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CONSERVATIVE TREATMENT OF ACUTE APPENDICITIS VERSUS EMERGENCY APPENDECTOMY: A RAPID SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Currently, increasing scientific evidence suggests that perforation is not an inevitable outcome of appendiceal obstruction. Over the past 25 years, the scientific literature has increasingly demonstrated the safety of non-operative treatment of Acute Appendicitis (AA) with antibiotics. Method: This study is a rapid systematic literature review. Studies were extracted from the PubMed databases of the National Library of Medicine, EMBASE, SCIELO, and the Virtual Health Library (VHL). Only randomized controlled clinical trials comparing conservative treatment with antibiotics to urgent surgical treatment in adults over 18 years old with uncomplicated acute appendicitis were included. Results: This meta-analysis found an effectiveness of 83.8% (95% CI: 87.99% - 78.17%) for surgical treatment and a global effectiveness rate of 68.77% (95% CI: 65.20% - 72.53%) for the conservative management of uncomplicated AA, increasing to 75.20% (95% CI: 71.50% - 79.09%) after sensitivity analysis excluding articles with a high risk of bias. Conclusion: Conservative treatment with antibiotics is safe and associated with lower risks of complications; however, it is significantly less effective than appendectomy in adults with uncomplicated AA without appendicolith.

Keywords: Acute appendicitis. Management. Cost-effectiveness. Rapid review.

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INTRODUCTION

Appendectomy is a surgical intervention performed to remove the cecal appendix, usually in cases of appendicitis. Approximately 8% of the population will develop Acute Appendicitis (AA) in their lifetime, with an incidence of 5.7-50 cases per 100,000 inhabitants per year. AA predominantly affects individuals between 10 and 30 years of age(1), occurring more frequently in men than women, though misdiagnosis is more common in females(2).

Diagnosing AA can be challenging, leading to diagnostic delays and negative appendectomies. Several scoring systems, such as the Modified Alvarado Scoring System (MASS) and the RIPASA score (Raja Isteri Pengiran Anak Saleha Appendicitis score), have been developed to improve diagnostic accuracy. A prospective study found that the RIPASA score is more accurate than MASS (72.22% vs. 91.66%), particularly in younger patients(3).

AA results from luminal obstruction due to fecaliths, lymphoid hyperplasia, foreign bodies (parasites, seeds, etc.), or tumors. This obstruction increases intraluminal pressure, leading to ischemia and potential perforation. The early phase is characterized by diffuse abdominal pain, often periumbilical, associated with nausea and vomiting. As ischemia progresses, bacterial colonization leads to localized pain and eventual peritonitis if untreated(4).

Recent evidence differentiates between complicated and uncomplicated AA. Surgery is mandatory for complicated AA, but numerous studies suggest that uncomplicated cases can be effectively treated with antibiotics alone, with high success rates and no increased risk of complications(5).

Between 2008 and 2014, approximately 684,278 appendectomies were performed in Brazil, averaging over 97,000 annually. In the United States, 300,000 appendectomies are performed yearly, predominantly laparoscopically. Appendicitis incidence varies geographically, with the U.S. reporting a 9% lifetime risk, Europe 8%, and Africa 2%.(6) In Brazil, in 2019, the Southeast region had 48,803 hospitalizations due to AA, followed by the Northeast (29,178), South (26,040), North (13,418), and Center-West (12,044), totaling 129,483 hospitalizations nationwide.(7,8)

Surgical techniques have evolved, with laparoscopic appendectomy increasingly preferred due to lower complication rates, reduced morbidity, shorter hospital stays, and better postoperative quality of life. Between 2008 and 2014, laparoscopic appendectomy in

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Brazil increased by 279.7% due to greater availability of technology. The Southeast and South regions still perform most of these procedures.(8)

Recent studies suggest that appendiceal perforation is not an inevitable consequence of obstruction, with perforation rates ranging from 16% to 40%, particularly at age extremes.(9) Mortality is below 0.1% for uncomplicated AA but rises to 5% in perforated cases.(1)

Over the last two decades, scientific production has increased regarding the safety of non-operative AA treatment using antibiotics. Recent meta-analyses report a 68.4% success rate for conservative treatment, with a 27.4% recurrence rate within one year and an 8% failure rate during primary hospitalization. The 2020 WSES Jerusalem consensus concluded that conservative treatment is safe for patients with uncomplicated AA.(1)

OBJECTIVE

To compare the clinical management of uncomplicated Acute Appendicitis with antibiotic therapy (non-operative management) versus emergency appendectomy (operative management).

METHODOLOGY STUDY TYPE

This is a rapid systematic review, in which, according to the Cochrane Rapid Reviews Methods Group, a transparent and rigorous search and synthesis process is conducted. As a systematic review, it follows a pre-established methodology and available tools for systematic reviews. The main difference lies in the adaptation of the scope and depth of processes, allowing specific stages to be restricted transparently to shorten the review process while maintaining the research objective (18).

The PICO strategy was applied as follows: P = adults over 18 years old diagnosed with uncomplicated acute appendicitis, I = non-operative management, C = emergency appendectomy, O = effectiveness at one year, complication and recurrence rates at one year, and length of hospital stay compared to emergency appendectomy. Accordingly, the research question was: What is the effectiveness of non-operative management with antibiotic therapy (conservative treatment) versus surgical treatment for uncomplicated AA?

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ELIGIBILITY CRITERIA

Only experimental studies (randomized controlled and non-controlled clinical trials) that compared conservative treatment with surgical treatment in adult patients over 18 years old with uncomplicated AA were included in this review. Studies had to be available in full text in English, Spanish, or Portuguese. Studies addressing complicated appendicitis or comparing antibiotic management with emergency appendectomy in children and adolescents were excluded.

SEARCH STRATEGY

The search was conducted on May 10, 2023, in the PubMed, EMBASE, SCIELO, and Virtual Health Library (VHL) databases, without filters, time limits, or language restrictions. The search terms and keywords used were: “Conservative Treatment” AND “Acute Appendicitis.”

STUDY SELECTION, DATA EXTRACTION, AND SUMMARIZATION

After retrieving articles from the databases, studies were imported into a reference management software. Duplicate articles were automatically identified and manually excluded after title and abstract screening.

For the selection process, the Rayyan.ai tool was used by a single reviewer (BM). Randomized controlled trials or clinical trials comparing conservative management (antibiotic therapy) versus emergency appendectomy for uncomplicated AA in adults were selected. After applying predefined filters, studies were screened based on a thorough reading of titles and abstracts, selecting those that met the eligibility criteria.

Following this step, the selected articles were fully read, and their results were synthesized descriptively in tables. Extracted information included details on interventions, effectiveness of conservative and surgical treatment, complication rates in each group, hospital stay duration, treatment failure rates within one year, sample sizes, study methods, and key results. Study results were synthesized both narratively, presenting key study characteristics such as authors, year of publication, study design, sample size, comparison groups, antibiotic regimens used in the conservative group, hospital stay duration across groups, recurrence rate at one year, and treatment effectiveness in each management approach.

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RESULTS

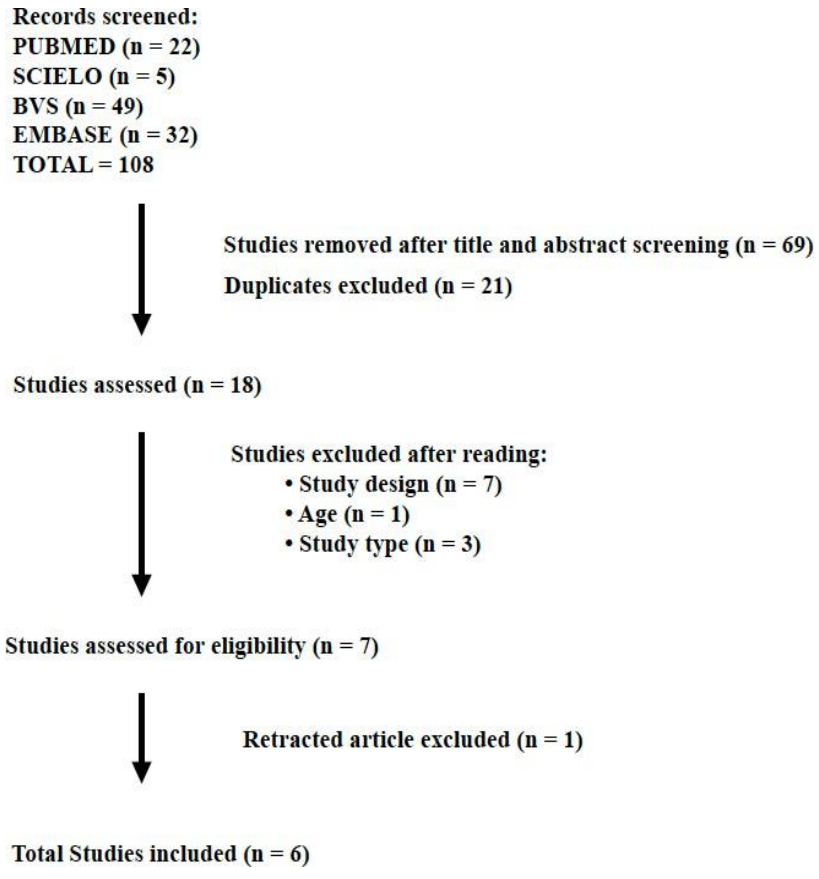
Of a total of 108 articles, 21 were excluded as duplicates after automatic identification by the Rayyan tool. Additionally, 69 articles were excluded after title and abstract screening for not meeting the predefined inclusion criteria, which were established using the PICO strategy in terms of population and study type.

Eighteen articles were classified as “maybe” in the Rayyan tool for a more in-depth methodological analysis. Of these, 7 were excluded for not being Randomized Controlled Trials (RCTs) comparing conservative treatment with antibiotics versus urgent surgical treatment in adults over 18 years old. One article was excluded because a portion of its population did not meet the inclusion criteria of this review, and another was excluded for being a study type other than an RCT.

Among the 7 articles eligible for inclusion in this review, one had to be excluded as it was retracted by the authors, while 6 were included for meeting all the selection criteria and the PICO strategy.

The study selection process in the databases is illustrated in Figure 1.

Figure 1. Flowchart for new systematic reviews including searches in databases, protocols, and other sources.



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The 6 included RCTs compared antibiotic therapy management with appendectomy at diagnosis in adults. Different antibiotic regimens were detected in the group randomized to conservative treatment, as well as different strategies regarding clinical criteria and imaging examinations for selecting patients with uncomplicated acute appendicitis. A total sample of 1,611 patients was obtained for the meta-analysis, with 817 randomized to conservative treatment and 794 to surgical treatment. These and other data are summarized in Table 1.

Table 1. Data information from the included studies.

Author	Ceresoli M	Hansson J	O'leary P	Salminen P	Styrud J	Vons C
Year	2019	2009	2021	2015	2006	2011
Publisher	Updates in Surgery	Journal of British Surgery	Annals of surgery	Jama	World journal of surgery	The Lancet
Country	Itália	Suécia	Irlanda	Finlândia	Suécia	França
Subjects in Conservative group	19	202	91	257	128	120
Subjects (%) of effective treatment in the conservative group	15 (78,9%)	83 (41,1%)	68 (74,7%)	186 (72,4%)	97 (75,8%)	81 (67,5%)
Subjects in surgery group	22	167	89	273	124	119
Subjects (%) of effective treatment in the surgery group	20 (90,9%)	142 (85%)	80 (89,9%)	270 (98,9%)	120 (96,8%)	117 (98,3%)
Antibiotic regimen	Ertapenem 1g IV, 3 times a day during internment durante a Hospitalization + Amoxicillin/Clavulanate 3 times a day for 5 days	Amoxicillin/Clavulanate 1.2g IV, 3 times a day until clinical recovery + Amoxicillin/Clavulanate more 5 days (625mg 3 times a day oral for more 5 days)	Cefotaxim 1 g two times e Metronidazol 1.5g one time for 24h. + Ciprofloxacin 500mg 2 times a day and Metronidazol 400mg 3 times a day for 10 days.	Ertapenem IV (1 g/day) for 3 days, followed by 7 days Levofloxacin oral (500 mg 1 time a day) and Metronidazol (500 mg 3 times a day)	Cefotaxime IV, 2g 2 times a day for 2 days and Tinidazole 0.8 g, followed by Ofloxacin 200 mg 2 times a day and Tinidazole 500 mg 2 times a day for 10 days	Amoxicillin/Clavulanate (3g per day) for 8 to 15 days

All studies had a pre-published and pre-approved clinical trial protocol. However, Hansson *et al*. employed multiple measurements and analyses in reporting results, opting for per-protocol analyses as the primary outcome measure due to significant deviations in the intention-to-treat groups. Consequently, it was classified as having a high risk of bias.

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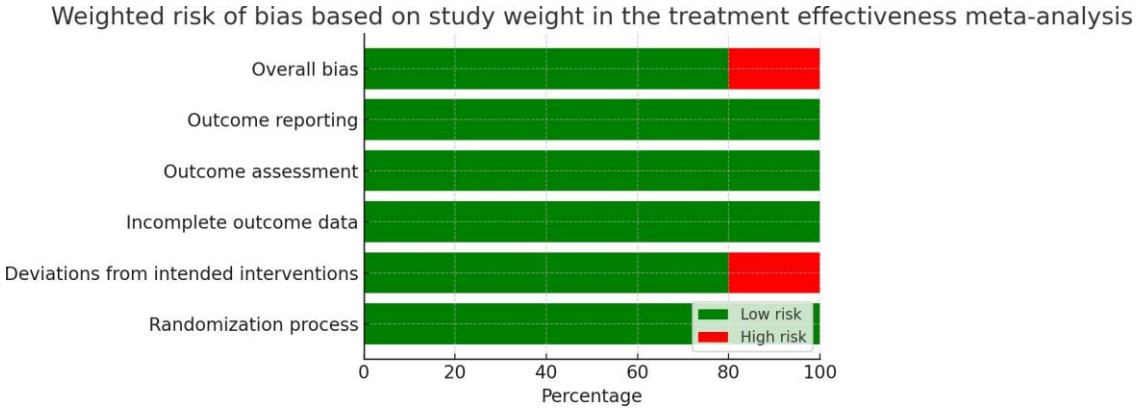
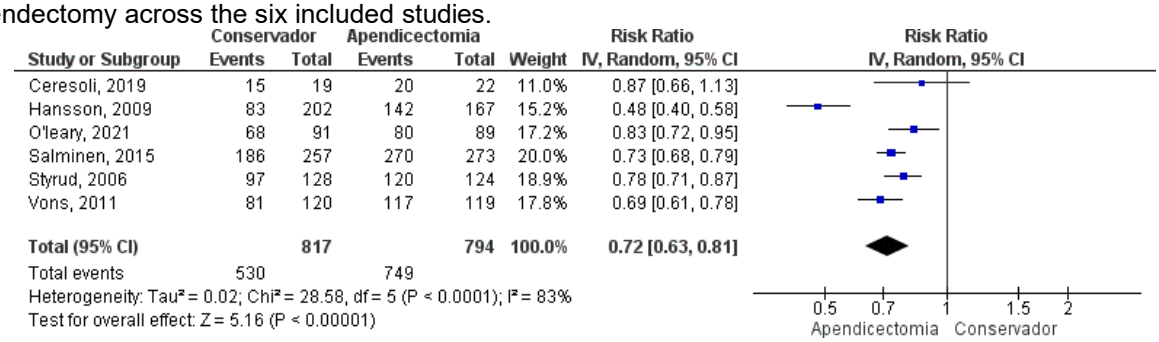
The remaining studies conducted predefined primary and secondary outcome analyses based on the randomized intention-to-treat groups, using appropriate statistical methods. Figure 2 illustrates the weighting of each bias based on the study's contribution to the meta-analysis.

Figure 2. Weighted risk of bias according to the study weight in the meta- analysis of treatment effectiveness.



Appendectomy is more effective compared to conservative treatment with antibiotics. Methodological differences, inclusion criteria, or variations in antibiotic regimens are reflected in the heterogeneity of the studies (I^2 = 83%). Although surgery is more effective, some studies still indicate the efficacy of conservative treatment, particularly in well- selected cases, as shown in Figure 3.

Figure 3. Forest plot depicting the one-year effective treatment rates for conservative management and appendectomy across the six included studies.



DISCUSSION

Appendectomy is considered the gold standard for managing both complicated and uncomplicated AA due to its high success rates and low risk of complications and mortality(1). In this study, an effectiveness rate of 83.8% (95% CI: 87.99% - 78.17%) was

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observed for surgical treatment, considering success not only as the resolution of all symptoms but also as confirmation via histopathological examination.(10)

However, the conservative management of uncomplicated AA has proven to be safe and effective for most patients, with an overall effectiveness rate of 68.77% (95% CI: 65.20% - 72.53%) and 75.20% (95% CI: 71.50% - 79.09%) found in this study.(11–13)

Additionally, a 71.0% relative risk reduction (95% CI: 86.0% – 38.0%) in complications was observed with conservative management, aligning with the evidence from the 2020 WSES Jerusalem guidelines. These guidelines indicate that conservative management does not increase the complication or perforation rate of uncomplicated AA in adults, with the APPAC RCT reporting an overall complication rate of 6.5% for conservative management versus 24.4% for appendectomy (1,5).

The risk of treatment failure was significantly higher in the conservative group, with an RR of 6.16 (95% CI: 2.95 – 12.86). (11–16)Thus, patients opting for this approach to avoid surgery should be aware of the significantly higher risk of symptom recurrence. A study following patients treated with antibiotics found recurrence rates of 27.3% at one year and up to 39.1% at five years.(17) Moreover, the presence of appendicolith, even in uncomplicated AA, was strongly associated with higher treatment failure rates, with some studies reporting a 60% failure rate within one year in patients with calcifications detected on imaging. Therefore, such patients should not be considered suitable candidates for conservative management alone.(1)

In this review, hospital stay duration during the initial hospitalization showed no statistically significant difference between the two management strategies, with a weighted mean difference of 0.01 days (95% CI: -0.17 – 0.20 days). Harnoss et al. reported a significantly longer hospital stay for conservatively managed patients (RR 0.3 days; 95% CI: 0.07 – 0.53; P = 0.009; I = 49%).(17) However, this difference was statistically significant, likely due to the necessity of completing a 24-hour antibiotic regimen.(14)

Our findings were consistent with those from a subgroup analysis by Yang et al., which included only RCTs and reported a mean difference of 0.01 days (95% CI: -0.03 – 0.05 days). The same meta-analysis, when including all eligible studies, found an additional 0.47 days (95% CI: 0.45 – 0.50 days) of hospitalization for the conservative group.(6) This suggests that when only RCTs are analyzed, no statistical difference in hospital stay duration is found, whereas including studies with different methodologies reveals a longer stay for conservatively managed patients.

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Regarding cost-effectiveness, only two of the included RCTs provided data on the average cost of each intervention per intention-to-treat group. Both studies indicated a lower cost associated with conservative treatment, particularly in cases where it was fully effective after one year of follow-up. However, there are no comparable cost- effectiveness studies in the literature that consider standardization of procedures and resource utilization for a comprehensive analysis. Future research should focus on standardizing protocols to allow for a more in-depth evaluation with a higher degree of evidence certainty.(14,15)

This study considered only data from intention-to-treat groups and effectiveness outcomes at one year of follow-up. Consequently, differences may be observed when comparing our findings with previously published systematic reviews that included longer follow-up periods. The analyzed data were limited to RCTs comparing conservative management with appendectomy in adults with uncomplicated AA, meaning that the conclusions drawn here cannot be generalized to other populations or disease presentations. Among the six included RCTs, there were few data on populations over 65 years old, and no separate analyses were conducted for this age group. Therefore, we believe that the evidence presented should not be extrapolated to elderly populations. Additionally, significant variations in antibiotic protocols were observed among the included RCTs, making it impossible to determine whether different regimens influenced treatment effectiveness.(11–16)

CONCLUSIONS

This meta-analysis indicates that antibiotic treatment for uncomplicated AA is safe and associated with lower complication risks but is significantly less effective than appendectomy. In settings where surgery is unavailable or in patients reluctant to undergo surgery, antibiotic therapy is a viable alternative. No significant difference in hospital stay duration was found. Further research is required to determine the cost-effectiveness of these treatment options.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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