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Comparison of the Effectiveness of Antibiotic Therapy and Surgical Treatment in Patients with Acute Appendicitis

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Abstract

Acute appendicitis is one of the most common causes of abdominal pain requiring emergency surgical intervention. While appendectomy has long been the standard treatment, recent evidence has explored the use of antibiotics as a non-operative alternative, particularly for uncomplicated cases. In this study, we want to compare the effectiveness, safety, and long-term outcomes of antibiotic therapy versus surgical appendectomy in the management of acute appendicitis. A comprehensive review of recent randomized controlled trials (RCTs),

including the APPAC and CODA trials, as well as meta-analyses, was conducted to evaluate treatment success rates, recurrence, complications, costs, and patient preferences.

Results: Antibiotic therapy successfully avoided surgery in most of the cases (approximately 73%) of patients within one year,. However, recurrence rates reached up to 39%. Surgical treatment was associated with lower recurrence (<5%) but higher direct costs and longer recovery. Antibiotic therapy resulted in shorter hospital stays and reduced overall treatment costs. Patient-centered decision-making was found to play a crucial role in selecting the appropriate therapy.

Conclusions: Antibiotic therapy represents a safe and cost-effective alternative to appendectomy for selected patients with uncomplicated acute appendicitis. However, shared decision-making and proper patient selection are essential to optimize outcomes and minimize risks. Further research is needed to refine the criteria for non-operative management and ensure long-term safety.

Keywords:

acute appendicitis, appendectomy, Open Appendectomy (OA), Laparoscopic Appendectomy (LA), antibiotic therapy

The aim of the study:

This study aims to compare the effectiveness, safety, and long-term outcomes of antibiotic therapy versus surgical appendectomy in the management of acute appendicitis.

Introduction

Acute appendicitis (AA) is one of the most common causes of acute abdominal pain and a leading indication for emergency abdominal surgery worldwide. Its annual incidence is estimated at approximately 100 cases per 100,000 individuals, with the highest risk observed

in people aged 10 to 30 years [1]. For over a century, appendectomy has been the standard of care, yet in recent years, less invasive alternatives, particularly antibiotic therapy, have gained increasing attention, especially in patients with uncomplicated appendicitis.

Several randomized controlled trials have evaluated the safety and efficacy of non-operative treatment. One of the landmark studies in this field, the Finnish APPAC trial, demonstrated that 72.7% of patients treated with antibiotics did not experience a recurrence of symptoms within one year, suggesting that antibiotics may be an effective alternative in selected cases [4]. Similar findings were reported in the large U.S.-based Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) trial, which confirmed that antibiotics can be a safe and viable treatment option for many patients with uncomplicated AA [5].

This paper aims to review and critically analyze the current scientific literature comparing the effectiveness and safety of antibiotic therapy versus surgical treatment in patients with AA. The objective is to evaluate whether antibiotics can serve as a realistic alternative to appendectomy in the treatment of uncomplicated AA and to assess the benefits and limitations associated with each therapeutic approach.

Pathophysiology and Classification of Appendicitis (Acute, Uncomplicated vs. Complicated)

The pathophysiology of AA typically involves obstruction of the appendiceal lumen due to a fecalith, lymphoid hyperplasia, parasites, or, less commonly, neoplasms. This obstruction leads to mucus accumulation, bacterial overgrowth, localized inflammation, and eventually mucosal necrosis, which can progress to wall perforation and generalized peritonitis if left untreated [2].

Modern classifications of AA distinguish between **uncomplicated** and **complicated** forms. Uncomplicated appendicitis refers to inflammation confined to the mucosa and submucosa, without perforation, gangrene, or the formation of an abscess. In contrast, complicated appendicitis includes cases involving perforation, periappendiceal abscess, inflammatory phlegmon, or gangrene [3]. This distinction is crucial in guiding treatment decisions—while complicated cases generally require surgical intervention, there is growing interest in exploring conservative management for uncomplicated cases using antibiotic therapy.

Traditional Surgical Treatment (Appendectomy)

Appendectomy has long been the standard treatment for AA, offering definitive removal of the inflamed organ and thereby eliminating the risk of recurrence. The procedure can be

performed via two primary techniques: open appendectomy (OA) and laparoscopic appendectomy (LA).

Open Appendectomy

OA involves a right lower quadrant incision, typically at McBurney's point, followed by dissection through the layers of the abdominal wall to access the peritoneal cavity. The appendix is then isolated, ligated at its base, and removed. In cases of complicated appendicitis (e.g., perforation, gangrene, or abscess), the procedure may include peritoneal lavage and drainage. OA is straightforward and effective, but it is associated with a longer recovery period, increased postoperative pain, and a higher rate of wound infections compared to laparoscopic techniques [6]

Laparoscopic Appendectomy

Introduced in the late 1980s, LA has become the preferred approach in many centers. The procedure is minimally invasive and typically involves the insertion of three trocars: one at the umbilicus for the camera, and two additional ports in the lower abdomen for instruments. The appendix is visualized, mobilized using graspers and energy devices, and then stapled or ligated and removed through one of the ports. This approach allows for enhanced visualization of the abdominal cavity, which is particularly advantageous in atypical presentations or when the diagnosis is uncertain [7]

Both surgical techniques have excellent safety profiles, with overall complication rates for appendectomy reported to be less than 5% in most cases. Laparoscopic surgery is particularly beneficial in obese patients, women of reproductive age (where gynecologic pathologies may mimic appendicitis), and elderly patients. In summary, appendectomy—whether open or laparoscopic—remains a highly effective and safe procedure that provides definitive resolution of AA. Despite the growing interest in non-operative management, surgery continues to be the reference standard, especially in complicated presentations.

Efficacy and Outcomes

Surgical Success and Efficacy- Both OA and LA are effective treatments for AA, with high success rates. However, LA has gained popularity due to its minimally invasive nature and associated benefits. A meta-analysis encompassing 25 randomized controlled trials (RCTs) with 4,694 patients found that LA resulted in fewer postoperative complications compared to OA (Odds Ratio [OR] = 0.74; 95% Confidence Interval [CI]: 0.55–0.98; $p = 0.04$). [8]

Postoperative Complications- LA is associated with a significantly lower risk of Surgical Site Infections (SSI). An umbrella review reported that LA reduced SSI rates by 48% to 70% compared to OA. [9]

Intra-Abdominal Abscesses (IAA) Some studies indicate a slightly higher incidence of IAA with LA. The same umbrella review noted that LA had a 1.34 to 2.20 times higher risk of IAA than OA. [9]

Recovery and Hospitalization- Hospital Stay: LA patients experienced shorter hospital stays. A meta-analysis reported a weighted mean difference (WMD) of -0.68 days favoring LA [8,]. Return to Normal Activities: Patients undergoing LA returned to normal activities sooner, with a WMD of -4.73 days compared to OA. [8]

Operative Time- LA generally requires a longer operative time. The same meta-analysis found that LA had an increased operative time by approximately 10.71 minutes compared to OA. [8]

Pain and Analgesia- LA patients reported less postoperative pain and required shorter durations of analgesia. The meta-analysis indicated a WMD of -0.53 days in analgesia use favoring LA. [8]

Cost Considerations- While LA may have higher initial operative costs due to equipment and longer surgery time, the overall hospital costs are comparable to OA when considering shorter hospital stays and quicker recoveries. [8]

Both open and laparoscopic appendectomies are effective treatments for AA. However, LA offers advantages in terms of reduced postoperative complications, shorter hospital stays, quicker return to normal activities, and less postoperative pain, albeit with a slightly longer operative time and a marginally increased risk of intra-abdominal abscesses. The choice between the two methods should be individualized based on patient factors, surgeon expertise, and available resources.

Antibiotic Therapy in the Management of Acute Appendicitis

In recent years, antibiotic therapy has emerged as a viable alternative to surgical intervention for selected patients with uncomplicated AA. This approach aims to treat the infection conservatively, avoiding surgery and its associated risks.[11]. Commonly Used Antibiotic Regimens include the following.

Several studies have investigated various antibiotic protocols for treating uncomplicated appendicitis. Notably, the Appendicitis Acuta (APPAC) randomized clinical trial conducted in Finland provides a well-documented regimen: Intravenous Phase (3 days):- *Ertapenem* 1 g once daily.

Oral Phase (7 days): *Levofloxacin* 500 mg once daily., *Metronidazole* 500 mg three times daily. This 10-day regimen demonstrated that approximately 73% of patients treated with antibiotics did not require surgery within the first year of follow-up. [4]

Alternative regimens have also been explored. For instance, a meta-analysis reviewed antibiotic therapies involving: Intravenous Phase: *Amoxicillin-clavulanic acid*, *cefotaxime*, or a fluoroquinolone. Often combined with *metronidazole* or *tinidazole*. Oral Phase: Continuation with appropriate oral antibiotics to complete a total duration of 8 to 15 days.

These studies reported that 63% to 78% of patients treated with antibiotics alone remained asymptomatic without recurrence during follow-up periods ranging from one month to one year. [12]

In the study conducted by Hansson and colleagues, patients allocated to the antibiotic treatment group received a specific regimen designed to address AA without surgical intervention. The treatment protocol was as Intravenous Phase (Initial 24 hours): *Cefotaxime* 1 g administered twice daily, *Metronidazole* 1.5 g administered once daily.

Oral Phase (Subsequent 10 days): *Ciprofloxacin* 500 mg taken twice daily., *Metronidazole* 400 mg taken three times daily [14]

Dosage and Duration Considerations

The total duration of antibiotic therapy typically spans 8 to 15 days, starting with an intravenous course followed by oral administration. The specific choice of antibiotics and treatment duration may vary based on patient characteristics, local resistance patterns, and clinician preference. For example, in cases where ertapenem is contraindicated, alternatives such as *piperacillin-tazobactam* or *ceftriaxone* with *metronidazole* are used intravenously, followed by oral regimens like *amoxicillin-clavulanate* or *ciprofloxacin* plus *metronidazole*.[13]

One of the key challenges in evaluating the effectiveness of antibiotic therapy across clinical trials is the lack of a universally accepted, standardized antibiotic regimen. Studies differ significantly in terms of: Antibiotic selection, Dosage and frequency, Duration of therapy, Criteria for switching from IV to oral therapy

This heterogeneity makes direct comparison of outcomes between studies difficult and limits the generalizability of results. It also complicates the development of unified clinical guidelines and decision-making tools for clinicians.

Indications for Antibiotic Therapy in Acute Appendicitis

Imaging-Confirmed Uncomplicated Appendicitis- Antibiotic therapy is primarily recommended for patients with uncomplicated appendicitis confirmed by imaging, typically computed tomography (CT) or ultrasound (US). Imaging should show a non-perforated, non-abscessed, inflamed appendix with no signs of necrosis or fecalith. CT scans are highly sensitive and specific in detecting appendiceal inflammation and ruling out complications such as perforation or abscess. US is often used in children and pregnant patients, although its diagnostic accuracy is more operator-dependent. [15, 4]

Stable Clinical Presentation- Patients with stable vital signs, localized pain in the right lower quadrant, and no signs of systemic infection (e.g., sepsis or generalized peritonitis) are good candidates for non-operative management. These patients should not present with: High-grade fever, Marked leukocytosis, Diffuse abdominal tenderness or rebound. This clinical stability supports safe outpatient or short inpatient antibiotic treatment. [16]

Patient Preference and Informed Consent- Shared decision-making plays a central role in choosing antibiotic therapy. Patients who are well-informed about the benefits (e.g., avoidance of surgery, quicker recovery) and the risks (e.g., recurrence, potential delayed surgery) can reasonably choose non-operative treatment. The CODA trial emphasized that antibiotic therapy aligns with patient-centered care when outcomes and preferences are clearly communicated. [5]

Absence of High-Risk Features- Antibiotic therapy is more effective when certain high-risk anatomical or clinical features are absent. These include: Appendicolith (fecalith), which significantly increases the risk of treatment failure and recurrence. Severe comorbidities (e.g., immunosuppression, poorly controlled diabetes) could reduce the efficacy of antibiotics and complicate outcomes. Studies like APPAC and CODA found that presence of an appendicolith nearly doubled the risk of treatment failure. [5,]

Contraindications to Antibiotic Therapy

Complicated Appendicitis (Perforation, Abscess, or Generalized Peritonitis)- Antibiotic therapy is generally contraindicated in complicated appendicitis, including perforation, abscess formation, or generalized peritonitis. These conditions often necessitate prompt surgical intervention to prevent further complications. The World Society of Emergency Surgery (WSES) guidelines emphasize that non-operative management should be reserved for

uncomplicated cases, as complicated appendicitis carries a higher risk of treatment failure and adverse outcomes when managed conservatively. [15]. Imaging studies, such as contrast-enhanced CT scans, are crucial in differentiating between uncomplicated and complicated appendicitis to guide appropriate treatment decisions.

Presence of Appendicolith (Fecalith) The presence of an appendicolith is associated with a higher risk of treatment failure and recurrence when managing appendicitis non-operatively. A meta-analysis published in *JAMA Pediatrics* found that pediatric patients with an appendicolith had a significantly increased risk of treatment failure with antibiotics compared to those without. [17]. Similarly, the CODA trial reported higher rates of complications and subsequent appendectomies in patients with an appendicolith who were initially treated with antibiotics. [5]. Given these findings, the presence of an appendicolith is considered a relative contraindication to antibiotic-only treatment.

Immunocompromised Status- Patients with immunocompromised conditions, such as those undergoing chemotherapy, organ transplant recipients, or individuals with HIV/AIDS (human immunodeficiency virus/Acquired Immune Deficiency Syndrome), may not respond adequately to antibiotic therapy alone due to their impaired immune systems.

The WSES guidelines recommend caution in using non-operative management for immunocompromised patients, as their ability to contain and resolve infections is compromised, increasing the risk of treatment failure and complications. [15]

Pregnancy- The management of AA during pregnancy presents unique challenges. While some studies suggest that conservative management with antibiotics may reduce the risk of preterm labor, others indicate a higher risk of complications, such as sepsis and peritonitis, particularly in cases of complicated appendicitis. A systematic review and meta-analysis highlighted the need for individualized treatment strategies, considering both maternal and fetal outcomes. [18]. Therefore, antibiotic therapy should be considered cautiously in pregnant patients, with surgical intervention remaining the standard of care in many cases.

Inability to Ensure Close Follow-Up- Successful non-operative management of appendicitis requires close follow-up to monitor for signs of treatment failure or recurrence. Patients who are unable or unlikely to adhere to follow-up appointments, due to factors such as limited access to healthcare, cognitive impairments, or social circumstances, may not be suitable candidates for antibiotic-only treatment. Ensuring patient compliance and the ability to promptly address any deterioration in condition is essential for the safe implementation of conservative management strategies. [13].

Effectiveness of Antibiotic Therapy vs. Surgical Treatment

Antibiotic therapy has emerged as a viable alternative to appendectomy for patients with uncomplicated AA. Numerous meta-analyses have assessed the efficacy of antibiotic therapy in treating uncomplicated AA. While success rates vary across studies, antibiotics are generally considered a viable alternative to surgery for selected patients. Below is a summary of findings from key meta-analyses:.

Summary Table:

Study	Antibiotic Success Rate	Recurrence Rate	Complication Rate	Conclusion
Podda et al., 2019 [19]	67.2%	19.2%	Not specified	Surgery more effective; antibiotics feasible option
Yang et al., 2019 [20]	68–88%	68–88%	Lower than surgery	Antibiotics less effective but fewer complications
Sallinen et al., 2016 [21]	75.3%	Not specified	3.6% vs. 11.6%	Fewer complications with antibiotics
Huang et al., 2017 [22]	68%	32%	Not specified	Higher recurrence with antibiotics
Liu et al., 2019 [23]	82.8%	5.6% reoperation	Lower than surgery	Fewer complications; higher recurrence

Meta-analyses indicate that antibiotic therapy can be an effective treatment for uncomplicated AA in selected patients, offering benefits such as fewer complications and shorter hospital

stays. However, it is associated with a higher risk of recurrence compared to surgical treatment

Cost Considerations

From an economic perspective, antibiotic therapy has been shown to be more cost-effective than surgical intervention. A five-year follow-up study reported that the overall costs associated with appendectomy were 1.4 times higher (€5,716) compared to antibiotic therapy (€4,171), resulting in cost savings of €1,545 per patient in the antibiotic group. [24]

Additionally, patients treated with antibiotics had shorter durations of sick leave (median of 11 days) compared to those who underwent surgery (median of 22 days), further contributing to economic benefits through reduced productivity losses. [24]

Ethical Aspects and Patient Decision-Making

The choice between antibiotic therapy and surgical treatment involves ethical considerations centered around patient autonomy, informed consent, and shared decision-making.

A study assessing patient preferences found that individuals who chose antibiotic therapy prioritized avoiding surgery, even if it meant accepting a higher risk of recurrence.

Conversely, those who opted for surgery valued quick treatment and minimizing the chance of recurrence. [17]

Healthcare providers have an ethical obligation to present patients with comprehensive information regarding the risks and benefits of each treatment option, ensuring that patients can make informed decisions aligned with their values and preferences.

Conclusion

The management of acute uncomplicated appendicitis is evolving, with robust evidence supporting both surgical and non-operative approaches. Antibiotic therapy has been shown to be an effective and safe alternative to appendectomy in selected patients, offering benefits such as shorter recovery time, reduced healthcare costs, and avoidance of surgical risks. However, the potential for recurrence—particularly within the first year—remains a significant consideration.

Appendectomy continues to provide a definitive cure with minimal risk of recurrence, making it the preferred option for patients seeking a one-time intervention or those with complicated or unclear diagnoses. The choice of treatment should be individualized, taking into account clinical presentation, comorbidities, the patient's ability to adhere to follow-up, and—most importantly—their preferences.

Shared decision-making, grounded in transparent communication of risks and benefits, is essential to ensuring optimal outcomes. As the field continues to shift toward more personalized care, future research should aim to refine patient selection criteria and evaluate long-term outcomes of non-operative strategies across broader populations.

Disclosure

Author's Contributions Statement

Conceptualization: BR

Methodology: BR

Software: BR, KW, ZC, KG, LC

Check: BR, KW, KJ, LC, KK

Formal analysis: BR, KJ, AR, KK

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Writing – review and editing: BR, AC, ZC, MB

Visualization: BR, KG, AR, LC

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The authors declare that there are no conflicts of interest regarding the publication of this review. No financial or personal relationships have influenced the work reported in this manuscript

Informed Consent Statement

Not applicable.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article's bibliography.

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