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REVIEW

Treatment options of inflammatory appendiceal masses in adults

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Abstract

At present, the treatment of choice for uncomplicated acute appendicitis in adults continues to be surgical. The inflammation in acute appendicitis may sometimes be enclosed by the patient's own defense mechanisms, by the formation of an inflammatory phlegmon or a circumscribed abscess. The management of these patients is controversial. Immediate appendectomy may be technically demanding. The exploration often ends up in an ileocecal resection or a right-sided hemicolectomy. Recently, the conditions for conservative management of these patients have changed due to the development of computed tomography and ultrasound, which has improved the diagnosis of enclosed inflammation and made drainage of intra-abdominal abscesses easier. New efficient antibiotics have also given new opportunities for nonsurgical treatment of complicated appendicitis. The traditional management of these patients is nonsurgical treatment followed by interval appendectomy to prevent recurrence. The need for interval appendectomy after successful nonsurgical treatment has recently been questioned because the risk of recurrence is relatively small. After successful nonsurgical treatment of an appendiceal mass, the true diagnosis is uncertain in some cases and an underlying diagnosis of cancer or Crohn's disease may be delayed. This report aims at reviewing the treatment options of patients with enclosed appendiceal inflammation, with emphasis on the success rate of nonsurgical treatment, the need for drainage of abscesses, the risk of undetected serious disease, and the need for interval appendectomy to prevent recurrence.

Key words: Appendicitis; Phlegmon; Abscess; Computed tomography; Antibiotics; Percutaneous drainage; Surgery

Core tip: The management of adult patients with inflammatory appendiceal masses is controversial. This report aims at reviewing the treatment options of these patients, with emphasis on the success rate of nonsurgical treatment, the need for drainage of abscesses, the risk of undetected serious disease, and the need for interval appendectomy to prevent recurrence. The debate arises over the importance of the complication rate of interval appendicectomy. Moreover, if appendicectomy is not performed, consideration needs to be given to what investigations should be undertaken and in which patients. It is also worth recalling that the appendix is used in reconstructive surgery.

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INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen and can be classified into uncomplicated and complicated. The life-time risk of appendicitis is 7%-8%, with the highest incidence in the second decade. The inflammation in acute appendicitis may sometimes be enclosed by the patients own defense mechanisms, by the formation of an inflammatory phlegmon or a circumscribed abscess. The management of these patients is controversial. Immediate appendectomy may be technically demanding because of the distorted anatomy and the difficulties to close the appendiceal stump because of the inflamed tissues. The exploration often ends in ileocecal resection or a right-sided hemicolectomy due to the technical problems or a suspicion of malignancy because of the distorted tissues[1-9]. Recently, the conditions for conservative management of these patients has changed due to the development of computed tomography (CT) and ultrasound (US), which has improved the diagnosis of enclosed inflammation and made drainage of intra-abdominal abscesses easier[10-15]. New efficient antibiotics have also given new opportunities for nonsurgical treatment of appendicitis[16-21]. The traditional management of these patients is nonsurgical treatment followed by interval appendectomy to prevent recurrence. The need for interval appendectomy after successful nonsurgical treatment has recently been questioned because the risk of recurrence is relatively small[22-27]. After successful nonsurgical treatment of an appendiceal mass, the true diagnosis is uncertain in some cases and an underlying diagnosis of cancer or Crohn's disease (CD) may be delayed[27].

This report reviews the treatment options of patients with enclosed appendiceal inflammation, with emphasis on the success rate of nonsurgical treatment, the need for drainage of abscesses, the risk of undetected serious disease, and the need for interval appendectomy to prevent recurrence. The debate arises over the importance and level of the complication rate of interval appendicectomy. Moreover, if appendicectomy is not performed, consideration needs to be given to what investigations should be undertaken and in which patients. It is also worth recalling that the appendix is occasionally used in reconstructive surgery[26,28].

DEFINITIONS

Acute appendicitis is inflammation of the vermiform appendix and remains the most common cause of the acute abdomen in young adults. The term complicated appendicitis is often used to describe a palpable appendiceal mass, an appendiceal phlegmon, or a localized abscess without distinction. A phlegmon is an inflammatory tumor consisting of the inflamed appendix, its adjacent viscera and the greater omentum, whereas an abscess is a pus-containing appendiceal mass[27-31]. The diagnosis of enclosed inflammation is made by finding a palpable mass at clinical examination before or after anesthesia, or by finding an inflammatory mass or a circumscribed abscess by CT, US or at surgical exploration of the abdomen. We consider that nonsurgical treatment has failed when the patient undergoes appendectomy during the same hospital stay after attempted nonsurgical treatment. The patients treated with drainage are those who had drainage (without appendectomy) of an abscess either percutaneously or by surgical exploration. Morbidity includes postoperative infectious complications, intestinal fistula, small bowel obstruction, and recurrence after initially successful nonsurgical management[27].

TREATMENT OPTIONS OF NONCOMPLICATED ACUTE APPENDICITIS

Although the etiology of acute appendicitis is poorly understood, it is probably caused by luminal obstruction in the majority of cases. Luminal obstruction can be caused by fecaliths, lymphoid hyperplasia, foreign bodies, parasites and both primary (carcinoid, adenocarcinoma, Kaposi sarcoma and lymphoma) and metastatic (breast and colon) tumors. Once appendiceal obstruction occurs, the continued secretion of mucus results in elevated intraluminal pressure and luminal distention. This eventually exceeds capillary perfusion pressure, which leads to venous engorgement, arterial compression, and tissue ischemia. As the epithelial mucosal barrier becomes compromised, luminal bacteria multiply and invade the appendiceal wall, which causes transluminal inflammation. The most common bacteria that can cause acute appendicitis are intestinal bacteria including *Escherichia coli* and bacteria belonging to the *Bacteroides fragilis* group. Continued ischemia results in appendiceal infarction and perforation[29-31]. However, the observation of spontaneous resolution of acute appendicitis cases and some reports of a good outcome in patients treated with antibiotics suggest that not all cases of acute appendicitis are caused by mechanical obstruction and progression to complicated disease. Some researchers have suggested that uncomplicated and complicated forms of appendicitis are two distinct diseases, with different etiologies. As in other intra-abdominal infections, such as salpingitis, diverticulitis and enterocolitis, which are often treated only with antibiotics, the infectious etiology of acute appendicitis is advocated by some scholars. Conservative treatment is most effective when administered within 12 h of symptom onset, ideally within the first 6 h[16-21,29-33]. Antibiotic therapy is associated with a 68%-84% success rate and a trend toward decreased risk of complications without prolonging hospital stay. The authors have described a low morbidity and mortality rate, and a recurrence rate between 5% and 15%[25-33].

At present, the treatment of choice for uncomplicated acute appendicitis in adults continues to be surgical (open or laparoscopy) and it is the gold standard. The most common operative complications are wound infection, intra-abdominal abscess, and ileus caused by intra-abdominal adhesions (Dindo *et al*[34] classification), which vary in frequency between open and laparoscopic appendectomy. The overall complication rates for open and laparoscopic appendectomy are respectively 11.1% and 8.7%, with a mortality rate $< 0.5\%$[35-41]. The exclusive treatment with antibiotics cannot be routinely recommended in current medical practice and should only be considered in selected patients or conditions in which surgery is contraindicated or in the context of clinical studies[18,19,31,32].

PROPORTION OF PATIENTS WITH APPENDICITIS WHO DEVELOP ENCLOSED APPENDICEAL INFLAMMATION AND CLINICAL PRESENTATION

Circumscribed appendiceal inflammation is common and often undiagnosed preoperatively. The proportion of all patients with appendicitis treated for enclosed inflammation is 3.8%-5.0%. The risk of perforation is negligible within the first 12 h of untreated symptoms, but then increases to 8.0% within the first 24 h. It then decreases to 1.3%-2.0% during 36-48 h, and subsequently increases again to 5.8%-7.6% for each ensuing 24-h period[42-47].

The diagnosis is suspected in patients with a palpable mass or with symptom duration > 3 d and is more common in children, especially in those aged < 5 years. Delay in presentation, age > 55 years, and elevated temperature (> 38.8 ℃) on admission are predictors of perforated appendicitis. Additionally, patients older than 55 years of age have a 29% prevalence of perforated appendicitis in the first 36 h from symptom onset. Patients with hyperbilirubinemia and clinical symptoms of appendicitis should be identified as having a higher probability of appendiceal perforation than those with normal bilirubin levels[48,49].

Enclosed inflammation is found more often in studies in which the diagnosis is based on CT or US than in those based on clinical diagnosis (14.2% *vs* 5.1%). It is also more common in children than in adults as shown by the trend of 8.8% in children, 6.5% in patients of all ages, and 4.8% in adults. There is an early risk of perforation even within the first 36 h of symptom onset, which may be higher in men than women. This suggests that diagnostic imaging should be used more frequently in children, in patients with a long duration of symptoms, and in patients with a palpable mass. Appendectomy should be performed without delay in adults, especially men and those aged > 55 years once diagnosis is confirmed[42-47].

RADIOLOGICAL DIAGNOSIS

There is continued debate about the relative merits of US and CT[10-15,50-59]; the latest meta-analysis has concluded that CT[60-69] is significantly more sensitive than US for the diagnosis of appendicitis, but that US should be considered in children. Sonography has high sensitivity (86%-100%), specificity (88%-95%), and accuracy (91%-92%) in diagnosing acute appendicitis. CT is comparable to sonography with respect to sensitivity, specificity, and accuracy for adults (90%-97%, 93%-100%, and 94%-99%, respectively) and children (95%-97%, 91%-99%, and 96%, respectively) with appendiceal diameter > 6 mm, although some studies have revealed lower diagnostic rates in children than in adults. The major area of debate is regarding which patients suspected of having acute appendicitis should have a CT scan before appendectomy. There are several articles in the literature that argue against routine preoperative imaging of patients with suspected acute appendicitis. In these articles, the routine use of imaging has not been shown to decrease the rate of negative appendectomy, and may actually delay the diagnosis and appropriate intervention in cases of acute appendicitis. Other studies have shown a benefit from preoperative imaging in suspected acute appendicitis, and the development of guidelines for CT in patients with an equivocal presentation has decreased the rate of negative appendectomy from 25% to 6%. A review of a large, prospectively gathered database of general surgical procedures in Washington state has found the negative appendectomy rate to be 9.8% in patients with no preoperative imaging and only 4.5% in those who had a preoperative CT scan. This difference was statistically significant. Based on these findings, CT scans seem to have significant benefit in the evaluation of patients with suspected acute appendicitis, to exclude other pathology, in selected patients such as elderly people[52,70].

Various CT techniques have been described for diagnosing acute appendicitis, including enhanced CT with rectally administered colon contrast medium, enhanced focused CT with thin collimation (3-5 mm), nonfocused technique with oral and intravenous contrast material, focused technique with oral contrast medium, and focused helical CT with colonic contrast medium, and have a high diagnostic accuracy. CT provides a rapid complete diagnostic evaluation of the right lower quadrant, with reported accuracy rates in the diagnosis of appendicitis of up to 95%-100%[11,52,66]. The obvious disadvantages of CT include exposure to ionizing radiation and the potential for contrast medium reactions. Those who benefit most from preoperative imaging are those with an atypical presentation and women of childbearing age. However, it is recognized that this is not without increased cost, radiation exposure and a potential delay in diagnosis. The use of US is particularly important in children and can be of use in premenopausal women[50-52,58]. Institution of a clinical pathway using CT can lead to a substantial decrease in the number of negative appendectomies from 16% to 4%. CT has greater potential than US to reveal alternative diagnoses and complications, such as perforation and abscess formation. US has lower sensitivity than CT in the setting of appendiceal perforation. The appendix is significantly larger in diameter in perforated appendicitis than in appendicitis with no perforation (15 mm *vs* 11 mm). Direct CT signs (*i.e.*, phlegmon, abscess, and extraluminal air) are more specific for perforated appendicitis. Indirect signs (bowel wall thickening, ascites, ileal wall enhancement, intraluminal air, and combined intraluminal air and appendicolith) are also found with higher incidence in appendiceal perforation[13,53,54,61,63]. Intraluminal appendiceal air in the setting of acute appendicitis is a marker of perforated or necrotic appendicitis.

Recognition of this finding in otherwise uncomplicated appendicitis at imaging should raise suspicion for image-occult perforation or necrosis[56]. Defect in the enhancing appendiceal wall allows excellent sensitivity (94.9%) and specificity (94.5%) for the diagnosis of perforated appendicitis when evaluated in a group of patients with known appendicitis. A defect in the enhancing appendiceal wall has the highest sensitivity (64.3%) of any individual finding[53]. Detecting a defect in the enhancing appendiceal wall by using cine mode display of transverse thin-section CT images allows 96.1% accuracy for diagnosing appendiceal perforation[55]. In one series, appendicolith, free fluid, a focal defect in the enhancing appendiceal wall, and enlarged abdominal lymph nodes were not sensitive or specific for the presence of perforation. That study has concluded that unless abscess or extraluminal gas is present multidetector CT cannot establish the diagnosis of perforation[63].

The range of diagnoses that can mimic appendicitis is wide and includes right ureteric calculus, epiploic appendagitis, torsion of Meckel's diverticulum, mesenteric adenitis, inflammatory bowel disease, colitis, gynecological disorders, and right-sided diverticulitis. CT is useful in differentiating between these disorders[63].

Magnetic resonance imaging (MRI) has had little role in the evaluation of acute abdominal pain. However, increasing concerns over the potentially hazardous effects of ionizing radiation associated with CT have made MRI the study of choice to evaluate pregnant women and children with symptoms of appendicitis and equivocal US findings. MRI is highly accurate with a sensitivity of 100%, specificity of 98%, positive predictive value of 98%, and negative predictive value of 100%. Although MRI may be used in any patient with suspected acute appendicitis, there is a special role for MRI in pregnant women with new-onset abdominal pain. MRI has many advantages. It is valuable in the imaging of pregnant women and children because there is no exposure to ionizing radiation. Although MRI is safe during pregnancy, no intravenous contrast should be used during pregnancy because gadolinium is a category C drug and potentially teratogenic. However, noncontrast MRI provides detailed images, which usually provide the correct diagnosis. MRI is operator independent and the results are highly reproducible. MRI is more useful than US in obese patients and in patients with a retrocecal appendix, which is difficult to visualize on US. Drawbacks of MRI are that it is more expensive than other imaging modalities and not as widely available. The examination itself takes longer to perform and may be degraded by motion artifact. There are concerns that, with the exception of trained radiologists, other health care providers are not comfortable interpreting MRI findings[52,70-73].

IMMEDIATE SURGICAL TREATMENT *VS* NONSURGICAL TREATMENT

Emergency appendectomies are still considered the primary means of treating acute appendicitis, with mortality rates of 0.5%-2.4% and 0.07%-0.7% for patients with and without perforation, respectively. Overall, post-appendectomy complication rates are typically 10%-19% for acute appendicitis without perforation and reach 12%-30% for perforated acute appendicitis[19]. Perforation increases the mortality rate of acute appendicitis from 0.0002% to 3% and increases the morbidity from 3% to 47%[52]. Perforated appendicitis may be treated first by conservative treatment or percutaneous abscess drainage with great improvement of the clinical symptoms[74-80]. This is in contrast to nonperforated appendicitis, which requires operation as early as possible in order to reduce morbidity. Immediate surgical treatment of enclosed appendiceal inflammation is associated with a > 3-fold increase in morbidity compared with conservative management, and may result in an unnecessary ileocecal resection or right-sided hemicolectomy for technical reasons or suspicion of malignancy in about 3% of patients[9,27]. Nonsurgical treatment is successful in about 93% of patients, but may need percutaneous drainage of abscesses in about 20%. Most perforated appendicitis give way to generalized peritonitis and cannot be drained. Indications of drainage are absence of generalized peritonitis and presence of percutaneously or surgically drainable abscess[75-78]. Nonsurgical treatment is associated with lower morbidity and shorter hospital stay compared with immediate appendectomy. The results of immediate surgery compared with those of nonsurgical treatment, eventually followed by interval appendectomy, have been reported in 19 retrospective studies[27]. Right-sided hemicolectomy for suspicion of a malignant disease or for technical reasons, but where only inflammatory changes could be found at histopathological examination, has been reported in 17 of 493 adult patients. In all but three of the studies, the authors have concluded that nonsurgical treatment is to be recommended. Conservative treatment is associated with significantly fewer overall complications, wound infection, abdominal/pelvic abscess, ileus/bowel obstruction, and reoperation. No significant difference has been found in the duration of first hospitalization, overall duration of hospital stay, and duration of intravenous antibiotics[79]. Immediate surgery is associated with morbidity in 35.6% of patients compared with 13.5% in nonsurgical treatment and an additional 11.0% after interval appendectomy. The majority of the studies have practiced elective interval appendectomy after successful nonsurgical treatment.

PRIMARY NONSURGICAL TREATMENT FOLLOWED BY DELAYED OR INTERVAL APPENDECTOMY OR WITHOUT APPENDECTOMY

The results of primary nonsurgical treatment followed by delayed appendectomy during the same hospital stay have been compared with those of interval appendectomy and with or without surgical intervention 6-12 wk later (interval appendectomy)[80-88]. Delayed appendectomy[89-93] is associated with morbidity in 18.2% compared with 12.4% after interval appendectomy. The return to work takes longer for patients treated with interval appendectomy, mainly because the patients want to have the planned interval appendectomy done before they are willing to return to work. One prospective study[7] has randomized patients to primary nonsurgical treatment followed by delayed or interval or no appendectomy. The group with nonsurgical treatment without appendectomy had the lowest morbidity and the shortest length of stay. In patients with an appendiceal mass, the authors have concluded that conservative treatment without interval appendicectomy is the best treatment.

FAILURE RATE OF NONSURGICAL TREATMENT AND NEED FOR ABSCESS DRAINAGE

All studies have reported a low failure rate for nonsurgical treatment without appendectomy; some of them even without giving antibiotics[75-80]. The failure rate for all the studies was 7.2%. Failure was associated generally with abscess diameter > 4-5 cm[77-79]. The proportion of patients in need of abscess drainage is strongly related to how the diagnosis is made, with 100% in studies of patients selected because of a drained abscess, 47.5% in patients with a palpable mass or preoperatively found abscess, 27.6% in patients with an abscess or phlegmon diagnosed by CT or US, 9.5% in patients with a palpable mass, and no need for drainage in studies of patients with a phlegmon diagnosed by CT or US. There is no association between the need for drainage and patient age.

COMPLICATIONS FOLLOWING INTERVAL APPENDICECTOMY

The morbidity of interval appendectomy has been reported in a few studies with a pooled value of 11.0%[94-97]. The age of the included patients had no influence on the results. The complication rate following interval appendicectomy is a consideration to be balanced against the recurrence rate. The complication rate varies from 8% to 23%. True surgical complications include wound infection (15.0%), pelvic abscess (5.0%), and aspiration pneumonia (1.5%). Another retrospective study reported a complication rate of 13%, but a prolonged fever, which others may not have cited as a true complication, accounted for almost half of these complications and only one wound infection occurred in 38 interval appendicectomies. An 8% complication rate was reported in a review of 50 interval appendicectomies, but about 25% of these were prolonged fever, about 50% cecal damage, and the remainder subcutaneous abscesses. Laparoscopic interval appendicectomy may decrease the complication rate and length of hospital stay[36,92]. A small retrospective study of 10 patients undergoing laparoscopic interval appendicectomy reported no complications and all patients were discharged on the day after surgery. A prospective study of open and laparoscopic appendicectomy for acute appendicitis in 65 patients showed a significantly lower wound infection rate in the laparoscopic group; however, it is not possible to extrapolate directly this finding to interval appendicectomy, even though one would expect a lower wound infection rate. In one study, the morbidity rates, particularly for intra-abdominal abscesses and wound infection, were lower for laparoscopic appendectomy in complicated appendicitis than those reported in the literature for open appendectomy, whereas operating times and hospital stays were similar[88].

RISK OF RECURRENCE

The recurrence rate of appendiceal pathology if appendicectomy is not performed is central to the debate over the use of routine interval appendicectomy. For some authors, the risk of recurrence after successful nonsurgical treatment was about 10% (3%-25% in the literature) and was often associated with an appendicolith. The majority of recurrences occur within 6 mo after initial hospital stay. Recurrence is characterized by a milder course than the primary attack in most cases. Elective interval appendectomy is associated with morbidity in about 11% (0%-23%) of patients. These results do not motivate routine elective interval appendectomy after successful nonsurgical treatment[16,20,27,98]. The literature review shows that at least 75%-90% of routine interval appendicectomies in adults are unnecessary. It would be reasonable and perhaps safer, as malignancy can be missed at appendicectomy, to replace routine interval appendicectomy with adequate follow-up of symptoms, performing appendicectomy only if symptoms recur or persist. Appropriate investigation should be done if the appendix is not removed, provided the patient has access to surgical care should symptoms recur[27].

HISTOLOGY

Several studies have examined the microscopic changes in the interval appendicectomy specimen. Many specimens show chronic inflammatory changes (52%)[5] and acute inflammation (50%)[3,8]. However, this may be of little clinical importance in the asymptomatic patient. The real concern is whether leaving the appendix *in situ* will prevent the detection of a cecal carcinoma or an ileal or appendicular malignancy[27].

RISK OF MISSING OTHER DIAGNOSES

Nonsurgical treatment is associated with a risk of missing or delaying an underlying cancer diagnosis or CD in about 2% of patients. The concern of failing to diagnose a rare case of appendiceal malignancy without interval appendicectomy may persist even with colonic investigation, although it is likely that these patients will have recurrent symptoms[99-101]. Most of the cancer cases occur in patients aged > 40 years. The risk of missing an important alternative diagnosis is probably lower if imaging is used for the diagnosis of enclosed appendiceal inflammation. This underlines the need of follow-up after nonsurgical treatment, especially in patients aged > 40 years. By tradition, this follow-up consists of colonoscopy or a barium study of the colon, but a virtual colonoscopy, CT scan, or US is probably more accurate to detect malignant conditions outside the colon or CD. Malignant disease was detected during follow-up in 1.2% of patients. This risk was related to age at diagnosis with 0.2% in children, 1.8% in studies of all ages, and 1.4% in adults. There was no difference in relation to how the diagnosis was done. CD was detected in 0.7% during follow-up after nonsurgical treatment. This risk was related to age with 0.1% in children, 0.8% in all ages, and 1.5% in adults. There was no difference in relation to how the diagnosis was done. Appendicular malignancy is rare and may be missed if appendicectomy is not performed; however, it is likely that such patients will have either a nonresolving mass or early recurrence. Colonic malignancy is a more common concern, but interval appendicectomy is not a reliable method of detecting a cecal tumor. Imaging is needed when cecal malignancy is possible. Colonic investigation should be a consideration regardless of whether interval appendicectomy is performed[27].

CONCLUSION

In patients with suspicion of contained appendiceal inflammation, based on a palpable mass or long duration of symptoms, the diagnosis should be confirmed by imaging techniques, especially CT scan. The patient should receive primary nonsurgical treatment with antibiotics and abscess drainage as needed. After successful nonsurgical treatment, no interval appendectomy is indicated in some cases, but the patient should be informed about the risk of recurrence especially in the presence of appendicolith. The risk of missing another underlying condition (cancer or CD) is low, but motivates a follow-up with a colon examination and/or a CT scan or US, especially in patients above the age of 40 years.

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