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**Management of complicated acute appendicitis in children: Still an existing controversy**

Zavras N *et al.* Management of CAA in children

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**Abstract**

Complicated acute appendicitis (CAA) is a serious condition and carries significant morbidity in children. A strict diagnosis is challenging, as there are many lesions that mimic CAA. The management of CAA is still controversial. This review aims to study the current data on operative *vs* non-operative management for CAA in children and to extract any useful information from the literature. There two options for treatment: Immediate operative management and non-operative management with antibiotics and/or drainage of any abscess or phlegmon. Each method of treatment has advantages and disadvantages. Operative management may be difficult due to the presence of inflamed tissues and may lead to detrimental events. In many cases, non-operative management with or without drainage and interval appendectomy is advised. The reasons for this approach include new medications and policies for the use of antibiotic therapy. Furthermore, advances in radiological interventions may overcome difficulties such as diagnosing and managing the complications of CAA without any surgeries. However, questions have been raised about the risk of recurrence, prolonged use of antibiotics, lengthened hospital stay and delay in returning to daily activities. Moreover, the need for interval appendectomy is currently under debate because of the low risk of recurrence. Due to the paucity of high-quality studies, more randomized controlled trials to determine the precise management strategy are needed.

**Key words:** Complicated acute appendicitis; Operative treatment; Non-operative treatment; Antibiotics; Children

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**Core tip:** The management of paediatric patients with complicated acute appendicitis (CAA) is controversial. There are two options for treatment: non-operative management with antibiotics and/or drainage of any abscess or phlegmon and immediate operative management. Each method has advantages and disadvantages. However, operative management is suggested for CAA with perforation, while non-operative management is advised for CAA with abscess or phlegmon. There is a paucity of high-quality studies in the current literature. Further investigations with randomized control studies are warranted.

**INTRODUCTION**

Appendectomy for acute appendicitis (AA) in children persists as the most common abdominal surgery for paediatric surgeons[1]. It has been estimated that 70000 children are operated on for AA every year in the United States[2]. The lifetime risk of appendectomy is 23.1% for females and 12% for males[3], and the lifetime risk of developing AA is 6.7% for females and 8.6% for males[4]. Interestingly, the peak incidence of AA occurs from ages 10-14 years for males and 15-19 years for females[4].

The clinical history of AA can vary from mild symptoms (uncomplicated AA) to those with sepsis and bowel obstruction [complicated AA (CAA)] with perforation of the appendix and probably development of an intraperitoneal abscess[5]. Approximately 30%-74% of children present with CAA[6], with rates ranging between 69%-93% for children aged 2 to 5 years and up to 100% for 1-year-old children[7]. Although operative management has been considered for many years as the mainstay of treatment in children with AA[8], the presence of distorted anatomy due to inflamed tissues may lead to harmful events such as injury to the surrounding tissues and bowel wall, dissemination of the infection, blood loss, postoperative bowel obstruction, abscess or fistula formation, and postoperative wound complications[2,9,10].

The evidence that AA can be managed with non-operative management is not new. The first case of a spontaneous resolution of CAA was published in 1910[11]. In 1956 and in 1959, Coldrey[12] published a series of 137 patients with AA successfully treated with non-operative management. Almost two decades later, Janik *et al*[13] reported the successful management of 31/37 children with a palpable mass and no established peritonitis with the administration of fluids and close monitoring. In the mid-1990s, the interest in non-operative management in the adult population was renewed, and since then, a number of studies have investigated the efficiency and safety of non-operative management, first in uncomplicated AA and later in CAA[14,15]. Although the literature on paediatric patients is still limited, ongoing evidence indicates that non-operative management may be effective and safe for the management of uncomplicated AA[16,17].

Despite modern diagnostic adjuncts such as imaging techniques and improvements in anaesthetic and surgical care, controversies in the optimal management of CAA in the paediatric population still exist[18].

Taking into account recent improvements in the management of CAA, this review aims to provide an update on the existing controversies in operative management *vs* non-operative management for children with CAA.

**Literature search**

A literature review was performed through PubMed and Google Scholar for original articles, reviews and meta-analyses from 1980 to December 2019using the following Medical Subjects Headings (MeSH) terms: “appendicitis” [MeSH] and “complicated appendicitis” [MeSH] or “appendicular mass” [MeSH] or “abscess” [MeSH] or “phlegmon” [MeSH] or ‘’perforated” [MeSH] or “conservative treatment” [MeSH] or “operative treatment” [MeSH] or “interval appendectomy” [MeSH] and “children”. A secondary search of the most relevant articles was also conducted manually or through PubMed based on the related articles. All randomized controlled trials (RCTs), prospective and retrospective articles and systematic reviews were included. Articles including both adult and paediatric populations and papers based on case reports, case series, abstracts and letters were excluded. All articles were selected systematically for inclusion and critically evaluated.

***Definitions***

CAA was defined as perforated appendicitis with or without the presence of an abscess or phlegmon[2] based on the surgeon’s findings during operation or the pathology report[19]. A phlegmon was defined as an inflammatory mass without an apparently defined abscess[19].

Operative management was defined as an early appendectomy performed either with laparotomy or laparoscopy within the first 24 h of hospitalization[20].

Non-operative management was defined as initial treatment with or without percutaneous abscess drainage for an abscess followed by interval appendectomy[21].

Treatment failure of operative management or non-operative management and percutaneous abscess drainage was defined as the need for an appendectomy operation during the same hospitalization period or within 7 d after discharge[22].

The complications included any surgical, medical or interventional adverse events (postoperative wound infection, small bowel obstruction, abscess or fistula formation)[2,9,10]. Hospital length of stay (LOS) for both operative management and non-operative management was defined as the total number of hospitalization days from admission to discharge and was calculated after reading the relevant articles in the literature.

We included 47 articles published from August 1980 to December 2019 relevant to the management of CAA in children. Of them, three[23-25] were systematic reviews and meta-analyses, two[26,27] were prospective RCTs, seven were prospective non-randomized trials[28-34], one was a prospective observational study[35], and thirty-four[9,13,19-21,36-64] were retrospective studies (Figure 1). The therapeutic options regarding CAA are analysed in detail below.

**MANAGEMENT**

Once a paediatric surgeon has to treat a patient with CAA, there are three strategies available for treatment: antibiotics only, antibiotics followed by interval appendectomy, and appendectomy on admission (Table 1). We will separately discuss the three options with the pros and cons of each strategy.

***Non-operative management***

**Advances in antibiotic policy:** Currently, the standard of care endorses the prompt administration of antibiotics in the management of CAA[65,66]. A survey of the European Pediatric Surgeons’ Association covering 42 countries (24 were from Europe) showed that 96% of surgeons start antibiotic therapy preoperatively in the case of CAA[66]. The same study showed that most surgeons choose a triple “standard therapy” comprising an aminoglycoside, a β-lactam and a regimen covering anaerobes. However, there is growing evidence that broad-spectrum single (piperacillin/tazobactam) or double-agent (ceftriaxone + metronidazole) therapy is equally effective and less expensive than triple-agent therapy and may lead to a shorter LOS[67-70]. This is in line with the recommendations of the American Pediatric Surgical Association (APSA) that state that broad-spectrum single or double-agent therapy is equally efficient and more cost-effective than three drugs[65]. It is noteworthy that a slight shift toward mono- or dual-agent therapy could be observed in the literature after the publication of the APSA recommendations[21,54].

A major issue arises from the use of broad-spectrum anti-Pseudomonas antibiotics such as piperacillin/tazobactam, imipenem or meropenem, *vs* narrow-spectrum antibiotics such as cefoxitin or cefazolin with metronidazole[70]. The clinical guidelines recommend the use of narrow-spectrum antibiotics in adults with complicated intra-abdominal infections and in most previously healthy children with uncomplicated AA who are not assumed to be susceptible to *P. aeruginosa*[71]. Kronman *et al*[71], in a large, retrospective cohort study of children suffering from either uncomplicated AA or CAA, showed that broad-spectrum antibiotics are not superior to narrow-spectrum antibiotics with respect to short-term postoperative complications, *e.g.*, readmission rates, wound infections, bowel obstruction, and percutaneous drainage of abscesses, within 30 d of discharge. Researchers have shown that antibiotic agents with an expanded spectrum against *P. aeruginosa* and *Enterococcus* were efficient in 78% of patients who failed first-line antibiotics and helped them achieve successful non-operative management[72]. In such cases, second-line antibiotics are recommended before surgical intervention[71]. An important question concerns the duration of antibiotics use in children with CAA and non-operative management. The APSA recommendations suggest that the length of antimicrobial agent use should be based on clinical criteria such as pain, fever, bowel function and white blood cell count[43]. Usually, a 5-d policy for intravenous antibiotics followed by a 2-d regimen of oral antibiotics (total 7-d length of antibiotics use) is recommended[65]. This suggestion was supported further by a very late systematic review and meta-analysis that showed that the transition from intravenous to oral administration did not raise the risks for complications such as wound infection, postoperative abscess and re-admission[73].

***Antibiotic treatment***

The common indications that CAA demands urgent operative intervention has changed in the last decade. Several centres have reported the results of children with appendiceal abscesses or masses treated with antibiotics, both with or without drainage[29,32,35,36,40,43,50,54-56,58,59]. Most of these studies revealed a success rate between 60-100%. However, Svensson *et al*[74] questioned the results of some of these studies because the majority of them were retrospective and included meaningful selection bias. Furthermore, without an operation, it is difficult to declare that all patients had definite CAA despite appropriate blood tests and radiological imaging. Although the presence of an appendicolith is thought to be a predictor of non-operative management failure[50,54] and recurrence, other researchers found no correlation between this factor and the outcomes[75].

We conclude that the optimal antimicrobial therapy and duration of antibiotics use in children with CAA need further investigation with RCTs.

**Percutaneous abscess drainage:** During the 1980s, a period of growth and acceptance of radiological interventional techniques in children started[76]. Percutaneous abscess drainage is a well-established procedure of choice for treating intra-abdominal abscesses of various aetiologies[77]. In the case of CAA, an intra-abdominal abscess may occur either before or after appendectomy and may be found anywhere in the abdominal cavity and/or pelvis[64]. Drainage is usually performed with the Seldinger technique under ultrasound or computed tomography (CT) guidance or a combination of both imaging modalities[64]. In the case of peri-appendicular abscesses, the anterior abdominal transperitoneal approach is usually performed[78,79], while for abscesses located anterior to the rectum, the transrectal or transgluteal approach may be used[79].

The incidence of intra-abdominal or pelvis abscesses is estimated to be approximately 3.8% in patients with CAA[80]. A delay in the diagnosis of AA is a possible risk factor, although there is evidence that some patients might be prone to abscess formation despite prompt management[81]. Several authors[26,53,54,57,61,62] have documented beneficial results with percutaneous abscess drainage in terms of reduced complication rates, acceptable LOS, and rapid recovery to oral feeding and return to normal activities. In a European Pediatric Surgeons’ Association survey, 59% of paediatric surgeons suggested a combination of antibiotics and percutaneous abscess drainage[66]. Luo *et al*[57], in a large series of children with appendiceal abscesses, found that patients treated with non-operative management and percutaneous abscess drainage had a significantly lower percentage of recurrent appendicitis, a lower possibility of requiring an interval appendectomy, and fewer postoperative complications after interval appendectomy than those without percutaneous abscess drainage. In contrast, Bonadio *et al*[58] reported a greater LOS, longer mean duration of fever, longer period of antibiotics use, more radiological procedures, higher complication rates and more unscheduled hospitalizations after discharge for patients who received percutaneous abscess drainage. Keckler *et al*[52] mentioned that multiple CT scans and major complications may follow percutaneous abscess drainage, such as ileal, colonic and bladder perforation and buttock/thigh abscesses, while in the interval appendectomy group, only one patient developed a pelvic phlegmon that responded to intravenous antibiotics. Gasior *et al*[64] suggested that only abscesses greater than 20 cm2 should be drained. Some authors advocate for the installation of a tissue plasminogen activator into the abdominal cavity[82] to facilitate drainage of thick and septated abscesses. In a recent RCT, St Peter *et al*[83] found that compared to the control group. patients who underwent tissue plasminogen activator installation had a longer duration of hospitalization, while no differences concerning the use of antibiotics, drainage duration or total hospitalization were found.

We could conclude that although arguments may be raised for percutaneous abscess drainage, there is evidence that drainage of the abdominal cavity may have favourable results in selected patients.

***Operative management***

**Immediate operative management** *vs* **non-operative management with delayed appendectomy:** Although many studies[23,26,27,55] propose early operative management for children with CAA, there are only two RCTs supporting this option for treatment. In the first study[26], 40 patients with similar characteristics on admission and a diagnosis of CAA were randomized to immediate operative management and non-operative management group, with the latter undergoing delayed appendectomy. Patients operated on early had fewer health care visits and CT scans than those with delayed surgery. No better outcomes were found in the non-operative management group than in the operative management group. Blakely *et al*[27] studied a cohort of 131 patients who were diagnosed with perforated appendicitis without abscess on admission, and they were randomized in a non-blinded manner for early operative management or non-operative management followed by interval appendectomy. The authors found that patients in the non-operative management group had higher complication rates and higher hospital charges than those in the operative management group. On the other hand, a meta-analysis by Duggan *et al*[23] showed that early appendectomy for patients with perforated appendicitis without abscess significantly reduced unplanned readmissions [Odds ratio (OR) = 0.08, 95% confidence interval (CI): 0.01-0.67], adverse events (OR = 0.28, 95%CI: 0.1-0.77) and total charges. A recent meta-analysis by Vaos *et al*[24] reported that operative management was associated with shorter LOS (SD = 0.25, 95%CI: 0.07-0.43, *P* = 0.007), but the overall complication rates (OR = 0.22, 95%CI: 0.14-0.38, *P* = 0.001) and incidence of wound infection(OR = 0.40, 95%CI: 0.17-0.96, *P* = 0.041) were significantly lower with non-operative management. The presence of intra-abdominal abscess and postoperative ileus was not affected by the treatment option. In a recent meta-analysis, Fugazzola *et al*[25] separately studied patients with free perforated appendicitis and those with abscess or phlegmon. The researchers reported better outcomes regarding complication rates and readmissions in patients with appendicular abscess or phlegmon treated with non-operative management than in those treated with operative management In contrast, the authors found a lower complication rate and fewer re-admissions for the group of patients with free perforated appendicitis than for those with appendicular abscess or phlegmon.

Summarizing the results of the abovementioned studies, it seems that there are two main types of CAA: CAA with perforation without abscess and CAA with abscess or phlegmon. The main conclusion is that operative management is the preferred treatment option for patients with perforated appendicitis without abscess, while non-operative management is advised in cases of perforated appendicitis with abscess or phlegmon.

**CONCLUSION**

Although AA is a common surgical disease, it may be expressed with a wide range of severity, ranging from simple to severe. In the case of CAA, operative management seems to be the preferable choice of treatment, while non-operative management is recommended for CAA with abscess or phlegmon. However, because of the paucity of high-quality studies, there is a need for more RCTs to determine the precise management strategy.

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**Figure Legends**

Articles retrieved in initial search: 57

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Systematic reviews and meta-analyses: 3

Prospective non-randomized trials: 7

Prospective observational study: 1

Retrospective studies: 34

**Figure 1 Study selection flowchart.** RCTs: Randomized controlled trials.

**Table 1 Management options of complicated acute appendicitis**

|  |  |
| --- | --- |
| **Non-operative management** | **Operative management** |
| Antibiotic treatment | Immediate operative management |
| Percutaneous abscess drainage | Non-operative management followed by interval appendectomy |