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SAGES guideline for the diagnosis and treatment of appendicitis

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Abstract

Background Appendicitis is an extremely common disease with a variety of medical and surgical treatment approaches. A multidisciplinary expert panel was convened to develop evidence-based recommendations to support clinicians and patients in decisions regarding the diagnosis and treatment of appendicitis.

Methods A systematic review was conducted from 2010 to 2022 to answer 8 key questions relating to the diagnosis of appendicitis, operative or nonoperative management, and specific technical and post-operative issues for appendectomy. The results of this systematic review were then presented to a panel of adult and pediatric surgeons. Evidence-based recommendations were formulated using the GRADE methodology by subject experts.

Results Conditional recommendations were made in favor of uncomplicated and complicated appendicitis being managed operatively, either delayed (>12h) or immediate operation (<12h), either suction and lavage or suction alone, no routine drain placement, treatment with short-term antibiotics postoperatively for complicated appendicitis, and complicated appendicitis previously treated nonoperatively undergoing interval appendectomy. A conditional recommendation signals that the benefits of adhering to a recommendation probably outweigh the harms although it does also indicate uncertainty.

Conclusions These recommendations should provide guidance with regard to current controversies in appendicitis. The panel also highlighted future research opportunities where the evidence base can be strengthened.

Keywords Appendicitis · Complicated · Appendectomy · Pediatrics · Antibiotics · Guideline · Nonoperative

Abbreviations

CT	Computed tomography scan
EtD	Evidence to decision
GRADE	The Grading of Recommendations Assessment, Development, and Evaluation
h	Hours
IBD	Inflammatory bowel disease

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ICTRP	International Clinical Trials Platform
ICU	Intensive care
IR	Interventional radiology
KQ	Key question
LOS	Length of stay
OR	Operating room
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
QOL	Quality of life
RIGHT	Essential Reporting Items for Practice Guidelines in Healthcare
SAGES	The Society of American Gastrointestinal and Endoscopic Surgeons

Executive summary

Background

Appendicitis is extremely common and is currently the most frequently encountered acute surgical pathology in both adults and children. A multidisciplinary expert panel of surgeons developed recommendations based on the available evidence to assist clinicians, patients, and others in making diagnostic and therapeutic decisions for appendicitis.

Methods

Systematic literature reviews were conducted for 8 key questions regarding appendicitis. PubMed, Cumulated Index to Nursing and Allied Health Literature, Embase, Cochrane Library, and Clinicaltrials.gov were searched to identify randomized control trials and non-randomized comparative studies. Evidence-based recommendations were formulated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology by subject matter experts. GRADE is a transparent framework used in the development of clinical practice guidelines, using the highest-level evidence available. Expert opinion was utilized in cases of insufficient data for an evidence-based recommendation.

Recommendations for future research were also proposed.

Interpretation of strong and conditional recommendations

All guideline recommendations were assigned either a "strong" or "conditional" recommendation. The words "the guideline panel recommends" are used for strong recommendations, and "the guideline panel suggests" for conditional recommendations, as per the GRADE approach. A conditional recommendation signals that the benefits of adhering to a recommendation probably outweigh the harms although it does also indicate uncertainty. This uncertainty may be due to a lack of high-quality evidence or variability in how individual patients value the outcomes of interest.

How to use these guidelines

The primary aim of these guidelines is to make recommendations for the diagnosis and management of appendicitis to aid physicians facing clinical dilemmas. They are also intended to provide education for patients, inform advocacy, and describe future areas for research. The guidelines are meant to provide a suggested, not prescribed, approach for the management of appendicitis, especially given the lack of strong evidence. The wide spectrum of severity and symptoms with which appendicitis presents means specific clinical situations may require adjustment of treatment plans to suit the needs and priorities of the individual patient. Finally, because the guidelines take a patient-centered approach, patients can use these guidelines as a source of information and basis for discussion with their physicians.

Key questions addressed by these guidelines

1. Should abdominal CT versus alternative imaging be used for diagnosing acute appendicitis?
2. Should adult and pediatric patients with acute, uncomplicated appendicitis be managed nonoperatively versus operatively?
3. Should adult and pediatric patients with complicated appendicitis be managed operatively or nonoperatively?
4. Should adult and pediatric patients with acute, uncomplicated appendicitis undergo delayed (> 12 h) or immediate operation (< 12 h)?
5. In patients undergoing appendectomy for perforated appendicitis, should suction and lavage versus suction alone be used?
6. In patients undergoing appendectomy for complicated appendicitis, should routine drain placement versus no routine drain placement be used? (society perspective)
7. Should patients who undergo appendectomy for complicated appendicitis be given postoperative antibiotics for short-term vs. long-term (as defined by authors)?
8. In asymptomatic patients with previous complicated appendicitis treated nonoperatively, should an interval appendectomy be performed versus observation?

Recommendations

1. Should abdominal CT versus alternative imaging be used for diagnosing acute appendicitis?

1. Ultrasound is a reasonable first line study given its low cost and lack of radiation. However, CT and MRI are the most definitive imaging modalities (*Expert opinion; GRADE not utilized*)

2. Should adult and pediatric patients with acute, uncomplicated appendicitis be managed nonoperatively versus operatively?

2. The panel suggests that adult and pediatric patients with uncomplicated appendicitis be managed operatively (*Conditional recommendation, low certainty of evidence in adults and very low certainty of evidence in pediatrics*)

3. Should adult and pediatric patients with complicated appendicitis be managed operatively or nonoperatively?

3. The panel suggests that adult and pediatric patients with complicated appendicitis be managed operatively (Conditional recommendation, very low certainty of evidence in adults and low certainty of evidence in pediatrics)

4. Should adult and pediatric patients with acute, uncomplicated appendicitis undergo delayed (> 12 h) or immediate operation (< 12 h)?

4. The panel suggests that adult and pediatric patients with uncomplicated appendicitis may undergo either delayed (> 12 h) or immediate operation (< 12 h). (*Conditional recommendation, very low certainty of evidence*)

5. In patients undergoing appendectomy for perforated appendicitis, should suction and lavage versus suction alone be used?

5. The panels suggests that adult and pediatric patients with complicated appendicitis should undergo either suction and lavage or suction alone based on surgeon preference. (*Conditional recommendation, very low certainty of evidence in adults and low certainty of evidence in pediatrics*)

6. In patients undergoing appendectomy for complicated appendicitis, should routine drain placement versus no routine drain placement be used? (society perspective)

6. The panel suggests no routine drain placement for both adult and pediatric patients undergoing appendectomy for complicated appendicitis (*Conditional recommendation, very low certainty of evidence*)

7. Should patients who undergo appendectomy for complicated appendicitis be given postoperative antibiotics for short-term vs. long-term (as defined by authors)?

7. The panel suggests that adult and pediatric patients who have undergone appendectomy for complicated appendicitis should be treated with short-term antibiotics postoperatively. (*Conditional recommendation, very low certainty of evidence*)

8. In asymptomatic patients with previous complicated appendicitis treated nonoperatively, should an interval appendectomy be performed versus observation?

8. The panel suggests adult patients with complicated appendicitis previously treated nonoperatively should have an interval appendectomy (*Conditional recommendation, low certainty of evidence in adults and expert opinion in pediatrics*)

Introduction

Aim of these guidelines and specific objectives

The purpose of these guidelines is to provide evidence-based recommendations from a surgeon and patient perspective pertaining to appendicitis. This review evaluated outcomes of abdominal computed tomography (CT) scan versus alternative imaging for diagnosis of acute appendicitis, operative versus nonoperative treatment of uncomplicated and complicated acute appendicitis, interval appendectomy versus observation for complicated acute appendicitis, late or early appendectomy in uncomplicated appendicitis, short- or long-term antibiotic treatment after appendectomy for complicated appendicitis, and intraoperative decisions during appendectomy for complicated appendicitis: suction and lavage versus suction alone and routine drain placement versus no drain placement. The key target audience includes adult and pediatric surgeons, patients, hospitalists, emergency medicine physicians, primary care physicians, and pediatricians in a clinical setting. Given that a patient-surgeon perspective was taken, not a population perspective, considerations such as cost effectiveness from a systems-standpoint were not evaluated.

The recommendations included in this guideline are based on a systematic review of the published literature [1]. The strengths and weaknesses of the available evidence are highlighted.

Description of the health problem

Appendicitis is one of the most common indications for surgery in both adult and pediatric patients, with a lifetime incidence of 6.7–8.6% [2]. It imposes a significant burden on patients, families, and healthcare systems with high hospital costs, rates of emergency department and outpatient clinic revisits, prolonged antibiotic treatment courses, and incidence of postoperative complications [3–5]. Diagnosis is typically determined by clinical assessment,

including history and physical exam, as well as imaging. The ideal imaging modality for accurate diagnosis, distinguishing between acute and complicated appendicitis, and optimal resource utilization has not yet been determined [6].

While appendectomy has traditionally been the mainstay of treatment for appendicitis, the past decade has witnessed increased popularity of non-operative management in both acute and complicated appendicitis [7, 8]. With the increased utilization of nonoperative initial management, the necessity of interval appendectomy has also been debated [9, 10]. Additionally, operative technique and post-operative antibiotic duration for complicated appendicitis are areas of active research.

Methods

A systematic review of the evidence informed the guideline recommendations. The guideline panel determined the certainty of evidence, and the direction and strength of recommendations, with the widely used *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) approach [11, 12] using the GRADEpro guideline development tool [13]. Reporting of the guideline adheres to the *Essential Reporting Items for Practice Guidelines in Healthcare* (RIGHT) checklist [14]. Evidence addressing the guideline questions was synthesized according to the SAGES Guidelines Committee's standard operating procedure [15]. Due to the diagnostic nature of key question 1, GRADE methodology was not employed; instead, the data were reviewed by the panel and used to formulate a consensus statement.

PubMed, Embase, Cochrane, Clinicaltrials.gov, and International Clinical Trials Platform (ICTRP) were searched (2010–2022) to identify randomized control trials and non-randomized comparative studies (Online Appendix A).

Two independent reviewers screened retrieved records for eligibility. Screening criteria and "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" screening flow diagrams for each KQ are provided in Online Appendix B. Studies were included if they were published in the English language and included more than 50 patients for case series. Exclusion criteria included pregnant patients, studies where the majority of appendectomies were performed open, and case reports.

Study quality was assessed using the Cochrane Risk of Bias 2.0 and Newcastle Ottawa Scale for randomized and non-randomized studies, respectively. Random effects meta-analysis was performed on available comparative data.

Guideline panel organization

The panel consisted of seven practicing adult and pediatric surgeons from the SAGES membership. A methodologist with guideline development expertise (M.T.A.) and the SAGES Guidelines Committee Fellow (S.S.K.) facilitated guideline panel meetings as non-voting members of the panel.

Guideline funding and declaration and management of competing interests

Funding for the methodologists, the librarian, and partial salary support for the fellow were provided by SAGES. Part of this funding came from a SAGES Education & Research Foundation grant. All disclosed potential conflicts of interest were reviewed by the senior author and are listed at the end of the manuscript and in Appendix C.

Selection of questions and outcomes of interest

The preoperative imaging and treatment of appendicitis are the focus of this guideline. The final set of outcomes for each KQ were chosen by simple majority. Outcomes were designated "critical" or "important" to decision-making for each KQ. Given their long-standing experience with patients, panel members used their own judgment as a proxy for what patient-surgeon dyads would consider important or critical for decision-making. The importance of these outcomes was re-visited by panel members during the formulation of recommendations after reviewing the systematic review evidence.

Determining the certainty of evidence

Methods outlined in the GRADE handbook were used to judge the certainty of evidence for each outcome of interest [16]. GRADEPro evidence tables were created. The highest-level of data available was used for the tables; less rigorous data that addressed the same outcomes was reviewed but not used in decision-making. In brief, the guidelines systematic review working group judged the certainty of the body of evidence across the domains of risk of bias, inconsistency, indirectness, and imprecision. If there was concern in any one of these domains, the certainty was downgraded. This data were then imported into the Evidence to Decision (EtD) table for each KQ. The EtD tables serve as a framework through which the final recommendations are developed.

Assumed values and preference

As this guideline took a patient-centered rather than a societal perspective, the panel members used their collective

patient experience to make judgements about patient values and preferences. The panel members recognize that patients may vary in the value placed on an outcome. The absence of a patient representative on the panel does limit the certainty of its recommendations. The target audience of this guideline includes patients, surgeons, emergency medicine physicians, primary care physicians, and pediatricians.

Development of recommendations

Critical and important to decision-making outcomes were imported into GRADEPro Evidence to Decision tables (EtD) as desirable or undesirable effects for the intervention. The panel then discussed the magnitude of desirable and undesirable effects, listed as absolute effect size unless stated otherwise, the certainty of evidence, any variation in values that patients may assign to outcomes, and the balance of these effects. Absolute percent differences were calculated by the GRADEPro software based on imported systematic review data. After determining whether the intervention, comparator, or both/neither was favored by the balance of these considerations, the panel discussed the acceptability and feasibility of this judgment. For each decision, the available evidence was discussed as well as any additional considerations based on panel members' experience or interpretation of the evidence. Based on the balance of effects and the acceptability and feasibility of a favored option, the panel voted on the final recommendation for that KQ. A consensus of 80% panel agreement was mandatory for all final recommendations. Voting was done anonymously. Subgroups, such as pediatric patients, were addressed in discussion for the justification for each recommendation and are specified for each key question below. Making a "strong" recommendation required a high certainty of evidence. Full evidence to decision tables are presented in Appendix D and summarized in the following recommendations.

Guideline document review

This guideline was reviewed and edited by all panel members. In accordance with SAGES Guidelines Committee policies, the revised draft was distributed to the committee for comments. After incorporating these edits, the final guideline was then submitted to the SAGES Executive Board for approval and published online on its website (www.sages.org) for public comment.

Key questions

KQ1: Should abdominal CT versus alternative imaging be used for diagnosing acute appendicitis?
KQ2: Should adult and pediatric patients with acute, uncomplicated appendicitis be managed nonoperatively or operatively?
KQ3: Should adult and pediatric patients with complicated appendicitis be managed operatively or nonoperatively?
KQ4: Should adult and pediatric patients with acute, uncomplicated appendicitis undergo delayed (> 12 h) or immediate operation (< 12 h)?
KQ5: In adult and pediatric patients undergoing appendectomy for perforated appendicitis, should suction and lavage versus suction alone be used?
KQ6: In adult and pediatric patients undergoing appendectomy for complicated appendicitis, should routine drain placement versus no routine drain placement be used? (society perspective)
KQ7: Should patients who undergo appendectomy for complicated appendicitis be given postoperative antibiotics for short-term vs. long-term (as defined by authors)?
KQ8: In asymptomatic patients with previous complicated appendicitis treated nonoperatively, should an interval appendectomy be performed versus observation?

Recommendations

KQ1 Should abdominal CT versus alternative imaging be used for diagnosing acute appendicitis?

Ultrasound is a reasonable first line study given its low cost and lack of radiation. However, CT and MRI are the most definitive imaging modalities (*Expert opinion; GRADE not utilized*).

Introduction

Although history, physical exam, and laboratory values are used to diagnose appendicitis, imaging plays an important role in the work up as well. Ultrasound, computed tomography (CT) scan, and magnetic resonance imaging (MRI) are the most frequently utilized imaging modalities [17, 18]. They serve as adjuncts to clinical diagnosis to minimize the potential for misdiagnosis resulting in either disease progression or negative appendectomy. However, there are disadvantages to unnecessary or noncontributory imaging including radiation exposure, cost, and delay to treatment. In addition, all imaging modalities have limitations in distinguishing between complicated and uncomplicated appendicitis.

Table 1 Diagnostic imaging for appendicitis in the adult population

	Sensitivity (%)	Specificity (%)	# of patients	Nondiagnostic study (%)	Additional imaging (%)	Negative appendectomy (%)
Ultrasound	68.8	67.0	19,974	38.7	32.3	8.7
CT	96.9	92.4	20,615	1.9	0.7	5.2
MRI	95.7	92.4	2113	9.7	0.0	7.3

Table 2 Diagnostic imaging for appendicitis in pediatric population

	Sensitivity (%)	Specificity (%)	# of patients	Nondiagnostic study (%)	Additional imaging (%)	Negative appendectomy (%)
Ultrasound	90.3	92.0	18,592	35.7	17.3	9.6
CT	93.0	94.2	2326	5.5	0.3	6.7
MRI	96.9	96.5	3007	13.9	0.7	8.4

Summary of the evidence

The literature search revealed 174 unique publications addressing imaging for appendicitis, the results of which are summarized in Tables 1 and 2 [1].

Decision criteria and additional considerations

There are a number of factors in addition to the sensitivity and specificity of the tests that need to be considered when deciding which modality to use for the diagnosis of appendicitis. The increased radiation exposure with CT scans is less of a consideration in adults but is particularly important for the pediatric population. In addition, facilities may not have expedient access to MRI, potentially limiting the practicality of this imaging modality. Furthermore, a pediatric MRI may require anesthesia for an adequate study, creating another barrier to its use. While ultrasound does not increase radiation exposure and is accessible in most hospitals, it is an operator-dependent study. This may reduce its accuracy, leading to bias against it, further imaging, and delayed care. It is often difficult to identify complicated appendicitis with ultrasound alone. Ultrasound is also associated with a high rate of non-visualization of the appendix, particularly in patients with obesity, limiting its utility. There is evidence that the reliability of ultrasound can be improved by a standardized reporting structure [18]. Finally, the clinical picture, physical exam, and clinical score all aid in determining the pre-test probability of appendicitis and which imaging modality is most appropriate for a particular patient.

Research recommendations

Research recommendations include additional studies comparing the different imaging modalities with standardized outcomes and endpoints, including their potential for negative impact on care, such as radiation exposure, delay in diagnosis, or need for anesthesia to obtain the test.

KQ2 Should adult and pediatric patients with acute, uncomplicated appendicitis be managed nonoperatively or operatively?

Recommendation

The panel suggests that adult and pediatric patients with uncomplicated appendicitis be managed operatively (*Conditional recommendation based on low certainty of evidence in adults and very low certainty of evidence in pediatrics*).

Introduction

While operative management of acute appendicitis has historically been the standard of care, medical management with antibiotics has become more widely utilized. Studies have demonstrated a 58–75% 1-year success rate in adults and children with no increase in complications if recurrence occurs [19, 20]. The advantage of nonoperative treatment is primarily the avoidance of surgery, general anesthesia, and their associated risks. On the other hand, appendectomy provides a definitive cure for appendicitis without the risk of recurrence and later need for surgery. There have been numerous systematic reviews suggesting that antibiotic therapy could be a reasonable alternative to appendectomy if the patient accepts the subsequent risk of recurrence [21–25].

Summary of the evidence

Uncomplicated appendicitis was defined as cases without preoperative evidence of abscess or perforation. The highest-level of evidence available for each outcome deemed critical or important to decision-making was utilized to inform the panel's recommendation. In the adult population, six RCTs were identified [1]. In the pediatric population, four RCTs and nine observational studies were identified.

There were five RCTs that investigated length of stay. All but one found that appendectomy had a shorter length of stay. However, the antibiotic arm had significant heterogeneity in treatment strategy. For example, in the study by Ceresoli et al. patients were mandated to receive 3 days of intravenous antibiotics, artificially inflating the length of stay, while in the CODA Collaborative trial, a patient was potentially eligible for discharge after a single dose of intravenous antibiotics with 24 h of bioavailability [26, 27]. Due to this, the panel decided this was ultimately not an informative outcome.

One included RCT investigated the comparative cost of the two arms. O'Leary et al. found that the mean total cost of antibiotic treatment was cheaper than surgical treatment, at a mean of €3077 as opposed to €4816 [28]. While the panel acknowledged that antibiotic treatment was likely cheaper than surgical treatment, it is difficult to extrapolate this to different health systems, and the lack of lifetime risk of appendicitis recurrence limits the utility of these point estimates.

Both the study by O'Leary et al. and the CODA Collaborative trials investigated quality of life as an outcome. The CODA Collaborative found a slightly superior quality of life at 30 days post management for antibiotic therapy [27]. The study by O'Leary et al. had similar results at 30 days, but the authors also followed their patients out to one year [28]. At three months post management, only 42% of the antibiotic arm was in full health while 90% of the surgical arm reported the same. At one year, the results were similar: 44% versus 87.6%.

The CODA Collaborative trial was the only study to report on rate of Clostridioides difficile infection; it found a rate of 0.6% in each arm.

Of the pediatric RCTs, one reported on cost and one reported quality of life data. Patkova et al. found similar costs between the two groups, with the nonoperative group costing a medianof 40,547 (range 34,467–112,936) Swedish krona and the operative group costing 42,099 (range 38,107–81,067) [29]. Hall et al. measured Parental PedsQL scores at 30 days and did not find a meaningful difference between the two groups: nonoperative median 91.3 (IQR 82.6–98.9) and operative median 90.2 (IQR 70.1–97.0) [30].

Adult

Benefits

There were four outcomes with desirable effects for antibiotic management including return to work, cost, quality of life, and need for a new course of antibiotics. The magnitude of these desirable effects was determined to be small.

Return to work 1.78 days shorter (95% CI 0.08 lower to 3.48 lower) based on four RCTs with 1411 patients.
Need for a new course of antibiotics 9 fewer per 1000 patients (95% CI 68 fewer to 469 more) based on 1 RCT with 30 patients.

Harms and burdens

From the available outcomes that were critical or important for decision-making, there were five outcomes with undesirable effects for antibiotic management including length of stay, readmission, post-treatment abscess, need for interventional radiology (IR) drainage, and conversion to operative management or reoperation. The magnitude of effect was deemed to be large by the panel.

Readmission 201 more per 1,000 patients (95% CI 137 more to 277 more) based on two RCTs with 1428 patients.
Post-treatment abscess 9 more per 1000 patients (95% CI 6 fewer to 78 more) based on three RCTs with 399 patients.
Need for IR drainage 14 more per 1000 patients (95% CI 3 more to 38 more) based on one RCT with 1332 patients.
Conversion to operative management or reoperation 91 more per 1,000 patients (95% CI 22 more to 279 more) based on four RCTs with 381 patients.

Certainty of evidence

The certainty of the above evidence was rated low based on the outcomes deemed critical to decision-making by the panel. These critical outcomes were primarily limited by their lack of power. (see evidence profile in the EtD framework, Appendix D).

Pediatric

Benefits

The main desirable effects of antibiotic management were return to school, cost, ICU admission, post-treatment abscess, and need for IR drainage. Overall, the panel felt that the combined magnitude for the desirable was small.

Return to school 2 days shorter (95% CI 6.2 days shorter to 2.2 days longer) based on one RCT with 39 patients.
ICU admission 39 fewer per 1000 patients (95% CI 52 fewer to 206 more) based on one observational study with 44 patients.
Post-treatment abscess 18 fewer per 1000 patients (95% CI 21 fewer to 6 more) based on four observational studies with 284 patients.
Need for IR drainage 8 fewer per 1000 patients (95% CI 9 fewer to 49 more) based on two observational studies with 216 patients.

Harms and burdens

From the available outcomes, there were four outcomes with undesirable effects for antibiotic management: LOS, QOL, readmission, and conversion to operative management or reoperation. The panel determined that the undesirable effect was large.

LOS 1.4 days longer (95% CI 0.6 days shorter to 3.4 days longer) based on six observational studies with 77,146 patients.
Readmission 220 more per 1,000 patients (95% CI 37 more to 575 more) based on four RCTs with 193 patients.
Conversion to operative management or reoperation OR 38.3 (95% CI 4.9 to 299.7) based on two RCTs with 100 patients.

Certainty of evidence

The certainty of evidence for the outcomes of readmission and conversion to operative management was high but the overall evidence for other outcomes was deemed very low. These critical outcomes were primarily limited by high-risk of bias and imprecision.

Decision criteria and additional considerations

These recommendations may not apply equally to all adult and pediatric patients. Nonoperative management may be less successful in immunocompromised patients who are unable to mount a normal immune response. Patients with poor access to medical care may benefit from definitive operative management at the time of presentation. For patients with inflammatory bowel disease (IBD), nonoperative management may be preferred in the setting of an equivocal diagnosis of appendicitis or significant cecal inflammation. The failure rate of nonoperative treatment in patients with recurrent appendicitis is unclear; there is limited data on this and when recurrence occurs it is typically managed operatively. There is some evidence that patients with a fecalith are at higher risk of recurrence than those without, and therefore the benefits of operative management may be greater in this population [31–35]. For patients with significant medical comorbidities or hostile abdomens, the risks and benefits of operative management must be assessed on a case-by-case basis. Finally, the panel did not evaluate the literature regarding appendicitis during pregnancy as this is addressed in another SAGES Guideline.

Of note, there may be a lower threshold for initiating antibiotic treatment in equivocal cases of appendicitis. However, increased and potentially unnecessary antibiotic usage may lead to increased antibiotic resistance and subsequent gastrointestinal infections, including Clostridium difficile.

Research recommendations

Further long-term outcome and quality of life data are needed for both treatment options. These studies should transparently report the diagnostic criteria as well as treatment protocols. Evidence of the value placed by patients or parents on the avoidance of appendectomy relative to the risk of recurrence would be useful when this guideline is updated as it could alter the strength of the current recommendation. Further evidence addressing many of the subgroups mentioned above would also be useful in tailoring care to these patients.

Conclusion

The panel suggested operative management for both adult and pediatric patients with uncomplicated appendicitis. This is a conditional recommendation based on low and very low certainty of evidence, respectively. Thus, the panel believes in general most patients will derive greater benefit from operative than from nonoperative management. However, there is uncertainty in this recommendation both due to the quality of the evidence and the variation across how individual patients value the outcomes assessed. Important considerations include how highly the patient values avoiding an operation as well as their access to care and medical comorbidities.

KQ3 Should adult and pediatric patients with complicated appendicitis be managed nonoperatively or operatively?

Recommendation

The panel suggests that adult and pediatric patients with complicated appendicitis be managed operatively (*Conditional recommendation based on very low certainty of evidence in adults and low certainty of evidence in pediatrics).*

In patients with significant cecal inflammation, longer symptom duration/delayed presentation, or a well-formed abscess, the panel notes that greater consideration can be

given to initial nonoperative management in an effort to minimize surgical risks.

Introduction

Approximately 30% of adult and pediatric patients with appendicitis present with complicated appendicitis [10]. Similar to the treatment of uncomplicated appendicitis, complicated appendicitis has been increasingly managed nonoperatively. The presence of an abscess or phlegmon has been associated with a higher risk of morbidity as well as the need for wider resections including ileocecectomy [36]. Percutaneous drainage is also an option for patients that present with a well-formed abscess.

Summary of the evidence

Complicated appendicitis was defined as cases with preoperative evidence of abscess or perforation. The data for the adult population came from one RCT and one retrospective study with direct comparative data [1]. Of the 30 RCT patients managed nonoperatively, 28 had attempted IR drainage. Ultimately 16 had aspiration of their abscess while 3 had drains placed. There was also one paper which examined the question of cost, including the hospital charges for the initial admission and any subsequent readmissions [37]. The authors found that the mean cost for operative management of complicated appendicitis was \$28,034 ± 24,166 and nonoperative management was \$28,158 ± 36,432.

The data for the pediatric population consisted of two RCTs and one retrospective study [1]. There was one additional paper investigating cost and one investigating quality of life. Myers et al. was an RCT of immediate compared to interval appendectomy in pediatric patients with complicated appendicitis; they found a medial total hospital charge of \$37,088 for immediate appendectomy and \$47,936 for interval appendectomy [38]. Schurman et al. investigated quality of life at 2 and 12 weeks for immediate appendectomy compared to interval appendectomy using the Pediatric Quality of Life Scale Version 4.0; at 2 weeks, they found no difference between early and interval appendectomy groups (81.93 ± 3.84 vs 74.25 ± 3.36) but at 12 weeks they found an increasing difference, favoring the early appendectomy group (96.77 ± 4.35 vs 84.37 ± 4.09) [39].

Adult

Benefits

ICU admission was the sole outcome with desirable effects for antibiotic management.

The magnitude of this desirable effect was determined to be trivial.

ICU admission: 83 fewer per 1000 patients (95% CI 18 fewer to 97 fewer) based on one observational study with 183 patients.

Harms and burdens

From the available outcomes that were critical or important for decision-making, there were six outcomes with undesirable effects of antibiotic management including LOS, cost, readmission, death, post-treatment abscess, and conversion to operative management or reoperation. The cost data are discussed in the Summary of Evidence above. The magnitude of effect was deemed to be large by the panel.

LOS 1.12 days more per 1000 patients (95% CI 0.65 more to 1.59 more) based on one RCT with 60 patients.
Readmission 233 more per 1000 patients (95% CI 7 more to 724 more) based on one RCT with 60 patients.
Death OR 7.39 (95% CI 0.15 to 372.38) based on one RCT with 60 patients.
Post-treatment abscess 167 more per 1000 patients (95% CI 21 fewer to 506 more) based on one RCT with 60 patients.
Conversion to operative management/reoperation 467 more per 1000 patients (95% CI 74 more to 859 more) based on one RCT with 60 patients.

Certainty of evidence

The certainty of the above evidence was judged as very low based on the outcomes deemed critical to decision-making. The biggest issue limiting the certainty of this evidence was the lack of quality of life data which the panel deemed critical to this judgement.

Pediatric

Benefits

There were no desirable effects for non-operative management.

Harms and burdens

There were 8 outcomes with undesirable effects associated with nonoperative management: return to school, LOS,

cost, QOL, readmission, post-treatment abscess, need for a new course of antibiotics, and conversion to operative management or reoperation. The cost and quality of life data are discussed in the Summary of Evidence above. The panel felt that the undesirable effect was large.

Return to school 5.6 days more (95% CI 2.8 more to 8.4 more) based on one RCT with 131 patients.
LOS 1.2 days more (95% CI 1.2 fewer to 3.6 more) based on two RCTs with 171 patients.
Readmission 235 more per 1000 patients (95% CI 60 more to 488 more) based on one RCT with 131 patients.
Post-treatment abscess 154 more per 1,000 patients (95% CI 15 more to 324 more) based on two RCTs with 171 patients.
Need for a new course of antibiotics: 60 more per 1000 patients (95% CI 0 fewer to 178 more) based on one observational study with 316 patients.
Conversion to operative management/reoperation: OR 11.18 (95% CI 0.56 to 222.98) based on one RCT with 40 patients.

Certainty of evidence

The certainty of the above evidence was judged as low for children based on the outcomes deemed critical to decision-making by the panel.

Decision criteria and additional considerations

The considerations for adult and pediatric patients described in KQ2 apply equally to KQ3. In addition, patients with a discrete abscess, significant cecal inflammation, or symptoms for longer than a week may benefit from initial nonoperative management given the higher operative risks in these patient populations. This decision should be made based on shared decision-making.

Research recommendations

The research recommendations are similar to those for uncomplicated appendicitis. Studies of complicated appendicitis should analyze patients with discrete abscesses, phlegmons, and symptoms for greater than a week separately.

Conclusion

The panel suggested operative management for both adult and pediatric patients with complicated appendicitis. This is a conditional recommendation based on very low and low certainty of evidence, respectively. Thus the panel believes in general most patients will derive greater benefit from operative than from nonoperative management. However, there is uncertainty in this recommendation both due to the quality of the evidence and the variation across individual patients in how they value the outcomes assessed. Important considerations include how significant the patient's inflammatory process is; significant inflammation may lead to extended resection and such patients would likely benefit from initial nonoperative management.

KQ4 Should adult and pediatric patients with acute, uncomplicated appendicitis undergo delayed (> 12 h) or immediate operation (< 12 h)?

Recommendation

The panel suggests that adult and pediatric patients with uncomplicated appendicitis may undergo either delayed (> 12 h) or immediate operation (< 12 h). (*Conditional recommendation, based on very low certainty of evidence*).

Introduction

The ideal timing of appendectomy is controversial [40]. Advocates for delayed operation argue initial treatment with antibiotics allows for better preoperative resuscitation. In addition, there are practical concerns such as OR availability, staffing, surgeon schedule, and patient considerations which may require delay. On the other hand, proponents of immediate operation worry that delay may lead to perforation and subsequently higher incidence of postoperative abscess or other complications.

Summary of the evidence

Data for this KQ consisted of nine retrospective studies in the adult population and three retrospective studies in the pediatric population [1].

Adult

Benefits

There were two desirable outcomes for delayed operation: reoperation and postoperative IR drainage. This effect size was deemed trivial.

Reoperation 2 fewer per 1000 patients (95% CI 14 fewer to 14 more) based on one observational study with 2559 patients.
Postoperative IR drainage 9 fewer per 1000 patients (95% CI 24 fewer to 25 more) based on one observational study with 863 patients.

Harms and burdens

There were three undesirable outcomes for delayed operation: LOS, postoperative, abscess, and readmission. This effect size was deemed trivial as well.

LOS 0.59 days more (95% CI 0.17 more to 1 more) based on four observational studies with 7,181 patients.
Postoperative abscess 6 more per 1000 patients (95% CI 0 to 13 more) based on eight observational studies with 10,432 patients.
Readmission 2 more per 1000 patients (95% CI 4 fewer to 10 more) based on four observational studies with 5968 patients.

Certainty of evidence

The certainty of the above evidence was graded very low.

Pediatric

Benefits

In the pediatric population there was one desirable outcomes for delayed operation: readmission. This effect size was deemed trivial.

Readmission 17 fewer per 1000 patients (95% CI 27 fewer to 2 fewer) based on one observational study with 2,756 patients.

Harms and burdens

There were two undesirable outcomes for delayed operation: postoperative abscess and reoperation. This effect size was deemed small.

Postoperative abscess 79 more per 1000 patients (95% CI 54 fewer to 829 more) based on two observational studies with 3004 patients.
Reoperation: 0 more per 1000 patients (95% CI 27 fewer to 2 fewer) based on one observational study with 2756 patients.

Certainty of evidence

The certainty of the above evidence was graded very low.

Decision criteria and additional considerations

For both children and adults, if there is concern the patient may actually be perforated, the patient may benefit from expedited source control. In addition, hospital resources including OR availability, staffing, and surgeon availability may affect the decision between immediate and delayed operation. For example, lack of OR availability the following day may justify performing the appendectomy overnight despite no difference in patient outcomes with waiting until the daytime. Similarly, if a surgeon or the OR staff are not in-house overnight it may be reasonable to delay the case until the following day.

Research recommendations

Future research should investigate whether the morbidity of operation increases past an upper limit of delay. In addition, better risk stratification for perforation will permit more expedient care for high-risk patients.

Conclusion

The panel suggested that both adult and pediatric patients with uncomplicated appendicitis undergo either immediate or delayed operation. This is a conditional recommendation based on very low certainty of evidence. Thus, the panel believes in general most patients will derive equal benefit from immediate or delayed operation. However, there is uncertainty in this recommendation due to the quality of the evidence. Important considerations include the patient's clinical status, risk for complicated appendicitis, and the hospital system's resources.

KQ5 In patients undergoing appendectomy for complicated appendicitis, should suction and lavage versus suction alone be used?

Recommendation

The panel suggests that adult and pediatric patients with complicated appendicitis should undergo either suction and lavage or suction alone based on surgeon preference. (*Conditional recommendation based on very low certainty of evidence in adults and low certainty of evidence in pediatrics*).

Introduction

Intraabdominal abscess formation occurs after appendectomy for complicated appendicitis in approximately 5–20% of patients and leads to increased hospital stays or readmission, ileus, and pain, often requiring a drainage procedure for treatment [31, 41]. Irrigation with lavage has been proposed as a method to decrease the incidence of postoperative abscesses. However, studies have shown mixed clinical outcomes and generally demonstrate longer operating room times with irrigation [42–44]. Potential reasons for the ineffectiveness of irrigations include bacterial adherence to peritoneal surfaces, irrigation disseminating the bacteria, and dilution of immunogenic responders [45].

Summary of the evidence

In adults, data from four RCTs from the systematic review were deemed critical or important to clinical decision-making for this question and were used to inform the panel's decision [1]. In children, four RCTs on suction and lavage versus suction alone were used to inform the panel's decision. Of note, cost data were not used by the panel for decision-making but there was a study in the pediatric population which found that cost was similar in both groups [45].

Adult

Benefits

There were four outcomes with desirable effects for suction and lavage including: hospital length of stay, death, postoperative abscess, and readmission. The magnitude of these desirable effects was determined to be small.

LOS 1.28 fewer days (95% CI 3.32 fewer to 0.76 more) based on two RCTs with 546 patients.
Death 8 fewer per 1000 patients (95% CI 11 fewer to 62 more) based on one RCT with 286 patients.
Postoperative abscess 7 fewer per 1000 patients (95% CI 55 fewer to 98 more) based on four RCTs with 713 patients.
Readmission 12 fewer per 1000 patients (95% CI 77 fewer to 150 more) based on two RCTs with 367 patients.

Harms and burdens

From the available outcomes that were critical or important for decision-making, there were two outcomes with undesirable effects for suction and lavage: post-operative drain placement and reoperation. The magnitude of effect was deemed to be small by the panel.

Postoperative drain placement 6 more per 1000 patients (95% CI 24 fewer to 65 more) based on three RCTs with 453 patients.
Reoperation 21 more per 1000 patients (95% CI 13 fewer to 117 more) based on three RCTs with 453 patients.

Certainty of evidence

The certainty of the above evidence was evaluated as very low for adults based on the outcomes deemed critical to decision-making by the panel. These critical outcomes were primarily limited by high-risk of bias and imprecision. (see evidence profile in the EtD framework, Online Appendix D).

Pediatric

Benefits

The main desirable effects of suction and lavage included organ space infection, post-operative drain placement, length of stay, and readmission. Overall, the panel felt that the combined magnitude for the undesirable effects of suction and lavage was small.

Postoperative abscess 11 fewer per 1000 patients (95% CI 62 fewer to 70 more) based on three RCTs with 406 patients.
Postoperative drain placement 25 fewer per 1000 patients (95% CI 63 fewer to 53 more) based on two RCTs with 320 patients.
LOS 0.33 fewer days (95% CI 0.97 fewer to 0.32 more) based on two RCTs with 320 patients.
Readmission 28 fewer per 1000 patients (95% CI 36 fewer to 17 more) based on two RCTs with 320 patients.

Harms and burdens

There was one outcome with undesirable effects from suction and lavage: reoperation. The panel felt that the undesirable effect was small.

Reoperation 8 more per 1000 patients (95% CI 3 fewer to 63 more) based on four RCTs with 1105 patients.

Certainty of evidence

The certainty of the above evidence was evaluated as low for pediatrics. These critical outcomes were primarily limited by small sample size and nonsignificant confidence intervals.

Decision criteria and additional considerations

This recommendation likely does not apply equally to adult and pediatric patients who are immunocompromised or have widely perforated appendicitis (i.e., purulent fluid in all quadrants of the abdomen). Particularly in the immunocompromised group, the initial presentation and morbidity of postoperative abscess may differ from the general population.

Research recommendations

Future studies on suction and lavage versus suction alone should include comparative studies with a standardized technique of irrigation as well as type and volume of irrigant.

Conclusion

The panel suggested that adult and pediatric patients with complicated appendicitis should undergo either suction and lavage or suction alone. This is a conditional recommendation based on very low and low certainty evidence, respectively. Thus, the panel believes in general most patients will derive equal benefit from suction and lavage or suction alone. However, there is uncertainty in this recommendation due to the quality of the evidence. Important considerations include how widespread the intraabdominal contamination is.

KQ6 In patients undergoing appendectomy for complicated appendicitis, should routine drain placement versus no routine drain placement be used?

Recommendation

The panel suggests no routine drain placement for both adult and pediatric patients undergoing appendectomy for complicated appendicitis (*Conditional recommendation based on very low certainty of evidence*).

Introduction

Proponents of routine drain placement after appendectomy for complicated appendicitis advocate for the necessity of monitoring and preventing postoperative intraabdominal abscess formation [46–48]. Others have questioned whether the presence of a drain prevents postoperative abscesses, especially since there can be drain dysfunction due to a number of factors and the tip of the drain may fail to remain in the space where an abscess forms. Routine drainage may also lead to increased pain, increased length of stay, and decreased bowel function.

Summary of evidence

From the recent systematic review, six observational studies on routine drain placement versus no drain placement in adults were used to inform the panel's decisions and three observational studies in children were used [1].

Adult

Benefits

Two outcomes, postoperative drain placement and length of stay were desirable effects for routine drain placement in adults. The panel felt that the effect magnitude was trivial.

Postoperative drain placement 8 fewer per 1000 patients (95% CI 55 fewer to 126 more) based on 3 observational studies with 476 patients.
LOS 0.21 days fewer (95% CI 0.77 fewer to 0.34 more) based on two observational studies with 250 patients.

Harms and burdens

Organ space infection, new course of antibiotics, readmission, reoperation, and death were undesirable effects for routine drain placement in adults. The overall magnitude of the undesirable effects was deemed moderate.

Organ space infection 10 more per 1000 patients (95% CI 20 fewer to 50 more) based on six observational studies with 1727 patients.
New course of antibiotics 37 more per 1000 patients (95% CI 23 fewer to 154 more) based on two observational studies with 327 patients.
Readmission 16 more per 1000 patients (95% CI 15 fewer to 68 more) based on two observational studies with 991 patients.
Reoperation 30 more per 1000 patients (95% CI 20 fewer to 173 more) based on one observational study with 225 patients.

Certainty of evidence

The certainty of evidence was evaluated as very low. These critical outcomes were primarily limited by high-risk of bias, large, nonsignificant confidence interval and small study sample size. (see evidence profile in the EtD framework, Online Appendix D).

Pediatric

Benefits

The only critical or important desirable outcome for routine drain placement was postoperative drain placement. The magnitude of the effect was deemed small.

Postoperative drain placement 57 fewer per 1000 patients (95% CI 99 fewer to 14 more) based on one observational study with 379 patients.

Harms and burdens

Organ space infection, readmission, and reoperation were undesirable outcomes for routine drain placement in children. The overall undesirable effect was deemed moderate.

Organ space infection 57 more per 1000 patients (95% CI 10 fewer to 187 more) based on two observational studies with 571 patients.
Readmission 5 more per 1000 patients (95% CI 15 fewer to 44 more) based on two with 2141 patients.
Reoperation 19 more per 1000 patients (95% CI 1 more to 52 more) based on two observational studies with 2141 patients.

Certainty of evidence

The certainty of evidence was evaluated as very low. These critical outcomes were primarily limited by high-risk of bias, large, nonsignificant confidence interval and small study sample size. (see evidence profile in the EtD framework, Online Appendix D).

Decision criteria and additional considerations

There are other disadvantages to routine drains in adult and pediatric patients that were not taken into consideration in the outcomes such as the drain falling out postoperatively, the emotional burden of caring for a drain, irritation of the skin, and pain at the site that might strengthen the recommendation against routine drain placement. In addition, immunosuppressed patients may develop an abscess at a later time after recovering their white blood cell count. As such, these patients who have a drain placed routinely may still require percutaneous drain placement in the future.

Research recommendations

Future recommendations were made by the panel for randomized controlled studies particularly with standardized types and sizes of drains, post-operative care and antibiotic regimen, and documentation of peritoneal contamination.

Conclusions

The panel suggested no routine drain placement for both adult and pediatric patients undergoing appendectomy for complicated appendicitis. This is a conditional recommendation based on very low certainty evidence. Thus, the panel believes in general most patients will derive greater benefit from no routine drain placement. However, there is uncertainty in this recommendation due to the quality of the evidence. Important considerations include complications of the drain and immunosuppression.

KQ7 Should patients who undergo appendectomy for complicated appendicitis be given short-term versus long-term postoperative antibiotics?

Recommendation

The panel suggests that adult and pediatric patients who have undergone appendectomy for complicated appendicitis should be treated with short-term antibiotics postoperatively. (*Conditional recommendation based on very low certainty of evidence*).

Introduction

There is significant debate regarding the duration of antibiotics for treating complicated appendicitis [49, 50]. Due to the link between antibiotic use and resistance, there has been increased emphasis on its judicious use. Although there is no clear definition of a short course, 3–5 days is often used as a cutoff. In addition, complications of prolonged antibiotic duration include Clostridium difficile (C. diff.) infections and urinary tract infections. This must be weighed against the possible post-operative risk of increased surgical site infections and intra-abdominal abscesses.

Summary of the evidence

In adults, data from eight (one RCT and seven retrospective comparative) studies were deemed critical or important to clinical decision-making on short versus long-term antibiotics postoperatively and were used to inform the panel's decision [1]. One study did not specify the type of regiment used. In all other studies, patients started with intravenous antibiotics prior to occasionally transitioning to oral antibiotics in the long-term arm. In children, eight (two RCTS, six retrospective comparative) were used to inform the panel's decision. Two of these retrospective studies used intravenous antibiotics exclusively while all other used intravenous initially with a potential to transition to oral antibiotics.

Adult

Benefits

There were five outcomes with desirable effects for short-term postoperative antibiotics including organ space infection, C. diff. infection, length of stay, reoperation, and total complications. The magnitude of these desirable effects was determined to be moderate.

Organ space infection 45 fewer per 1000 patients (95% CI 102 fewer to 178 more) based on one RCT with 80 patients.
C. diff. infection 9 fewer per 1000 patients (95% CI 10 fewer to 15 more) based on two observational studies with 636 patients.
LOS 0.9 fewer days (95% CI 1.65 fewer to 0.15 fewer) based on one RCT with 80 patients.
Reoperation 16 fewer per 1000 patients (95% CI 70 fewer to 123 more) based on two observational studies with 885 patients.
Total complications 114 fewer per 1000 patients (95% CI 214 fewer to 117 more) based on one RCT with 80 patients.

Harms and burdens

From the available outcomes that were critical or important for decision-making, there were three outcomes with undesirable effects for short-term antibiotics: new course of antibiotics, post-operative drain placement, and readmission. The magnitude of this effect was deemed to be trivial by the panel.

New course of antibiotics 4 more per 1000 patients (95% CI 56 fewer to 285 more) based on one RCT with 80 patients.
postoperative drain placement 2 more per 1000 patients (95% CI 41 fewer to 298 more) based on one RCT with 80 patients.
Readmission 4 more per 1000 patients (95% CI 56 fewer to 285 more) based on one RCT with 60 patients.

Certainty of evidence

The certainty of the above evidence was evaluated as very low for adults based on the outcomes deemed critical to decision-making by the panel. These critical outcomes were primarily limited by high-risk of bias and imprecision. (see evidence profile in the EtD framework, Online Appendix D).

Pediatric

Benefits

The main desirable effects of short-term antibiotics included organ space infection, new course of antibiotics, C. diff. infection, postoperative drain placement, length of stay, and readmission. Overall, the panel felt that the combined magnitude for the undesirable was moderate.

Organ space infection 4 fewer per 1000 patients (95% CI 52 fewer to 58 more) based on two RCTs with 788 patients.
New course of antibiotics 12 fewer per 1000 patients (95% CI 102 fewer to 129 more) based on one observational study with 179 patients.
C diff infection 6 fewer per 1000 patients (95% CI 15 fewer to 22 more) based on one RCT with 686 patients.
Postoperative drain placement 33 fewer per 1000 patients (95% CI 65 fewer to 22 more) based on three observational studies with 1010 patients.
LOS 0.33 fewer days (95% CI 4.0 fewer to 3.4 more) based on two RCTs with 788 patients.
Readmission 37 fewer per 1000 patients (95% CI 52 fewer to 6 fewer) based on one RCT with 686 patients.

Harms and burdens

There was one outcome with undesirable effects for short-term antibiotics which was reoperation. The panel felt that the undesirable effect was small.

Reoperation RR 6.72 (95% CI 0.35 to 129.62)

Certainty of evidence

The certainty of the above evidence was evaluated as very low for pediatrics. These critical outcomes were primarily limited by high-risk of bias and imprecision.

Decision criteria and additional considerations

The value that both the patient and surgeon places on these outcomes in both adult and pediatric patients may differ in the immunocompromised population.

To improve the implementation of this recommendation, the panel felt that additional education would be needed for patients and physicians (especially infectious disease, primary care physicians, and hospitalists). Once the recommendation of short-term antibiotics treatment for patients with complicated appendicitis that have undergone appendectomy is adopted, it will be important to monitor readmission and post-operative infection (both superficial and deep) at individual institutions.

Research recommendations

Future studies should investigate how short a course of antibiotics is still effective, when the transition to oral antibiotics can be made, and the optimal antibiotic from the perspective of stewardship and efficacy.

Conclusion

The panel suggested that adult and pediatric patients who have undergone appendectomy for complicated appendicitis should be treated with short-term antibiotics postoperatively. This is a conditional recommendation based on very low certainty of evidence. Thus, the panel believes in general most patients will derive greater benefit from short-term antibiotics. However, there is uncertainty in this recommendation due to the quality of the evidence. There is still uncertainty surrounding the ideal number of days of antibiotics postoperatively. However, the STOP-IT trial demonstrated that antibiotics for four days after adequate source control is sufficient and this can logically be applied to patients with complicated appendicitis as well [51].

KQ8 In asymptomatic patients with complicated appendicitis previously treated nonoperatively, should an interval appendectomy be performed versus observation?

Recommendation

The panel suggests that adult patients with complicated appendicitis previously treated nonoperatively should have an interval appendectomy (*conditional recommendation based on low certainty of evidence in adults and expert opinion in pediatrics*).

Introduction

Controversy exists whether interval appendectomy after initial conservative management of complicated appendicitis is necessary [52]. The advocates of interval appendectomy note that it is a definitive treatment and provides a definitive diagnosis, which is especially important as malignancy is a concern in patients with complicated appendicitis. Opponents argue that the appendectomy is unnecessary and places the patient at risk for operative complications without benefit.

Summary of the evidence

The literature search identified seven studies addressing the neoplasm rate in the adult population [1]. The neoplasms identified included serrated adenoma, mucinous neoplasm, carcinoid, lymphoma, signet ring cell carcinoma, and adenocarcinoma. The pooled event rate in patients undergoing interval appendectomy was 14% and ranged from 6 to 34%, with higher rates found in studies with an older population. The risk for neoplasm seems to increase most significantly around age 40. Of note, the one randomized controlled trial addressing this question [53] was terminated early due to ethical concerns over the high tumor burden identified over the first 60 patients enrolled in the study.

There was no comparative data identified in the pediatric population.

Adult

Benefits

There were three outcomes with desirable effects for interval appendectomy: death, conversion to operative management/reoperation, and neoplasm detection. The magnitude of these desirable effects was determined to be large.

> *Death* 40 fewer per 1000 patients (95% CI 47 fewer to 68 more) based on one observational study with 170 patients. *Conversion to operative management/reoperation* 681 fewer per 1000 patients (95% CI 428 fewer to 704 fewer) based on one RCT with 52 patients.

Harms and burdens

There were three outcomes with undesirable effects for interval appendectomy: length of stay, abscess, and drain

placement. The magnitude of effect was deemed to be trivial by the panel.

LOS 0.33 more days (95% CI 3.41 fewer to 4.07 more) based on one observational study with 29 patients.
Abscess RR 3.23 (95% CI 0.14 to 75.83) based on one RCT with 52 patients.
Drain placement RR 3.23 (95% CI 0.14 to 75.83) based on one RCT with 52 patients.

Certainty of evidence

The overall certainty of evidence was judged to be low based on underpowered patient cohorts and concerns over the comparability of groups in the observational study.

Pediatric

Primarily single arm data were available for this question and given the low quality of evidence the panel determined they were unable to make an evidence-based recommendation. Of note, the pooled risk of appendiceal carcinoid across 5 single arm studies with 9,091 children undergoing interval appendectomy was < 1%. Prior studies estimated the risk to be about 2–5 per 1000 [54].

The decision to proceed with interval appendectomy should be based on a discussion with parents regarding the risks and benefits of interval appendectomy. Until further studies are done, both options are reasonable. In pediatric patients with a family history of malignancy at a younger age or poor access to care, stronger consideration for appendectomy should be given. In patients with recurrent appendicitis, immediate or interval appendectomy depending on the clinical status should be performed.

Decision criteria and additional considerations

For both adult and pediatric patients with complicated appendicitis initially treated with antibiotics, one of the major considerations regarding interval appendectomy is the concern for missing a malignancy. Of note, patients with neoplasms were all over 40 years of age. Therefore, the benefits of interval appendectomy may be less in pediatric patients or younger adults. However, there may be strong patient, surgeon, or parental preference for an appendectomy to be performed. Patients with a family history of malignancy, especially colorectal or gastrointestinal malignancy, may also benefit from stronger consideration of interval appendectomy.

Furthermore, patients with poor access to care may have difficulty returning to the hospital if appendicitis recurs and a planned interval appendectomy may be preferred. Finally, for pediatric patients and younger adult patients, given the longer lifespan after appendicitis, there could be a higher rate of recurrence.

Research recommendations

Studies with long-term outcomes in younger patients that do not undergo interval appendectomy are needed to determine the recurrence rate and rate of future detected malignancy.

Conclusion

The panel suggested that adult and pediatric patients who have undergone nonoperative treatment for complicated appendicitis should be treated with interval appendectomy. This is a conditional recommendation based on low certainty of evidence and expert opinion, respectively. Thus, the panel believes in general most patients will derive greater benefit from interval appendectomy. However, there is uncertainty in this recommendation due to the quality of the evidence and variation in individual patient values. Important considerations include the patient's values, medical comorbidities and access to care, and potential risk of malignancy.

Discussion

What is new in this guideline?

The European Association of Endoscopic Surgery (EAES) generated consensus guidelines on appendicitis in 2015 [55]. Similar to this guideline, they stated that appendectomy remains the gold standard in acute uncomplicated appendicitis. In addition, the EAES guidelines recommended that diagnostic imaging begin with ultrasound with advanced imaging as needed, suction alone without lavage, no routine use of drains for complicated appendicitis, and no postoperative antibiotics for uncomplicated appendicitis—all recommendations consistent with this panel's recommendations. While the EAES review did not cover whether interval appendectomy should be performed following non-operative management of complicated appendicitis, the current review utilized new evidence that reveals a relatively high rate of neoplasm in interval appendectomy specimens and therefore recommends eventual appendectomy, particularly in patients over the age of 40 years. The EAES also recommended immediate appendectomy in cases of uncomplicated appendicitis in order to decrease perforation risk, however our authors did not uncover sufficient evidence to confirm this recommendation and therefore make a conditional recommendation for either immediate or delayed appendectomy (> 12 h) depending upon individual patient, surgeon, or logistical factors. Most recent reviews are in agreement regarding

implementing a shorter course of postoperative antibiotics in cases of complicated appendicitis; the current review has additionally recommended that duration be kept in the range of 3–5 days as opposed to longer courses in order to avoid resistance, *C. difficile* and urinary tract infections with no evidence of added benefit in abscess reduction.

The guideline of the Eastern Association of Surgery for Trauma (EAST) could not make a recommendation for or against nonoperative management as primary treatment for uncomplicated AA [56]. They recommended against routine interval appendectomy for patients initially treated nonoperatively for intra-abdominal abscess or phlegmon, again likely due to lack of availability of the most recent evidence.

The World Society of Emergency Surgery (WSES) reported on a consensus conference on the diagnosis and treatment of adult patients with acute appendicitis in 2015 and updated the recommendations in 2020 [57]. For diagnosis, they recommend the routine use of a combination of clinical parameters and US.

Implementation

The panel believes that it is feasible to successfully implement these recommendations into local practice and that the recommendations will be accepted by stakeholders. The main considerations regarding implementation of this guideline are the costs and availability of the testing and treatment options. The panel plans to survey physicians in the future to monitor and audit compliance with the recommendations put forth in this guideline.

Updating this guideline

SAGES plans to repeat a comprehensive literature review in approximately three years to reevaluate and identify any new evidence. Particular attention will be paid to any future studies that specifically address the research recommendations proposed in this guideline. A formal update will be generated when substantial literature is detected. The adoption and implementation of this guideline's recommendations will be assessed at an interval time in the future.

Limitations of this guideline

There are a number of limitations to this guideline. The main limitation is the low certainty of evidence for all of the key questions. There is minimal long-term data for both recurrence of appendicitis and malignancy rates, which decreases the ability to strongly advocate for a particular recommendation. In addition, the level of importance for the patient-centered outcomes was determined by the panel members rather than by patient advocates. As such, despite attempting to take this into account, different patients may place more or less weight on these individual outcomes, which would potentially change the balance of effects.

Health equity assessment

The pediatric literature is replete with evidence of racial and socioeconomic disparities in perforation rates among children with acute appendicitis [58, 59]. There is also evidence from the Southern California Kaiser Permanente system that these disparities can be eliminated when patients of all races and socioeconomic statuses have equal access to care [60]. The adult literature similarly describes evidence that the existing racial disparities in appendiceal perforation rates are due to insurance status and can be eliminated in environments with increased access to care [61, 62].

However, the same group from the Southern California Kaiser Permanente system reports persistent disparities in the utilization of laparoscopic appendectomy, with male, Black, low income, and older patients all less likely to undergo laparoscopic appendectomy [63]. Postoperative morbidity was also higher in male and older patients.

Noting known disparities in the appendicitis literature is essential to begin working towards eliminating them. Future randomized controlled trials should make efforts to recruit a patient population that reflects the diversity of the country in which they are conducted to ensure the conclusions of these trials will be applicable to their target population.

Conclusion

While the management of appendicitis continues to evolve, surgical management remains the gold standard therapy. This paper outlines recommendations for diagnosis, management, and intraoperative decision-making for adult and pediatric patients with uncomplicated and complicated appendicitis. The recommendations for future research outlined herein should allow for stronger recommendations in future updates of this guideline.

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Declarations

Disclaimer Clinical practice guidelines are intended to indicate the best available approach to medical conditions as established by a systematic review of available data and expert opinion. The approach suggested may not necessarily be the only acceptable approach given the complexity of the healthcare environment. This guideline is intended to be flexible, as the surgeon must always choose the approach best suited to the patient and to the variables at the moment of decision. This guideline is applicable to all physicians who are appropriately credentialed regardless of specialty and address the clinical situation in question. Some studies or treatment options may not be available in certain regions, and as such individual decision-making must be used. This guideline is developed under the auspices of SAGES, the guidelines committee, and approved by the Board of Governors. The recommendations of each guideline undergo multidisciplinary review and are considered valid at the time of production based on the data available.

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