Appendicitis

13

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Introduction

Patients of advanced chronologic age have predictable changes in anatomy and physiology, often combined with comorbidities muddying the diagnostic process of common surgical problems, complicating their treatment, and negatively impacting outcomes. While acute care surgeons are positioned to evaluate and treat surgical emergencies stemming from a wide range of pathology, the elderly present a particular challenge. In this population, disease states often present diagnostic and therapeutic challenges. Increasing life expectancy is leading to a bourgeoning population of aged patients and makes it critical for surgeons to have a firm understanding of all aspects of the aging process and its impacts on all facets of patient care from initial presentation and workup to recovery. Appendicitis epitomizes this challenging situation.

History

The anatomic discovery of the appendix in humans is attributed to Berengario da Carpi in 1521; however, the appendix was depicted in an anatomy drawing by Leonardo da Vinci [1]. Nearly 200 years later in 1711, Lorenz Heister first described its diseased state, appendicitis, when he speculated that a perforation of the appendix with an adjacent abscess may have been caused by inflammation of the appendix itself [2]. Claudius Amyand performed the first reported appendectomy a quarter century later (1735) on an 11-year-old boy whose appendix was perforated by a pin identified during a scrotal hernia repair [3]. Ironically, it was nearly another century before Francois Melier proposed removing the appendix as a treatment strategy during his description of six cases of postmortem appendicitis in 1827 [2, 4, 5]. Another 50 years passed before Lawson Tait in London presented his transabdominal appendectomy for gangrenous appendix in 1880. In 1886, Reginald Fitz coined the term "appendicitis," described the natural history of the inflamed appendix, and advocated for its surgical removal. Charles McBurney presented his case series of surgically treated appendicitis in 1889 and described the anatomic landmark that now bears his name. In the 1890s, Sir Frederick Treves advocated expectant management of acute appendicitis followed by appendectomy after the infection had subsided; sadly, his youngest daughter developed and later died from perforated appendicitis with this treatment paradigm [6–10].

Epidemiology

Abdominal pain is an extremely common presenting problem with a long differential diagnosis. Appendicitis has long been one of the leading causes. Clinicians associated it more strongly with younger patients because the highest incidence occurs in the second and third decades of life. Appendicitis tends to be less common in extremes of age (<5 years old, >50 years old). However, in recent decades, the incidence of appendicitis in the elderly appears to be increasing. Contributing factors may include longer life expectancies and a rapidly increasing proportion of senior citizens in our society [11–13]. The lifetime risk of appendicitis remains significant with nearly 1 of every 15 persons (7 %) developing acute appendicitis during their lifetime. After the age of 50, the risk of having appendicitis goes down (2 % for men and 3 % for women). Nonetheless, older patients still make up a significant portion of cases.

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Patients older than 60 account for 5–10 % of all diagnoses of appendicitis. Roughly 5 % of all older patients presenting with an acute abdomen will have appendicitis [14–20].

Interestingly, there is substantial variation in the rate of appendicitis between countries. The diagnosis of appendicitis is more common in industrialized countries, which has thrust nutritional and dietary factors into question as a possible variable. Diets with higher proportions of highly refined grains and lower proportions of dietary fiber may have increased risk. Populations of developing regions tend to consume whole foods which are less refined and higher in fiber [21, 22]. Studies on seasonal variations have additionally implicated fiber consumption as predisposing factor [23, 24]. The proposed mechanism is low-fiber diets which lead to less colonic water and inspissated fecal material and, thus, higher colonic pressures. These conditions predispose to the development of fecaliths. Obstructing fecaliths essentially create a closed loop obstruction resulting in eventually appendicitis. However, attempts to confirm this pathophysiology mechanism with case-controlled studies of fiber intake and appendicitis rates are inconclusive. Of note, the evidence for fecaliths as a factor in the development of appendicitis is stronger in children and in cases of uncomplicated appendicitis than in the elderly who are also more likely to be perforated [25]. Further confounding epidemiologic analysis is the role of heredity, as having a family history of appendicitis increases the relative risk of the disease by almost threefold [26].

Pathophysiology

Despite its frequency and our ability to diagnose and effectively treat appendicitis for nearly two centuries, our understanding of its etiology is relatively poor. Historically, appendicitis was attributed to obstruction of the lumen and resultant increased luminal pressure leading to distention. This process if left unfettered ultimately can lead to progressive tissue ischemia due to appendiceal wall venule occlusion and stasis of lymphatic flow, leading to gangrene and perforation [27–33]. Appendiceal obstruction may be caused by fecaliths, lymphoid hyperplasia, benign or malignant tumors, and infectious processes. The relative frequency of these processes may be related to the patient's age at presentation. Lymphoid follicular hyperplasia as a sequela of infection may be suspected in the young. In contrast, luminal obstruction in older patients is believed to be from fibrosis, fecaliths, and neoplasia. More recent research suggests there may be a difference between the pathophysiology of perforated and nonperforated acute appendicitis [34]. A review of the National Hospital Discharge Survey identified an increase in the rate of perforated appendicitis starting in 1995 after a quarter century of steady decline. In the same time frame, the rate of both negative appendectomy and incidental appendectomy was declining as the diagnostic accuracy of imaging was enhanced [28].

When perforation occurs, the flora varies based on the chronicity of symptoms. Aerobic organisms predominate early in the course, while mixed flora is more common in late perforated appendicitis. Common organisms include *Bacteroides fragilis* and *Escherichia* [35–37]. Other bacteria are often found and are typical of colonic flora [38]. Known physiologic changes associated with aging may hasten the clinical course of appendicitis in elderly patients [30, 39, 40]. Anatomic variations have been noted in the appendices of elderly patients which may cumulatively result in decreased appendicular wall strength. These variations include smaller-caliber lumens or even obliterated, thinned mucosa, attenuated levels of lymphoid tissue, and fibrous or fatty infiltration of the wall [12]. Other age-related medical comorbidities like atherosclerosis can predispose to ischemia. Any one or combination of these changes may require significantly less endoluminal pressure, as is more common in early appendicitis, to cause prompt rupture in elderly patients. Older patients can have immunosenescence, a predictably diminished inflammatory response [41]. This can lead to blunted signs and symptoms of appendicitis as compared to younger patients.

Presentation

Abdominal pain is the most common clinical symptom of appendicitis and is found in nearly all confirmed cases [42]. Unfortunately, abdominal pain is one of the most common presenting complaints for physician visits. For every 100 people in the USA, there are 35 physician visits for abdominal pain annually [43]. The classic clinical presentation of acute appendicitis is right lower quadrant abdominal pain, anorexia, nausea, and vomiting. The epitomic patient will relate more generalized periumbilical pain that later localizes to the right lower quadrant. This constellation of symptoms can be identified in more than half of patients with appendicitis [42, 44, 45]. Other signs and symptoms usually trail the onset of pain and include nausea, vomiting, fever, and leukocytosis. Fevers, when present, are typically minimal, up to 101.0 °F (38.3 °C) [42, 46–49].

Commonly, the clinical presentation of appendicitis in the elderly mirrors that of younger patients [15, 39, 50].

However, comorbidities and other potential diagnoses confound the diagnosis of appendicitis in elderly patients. Older patients (age >50) are more likely to have diagnostic errors as compared to their younger counterparts (30 % vs 8 %) despite similar presenting signs and symptoms [50, 51].

The greatest diagnostic challenge of appendicitis remains its atypical and nonspecific presentation in many patients irrespective of age. As initial signs and symptoms of appendicitis are often subtle, patients and clinicians may downplay their importance. By estimation, 25 % of patients with appendicitis do not have a classic presentation. Symptoms can be dependent upon the location of the appendix, as it is not anatomically fixed in position. The appendix may be found in the pelvis, retrocecal, adjacent to the terminal ileum or the right colon (paracolic). Unusual presentations have been implicated as a factor leading to a delayed diagnosis. Delays in diagnosis permit time for progression of inflammation increasing the possibility of perforation. Atypical presentation is associated with extremes of age and other medical conditions which also may interfere with establishing the diagnosis. The higher rates of perforation consistently reported in the literature for elderly patients may be from delay in seeking evaluation, physiological differences, or other factors [52–55].

Diagnosis

Scoring systems have been developed to objectively guide clinicians in the diagnosis of appendicitis. Of these, the Alvarado score is the most widely used [56, 57]. Alvarado identified seven signs and symptoms and assigned each a point value: migratory right iliac fossa pain (1 point), anorexia (1 point), nausea/vomiting (1 point), right lower quadrant tenderness (2 points), rebound tenderness in the right lower quadrant (1 point), temperature >37.5 °C (1 point), and leukocytosis (2 points). The sum of these points yields the total score used to guide management. Scores below 3 are considered low risk of having appendicitis and need no further workup [56, 58, 59]. Scores higher than 3 may have appendicitis and should prompt further evaluation. The system was devised in the era prior to routine cross-sectional imaging. More recently, the Alvarado score has been employed as a screening tool to limit unnecessary imaging studies [61]. Elderly men with very high scores (>7) are highly likely to have appendicitis and should undergo appendectomy [59]. Women, particularly those who are premenopausal, may benefit from a confirmatory test prior to appendectomy [56, 57, 59].

There has been an exponential increase in the use of imaging for the identification of acute appendicitis. Although the growing reliance on confirmatory imaging has greatly reduced the negative appendectomy rate, unnecessary diagnostic imaging has associated costs and risks that could otherwise be avoided when the diagnosis can be made based on other clinical signs and symptoms [60–62].

Imaging should be performed when the diagnosis of appendicitis is suspected or unclear, which is often the case in elderly patients. Either ultrasound or cross-sectional imaging, with computed tomography or magnetic resonance imaging, can be used. Ultrasound is generally considered reliable for identifying acute appendicitis, but its sensitivity is suboptimal and dependent on many variables. It has little added value when the clinical presentation is clear [63]. Ultrasonographic findings of appendicitis include:

1. Blind-ended, tubular, noncompressible, aperistaltic structure
2. Diameter > 6 mm, laminated wall
3. Increased periappendiceal echogenicity
4. Appendicolith: echogenic with distal shadowing
5. Doppler: increased circumferential flow
6. Perforation/abscess: thickening of adjacent bowel wall, fluid collections, and hypoechoic mass

The overall diagnostic accuracy of ultrasound is 85 % (Fig. 13.1) [42, 63–65].

Sonography is increasingly available, does not require ionizing radiation, the results are immediately available, and does not require delays for administration of contrast agents. The accuracy of ultrasound is, however, dependent on the skill of the operator. Furthermore, patient factors related to body habitus or the presence of significant bowel gas can limit its utility in some patients. Currently, there are no studies focusing on the use of ultrasound in elderly patients [42, 64–66]. Increased use of ultrasound could reduce the growing reliance on CT scanning for the diagnosis of appendicitis by as much as 25 % [67]. There is increasing evidence to support the use of ultrasound as the initial screening modality, reserving cross-sectional imaging for nondiagnostic or equivocal results. However, the false-positive rate may be higher with this approach [68].

Computed tomography of the abdomen and pelvis is the most sensitive and specific modality for the diagnosis of appendicitis. The campaign against unnecessary operations, the negative appendectomy rate, has driven clinicians to

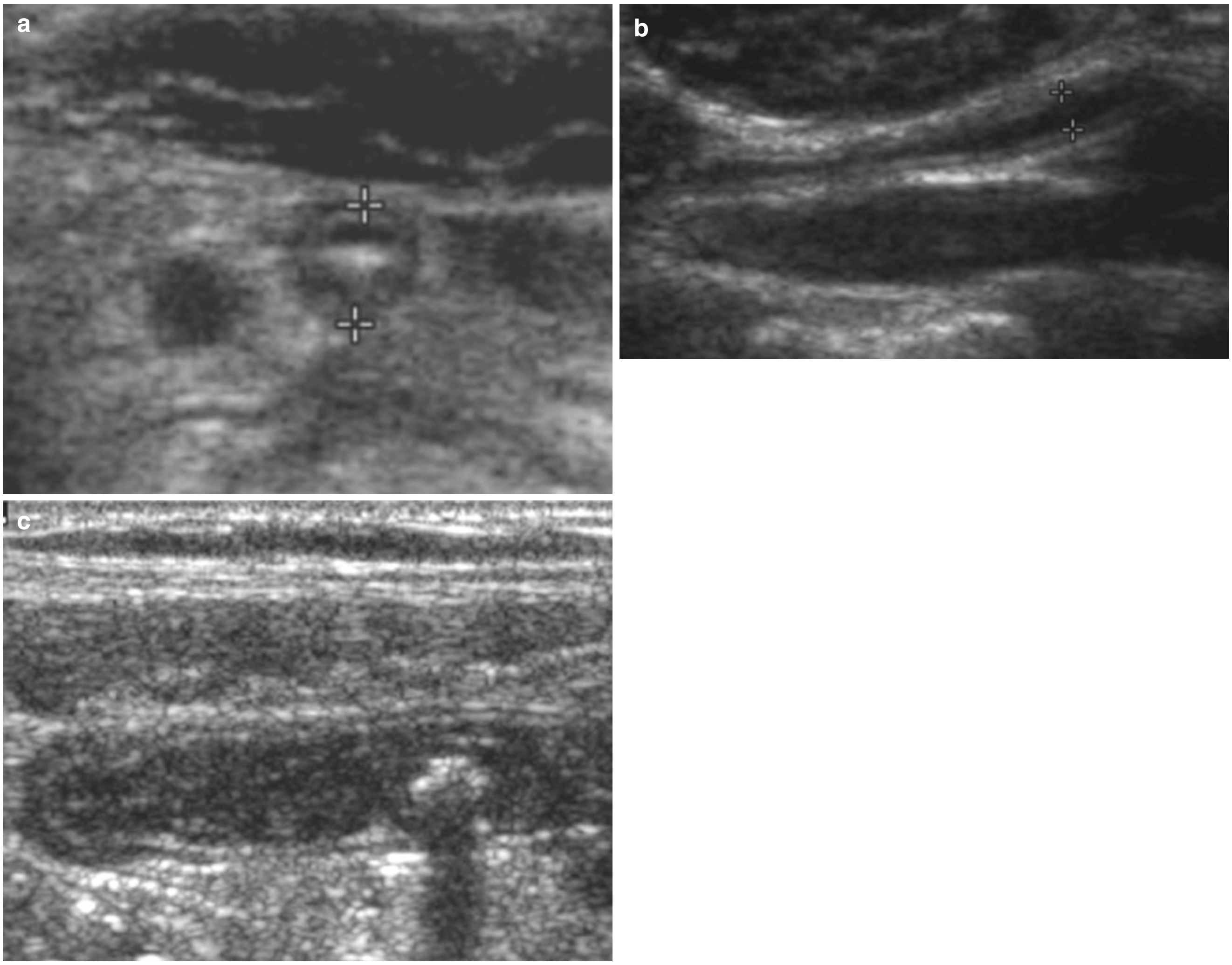

Fig. 13.1 (**a**) Ultrasound demonstrating a noncompressible tubular structure on ultrasound, with a transverse diameter of >6 mm, consistent with acute appendicitis. (**b**) Ultrasound demonstrating a longitudinal view of a noncompressible tubular structure with thickened laminated walls consistent with acute appendicitis. (**c**) Endolumenal fecolith on ultrasound with distal shadowing

become increasingly reliant on CT. CT findings of appendicitis include:

1. Enlarged, inflamed appendix (>6 mm)
2. Appendicolith (20–40 %)
3. Absence of luminal oral contrast
4. Appendiceal wall thickening
5. Periappendiceal fat stranding
6. Abscess or phlegmon
7. Focal cecal thickening (arrowhead sign)
8. Target sign

It is well accepted that CT has a high sensitivity and specificity in all patient populations. Older patients with suspected appendicitis can be diagnosed by CT with an accuracy of >99 %. Despite a lower overall rate of acute appendicitis when compared to younger patients, the sensitivity and specificity of CT in elderly patients with clinically suspected appendicitis are statistically comparable to that of younger patients (Fig. 13.2) [69, 70].

Efforts to reduce unnecessary risk of radiation exposure and radiocontrast nephropathy have led to the suggestion that magnetic resonance imaging (MRI) may be used as an alternative to CT scanning [71, 72]. Most studies of MRI in appendicitis have focused on pregnant women, where the risk of radiation to the fetus is paramount [73, 74]. A Dutch group evaluated this modality for all adult patients and found it to be comparable to CT scan as a second-line study after inconclusive or nondiagnostic sonograms [72]. In the elderly patient, radiation exposure is less of a concern, but underlying renal insufficiency may make potential renal toxicity more concerning. There are no studies to evaluate MRI for appendicitis in the elderly.

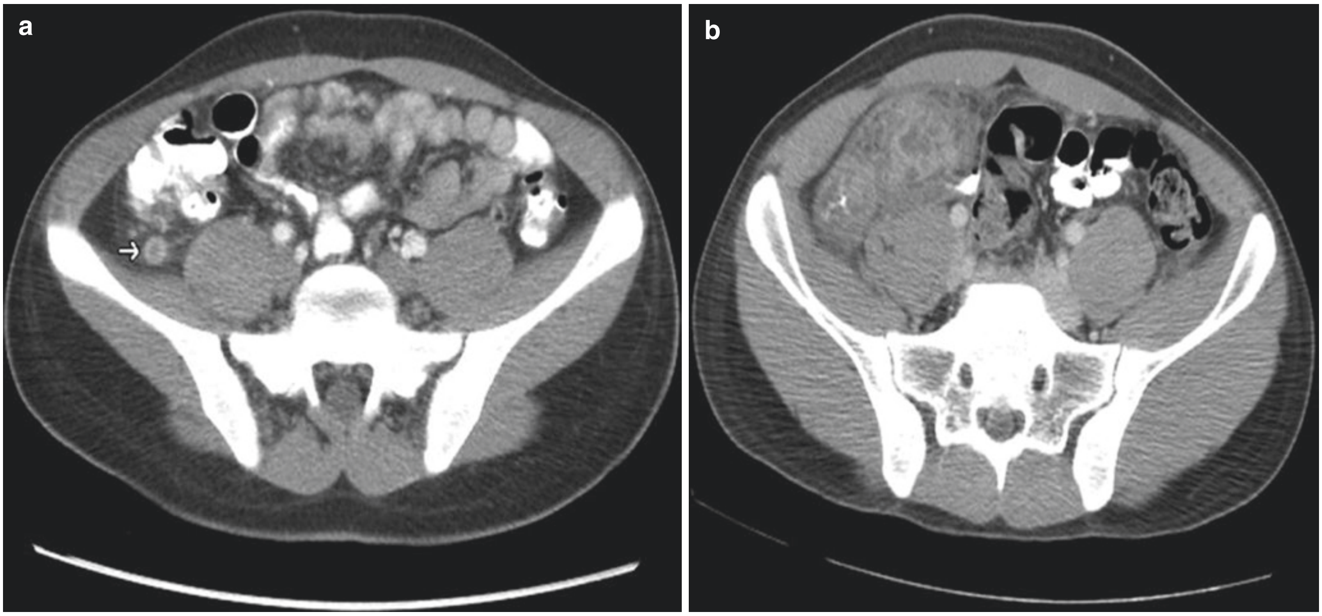

Fig. 13.2 (**a**) A target sign on CT scan of the abdomen and pelvis consistent with acute appendicitis. (**b**) Periappendiceal inflammation suspicious for perforated appendicitis

Treatment

The goals of therapy for acute appendicitis have historically been timely diagnosis followed by prompt surgical intervention. Advanced imaging technology has decreased negative appendectomy rates to roughly 10 %. The evaluation of abdominal pain and the diagnosis of appendicitis are more complex with longer intervals between the onset of symptoms and initial medical visit, especially in elderly patients [42, 51, 53–55, 59–62, 64–66, 75].

Surgical intervention remains the standard of care for elderly patients for uncomplicated appendicitis as well as patients with early perforation without defined phlegmon or abscess. For open appendectomy, a McBurney's incision in the right lower quadrant is the standard choice. Alternative incisions, namely, paramedian and vertical midline, are associated with higher postoperative infectious complications [55, 76]. Laparoscopic appendectomy has been proven safe and effective in the aged population with benefits of decreased length of stay, postoperative complications, and mortality. This holds true for older patients with both perforated and nonperforated appendicitis [77–79].

There are some uncommon clinical scenarios when appendectomy should be delayed. Patients with delayed presentation or longer duration of symptoms (>72 h) are more likely to have complicated appendicitis. Diagnostic imaging may confirm a phlegmon or abscess. Early operative intervention in such cases is correlated with increased morbidity, due to the technical challenges of dense adhesions and inflammation. Additionally, when there is extensive inflammation, appendectomy may not be a safe surgical option, and an ileocecectomy may be required to avoid postoperative complications such as appendiceal stump leak. In patients with a defined phlegmon or abscess without severe sepsis physiology, a nonoperative approach can be considered to avoid these potential complications. Nonoperative management includes antibiotics, intravenous fluids, and bowel rest [80–83]. Many patients will respond to nonoperative management since the inflammatory process has already been sequestered by natural host defenses. Repeat imaging may be necessary to document resolution of the phlegmon, or progression to abscess formation.

If initial or follow-up imaging identifies a defined abscess cavity, percutaneous image-guided drainage can be performed if the patient's clinical condition permits [83–85]. Patients who have an abscess are ideal candidates for percutaneous drainage and nonoperative management, with success rates of 80 %. This approach to appendiceal abscesses results in a decrease in morbidity and shorter lengths of stay [82, 86, 87]. Inpatient admission and close monitoring for signs of treatment failure are warranted. Failure of this approach includes bowel obstruction, ongoing or worsening sepsis, persistent pain, fever, or leukocytosis. In the majority of patients, nonoperative management is successful. However, in the patients who fail nonoperative management, the next step should be prompt operative intervention for source control of the sepsis.

Traditionally, an interval appendectomy has been recommended for patients managed nonoperatively at 6–8 weeks after treatment [88]. The rationale for this has been to prevent recurrent appendicitis [89, 90] and to exclude neoplasms (such as carcinoid, adenocarcinoma, mucinous cystadenoma, and cystadenocarcinomas) [91, 92]. Recent studies suggest that interval appendectomy is unnecessary [93–95]. Recurrent appendicitis is uncommon and appendectomy can be performed at the time of recurrence [94, 95].

In the general population, the risk of malignancy is quite low but increases with advanced age [94, 96]. As with all surgical decisions, and especially in the case of elderly patients, clinicians must be circumspect. The benefit of interval appendectomy should be weighed against the risks of surgical intervention. Colonoscopy should be considered prior to appendectomy in patients over 50 years old who have not had a recent colonoscopy to rule out concurrent colonic pathology necessitating resection.

Antimicrobial management of complicated appendicitis is varied. Traditionally, antibiotics would be continued for 10–14 days in hopes of reducing the likelihood of postoperative abscesses with little evidence. Some have advocated for using clinical markers such as fever and leukocytosis to guide the duration of therapy [97]. The most recent evidence shows no benefit to continuing antibiotics beyond 4 days after appendectomy regardless of systemic inflammatory signs [98, 99]. The appropriate length of antibiotics has not been studied in the elderly but the average of patients in the STOP-IT trial was over 50 [98]. Whether significant immunosenescence should be factored into determining the appropriate length of antibiotics is not clear. There is also limited data to suggest that uncomplicated cases of appendicitis be treated with antibiotics alone, reserving surgical intervention for those who fail nonoperative management [100–102].

Outcomes

Despite improvements in the diagnosis and management of geriatric surgical patients, morbidity and mortality for appendicitis remain high. Morbidity rates (28–60 %) and mortality rates (up to 10 %) are all significantly higher than younger patients. In 2004, deaths from appendicitis were rare, but nearly 70 % of patients who died from appendicitis were ≥65 years old [103]. This is typically attributed to delays in diagnosis and higher rates of perforation. Perforated appendicitis portends to longer hospital stays, an increased risk of wound, and other nosocomial infections. Intra-abdominal sepsis is seen almost exclusively in patients with perforation. The additive burden of disease in elderly patients where cardiac, pulmonary, and malignant comorbidities are far more common not surprisingly yields a higher mortality rate [50–53, 55, 75, 76].

Malignancy and Mucocele

Malignancy of the appendix is uncommon, occurring in approximately 1 % of appendectomy specimens, and accounts for roughly 0.5 % of intestinal neoplasms. Carcinoid tumors are the most common, comprising over 50 percent of appendiceal neoplasms. As is the case with other carcinoid tumors arising in the intestines, appendiceal carcinoids can secrete serotonin and other vasoactive substances. These substances are responsible for the carcinoid syndrome, which is characterized by episodic flushing, diarrhea, wheezing, and right-sided valvular heart disease. Nearly all appendiceal carcinoids are found incidentally during an operation for acute appendicitis, and the majority of those are located at the tip of the appendix [104, 105]. This incidence in patients over 40 is higher than their younger cohorts [96].

Additional surgical management for appendiceal carcinoids is a subject of some debate. Tumor size is an important determinant of the need for further surgery [106]. Very small carcinoid tumors of the appendix (<1 cm) are generally considered benign. However, slightly larger (1–2 cm) tumors have rarely been reported to metastasize regionally and have deep invasion. Appendiceal carcinoid tumors ≥2 cm have a 5-year mortality of approximately 30 %. In contrast, 1 cm appendiceal tumors have a 5 % mortality at 5 years [107]. Whether colectomy should be performed in patients with smaller tumors is unclear, but the latest recommendations do not support formal colectomy for small (<2 cm) tumors [108].

Oncologic right colon resection should be performed for patients with tumors >2 cm, tumors at the base of the appendix, and incompletely resected tumors. Other debated indications for right hemicolectomy include tumors <2 cm, mesoappendiceal invasion, lymphovascular invasion, intermediate- to high-grade pathologic features, mixed histology (goblet cell carcinoid, adenocarcinoid), or obvious mesenteric nodal involvement. Some dissenting authors consider appendectomy alone adequate for tumors <2 cm, regardless of mesoappendiceal invasion. Most agree that for carcinoids <2 cm in size without evidence of mesoappendiceal invasion or nodal involvement, simple appendectomy alone is adequate [107, 109–112].

In contrast to other appendiceal neoplasms, the majority of patients with adenocarcinomas present with symptoms consistent with acute appendicitis. Patients can also present with ascites, generalized abdominal pain, or abdominal mass. Appendiceal adenocarcinomas fall into one of three separate histologic types: the most common is the mucinous type, intestinal or colonic type (which closely mimics adenocarcinomas found in the colon), and, the least common, signet-ring cell adenocarcinoma [113–115].

In general, the optimal treatment for most appendiceal adenocarcinomas is a right colectomy. Some authors advocate a simple appendectomy for adenocarcinomas that are confined to the mucosa or well-differentiated lesions that invade no deeper than the submucosa. Although this distinction can be difficult to make intraoperatively, a more common scenario is the unexpected finding of an adenocarcinoma when the surgical report of an appendectomy specimen is finalized. In such cases, a right colectomy need not be pursued for appendiceal adenocarcinomas that are confined to the mucosa or well-differentiated lesions that invade no deeper than the submucosa [116]. The role of adjuvant chemotherapy for adenocarcinoma of the appendix remains unknown. The low incidence of this disease has precluded the performance of randomized studies, and few institutions see sufficient numbers of patients to report series of homogeneously treated patients.

The term appendiceal mucocele refers to any lesion that is characterized by a distended, mucus-filled appendix. It may be either a benign or malignant condition. The course and prognosis of appendiceal mucoceles are related to their histologic subtypes which include mucosal hyperplasia, simple or retention cysts, mucinous cystadenomas, and mucinous cystadenocarcinomas. Mucoceles that are due to hyperplasia, or that arise from an accumulation of mucus distal to an obstruction in the appendiceal lumen, even if they rupture, are asymptomatic, are benign, and do not recur. They may be diagnosed incidentally on a CT scan done for another purpose. In contrast, mucoceles that develop from true neoplasms (cystadenomas or cystadenocarcinomas) when ruptured can lead to intraperitoneal spread and the clinical picture of pseudomyxoma peritonei.

Surgical resection should be pursued, even for a benign-appearing appendiceal mucocele, since it may harbor an underlying cystadenocarcinoma [117–120]. An oncologic right hemicolectomy is advocated for patients with complicated mucoceles involving the terminal ileum or cecum. If there is no evidence of peritoneal disease and the final pathology after traditional appendectomy shows a cystadenocarcinoma, a right colectomy could be considered to remove lymph nodes; however, the chance of nodal spread is quite small. An acceptable approach (assuming negative resection margins) is observation alone. If, on the other hand, there is evidence of peritoneal disease at laparoscopy, then the procedure should be converted to an open laparotomy for debulking.

It is important to remember the association between appendiceal mucoceles and other tumors involving the GI tract, ovary, breast, and kidney [121, 122]. This possibility should be evaluated either preoperatively or intraoperatively.

Conclusions

Appendicitis is uncommon in elderly patients. However, when it does occur, elderly patients have poorer outcomes. Delayed presentation, preexisting medical conditions, and more rapid progression of disease contribute to increased morbidity and mortality. Elderly patients with significant comorbidities do not tolerate complications that are associated with advanced appendicitis well. It is critical that clinicians have appendicitis in their differential diagnosis when an elderly patient presents to the hospital with abdominal pain. Expeditious evaluation and treatment are imperative.

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