

Original Investigation

Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial

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IMPORTANCE An increasing amount of evidence supports the use of antibiotics instead of surgery for treating patients with uncomplicated acute appendicitis.

OBJECTIVE To compare antibiotic therapy with appendectomy in the treatment of uncomplicated acute appendicitis confirmed by computed tomography (CT).

DESIGN, SETTING, AND PARTICIPANTS The Appendicitis Acuta (APPAC) multicenter, open-label, noninferiority randomized clinical trial was conducted from November 2009 until June 2012 in Finland. The trial enrolled 530 patients aged 18 to 60 years with uncomplicated acute appendicitis confirmed by a CT scan. Patients were randomly assigned to early appendectomy or antibiotic treatment with a 1-year follow-up period.

INTERVENTIONS Patients randomized to antibiotic therapy received intravenous ertapenem (1 g/d) for 3 days followed by 7 days of oral levofloxacin (500 mg once daily) and metronidazole (500 mg 3 times per day). Patients randomized to the surgical treatment group were assigned to undergo standard open appendectomy.

MAIN OUTCOMES AND MEASURES The primary end point for the surgical intervention was the successful completion of an appendectomy. The primary end point for antibiotic-treated patients was discharge from the hospital without the need for surgery and no recurrent appendicitis during a 1-year follow-up period.

RESULTS There were 273 patients in the surgical group and 257 in the antibiotic group. Of 273 patients in the surgical group, all but 1 underwent successful appendectomy, resulting in a success rate of 99.6% (95% CI, 98.0% to 100.0%). In the antibiotic group, 70 patients (27.3%; 95% CI, 22.0% to 33.2%) underwent appendectomy within 1 year of initial presentation for appendicitis. Of the 256 patients available for follow-up in the antibiotic group, 186 (72.7%; 95% CI, 66.8% to 78.0%) did not require surgery. The intention-to-treat analysis yielded a difference in treatment efficacy between groups of -27.0% (95% CI, -31.6% to -22.4%) ($P = .89$). Given the prespecified noninferiority margin of 24%, we were unable to demonstrate noninferiority of antibiotic treatment relative to surgery. Of the 70 patients randomized to antibiotic treatment who subsequently underwent appendectomy, 58 (82.9%; 95% CI, 72.0% to 90.8%) had uncomplicated appendicitis, 7 (10.0%; 95% CI, 4.1% to 19.5%) had complicated acute appendicitis, and 5 (7.1%; 95% CI, 2.4% to 15.9%) did not have appendicitis but received appendectomy for suspected recurrence. There were no intra-abdominal abscesses or other major complications associated with delayed appendectomy in patients randomized to antibiotic treatment.

CONCLUSIONS AND RELEVANCE Among patients with CT-proven, uncomplicated appendicitis, antibiotic treatment did not meet the prespecified criterion for noninferiority compared with appendectomy. Most patients randomized to antibiotic treatment for uncomplicated appendicitis did not require appendectomy during the 1-year follow-up period, and those who required appendectomy did not experience significant complications.

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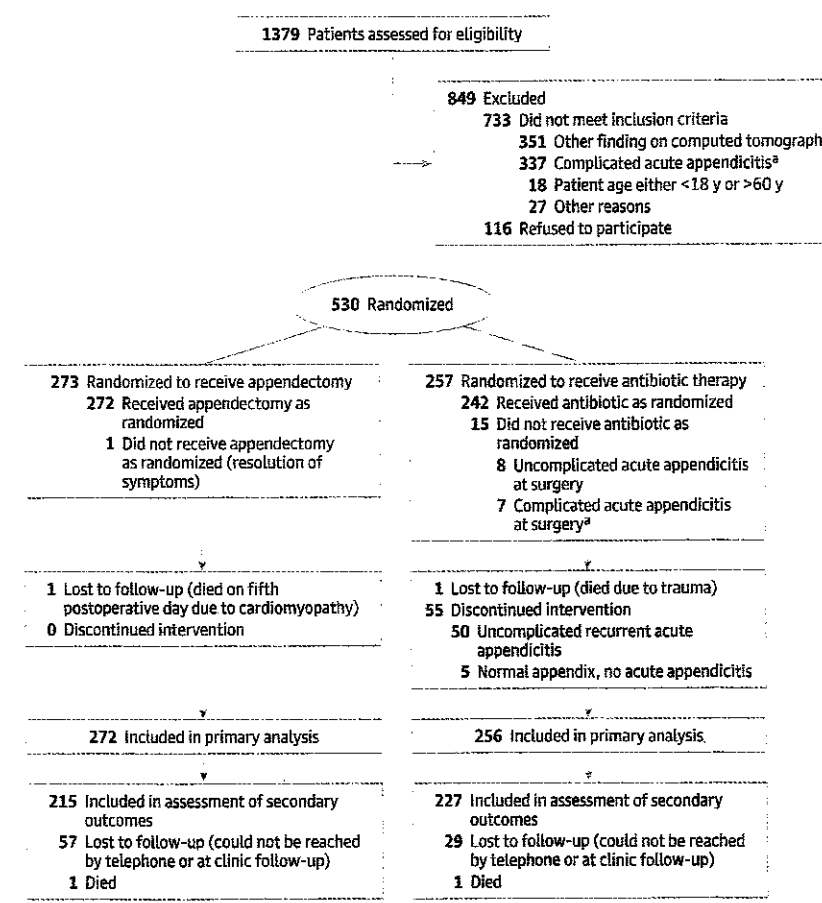
Table 1. Major Randomized Clinical Trials Comparing Antibiotic Therapy With Appendectomy in Patients With Acute Appendicitis

Source	Inclusion Criteria	Age Group, y	No. of Patients	Antibiotic Used for Nonsurgical Patients	Completeness of 1-Year Follow-up	Appendectomy in Patients Treated With Antibiotics*	Limitations
Styrud et al, ⁸ 2006	Clinical diagnosis and CRP >10 mg/L	18-50	Surgery: 124 Antibiotic: 128	IV: cefotaxime plus tinidazole Oral: ofloxacin plus tinidazole	Not stated	31/128 (24)	Female patients excluded, primary end point unclear
Hansson et al, ⁷ 2009	Clinical diagnosis	>18	Surgery: 167 Antibiotic: 202	IV: cefotaxime plus metronidazole Oral: ciprofloxacin plus metronidazole	Surgery: 47% Antibiotic: 54%	96/202 (48)	52.5% of patients in the antibiotic group crossed over to the surgery group
Vons et al, ⁹ 2011	CT imaging	>18	Surgery: 119 Antibiotic: 120	IV: amoxicillin plus clavulanic acid Oral: amoxicillin plus clavulanic acid	Surgery: 87% Antibiotic: 90%	44/120 (37)	Included patients with complicated acute appendicitis (appendicolith), suboptimal antibiotic for intra-abdominal infections

Abbreviations: CRP, C-reactive protein; CT, computed tomography; IV, intravenous.

* Data are expressed as No./total (%).

Figure. Path of Patients in the Appendicitis Acuta (APPAC) Trial



* Includes appendicolith, perforation, abscess, or suspicion of tumor.