

Evolution and Current Trends in the Management of Acute Appendicitis



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KEYWORDS

- Acute appendicitis • Alvarado score
- Nonoperative management of acute appendicitis
- Medical imaging in acute appendicitis • Epidemiology of acute appendicitis

KEY POINTS

- Since the first surgical appendectomy in the 18th century the treatment of appendicitis has changed.
- The use of scoring systems has helped refine the diagnosis of acute appendicitis.
- Medical imaging techniques, such as ultrasound, CT scans, and MRI, have assisted in the diagnosis of acute appendicitis.
- Nonoperative management is being investigated and may prove to be acceptable in most cases of acute appendicitis.
- The microbiome of the appendix is being investigated and may prove to have a role in the development of acute appendicitis; treatment in the future may focus on modifying the microbiome.

INTRODUCTION

The appendix is a vestigial organ of dubious utility; its function and normal physiology remain unclear. The appendix is notable in medicine because appendicitis (the inflammatory state of this organ) is the most common indication for emergent surgery

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worldwide¹; it is the most common nonobstetric surgical emergency during pregnancy^{2,3} and it is the most common surgical emergency in childhood.⁴ A small organ located at the base of the cecum, the appendix has a unique position in history, is a medical oddity, and is even the subject of a beloved children's book.

A 27-year-old Leonid Rogozov performed an autoappendectomy on April 30, 1961, while isolated with a team of Soviets on an expedition to the Antarctic.⁵ As medical officer, meteorologist, and driver he was the only one qualified to perform this surgical procedure. After a brief therapeutic attempt at unsuccessful nonoperative management he realized that his survival depended on a surgical intervention. Using his teammates as his surgical team, he directed them to carefully sterilize the instruments required, perform an appropriate surgical wash, and then assist him as he performed his own open appendectomy under local anesthetic. When asked to comment about this in later years Dr. Rogozov is recorded to have replied, "A job like any other, a life like any other."

In 1939, Ludwig Bemelmans published the first in his series of *Madeline* books, a favorite of children, describing the heroine's travails with acute appendicitis.⁶ An additional oddity, Dr Jeffrey Sedlack founded a virtual online museum of the appendix and appendicitis (www.appendicitis.pro).⁷ Because of the prevalence of acute appendicitis, Sir Alexander Cope, in his classic treatise *Early Diagnosis of the Acute Abdomen*,⁸ stated that "appendicitis should never be lower than second" when considering the differential diagnosis of abdominal pain.

Since the first documented appendectomy in 1735 by Claudius Amyand there have been many changes in the management of the appendix and its surgical pathology. The appendectomy performed by Amyand was on an 11-year-old boy with a fecal fistula through an inguinal hernia. After surgical intervention it was noted that the boy had an inguinal hernia that contained the appendix. He had swallowed a pin, and this led to the fistula formation. The eponymous Amyand hernia now defines the condition of an appendix in the inguinal canal.⁹ The French physician, Mestier is credited with performing the first appendectomy for acute appendicitis in 1759.^{10,11}

Although the works of Charles McBurney¹²⁻¹⁴ and Reginald Fitz¹⁵ are frequently quoted when discussing the history of acute appendicitis, perhaps the most famous case of acute appendicitis is the case of King Edward of England. King Edward developed symptoms of abdominal pain in late May 1902, a short time before his scheduled coronation on June 16, 1902. Tended by Sir Frederick Treves, Sir Joseph Lister, and other eminent surgeons of the era, the future King is said to have refused surgical intervention initially. He waxed and waned clinically and eventually underwent an incision and drainage of a large periappendiceal abscess by Treves just 2 days before his scheduled coronation. The coronation was delayed and eventually the King was crowned on August 8, 1902.^{7,16}

EPIDEMIOLOGY

Inquiries as to the distribution of this pathology within the population have produced similar results globally.¹⁷⁻²⁵ These assessments are limited by their retrospective nature and because there is little or no controlled prospective evaluations. Additionally, there is a question as to the detail of the databases that are used to collect the data because these are often administrative databases.²⁴ Certain studies focus on limited populations, such as active duty or reserve military¹⁸ or children.²¹ The lifetime risk has been estimated to range from 8.6% to 12% in males and 6.7% to 23.1% in females.^{1,19} When analyzed by age, the greatest frequency of appendicitis is seen in the age range of 10 to 19 years of age.^{19,20,22,24} However, Andreu-Ballester and colleagues,²³ in a large study from Spain, found that the highest incidence was in the 1 to

4 years of age group. Seasonal variation has also been noted in multiple studies; the incidence of acute appendicitis is more prevalent in the summer months.^{20,22} Cases of perforated appendicitis have decreased over time, although no rationale was given for the cause.²⁶ Not surprisingly, cases of perforated appendicitis have a hospital length of stay that was much longer and a cost that was almost double cases of nonperforated appendicitis.²⁶

ANATOMY

The vermiform or “wormlike” appendix is an antimesenteric luminal outpouching found at the base of the cecum where the three bands of colonic longitudinal smooth muscle or taeniae coli coalesce. The size of the appendix varies but averages 10 cm in length. Its histology resembles that of other luminal abdominal structures in that it is composed of mucosal, submucosal, muscular, and serosal layers; however, it is distinct in that it contains lymphoid aggregates and a subepithelial neurosecretory layer. It contains the polymicrobial flora of bacterial species seen in the colon, such as *Escherichia coli*, *Bacteroides*, *Enterococcus*, and *Pseudomonas*. The vascular supply is from the appendiceal artery, a branch of the ileocolic artery arising from the distal superior mesenteric artery. Venous and lymphatic drainage follow that of the arterial supply. It receives autonomic parasympathetic innervation from fibers of the vagus nerve that passes through the superior celiac plexus. Sympathetic fibers arise from the thoracic spinal cord as splanchnic nerve fibers. The vessels, lymphatics, and nerves enter the appendix through its mesentery or mesoappendix to which it is adherent to the mesentery of the adjacent ileum. In its normal position, it is an entirely intraperitoneal structure with the overlying peritoneum in close relation, lying deep in the right pelvis. However, its location varies greatly and has been described as located in almost any location in the abdomen.⁸ The anatomy and embryology are relevant to explain the typical clinical findings seen during an acute episode of appendicitis.

Pathophysiology of Appendicitis

Acute appendicitis has been thought of as a sequence of events with an initial enticing event and natural progression, keeping in mind that patients presenting at different points in time present with different clinical pictures. Appendicitis is thought to begin with outflow obstruction of the lumen. Fecaliths (a hard mass of stool also known as appendicoliths when originating in the appendix) have often been cited as a cause for appendicitis and common teaching is to look for a fecalith in the abdominal radiograph; however, there is no clear-cut evidence that this is the case.²⁷ Other proposed causes include lymphoid hyperplasia preceded by a viral illness or a bacterial enteritis. Most cases occur without a known cause and is rarely of clinical significance. One exception is middle-aged to elderly patients with appendicitis, because an obstructing tumor is not an uncommon cause of obstruction in this group.

The mucosal and secretory function of the inflamed appendix continues, and without a patent lumen, this causes increased intraluminal pressure, leading to bowel wall distention. This is transmitted as visceral pain, via afferent sympathetic autonomic nerve fibers of the splanchnic origin to the dorsal root ganglion of the thoracic spinal cord segments that are shared with the other abdominal organs of midgut embryologic origin. This is manifested as the earliest symptom: poorly localized midabdominal pain. This point in time is considered early acute appendicitis. With ongoing luminal obstruction and stasis of intraluminal contents, enteric bacterial overgrowth ensues simultaneously as venous outflow ceases followed by loss of arterial inflow. The culmination of these events leads to initiation of the systemic acute inflammatory response,

with cytokine release and leukocyte activation, causing neutrophil migration to the site of inflammation. The combination of these events results in acute transmural inflammation of the appendiceal wall and the overlying parietal peritoneum. Irritation of the peritoneum, which is under somatic sensory innervation, causes localized pain in the right lower abdomen and corresponding point tenderness to palpation. The systemic inflammatory response gives rise to the fever, leukocytosis, and anorexia seen at this stage, which is considered as late acute appendicitis. Gross examination of the appendix reveals a purulent or suppurative appendix, caused by neutrophil response to infection. Without arterial supply, the appendicular wall becomes ischemic, gangrenous, until free wall perforation occurs. This late presentation is considered complicated appendicitis and typically occurs 2 to 3 days after symptom onset. Appendiceal wall perforation can progress into abscess formation or gross intraperitoneal spillage with peritonitis. The latter results in inflammation of the entire peritoneum causing the severe diffuse abdominal pain of peritonitis. Untreated, this ultimately leads to transmigration of enteric bacteria into the bloodstream, septic shock, circulatory collapse, and death. More commonly, perforation leads to abscess formation with persistent right lower quadrant pain and ongoing signs and symptoms of systemic inflammation.

DIAGNOSIS

History

The presentation of acute appendicitis generally follows a typical sequence of events: the sudden or gradual onset of vague periumbilical or epigastric pain followed by anorexia, nausea, and vomiting. Often, there is a preceding history of bowel distress, either in the form of diarrhea or constipation. The initial onset of periumbilical or epigastric pain is postulated to be the result of hyperperistalsis of the appendix to overcome luminal obstruction and to be visceral in origin. At times the initial pain may be felt all over the abdomen. Nausea and anorexia (with or without emesis) are the next symptoms to follow, a consequence of bowel wall distention. Many clinicians consider a lack of appetite as the most consistent symptom, so much so that its absence should give rise to alternative diagnoses; however, this claim is unsupported by evidence.

About 24 hours after the onset of symptoms, the pain often shifts and is localized to the right lower quadrant with accompanying tenderness to palpation. Because the anatomic position of the appendix varies, the localization and character of pain also varies. Three anatomic positions that are well described include the ascending appendix, iliac appendix, and pelvic appendix. When located in the retrocecal position, localizing symptoms are often mild or even absent. Pelvic appendices may give rise to suprapubic pain and urinary symptoms, or symptoms of painful defecation when in proximity to the rectum. Patients often describe exacerbation of the pain on the car ride to hospital, especially when going over bumps.

Fever and anorexia follow as the infection progresses from a localized to a systemic inflammatory process. The disease may progress to perforation and peritonitis within 2 to 3 days of symptoms onset. If perforation happens to occur in an area of the abdomen that is contained within other loops of bowel, mesentery, or omentum, the infection remains localized to the right lower quadrant, causing continued right lower quadrant pain without signs and symptoms of peritonitis, and occasionally a mass is palpated.

Physical

Fever is a consistent finding but may be absent at early onset of symptoms. Tachycardia may present because of sympathetic response to abdominal pain; however,

persistent tachycardia despite pain control in conjunction with hypotension may be caused by the systemic inflammatory response or sepsis. Abdominal examination reveals tenderness, most often in the right lower quadrant near the iliac fossa; this is known as McBurney point after Charles McBurney, who initially described this clinical finding.^{12,14} The exact point of maximal tenderness varies and is affected by the position of appendix in relation to surrounding structures. Rebound tenderness, elicited either by gentle percussion or rapid release of pressure from the abdomen, indicates inflammatory irritation of the parietal peritoneum. A useful technique in children includes having them hop or cough (Dunphy sign), or shaking the bed. Involuntary guarding may also be present with peritoneal irritation and Rovsing sign, right-sided abdominal pain elicited with left-sided abdominal palpation. When the appendix is located near the psoas or obturator internus muscles, inducing contraction of these muscles by hip flexion or external rotation, respectively, causes severe pain (the so-called psoas sign). Similarly, in women, cervical motion tenderness during pelvic examination occurs when the cervix and other pelvic organs are brought into contact with an inflamed appendix. Rectal examination may elicit pain when palpation of an inflamed pelvic appendix in proximity to the rectum occurs.

Laboratory

Laboratory studies classically include a basic or comprehensive metabolic panel, a complete blood count, and urinalysis. Coagulation parameters should be obtained if the patient has a history of bleeding dyscrasia or is currently on antiplatelet or anticoagulation medications. These studies can help determine if the patient has electrolyte disturbances, is dehydrated, or has a leukocytosis, all elements that can help rule in or out acute appendicitis or other pathology. The urinalysis may also help in determining if the complaints and findings on clinical examination are of urologic origin. Females should also have a pregnancy test.

Markers

It would be ideal and facilitate the diagnosis of acute appendicitis if the appendix had a unique biochemical marker that would be highly diagnostic of acute appendicitis if positive. Unfortunately, this is not the case. Multiple studies have looked at various markers independently and jointly to help in the diagnosis of acute appendicitis. Although the white blood cell count remains the most common laboratory marker, other markers, such as C-reactive protein, bilirubin, granulocyte colony-stimulating factor, fibrinogen, interleukin, procalcitonin, the APPY1 test, and calprotectin, have been investigated.^{28–41} An industry-sponsored study claims 97% sensitivity for a biomarker produced by the sponsor.^{34,36,37}

Thuijls and coworkers³⁹ reported that lactoferrin and calprotectin are significantly elevated in cases of acute appendicitis. Kwan and Nager³⁸ concluded that elevated C-reactive protein, in conjunction with a leukocytosis, increased the likelihood of appendicitis; D-lactate was not useful. Bilirubin may be a marker to consider; a prospective study showed hyperbilirunemia had a high specificity for acute appendicitis, especially when the appendix is perforated.³³ A meta-analysis proposed that an elevated bilirubin along with clinical signs of acute appendicitis should be considered for early appendectomy because there was a greater chance of appendiceal perforation.³⁵ Fibrinogen has also been proposed as a marker of perforated appendicitis.³⁰ The recent World Society of Emergency Surgery Jerusalem Guidelines for Diagnosis and Treatment of Acute Appendicitis makes no recommendation for use of any of these markers.⁴²

Scores

Since its earliest description, appendicitis has remained a diagnostic challenge for clinicians. A negative appendectomy rate has been used as a quality measure; this has been a moving target as diagnostic technology has improved. History and physical examination have been the most important modalities in the evaluation of a patient with suspected appendicitis. The addition of routine laboratory values further aides in the diagnosis. The Alvarado score, first described in 1986,⁴³ uses eight predictive factors from history, physical examination, and laboratory studies, to categorize suspected appendicitis into probability groups. Factors include (in order of strongest predictive value) localized right lower quadrant abdominal tenderness, new-onset leukocytosis, pain migration, left shift, fever, nausea/vomiting, anorexia, and direct rebound pain. A prospective clinical trial by Owen and coworkers⁴⁴ validated the Alvarado score in 215 patients, reducing the negative appendectomy rate without increasing morbidity or mortality. Since its description, clinicians have adopted its use with varying degrees of success in reliably predicting appendicitis. Rodrigues and colleagues⁴⁵ came to a similar conclusion while performing a prospective assessment of the Alvarado score concluding that a score of 7 to 10 “virtually confirmed the diagnosis” and that patients with score one to four can be “discharged unless otherwise indicated.” However, as use of computed topographic imaging became more readily available with improved imaging quality, clinicians have become less reliant on thorough clinical judgment. As evidence of the association with radiation and the increased lifetime risk of cancer began to surface, attention again turned to scoring systems, such as the Alvarado score, to help stratify when computed tomography (CT) scan was necessary and which patients could be spared from radiation. In 2008, the Appendicitis Inflammatory Response Score proposed by Andersson and Andersson⁴⁶ was shown to outperform the Alvarado score in predicting advanced and all appendicitis.⁴⁷ A recent prospective evaluation concluded that the use of the Appendicitis Inflammatory Response Score would reduce the use of diagnostic imaging.⁴⁸ This score used similar factors from the history and physical examination, such as pain, rebound, guarding, leukocytosis, fever, vomiting, and left shift, but with the addition of C-reactive protein.

In 2014 Sammalkorpi and coworkers¹ published results from a prospective study of 829 patients using a New Adult Appendicitis Score that showed further predictive accuracy by incorporating duration and timing of symptoms. Similar to the Alvarado score, the Pediatric Appendicitis Score⁴⁹ uses a simple 10-point scale, specifically designed for children. This was later validated by Goldman⁵⁰ in a prospective evaluation, who determined that 61% of patients with a score of greater than or equal to seven had acute appendicitis. The RIPASA (from the Raja Isteri Pengiran Anak Saleha Hospital in Brunei Darussalam) score was developed in 2010 to address the poor sensitivity and specificity of the other scores when applied to Middle Eastern and Asian populations.⁵¹ **Table 1** compares the components of each of these scores.

Apisarnthanarak and coworkers⁵² performed a retrospective study comparing reliability of the Alvarado score with CT scans. The conclusion was that the Alvarado score was not as reliable as CT scans because almost 50% of the patients in the study with documented acute appendicitis had low or equivocal Alvarado scores.

Imaging Studies

As part of the work-up of acute abdominal pain, classically an obstructive series has been performed of the abdomen. Although rarely helpful, the presence of a fecalith in the right lower quadrant, and there suspected in the appendix, was supportive of the working diagnosis of acute appendicitis. It is probably most useful in ruling out other

Table 1
A comparison of different scoring systems in acute appendicitis

Finding	Alvarado	PAS ⁴⁹	RIPASA ⁵¹	New Score	AIRS ⁴⁶	
RLQ pain	1	—	0.5	—	1	
Gender	—	—	—	—	—	
Male			1.0			
Female			1.5			
Age	—	—	—	—	—	
<40			0.5			
>40			1.0			
Migration of pain (relocation)	—	1	0.5	2	—	
Nausea/vomiting	1	1	1.0	—	1	
Duration, h	—	—	—	—	—	
<48			1.0			
>48			0.5			
Anorexia	1	1	1.0	—	—	
Guarding	—	—	2.0	—	Pts	—
				Mild	2	
				Moderate/severe	4	
RLQ tenderness	2	1	1.0	3/1 ^a	—	
Rebound	1	1	1.0	—	Light	1
					Medium	2
					Strong	3
Rovsing sign	—	—	2.0	—	—	
Exacerbation with hopping/cough/percussion	—	1	—	—	—	
Fever	1	1	1.0	—	—	
Leukocytosis	2	1	1.0	—	Pts	—
WBC ($\times 10^9$)				7.2–10.9	1	10–14.9
				10.9–14.0	2	>15
				>14	3	2
CRP, mg/dL	—	—	—	<48-h symptoms	Pts	—
				4–11	2	1–4.9
				11–25	3	>5
				25–83	5	
				>83	1	
	—	—	—	>48-h symptoms	Pts	—
				12–53	2	
				53–152	2	
				>152	1	
Negative urinalysis	—	—	1.0	—	—	
Left shift	1	1	—	%	Pts	%
				62–75	2	70–84
PMN, %				75–83	3	>85
				>83	4	2
Sum total	10	10	16.5	—	12	
Low-probability group	5–6	<5	—	<16	0–4	
Intermediate group	7–8	5	—	16–18	5–8	
High-probability group	9–10	6–10	—	>18	9–12	

The Alvarado score⁴³: 8 factors with the resultant score being characterized as low probability, moderate probability, and high probability.

New Appendicitis Score.¹

Abbreviations: AIRS, Appendicitis Inflammatory Response Score; CRP, C-reactive protein; PAS, Pediatric Appendicitis Score; PMN, polymorphonuclear leukocytes; RIPASA, from the Raja Isteri Pengiran Anak Saleha Hospital in Brunei Darussalam; RLQ, right lower quadrant; WBC, white blood count.

^a New score age: men and women age 50+/women age 16–49.

causes of abdominal pain, such as free air in the case of a perforated viscus, or a small bowel obstruction.

Other medical imaging technologies are also helpful in the assessment of the acute abdomen. The most commonly used modalities used are ultrasonography (UC), CT scan, and MRI. Each of these has advantages and disadvantages, such as sensitivity, specificity, costs, and exposure to ionizing radiation. Although UC is inexpensive and has no exposure to ionizing radiation, it is operator dependent and only has a specificity of 83% and a sensitivity of 78%. CT scans have a specificity of 90% and a sensitivity of 94%, but is more costly and exposes the patient to nonnegligible ionizing radiation.^{53,54} CTs have not been demonstrated to be reliable at determining if there is appendiceal perforation.⁵⁵

The diagnostic accuracy of MRI is comparable with CT and better than US.⁵⁶ MRI has a sensitivity of 97% and a specificity of 97% but without the ionizing radiation; however, there is increased cost relative to CT.^{57,58} Reddy and coworkers⁵⁹ proposed a combined US-Alvarado score could reduce the need for CT scans in patients suspected of having appendicitis.

SURGICAL APPROACHES

Open Surgery

Open appendectomies are now rarely performed as the initial operation, and many surgical residents now complete their training having never performed one. However, familiarity with this approach is important because it may be necessary when contraindications to laparoscopy or difficult adhesions are encountered or in austere environments where laparoscopy is not available. In 1894 Charles McBurney described the oblique right lower quadrant incision and muscle-splitting approach, which continued to be used until the late 20th century (before this, surgeons typically used a midline laparotomy approach). A Rockey-Davis or transverse right lower quadrant incision just lateral to the rectus muscle and through McBurney point is thought to provide a better cosmetic outcome and more access to the pelvis. After incising the skin and sharply incising the aponeurosis of the external oblique muscle, the three layers of the abdominal wall lateral to the rectus are bluntly dissected and retracted to gain access to the peritoneum. On entering the peritoneal cavity, the appendix is identified at the base of the cecum. Tracing the taenia coli of the ascending colon proximally can facilitate identification. The appendiceal artery is identified as a branch of the mesentery of the appendix and ligated. The base of the appendix is then ligated with suture and removed. Inversion of the appendiceal stump into the cecum, historically thought to decrease risk of fistula, has now largely been abandoned after multiple studies proved no significant difference in outcomes.^{60,61} The peritoneal cavity is then irrigated with saline solution, and the muscle, fascia, and skin are closed separately in layers.

Laparoscopic Surgery

Semm, a German gynecologist and pioneer of laparoscopic surgery, performed the first laparoscopic appendectomy in 1980, which had previously been used mainly as a diagnostic tool in gynecologic surgery. His attempts to bring this new technique to mainstream surgery were met by a great deal of skepticism and backlash from the surgical community. Over the next several years, his efforts to promote laparoscopic surgery ultimately brought about the "laparoscopic revolution" leading to its widespread adoption in not only appendectomy but also cholecystectomy.⁶² Several advances in technique and instrumentation have evolved, and numerous studies have

solidified laparoscopic appendectomy as the current gold standard treatment of appendicitis with improved outcomes compared with the open approach.

Comparison of Open Versus Laparoscopic

Numerous studies of level I evidence have compared open and laparoscopic appendectomies. A meta-analysis of 33 prospective randomized controlled trials, accounting for more than 3500 patients, showed that laparoscopic appendectomy in adults had a statistically significant decrease in incidence of wound infection, length of hospitalization, and postoperative complication, and an earlier returned to work. This conclusion did not apply to the pediatric population.⁶³

Single Incision Laparoscopic Surgery

Single incision laparoscopic surgery (SILS) has been described since 1997 for cholecystectomy.⁶⁴ This technique uses one incision to access the peritoneal cavity, placing multiple operative ports through this incision. The primary motive to this procedure is cosmesis.⁶⁵ Multiple studies have demonstrated the feasibility of this technique.^{65–70} However, SILS has a longer operative time^{65,67} and is more expensive.⁷⁰ In addition, at least one study has found that SILS patients had more postoperative pain.⁶⁵

Natural Orifice Transluminal Surgery

Natural orifice transluminal surgery (NOTES) is a procedure whereby the peritoneal cavity is accessed via a natural orifice: the stomach via the mouth, the vagina in women, or the rectum. Once the peritoneal cavity is accessed in this fashion the surgical procedure is performed. First described in 2007 it has been used to perform appendectomies and even colon resections. Additional acronyms for this procedure exist: transgastric appendectomy (TGAE) and transvaginal appendectomy (TVAE). In 2008 the German Society of General and Visceral Surgery formed the German NOTES Registry (GNR) to track and follow NOTES surgery performed in Germany.⁷¹

In 2014, a total of 13 cases were described with successful outcomes. These cases were part of the GNR.⁷² An analysis of the first 217 appendectomies entered into the GNR was published recently.⁷¹ The hybrid NOTES nomenclature is used for cases where additional transabdominal trocars are used. There were 181 TVAE performed with a median time of 35 minutes duration, without any conversions to laparotomy. The median postoperative hospital stay was 3 days. Only one center was designated as a TGAE center, performing 36 of these procedures. The median duration of this procedure was 96 minutes, with two conversions to laparotomy, and a median postoperative hospital stay of 3 days. Complications occurred in 6.5% of the patients and included pouch of Douglas abscesses, other intra-abdominal infections, intra-abdominal bleeding, and a case of gastric leak of the gastric clip closure.

The overall conversion rate for both procedures was conversion to laparoscopy of 2.8% and a conversion rate to laparotomy of 0.9%, the latter two cases from the TGAE group. The purported advantage of NOTES is to decrease the risk of wound infections, trocar hernias, and neuropathic scar pain.

Endoluminal Surgery

Recently, an endoluminal appendectomy was performed in Brazil.⁷³ The patient, a 67-year-old man with a history of a transverse colostomy, presented with abdominal discomfort. After ultrasonography demonstrated an enlarged appendix the patient underwent an endoluminal appendectomy: a modified colonoscope was passed, the appendiceal lumen was cannulated with a shark tooth grasping forceps, and the appendix was inverted. An endoloop was placed at the base of the appendix, the

appendiceal base was then transected with a snare loop. Hemostatic clips were then used to reinforce the closure of the appendiceal lumen.

Nonoperative Management

In 1902 Ochsner wrote in his *Handbook of Appendicitis*,⁷⁴ “I say this because I am confident that with proper non-operative treatment almost all of the cases which are diagnosed reasonably early may be carried through any acute attack, no matter what its character may be.” Stengel⁷⁵ also wrote at the beginning of the twentieth century, “Treated in a purely medical or tentative manner, the great majority of patients with appendicitis recover.” Coldrey^{76,77} was a proponent of nonoperative management in the 1950s, but this never caught on. Buckley and coworkers⁶⁸ state “During the course of over 30 years of surgery, a good deal of which has been emergency surgery, I have gradually been tending more and more to conservative treatment in cases of advanced appendicitis. For many years I have believed it best to treat appendix abscesses conservatively. For more than 4 years I have believed it best to treat all cases of acute appendicitis over 24 hours old conservatively. It is probably wise to treat all cases of acute appendicitis under 24 hours old by an emergency appendectomy, and this is our usual custom. One sometimes wonders whether it would not be a sound procedure to treat all cases of acute appendicitis conservatively. They seem to settle down quite nicely, and some never seem to have any further trouble: the appendix has wizened. We should then be left with appendectomy for recurrent acute appendicitis, and for chronic appendicitis—the ‘grumblers’ with fecaliths in the appendix, with kinks, and with adhesions. Looking into the future, one cannot help feeling that our successors will be more conservative in their outlook in this matter, and may look back on us as having been too ‘appendectomy-minded’.”⁶⁸

Nonoperative management of acute appendicitis has regained more popularity recently and has been supported by several studies. Nonoperative management terminology includes nonoperative management (the concept of not performing an appendectomy on a patient with a diagnosis of acute appendicitis), treatment failure (wherein the patient’s symptoms worsen and requires a surgical intervention while still under nonoperative therapy), and recurrence (when the patient develops appendicitis after successful completion of a course of nonoperative management).

The Appendectomy vs Antibiotics in the Treatment of Acute Uncomplicated Appendicitis (APPAC) study,^{78,79} a randomized, prospective controlled study, assessed nonoperative management versus surgery using ertapenem as antibiotic of choice initially, followed by levofloxacin with metronidazole. Of those patients managed nonoperatively almost 73% did not require surgical appendectomy within the first year of their enrollment. This study was later followed up with an economic assessment.⁸⁰ Not surprisingly, surgical intervention cost was 1.6 times greater than nonoperative management; surgical patients required more sick leave, leading the authors to conclude surgical intervention has greater societal costs.

DiSaverio and coworkers,⁸¹ in the Non-Operative Treatment for Acute Appendicitis (NOTA) study, prospectively followed 159 patients with suspected acute appendicitis based on clinical assessment. The patients were treated with amoxicillin/clavulanate for up to 7 days. Treatment failure was 12%. The recurrence rate was an additional 14%, but these patients were all treated successfully with antibiotics.

Additional reviews and meta-analyses have shown that nonoperative management is successful in upward of 70% of patients.^{82,83} There is some evidence that appendicitis should be stratified into noncomplicated and complicated, and that those cases that are complicated should undergo a surgical intervention.⁸⁴ In this study complicated appendicitis was defined as “patients with evidence of perforation,

peri-appendiceal abscess, or phlegmon, or duration of symptoms greater than 48 h prior to admission to the Emergency Department.”⁸⁴

A recent World Wide Web–based survey of almost 2000 persons found that those surveyed predominantly favored laparoscopic appendectomy for themselves and their children; the survey was unbalanced, however, with a preponderance of females (70.9% of respondents) and non-Hispanic white (90.5%) respondents.⁸⁵ More recently, the Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) trial⁸⁶ was initiated in the United States with a goal to recruit 1500 patients. This study is currently enrolling patients.

Bacteriology

The microbiome of the appendix in normal state and in acute appendicitis has been analyzed as a possible factor in acute appendicitis. One of the classic theories of the development of acute appendicitis has been luminal occlusion of the appendix by either a fecalith or hypertrophic lymphoid tissue.⁸⁷ Subsequently, this blind pouch becomes a breeding ground for bacteria, leading to acute appendicitis. Although some of the original studies did not demonstrate a difference in the microbiome in patients with acute appendicitis confirmed by pathology versus normal appendix as confirmed by pathology,⁸⁸ it was suspected that a higher preponderance of anaerobic bacteria was present in the appendix and ileum in patients with acute appendicitis.⁸⁹

Technological advances, such as gene sequence analysis, have allowed for better assessment of the microbiome and better quantification and qualification of the microbiome has become possible. With these differences, the hypothesis that a shift in the appendiceal microbiome may play a key role in the pathophysiology of acute appendicitis was postulated.^{90,91} Further investigation shows that *Fusobacterium* is more predominant in patients with acute appendicitis with a concomitant decrease in the *Bacteroides* population.^{87,91–93}

The inferences of these studies are challenged by small numbers of patients studied to make some of the conclusions put forth; for example, Salö and coworkers⁹² documents a nonstatistical increase in *Fusobacterium* and an associated decrease in *Bacteroides* in phlegmonous appendicitis and perforated appendicitis compared with control subjects. However, he found that the microbiome is similar in gangrenous appendicitis and control subjects. These conclusions were made after studying only 22 patients.

These findings support the hypothesis that appendicitis is actually a disease of inflammation and changes in immune function.⁸⁷ This concept still needs refinement; support for this is the fact that appendicitis has some cultural findings, with appendicitis remaining stable in industrialized countries, but rapidly increasing in newly industrialized countries.²⁵ This knowledge can be used to drive antibiotic management in cases of nonoperative management.

SPECIAL CIRCUMSTANCES

Interval Appendectomy

Patients may present late in the natural course of the appendicitis, after perforation has occurred. If the perforation is contained, an intra-abdominal abscess or phlegmon forms within 5 days. This causes persistent right lower quadrant pain and tenderness, sometimes associated with a palpable mass and is typically diagnosed with CT scan or US. Percutaneous drainage along with antibiotic therapy is currently the standard of care. Immediate surgical intervention in setting of an abscess or phlegmon carries an increased risk of adjacent bowel injury, potentially requiring more extensive resection, such as a right hemicolectomy or ileocecectomy.⁹⁴ There has been much debate and

research in the pediatric and adult population regarding outcomes, cost, morbidity, and recurrence rates for each of these options. In the pediatric population, percutaneous drainage and antibiotics with interval appendectomy compared with immediate appendectomy resulted in no difference regarding cost, length of hospitalization, or abscess recurrence rate.⁹⁵ Initial nonoperative management may also have negative psychosocial impact on the family, decreasing the quality of life because of a delay in definitive treatment.⁹⁶

After successful nonoperative management of appendicitis or an appendiceal abscess, an interval appendectomy may be performed. Proponents of interval appendectomy justify this based on a reported recurrence rate ranging from 6% to 20%, with most recurrences within the first 6 months.⁹⁷ Interval appendectomy is most often performed in the pediatric population, who are believed to have higher recurrence rates and lower surgical complication rates.^{98,99} A larger retrospective study combining adult and pediatric populations showed recurrence of 5% within 4 years, with the authors concluding that the practice of interval appendectomy should be abandoned.¹⁰⁰ Multiple factors should be considered in deciding when to do an interval appendectomy. Very young children and elderly adults are more likely to present after perforation, because of inability to independently seek medical attention and communicate effectively. Elderly patients are also less likely to tolerate a second episode of acute appendicitis and are more apt to progress to sepsis because of weakened immune system and comorbid conditions. There is also a higher likelihood of associated malignancy or undiagnosed inflammatory bowel disease in those 40 years of age and older.⁹⁴

For these reasons, interval appendectomy should be strongly considered in these select populations. Healthy adolescents and young adults are least likely to have serious sequelae from an appendicitis recurrence. Routine interval appendectomy is not recommended in this population.

Pregnancy

Acute appendicitis is the most common nonobstetric surgical emergency during pregnancy with a prevalence of 1 in 500 pregnancies.^{2,3} The diagnosis is somewhat challenging because some of the diagnostic modalities used to diagnose acute appendicitis in the nongravid patient are often confounded by the gravid state. The physical examination is altered because of displacement of the appendix. The state of pregnancy tends to leukocytosis and therefore the use of leukocytosis to help make the diagnosis of acute appendicitis is challenged. Imaging adjuncts to help with the diagnosis are also affected. US may not locate the pathologic appendix as easily. Although a CT scan has good sensitivity and specificity, it is preferred to not expose the fetus to a high level of radiation. MRI has not been known to affect the fetus.¹⁰¹ The American College of Radiology has created appropriateness criteria with frequent revisions. Under the rubric of "Right Lower Quadrant Pain – Suspected Appendicitis," the latest revision, dated 2013, has four variants.¹⁰² The third variant, specifically addressing the pregnant patient, rates the MRI of the abdomen and pelvis without intravenous contrast a seven of a maximum nine. Abdominal US received the highest rating with a rating of eight. The specificity of MRI is 98%, sensitivity of 97%, positive predictive value of 92.4%, and negative predictive value of 99%, challenged by the fact that the nonvisualization may be high.^{2,3,57} Although limited by this, MRI should be considered the choice imaging modality for assessing the pregnant patient suspected of acute appendicitis.² However, because of the cost of MRIs, many authors recommend an US as the first step in the work-up of the pregnant patient with a follow-up MRI if the results of the US are not conclusive.^{2,101} Unfortunately, not all hospitals have an MRI machine or the radiologists trained to read the images.

Rapid and accurate diagnosis of acute appendicitis in pregnancy is paramount because of the effect that untreated acute appendicitis can have on the outcome of the pregnancy. Surgery can either be open or laparoscopic depending on surgeon comfort.²

Other Possible Diagnoses

In the differential diagnosis consideration must be given to alternative pathologies that may present in a fashion similar to acute appendicitis. Gynecologic pathology, such as ovarian torsion, ectopic pregnancy, and pelvic inflammatory disease, must be considered the differential diagnosis. In the elderly, concern that this may be an initial presentation of a neoplastic disease must be entertained. In addition, this may be the initial presentation of inflammatory bowel disease; in one study 0.3% of pediatric appendectomies were later found to have Crohn disease.¹⁰³ Parasites have also been known to cause or contribute to acute appendicitis,^{104–106} as has tuberculosis.¹⁰⁷

SUMMARY

Appendicitis continues to be a frequent cause of emergency surgery because of its high prevalence in society. Diagnosis continues to remain a challenge and adjuncts, such as new biomarkers and advanced imaging technology, are being used to help facilitate this diagnosis. Although the new biomarkers may hold some promise, additional work needs to be done. Advanced imaging technology, such as CT and MRI, have high sensitivity and specificity but are costly and, in the case of CT scans, subject the patient to significant ionizing radiation. Nonoperative management continues to be investigated and as a better understanding of the true pathophysiology of acute appendicitis matures this will have a significant effect on the number of surgical interventions for acute appendicitis.

Clinical equipoise is still mandatory in the assessment of the patient who presents to the emergency department with right lower quadrant pain suspicious of appendicitis. Clinical scores, biomarkers, and advanced imaging technology help facilitate this challenging diagnosis.

Historically, nonoperative management has been underappreciated but is now seeing a resurgence in academic support and may be more cost effective. The future may see a new approach combining a more detailed physical examination and better usage of laboratory studies and medical imaging, leading to more nonoperative management being safely justified.

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