, with 59% of respondents to a questionnaire

expressing a preference for non-operative treatment over surgery [30]. Emphasis on shared decision making empowers parents who are uniquely placed to comprehend the relevant wider factors in their child's life [31]. At least one more randomised controlled trial is ongoing, namely the CONTRACT-2 (CoNservative TRreatment of Appendicitis in Children-2) study in the UK. Once further results become available, they have the potential to help refine our management of uncomplicated paediatric appendicitis [25,32].

5. Management of Complicated Appendicitis

Complicated appendicitis sits at the other end of the spectrum of disease and can be defined as appendicitis with perforation, the presence of a peri-appendicular abscess or peritonitis [8]. There is less interest in treating this cohort of patients non-operatively, except for in cases of well-established appendicular abscess. Many studies present heterogeneous outcome data encompassing all sub-categories of complicated appendicitis. Arguably, this limits our ability to determine the most effective course of treatment. To overcome this limitation, one systematic review and meta-analysis investigated the non-operative management of complicated appendicitis in children, ensuring stratification of disease into two groups (perforation with an abscess/phlegmon and perforation without abscess/phlegmon). Fourteen studies were included with a total of 1288 patients. In children with free perforated appendicitis, operative management showed a lower complication (risk ratio [RR] = 1.86) and readmission rate (RR = 1.49). This was contrary to the results in patients with an abscess/phlegmon in whom non-operative management had lower complication (RR = 0.07) and readmission rates (RR = 0.35) [33]. This highlights the importance of stratifying patients into these two groups to guide their initial management. The efficacy of clinical examination to distinguish between free perforated appendicitis and abscess/phlegmon is unclear. This raises the question of whether additional investigations, such as ultrasound imaging, should be implemented. Ultrasound imaging is the first-line imaging for the diagnosis of paediatric appendicitis, with a diagnostic accuracy of 96% reported in one case series of 8555 scans [34]. Intuitively use of ultrasound is likely to enhance the distinction of free perforated appendicitis from abscess/phlegmon; however, this question is not addressed in the literature.

Perforated appendicitis can lead to the formation of an appendix abscess, which is characterised by a localised collection of pus. Management of peri-appendicular abscesses can be with early surgery or non-operative treatment with antibiotics and consideration of drain insertion if the anatomical location is accessible under radiological guidance [35]. A Cochrane review considered early versus delayed laparoscopic appendectomy for appendiceal abscesses. The available data were very sparse, with only one trial involving 40 paediatric patients suitable for inclusion, which did not report overall complications and prevented any robust conclusions. Of note, the majority of patients in the delayed appendectomy group had undergone percutaneous abscess drainage as initial management [36]. There is evidence to support the therapeutic effectiveness of percutaneous drainage in the management of paediatric appendiceal abscess, with lower rates of recurrent appendicitis compared with antibiotics alone [35].

Complicated appendicitis is associated with greater morbidity after appendectomy than uncomplicated appendicitis [37]. One complication is the formation of an intra-peritoneal abscess following operative management. This is different from the previously discussed peri-appendicular abscess that arises as a primary pathology. It is estimated that intra-peritoneal abscesses occur post-operatively in 10–20% of cases of complicated appendicitis [38–40]. The placement of prophylactic intra-peritoneal drains during appendectomy in these cases remains controversial. The perceived benefits are to reduce the accumulation of fluid by external drainage to prevent abscess formation. Conversely, the drain is a foreign body that acts as a potential nidus and conduit of infection. A recent systematic review and meta-analysis found no clinical benefit to the placement of intra-peritoneal drains in children. In fact, drain placement was associated with an increased risk of abscess formation (odds ratio (OR) = 1.61), longer operative time and longer hospital admission [41]. Alternative techniques to reduce abscess formation include intraoperative suction and irrigation. A prospective randomised controlled trial compared peritoneal irrigation and suction only. They found equivalence of these techniques with only one post-operative abscess developing and no significant difference in length of stay [42]. Overall, there is a paucity of research into the role of non-operative management in complicated appendicitis, likely because it represents a less viable clinical option in the context of advanced disease.

6. Management of Appendix Mass

The management of an appendiceal mass is anomalous amongst the spectrum of paediatric appendicitis, with primary antibiotic therapy being well established in clinical practice [43]. An appendix mass refers to an inflammatory mass of bowel and omentum that surrounds and adheres to an inflamed appendix [9]. It is estimated that up to 9% of children present with an appendix mass [43]. This is of

particular concern in the pre-school population, who often present late and with undifferentiated symptoms [44]. The rationale for non-operative treatment of an appendix mass arises from the increased technical difficulty of appendectomy and the potential risk of damage to adjacent structures when dissecting the inflammatory mass [7].

Despite this, some surgeons remain proponents of early surgery for cases of appendix mass during initial hospital admission. A recent Cochrane review addressed the question of operative timing in appendix mass by considering evidence from 7 studies, which included 788 children and adults. The evidence was found to be very uncertain about the effect of early versus late appendectomy on morbidity (including wound infection, bowel obstruction, faecal fistula and unplanned bowel resection). Whilst early appendectomy was associated with a lower rate of abdominal abscess (by 43 per 1000 participants) and shorter length of stay (by approximately 2 days), it was also associated with increased time away from normal activities by 5 days. There are significant limitations to this data, and further randomised controlled trials are needed to provide robust conclusions [45].

Further controversy exists around whether there is an absolute necessity to perform appendectomy following successful non-operative management of an appendix mass. The Children's Interval Appendectomy (CHINA) study, an international multicentre randomised controlled trial, compared routine interval appendectomy with active observation in a cohort of 106 patients to address this question. They found that only 12% of children who had successful conservative treatment of appendicitis had a histologically proven recurrence of appendicitis within 1 year. Of note, the presence of a faecolith had no effect on this outcome [46]. This provides a strong rationale for adopting an expectant approach in clinical practice, which was contrary to the routine advice of UK-based paediatric surgeons at the time, with 68% recommending interval appendectomy [47]. Furthermore, interval appendectomy was associated with severe complications in 6% of children, which must be weighed against the risk of recurrent appendicitis. Active observation had the additional benefits of reduced cost, shorter hospital admission and less time away from normal daily activities. One final consideration when determining the time of operative intervention is the risk of non-diagnosis of significant conditions, such as carcinoid tumours, whose presentation can be homologous to appendicitis. The estimated risk of carcinoid tumour in this population is less than 1%, which lies within the range of the overall incidence in the general population [46]. Therefore, this does not present a contraindication to expectant management of an appendix mass in the paediatric population.

7. Who Should Care for the Patient?

Inevitably, with the acknowledgement that some cases of appendicitis are amenable to successful treatment with-

out surgery, there may be a drift towards both diagnosis and management of appendicitis by non-surgical clinicians. We do not support this and would argue against it. In the interests of antibiotic stewardship and avoidance of unnecessary treatment, we would not support a move away from the diagnosis of appendicitis by a surgeon (as is the case in UK practice currently). Such a move may risk widespread use of antibiotics for cases of abdominal pain without a definite diagnosis of appendicitis being made. Furthermore, we believe surgeons are best placed to monitor cases of appendicitis being managed non-operatively so as to identify early cases that may require surgery and allow for early recognition and treatment of any complications that may arise. As such, we propose that surgeons maintain a key role as both diagnosticians and clinicians overseeing the treatment of children with appendicitis (jointly with paediatricians where appropriate) so that cases can be managed appropriately, whether with surgery or non-operative treatment. We do recognise, however, that with improvements in our understanding of which children with which type of appendicitis are most likely to respond to non-operative management, treatment outside of the inpatient hospital setting may become a reality in the future.

8. Conclusion

Appendicitis is a common cause of acute abdominal pain in the paediatric population and represents a significant burden on our healthcare system. Appendectomy has been a well-established treatment throughout history and continues to have an important role in the management of paediatric appendicitis. However, emerging evidence supports a role for non-operative management in selected cases. Although further studies are necessary to determine how outcomes compare to appendectomy in unbiased populations over longer follow-up periods, the dogma that appendectomy is the default management for all appendicitis is certainly outdated. Discussion of non-operative treatment and appendectomy should form part of a shared decision-making and informed consent process with parents and patients.

Key Points

- Appendicitis constitutes a wide spectrum of disease, ranging from uncomplicated (simple) to complicated.
- Both operative and non-operative management of acute appendicitis can be safe and valid treatment options in appropriately selected patients.
- Complicated appendicitis is associated with higher morbidity, longer hospital admissions, higher re-admission rates and poses a significant financial burden on our healthcare system.
- There is ongoing research into non-operative management of uncomplicated appendicitis with large-scale randomised controlled studies underway in order to help establish its role in future clinical practice in the UK.

- Shared decision-making with patients and parents to convey the options of non-operative and operative management is warranted based on the current evidence.

Availability of Data and Materials

Not applicable.

Author Contributions

KL and NJH: conceptualisation, drafting, review & editing. Both authors contributed to the important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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