Non-operative Management of Complicated Appendicitis

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Case Example
A 10-year-old girl presents to the emergency department with her parents complaining of 5 days of right lower quadrant abdominal pain. She has been intermittently febrile at home to 38.5 °C and she has a leukocytosis of 16.1 × 10^9/L. On examination, she is noted to have a palpable mass in the right lower quadrant, which is confirmed on ultrasound to be a 3 × 3 cm abscess, likely due to perforated appendicitis. She is admitted, placed on intravenous antibiotics until resolution of her fevers and improvement of her abdominal pain and leukocytosis. She is then discharged home on oral antibiotics once tolerating a diet. She is scheduled to return to clinic for evaluation for interval appendectomy.

Introduction

Acute appendicitis has a spectrum of presentations, from simple inflammation of the appendix to perforation with gross fecal contamination. Complicated appendicitis itself includes a wide spectrum, from gangrenous to perforated, with the possibility of the development of an associated phlegmon or abscess or with diffuse peritonitis. The incidence of perforated appendicitis in the pediatric population is approximately 30% [1]; this number has even been estimated as high as 38.7% in other studies, with the finding that up to 65.8% of pediatric patients under age 4 years will present with perforation [2]. Once perforated, the course of care is complicated by a longer length of stay, longer duration of antibiotics, and greater

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financial expense as compared to non-complicated acute appendicitis [2]. In addition to the variable course of complicated appendicitis, there is significant provider variability in the management of this disease process. Multiple studies have described the benefits of early appendectomy, even in the setting of complicated appendicitis [3–13]. However, non-operative therapy can also be effective in the management of complicated appendicitis and in certain circumstances should be the preferred approach. In this chapter, we will explore the non-operative management of complicated pediatric appendicitis and provide treatment recommendations for practice.

The Role for Non-operative Management

The optimal treatment of complicated appendicitis (gangrenous or perforated plus or minus an associated phlegmon or abscess) remains controversial. A 1981 study by Jordan et al. of 45 patients presenting with an abdominal or pelvic mass with appendicitis demonstrated a 33.7% complication rate in the 90.5% of patients who underwent appendectomy within 24 hours of admission (primarily wound infections) [3]. Despite this, multiple studies are in support of early appendectomy, even in patients presenting with complicated appendicitis who are at higher risk of complications. Blakely et al., in a 2011 study of 131 patients with perforated appendicitis without mass or abscess, randomized patients to early appendectomy (within 24 hours of admission) versus initial non-operative management with interval appendectomy (within 6–8 weeks); they found adverse events in 30% of early appendectomy patients as compared to 55% of interval appendectomy patients, as well as a reduced time away from normal activities for early appendectomy patients in addition to a 34% failure rate for patients randomized to the interval appendectomy group due to failure to improve or recurrent symptoms of acute appendicitis [5]. In light of these findings, they suggested that early appendectomy was better than non-operative management with interval appendectomy [5]. The results of this single randomized trial have dominated the recommendations of multiple meta-analysis studies and led to the recommendation of early appendectomy for complicated appendicitis [9, 10]. Retrospective reviews have also found that early appendectomy is associated with decreased length of stay, morbidity, and overall complications [4, 7, 8, 12, 13], as well as lower hospital costs and healthcare utilization as compared to non-operative management with interval appendectomy [6, 11].

Despite the findings of these studies, there has also been ample evidence to support a trial of non-operative management for complicated appendicitis in certain patients. As early as 1980, Janik et al. described an ultraconservative approach to non-operative management of late-presenting complicated appendicitis in which 37 children were observed in the hospital without antibiotic management until they had improvement in symptoms; 81% of the children demonstrated clinical improvement in 5–22 days, and only 19% required abscess drainage within 2–10 days of presentation, with only 1 child presenting with recurrent symptoms [14]. They concluded that non-operative management without antibiotics is safe with close observation

and that interval appendectomy can be performed up to 20 weeks after symptom resolution [14]. In 1981, Powers et al. described non-operative or conservative management of perforated appendicitis with interval appendectomy 4–6 weeks later if there was good clinical response and described good safety with this approach; however, they cautioned that if there was no clinical improvement on antibiotics within 12–24 hours, then appendectomy was indicated at that time [15]. Skoubo-Kristensen and Hvid, in 1982, described a series of 193 adult and pediatric patients with an appendiceal mass or abscess treated over a period of 10 years with non-operative management; they found an 88% success rate with non-operative management, with a 7.1% recurrence rate over a 3-month period [16]. They felt that patients presenting with appendicitis with an appendiceal mass were successful in most patients, with low complication rates for interval appendectomy [16]. In 1987, Bagi and Dueholm described using non-operative management with intravenous antibiotics and percutaneous drainage if there was a verified abscess which could be safely drained for patients presenting with appendicitis with an appendiceal mass [17]. They found that non-operative management was safe, with relatively few complications or late sequelae; patients do, however, require close monitoring upon discharge [17].

These early studies laid the groundwork for future work describing successful non-operative management of complicated appendicitis. One aspect to consider is whether the patient is presenting simply with a perforated appendicitis or whether they are presenting with a perforated appendicitis with a well-formed appendiceal mass or abscess. A number of studies have examined the success of conservative management with initial intravenous antibiotics with the addition of percutaneous drainage if possible in the treatment of perforated appendicitis with a well-defined abscess or mass [18–29]. In a large study of 427 children presenting with abdominal mass with appendicitis at three children's hospitals, 16 underwent immediate appendectomy and 411 were treated conservatively; the authors described an 84.2% success rate of initial non-operative management, with a median length of stay of 6 days. The complication rate following interval appendectomy 4–6 weeks later was only 2.3% [19]. Roach et al., in a study of 92 pediatric patients with complicated appendicitis and an intra-abdominal abscess or phlegmon, where 60 were taken immediately to the operating room and 32 were treated with intravenous antibiotics and abscess drainage followed by interval appendectomy around 6 weeks later, found that the conservative management group demonstrated no difference in length of stay and no readmissions, while there were 6 readmissions in the immediate operation group; they concluded that patients presenting with more than 5 days of symptoms with a well-defined mass or abscess could be successfully treated with antibiotics and drainage when possible [22]. These and other similar studies support the use of non-operative management for pediatric patients presenting with appendicitis with an associated appendiceal mass or abscess, with good success rates and minimal complications as compared to those patients undergoing immediate or early appendectomy.

The success of non-operative management extends beyond the treatment of patients presenting with appendiceal mass or abscess, however. Successful

non-operative management has also been described in groups of patients presenting with complicated appendicitis with no distinction based on the presence or absence of appendiceal mass or abscess [30–36], as well as in mixed populations of patients presenting with and without abscess or mass [37–40]. A 2003 study of 96 children being treated for perforated appendicitis, where 71 underwent immediate appendectomy and 25 were treated initially non-operatively with antibiotics and percutaneous drainage if necessary, demonstrated a success rate of 64%; however, in the 9 children who required earlier appendectomy (after 3–12 days), those patients had fewer wound complications and abscesses postoperatively compared to those patients undergoing immediate appendectomy, therefore favoring initial delayed or non-operative management [37]. Vane and Fernandez compared 86 children presenting with complicated appendicitis based on those undergoing immediate appendectomy within 72 hours (59 children) and those undergoing initial non-operative management with interval appendectomy (27 children); they found that the length of stay was 4.9 days for the immediate group and 4.1 days for the interval group plus an additional 0.9 days for the interval appendectomy and that all of the complications occurred in the immediate appendectomy group, further supporting the use of non-operative management in complicated appendicitis [31]. In a 2013 study of children presenting with complicated appendicitis being treated non-operatively, the authors expanded the criteria for non-operative management to include almost anyone beyond those presenting with simple appendicitis; they found the average length of stay to be 5.6 days, and only 4.9% required appendectomy prior to discharge for failure to improve [40]. In a meta-analysis comparing conservative treatment of complicated appendicitis versus immediate appendectomy, Simillis et al. looked specifically at studies pertaining to the pediatric population and demonstrated that as compared to conservative management, pediatric patients undergoing immediate appendectomy had more complications, including wound infections and intra-abdominal abscesses, with no difference in the initial length of stay, the rate of ileus or small bowel obstruction, or the need for reoperations; this large meta-analysis further supports the use of non-operative management in pediatric patients presenting with complicated appendicitis [41]. All of these studies taken together support a careful use of a trial of initial non-operative management, including intravenous fluid resuscitation, intravenous antibiotics, and percutaneous drainage if possible for complicated appendicitis, regardless of whether or not there is a well-formed abscess or mass at the time of presentation.

The Cost of Non-operative Management

When comparing initial non-operative management to early appendectomy, the hospital-related costs must also be taken into account. The majority of studies report that early appendectomy is associated with decreased costs as compared to interval appendectomy following non-operative management [6, 8, 11, 24, 42]. A study by Darwazeh et al. in 2016 found that interval appendectomy prevents a recurrence in only one of eight patients (pediatric and adult); therefore significant additional

operative costs are being used for a diminishing return [42]. Dennett found that while the total hospital costs were greater for the non-operative management group, the indirect costs to patients and their families were not significantly greater [8]. While Keckler et al. support a trial of non-operative management with antibiotics and possible percutaneous drainage, they did advise that this treatment methodology can be related to an increased number of visits, and increased CT scans, leading to overall increased costs [24].

One author encouraged continued non-operative management instead of interval appendectomy if the non-operative success rate is estimated to be 60% or greater, as the potential costs of repeat admissions and procedures did not outweigh the cost associated with routine interval appendectomies [43]. Similarly, a 2014 study questioned the usefulness of routine interval appendectomy, as only 12% of patients in the study developed recurrent appendicitis, and this could lead to significant potential cost savings [26].

The Role for Patient Selection in Non-operative Management

Proper patient selection for non-operative management is key to its success. Patients presenting with diffuse peritonitis or a short duration of symptoms are typically better served by early operative management [4, 23, 38, 44]. However, those patients presenting with a longer duration of symptoms (typically greater than 5 days) and no diffuse peritonitis may be candidates for non-operative management [22, 23]. Additionally, those patients presenting with a palpable mass or visualized abscess on imaging are typically better candidates for non-operative management [45].

The key to successful non-operative management is to attempt to identify those patients who will likely fail non-operative management early in the course of their treatment. Multiple studies have been done to attempt to identify risk factors which may contribute to the failure of non-operative management [34, 35, 38, 39, 45–48]. In a 2001 study, Kogut et al. found that 22% of children being treated non-operatively for perforated appendicitis failed to improve on antibiotics and went on to appendectomy; they found that the white count differential, and in particular bandemia >15%, was correlated with treatment failure and future complications [47]. Talishinskiy et al. similarly found that bandemia >15% was associated with non-operative treatment failure [35], and Whyte et al. demonstrated that a higher percentage of bands on admission white count differential was predictive of failure [48]. The presence of an appendicolith on initial imaging is also predictive of treatment failure, as described in multiple studies [25, 34, 44, 46]. In a 2005 study, Ein et al. described a recurrence rate of 72% for patients with an appendicolith, as compared to 26% with no appendicolith [44]. Nazarey et al. described the presence of an appendicolith along with a leukocytosis >15, or patients presenting with more than 2 days of symptoms, was associated with treatment failure [34]. Zhang et al., interestingly, found that not all patients with an appendicolith on initial imaging failed non-operative therapy, as most appendicoliths which are present on the admission imaging will resolve; however, if the appendicolith persists on subsequent

imaging, this is a risk factor for non-operative treatment failure [25]. Other predictors of non-operative treatment failure include lack of an abscess on admission imaging [46], evidence of disease extension beyond the right lower quadrant on admission imaging [39], requiring percutaneous drainage of an intra-abdominal abscess [38], and lack of fever response within 24 hours of initiation of treatment [48]. If these risk factors are not present, it is possible that patients will have greater success with non-operative management. It is important to make the decision early in the patient's presentation as to whether or not they will be a good candidate for non-operative management, as failure of non-operative management can lead to significant complications.

The Role for Antibiotic Selection in Non-operative Management

While individual hospitals or providers may have their own protocols for the non-operative management of complicated appendicitis, management typically is begun with fluid resuscitation, as well as initiation of broad-spectrum antibiotics.

Multiple antibiotic regimens have been described [4, 5, 11, 12, 30, 40, 49]. The classic starting regimen of intravenous antibiotics for perforated appendicitis includes the triple therapy of ampicillin, gentamicin, and clindamycin or metronidazole [4, 31]. Studies have since demonstrated efficacy with other antibiotic combinations such as ceftriaxone and metronidazole, which is felt to be less costly with no difference in length of stay or the rate of postoperative complications [4, 50, 51], or ticarcillin/clavulanate plus gentamicin, which was found to be clinically more effective than the traditional triple therapy [4, 52]. The use of piperacillin-tazobactam plus or minus metronidazole has also been described [40, 49]. Bufo et al. in 1998 described treatment with ceftazidime and clindamycin, with a non-operative failure rate of 17% [30].

The ideal antibiotic for discharge home has also been explored. Interestingly, higher numbers of treatment failures have been identified in patients remaining on intravenous antibiotics via a peripherally inserted central catheter (PICC) line upon discharge home. The treatment failures and revisits are thought to be due in part to complications arising from the PICC line [53]. Oral antibiotics which have been used with successful discharge include amoxicillin/clavulanate with metronidazole [40] and trimethoprim-sulfamethoxazole with metronidazole [23, 31].

The Role for Percutaneous Drainage in Non-operative Management

If an abscess is identified on admission imaging or the patient has a palpable mass on physical examination, percutaneous drainage can be a valuable addition to the success of non-operative management. Even starting as early as 1987, practitioners were abdicating for non-operative management in complicated appendicitis with

abscess, including percutaneous drainage of the abscess if possible [17]. A 2016 study by Luo et al. included 1225 pediatric patients with appendiceal abscess undergoing non-operative management; 150 underwent percutaneous drainage (2.2%), whereas 1075 (97.8%) were treated with antibiotics alone and no percutaneous drainage. The patients who underwent percutaneous drainage had a longer length of stay, but less recurrences and fewer complications following interval appendectomy if it was performed; the authors concluded that antibiotics plus percutaneous drainage was more effective treatment for appendiceal abscess than antibiotics alone [29]. McNeeley et al. similarly described significant symptom improvement with percutaneous drainage; however, they did find that more complicated abscesses had a higher rate of technical failure or possible subsequent recurrence or complications [54]. Roach et al., in a study of 92 pediatric patients with complicated appendicitis with intra-abdominal abscess in which 32 patients had percutaneous drainage and treatment with intravenous followed by oral antibiotics and 60 patients were taken immediately to the operating room, found that those patients undergoing non-operative management with interval appendectomy at a later date had no difference in length of stay and an improved readmission profile as compared to the immediate appendectomy group; they therefore support percutaneous drainage and interval appendectomy in patients who present with prolonged symptoms and a discrete abscess or phlegmon [22]. In a 2010 study, St. Peter et al. randomized children presenting with appendiceal abscess to early appendectomy or percutaneous drainage with antibiotics and an interval appendectomy; they found that 11 of 20 patients had successful placement of percutaneous drain, and three patients had aspiration of the abscess with no drain left (six patients had an abscess not amenable to drainage). The patients who were successfully drained had a quick return to regular diet as well as a shorter operation as compared to the early appendectomy group [55].

Depending on the size of the abscess, it is possible that no percutaneous drainage is necessary and that intravenous antibiotics alone are sufficient for treatment. In a 2013 study, Gasior et al. performed a retrospective review of 217 children presenting with appendiceal abscess with perforated appendicitis. They found that abscess less than 20 cm^2 may be successfully treated with antibiotics alone and no percutaneous drainage [56]. In a 1991 study, Hoffmann et al. described a series of 28 patients in which abscess drainage was avoided and the patients were treated with intravenous antibiotics and observation alone; there were no in-hospital complications, with a median stay of 10 days and only one patient presenting with recurrent appendicitis and one with recurrent abscess [18]. This suggests that it may be possible to treat complicated appendicitis with abscess with intravenous antibiotics alone.

The Role for Performance of Interval Appendectomy in Non-operative Management

Early supporters of non-operative management for complicated appendicitis included the recommendation for interval appendectomy anywhere from 4 to 20 weeks following resolution of acute appendicitis [14, 15]. Recent practice

guidelines for perforated appendicitis found that the risk of recurrence is approximately 8–15% (or 1–3% per year) and therefore made an argument for interval appendectomy [57]. Multiple other studies have supported interval appendectomy after successful non-operative management to prevent recurrence (especially in patients with appendicolith, the presence of which significantly increases the risk of recurrent appendicitis) and to rule out other pathologies such as carcinoid tumor [19–22, 31, 33, 37, 44, 58, 59]. A handful of studies have examined the histopathology of interval appendectomy specimens and have found that the rate of an obliterated appendiceal lumen is relatively low, which leaves the patient at increased risk of recurrent appendicitis since we are unable to determine whether or not the appendix lumen is obliterated without removing the specimen surgically [20, 33, 58].

Conversely, there have been multiple studies in recent years arguing against the routine performance of interval appendectomy following successful non-operative management of complicated appendicitis for all patients. Significant findings in these studies include a low risk of recurrence [42, 60–62], the associated costs with routine interval appendectomy [6, 26, 42, 43], and a lack of superiority evidence for interval appendectomy [63], in addition to the psychosocial impact on the patient and their family [64].

Conclusions

The optimal treatment of complicated appendicitis remains controversial. Whereas clinical practice guidelines have been developed for the operative management of perforated appendicitis with the ability to decrease resource utilization and improve patient outcomes [65, 66], the same has not yet been done for the non-operative management of perforated appendicitis. See Fig. 8.1 for a recommended treatment algorithm. Patients presenting initially with a short duration of symptoms (<5 days) or diffuse peritonitis should proceed to the operating room for early appendectomy following initiation of fluid resuscitation and broad-spectrum antibiotics. If, however, there is no diffuse peritonitis on exam and symptoms have been present for >5 days, the patient is potentially a candidate for non-operative management.

Patients should be adequately resuscitated with intravenous fluids and started on broad-spectrum intravenous antibiotics (preferably ceftriaxone/flagyl) while kept initially NPO. If there is an abscess present on imaging which is >20 cm^2 and amenable to percutaneous drainage, this should be performed by interventional radiology. If there is no abscess and only phlegmon, or the abscess is <20 cm^2, treatment should continue with intravenous antibiotics alone. Close clinical monitoring is necessary at the outset of non-operative treatment to identify those patients who are failing non-operative therapy. If there is no clinical improvement (decreased abdominal pain, improving leukocytosis, reduced fevers) within the first 24–48 hours, non-operative management should be abandoned, and the patient should be taken to the operating room for appendectomy.

The duration of intravenous antibiotic therapy is based on clinical parameters. Once a patient is afebrile for at least 24 hours, his or her pain is adequately

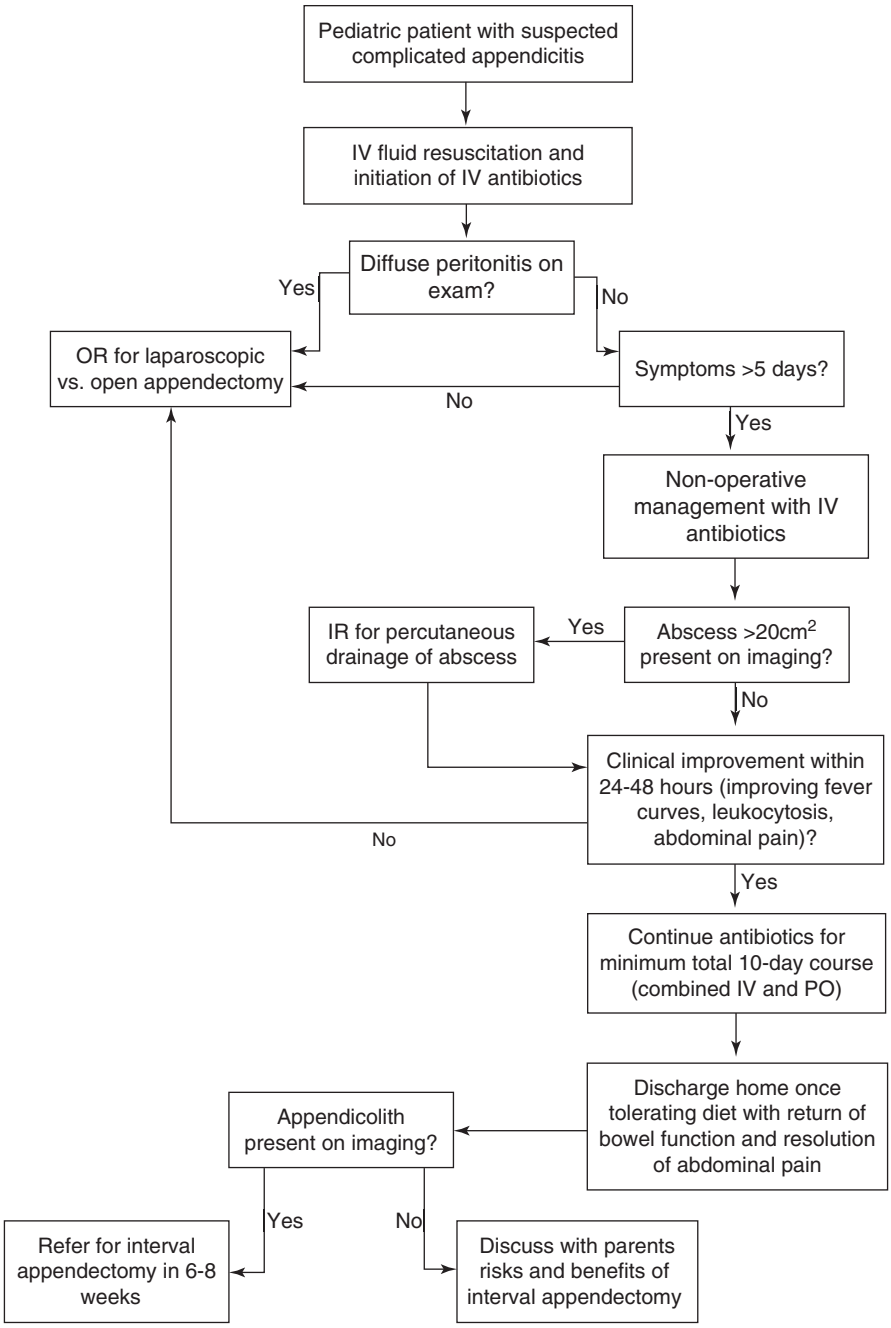

Fig. 8.1 Recommended treatment algorithm for pediatric complicated appendicitis

controlled, and he or she is tolerating a diet with normal bowel function, the patient is considered ready for discharge. The use of oral antibiotic regimens remains controversial; if administered, they should be similar in action to the intravenous regimen (such as amoxicillin/clavulanate plus metronidazole or trimethoprim-sulfamethoxazole plus metronidazole), and the total course of antibiotics (intravenous plus oral) should be 10 days.

Following successful non-operative management, patients with appendicolith should be followed up in clinic to arrange for interval appendectomy approximately 6–8 weeks after the episode of acute appendicitis; in patients with no appendicolith, a discussion should be had with the parents to discuss the risks and benefits of interval appendectomy, and the decision should be left up to them of whether or not to proceed with interval appendectomy.

Clinical Pearls

- Patients with >5 days of symptoms but without signs of peritonitis may be considered for non-operative management.
- Close clinical monitoring is necessary to ensure that patients are improving with non-operative management.
- In cases of failure of non-operative management, an operation is necessary.
- Interval appendectomy should be considered.

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