



Review

NONOPERATIVE TREATMENT FOR ACUTE UNCOMPLICATED APPENDICITIS IN CHILDHOOD

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ABSTRACT

Nonoperative treatment (NOT) has emerged as a potential alternative to surgery for acute uncomplicated appendicitis in children; although short-term outcomes are often favourable, concerns remain regarding the durability of treatment, the incidence of complications, and long-term failure. Updated meta-analyses of randomized clinical trials (RCTs) may help clarify the comparative safety and effectiveness versus appendectomy. **Objective:** To assess the safety and effectiveness of NOT compared with appendectomy for uncomplicated appendicitis in children using the highest level of available evidence. **Methods:** A systematic review of PubMed, Embase, Scopus, Cochrane, and Web of Science was conducted. **Results:** In this systematic review and meta-analysis of 8 randomized clinical trials including 1480 children and adolescents, NOT (nonoperative antibiotic treatment) was associated with a significantly higher risk of treatment failure at 1 year and an increased incidence of major complications compared to appendectomy. Although NOT resulted in a modestly faster return to school and daily activities, this benefit may be offset by higher rates of readmission and reintervention. **Conclusion:** Although NOT offers a shorter initial recovery, higher failure rates and major complications limit its role as a primary treatment strategy. The data suggest that appendectomy offers better outcomes in children and adolescents with uncomplicated appendicitis.

Keywords: uncomplicated appendicitis, childhood, treatment

Nonoperative treatment /NOT/ provides inferior outcomes compared to surgical therapy in children and adolescents with UA. NOT is associated with higher treatment failure rates, readmission rates, complications, and increased length of hospital stay; lower treatment success; a recurrence rate of appendicitis of 18.47 events/100 observations in 1 year; and shorter time to return to normal activities and school. Our primary results showed low heterogeneity, and the main results were supported by the TSA (test of statistical significance of antibiotics). Our findings differ from those of a previous major meta-analysis, which suggested that surgical treatment offered fewer complications in pediatric patients. Treatment with antibiotics alone and surgery are not directly comparable in terms of absolute treatment failure, so a non-inferiority analysis is essential for interpreting the results.

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As observed in a recent randomized controlled trial (RCT) by Helling TS and suggested by a Cochrane review, (24) a non-inferiority margin of 20% is considered a reasonable threshold to balance the lower efficacy of nonoperative management with its potential benefits.

The 2020 WSES consensus provides the following recommendations for conservative management of acute appendicitis (1-4):

1. Nonoperative antibiotic treatment is recommended as a safe alternative to surgical treatment in selected patients with uncomplicated appendicitis and in the absence of appendicitis. The possibility of failure or missed complicated appendicitis is emphasized.
2. Nonoperative management of acute appendicitis during pregnancy is not recommended until a higher level of evidence is available.
3. Nonoperative antibiotic treatment is proposed as a safe and effective alternative to surgical treatment in children with uncomplicated acute appendicitis in the absence of appendicitis, with attention being paid to the

possibility of failure and missed complicated appendicitis.

4. In cases of nonoperative treatment, initial intravenous antibiotic therapy is recommended with subsequent switching to oral antibiotics based on the patient's clinical condition.

Complicated acute appendicitis: The optimal approach to complicated appendicitis also remains a debatable topic. In the past, immediate surgical treatment has been associated with increased morbidity, while initial nonoperative treatment has been reported to have a success rate of over 90%, a recurrence risk of 7.4%, and the need for percutaneous drainage in only 19.7% of cases with abscess (5, 6). Meta-analysis of Similis (including 16 non-randomized retrospective studies and one non-randomized prospective study with a total of 1572 patients, of whom 847 were initially treated conservatively.

Three main factors are considered when undertaking conservative treatment. Shared decision-making after a thorough discussion between the patient and the surgeon, outlining the potential benefits and risks, including the possibility of disease recurrence and the need for potential surgical intervention in the future, is essential. The second main factor is adequate patient selection (form of appendicitis, factors indicating a greater chance of success such as low Alvarado score, small appendix diameter). The concomitant comorbidity and the patient's general condition are also considered in patient selection. The third factor is close observation. Patients undergoing conservative treatment require close dynamic monitoring for signs of deterioration, failure of the therapeutic approach, and detection and treatment. In the NOT analysis, there was a 1-year failure rate of 36.6% compared with 7.0% in the surgical group, indicating that appendectomy is more effective than antibiotics and surpasses the margin of previous RCTs. (7-9) This finding differs from previous meta-analyses and is consistent with the most recent RCTs. Our findings differ from the 2017 meta-analysis by Huang et al. (10-12), which supported antibiotics as a safe primary treatment, but was limited by a small sample size (404 patients), only 1 RCT, and reliance on cohorts, which increases bias. Their analysis used fixed-effects models and did not assess the robustness of the results by TSA. In contrast, our study included 8 randomized controlled trials (RCTs) and 1490 patients, with TSA (a history of emergency transplant) supporting the robustness of the

results in all primary outcomes. In cases where peri-appendicular abscess or phlegmon is present, some authors again advocate an initial therapeutic approach, while others recommend an aggressive surgical approach (13-15).

In 2007, Anderson demonstrated that immediate surgical treatment in these patients was associated with increased morbidity versus initial nonoperative treatment (16-18). Similis et al. in their meta-analysis of 17 studies showed that preoperative conservative treatment was associated with fewer complications (intra-abdominal abscess and intestinal obstruction) (19-21). Recent cohort studies have shown opposite results (22, 23). They argue for more aggressive treatment in cases of peri-appendicular abscess, based on the idea that there is a relatively high failure rate with conservative treatment. According to the 2015 EAES consensus, a new systematic review is needed. Until then, preoperative conservative treatment of periappendicular abscess is the preferred treatment option (24, 25).

In 2020 The WSES provides the following recommendations for the treatment of complicated acute appendicitis with periappendicular abscess or phlegmon (26, 27):

1. Preoperative antibiotic treatment and, if possible, percutaneous drainage are recommended in cases where laparoscopic expertise is not available.
2. In the presence of advanced laparoscopic expertise, a laparoscopic approach with a low risk of conversion is recommended as the treatment of choice.
3. Routine interval appendectomy is not recommended after nonoperative treatment of appendicitis in patients under 40 years of age and children. Interval appendectomy is recommended in cases of recurrence of symptoms.
4. In patients with appendicitis over 40 years of age, treated conservatively, colonoscopy and contrast-enhanced computed tomography are recommended to exclude underlying malignant pathology. Interval (delayed) appendectomy: The need for interval appendectomy after initial nonoperative treatment remains a subject of debate. Recommendations for interval appendectomy are based on the probability of missing an underlying malignancy (frequency 6%) and the chance of developing recurrent appendicitis (frequency from 5 to 44%) (28-30). Both conditions can be avoided by interval appendectomy, although there is a lack of data on its advantages. The reported average

recurrence rate in nonsurgical treatment of perforated appendicitis and phlegmon is 12.4% (8). In order to avoid this significant risk, some authors recommend routine elective interval appendectomy after initial nonoperative treatment. In a recent systematic review by Darwazeh, interval appendectomy and repeated nonoperative treatment in the case of recurrence were associated with similar morbidity rates (31-34).

Elective interval appendectomy

This updated and higher-quality evidence base supports surgery as the most effective and reliable strategy based on treatment outcomes and questions previous guideline changes to NOT (nonoperative treatment (35-37). Previous studies have shown that reduced recovery time and fewer hospital visits are associated with improved well-being and participation in school and social activities. (38-40) Patients who underwent surgery were found to return to school with 4.93 more days of normal activities, despite a shorter hospital stay without clinical significance. This is expected due to postoperative activity restrictions. (41-43) However, because one-third of nonsurgical patients did not experience treatment failure within one year, they may ultimately add to the burden of rehospitalizations. TSA showed insufficient data to draw firm conclusions about return-to-activity outcomes, highlighting the need for further research (44, 45).

CONCLUSIONS

1. Conservative treatment with antibiotics is a feasible treatment method for selected patients with uncomplicated acute appendicitis who would like to avoid immediate surgical treatment and understand the associated risks, mainly the risk of recurrence of the disease.
2. Initial conservative treatment in destructive and complicated forms is a recommended approach.
3. Appendectomy remains the gold standard in the treatment of acute appendicitis with its high and long-term effectiveness, and with good expertise available, laparoscopic treatment is recommended.

REFERENCES

1. Ziinovieva Y., M.Radionov. Conservative treatment in acute appendicitis. *Surgery*. Vol.89, 3,1-17 2025
2. Di Saverio S, Podda M, De Simone B, Ceresoli M, Augustin G et al. Diagnosis and treatment of acute appendicitis: update of the

- WSES Jerusalem guidelines. *World J Emerg Surg*.15:27-35. 2020
3. Ambrose NS, Donovan IA, Wise R, Lowe P. Metronidazole and ticarcillin in the prevention of sepsis after appendectomy. *Am J Surg.*,146:346–348, 1983
4. Basoli A, Zarba Meli E, Salvio A, Crovaro M, Scopelliti G, Mazzocchi P, Lomanto D, Fiocca F, Speranza V. Trends in the incidence of acute appendicitis in Italy during the past 30 years. *Minerva Chir.*;48:127–132, 1993
5. Andersson R, Hugander A, Thulin A, Nyström PO, Olaison G. Indications for operation in suspected appendicitis and incidence of perforation. *BMJ.*;308:107–110, 1994
6. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. *Ann Surg*.246:741–8.4,2007
7. Ansaloni L, Catena F, Coccolini F, Ercolani G, Gazzotti F, Pasqualini E, Pinna AD. Surgery versus conservative antibiotic treatment in acute appendicitis: a systematic review and meta-analysis of randomized controlled trials. *Dig Surg.*,28:210–221,2011
8. Haijanen J, Sippola S, et al. on behalf of the APPAC study group, Optimising the antibiotic treatment of uncomplicated acute appendicitis: a protocol for a multicentre randomised clinical trial (APPAC II trial). *BMC Surg*.18:117-23, 2018
9. Buckels JA, Brookstein R, Bonser R, Bullen B, Alexander-Williams J. A comparison of the prophylactic value of cefotetan and metronidazole appendectomy. *World J Surg*.9:814–818, 1985
10. Vons C, Barry C, Maitre S, Pautrat K, Leconte M et al. Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis. An open label, non-inferiority, randomised controlled trial. *Lancet*. 377:1573–1579, 2011
11. Coakley B, Sussman E, Wolfson T, Bhagavath A, Choi J, Ranasinghe N, Lynn E, Divino C. Postoperative antibiotics correlate with worse outcomes after appendectomy for nonperforated appendicitis. *J Am Coll Surg*.213:778–783, 2011
12. Darwazeh G, Cunningham SC, Kowdley GC. A systematic review of perforated appendicitis and phlegmon: interval appendectomy or wait-and-see? *Am Surg*. 82:11–5,2016

13. De Jonge J, Bolmers MDM, Musters GD, et al. Predictors for interval appendectomy in non-operatively treated complicated appendicitis. *Int J Colorectal Dis.*34:1325–32,2019
14. Deelder JD, Richir MC, Schoorl T, Schreurs WH. How to treat an appendiceal inflammatory mass: operatively or nonoperatively? *J Gastrointest Surg.*18:641–645, 2014
15. Gorter RR, Eker HH, Gorter-Stam MA, Abis GS, Acharya et al.. Diagnosis and management of acute appendicitis. EAES consensus development conference. *Surg Endosc.*30(11):4668-4690,2016
16. Hall NJ, Jones CE, Eaton S, Stanton MP, Burge DM. Is interval appendectomy justified after successful nonoperative treatment of an appendix mass in children? A systematic review. *J Pediatr Surg.*46:767–771, 2011
17. Elangovan S, Knapp DP, Kallail KJ. Incidence of acute appendicitis confirmed by histopathologic diagnosis. *Kans Med.*98:10–13.,1997
18. Eriksson S, Granstrom L. Randomized clinical trial of appendectomy versus antibiotic therapy for acute appendicitis. *Br J Surg.*82:166–169 1995
19. Hall NJ, Eaton S, Stanton MP, et al. Active observation versus interval appendectomy after successful non-operative treatment of an appendix mass in children (CHINA study): an open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol.*2:253–60, 2017
20. Hansson J, Körner U, Khorram-Manesh A, Solberg A, Lundholm K. Randomized clinical trial of antibiotic therapy versus appendectomy as primary treatment of acute appendicitis in unselected patients. *Br J Surg.*96:473–481, 2009
21. Hansson J, Khorram-Manesh A, Alwindawe A, et al. A model to select patients who may benefit from antibiotic therapy as the first line treatment of acute appendicitis at high probability. *J Gastrointest Surg.*18:961–7,2014
22. Kim JK, Ryoo S, Oh HK, Kim JS, Shin R, Choe EK, Jeong SY, Park KJ. Management of appendicitis presenting with abscess or mass. *J Korean Coloproctol.*;26:413–419,2010
23. Harnoss JC, Zelienska I, Probst P, et al. Antibiotics versus surgical therapy for uncomplicated appendicitis: systematic review and meta-analysis of controlled trials (PROSPERO 2015). *Ann Surg.*265:889–900, 2017
24. Helling TS, Soltys DF, Seals S. Operative versus non-operative management in the care of patients with complicated appendicitis. *Am J Surg.*214:1195–200.,2017
25. Huston JM, Kao LS, Chang PK, et al. Antibiotics vs. appendectomy for acute uncomplicated appendicitis in review of the evidence and future directions. *Surg Infect.*;18:527–35, 2017
26. Ilves I, Fagerström A, Herzig KH, Juvonen P, Miettinen P, Paajanen H. Seasonal variations of acute appendicitis and nonspecific abdominal pain in Finland. *World J Gastroenterol.*;20:4037–4042, 2014
27. Mason RJ, Moazzez A, Sohn H, Katkhouda N. Meta-analysis of randomized trials comparing antibiotic therapy with appendectomy for acute uncomplicated appendicitis. *Surg Infect (Larchmt)* 13:74–84, 2012
28. Kirby A, Hobson RP, Burke D, Cleveland V, Ford G, West RM. Appendectomy for suspected uncomplicated appendicitis is associated with fewer complications than conservative antibiotic management: a meta-analysis of post-intervention complications. *J Infect.* 70:105–110,2015
29. Liu K, Fogg L. Use of antibiotics alone for treatment of uncomplicated acute appendicitis: a systematic review and meta-analysis. *Surgery.*;150:673–683,2011
30. Livingston EH, Woodward WA, Sarosi GA, et al. Disconnect between incidence of nonperforated and perforated appendicitis: implications for pathophysiology and management. *Ann Surg.*,245:886–92,2007
31. Loftus TJ, Brakenridge SC, Croft CA, et al. Successful nonoperative management of uncomplicated appendicitis: predictors and outcomes. *J Surg Res.* 222:212–218,2018;
32. Mällinen J, Vaarala S, Mäkinen M, et al. Appendicolith appendicitis is clinically complicated acute appendicitis—is it histopathologically different from uncomplicated acute appendicitis. *Int J Colorectal Dis.*,34:1393–400, 2019
33. Salminen P, Tuominen R, Paajanen H, et al. Five-year follow-up of antibiotic therapy for uncomplicated acute appendicitis in the APPAC randomized clinical trial. *JAMA.*;320:125-9, 2018
34. Sartelli M, Chichom-Mefire A, Labricciosa FM, et al. The management of intra-abdominal infections from a global

- perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg.*,56,29-30. 2017
35. Podda M, Gerardi C, Cillara N, et al. Antibiotic treatment and appendectomy for uncomplicated acute appendicitis in adults and children: a systematic review and meta-analysis. *Ann Surg.*270:1028–40.,2019
 36. Nadler E, Reblock KK, Ford HR, Gaines BA. Monotherapy versus multi-drug therapy for the treatment of perforated appendicitis in children. *Surg Infect* ,4:327–333,2003.
 37. Pinto DJ, Sanderson PJ. Rational use of antibiotic therapy after appendectomy. *Br J Surg.*,280:275–277,1980
 38. Simillis C, Symeonides P, Shorthouse AJ, et al. A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis. *Surgery.*;147:818–829,2010
 39. Styrod J, Eriksson S, Nilsson I, Ahlberg G, Haapa et al. Appendectomy versus antibiotic treatment in acute appendicitis. A prospective multicentre randomized controlled trial. *World J Surg.* 30:1033–1037, 2006
 40. Sallinen V, Akl EA, You JJ, et al. Meta-analysis of antibiotics versus appendectomy for non-perforated acute appendicitis. *Br J Surg.*;103: 656–667,2016
 41. Singh JP, Mariadason JG. Role of the fecalith in modern-day appendicitis. *Ann R Coll Surg Engl.*, 95:48–51, 2013
 42. Svensson JF, Hall NJ, Eaton S, Pierro A, Wester T. A review of conservative treatment of acute appendicitis. *Eur J Pediatr Surg.*,22:185–194,2012
 43. Viniol A, Keunecke C, Biroga T, Stadjc R, Dornieden K. et al. Studies of the symptom abdominal pain—a systematic review and meta-analysis. *Fam Pract.*;31:517–529,2014
 44. Van Rossem CC, Schreinemacher M, Treskes K, Hogezaand RM, Geloven AAW. Duration of antibiotic treatment after appendectomy for acute complicated appendicitis. *Br J Surg.*101:715–719, 2014
 45. Wei W. PL, Chen CS, Keller JJ, Lin HC. Monthly variation in acute appendicitis incidence: a 10-year nationwide population-based study. *J Surg Res.*178:670–676,2012