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Acute Appendicitis

Evidence Based Medicine Guideline

Primary Author: Gabriel Diaz-Pagan, MD
Co-Authors: Sofia Barba, DO
Editors: Michael L. Cheatham MD, Chadwick Smith MD
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SUMMARY
Acute appendicitis is one of the most common acute surgical conditions worldwide. Appendectomy has historically been the gold standard for management, however, there is emerging data that support initial nonoperative management in both complicated and uncomplicated disease. This is a summary of the most up-to-date literature on the management of acute appendicitis workup and management in adults.

RECOMMENDATIONS

- **Level 1**
  - **CT abdomen/pelvis with IV-contrast is the first-line imaging modality for nonpregnant adults with suspected appendicitis.**
  - **For perforated appendicitis with generalized peritonitis or hemodynamic instability, surgery is recommended.**
- **Level 2**
  - **Nonoperative management with antibiotics can be offered to carefully selected patients with uncomplicated appendicitis.**
  - **The presence of an appendicolith should prompt surgical intervention due to the high rate of failure of non-operative management.**
  - **Laparoscopic appendectomy is recommended over open surgery when feasible due to fewer wound complications, shorter time to resume oral intake, and shorter hospital length of stay.**
  - **Postoperative antibiotics after non-perforated appendectomy are not required as they do not improve outcomes.**
  - **For peri-appendiceal abscess or phlegmon, IV antibiotics with either image-guided percutaneous drainage vs. surgery are recommended.**
  - **With adequate source control, 3-5 days of postoperative antibiotics in cases of complicated appendicitis are sufficient.**
  - **Given the increased risk of neoplasm, interval appendectomy should be considered in patients with recurrent symptoms and those over 40 years of age with appendicitis with phlegmon or abscess.**
  - **When surgery is indicated, operate within 24 hours of diagnosis to reduce complications.**
  - **Avoid routine intraperitoneal drains after appendectomy as they do not reduce abscess rates and may prolong hospitalization.**
- **Level 3**
  - **None**

INTRODUCTION

The overall incidence of acute appendicitis is approximately 6-86 per 100,000 patients per year and can be classified as complicated vs. uncomplicated. Complicated appendicitis is defined as having perforation as evidenced by a phlegmon, abscess or gross pneumoperitoneum with generalized peritonitis. Uncomplicated

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Supported by multiple, prospective randomized clinical trials or strong prospective, non-randomized evidence if randomized testing is inappropriate.
- **Level 2:** Supported by prospective data or a preponderance of strong retrospective evidence.
- **Level 3:** Supported by retrospective data or expert opinion.

appendicitis is defined as occurring without any of these features although additional factors may make uncomplicated disease higher risk for future perforation, recurrence or nonresolution without surgery. The highest incidence of uncomplicated appendicitis occurs among adolescents and young adults aged 13 to 40 years old. The incidence of perforated disease is 16-40% with a bimodal distribution involving children and adults over 50 years of age (1-3).

The two essential decisions in modern acute appendicitis treatment involve determining if 1) the condition is complicated or uncomplicated, and 2) deciding between initial surgical intervention vs. antibiotic treatment. Though surgery was historically the mainstay of treatment, nonoperative management is being increasingly accepted for the management of uncomplicated appendiceal disease. Duration of antibiotic treatment remains another area of debate both in the setting of nonoperative management as well as postoperatively in surgically managed disease. Additionally, there exists the challenge of who to select for interval appendectomy after initial conservative management (1-3).

LITERATURE REVIEW

Clinical Assessment and Risk Scores

The initial assessment for suspected appendicitis begins with bedside evaluation including history and physical examination, temperature measurement, and lab work with inflammatory markers. Risk-based pathways now combine these assessments with validated scores to determine imaging and treatment decisions. The Appendicitis Inflammatory Response (AIR) score demonstrates superior performance to the Alvarado score for adult patients because it includes C-reactive protein measurements and neutrophil grading along with clinical indicators (4). Andersson et al. prospectively evaluated 545 patients showing that AIR outperformed Alvarado in detecting advanced appendicitis ($p < 0.01$). The AIR algorithm used pre-defined thresholds to classify 63% of patients into low-risk or high-risk categories while achieving 97% accuracy in identifying acute appendicitis. The study provided a three-level system for adult patient assessment which classified patients into low-risk (<5), intermediate-risk (5-8) and high-risk (>8) categories (4). The 2021 multicenter validation study by Andersson et al. included 3,878 emergency patients to confirm AIR performance. This demonstrated a 99% negative predictive value for scores below 4 and 96% positive predictive value for scores above 8 in younger patients and 89% in male patients (5). They concluded that AIR should be used to direct patient management, but should not replace imaging because of overlapping symptoms with gynecologic and other gastrointestinal conditions.

Imaging Studies

The 2020 World Society of Emergency Surgery (WSES) Jerusalem guidelines establish specific imaging indicators which help determine disease severity (3). The first diagnostic test for nonpregnant adults should be IV–enhanced CT abdomen/pelvis because it provides both high sensitivity and specificity and enables the identification of critical features that guide treatment decisions (e.g., appendicolith, wall defect, extraluminal air, abscess/phlegmon) (6). According to the large, prospective, multicenter observational MUSTANG trial, CT was the primary diagnostic imaging modality for acute appendicitis in the United States with 90% of 3,597 patients undergoing CT imaging (7). Ultrasound is operator-dependent and provides best results when radiation exposure needs to be limited (such as for young patients or pregnant women). If an abdominal ultrasound examination is non-diagnostic in the pediatric or pregnant population, then performing a CT abdomen/pelvis would be the next step (3). MRI is a good alternative when both ionizing radiation and iodinated contrast are undesirable.

Stratifying uncomplicated vs complicated disease on CT

The decision between non-operative management (NOM) and surgery depends on whether the disease is uncomplicated or complicated. Uncomplicated appendicitis, based on imaging criteria, would be suggested by an appendiceal diameter > 6 mm, wall thickness > 2 mm, periappendiceal inflammation, and possibly a fecalith, without evidence of perforation, abscess, or phlegmon (6). Kim et. al. retrospectively examined multiple indicators including mucosal/wall enhancement defect, extraluminal (free) air, peri-appendiceal fluid collection, organized abscess/phlegmon, fascial thickening/ileus, and large or extraluminal appendicolith all of which indicate the presence of complicated disease (8). CT provides value for treatment planning in complex disease by showing abscesses that can be drained under image guidance, diffuse peritonitis that needs immediate laparoscopic surgery, and appendicolith size that indicates higher risk of complications (3).

Management of uncomplicated appendicitis (operative vs non-operative)

The selection of operative management for CT-confirmed uncomplicated appendicitis should lead to laparoscopic rather than open appendectomy because it provides reliable short-term benefits without raising septic complications. Athanasiou et al. conducted a systematic review and meta-analysis of adult appendicitis by combining 3 randomized trials with 154 laparoscopic appendectomy patients vs. 155 open appendectomy patients and 23 case-control studies with 2,034 laparoscopic appendectomy patients vs. 2,096 open appendectomy patients (9). The authors found that laparoscopic appendectomy produced better surgical-site infection outcomes (odds ratio [OR] 0.30, 95% CI 0.22–0.40; $p < 0.00001$), shorter time to oral intake (95% CI −1.09 to −0.86; $p < 0.00001$), and reduced hospital stay duration (95% CI −3.70 to −3.29; $p < 0.00001$) compared to open appendectomy without raising intra-abdominal abscess rates (OR 1.11, 95% CI 0.85–1.45; p=0.43). The overall operative time was slightly longer for laparoscopic compared to open appendectomy (95% CI 5.14–15.87; p=0.0001), but the randomized controlled trial subgroup did not show a significant difference and regression analysis indicated that hospital stays have become progressively shorter in more recent studies (p=0.007). The data supports the use of laparoscopy as the standard operative approach for adults with uncomplicated appendicitis since it offers comprehensive intraperitoneal inspection and the capability to treat alternative pathologies.

Non-operative management (NOM) with antibiotics is now a validated option for CT-confirmed uncomplicated appendicitis in carefully selected adults provided there is reliable follow-up and shared decision-making. In the randomized APPAC trial, 73% of patients treated initially with antibiotics avoided appendectomy at 1 year (10). At 5 years, the cumulative appendectomy rate after initial NOM was 39% with no increase in major complications among those who ultimately required surgery compared with immediate appendectomy. The CODA trial extended these findings to a broad U.S. population and found that antibiotics were noninferior to immediate appendectomy for 30-day health status, but 29% of patients assigned to antibiotics underwent appendectomy within 90 days (11). Notably, appendicolith status modified the recurrence risk where the 90-day appendectomy rate was 41% in those with an appendicolith vs. 25% in those without and serious complications were higher with antibiotics-only in those with an appendicolith. This data supports offering antibiotics-first to patients without an appendicolith, framing expectations about early failure, recurrence over several years, and the likelihood of additional visits or imaging.

In an additional study by Talan et al., NOM is a reasonable alternative to appendectomy for CT-confirmed uncomplicated appendicitis without an appendicolith if reliable follow-up is available (2). A 7-10 day antibiotic regimen (IV then oral) avoids immediate surgery for most patients, yields noninferior 30-day quality of life vs. surgery, but carries an approximate 25–40% chance of appendectomy within 1–5 years. Because an appendicolith increases early failure and complications, they stress shared decision-making, careful patient selection, narrow-spectrum antibiotics, and clear safety-netting with rapid surgical access if symptoms worsen (2). Prospective data from the MUSTANG study clarify who is likely to fail NOM early. Among thousands of adults initially treated with antibiotics, 21% required appendectomy within 30 days and predictors of failure or complicated disease included older age, longer symptom duration (>48 hours), higher inflammatory markers (e.g., WBC) and especially the presence of an appendicolith (7). Hemodynamic instability, generalized peritonitis, pregnancy, history of inflammatory bowel disease and immunodeficiency were also key factors in determining inadequate candidacy for NOM (1-3).

Management of complicated appendicitis

Patients with perforated appendicitis and diffuse peritonitis require immediate surgery to establish source control followed by brief antibiotic treatment. The SIS 2017 guidelines and IDSA 2024 update recommend using the most restricted antibiotic spectrum possible while keeping treatment durations as short as possible after patients show signs of improvement (12-13). The STOP-IT randomized trial by Sawyer et al. included 518 patients with complicated intra-abdominal infection who received either a fixed 4 ± 1-day antibiotic treatment or a symptom-guided approach until their fever, leukocytosis and/or ileus resolved for at least two days (14). The study showed no difference in the primary outcome of surgical-site infection and recurrent intra-abdominal infection and 30-day mortality between the short-course and control groups (21.8% vs 22.3%; absolute difference −0.5%). These findings show that extended treatment duration does not provide better results after source control achievement. The data support the implementation of antimicrobial stewardship in postoperative care by using a 4-day fixed treatment duration with extra days only for patients who develop sepsis or show signs of treatment failure. The WSES guidelines conclude that antibiotic duration of 3-5 days is usually sufficient and recommend against extending antibiotics beyond this time (3).

The treatment of adults with peri-appendiceal abscesses or phlegmons includes two established methods. First, NOM using IV antibiotics, image-guided percutaneous drainage for defined collections, and surgical intervention for

treatment failures or recurrences. Second, immediate appendectomy when surgeons can perform the procedure safely. A meta-analysis by Gavriilidis et al. compared appendectomy with conservative treatment (15). The analysis demonstrated that patients who received conservative treatment experienced lower rates of complications, abdominal/pelvic abscesses, wound infections and unplanned surgical procedures. On the other hand, a subgroup analysis of three RCTs in this study showed no substantial difference between treatment approaches regarding abdominal/pelvic abscess development (OR 0.46, 95% CI 0.17–1.29; p=0.14) and both groups had similar hospital stay durations (16). The results from these high-quality RCTs showed that patients who had laparoscopic appendectomy spent one day less in the hospital than patients who received conservative treatment (95% CI −1.31 to −0.67; p<0.0001).

In summary, the evidence supports a flexible treatment method that begins with IV antibiotics and image-guided drainage for defined abscesses but moves to early surgery in experienced centers to achieve quick source control and minimize hospital duration. Ultimately, the selection of treatment depends on individual patient characteristics.

Antibiotic regimens

Aerobic and anaerobic coverage is recommended for the treatment of acute intra-abdominal infections. Most trials support initial IV antibiotics for 1-3 days followed by oral antibiotics to complete a course of 7-10 days for intra-abdominal infections treated nonoperatively. Regimen options include piperacillin-tazobactam or carbapenems as single agents, or a combination regimen with metronidazole and a second or third-generation cephalosporin. Oral regimens include amoxicillin-clavulanate or combination therapy with metronidazole and either fluoroquinolone or advanced generation cephalosporin (2).

A single dose of broad-spectrum antibiotics is recommended preoperatively and within 60 minutes of incision. It is not recommended to continue antibiotics postoperatively in uncomplicated cases of appendicitis (3).

Interval appendectomy and neoplasm surveillance

The need for routine interval appendectomy after successful non-operative management (NOM) does not apply to every adult because most patients stay free from recurrence and studies show recurrence rates following NOM range between 12-24% across different patient groups. The primary reason for performing interval surgery on older adults is their higher risk of hidden appendiceal tumors when their appendicitis presents with abscesses or phlegmons. The multicenter Peri-Appendicitis Acuta clinical trial by Mällinen et al. randomized adults (18-60 years) with periappendiceal abscess successfully treated nonoperatively to either interval appendectomy (typically performed 6-8 weeks after initial presentation) or imaging-based surveillance with MRI and colonoscopy (17). The primary endpoint was treatment success defined as absence of postoperative morbidity (appendectomy group) or recurrence (surveillance group). The trial terminated early due to a high rate of neoplasms (20% overall, all in patients >40 years) detected at interval appendectomy raising ethical concerns. The findings suggest that interval appendectomy should be strongly considered in adults over 40 years with periappendiceal abscess given the substantial risk of underlying neoplasm. This approach aligns with the World Society of Emergency Surgery (WSES) Jerusalem Guidelines, which recommend reserving interval appendectomy for patients with recurrent symptoms or those at increased risk for neoplasm (e.g., age >40), rather than routine interval appendectomy for all patients after successful nonoperative management of complicated appendicitis (3).

Timing of appendectomy

The best evidence indicates that surgical intervention for stable adults with presumed uncomplicated appendicitis should take place within 24 hours after diagnosis but ultra-early procedures before 8-12 hours only benefit patients with sepsis. van Dijk et al. performed a meta-analysis of 45 studies with 152,314 participants demonstrating that hospital delays between 7-12 hours (adjusted OR for complicated appendicitis 1.07, 95% CI 0.98-1.17) and 13-24 hours (OR 1.09, 95% CI 0.95-1.24) did not raise the risk of complicated appendicitis (18). The analysis showed no rise in postoperative surgical-site infections or overall morbidity when delays took place between 24-48 hours (18). The authors determined that patients without preoperative signs of complicated disease can safely wait up to 24 hours for appendectomy because it allows for better staff availability and creates more time for potential diagnostic tests/imaging.

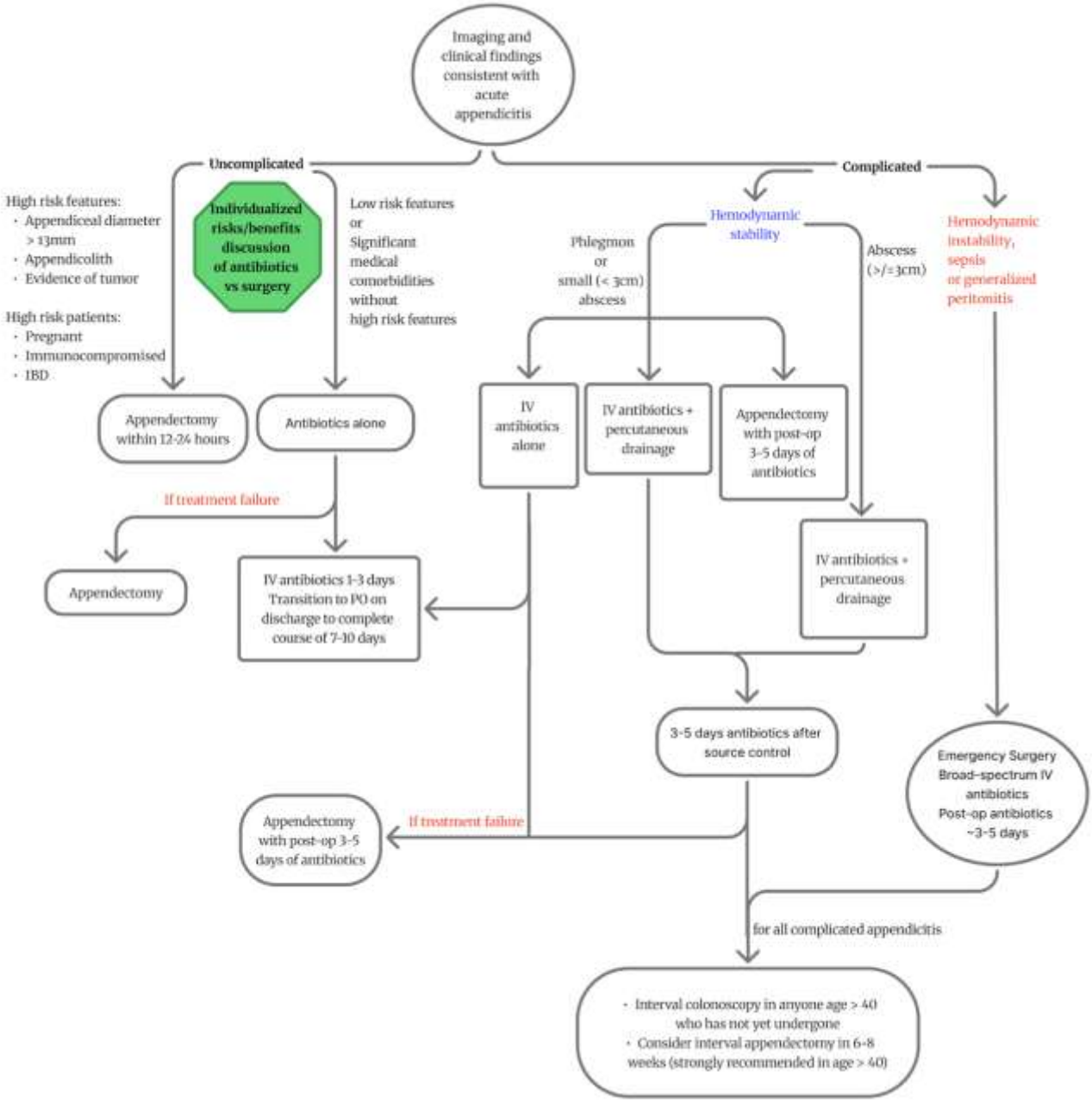
A 2024 systematic review and meta-analysis by Calpin et al. analyzed 16 studies involving 232,678 patients to show that patients who received surgery within 24 hours spent less time in the hospital compared to those who waited between 24 to 48 hours or more than 48 hours (19). They noted that hospital time under 24 hours produced superior results than both 24-48 hours and more than 48 hours, yet time-of-day variations between day, evening and night shifts did not affect the findings. Perforation rates stayed the same across all hospital-time intervals. Out of the

studies comparing outcomes based on total time (symptom onset to surgery), results demonstrated that patients who received surgery within 24 hours after symptom appearance needed 2.1 days of hospital care, whereas patients who received surgery between 24-48 hours needed 3.4 days, and patients who received surgery after 48 hours needed 5.4 days.

Intraperitoneal drains

Most adults should not receive routine intraperitoneal drainage following appendectomy because this procedure fails to stop intra-abdominal abscess formation and does not enhance recovery while potentially leading to negative short-term results. Liao et al. analyzed 1,241 patients who received laparoscopic appendectomy care at two medical facilities through a two-center retrospective cohort study (20). The 421 patients with complicated appendicitis (AAST ≥ II) received drain placement which resulted in higher overall complication rates (OR 2.44, 95% CI 1.60–3.73; $p < 0.0001$) without any decrease in postoperative intra-abdominal abscess formation (OR 1.66, 95% CI 0.49–5.62; $p=0.42$) when compared to no drain. The study results showed that drain placement resulted in longer recovery times which led to patients requiring 45.9 additional hours to begin eating soft foods (95% CI 34.5–57.3) and their hospital stay lengthened by 21 hours (95% CI 15.3–26.1); $p<0.0001$). The authors recommend against standard drain placement, but endorse its application when surgeons encounter uncontrolled contamination during surgery. The study results match previous research which shows that prophylactic drainage after complicated appendectomy does not provide clinical benefits but creates uncertainty about abscess and wound infection rates (21). In addition, drains have been shown to prolong hospital stay. In contrast, incorporating enhanced recovery elements such as early ambulation, multimodal (opioid-sparing) analgesia, and early feeding, have been associated with shorter length of stay and earlier postoperative dietary advancement without increases in readmission or surgical-site infection (22).

Treatment Algorithm



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