Chapter 9

ACUTE APPENDICITIS

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The cecal appendix is a closed-ended tube located in the cecal region. Acute appendicitis is characterized by luminal obstruction of the appendix, often caused by mucosal inflammation, lymphoid hyperplasia, or fecalith. This condition is considered one of the most common surgical emergencies worldwide, affecting both adults and children. The luminal obstruction promotes bacterial proliferation,

leading to organ distension, increased intraluminal pressure, and potentially progressing to suppurative transmural inflammation, infarction, and perforation. The inflamed appendix can be isolated by the omentum and surrounding viscera, forming an inflammatory mass. Conversely, perforation can result in generalized peritonitis or an isolated appendicular abscess (Gutierrez *et al.*, 2022; Jumah; Wester, 2022; Juremeira *et al.*, 2022; Stringer, 2017).

It is estimated that about 8% of the world's population undergoes surgical procedures to treat this condition throughout their lives, and approximately 30% of children with acute abdominal pain referred to pediatric surgical services have acute appendicitis. Diagnostic methods will be analyzed, emphasizing traditional and advanced techniques for accurate and early detection, as well as common signs and symptoms associated with the condition. Finally, the importance of effective treatment will be discussed, including the timing and modalities of surgical interventions, as well as new tools for managing appendicitis (Jumah; Wester, 2022; Stringer, 2017).

Technical and instrumental advancements have consolidated laparoscopic appendectomy as the current standard treatment. Studies show that in adults, this approach results in a statistically significant reduction in wound infection incidence, hospital stay length, and postoperative complications, as well as a quicker return to work; however, these conclusions do not apply to the pediatric population (Wagner; Tubre; Asensio, 2018). Additionally, non-operative treatment of uncomplicated acute appendicitis, including antibiotic therapy, has been proposed as an effective and safe primary option, with a lower complication profile and reduced cost, promising to avoid unnecessary surgeries in both adults and children (Jumah; Wester, 2022).

EPIDEMIOLOGY

Acute appendicitis is one of the most common causes of abdominal pain, affecting about 10% of the population, with a peak incidence in the second or third decade of life, especially during the summer. In developed countries, the rate is 100 cases per 100,000 inhabitants per year, resulting in more than 300,000 appendectomies annually in the United States, of which less than 10% involve healthy appendices (Juremeira *et al.*, 2022; Snyder; Guthrie and Cagle, 2018). The prevalence is higher in young adults, particularly in men, with a lifetime risk of 8.6% for them and 6.7% for women. Despite this, appendectomies are performed twice as often in women, even with lower prevalence (Snyder; Guthrie and Cagle, 2018). Although the incidence of appendicitis decreases with age, the risk of perforation and neoplasia increases (Perez; Allen, 2018).

Perforation is the most concerning complication of appendicitis, potentially causing abscesses, peritonitis, bowel obstruction, fertility issues, and sepsis. The perforation rate in adults ranges from 17% to 32%. In children, a delay of more than 48 hours from symptom onset to diagnosis and surgery increases the perforation rate and hospital stay length

(Snyder; Guthrie; Cagle, 2018).

Appendicitis is the most common non-obstetric surgical emergency during pregnancy, with an incidence of 6.3 per 10,000 pregnancies in the pre-partum period, increasing to 9.9 per 10,000 after delivery. In the United States, more than 300,000 appendectomies are performed annually, with less than 10% resulting in the removal of a normal appendix (Snyder; Guthrie and Cagle, 2018).

Appendix neoplasia is more common in patients with complicated appendicitis. In cases treated with interval appendectomy, the rate of mucinous neoplasia reaches 55%. Interval appendectomy is an alternative strategy, especially recommended for patients over 40 years old, aiming to reduce the risk of appendix neoplasia, which can occur in up to 12% of cases treated this way (Perez; Allen, 2018).

Between 1973 and 2004, 2,791 patients with malignant appendix neoplasms were studied. Adenocarcinomas were the most frequent, accounting for 65.4% of cases. During this same period, there was a 260% increase in appendix carcinoma rates. The 5-year survival rate for these patients was 46.5%. For mucinous cystadenocarcinoma, the 5-year survival rate was 59% across all stages, while for signet ring cell tumors, it was 20.3%. Goblet cell carcinoid tumors, which represent less than 5% of primary appendix tumors and are composed of a mix of goblet and neuroendocrine cells, have a 5-year survival rate ranging from 40% to 75%, which is lower than that of well-differentiated NETs (Teixeira *et al.*, 2017).

The incidence of appendicitis in the elderly shows a lower preoperative diagnosis rate, with an accuracy of 64% compared to 78% in younger age groups. Mortality in the elderly reaches 8%, while in younger patients it ranges from 0% to 1%. Furthermore, the rate of complicated appendicitis, with perforation or abscess, is higher in the elderly, varying from 18% to 70%, compared to 3% to 29% in younger patients. Postoperative complication rates are also higher in elderly patients, with increased postoperative mortality and morbidity (Fugazzola *et al.,* 2020).

DIAGNOSIS

Early diagnosis of acute appendicitis must be performed accurately and efficiently to reduce morbidity and mortality and minimize the risk of complications such as perforation, generalized peritonitis, and sepsis (Snyder; Guthrie and Cagle, 2018). Acute appendicitis is considered a challenge for the healthcare system due to its high global prevalence. Thus, early diagnosis is crucial to reduce the chances of complications and the high costs associated with hospitalizations (Juremeira *et al.*, 2022).

History taking and physical examination, along with laboratory findings, remain the basis for avoiding late diagnosis (Bom *et al.*, 2021). Clinically, periumbilical abdominal pain that intensifies over 24 hours and migrates to the right iliac fossa is common in

more than half of patients with acute appendicitis. Other symptoms include colic, nausea, vomiting, anorexia, and fever. Changes in bowel habits, such as constipation and diarrhea, are frequent, as well as urinary changes when the appendix is located near the bladder (Juremeira *et al*., 2022).

The pain caused by localized peritonitis can worsen with movements such as coughing or driving on bumpy roads (Baird *et al*., 2017). Fever and anorexia arise as the infection evolves from a localized inflammatory process to a systemic inflammatory process. The disease can progress to perforation and peritonitis within 2 to 3 days after symptom onset. If the perforation occurs in an area of the abdomen confined by other intestinal loops, mesentery, or omentum, the infection remains localized in the lower right quadrant, resulting in continuous pain in that region without signs and symptoms of peritonitis. Occasionally, a mass may be palpated (Wagner; Tubre and Asensio, 2018).

There are three well-described anatomical positions for the appendix: ascending appendix, iliac appendix, and pelvic appendix. When the appendix is located in the retrocecal position, local symptoms tend to be mild or even absent. Pelvic appendices can cause pain in the suprapubic region, urinary symptoms, or pain when defecating if they are close to the rectum (Wagner; Tubre and Asensio, 2018). The variable position of the appendix results in different clinical manifestations, making diagnosis challenging, especially in pregnant women and women with gynecological complaints such as pelvic inflammatory disease. In children, however, the absence or reduction of bowel sounds, psoas sign, obturator sign, and Rovsing's sign are more reliable for diagnosing acute appendicitis.

In adults, the main signs and symptoms of acute appendicitis include pain in the lower right quadrant, abdominal rigidity, and pain radiating from the periumbilical region to the iliac fossa. In the elderly, clinical characteristics may be more silent, often due to the formation of an appendicular abscess or obstruction by perforation (Snyder; Guthrie and Cagle, 2018; Juremeira *et al*., 2022). Specific physical examination findings for acute appendicitis include psoas sign, obturator sign, and Rovsing's sign (Snyder; Guthrie; Cagle, 2018). Abdominal examination usually reveals tenderness at McBurney's point, near the right iliac fossa (Wagner; Tubre and Asensio, 2018).

Blumberg's sign or rebound tenderness is provoked by gentle percussion or the rapid release of pressure at McBurney's point, indicating inflammatory irritation of the parietal peritoneum. Rovsing's sign involves palpation of the left iliac fossa that causes pain in the right iliac fossa. Psoas sign is positive when the appendix is located near the psoas or internal obturator muscles, inducing contraction of these muscles by flexing the hip or external rotation, respectively, causing intense pain. Obturator sign involves pain during passive internal rotation of the flexed thigh. Dunphy's sign is a useful technique in children, which includes making them jump, cough, or shake the bed. Rectal examination can provoke pain when palpating an inflamed pelvic appendix near the rectum (Wagner; Tubre and Asensio, 2018).

Laboratory tests alone have low sensitivity and specificity, but combined with patient

clinical data, they increase diagnostic accuracy, helping to exclude other pathologies and support the diagnosis of acute appendicitis (Hoffmann; Anthuber, 2019). The suspicion of appendicitis increases when there is an elevation in the white blood cell count, C-reactive protein concentration, granulocyte count, or the proportion of polymorphonuclear cells (Baird *et al.*, 2017). Other markers such as interleukins, procalcitonin, calprotectin, bilirubin, fibrinogen, and the APPY1 test have been studied. In cases of perforation, bilirubin should be considered, as studies show a specificity of 86% and sensitivity of 70%, compared to serum bilirubin levels in patients without perforation (Perez; Allen, 2018).

Urine examination can also help determine if the complaints and clinical findings are of urological origin. In women of childbearing age, it is important to rule out pregnancy as the cause of symptoms and consider alternative diagnoses such as renal colic or urinary tract infection. Due to the proximity of the appendix to the urinary tract, about 40% of patients with acute appendicitis may present leukocytes in the urine (Wagner; Tubre and Asensio, 2018).

Although the diagnosis of acute appendicitis is based on clinical history and physical examination, imaging exams such as ultrasound, abdominal computed tomography (CT), and magnetic resonance imaging (MRI) are frequently used (Perez; Allen, 2018). The more advanced the inflammatory process, the more evident the appendicitis will be in any of the imaging modalities. Each method has its advantages and disadvantages in terms of sensitivity, specificity, costs, and exposure to ionizing radiation (Baird *et al.*, 2017).

Computed tomography is highly sensitive (97-100%) and has a specificity of 90%, being considered the best diagnostic option despite its limitations in terms of cost, availability, and radiation exposure (Juremeira *et al.*, 2022; Wagner, Tubre and Asensio, 2018). It is contraindicated in pregnancy and relatively contraindicated in young people due to the increased risk of neoplasms. CT is useful for identifying inflammation, precise location, and excluding differential diagnoses, although it is unreliable for determining appendicular perforation (Hoffmann; Anthuber, 2019; Baird *et al.,* 2017). CT can define the diameter of the appendix, indicating appendicitis if greater than 6 mm, as well as the presence of fecaliths and/or periappendicular inflammation (Perez; Allen, 2018). Studies indicate that low-dose contrast-enhanced CT has comparable accuracy to normal CT and should be preferred. CT protocols generally use helical scanners with a slice thickness of 3 to 5 mm and an interval of 3 to 10 mm (Bom *et al.*, 2021).

Ultrasonography has a sensitivity of 80-94% and a specificity of 89-95%, being a non-invasive and economical option, but less accurate in obese patients and dependent on the operator's skill. It is safe for use in children and pregnant women (Juremeira *et al.*, 2022; Wagner; Tubre and Asensio, 2018). In sexually active women, transvaginal ultrasonography can be useful for visualizing gynecological organs. The accuracy of results depends on the operator's skill, with a specialist, such as a consultant radiologist, more likely to provide an accurate diagnosis (Baird *et al.*, 2017). In USG, it is important to mention whether the appendix is fully visualized, its diameter, and the state of its wall, as well as indirect signs of appendicitis such as free fluid, fat stranding, and small bowel dilation in the lower right

abdomen.

The diagnostic accuracy of magnetic resonance imaging is comparable to computed tomography and superior to ultrasonography, with a sensitivity of approximately 97% and specificity of about 97%, without the use of ionizing radiation. However, its cost is generally higher compared to CT and the procedure time is longer, making it not the first choice (Wagner; Tubre; Asensio, 2018; Perez; Allen, 2018). MRI or ultrasound techniques are more commonly used in pregnant women and children to avoid excessive radiation exposure (Hoffmann; Anthuber, 2019).

The Alvarado score, pediatric appendicitis score, and appendicitis inflammatory response score use clinical and laboratory findings to classify patients into low, moderate, or high risk, helping to make a more accurate diagnosis, as illustrated in Table 1 (Snyder; Guthrie and Cagle, 2018).

Table 1: Alvarado Score for Diagnosis of Acute Appendicitis

Clinical Criterion	
Symptoms	**Score**
Migratory pain to the right iliac fossa	1
Anorexia	1
Nausea or vomiting	1
Signs	
Pain on palpation in the right iliac fossa	2
Rebound (Blumberg)	1
Fever (>37.5°C)	1
Laboratory Findings	
Leukocytosis (>10,000/mm³)	2
Left shift of neutrophils	1
Total	10

Source: Snyder; Guthrie; Cagle, 2018.

Interpretation of the Score:

- 1-4: Low probability
- 5-6: Moderate probability
- 7-10: High probability

TREATMENT

Open appendectomy was described by Charlie McBurney in 1891, and the technique has remained largely unchanged (Téoule *et al.*, 2020). Regarding the choice

between conventional and laparoscopic surgery, numerous comparative studies have been conducted. For example, a meta-analysis of 33 prospective randomized controlled trials involving over 3,500 patients demonstrated that laparoscopic appendectomy in adults resulted in a statistically significant reduction in wound infection incidence, hospital stay length, and postoperative complications, as well as an earlier return to work, although with a longer operation time. However, this conclusion did not apply to the pediatric population (Wagner; Tubre and Asensio, 2018).

The Children's Interval Appendectomy (CHINA) study, a randomized multicenter clinical trial, addressed this issue in pediatric patients. Patients were randomized into two groups: one received antibiotic treatment and the other underwent appendectomy 66 days after treatment allocation. Appendectomy was associated with low complications and a high recovery rate; however, 6% of patients had severe complications and one patient required multiple surgeries (Jumah; Wester, 2022). Current evidence is insufficient to detect any significant advantage of antibiotic treatment compared to surgical treatment. Thus, surgery remains the treatment of choice for uncomplicated acute appendicitis in children (Teixeira *et al*, 2017).

Intravenous resuscitation is generally performed with normal saline solution, considering the patient's fluid deficit based on clinical signs of dehydration and tissue perfusion. In patients with generalized peritonitis, plasma electrolytes should be checked and fluids and electrolytes adjusted accordingly (Teixeira *et al*, 2017). Antibiotics are administered to prevent intra-abdominal abscess formation, wound infection, and sepsis. Antibiotic therapy, with cefuroxime plus metronidazole or amoxicillin/clavulanic acid, is initiated immediately after the diagnosis of acute appendicitis and always before surgery (Stringer, 2017).

Isolated antibiotic therapy, covering Gram-negative and anaerobic bacteria, has been increasingly used due to its potential to significantly reduce the costs associated with surgery (Iamarino *et al*, 2017). Given the risks associated with open and laparoscopic appendectomy, antibiotic therapy should be considered an effective option for adults and children. Patient management should always be performed in consultation with the surgical team, according to local hospital protocols and in a shared decision-making process (Snyder; Guthrie and Cagle, 2018).

Emerging evidence indicates that antibiotic therapy can be a first-line option for selected patients with uncomplicated appendicitis. A meta-analysis of five randomized clinical trials compared antibiotic treatments with appendectomy in 980 adults with uncomplicated appendicitis, demonstrating that antibiotic treatment resulted in a reduction in complication rates, fewer medical leaves or disability, and less need for analgesics. However, 40% of patients treated with antibiotics required appendectomy within the following year, compared to 8.5% of those who initially had surgery and needed a second intervention (Snyder; Guthrie and Cagle, 2018).

More recently, a randomized, multicenter, open-label clinical trial with 530 adults

aged 18 to 60 years with uncomplicated appendicitis reported a resolution rate of 73% with ertapenem (Invanz), 1 g per day intravenously for three days, followed by levofloxacin (Levaquin) for seven days, 500 mg per day, plus metronidazole (Flagyl), 500 mg three times a day (Snyder; Guthrie and Cagle, 2018).

Histological examination of the excised appendix is advisable for several reasons. Firstly, the histology should be consistent with the clinical diagnosis. Additionally, other pathologies may occasionally be found, such as carcinoid tumor, granulomas (which can be a feature of Crohn's disease or Yersinia infection), Enterobius vermicularis (pinworm) infestation, and eosinophilic infiltrates (Stringer, 2017).

In managing pain from acute appendicitis, a meta-analysis of nine randomized clinical trials revealed that opioid use did not significantly increase the risk of delayed or unnecessary surgeries in 862 adults and children with acute abdominal pain. Paracetamol and non-steroidal anti-inflammatory drugs should also be considered for pain management in patients with suspected acute appendicitis, especially those with contraindications to opioids (Snyder; Guthrie and Cagle, 2018).

Perforation is the most severe complication of acute appendicitis, potentially causing abscesses, peritonitis, bowel obstruction, fertility issues, and sepsis. Perforation rates among adults range from 17% to 32%, even with increased use of imaging, and can result in longer hospital stays, prolonged need for antibiotics, and more severe postoperative complications. A national prospective study showed that four out of 64 children (6%) with perforated appendicitis were treated with antibiotics due to suspected sepsis, even after surgery. Risk factors for perforation include advanced age, the presence of three or more comorbidities, and male sex. The time between symptom onset and diagnosis and surgery is directly associated with the risk of perforation (Snyder; Guthrie and Cagle, 2018).

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