

ANTIBIOTICS OR APPENDECTOMY FOR ACUTE NON-PERFORATED APPENDICITIS—HOW TO INTERPRET THE EVIDENCE?

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All surgeons during their residency perform appendectomy as it is the most common emergency surgery procedure worldwide. It has been taught for decades that appendicitis is a surgical emergency requiring prompt appendectomy to prevent inevitable perforation and subsequent peritonitis. However, the evidence for such dogma is weak. Over 20 years ago, a small randomized controlled trial (RCT) already suggested that uncomplicated appendicitis can be successfully treated with antibiotics, at least in selected cases, and that perforation is not an inevitable consequence of acute appendicitis (1). Although larger RCTs have later confirmed these findings (2–6), clinical practice has changed little. After the publication of the biggest RCT on this topic, the Finnish Appendectomy Versus Antibiotics in the Treatment of Acute Uncomplicated Appendicitis (APPAC) trial (5), it is time to assess the benefits and drawbacks of antibiotic therapy compared to appendectomy in patients with uncomplicated appendicitis.

A recent systematic review and meta-analysis (7) summarized data from five RCTs including 1116 patients (1, 2, 4–6). Pooled data demonstrated that only 8% of patients with acute non-perforated appendicitis initially treated with antibiotics required appendectomy within 1 month (7). However, a further 23% of patients initially treated with antibiotics had a recurrence (or suspicion) of appendicitis leading to surgery within the first year of follow-up. Both findings were based on high-quality evidence, and it is therefore unlikely that further research will substantially change these estimates. Obviously, an 8% failure rate is low, but should a 23% recurrence rate be considered high or low? In other words, 7 out of 10 patients avoid surgery, but every fourth patient suffers a recurrence of appendicitis within a year, including re-hospitalization causing substantial inconvenience and costs. Indeed, it is a preference sensitive decision how to balance this trade-off.

Although these randomized trials raise the quality of evidence regarding surgical versus medical treatment of appendicitis to a new level, many questions remain. First, these RCTs had follow-up up to 1 year only, and little is known about recurrence rates with longer follow-up. Furthermore, whether patients recruited in these trials represent the real world is also unknown. Only 16% of the eligible patients with uncomplicated appendicitis were recruited in the

APPAC trial, and 70% of them were successfully treated with antibiotics and suffered no recurrence within 1 year. If the prognosis in these 16% of patients differs from that in the 84% not recruited, the results may be very different. Regrettably, such information is not available for other trials.

Risk of complications after either treatment is of paramount interest, with some hope that conservative treatment may reduce the significant, albeit low, complication rate associated with appendectomy. Unfortunately, the quality of complication reporting is so poor as to permit only few conclusions. First, no RCT used any of the validated complication classification systems. Second, none of the RCTs reported antibiotic-related complications such as diarrhea or *Clostridium difficile* infection (7). In spite of a trend toward a lower complication rate with antibiotic therapy, one must not forget that in these trials, only 23% of appendectomies were laparoscopic. This is especially relevant as laparoscopic (compared to open) appendectomy reduces complication rates and the laparoscopic approach is the current gold standard in developed countries (8–10).

The length of hospital stay was slightly shorter (half a day) in patients treated with prompt appendectomy (7). Pragmatically speaking however, it was approximately 3 days in both groups (7). On the other hand, recent studies have reported that over 75% of patients with uncomplicated appendicitis undergoing appendectomy could be treated as outpatients (11), and in many centers, patients treated with appendectomy can be discharged earlier than in these RCTs. Yet, as more experience has accumulated, in-hospital antibiotic therapy (typically 3-day intravenous antibiotic treatment in these trials) may be shorter.

Currently, it is not possible without imaging to distinguish between complicated and uncomplicated appendicitis. Hence, all patients considered for antibiotic

therapy should undergo a computed tomography (CT) scan to rule out the possibility of complicated disease. Although the radiation exposure used in the scans has been reduced, it has recently been estimated that an abdominal CT scan will cause a potentially fatal cancer in 18–37/100,000 patients (12). While CT scan is increasingly used to diagnose appendicitis and to reduce the number of negative appendectomies (to 3% in some series (13)), it is not mandatory to confirm the diagnosis of appendicitis with CT scan in all patients prior to commencing surgical treatment. Indeed, extensive use of CT scan causes more harm than good: Routine CT confirmation of appendicitis has been estimated to avoid 12 negative appendectomies at a cost of one cancer death caused by the imaging (14)—a trade-off few would be willing to accept. Several clinical scoring systems have been developed to improve the diagnostics of appendicitis and to reduce the need for imaging (15–17). However, current scoring systems have not been developed to distinguish between uncomplicated and complicated appendicitis, and thus cannot be used in selecting patients for antibiotic therapy.

Given the current evidence, although most patients with appendicitis are still probably best treated with prompt appendectomy, the choice between antibiotic therapy and appendectomy in patients with clearly uncomplicated appendicitis is a value and preference decision. Some informed patients would choose immediate appendectomy and others antibiotic therapy. Only time will tell how many prefer antibiotics over immediate surgery. Future trials will provide valuable information regarding complications and recurrence rates beyond 1-year follow-up to back up this decision.

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