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WHO CAN SAFELY SKIP SURGERY? PREDICTORS OF SUCCESS AND FAILURE OF NONOPERATIVE MANAGEMENT IN ACUTE UNCOMPLICATED APPENDICITIS

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ABSTRACT

Introduction and objective: Acute appendicitis is one of the most common surgical emergencies worldwide. Although appendectomy remains the standard treatment, nonoperative management (NOM) with antibiotics has emerged as an alternative for selected patients with acute uncomplicated appendicitis. While randomized trials have confirmed the safety and noninferiority of NOM, treatment failure and recurrence remain important limitations. This review aims to summarize current evidence on predictors of success and failure of NOM in acute uncomplicated appendicitis.
Methods: A comprehensive literature search was performed in PubMed, Embase, Google Scholar, and Web of Science for studies published between January 2000 and January 2025. Randomized controlled trials, observational studies, systematic reviews and meta-analyses evaluating predictors of NOM outcomes were included. Due to heterogeneity among studies, results were synthesized narratively.
Results: Sixteen studies comprising 6,281 patients treated with NOM were analyzed. Overall, NOM demonstrated noninferiority to surgical treatment in selected patients; however, approximately 24% required subsequent appendectomy. The presence of an appendicolith was the most consistent predictor of NOM failure and recurrence. Increased appendiceal diameter, elevated C-reactive protein levels, fever, and imaging features suggestive of advanced inflammation were also associated with poorer outcomes. Demographic factors such as age and sex showed inconsistent associations.
Conclusions: Nonoperative management with antibiotics is a safe and effective option for carefully selected patients with acute uncomplicated appendicitis. The presence of an appendicolith, appendiceal diameter greater than 10mm and elevated inflammatory markers are key predictors of NOM failure and should be incorporated into clinical decision-making.

KEYWORDS

Acute Appendicitis, Nonoperative Management, Antibiotics, Predictors, Appendicolith

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1. Introduction

Acute appendicitis has a global annual incidence of approximately 100 new cases per 100,000 people, making it one of the most common causes of acute abdominal pain requiring emergency surgical intervention, that affects all age groups and both sexes (Téoule et al., 2020). Appendectomy has long been considered the standard treatment and is associated with low morbidity and excellent outcomes in both uncomplicated and perforated disease (Sartelli et al., 2018), particularly when performed laparoscopically (Köhler et al., 2021).

Over the past decade, however, nonoperative management (NOM) with antibiotics has emerged as a valid alternative to surgery for selected patients with uncomplicated appendicitis. This paradigm shift has been driven by evidence from large randomized controlled trials and meta-analyses, including the APPAC (Salminen et al., 2015) and CODA (Flum et al., 2020) trials, which have demonstrated that NOM can be safe and effective in many cases, with the added advantages of avoiding surgery and enabling faster initial recovery.

Despite these promising findings, accumulating evidence suggests that the success of NOM largely depends on careful patient selection and cannot be used as an alternative in all patients. Reported failure rates vary widely, and recurrent appendicitis remains a concern during long-term follow-up. (Farah et al., 2024; Flum et al., 2020; Poon et al., 2017; Salminen et al., 2015; Sevinç et al., 2025) Specific clinical, laboratory, and radiological factors appear to influence the likelihood of treatment success or failure, yet these predictors are not uniformly applied in clinical practice. Among them, the presence of an appendicolith, elevated C-reactive protein (CRP), fever and imaging features such as appendiceal diameter, presence of abscess or periappendiceal fluid, suggestive of more advanced disease, have repeatedly been associated with poorer outcomes, whereas patients with mild inflammatory responses and favorable imaging profiles may benefit

more from a conservative approach (Kohga et al., 2021; Lie et al., 2023; Loftus et al., 2018; Maxfield et al., 2014; Walker et al., 2019).

As interest in NOM increases among both practitioners and patients, determining which patients can safely forgo surgery has become a critical clinical question. Reliable identification of patients with a high probability of successful antibiotic therapy would allow clinicians to personalize treatment, reduce unnecessary surgeries, and improve shared decision-making.

The aim of this review is to synthesize current evidence on predictors of success and failure of nonoperative management in acute uncomplicated appendicitis. By examining demographic factors, clinical presentation, inflammatory markers and imaging characteristics such as presence of appendicolith and appendiceal diameter, we seek to clarify which patients are most likely to benefit from conservative therapy and which should be directed toward early surgery. Understanding these predictors is fundamental to optimizing patient outcomes and guiding future protocols for the selective use of NOM in clinical practice.

2. Methods

Search Strategy

A comprehensive literature search was conducted to identify studies evaluating predictors of success or failure of nonoperative management (NOM) in acute uncomplicated appendicitis. PubMed, Embase, Google Scholar, and Web of Science databases were searched for articles published between January 2000 and January 2025. The search included combinations of MeSH terms and free-text keywords such as: “acute appendicitis”, “uncomplicated acute appendicitis”, “nonoperative management”, “antibiotic treatment”, “predictors”, “risk factors”, “treatment failure”, “appendicolith”, “appendix diameter”, “C-reactive protein”, and “conservative treatment”.

Reference lists of key articles, meta-analyses, and randomized controlled trials (RCTs) were manually screened to identify additional eligible studies not captured in the database search.

Eligibility Criteria

Studies were considered eligible if they met the following criteria: **Population:** Adult, pediatric, or mixed populations diagnosed with acute uncomplicated appendicitis with and without presence of appendicolith. **Intervention:** Nonoperative management using antibiotics, with or without follow-up. **Outcomes**: Studies reporting predictors, risk factors, or determinants of treatment success or failure. **Study design:** Randomized controlled trials, prospective or retrospective cohort studies, case–control studies, systematic reviews, and meta-analyses. **Language:** Articles published in English.

Exclusion criteria: Perforated, gangrenous, phlegmonous, or abscess-forming appendicitis unless predictors for uncomplicated cases were reported separately; case reports and case series including fewer than three patients; and studies lacking extractable data on predictors.

Study Selection

Titles and abstracts were screened for relevance. Full texts of potentially eligible studies were retrieved and evaluated using predefined inclusion criteria. Disagreements were resolved through discussion and consensus. Studies were grouped based on the type of predictor evaluated: demographic, clinical, laboratory or imaging-related

Quality Assessment

The Newcastle–Ottawa Scale (NOS) was used to assess observational studies. Randomized controlled trials were evaluated using the Cochrane Risk of Bias tool, while systematic reviews and meta-analyses were appraised using the AMSTAR-2 framework. Study quality was considered when interpreting the level of evidence supporting each predictor.

Data Synthesis

Because of substantial heterogeneity in study populations, diagnostic criteria, antibiotic regimens, and follow-up periods, a formal meta-analysis was not performed. Instead, findings were synthesized narratively.

3. Results

The database search identified 1,342 records. After removing duplicates and screening titles and abstracts, 82 full-text articles were assessed for eligibility. A total of 16 studies met the inclusion criteria, encompassing 6,281 patients treated with nonoperative management for acute uncomplicated appendicitis. (Anwar et al., 2024; Becker et al., 2023; Kobayashi et al., 2021; Kohga et al., 2021; Kupietzky et al., 2025; Lee & Park, 2025; Lie et al., 2023; Loftus et al., 2018; Mahida et al., 2016; Prajapat et al., 2023; Ramadan et al., 2024; Scheijmans et al., 2025; Selänne et al., 2025; Silina et al., 2016; Wakasa et al., 2023; Walker et al., 2019)

Most studies evaluated patients diagnosed with uncomplicated appendicitis based on clinical criteria supported by imaging (ultrasound or CT). Successful NOM was generally defined as clinical improvement with resolution of symptoms and normalization of inflammatory markers without the need for appendectomy. Failure was defined as conversion to surgery before symptom resolution or the need for appendectomy during follow-up due to recurrence. (Anwar et al., 2024; Kohga et al., 2021; Kupietzky et al., 2025; Lee & Park, 2025; Loftus et al., 2018; Prajapat et al., 2023; Walker et al., 2019)

None of the studies demonstrated superiority of NOM over surgical treatment; however, the majority showed noninferiority of conservative therapy. Among 6,281 patients treated with NOM, 1,537 (24%) required surgery. Reported failure rates ranged from 10% to 60% (median 22%).

The most consistently investigated factor was the presence of an appendicolith. Most studies reported that appendicolith significantly increased the risk of NOM failure. In meta-analyses conducted by Lee et al. (2025)., surgery was required in 25% of patients without an appendicolith and in 41% of those with an appendicolith. Similar findings were reported by Scheijmans et al. (2025), with failure rates of 30% and 49%, respectively. Among the studies included in this review, only Silina et al. (2016) and Ramadan et al. (2024). did not observe a statistically significant difference between patients with and without an appendicolith. Kupietzky et al. (2025) reported that although appendicolith presence did not increase the initial failure rate, it was associated with earlier recurrence by approximately two months. Kohga et al. (2021) further stratified patients based on appendicolith incarceration and demonstrated that only incarcerated appendicoliths were associated with significantly worse outcomes.

Appendix diameter was the second most frequently reported imaging predictor. Although threshold values varied between studies, larger appendiceal diameter was generally associated with a higher risk of NOM failure, presumably due to an increased risk of perforation. Reported thresholds ranged from 10 to 15 mm (Kobayashi et al., 2021; Kupietzky et al., 2025; Loftus et al., 2018; Prajapat et al., 2023; Ramadan et al., 2024; Selänne et al., 2025). Only the study by Silina et al. (2016) did not demonstrate a statistically significant association.

Among indicators of ongoing inflammatory process, CRP and fever were most commonly evaluated. Prapajat et al. (2023) reported that CRP values above 20 mg/L and the presence of fever within 24 hours from symptom onset increased the risk of NOM failure. Fever within the first 6 hours of admission was also identified as a risk factor. (Loftus et al., 2018) Time from symptom onset to hospital admission showed inconsistent associations. In the study by Prapajat et al. (2023), patients presenting within two days had a higher risk of failure, whereas Loftus et al. (2018) reported a threshold of 25 hours. Conversely, Anwar et al. (2024) found that admission after 42 hours was associated with worse outcomes.

Data regarding sex and age were inconsistent. Most studies did not demonstrate a significant difference between sexes. However, Kobayashi et al. (2021). reported a higher risk of failure in males. Becker et al. (2023) identified age as a risk factor, reporting that children older than 14 years were more likely to fail conservative treatment. This finding has not been supported by other studies on pediatric populations, indicating the need for further investigations. Age above 40 years old was not directly associated with NOM failure, but was rather linked to comorbidities such as stroke (Kohga et al., 2021) or diabetes mellitus (Anwar et al., 2024), however those were scarcely reported.

4. Discussion

Across the included studies, NOM consistently demonstrated noninferiority to surgical treatment in terms of short-term safety and clinical outcomes, in line with findings from large randomized trials such as APPAC (Salminen et al., 2015) and CODA (Flum et al., 2020). Nevertheless, approximately one third of patients ultimately required appendectomy, due to lack of improvement or recurrence of symptoms, underscoring that NOM should not be viewed as a replacement for surgery but rather as a selective treatment strategy. Identifying patients at increased risk of failure or recurrence remains central to optimizing outcomes and avoiding delayed surgical intervention.

Among all evaluated predictors, the presence of an appendicolith emerged as the most robust and consistently reported risk factor for NOM failure. Multiple cohort studies and meta-analyses demonstrated significantly higher rates of early treatment failure and recurrence in patients with an appendicolith compared to those without. These findings are biologically plausible, as a fecalith may cause persistent luminal obstruction, increase in intraluminal pressure, and promote ongoing bacterial proliferation despite antibiotic therapy. Importantly, more recent studies suggest that not all appendicoliths confer equal risk. Incarcerated appendicoliths, as well as those associated with periappendiceal fluid, appear to be particularly predictive of poor outcomes (Kohga et al., 2021). Although a minority of studies did not confirm a statistically significant association, the overall body of evidence strongly supports the presence of an appendicolith as a relative contraindication to NOM.

Appendiceal diameter was the second most frequently reported imaging predictor of NOM failure likely reflecting more advanced inflammatory changes and a higher probability of impending perforation. Other imaging features, such as periappendiceal fluid, wall thickening, or inflammatory fat stranding, were less consistently analyzed, but tended to be associated with complicated disease and poorer outcomes when reported. Collectively, these findings reinforce the central role of high-quality imaging, particularly CT, in confirming truly uncomplicated appendicitis prior to initiating NOM.

Inflammatory markers, particularly C-reactive protein (CRP) above 20mg/L along with high posttreatment levels, were frequently evaluated as prognostic indicators, suggesting that a heightened systemic inflammatory response may reflect advanced local disease or early complications. Several studies also emphasized the prognostic value of early trends in CRP, with lack of improvement after antibiotic initiation indicating a higher likelihood of conversion to surgery. Fever, especially when present early in the disease course or shortly after admission, was similarly associated with poorer outcomes, although its predictive value was less consistent than that of imaging findings.

The relationship between symptom duration and NOM outcomes remains controversial. Some studies reported higher failure rates among patients presenting early after symptom onset, possibly reflecting rapidly progressive disease, while others found worse outcomes in patients with delayed presentation. These seemingly contradictory findings suggest that symptom severity and progression, rather than duration alone, may be more clinically meaningful and should be interpreted in conjunction with imaging and laboratory findings.

Demographic variables such as sex and age showed inconsistent associations with NOM outcomes. Isolated reports suggested higher failure rates in male patients. Age-related findings were similarly heterogeneous. In pediatric populations, older children and adolescents were reported in some studies to have higher failure rates, but this observation was not consistently replicated. In adults, advanced age was not directly associated with NOM failure; however, concerns regarding underlying appendiceal malignancy in patients over 40 years of age have led some authors to recommend surgical management or close follow-up in this group. Additionally, comorbidities such as diabetes mellitus or cerebrovascular disease were infrequently reported, but may contribute to poorer outcomes, highlighting the need for individualized risk assessment.

The findings of this review have important clinical implications. They support a selective approach to NOM, emphasizing the need for a multimodal assessment incorporating imaging, laboratory data, and clinical presentation. Patients with unequivocally uncomplicated appendicitis, absence of an appendicolith, limited appendiceal enlargement, and mild inflammatory responses appear to be the best candidates for antibiotic-first therapy. Conversely, patients with appendicoliths, marked inflammatory responses, or imaging features suggestive of advanced disease should be counseled regarding the higher risk of failure and the potential benefits of early appendectomy.

Despite growing evidence, several gaps remain. The heterogeneity of study designs, definitions, and follow-up periods limits direct comparison and precludes firm conclusions regarding optimal thresholds for many predictors. Additionally the antibiotics used in conservative treatment not only vary between studies, but

also within each article, making it impossible to compare the effect that antibacterial agents have on NOM success and to create universal guidelines Future research should focus on developing and validating standardized prediction models that integrate clinical, laboratory, imaging parameters and comparable treatment strategies. Such tools may facilitate shared decision-making, improve patient selection, and enhance the safety and effectiveness of NOM in routine clinical practice.

In conclusion, while nonoperative management with antibiotics is a viable option for selected patients with acute uncomplicated appendicitis, its success depends on careful evaluation of multiple predictive factors. A structured, evidence-based approach to patient selection is essential to maximize benefits and minimize the risks associated with delayed surgical intervention.

5. Conclusions

While nonoperative management with antibiotics is a viable option for selected patients with acute uncomplicated appendicitis, its success depends on careful evaluation of multiple predictive factors of which presence of appendicolith, diameter of appendix and elevated inflammatory markers seem to be the most crucial. A structured, evidence-based approach to patient selection is essential to maximize benefits and minimize the risks associated with delayed surgical intervention.

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