



# Appendicitis: Unusual Complications and Outcomes

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## Introduction

Children with uncomplicated appendicitis who undergo prompt laparoscopic appendectomy have a low incidence of complications (1–3%) and typically make rapid recovery to full wellness and return to normal activities [1]. In contrast, children with complicated or perforated appendicitis are at risk for substantial morbidity, long hospital stays, and have an adverse event rate of 15–40%. The morbidity in association with complicated appendicitis has generated robust inquiry, debate, and controversy as to best approach to improve outcomes.

Primary outcome measures in pediatric appendicitis include overall complication rate, incidence of surgical site infections and intra-abdominal abscess, postoperative bowel obstruction, incisional hernia, and fecal fistula.

Secondary outcome measures include length of hospital stay, readmission rate, time to return to full activities, treatment-related costs, resource utilization, quality of life, and parent and patient satisfaction scores.

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## Intraoperative Complications

The surgical management of acute appendicitis has been the standard of care for more than a century. In earlier times, without antibiotics and when all surgery was “open”, surgical complications were common in acute appendicitis. In current practice, with advanced laparoscopic techniques, intraoperative technical complications are rare.

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Bleeding may occur with failure to secure the appendiceal artery during dissection or inadvertent injury to the intestinal mesentery. Iatrogenic bowel injury or injury to adherent structures, while uncommon, can occur during dissection to mobilize the appendix or to identify the base in the setting of a dense inflammatory reaction. Direct injury to adjacent bowel is most often only serosal, rarely full-thickness bowel injury. The bladder and the fallopian tube in girls may, on rare occasion, be injured by direct manipulation or thermal injury from the electrocautery. All of these complications are generally easily managed when promptly recognized with minimal morbidity [2].

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## Laparoscopic Appendectomy

In the open appendectomy era, operative exploration, particularly in complicated or perforated appendicitis, was wrought with an intimidating degree of complications and morbidity: large incisions, high rates of wound infection and postoperative intra-abdominal abscesses, fascial dehiscence, bleeding, abdominal injuries to friable bowel or adjacent structures, and prolonged ileus and antibiotics postoperatively. Drains, central lines, and parenteral nutrition were commonplace; morbidity was substantial.

The clear emergence of the laparoscopic approach for appendectomy on numerous studies and meta-analyses as superior to open appendectomy on essentially all metrics has significantly reduced complications and improved outcomes: decreased risk of wound infection, decreased pain and use of analgesic medications, decreased hospital stay, reduced postoperative ileus, improved cosmesis, and faster return to normal activities. The Pediatric Health Information System database shows the laparoscopic approach is now used in >90% of appendectomies, both simple and complicated. During the early experience with laparoscopy for perforated appendicitis, some authors reported longer operative times and an increased incidence of postoperative intra-abdominal abscess nearly threefold compared to open appendectomy; however, more recent literature clearly confirms reduced operative times and no difference in abscess risk between the open and laparoscopic approach based on multiple prospective trials, meta-analyses, and large, multi-institutional comparative series [3].

The laparoscopic technique has increased risks in children compared to adults during trocar placement. Injury to the intestines, intra-abdominal viscera, or major blood vessels (aorta, iliac vessels, inferior vena cava) are all reported during trocar insertion, presumed related to laxity of the abdominal wall in children. These injuries may be more likely in obese children with a thickened abdominal wall leading to the need for excessive force to be applied during trocar insertion. The sequelae of abdominal wall vessel injury are generally minimal: pain and hematoma formation at the trocar site. Many pediatric surgeons prefer an open technique for trocar insertion at the umbilical site prior to insufflation for safety, particularly in young children and children with thin body habitus. Occasionally, device malfunction can contribute to these types of injuries.

The laparoscopic approach, with small incisions and protective trocars, significantly lowers the incidence of surgical site infections compared to open appendectomy [4]. Furthermore, the laparoscopic approach minimizes the morbidity of wound complications when they do occur, a perennial problem with open appendectomy. The administration of intravenous antibiotics once the diagnosis of acute appendicitis has been made or suspected and effective re-dosing at the time of surgery have been consistently shown to lower the incidence of superficial SSI in appendicitis. Cameron and colleagues recently used the PHIS and ACS-Pediatric NSQIP databases to investigate the use of extended spectrum (piperacillin/tazobactam) or narrow spectrum (cefoxitin or ceftriaxone and metronidazole) in uncomplicated (i.e., non-perforated) acute appendicitis. Costs of the different regimens were similar, and readmission rates and hospital revisits were similar between the matched groups. The surgical site infection rate was 1.8% overall with no difference for the extended versus the narrow spectrum antibiotics [5]. This may provide an opportunity for improved stewardship of the use of extended spectrum antibiotics in uncomplicated appendicitis.

Laparoscopic appendectomy has become the standard of care in children in acute uncomplicated appendicitis. It is generally a 30–60 minute operation with a low complication rate and excellent outcomes. The incidence of superficial surgical site infections (SSI) with laparoscopic appendectomy in uncomplicated appendicitis is 1%, and the incidence of postoperative intra-abdominal abscess is generally <1%. All other short- and long-term complications after laparoscopic appendectomy for uncomplicated appendicitis are exceedingly rare. Length of stay is generally 12–24 hours, and many pediatric centers now have clinical pathway guidelines that allow for same day discharge open appendectomy is reserved for selected cases based on preoperative assessment and imaging, such as marked abdominal distension, or when during the laparoscopic approach the procedure is deemed technically difficult or unsafe.

In contrast to simple appendicitis, complicated appendicitis (perforated appendicitis with peritonitis, appendicular inflammatory mass, and perforated appendicitis with well-defined abscess) is associated with a complication rate of 15–40%. Early complications include intra-abdominal abscess (20–30%), superficial SSI, and small bowel obstruction. Patient morbidity is high, and outcomes are challenged with a broad array of adverse events: increased length of hospital stay, need for postoperative CT scans, emergency room revisits, unplanned reoperations and interventional procedures (drains and PICC lines), use of parenteral nutrition, and significant delay in return to wellness and full activities. Hospital costs are doubled in complicated appendicitis, and nationwide the readmission rate is estimated at 12.8%.

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## Outcomes and Resource Utilization

Acute appendicitis is estimated to account for greater than one million pediatric hospital admission days per year and at a cost of >\$680 million per year. Despite the frequency of appendicitis in children, the heterogeneity of the patients across age

groups and severity of illness scale has been an obstacle to establishing standardized outcome measures. Optimal treatment remains elusive, particularly for complicated appendicitis, representing as much as one half the patients in many centers at presentation. Clinical management is characterized by marked variability in resource utilization, outcomes, and costs, both within children's hospitals and in the community [6, 7]. Variation in care has been identified as a key driver in healthcare costs and has been targeted for quality improvement efforts to steward resource utilization and improve outcomes [8].

Recent research efforts have sought to identify the influence of surgeon experience (operative volume, specialty training) and hospital factors (hospital designation) on outcomes in children with surgical illness [9, 10]. The American College of Surgeons has recently instituted a children's hospital verification designation program to optimize the surgical care of children. Numerous studies have demonstrated improved outcomes in acute appendicitis treated in specialty children's centers by fellowship-trained pediatric surgeons and other pediatric specialists, particularly in younger children [11].

Operative volume, fellowship-trained pediatric surgeons, pediatric anesthesiologists, and established evidence-based clinical pathways are likely critical drivers of these improved outcomes [12]. Despite these existing data, the 2012 report from the KIDS national database, a retrospective review found that 82.4% of patients ages 2–18 years who underwent appendectomy were treated at a non-children's hospitals. In hospitalizations for patients identified as having perforated appendicitis, the mean case volume per hospital was 7, and the median case volume per hospital was 2 [13]. These volumes are undoubtedly low.

Another area of controversy is drainage procedures for intra-abdominal abscesses [14]. Drainage procedures for intra-abdominal abscess by interventional radiology have their own potential complications and have been consistently identified as a major factor in increased length of stay and escalation of hospital costs in acute appendicitis. Risks associated with percutaneous drainage of intra-abdominal abscesses are reported in 2–3% of percutaneous drain procedures and include bleeding, intestinal perforation, bladder perforation, fecal fistula formation, soft tissue abscess (buttock/thigh), and post procedure sepsis. While the number of complications is not high, the hospital course and time to recovery are often significantly impacted [15]. In addition, current reviews and meta-analyses demonstrate patients with drains consistently have increased use of CT scans contributing to the cumulative lifetime radiation risk. A more selective approach to antibiotic-alone management of smaller, asymptomatic abscesses and clinical practice guidelines to limit postoperative CT imaging before postoperative day 7 and directed by clinical criteria is likely to substantially reduce hospital costs, resource utilization, and radiation exposure without compromise of quality or safety measures [16].

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## Postoperative Intestinal Obstruction

Postoperative bowel obstruction and ileus are uncommon after uncomplicated appendicitis treated by laparoscopic appendectomy. The risk of bowel obstruction requiring reoperation is consistently reported around 0.7% in numerous large

national database studies [17]. The risk is expectedly higher in open appendectomy and in patients with complicated or perforated appendicitis, historically reported from 0.5% to 10.7% in reviews with long-term follow-up. The laparoscopic approach is estimated to have as much as a fourfold decrease in the incidence of adhesive formation compared to open surgery. While adhesive postoperative bowel obstruction can occur as early as the first week postoperatively, the majority of cases occur following initial discharge in the first 1–2 years [18].

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## Unusual Pathology

Albeit rare, appendiceal carcinoid tumors are discovered incidentally in approximately 0.2% of children [19]. Typically these are small tumors with a low risk of lymphovascular invasion or extension. The rare occurrence of this finding may be cited in support of interval appendectomy following presumed perforated appendicitis, to prevent missing this diagnosis. In addition to rare tumor diagnoses, unusual infections may mimic appendicitis. For example, the pathologist may identify a parasite such as *Enterobius vermicularis* (pin worm) within the lumen of the appendix masquerading as appendicitis [20].

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## Rare Complications in Appendicitis

### Fecal Fistula

Fecal fistula is a rare complication in appendicitis, occurring in <1% of patients. This may occur as sequelae of intra-abdominal infection/abscess in patients with complicated appendicitis or as a procedure-related complication of percutaneous drainage of an intra-abdominal abscess. Similar to intestinal fistulae seen in other surgical settings, fecal fistula in the setting of appendicitis will most often close spontaneously (>90%) with non-operative management provided coexisting disease is absent including foreign body, immune deficiency, malnutrition, and distal bowel obstruction. An important consideration in a patient with fecal fistula is the possibility of incipient Crohn's disease.

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## Long-Term Complications

### Inflammatory Bowel Disease

The precise role of the appendix as part of the digestive tract remains unclear; however, some authors have suggested the appendix may have an immunological role. The appendix contains the highest amount of gut-associated lymphoid tissue (GALT) in the intestinal tract, and removal of the appendix may alter the intestinal tract bacterial microbiome. This finding has led to numerous studies investigating the possibility that removal of the appendix could have a role in the development of inflammatory bowel disease or cancer [21].

The incidence of Crohn's disease seems to be slightly higher after appendectomy [22]. Studies reporting on Crohn's disease demonstrated a median prevalence of 0.20% in patients who underwent appendectomy and 0.12% in study group controls. One study reported 2.3 times as many cases of Crohn's disease in the appendectomy group compared to the control group. Alternatively, it is also suggested that the higher prevalence of Crohn's disease, especially cases identified in early follow-up after appendectomy, might be related to the difficulties in diagnosing an incipient Crohn's disease [23, 24].

The incidence of ulcerative colitis is not changed after appendectomy. The mean prevalence of ulcerative colitis, reviewed in only a few studies, was 0.15% in patients after appendectomy and 0.19% in the studied controls. Andersson et al. actually reported a reduced risk of ulcerative colitis after appendectomy in patients <20 years of age, and this has been in other case-control studies [25].

## **Perforated Appendicitis and Subsequent Infertility in Girls**

Although perforated appendicitis has been considered a risk factor for tubal infertility in women, epidemiologic evidence supporting this relation is inconsistent. Earlier reports of an increase in tubal infertility after appendectomy had significant limitations: study patients were adult women who had undergone appendectomy for perforated appendicitis in adult life; case numbers were small, and detailed investigations of infertility were lacking. In one study suggesting increased infertility in women after perforated appendicitis, critical analysis revealed that 20% of the patients reported with primary infertility had a history of pelvic inflammatory disease compared with only 3% of patients in the control group. A 2001 study investigating risk factors for tubal infertility in 121 women attending in vitro fertilization clinics in Toronto, Canada, found that history of acute appendicitis or perforated appendicitis was not a statistically significant risk factor for tubal infertility in their patients [26].

There are minimal reports in the literature that have specifically investigated infertility in women who had undergone appendectomy in childhood. Recently, a large cohort study from Sweden investigated fertility patterns in women (9840 patients over a 20-year period) who had undergone appendectomy when aged <15 years and demonstrated similar rates of first birth and distribution of parity between women with history of perforated appendicitis and control women. Women with a history of perforated appendicitis had a similar rate of first births as the control women and a similar distribution of parity at the end of follow-up (mean age 31.6 years) [27].

In another recent systematic review and meta-analysis, including electronic databases from inception until 2013, no statistically significant association was found between appendectomy and infertility; however, appendectomy was associated with a significantly increased risk of ectopic pregnancy [28].

In summary, these data indicate that perforated appendicitis before puberty does not appear to have long-term negative effects on female fertility. These data have important implications for clinical practice for counseling patients and families

when young women present acutely with suspected acute appendicitis to refute a widely accepted approach that females should be considered for earlier surgery with a higher negative appendectomy rate to avoid perforation of the appendix and the concerns for future infertility.

## Portal or Splenic Vein Thrombosis

Also exceedingly rare in the pediatric literature is the occurrence of superior mesenteric vein, portal vein, or splenic vein thrombosis in association with appendicitis [29]. The diagnosis tends to be delayed due its nonspecific symptoms. The condition can occur at presentation, in a patient with history suggestive of appendicitis that went unrecognized or after appendectomy in complicated appendicitis. This condition, termed pylephlebitis, is presumed a consequence of a convergence of factors: intra-abdominal infection and local sepsis producing a hypercoagulable state, dehydration, and bacterial invasion into the mesenteric venous system [30]. While exceptionally rare in children, the condition can be fatal if left undiagnosed or untreated. Presenting signs and symptoms are typically nonspecific: fevers, vague abdominal pain, poor appetite, weight loss, sweats, chills, malaise, and occasionally diarrhea. If thrombosis of the portal venous system occurs, patients may demonstrate signs and symptoms of portal hypertension. Affected patients frequently have elevated serum inflammatory markers (CRP, ESR) and blood cultures positive for enteric organisms: *Escherichia coli*, *Bacteroides fragilis*, *Proteus mirabilis*, *Klebsiella pneumoniae*, and *Enterobacter species*.

Diagnosis is made by ultrasound or CT demonstrating thrombus formation in the portomesenteric venous system and may extend into the splenic vein. A 1–2-week course of broad-spectrum antibiotics targeting gram-negative enteric bacteria and anaerobes is foundational therapy, and therapeutic anticoagulation is indicated to limit extension of the thrombus and to enhance natural fibrinolysis. In patients when the mesenteric thrombus occurs acutely, catheter-directed thrombolysis by interventional radiology is an option. Anticoagulation therapy is generally continued for 3–6 months, although patients may show almost complete resolution of thrombus as early as the first month of treatment. Liver abscess can also occur. The patient typically demonstrates a large, tender liver. Treatment is aspiration and antibiotics.

## “Stump” Appendicitis

Incomplete removal of the appendix places a patient at risk for recurrent appendicitis, termed “stump” appendicitis. This is a rare event, and most surgeons will likely see only a few cases in a career. The time to occurrence is generally years after the initial surgery; however, occasionally stump appendicitis may occur even within the first year. Patients typically present with clinical signs and symptoms of acute appendicitis, and a definitive diagnosis is made with abdominal CT scan. Stump appendicitis has been reported after both laparoscopic and open

appendectomy. It appears to be more likely after complicated appendicitis. It may be related to an incomplete appendectomy, leaving a small “stump” of appendix in place at the time of removal. The diagnosis of “stump” appendicitis is associated with significant morbidity as patients who developed stump appendicitis were more likely on the second surgery to have complicated appendicitis, have an open procedure, and undergo colectomy in surgical management.

### **Incisional or Port Site Hernia**

The incidence of port site hernia following laparoscopy in adults is reported as 0.1–3%. In a recent systematic review, which included 37 studies, only four studies reported on the incidence of incisional hernia. The overall prevalence of incisional hernia was 0.7%. The vast majority of incisional hernias reported occurred in laparoscopic converted to open appendectomies. The data in children is expectedly sparse, and the incidence is likely underappreciated as many port site hernias would be asymptomatic and unrecognized. Limited studies suggest the incidence of port site hernia is higher in younger children, particularly children preschool age and younger. While risk factors for development of port site or incisional hernia in adults include infection, obesity, and diabetes, no risk factors have reliably been identified in children. Closure of all port sites does not obviate port site hernia; however, fascial closure of openings 10 mm or greater is performed by most pediatric surgeons.

### **Sarcopenia**

Sarcopenia is defined as a decrease in skeletal muscle mass and has been shown to be associated with longer postoperative recovery and an increased risk of complications in adult surgical patients. Children with delayed presentation and complicated appendicitis may experience, in the course of illness, treatment, and recovery, an extended period of inadequate nutrition and be at risk for sarcopenia and potential worse outcomes. A particular risk identified in patients with sarcopenia appears to be a higher risk of poor wound healing and postoperative surgical site infections. In a recent retrospective review from Nationwide Children’s Hospital in pediatric patients, nutritional assessment in select patients as part of preoperative risk assessment may provide important information that could identify patients who would benefit from early nutritional intervention and thereby potentially lower the incidence of complications and improve outcomes [31].

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### **Conclusion**

Complications in the management of appendicitis are low; however there are a few rare complications or outcomes that merit consideration especially when the post-management course follows an unexpected path. To minimize general complications and improve outcomes, it appears that management may best be performed by



specialized providers in a high-volume center. This is especially true for the youngest patients.

### Clinical Pearls

- Outcomes may be optimized by having specialized providers care for patients, and this is especially true for the younger patients.
- It appears unlikely that appendicitis significantly affects long-term fertility.
- Knowledge of rare outcomes and associations with appendicitis merit consideration when a patient has an unexpected postoperative course.

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