ACUTE APPENDICITIS: IS SURGERY STILL THE BEST OPTION? SPECIAL CONSIDERATION ON PEDIATRIC AND PREGNANT PATIENTS

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ABSTRACT

Acute appendicitis, being one of the most prevalent causes of the acute abdomen in adult and pediatric patients, is marked by inflammation of the remnant of the vermiform appendix. When pregnancy and general surgery cases are combined, acute appendicitis is also a leading concern. For more than 10 decades, open surgery was the sole normative treatment for acute appendicitis. Nonoperative management (NOM) is a management strategy in which patients receive antimicrobials with the aim of averting surgery. Appendectomy is reserved for patients who do not respond to antimicrobials or who experience a relapse of appendicitis. However, the decision to conduct NOM has increased since the outbreak of COVID-19. NOM is suitable for patients with a first attack who have clinical signs of uncomplicated appendicitis without physical findings of diffuse peritonitis or imaging evidence of a large abscess, phlegmon, perforation, or tumor. The limited contraindications to NOM include patients who have a delayed response to antimicrobials, those with an appendicolith finding, and older patients because of a higher chance of latent malignancy. Treatment failure, either clinically or radiographically, as proven by bowel obstruction, sepsis, or persistent pain, pyrexia, or leukocytosis, necessitates prompt appendectomy. NOM may be an option for children who can describe their symptoms verbally, have a reliable and reproducible abdominal examination, and after shared decision-making among the overseeing pediatric surgeon and the parents or primary caregivers. The success rate of NOM in pediatric patients is about 67%–91%. The customary treatment of acute appendicitis in pregnancy remains appendectomy, with laparoscopic appendectomy being preferable to open appendectomy. The selection of strategy is based on clinical status and preferences, gestational age, and the surgeon's level of experience. Under consideration of gestational age, NOM was more frequently chosen than appendectomy in the first and third trimesters. The overall success rate of NOM is 93%.

***Keywords**: Acute appendicitis; Nonoperative management (NOM); Anti-microbials; Pediatric patient; Pregnant patient*

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INTRODUCTION

Acute appendicitis, one of the most prevalent causes of the acute abdomen in adult and pediatric patients, is marked by inflammation of the vermiform appendix. Typically, appendicitis is an indication for emergency abdominal surgery. Acute appendicitis is also the leading general surgical concern encountered during pregnancy. The prevalence of abdominal and gastrointestinal distress is generally high in pregnant patients, making the diagnosis of acute appendicitis difficult, particularly given anatomic alterations related to uterine enlargement and the physiological leukocytosis of pregnancy.[1–5]

Etiology & Anatomy

The vermiform appendix is usually located in the right lower quadrant (RLQ) of the abdomen, although it can be located elsewhere in the abdomen, depending on the presence of developmental abnormalities or related histories such as prior surgery or pregnancy in female patients. Children with congenital anomalies of intestinal location (e.g., uncorrected malrotation) may have the appendix located in the upper abdomen or on the left side, as seen in situs inversus totalis. Other abnormalities that may affect appendix location include postsurgical correction of diaphragmatic hernia, gastroschisis, and omphalocele.[3–8]

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The appendix is called a true cecal diverticulum, meaning that the appendiceal wall contains all layers of the large intestine: mucosa, submucosa, muscularis (longitudinal and circular), and serosa. The mucosa and submucosa of the appendiceal lamina propria contain B and T lymphoid cells, making the appendix histologically distinguishable from the cecum. Hyperplasia of this lymphoid tissue can promote appendiceal obstruction and lead to appendicitis.[1]

The connection of the appendix to the base of the cecum is fixed, but the appendiceal tip can extend into preileal, postileal, subcecal, retrocecal, and pelvic positions; it is most commonly retrocecal, occurring in more than 60% of patients. The diagnosis of appendicitis can be complicated by these normal anatomical variations because the location of pain and clinical examination findings reflect the anatomical position of the appendix.[1,6]

Several anatomic features of the appendix can increase the frequency and presentation of appendicitis during childhood. These features include a funnel-shaped appendix in the first year of life, which may make obstruction less likely. Lymphoid follicles are embedded within the colonic epithelium bordering the appendix and may cause obstruction; these follicles reach their largest diameter during the teenage years. The omentum is exceptionally thin and immature in toddlers and usually cannot contain purulent material, which may partly explain the diffuse peritonitis that commonly follows perforation in younger children.[6]

Epidemiology

The incidence of acute appendicitis ranges from 98 to 110 per 100,000 person-years in North America and Europe and from about 100 to 223 per 100,000 person-years worldwide. The second and third decades of life are the periods during which appendicitis occurs most frequently. The incidence is highest among teenagers and lowest in children ≤9 years old. The male proportion exceeds the female proportion by approximately 1.4:1.[1,4,6–10]

The incidence of appendicitis in pediatric patients from birth to the toddler years is 1 to 6 per 10,000 children, whereas in children younger than 14 years of age, it is 19 to 28 per 10,000 children. Disease progression in appendicitis is more common and more rapid in toddlers, occurring in almost 60% of cases, partly due to the presence of nonspecific symptoms, which leads to a delay in diagnosis.[6,7,8,11–13]

The acute form of appendicitis is suspected in 1 in 600 to 1 in 1,000 pregnancies and confirmed in 1 in 800 to 1 in 1,500 pregnancies. Appendicitis occurs less commonly in pregnant or postpartum women than in nonpregnant women. The incidence is higher during the second trimester than in the first or third trimesters, or after childbirth.[3,14–18]

Pathogenesis and Clinical Manifestations

Inflammation of the appendiceal surface characterizes early appendicitis, followed by localized ischemia, perforation, and the formation of a contained abscess or generalized peritonitis. Appendiceal obstruction is frequently implicated but not always identified, most commonly caused by hard fecal masses called fecaliths, infectious agents such as intestinal parasites, lymphoid hyperplasia, and tumors (benign or malignant). However, the majority of acute appendicitis patients do not have a fecalith, and some patients with a fecalith have a histologically normal appendix.[1,4,18]

Obstruction of the appendix causes the lumen to fill with mucus and become swollen, leading to increased luminal and intramural pressure, thrombosis, occlusion of small appendiceal vessels, and lymphatic stasis. As the appendix becomes distended, the wall thickens, the mucosal barrier is disrupted, ischemia occurs, and the appendix may become necrotic and potentially perforated. The visceral afferent nerve fibers of T8 to T10 are then stimulated, causing poorly localized central or periumbilical abdominal pain. When inflammation reaches the adjacent parietal peritoneum, the pain becomes well localized.[1,4,6,9]

The mechanism of luminal obstruction varies with the age of the patient. In younger children, the most common cause is hyperplasia of lymphoid follicles due to infection. In older patients, the obstruction is more likely to be caused by fibrosis, fecaliths, or neoplasia (carcinoid, adenocarcinoma, or mucocele). In endemic regions, parasites can cause obstruction at any age.[1,4,7,12]

Bacterial overgrowth occurs within the diseased appendix. Aerobic organisms predominate in early appendicitis, whereas mixed infections are more common in late appendicitis. Common organisms involved include the normal fecal flora, mainly aerobic and anaerobic Gram-negative rods

such as *Escherichia coli*, *Peptostreptococcus* species, *Bacteroides fragilis*, and *Pseudomonas* species. Intraluminal microbes then invade the appendiceal wall, stimulating a neutrophilic exudate. The influx of neutrophils causes a fibropurulent response on the serosal surface, which irritates the parietal peritoneum.[1,4,6,13]

Within the first 24 hours after the onset of symptoms, around 90% of patients have inflammation and possibly necrosis of the appendix, but perforation has not yet occurred. This can lead to localized abscess formation or diffuse peritonitis. Approximately 20% of patients develop perforation within 24 hours of symptom onset, whereas 65% of patients have symptoms for longer than 48 hours. If the bowel loops and omentum do not contain the infection, generalized peritonitis can develop.[1,4,6,19]

Less commonly, enteric pathogens can directly infect the appendix or cause localized hyperplasia of appendiceal lymphoid tissue, leading to obstruction in pediatric patients. Specific organisms include adenovirus (sometimes associated with intussusception), rubeola virus, Epstein-Barr virus, *Actinomyces israelii*, *Enterobius vermicularis* (pinworms), and *Ascaris lumbricoides* (roundworms). Some cases of acute pediatric appendicitis arise from other conditions such as Crohn's disease (in which granulomatous inflammation involves the appendix), appendiceal duplication, Burkitt lymphoma, or inspissated mucous obstruction of the appendiceal lumen, as seen in cystic fibrosis.[6]

DIAGNOSIS

History and Physical Examination

Initial assessment of acute appendicitis comprises clinical and laboratory evaluation. Unfortunately, neither is sufficiently sensitive or specific to definitively exclude or diagnose appendicitis. Diagnostic accuracy based on clinical assessment often depends on the proficiency of the examining pediatrician. Persistent acute abdominal pain should be carefully evaluated, including a digital rectal examination. In female patients, a pelvic examination should also be performed. Women of childbearing age should be assessed for the possibility of pregnancy.[2]

The early signs of appendicitis are frequently nonspecific. There may be a low-grade fever up to 38.3°C. Abdominal pain is the most common presenting symptom, occurring in nearly all confirmed cases of acute appendicitis. Classical symptoms include right lower quadrant (RLQ; right anterior iliac fossa) abdominal pain, anorexia, nausea, and vomiting. The pain is typically periumbilical initially, with subsequent migration to the RLQ as inflammation progresses. Classical signs of peritoneal irritation (e.g., rebound tenderness, muscle guarding, rigidity, referred pain) may also be present. Other signs, such as the psoas or obturator signs, may help clinicians localize the inflamed appendix. Once the inflammation reaches the RLQ, symptoms may vary depending on the position of the appendiceal tip. An anterior tip appendix produces marked, localized pain in the RLQ, whereas a retrocecal appendix produces dull abdominal pain. Tenderness below McBurney's point may be noted in patients with a pelvic appendiceal tip. Patients with a pelvic tip may also report dysuria, urinary frequency, or rectal symptoms such as tenesmus and diarrhea. If the appendix is long (usually more than 10 cm) and becomes inflamed, pain may also present in the left lower quadrant (LLQ) of the abdomen.[1,2,4,7]

Patients with a retrocecal appendix are more likely to have positive findings on rectal and/or pelvic examination than on abdominal examination. However, distinguishing tenderness of pelvic origin from that of appendicitis may be difficult in female patients. In older and debilitated patients, appendicitis can present with atypical symptoms, such as diffuse abdominal discomfort or a lack of leukocytosis. Early features may also be nonspecific or subtle, including flatulence, diarrhea, acid reflux, bowel irregularities, and even generalized restlessness.[1,2]

The clinical features of appendicitis in teenagers are similar to those in adults. Information regarding menstrual history and sexual activity can be helpful in distinguishing gynecologic conditions from appendicitis in postmenarchal girls.[6]

Commonly described physical signs include McBurney's point tenderness (3.5 to 5 cm from the anterior superior iliac spine [ASIS] along a line to the umbilicus); Rovsing's sign, which refers to pain in the RLQ with palpation of the LLQ (also called indirect tenderness or referred pain); Obturator sign (pain on flexion and internal rotation of the right hip), associated with pelvic appendicitis; Psoas sign (pain with passive extension of the right hip), associated with retrocecal appendicitis; Iliopsoas sign (pain on

raising the right leg), also typically seen in retrocecal appendicitis; and rebound tenderness (elicited by steady pressure on the RLQ for 10 to 15 seconds followed by sudden release, considered positive if pain increases on release). Some clinicians also use Dunphy's sign (intensified abdominal pain with coughing or any activity that increases intra-abdominal pressure) to assess suspected appendicitis.[1,3,4,6,7]

Because classic symptoms and signs are often absent, diagnosing appendicitis in children is frequently challenging, and clinical findings are often obscured by other conditions. Signs commonly observed in adults, such as the obturator, Rovsing, and iliopsoas signs, may be difficult to elicit in toddlers. However, the absence of these classic signs should not prevent the clinician from considering a diagnosis of acute appendicitis. These signs have high specificity for acute appendicitis in children from toddler age to early adolescence.[6,7,19]

Appendicitis in neonates is rare. In suspected neonatal appendicitis, clinicians should evaluate the possibility of Hirschsprung disease, although this condition is also uncommon. Case reports of neonates with appendicitis mostly describe abdominal distension, vomiting, and anorexia as the most commonly reported findings. These symptoms are nonspecific and overlap with other more prevalent neonatal surgical conditions, particularly volvulus and necrotizing enterocolitis (NEC).[6]

Appendicitis is also uncommon in infants and preschool children. The predominant physical findings leading to the suspicion of appendicitis are fever and diffuse abdominal tenderness with rebound or muscle guarding. In addition, irritability, grunting respirations, difficulty with or refusal to ambulate, and right hip discomfort may be present. The rates of perforation and even peritonitis are high in this age group, consistent with the frequent occurrence of rebound or diffuse tenderness and guarding. Historical findings are often nonspecific, such as fever, vomiting, and abdominal pain, all of which may also occur in other surgical conditions, such as intussusception. Diarrhea is also relatively common, making acute appendicitis difficult to distinguish from other conditions in this age group, such as acute gastroenteritis. Extensive inflammation of the rectosigmoid colon or irritation from a nearby hip infection may contribute to diarrhea as part of the presenting symptoms of acute appendicitis.[6,19]

A careful abdominal examination is essential for the diagnosis of pediatric acute appendicitis, despite its limitations. Analgesia proportional to the level of pain may be administered initially to facilitate examination of children with suspected appendicitis, including intravenous (IV) opioid medications if necessary. Analgesics in pediatric patients may actually support prompt diagnosis by making physical examination and diagnostic imaging easier to perform. Some studies in children have shown that IV opioid administration for pain control does not significantly affect the diagnosis of appendicitis nor have any notable adverse effects on surgical management. In children, rectal examination does not provide additional information regarding appendicitis.[6,7,19]

Appendicitis in pregnant patients often presents atypically, especially in late pregnancy, with symptoms such as heartburn, bowel irregularity, flatulence, restlessness, or diarrhea. Rectal or vaginal examination in these patients is more likely to elicit pain than abdominal examination. The position of the appendix shifts upward by several centimeters due to the enlarging uterus, so in the third trimester, pain may occur in the mid-abdomen or even the upper right quadrant (URQ). McBurney's point tenderness is rarely observed during pregnancy because the gravid uterus elevates and displaces the anterior abdominal wall away from the inflamed appendix. Rebound tenderness or guarding is also less pronounced in pregnant patients because direct contact between the site of inflammation and the parietal peritoneum is limited. The gravid uterus may also restrict contact between the omentum and the inflamed appendix.[3,5,9,17,18]

Laboratory Aspect of Diagnostic Examination

Laboratory tests should not be used in isolation to replace history taking or physical examination for the diagnosis of appendicitis. Evaluation should include a white blood cell (WBC) count with differential, serum C-reactive protein (CRP), and a pregnancy test in women of reproductive age to help rule out ectopic pregnancy.[2,3,6,7,9]

Mild leukocytosis (WBC count >10,000 cells/μL) is observed in approximately 80% of patients with acute appendicitis (14,500 ± 7,300 cells/μL). Although an elevated C-reactive protein (CRP) level occurs in appendicitis, it is a nonspecific marker of inflammation. The specificity for appendicitis increases to approximately 90% when

both WBC and CRP are elevated, but sensitivity remains low at around 40%.[1,2,3,4,6,10]

The finding that either the WBC or the absolute neutrophil count (ANC) is elevated in approximately 96% of children with acute appendicitis is nonspecific, since many other conditions can mimic acute appendicitis (e.g., streptococcal pharyngitis, pneumonia, pelvic inflammatory disease [PID], or gastroenteritis).[6]

WBC is not a particularly useful test in pregnant patients. Mild leukocytosis can be a normal finding in pregnant patients, whether or not appendicitis is present. WBC counts may be as high as 16,500 cells/µL in the third trimester and rise up to 28,500 cells/µL during labor, often with a slight left shift.[3,5,9]

Urinalysis is typically performed in children to identify alternative conditions, such as urinary tract infection (UTI) or nephrolithiasis, rather than to diagnose acute appendicitis. Some patients, both children and adults, with acute appendicitis may develop pyuria (bacteria are not usually detected in a clean-catch specimen), and some may have hematuria due to appendiceal irritation of the ureter or bladder. This occurs when the tip of the inflamed appendix is in contact with the bladder or near the ureter.[3,6,10]

Radiologic Aspect of Diagnostic Examination

Clinical examination is primarily used to diagnose acute appendicitis. Imaging modalities may not be necessary when the diagnosis is clear, but they are used to improve the specificity of a suspected diagnosis. Plain abdominal X-ray is generally not helpful for establishing the diagnosis of appendicitis and should not be performed routinely. Abdominopelvic CT (computed tomography) is the preferred imaging test for suspected appendicitis in adults. CT can be performed quickly and is usually better tolerated by patients than ultrasound (which requires compression) or MRI (which requires the patient to remain in a confined space for an extended period).[1,2,4,7,20]

The drawbacks of CT include exposure to ionizing radiation and the use of iodinated contrast. However, 10% to 20% of examinations may still result in nonvisualization of the appendix (a nondiagnostic result). Overall, the sensitivity of CT is 85–94% and specificity is 94–97%. CT imaging can reduce the negative appendectomy rate in adult women compared with men (21% versus 8%). The main findings of appendicitis on CT are inflammation in the RLQ, a nonfilling tubular structure enlargement, and/or an appendicolith.[2,3]

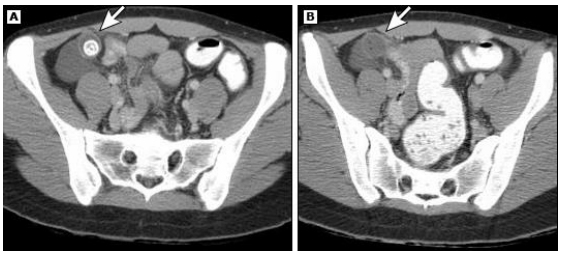

Figure 1. Acute appendicitis. Pelvic images from a CT scan with intravenous (IV) and oral contrast show a thickened appendix (arrow) containing an appendicolith and adjacent fluid indicating inflammation.[1]

The preferred imaging test in children with suspected appendicitis is abdominal ultrasound (US). If the appendix is visualized on US and shows no signs of appendicitis, then CT or magnetic resonance imaging (MRI) is not required. However, when a clinical diagnosis of appendicitis cannot be established and concerning clinical features persist, repeat US (serial examination over 12 to 24 hours) may be performed.[6,7,11,20,21]

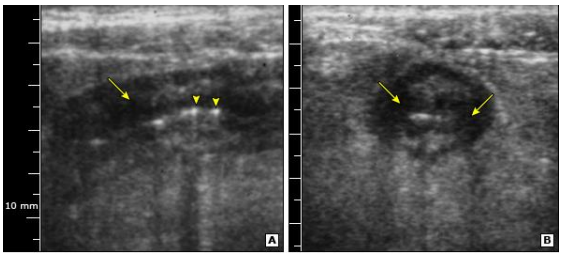

Figure 2. Acute appendicitis. Grayscale ultrasound of the appendix is shown in the longitudinal (A) and transverse (B) planes. The appendix is noncompressible, with a diameter of approximately 2 cm. The echogenic mucosal and submucosal layers of the wall are disrupted (arrows).

Approximately 50% to 85% of normal appendices are not visualized, so nondiagnostic ultrasound examinations for acute appendicitis remain common. Sonographic features of acute appendicitis include a noncompressible appendix with a double-wall thickness diameter >6 mm, focal tenderness over the appendix with compression, appendicolith, increased echogenicity of inflamed periappendiceal fat, and fluid in the RLQ.[1,2,7,20,22,23]

Ultrasound (US) or MRI may be performed in younger women (<30 years old) who are particularly concerned about radiation exposure, as well as in pregnant patients. Another advantage of US is that it can be performed at the bedside. However, US has lower diagnostic accuracy than CT or MRI. The results of US are highly variable and depend on patient-specific factors (e.g., body habitus, discomfort and cooperation, appendix position relative to the bowel) and operator-specific factors (e.g., experience).[1,2,3]

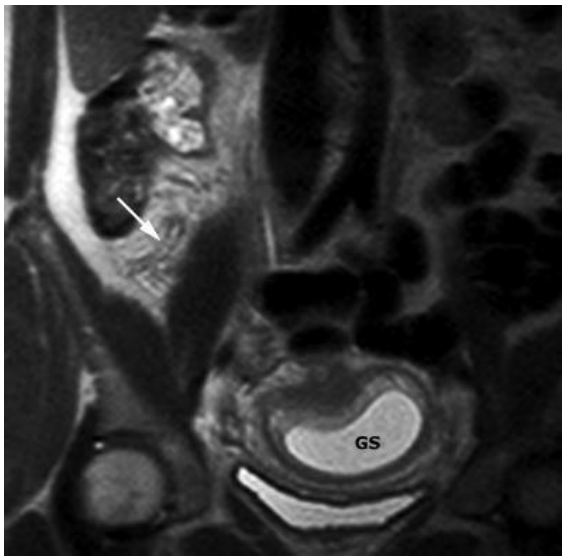

Figure 3. T2-weighted MRI of a woman at 2 months of gestation with appendicitis. The appendix was fluid-filled and measured 0.7 cm in diameter (arrow). The gestational sac (GS) is shown inferiorly in the pelvis.[1]

For pregnant women whose US results are inconclusive for appendicitis, MRI is the preferred next test because it avoids the ionizing radiation of CT and is relatively cost-effective. MRI in pregnant patients is usually performed without contrast. MRI is superior to ultrasound, with a high sensitivity of 95%–96% and specificity of 97%–99%. However, MRI may be intolerable for claustrophobic patients, children, or those in significant pain, since the patient is typically required to lie still in the magnet for more than 10 minutes. Common relative contraindications to MRI include cardiac pacemakers and implanted metallic surgical devices.[2,3,5,9,10,16,17,18,24]

The rate of nondiagnostic CT examinations remains high, with 20–40% of normal appendices not visualized. If clinical suspicion of acute appendicitis is high but imaging is negative, surgery is indicated. Surgery is also warranted in pregnant patients with findings suggestive of appendicitis despite inconclusive US results.[2,3]

DIFFERENTIAL DIAGNOSIS

Perforated appendix is a major consideration in the differential diagnosis of acute appendicitis. Within less than 24 hours after the onset of symptoms, nearly 20% of patients may develop perforation. If a patient has a temperature exceeding 39.5°C, clinicians should consider perforated appendix rather than simple acute appendicitis. The same applies to a WBC count greater than 15,000 cells/µL or if imaging reveals a fluid collection in the RLQ.[1]

Other differential diagnoses include cecal diverticulitis, Meckel's diverticulitis, acute ileitis, Crohn's disease, tubo-ovarian abscess (TOA), pelvic inflammatory disease (PID), ruptured ovarian cyst, mittelschmerz, ovarian or fallopian tube torsion, endometriosis, ovarian hyperstimulation syndrome, ectopic pregnancy, acute endometritis, renal colic, testicular torsion, and epididymitis.[1,3,4,18]

Numerous conditions can mimic acute appendicitis in children, including bowel obstruction, intestinal malrotation, intussusception, Crohn's disease, lymphoma, cystic fibrosis, ovarian torsion, ectopic pregnancy, testicular torsion, omental torsion, hemolytic uremic syndrome, diabetic ketoacidosis, primary peritonitis, pneumonia, streptococcal pharyngitis, urinary tract infection (UTI), nephrolithiasis, sickle cell disease, immunoglobulin A vasculitis (IgAV; Henoch-Schönlein purpura [HSP]), pelvic inflammatory disease (PID), ovarian cyst, mittelschmerz, gastroenteritis, and mesenteric lymphadenitis.[6,7,20]

The differential diagnosis of suspected acute appendicitis in pregnant patients includes conditions typically considered in nonpregnant individuals, such as ectopic pregnancy, indigestion, round ligament pain, pyelonephritis, preeclampsia, abruptio placentae, uterine rupture, HELLP (Hemolysis, Elevated Liver enzymes, Low Platelets) syndrome, and ovarian vein thrombophlebitis (OVT).[3,18]

THERAPY (MANAGEMENT)

Open appendectomy was the only standard treatment for acute appendicitis for more than 10 decades. Modern approaches for acute appendicitis

are more advanced and less invasive: laparoscopic appendectomy has surpassed open appendectomy in usage. Even some patients with perforated appendicitis may benefit from initial antimicrobial therapy followed by interval appendectomy, and several studies have suggested that it is possible to manage uncomplicated acute appendicitis nonoperatively with antimicrobials alone in otherwise healthy patients.[25]

Nonoperative management (NOM) is a strategy in which patients receive antimicrobials with the aim of avoiding surgery. Surgical intervention is reserved for patients who fail antimicrobial therapy or experience a recurrence. NOM is not a new approach, as it was first formally introduced by Harrison in 1953. The use of NOM has increased since the outbreak of COVID-19 and continues to the present. NOM may offer some benefits, such as faster recovery and fewer days away from work or other activities, but patients must be informed and comply with the understanding that there is a higher risk of disease progression despite antimicrobials, infection recurrence, or even a missed neoplasm.[25,26,27,28,29,30]

NOM is suitable for patients experiencing a first episode of acute appendicitis who have a clinical diagnosis of uncomplicated appendicitis, without physical signs of diffuse peritonitis or imaging evidence of large abscess, phlegmon, perforation, or tumor. Relative contraindications to NOM include patients with delayed response to antimicrobials, those with an appendicolith, and older patients due to a higher likelihood of underlying malignancy. NOM is contraindicated in patients with peritonitis, sepsis, pregnancy, immunocompromise, or a history of inflammatory bowel disease, as it has not been adequately studied and there is insufficient evidence that NOM is superior to surgery.[23,25,26,27,31,32,33]

NOM is also useful in patients with a longer duration of symptoms and the presence of phlegmon or abscess, due to dense adhesions and inflammation. NOM during the initial hospitalization allows the locally inflamed appendix to resolve, and interval appendectomy can then be performed at a lower risk. Fortunately, many of these patients respond to initial NOM because the appendiceal process has already been "walled off."[19,25,34]

Patients should be closely monitored and hospitalized during the period of NOM. Clinical or radiographic treatment failure, evidenced by bowel obstruction, sepsis, or persistent pain, fever, or leukocytosis, requires prompt surgical management. If fever, tenderness, and leukocytosis improve, nutritional intake can be gradually advanced, typically within 3 to 5 days. Patients who respond well to initial antimicrobial therapy can be discharged home with oral antimicrobials to complete a 7- to 10-day course and return for follow-up in 1.5 to 2 months.[25,28]

Older adults (over 65 years old) tend to have a reduced inflammatory response, exhibit less frequent leukocytosis, and show fewer abnormal findings on history and physical examination. For these reasons, older adults often delay seeking medical care and, as a result, have a significantly higher rate of perforation. They may also have comorbid cardiac, pulmonary, or renal conditions that can worsen their overall status. Additionally, an elongated sigmoid colon in older adults can cause right-sided pain from sigmoid pathology, making CT imaging important to improve diagnostic accuracy. More than 28% of appendiceal cancers in patients over 65 years were initially misdiagnosed as inflamed appendicitis. Therefore, NOM should be offered to older adults more cautiously and only with follow-up imaging and interval appendectomy as part of management.[25]

Immunocompromised patients are more susceptible to infection, and their immune response is often suppressed due to immunosuppressive drugs or underlying illness. As a result, these patients may exhibit only mild tenderness on examination, which is not typical for appendicitis. Furthermore, supportive laboratory tests may not reflect the expected degree of inflammation. The extended differential diagnosis includes, but is not limited to, opportunistic infections (e.g., mycobacterial), viral infections (e.g., cytomegalovirus), fungal infections, secondary malignancies (e.g., lymphoma and Kaposi's sarcoma), and typhlitis (neutropenic enterocolitis). Due to this broad differential, diagnosis is often delayed, surgical evaluation may be postponed, and the risk of perforation increases. If appendicitis is strongly suspected, physicians should not delay surgical intervention, as there is no absolute contraindication to surgery in immunocompromised patients. NOM is not routinely recommended in this group.[25]

There is broad consensus that most children with appendicitis require appendectomy. However,

if there are no signs of perforation on examination, the child may be a candidate for NOM. The rate of appendiceal malignancy in children is very low (approximately 0.3%), which further supports consideration of NOM for pediatric patients. NOM may be an option for children who can verbally describe their symptoms, have a reliable and reproducible abdominal examination, meet strict criteria, and undergo shared decision-making between the supervising pediatric surgeon and the parent or primary caregivers. NOM may be most appropriate in children at low risk for perforation and those with comorbidities that increase the risk associated with appendectomy or general anesthesia.[19,21,22,31,32,35]

Clinicians should exclude NOM in pediatric patients with appendicitis if there are signs of suspected perforation, including abdominal tenderness for ≥48 hours, WBC count >18,000/μL, elevated CRP, presence of appendicolith on imaging, appendix diameter >1.1 cm, or preoperative concern for rupture based on clinical findings. Additionally, appendicolith detected on imaging has been shown to be the strongest risk factor for NOM failure. Children undergoing NOM have a higher rate of emergency department visits and hospital admissions. The success rate of NOM in pediatric patients is approximately 67% to 91%.[11,12,13,19,21,22,31,32,35]

The standard treatment of acute appendicitis in pregnancy remains surgical management, with laparoscopic appendectomy preferred over open appendectomy due to lower wound infection rates and shorter hospital stays. NOM is not recommended because it is associated with both short- and long-term failure, and limited outcome data are available for pregnant patients. Some studies report increased risks (approximately 23%) with antibiotic-only management, including preterm premature rupture of membranes and preterm labor or delivery (15–45%). More than half of patients ultimately require urgent surgery. Importantly, the rate of fetal loss is increased when the appendix perforates (over 35%).[3,5,9,14,15,16,18]

Although antibiotic-only treatment in pregnancy is not the standard of care, pregnant patients for whom antibiotics may be appropriate include those who refuse surgery or patients in remote areas where timely surgical intervention or expertise may not be available. Physicians must also consider the safety of antibiotic use with respect to the first and second trimesters, as some agents may cause premature birth or miscarriage. The choice of strategy is based on the patient's clinical condition and preferences, gestational age, and the surgeon's level of experience. Considering gestational age, NOM is more frequently chosen than appendectomy in the first and third trimesters. When the diagnosis is sufficiently certain, either open or laparoscopic appendectomy can be considered. Some studies report that laparoscopic appendectomy is preferable in the first and second trimesters, while open appendectomy is preferred in the third trimester, primarily due to fetal safety.[3,5,9,17,24,36,37]

NOM should not be promoted solely as a cost-saving measure or considered routine in resource-limited settings for several reasons: lack of advanced imaging, inadequate follow-up, or limited surgical expertise. In resource-limited settings, shared decision-making is preferable to help patients choose between antibiotics and appendectomy based on their individual circumstances, characteristics, and preferences. It should also be noted that NOM may increase complications and prolong hospitalization.[23,25,26,27,28,30,35,38,39]

The success of NOM is defined as the resolution of pain, fever, leukocytosis, and anorexia within 1 to 2 days after initiating antibiotics. The response to antibiotics may be slower in adults aged 45 years or older and in patients with appendicoliths, extraluminal fluid or air, fever, elevated inflammatory markers, or symptoms lasting more than 2 days, all of which are associated with appendiceal abscess.[21,25,31,32,34]

The minimum failure rate of NOM is 7%. About 10% to 20% of patients experience failure of NOM within 30 days, 30% to 40% have a relapse within 1 year, and 40% to 50% experience relapse within 5 years. When appendicitis recurs, surgical management is usually performed and may be preferred in adults aged 40 years or older, considering the possibility of malignancy. Repeat antibiotic treatment is an option in pediatric patients, although the failure rate of NOM is slightly higher. The failure rate of NOM in pregnant patients is also considered higher than in adult or pediatric patients, with some studies reporting a success rate of only up to 71%.[9,10,19,25,28,30,34,35,36,40,41,42]

Ramadan et al. propose that abscess formation and appendiceal distension >10 mm are potential

risk factors for recurrent acute appendicitis after successful initial NOM. Consequently, these factors should also be considered when deciding between NOM and surgery. Patients should be informed about these recurrence rates and the possible management strategies before opting for NOM. Some studies recommend close monitoring for 6 months to 1 year to detect recurrences.[33,39,43,44,45,46,47]

In NOM protocols, the choice of anti-microbials is not standardized, but it usually involves initiating IV antibiotics for 24 to 72 hours, followed by oral antibiotics to complete a total course of 7 to 10 days. Adequate coverage can be achieved with piperacillin-tazobactam 3.375 g IV every 6 hours, or a combination of metronidazole 500 mg IV every 8 hours with cefazolin 1–2 g IV every 8 hours, cefuroxime 1.5 g IV every 8 hours, ceftriaxone 2 g IV every 24 hours, cefotaxime 2 g IV every 8 hours, or ciprofloxacin 400 mg IV every 12 hours. The preferred choice of anti-microbials in pediatric patients is generally the same as in adults. Penicillins, beta-lactam/beta-lactamase inhibitors, and cephalosporins are also widely considered safe for use in pregnant patients.[9,10,21,22,25,30,48,49]

Before surgery, patients should receive adequate hydration with IV fluids, correction of electrolyte abnormalities, pain control, and perioperative antibiotics. Prophylactic antibiotics typically include cefazolin 2 g IV, with or without metronidazole 500 mg IV. Postoperative antibiotics are usually unnecessary. For patients allergic to penicillins or cephalosporins, clindamycin 900 mg IV or vancomycin 15 mg/kg IV can be used. The recommended antibiotic choices in pediatric patients are the same as in adults.[10,22,25,31]

A postponement of up to 1 day (24 hours) before surgery in patients with simple appendicitis did not result in a heightened risk of perforation or other complications compared with surgery within 8 hours. Deferring appendectomy for more than 2 days may increase surgical site infections (SSI) and other complications. This also applies to pediatric patients. The use of certain anticoagulants, such as aspirin or clopidogrel, should not delay surgery, whereas the use of direct oral anticoagulants should be stopped 24 to 48 hours before surgery.[12,25,31,50]

COMPLICATIONS

Acute appendicitis that is left untreated can result in severe complications, such as diffuse peritonitis and sepsis, which can lead to death (0.28%). The most prominent complication of appendectomy is surgical site infection (SSI). Other common complications of appendectomy include hematomas, postoperative pain, adhesions, and bowel obstruction. Long-term complications of appendectomy include incisional hernia. Recurrent episodes of appendicitis can occur in up to 49% of patients managed with nonoperative management (NOM). Stump appendicitis is a form of recurrent disease that is associated with incomplete removal of the appendix, leaving an excessively long appendiceal stump after surgery, either open or laparoscopic. This is particularly common in cases of perforated appendicitis. This complication can be minimized by cross-cutting the appendix no more than 50 mm from its junction with the cecum and ensuring complete removal. In cases of stump appendicitis, stump resection can be performed surgically, either open or laparoscopically; however, it often requires a longer bowel resection for management.[4,7,8,21,25,45]

Complications such as wound infection or abscess in pediatric patients occur in approximately 1% to 5% of cases. The usual symptoms that can be identified include fever, anorexia, inability to tolerate a normal diet, and pain in and around the incision site. Some patients may also experience intestinal dysfunction, including paralytic ileus, constipation, or mechanical obstruction due to adhesions.[7,12,22,26,30,31,40]

In general, surgical management performed during pregnancy does not appear to adversely affect the offspring. Risk factors significantly associated with adverse obstetric outcomes include cervical abnormalities, preterm labor during the current pregnancy (but prior to surgery), vaginitis or vulvovaginitis, and sepsis.[3,4]

PROGNOSIS

The mortality associated with acute appendicitis is low. In developed countries, the death rate is less than 0.24%, whereas in economically developing nations, the rate is higher, up to 4%. Risk factors for mortality include age >80 years, immunosuppression, advanced cardiovascular disease, previous episodes of suspected appendicitis, prior treatment with antimicrobials, and a pathologic report of perforation. Delaying surgery while administering antimicrobials does not increase the

risk of perforation, which is a major patient concern and limitation of nonoperative management (NOM).[4,25]

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