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Doubts, Problems and Certainties about Acute Appendicitis

Edited by Angelo Guttadauro

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Published in London, United Kingdom

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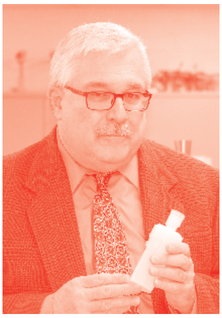



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http://dx.doi.org/10.5772/intechopen.91502
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First published in London, United Kingdom, 2022 by IntechOpen
IntechOpen is the global imprint of INTECHOPEN LIMITED, registered in England and Wales, registration number: 11086078, 5 Princes Gate Court, London, SW7 2QJ, United Kingdom
Printed in Croatia

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Additional hard and PDF copies can be obtained from orders@intechopen.com

Doubts, Problems and Certainties about Acute Appendicitis
Edited by Angelo Guttadauro
p. cm.
Print ISBN 978-1-83968-855-3
Online ISBN 978-1-83968-856-0
eBook (PDF) ISBN 978-1-83968-857-7

Meet the editor

Dr. Angelo Guttadauro is a researcher at the University of Milano-Bicocca, Italy, and first-level manager at the U.O.C. of General Surgery, Zucchi Clinical Institute, Monza. He is the founder and head of the "Hernia Center" of Monza-Brianza. He has participated in research projects of the Ministry of University and Scientific and technological research. In 2015, Dr. Guttadauro obtained an international patent for a prosthesis for inguinal hernioplasty and standardized a new surgical technique for the application of the prosthesis. In 2017, he won the Innovation Grant award from the University of Milano-Bicocca. He is the author of ninety scientific publications, books, and abstracts in national and international journals and book chapters. He has presented his works in around 250 national and international congresses worldwide.

Contents

Preface

Acute appendicitis, which has been studied and treated for hundreds of years, is still a subject of debate today.

Its clinical presentation is atypical in 30%–40% of cases and diagnostic delays, especially in the elderly, make the diagnosis challenging and often hinder the prevention of complications.

Despite the greater frequency of this disease in children and adolescents, in which the diagnosis is generally simple, acute appendicitis can occur at any age.

The great heterogeneity of the population that can be affected by this disease makes it difficult to establish a universally valid diagnostic procedure. An individualized approach based on age, sex, comorbidities, and clinical manifestations is therefore always necessary.

This book, which includes contributions from experts around the world, takes stock of the current situation in acute appendicitis to help surgeons administer proper and timely treatment.

I sincerely thank the contributing authors without whom this book would not have been possible.

Dr. Angelo Guttadauro
University of Milano-Bicocca,
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Foreword

Acute appendicitis affects 7% of the world's population, with 1% of those affected undergoing appendectomy. Mortality from appendicitis is 0.3% and increases to more than 1.5% in complicated forms of the disease. Although prevalent in young patients, appendicitis also occurs in the elderly, with clinical pictures that are often difficult to diagnose.

About 60,000 appendectomies are performed in Italy every year. The risk of serious complications, such as peritonitis, leads to an increase in the number of operations, with the risk of unnecessary appendectomies, up to 20-30% of cases. Hence the need to improve diagnosis. From the classic, simple evaluation of symptoms and objectivity, healthcare professionals today use more rigorous methods to diagnosis appendicitis, including Alvarado score and preoperative imaging diagnostics such as ultrasound, which is simple to perform, inexpensive, and has a diagnostic accuracy of up to 90% when used properly.

I am happy to present this volume edited by Dr. Angelo Guttadauro and written by experts from around the globe. Chapters examine and discuss the diagnosis of acute appendicitis as well as interventions and surgical tactics. This book is a useful reference for gastroenterologists and surgeons.

Francesco Gabrielli
Professor,
Full Professor in General Surgery,
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Section 1

Introduction

Chapter 1

Introductory Chapter: Doubts, Problems, and Certainties about Acute Appendicitis

Angelo Guttadauro

1. Introduction

Acute appendicitis (AA) is one of the most common abdominal surgical emergencies, studied and treated for hundreds of years. Although the progress of medicine, in particular radiology, has allowed a safer diagnosis, its treatment is still under discussion.

AA disease can affect people of all ages with a prevalence in subjects between 10 and 20 years. Its incidence rate is reduced with increasing age. There is a predominance of cases in the male sex, although the female sex receives appendicectomy in more cases. The estimated lifetime risk of AA is between 7 and 9%.

The precise etiology of appendicitis is not yet fully understood. Probably an obstruction of the lumen due to coprolites, foreign bodies, lymphoid hyperplasia, or tumors leads to a subsequent blood stasis, necrosis, and perforation of the organ. Symptomatology does not always occur in a similar manner, but in most cases the patient refers center-abdominal pain migrating to the right iliac fossa, usually accompanied by fever, nausea, vomiting, anorexia, and/or diarrhea and, in the most advanced cases, signs of peritoneal irritation. The symptomatology in the elderly patient is more nuanced and difficult, and often the aid of radiodiagnostics is needed to diagnose AA.

1.1 Diagnosis

Due to the differences in symptoms dependent on age, sex, and comorbidities, it is not possible to follow a flowchart for the diagnosis but it is necessary to adopt an individualized approach. There are useful scores for diagnosis and treatment that consider the age of the patient.

In most cases, in a young patient, already with a history and objective examination, it is possible to diagnose an acute appendicitis with a good probability. In support of a differential diagnosis with other diseases, there are no specific laboratory tests. WBC count, PCR, and VES increase during appendicitis, but they are universal signs of any type of inflammation. More help is provided by radiodiagnostic tests. Ultrasound and a CT scan allow safe diagnosis in severe or blurred cases as in advanced age.

Current guidelines recommend the use of the abdominal ultrasound as the first diagnostic test. Advantages include low cost, easy accessibility, and the absence of ionizing radiation, generally contraindicated in younger women and in pregnancy. The main limits of this method are a lower sensitivity and specificity compared to CT, which are also related to the operator's experience. In cases where the ultrasound is not straight and the patient cannot be subjected to CT, MRI is a valid alternative. It has excellent sensitivity and specificity but is little used because of the costs, duration, motion artifact, and poor accessibility. Whichever method is used, the most suggestive radiological characteristics of AA are the thickening of the walls, a noncompressible lumen with a diameter of more than 6 mm, the presence of coprolites, the heterogeneity of the peri-appendicular fat, and the presence of free fluid in the abdomen and/or lymphadenopathy.

1.2 Treatment

Regarding treatment, although until a few years ago the most practiced surgery was open appendicectomy, today's guidelines recommend the use of a laparoscopic approach, where, of course, the surgeon has practical skills. This method is now recognized as safe and executable on patients of all ages and also in complicated cases. Recent meta-analyses have shown that, despite a longer duration of surgery and a higher surgical cost, the laparoscopic surgery is associated with a lower postoperative pain, less length of hospital stay, faster resumption of daily activities, better esthetic result, and lower rate of surgical wound infections. In the past, some studies had found a higher rate of postoperative intra-abdominal abscess associated with the laparoscopic technique, but recent work has shown that this complication occurs equally.

There are two other surgical techniques available: the laparoscopic appendicectomy through single incision and the NOTES (Natural Orifice Transumbilical/gastric/vaginal Endoscopic Surgery) approach. The approach by single incision showed no clear advantages due to the long learning curve and due to the difficult accessibility of the equipment, despite some evidence in the literature of lower post-operative pain and shorter hospitalization.

The NOTES approach, which uses a natural orifice (oral or vaginal) as mininvasive access in the abdomen, although there is some positive feedback such as the reduction of the postoperative pain, surgical wound infections, hernias and abdominal adherences, is performed only in very specialized centers due to the long learning curve and the high cost of the intervention.

Regarding the stages of surgery, there are many points that are debated.

The current guidelines, based on the latest studies and meta-analysis, no longer consider it useful to irrigate the peritoneum in cases of complicated AA compared to aspiration alone.

There are no substantial differences in terms of clinical outcomes, length of stay, and rate of complications depending on the technique used for the dissection of the mesenteriol.

The use of an endostapler for the closure of the appendicular stump is not advantageous compared to the endoloops, even in complicated cases. There are also no real advantages of the introflexion of the appendicular stump after its section.

There is no concrete evidence of benefits related to the use of intra-abdominal drainage even in complicated cases. In fact, the use of the drainage is related to a longer duration of the surgical time and of the hospital stay as well as a higher rate of wound infections.

An important aspect is the use of a nonsurgical treatment in selected cases. In fact, not all AAs progress toward perforation, and a resolution can commonly occur with an appropriate medical therapy. Although appendicectomy must remain in my opinion the first-line therapy in acute and/or complicated forms, in some patients, it can be considered a reasonable first approach with only antibiotic therapy and support.

Conservative treatment with antibiotic therapy can be considered, for example, when clinical conditions are not serious, laboratory tests are not extremely altered, there are doubts about the diagnosis, the patient has severe comorbidities, or the patient refuses the intervention.

Numerous studies have shown the applicability and safety of this approach in selected patients with uncomplicated forms of AA although in these patients, there could be a recurrence rate of up to 38%. Some recent works have shown that some forms of uncomplicated AA can be treated with the support therapy only (rehydrating, analgesics, antipyretic) and without the use of antibiotics, reducing the duration and costs of the hospital stay.

The administration of a broad-spectrum antibiotic therapy has shown benefit before surgery. Postoperative administration is now recommended only for complicated forms. The duration of the treatment must be evaluated depending on clinical and laboratory data, but in general a treatment period of 3–5 days is considered appropriate.

There are also two categories in which a personalized approach is needed: in elderly patients (>65 years old) and in pregnant women. In elderly patients, the incidence of AA is much lower than in younger people, but the mortality rate reaches up to 8%, compared to 0–1% of the rest of the population. For this reason, it is necessary to pay particular attention when there is a suspect of AA in these subjects; in particular, clinical examination and blood tests should be completed with a radiological test. Also, in these cases, it is necessary to consider the surgery as a first-line treatment, paying particular attention to the clinical history of the patient and assessing a precise balance of risks–benefits.

Regarding pregnant women, the main recommendations concern diagnostic imaging, which involves only those methods that do not use ionizing radiation. The surgical option remains the best choice for this category as well. Until recently, it was believed that laparoscopy is related to a higher risk of fetal death and premature childbirth, but more recent studies have shown that these complications occur in equal measure both with the open approach and with the laparoscopic one. For that reason, the laparoscopic approach also remains the gold standard in pregnancy.

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Section 2

Acute Appendicitis: Doubts, Problems and Certainties

Chapter 2

Management of Appendicitis

Vishal P. Bhabhor

Abstract

Appendicitis is one of the most common causes of acute abdomen with life time risk between 6 and 8% and it's a most common non obstetric surgical emergency during pregnancy. Appendicitis is claimed to be unknown in the villages of India and China in paper by A. M. Spencer. The reason is simply due to the fact that diagnostic facilities do not exist and cases are not recognized. So diagnosing acute appendicitis accurately and efficiently can reduce morbidity and mortality from perforation and other complications. Surgical intervention is the first choice for appendicitis with medical management being reserved for special situations.

Keywords: diagnosis of appendicitis, appendectomy, appendectomy in pregnancy

1. Introduction

It is widely accepted that the inciting event in most instances of appendicitis is obstruction of the appendiceal lumen. This may be due to lymphoid hyperplasia, inspissated stool (fecolith), or some other foreign body. In this chapter clinical signs, diagnostic tools and surgical approach towards appendicitis is covered.

2. Clinical features

1. Pain: first noticed in periumbalical region with progressive inflammation of appendix, the parietal peritoneum in RIF becomes irritated, producing more intense, constant and localized somatic pain

2. Pyrexia: usually low-grade, and occur within first 24 hours of onset of pain with corresponding increase in the pulse rate

3. Tenderness: seen on right iliac fossa by superficial to deep palpation

4. Rebound tenderness: (Blumberg sign) asking the patient to cough or gentle percussion over the site of maximum tenderness will elicit rebound tenderness

5. Rovsing sign: elicited by pressure over left iliac fossa causing pain over right iliac fossa

6. Psoas sign: stretching of right thigh causing irritation to inflamed appendix over psoas muscle

7. Obturator sign: In supine position with passive rotation of the flexed right hip causing pain

8. Baldwin's sign: A hand is placed over the right flank and patient is asked to raise the right lower limb with knee extended causes pain

9. Ligat's sign: Hyperaesthesia in Sherren's triangle (formed by lines joining the umbilicus, right anterior superior iliac spine and symphysis pubis) is an occasional but inconstant accompaniment of gangrenous appendicitis

3. Differential diagnosis

- Children:

  1. Gastro enteritis
  2. Mesenteric adenitis
  3. Meckel's diverticulitis
  4. Intussusception
  5. Henoch-Schonlein purpura
  6. Right Lobar pneumonia

- Adult:

  1. Regional enteritis
  2. Ureteric colic
  3. Perforated peptic ulcer
  4. Torsion testis
  5. Pancratitis
  6. Rectus sheath hematoma

- Adult female:

  1. Mittleschmertz
  2. PID
  3. Ectopic pregnancy
  4. Torsion/rupture of ovarian cyst
  5. Endometriosis

- Elderly:

  1. Diverticulitis
  2. Intestinal obstruction

3. Colonic carcinoma

4. Mesenteric infarction

5. Leaking aortic aneurysm

4. Investigations

Despite advances in other diagnostic modalities, appendicitis remains a diagnosis based primarily on history and physical examination.

4.1 Alvarado score

Alvarado scoring system is purely based on history, clinical examination and few laboratory tests and is very easy to apply (**Table 1**) [1].

Symptoms	Score
Migratory right iliac fossa pain	1
Anorexia	1
Nausea/vomiting	1
Signs	
Tenderness in right iliac fossa	2
Rebound tenderness	1
Elevated temperature	1
Laboratory findings	
Leucocytosis	2
Shift to left of neutrophils	1
Total score	10

Probability of acute appendicitis is decided by score which as following:
Score less than 5: Not sure.
Score between 5 and 6: Compatible.
Score between 6 and 9: Probable.
Score more than 9: Confirmed.

Table 1.
Alvarado scoring for appendicitis.

4.2 Leucocytosis

It is clear that 80–85 percent of patients with acute appendicitis will have a total white blood cell count of over $10000/m^3$. Neutrophilia of >75 percent will occur in 78 percent of patients. However, the white cell count is raised in 25–70 percent of patients with other causes of acute right iliac fossa pain.

A raised white cell count is highly sensitive for acute appendicitis, it is rendered almost useless by a low specificity and it has little diagnostic value.

4.3 Serum fibrinogen

Fibrinogen is an acute-phase reactant, meaning that elevated fibrinogen levels can be seen the following conditions:

- Inflammation
- Tissue damage/trauma
- Infection
- Cancer

As the acute appendicitis is an acute inflammatory condition serum fibrinogen is useful as novel indicator of ongoing inflammatory process.

4.4 Plain radiograph

However, there is no single sign that is pathognomic of acute appendicitis in a plain film. Brooks et al. described (1965) several signs in a case of acute appendicitis.

a. Presence of appendicolith.

b. Sentinel loop—dilated atonic containing fluid level present in right iliac fossa.

c. Dilated ceacurn.

d. Widening/blurring of preperitonial fat line.

e. Haziness in right lower part.

f. Scoliosis concave to right.

g. Right lower quadrant mass indenting caecum.

h. Blurring of right psoas outline.

i. Gas in the appendix.

Plain radiograph has less specificity. It has similar findings and normal findings as well as in other conditions.

Furthermore, irradiation hazard s especially to two groups' most frequently requiring elucidation, namely women of reproductive age and children, as well as the cost and overloading of radiology departments make this investigation of low diagnostic yield unattractive.

4.5 Ultrasound

If the appendix can be seen on ultrasound examination, this is taken to indicate the presence of acute appendicitis and idea about its position [2]. Structure which is blind-ended, immobile, non-compressible and cannot be displaced by ultrasound probe is appendix. The eco density of appendicular lumen is varying and with changed mucosa and thickened wall gives picture of a bull's eye on ultrasound.

There may be presence of fluid or faecolith in the lumen of the appendix confirming the appendicitis. The ultrasound examination will be non-diagnostic in

3–11 percent of cases because of pain, guarding, obesity or overlying gas. Among seven studies in literature, the sensitivity ranges from 75 to 89 percent and the specificity from 86 to 100 percent. Poorer results are also reported for retrocaecal appendices, early appendicitis and perforated appendices.

In the hands of expert ultrasound is highly specific, along with that it has further advantages. Diseases such as mesenteric adenitis, terminal ileitis, ureteric stones and some gynecological disorders can be accurately diagnosed by ultrasound which may not require surgery. In pregnancy ultrasound has major diagnostic role. Need of expertise and special equipment are major disadvantages. Other than this it's difficult to use in obese patients and distended abdomen and low sensitivity in some studies are also disadvantages of the ultrasound.

4.6 CT scanning

Initial studies evaluated sequential (nonhelical) CT scanning in the diagnosis of appendicitis (**Figure 1**) [2].

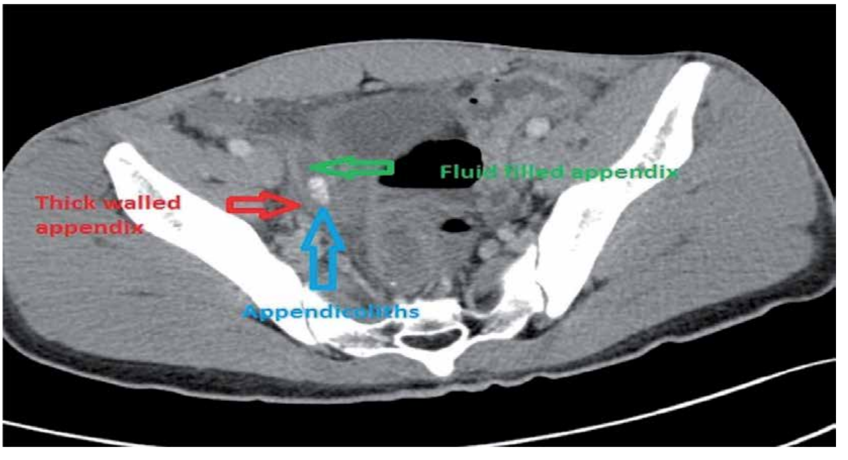

Figure 1.
Showing inflamed appendix arrows (single headed) pointing to abscess (https://www.google.com/url?sa=i&url=https%3A%2F%2Fradiopaedia.org%2Fcases%2Facute-appendicitis-25&psig=AOvVaw2YLkUq9GxMka1g1e4cq3Oo&ust=1626969528328000&source=images&cd=vfe&ved=0CAgQjRxqFwoTCJCyt_zD9PECFQAAAAAdAAAAABAD).

4.7 Diagnostic peritonial aspiration or lavage

Peritoneum was punctured with fine bore catheter to aspirate fluid which can detect pus or an abnormal number of leucocytes which can be seen in acute appendicitis. Other than appendicitis gynecological infections and mesenteric adenitis may have same results in aspirated fluid examination. Normal findings of aspiration usually rule out all above mentioned conditions.

4.8 Radio isotope scanning

Two types of imaging modalities are used:

1. Radiolabelled white blood cell (Tc^{99}mm WBC).
2. Immunoglobulin G (Tc^{99} IgG).

These techniques relay on the localization of the leukocyte and IgG at the site of appendiceal inflammation, with the use of scintigraphy, the inflamed tissue is observed in the right lower quadrant.

The true potential usefulness of these studies occurs in - patient with persistent symptoms and negative ultrasound and CT studies.

4.9 Diagnostic laparoscopy

Laparoscopy has the attraction of being the only investigation that can view the appendix directly. The criteria used for the diagnosis of acute appendicitis are the identification of an inflamed appendix or the presence of sign of inflammation in the right iliac fossa when no other pathology can be found to account.

Huffman summed up the science of acute appendicitis in laparoscopy:

- Partial or complete visualization of the inflamed appendix.
- Pus in right iliac fossa.
- Omen tum adherent to the structure of right iliac fossa.
- Inflammation of pericaecal tissues.

The major disadvantage of laparoscopy is its invasiveness. It requires a general anesthesia (although some perform laparoscopy under local anesthesia) and is in fact an operation that may result in many of the complications of an abdominal procedure.

4.10 Histopathological diagnosis of acute appendicitis

Histopathology is considered the gold standard for confirmation of the diagnosis of acute appendicitis [3]. The histologic criterion for the diagnosis of acute appendicitis is neutrophilic infiltration of the muscularis propria (**Figures 2–10**).

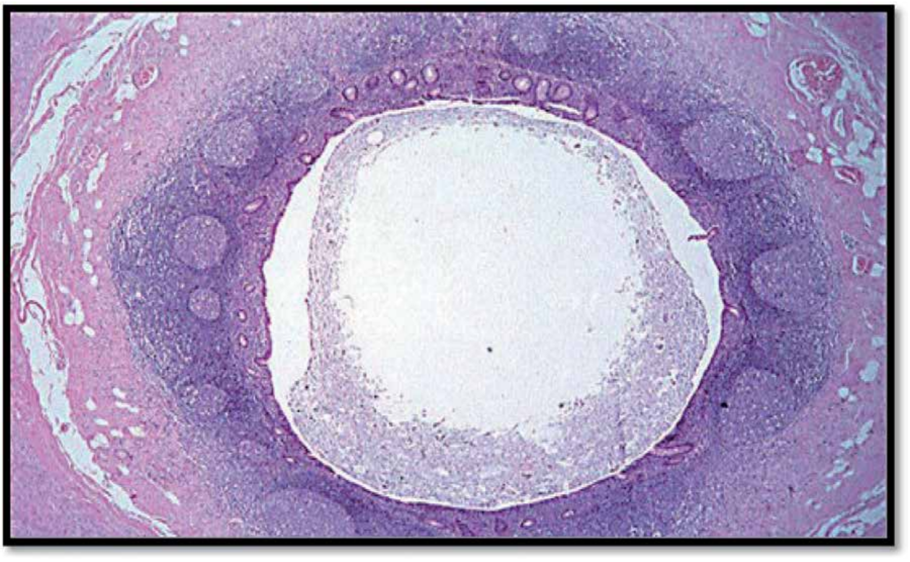

Figure 2.
Microscopy of normal appendix, showing the lumen (low power).

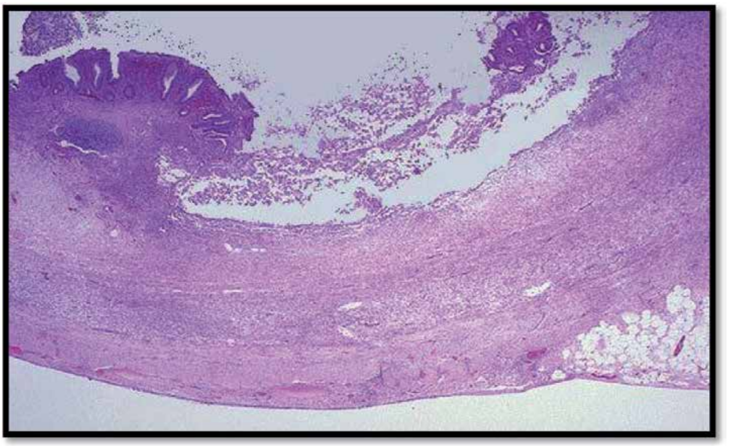

Figure 3.
Microscopy of acute appendicitis is marked by mucosal inflammation and necrosis.

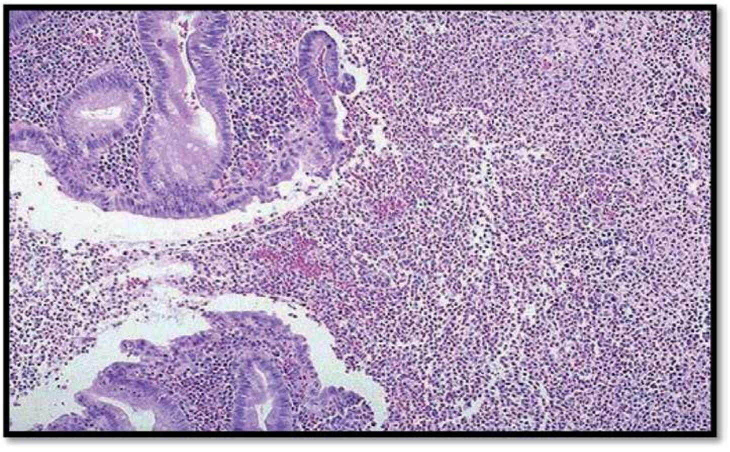

Figure 4.
Acute appendicitis: (Low power) Mucosa shows ulceration and undermining by extensive neutrophilic exudates.

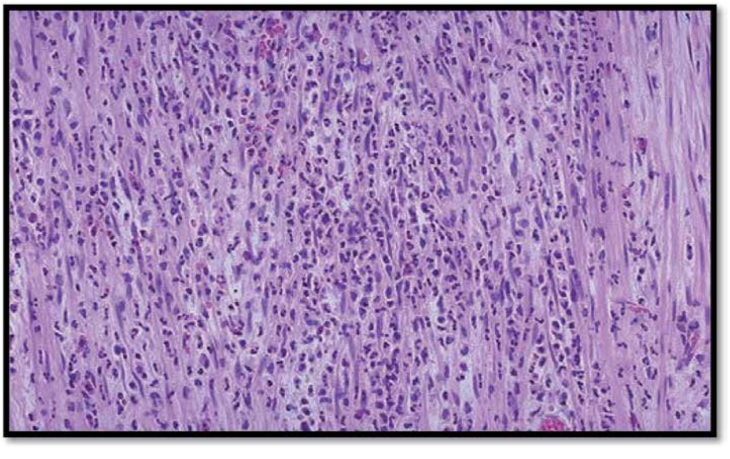

Figure 5.
Acute appendicitis: (High power) Neutrophils extend into and through the wall of appendix.

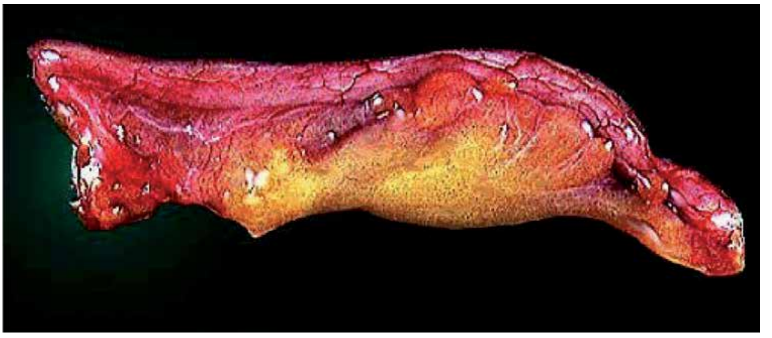

Figure 6.
Gross specimen: Normal appendix.

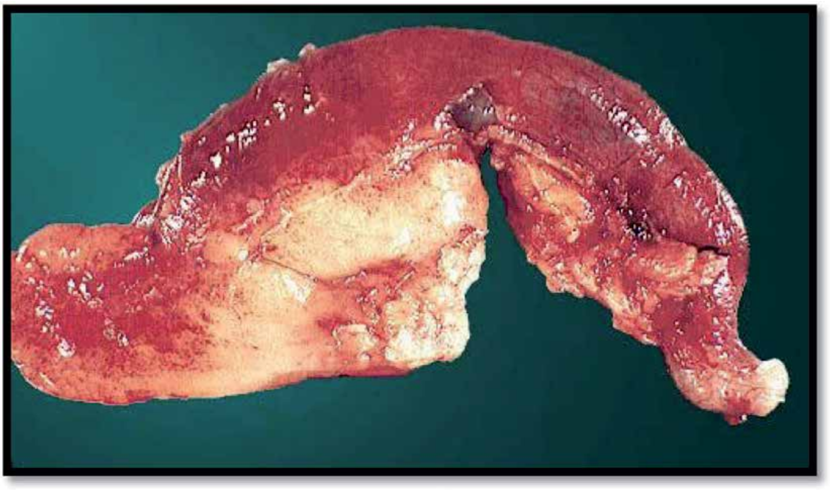

Figure 7.
Gross specimen: Acute appendicitis.

Figure 8.
Gross specimen: Appendix cut open with fecoliths in the lumen.

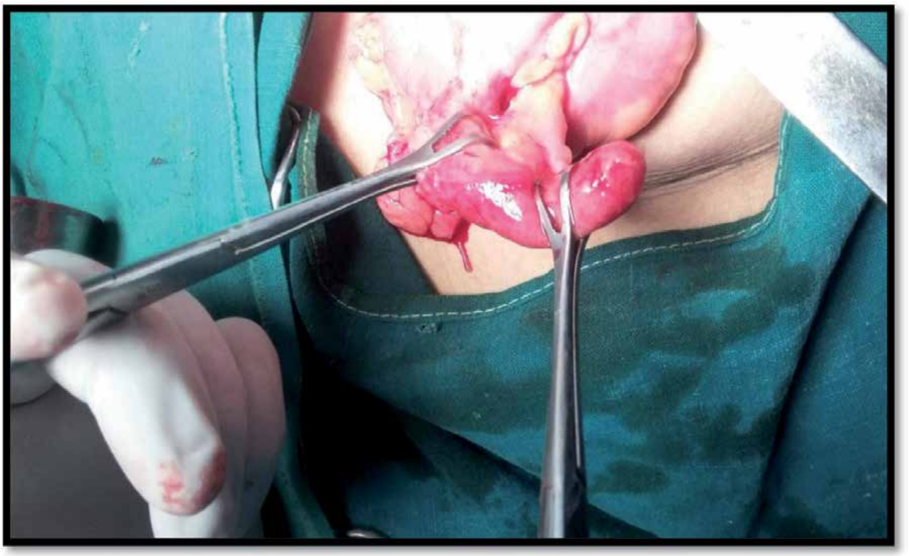

Figure 9.
Gross specimen: Acute appendicitis.

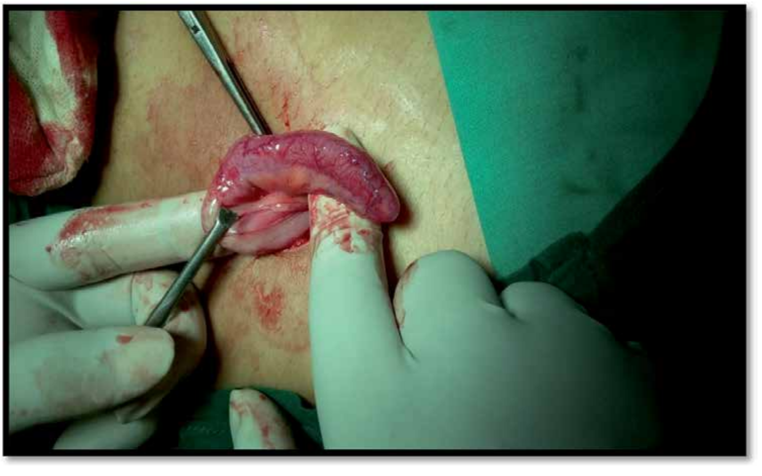

Figure 10.
Gross specimen: Acute appendicitis.

5. Modalities of treatment

- Open appendicectomy
- Laparoscopic appendicectomy
- Conservative management
- Management of complications

6. Appendectomy

6.1 Incisions for appendectomy

a. McBurneys: oblique, muscle splitting incision.

b. Lanz: 4–7 cm incision along the lines of Langer, about the level of anterior superior iliac spine.

c. Rutherford Morison's incision: an oblique muscle cutting incision, which can be extended, obliquely upwards and laterally as necessary. Useful if the appendix is paracaecal or retrocaecal and fixed.

d. Davis-Rockey: a transverse right lower quadrant skin incision.

e. Fowler-Weir extension: extension of McBurneys incision via a staged separation of muscles.

f. Para median: just lateral to the rectus in vertically midline (**Figure 11**).

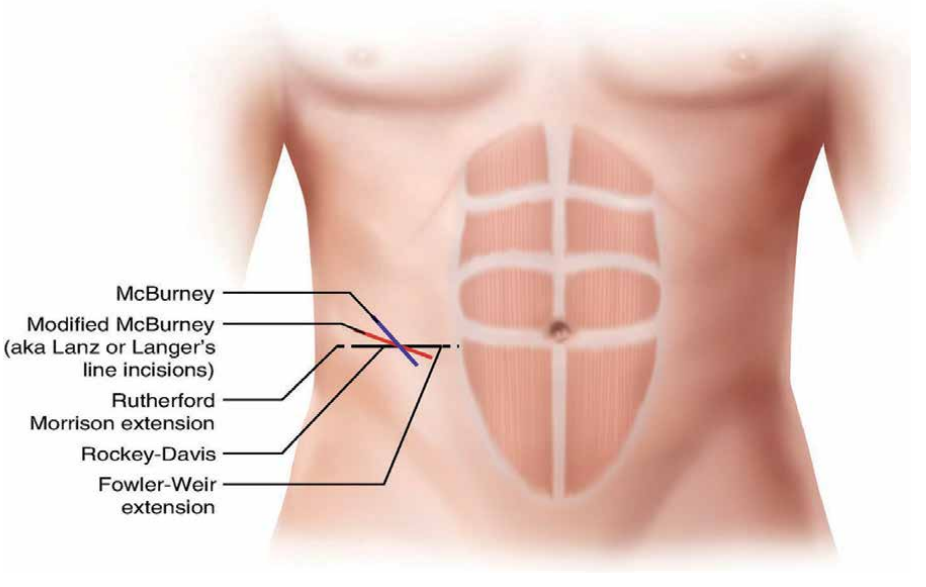

Figure 11.
Incision for appendectomy.

6.2 Procedure of open appendectomy

Abdomen is opened and caecum was identified. Appendix located at illeo caecal junction and mesoappendix dissected and clamped and tied.

Appendix was cut at the base after securing with purse string or Z stitch. Invagination of appendicular stump can be done. When the appendix is retrocaecal and adherent, it is advantageous to do retrograde appendicectomy.

See for Meckel's diverticulum. Put a drain if pus is there or in case of extensive dissection.

The definitive treatment of acute appendicitis is appendectomy and the sooner it is done, the better. There are four exceptions to this excellent rule:

1. The patient is moribund with advanced peritonitis. Conservative supportive treatment can be done in an attempt to get the patient fit for surgery.

2. The attack has already resolved. Interval appendectomy is done later.

3. Circumstances make operation difficult or impossible.

4. Appendicular mass has formed.

6.3 Management of appendicular mass

Ideal is to manage by the Ochsner-Scherren regimen (conservatively). In that regimen patient is treated by starting IV antibiotics and symptomatic treatment.

Patient is allowed orally only when it's tolerated otherwise to start IV fluids at initial part. Stop treating conservatively if:

1. Persistent fever

2. Rising pulse

3. Signs of obstruction

4. Increase in size of abscess

6.4 Laparoscopic appendectomy

As per some studies laparoscopic surgery is comparable or sometimes superior to open surgery in appendectomy. So while going for surgical management of appendicitis laparoscopy is preferred irrespective of clinical condition and diagnostic value [4].

Appendicular stump closure by single endoligature (endoloop) is procedure of choice as tactical modification nowadays. Other alternatives like endostapler, metal clips, bipolar endocoagulation, and polymer clips [5].

All alternative methods have never been assessed in prospective randomized studies but with proper knowledge about them one can do safe and cost-effective procedure [6].

In inflamed appendicular stump one can use enostapler which causes closing and transecting the appendix in one step but it's expensive [7].

Endoclip and endoloop are other methods which are equally cost effective but endoclip is easier to mastered than endoloop. Both offers closing and cutting the appendix before dissecting the mesoappendix. Appendicular base up to 16 mm can be clipped is a limitation of endoclip which is not offered by endoloop [7].

In bipolar coagulation technique there is no need of clip applicators, needle holders or knot pushers required and it is very simple and economical method. But it should be carried out by experienced surgeon [8].

6.5 Advantages (laparoscopic appendectomy)

- Fully exposed peritoneal cavity facilitates diagnosis and treatment of additional pathology especially in females in same sitting.

- Easy to treat subhepatic appendix and appendix in situs inversus.

- Less hospitalization (24 hours) and in uncomplicated cases sometimes as day care surgery.

- Less traumatic access and postoperative pain; early recovery and return to work.

- Less incidence of wound complications.
- Avoids laparotomy and gives good cosmesis.

6.6 Procedure (iaparoscopic appendectomy)

Port placement can be done as shown in the figure after creating pne umoperito-neum (**Figure 12**).

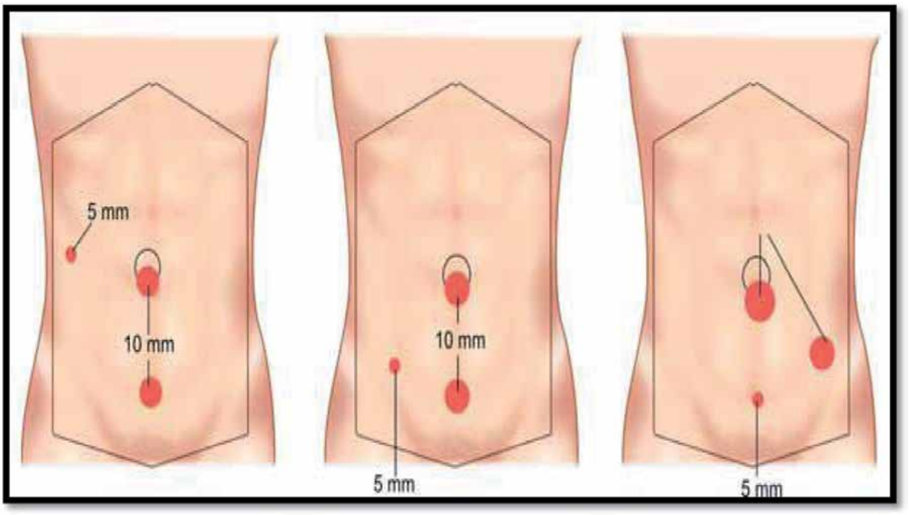

Figure 12.
Port placement.

Appendix was skeletonized and mesoappendix was secured by bipolar coagulation forceps. As described above appendicular base is secured by various different techniques (**Figures 13** and **14**).

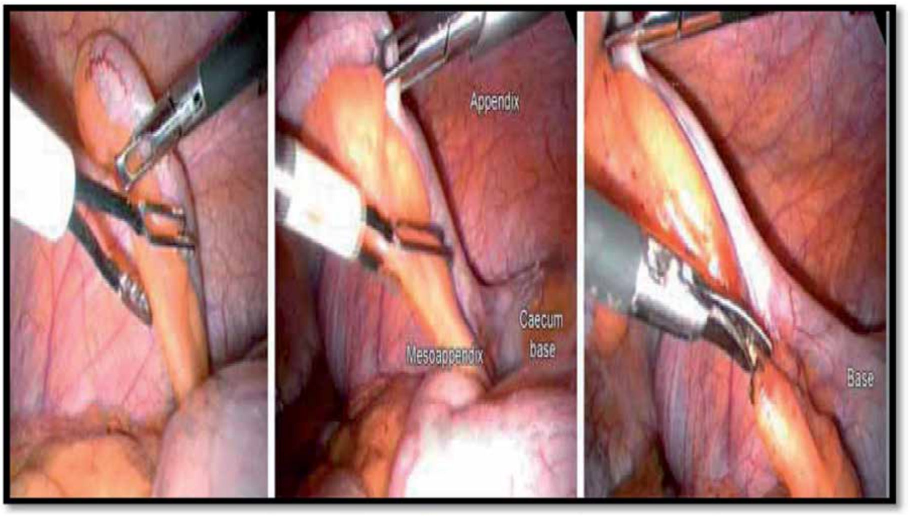

Figure 13.
Securing mesoappendix.

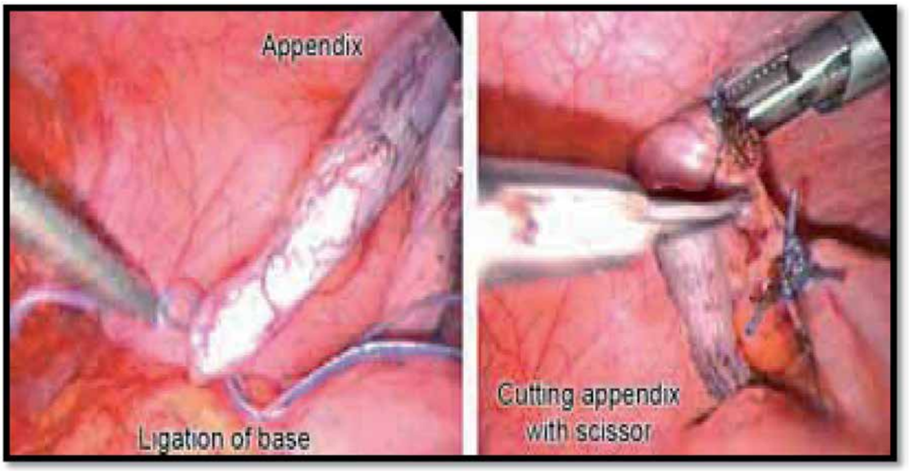

Figure 14.
Removal of Appendix.

Port site infection is prevented by using specimen retrieval bag when appendix is friable or badly infected. After complete examination of pelvic cavity, thorough wash is given and a drain may be kept if needed.

6.7 Complications of appendectomy

1. In 5 to 10% of cases chances of wound infection is there.
2. Perforated pelvic appendicitis may cause pelvic abscess after operation.
3. There may be a brief peiod of paralytic ileus.
4. Chances of fecal fistula (rare).
5. Gangrenous appendicitis may cause pylephlebitis in rare cases.
6. In women taking oral contraceptive pills can develop venous thrombosis and embolism.
7. Delayed complications:

- Adhesions and intestinal obstruction.
- Iliohypogastric nerve injury can cause right sided inguinal hernia.

6.8 Appendectomy in pregnancy

Incidence of appendicitis is same in pregnant and non-pregnant female (1 in every 1400 pregnancies) [9]. Appendicitis is more common during second trimester [9, 10]. Due to longer duration from onset of symptoms to operation perforation is more common during third trimester [10].

Appendectomy is performed in all pregnant having appendicitis. Due to difficulty in diagnosis over one third cases are of negative appendectomy during pregnancy [11, 12]. Due to high risk to the fetus negative appendectomy is accepted as risk reducing surgery in pregnancy when suspected [13].

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Chapter 3

Faecoliths in Appendicitis: Does It Influence the Course and Treatment of the Disease in the Acute Setting?

Rossi Adu-Gyamfi

Abstract

Luminal obstruction has been widely considered as one of the major causes of appendicitis. Faecolith, in this case called appendicolith, is a hardened lump of faeces in varying sizes, have over the years been closely associated with appendicitis as a potential cause of luminal obstruction. There are varying opinions with regards to role of appendicolith in both uncomplicated and complicated acute appendicitis. While some authors have reported that the presence of appendicolith is a predictive factor for high failure rates, others are of the opinion that appendicolith does not necessarily predict non-operative treatment failure, and even if so, not as an independent factor. Opinions also seem to be divided on the correlation between complicated appendicitis and the presence of appendicolith. This chapter seeks to discuss the evidence available and attempt to clarify the controversies surrounding the role of appendicolith in acute appendicitis using current evidence available.

Keywords: Faecolith, Appendicitis

1. Introduction

There are numerous theories with regards to the aetiology of acute appendicitis. These theories include genetic factors, environmental influences, luminal obstruction and infections. However, of all these theories, the debate between luminal obstruction with possible secondary infective process and primary infective causes has been the fiercest. With the latter raising more questions than answers.

Even though many infectious agents have been linked with acute appendicitis, quite a number of them are still unknown and this makes the understanding of the pathophysiology even more difficult [1–3]. In addition to the aforementioned, most organisms isolated from patients are typically normal colonic flora and that is in sharp contrast to the original postulation of the temporal and geographic distribution of organisms.

Luminal obstruction of the appendix results from a variety of causes and is associated with increased pressure within the lumen. Causes of appendiceal luminal obstruction include lymphoid hyperplasia due to inflammatory bowel disease or infections (commonly viruses), parasites, foreign bodies, neoplasms and faecoliths. The increased pressure results from continuous secretion and stagnation of fluids and mucus from the mucosal epithelial cells. This serves to provide a conducive milieu for intestinal flora to multiply and flourish. This multiplication leads to local increase in bacteria load, with its accompanying translocation and the subsequent inflammatory process which ensues, resulting in the formation of pus and a further increase in intraluminal pressure.

Appendiceal venous outflow obstruction occurs as the intraluminal pressure rises above the appendiceal venous pressure. A further increase in luminal pressure also impairs arterial blood flow to the appendix. The above-mentioned vascular compromise gives rise to a loss of epithelial integrity and wall ischaemia, which in addition to the luminal bacteria overgrowth, and rapid bacteria translocation are often complicated by peritonitis, perforation, gangrene of the appendix and/or peri-appendicular abscess with or without peritonitis.

2. Faecoliths as a causal agent of acute appendicitis

Faecolith, also known as appendicolith, appendiceal calculi/enterolith or corpolith, is a combination of firm, dense stool and mineral or calcified deposits which usually has a laminar structure [4]. Although the formation of a faecolith is not clearly understood, there have been previous instances where foreign bodies and gallstones have been implicated [5, 6]. As a matter of fact, for a long time, there was a myth which seemed to have suggested that accidental swallowing of seeds could cause acute appendicitis.

Early on, faecoliths were noted to be one of the most common causes of acute appendicitis resulting from luminal obstruction. In the early 19th century Volz observed faecoliths to be a "pathognomonic agent" for typhlitis [7]. Later that century, Fitz revealed that in patients who presented with perforated appendicitis, 47% of them had hardened stools in the lumen of the appendix [8]. These findings raised enough suspicions which linked faecoliths to acute appendicitis and possibly its complicated forms. As a result, many other observations were published [9–11]. Most of these studies, however, remained experimental until Bowers conclusively showed in the late 1930s that obstruction by a faecolith was a major cause of acute appendicitis [12].

The other issue with respect to faecoliths in acute appendicitis has to do with its consistency. This has led to the suggestion that faecoliths should be classified based on consistency and calcium content due to their correlation with perforation. On the contrary, other authors have also suggested that even the softer form presents more commonly with appendicitis than the harder ones [13, 14].

In fact, the prevalence of faecoliths in the vermiform appendix has been recently reported to be 3% in a population study by Jones et al. [15]. In this study, the investigators observed an increased incidence in populations with increased intake of low-fibre diets. Other studies have shown higher prevalence in paediatric and young adult population, with increased male preponderance [16]. There are also reports of increased incidence of faecoliths among patients with a retrocaecal appendix, but these are yet to be substantiated.

From the discussions so far, it can therefore be concluded that the presence of faecoliths does not confirm a diagnosis of acute appendicitis without the presence of appendiceal wall inflammation involving the muscularis propria on histological assessment or peri-caecal inflammatory changes/appendiceal wall enhancement clinically. On this matter, there have been numerous conflicting reports on the relationship between the presence of faecoliths and appendicitis especially in different age groups [17–19]. There are reports by some authors that up to 49% appendices with luminal obstruction were normal on histological assessment. The same study also found that 49% of appendices with luminal obstruction had microscopic evidence of acute inflammation even though they looked normal macroscopically. Some of these studies initially led to the performance of an appendicectomy in asymptomatic patients with a faecolith by some surgeons. This practice, however, is currently controversial. At the moment, the widely accepted evidence is what Butler et al. [20] reported. They found faecoliths in 10% of patients, with 90% of them subsequently going on to develop appendicitis. The purpose of this chapter is however to look at the effect of faecoliths on the disease process of acute appendicitis.

The discussion on the role of faecoliths in appendicitis, in general, could be as old as the disease process itself and as result many theories have been postulated in times past. This chapter will be broken down into subheadings on important aspects of the role of faecoliths in acute appendicitis.

3. Incidence and diagnosis

The incidence of faecoliths in population and patient studies have been generally discussed in previous paragraphs of this chapter. With the introduction of modern abdominal imaging modalities from plain abdominal radiography, ultrasound examination, computed tomography (CT) scan to magnetic resonance imaging, the association of faecoliths as an important cause of luminal obstruction in acute appendicitis have become very clear and recent data reports prevalence of about 20% in pathological specimens either with or without the presence of acute appendicitis.

Faecoliths are usually one the main causes of non-specific intermittent abdominal pain. In some cases, it even mimics genitourinary conditions such as urolithiasis. They are usually less than a centimeter in diameter and those that are more than two-centimeters are classified as giant faecoliths. Even though those greater than two-centimeters are considered uncommon, the largest ever recorded is 3.5 cm [21, 22].

A study by Ishiyama et al. [23] to investigate the significance of appendicoliths as an exacerbating factor of acute appendicitis using multivariate analysis resulted in very interesting findings. First of all, they were able to show that the presence of a faecolith is usually associated with more severe disease. In addition, the study identified a significant relationship between severe disease and size, and location of the faecolith. The larger the size and/or the more proximal the location in the vermiform appendix, the more likelihood of severe disease. The radiological characteristics of faecoliths associated with acute appendicitis were recently described by Khan [24]. He and his colleagues concluded that, in addition to a faecolith of 5 millimetres or more, multiple faecoliths were also identified to be an independent factor associated with acute appendicitis.

The diagnosis of acute appendicitis in a patient who presents with abdominal pain has markedly improved with the advent of numerous imaging modalities. In the presence of a faecolith, an abdominal plain radiography study alone can be considered as adequate when there is associated abdominal pain, with a specificity of 100% [25]. The use of CT scans in the assessment of patients suspected to have appendicitis has shown that the incidence of faecoliths is higher in the general population than previously reported. Two studies by Balthazar et al. and Rao et al. reports of incidence between 43 and 50% in predominantly adult patients diagnosed with acute appendicitis [26, 27]. In the paediatric population, Lowe and her friends showed that the incidence of faecoliths in patients with confirmed acute appendicitis was 65% [28]. This detection rate could be diminished by the administration of oral contrast. CT scans have been extensively used in the diagnosis of acute appendicitis.

At the time of writing this chapter, there was no study or literature dedicated to the diagnostic capabilities of ultrasound (US) scan in faecolith-related acute appendicitis. However, in general, the accuracy of US scan in the diagnosis of acute appendicitis is between 71–95% with sensitivity and specificity of 94.7% and 88.9% respectively when graded compression ultrasonography is done [29, 30]. Magnetic Resonance Imaging (MRI) has the advantage of no ionizing radiation exposure and the absence of nephrotoxic contrast agents. Availability and cost are among the main reasons why it is underutilised, although it has a sensitivity and specificity of 96.8% and 97.4% respectively. At the moment, there is very little data on its role and position in the workup of appendicitis, except in very special circumstances [31].

4. Role of faecoliths in disease presentation and failure of conservative treatment

Literature on what role and effect faecoliths have on clinical scoring systems in acute appendicitis was very scanty to come by and therefore this chapter cannot provide a comment on that currently. Nonetheless, some studies, like that of Ishiyama and colleagues as mentioned in the previous paragraph have observed severe disease presentations in patient with faecoliths compared to those without.

In addition, faecoliths have been known to be more frequently associated with perforations and abscess formation [32]. Flum et al. found that the presence of faecoliths was identified to be a significant contributor of post treatment complications and adverse effects in patients who received antibiotics alone compared with those who had surgery. They also realised that though the perforation rate was high in patients initially treated with antibiotics, this high rate was attributable to patients with a faecolith. They reported about a 3-fold rise in perforations among the faecolith group. This, however, did not lead to a higher rate of extensive resections in the antibiotic group. Looking at the group that had appendicectomy done as initial treatment, there was not much difference in the perforation rate between patients with faecoliths and those without.

As a result, the finding of an appendicolith may be sufficient evidence to perform an appendectomy in patients earmarked for conservative management, given the higher rate of perforation at the time of failure of antibiotic treatment. This position is so explicitly stated in the recommendations made in the Jerusalem guidelines of 2020 and seems to be consistent with what Von and his friends found. It is however the author's strong believe that every patient's situation should be uniquely assessed, and a tailored treatment advocated with the patient's express consent of course.

5. Effect on treatment and complications

In the management of acute uncomplicated appendicitis using laparoscopy, Finnerty et al. [33] showed that age, presence of diabetes, raised BMI, presence of imaging confirmed complicated appendicitis, male gender and ethnicity were independent predictor of failure in laparoscopic management of acute uncomplicated appendicitis. At the moment, there is no evidence to support which method of treatment is best in the presence of faecolith in acute uncomplicated appendicitis, even though current evidence favours laparoscopy in the management of uncomplicated acute appendicitis generally. The presence of faecolith has been shown to have significant effect on therapeutic interventions and therefore the treating surgeon must be informed about the presence of faecolith for certain considerations to be taken into account. For instance, there have been several studies and case reports to show that dropped faecolith is a major contributor of post interventional morbidity with increased incidence of pelvic abscesses especially after laparoscopic appendicectomy.

The results from the CODA trial showed a noninferiority in managing patient with acute appendicitis conservatively with antibiotics in terms of 30-day post treatment health status, which was the primary outcome of the study. At 90-day post treatment, 29% of patients in the antibiotic arm had undergone appendicectomy. When a subgroup analysis was done, the number of patients with faecolith who required appendicectomy in the antibiotic group was almost twice patients without faecolith in the same subgroup. Even though all these are evolving areas of controversy, the surgeon's awareness of the presence of faecolith is key to enable adequate decision making and planning for possible retrieval of faecolith if so needed [32, 34, 35].

6. Faecolith as a predictor for extensive resection

The Gridiron incision, also known as McBurney's incision, is the most commonly used open method in the management of acute uncomplicated appendicitis. In addition to this type of incision offering a minimally invasive and direct access to the diseased appendix, it provide good cosmesis and in lean (healthy BMI) patients, it is usually comparable to laparoscopic technique in terms of access, time of surgery, hospital stay and cosmetic advantage. In situations of delayed presentation or complications, McBurney's technique becomes extremely challenging and, in such situations, larger laparotomy incisions are made with accompanied extensive bowel resection in some cases. The most common extensive bowel resection in acute appendicitis is ileocaecectomy with or without primary anastomosis of bowel. Recent evidence suggests that appendiceal mass, non-visualization of appendix, delayed admission, and CRP are strong predictors of extensive resection in acute appendicitis [36]. Additionally, faecolith was also identified as a preoperative predictor of extensive resection for acute appendicitis. Other preoperative predictors of extensive resection found in these studies included age, ascites, and extraluminal air. The role of faecolith in predicting the possibility of extensive resection obviously require further robust research but should not be underestimated.

7. Role of routine interval appendectomy in the presence of faecoliths

Consensus on routine interval appendicectomy after conservative management of acute appendicitis is another highly debated subtopic in acute appendicitis. As a principle, surgeons are more inclined to do routine interval appendicectomy especially in patients in their mid-forties and above as there is an increased risk of malignancy in this groups. However, one can question the essence of this practice especially when there are very accurate diagnostic imaging modalities available to assist with confirming the presence of a tumour. While some have argued for routine interval appendicectomy when a faecolith is involved because of its possible association with increase recurrence rate, others have suggested otherwise as there have not been adequate evidence to support this idea especially when patients remained asymptomatic [37, 38].

To conclude, the role of faecoliths in causing acute appendicitis, and not just the disease but the worse form of it cannot be underestimated. Its ability to accelerate complications in the disease process and in addition cause significant headaches for surgeons and patients cannot be in dispute. The several contrasting opinions with regards to what to do with it confirms how complicated the situation is. It is the author's firm opinion that more focused research should be done on this subject. Also, a lot of commendations should go to the designers and authors of the CODA trial who have thrown more light on this subgroup of patients.

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Chapter 4

Appendicitis in Children: Fundamentals and Particularities

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Abstract

Acute appendicitis in children under 5 years of age is a diagnostic challenge, its delay is usually dramatic and leaves serious sequelae. It is one of the main causes of surgical intervention, it is common for other diseases to be associated with it and to simulate it. Acute appendicitis is of obstructive etiology and its pathophysiology, the bacteriology involved and the evolution of the disease progresses through its phases, from the simple to the complex, is addressed in each case. The typical abdominal pain of appendicitis, in addition to vomiting and fever at a young age, is most often accompanied by an atypical clinical picture such as diarrhea. Integrating the clinical signs at this age requires the full capacity and good sense of the pediatric surgeon. For a correct and timely diagnosis, unfortunately many pediatric patients present in complicated stages of the disease, which implies decision-making regarding the type of surgical intervention and subsequent treatments.

Keywords: acute appendicitis, children, classification, treatment, special conditions

1. Introduction

Acute appendicitis is the main cause for abdominal surgery, and it is also one of the main diseases in pediatrics that requires surgical treatment. It is among the primary reasons for hospital care in developing countries [1]. The most frequent age of presentation is in the second decade of life; however, we must pay special attention to children under 5 years of age, as they have an atypical clinical presentation that can delay diagnosis and treatment [1]. According to our experience, based on the management of up to 1,200 appendicitis cases a year at the Surgery Unit of the Moctezuma Pediatric Hospital of the Mexico City Secretary of Health, a regional referral center in a densely populated area, we observed a predominance of males, and children under 10 years of age accounted for almost 85% of the cases. We combined a series of more than 300 children three years of age or less. Pediatric appendicitis is a common sporadic event; however, it is often associated with specific regional diseases such as Hirschsprung's disease [2]. The appendix serves as a reservoir for normal intestinal flora and has a high concentration of gut-associated lymphoid tissue [3]. A family history of appendicitis imparts a risk. Although a specific gene has not been identified, the likelihood of appendicitis is approximately three times greater in family members with a positive history than in those with a negative history [3, 4].

2. Etiology

The most frequent, almost exclusive, cause is the luminal obstruction of the proximal segment, the appendico-caecal junction, which makes practical sense as this structure is like the finger of a glove. Everything that prevents the natural drainage of mucus that normally accumulates inside, be it an appendicolith, foreign body, a vegetable seed, intestinal parasites (*Ascaris lumbricoides*), even hyperplasia and hypertrophy of lymphoid tissue, primary tumors (carcinoid, adenocarcinoma, Kaposi's sarcoma and lymphoma) or metastatic tumors will cause structural and physiological changes and depending on the time it remains occluded, the clinical and histopathological stages of the disease can be obtained [5].

2.1 Fecaliths/appendicular stones

The formation of a fecalith and a stone occurs when feces, trapped within the appendicular lumen, are continuously bathed with minerals and thickened. Like gallstones, fecaliths and appendix stones can enlarge to a critical diameter, resulting in complete lumen obstruction. The consequence is an increase in intraluminal pressure in the obstructed part of the appendix, which interferes with the circulation in the intestinal mucosa and alters venous drainage, causing a thrombosis of the terminal appendicular artery, which results in a transmural infarction and perforation [6]. The presence of fecaliths or appendicular stones is associated with a higher number of complicated acute appendicitis, with perforation in 18% of cases and appendicular abscess in 42%. Therefore, fecaliths and appendicular stones play an important role in the pathogenesis of appendicitis [6].

2.2 Bacterial infection

Most opponents of the obstruction theory advocate an infectious pathogenesis for acute appendicitis. The lack of increased bacterial counts in acute inflammation suggests that the environment for bacterial growth is unfavorable and that the number of organisms invading the wall is low compared to those in the lumen or associated with the mucosa [6].

2.3 Hiperplasia linfoide

Since the cecal appendix is rich in lymphatic follicles, lymphoid hyperplasia can lead to obstruction of the lumen of the appendix. In a pathology analysis of 405 appendages, Babekir and Devi found significant lymphoid hyperplasia in 25% of acutely inflamed appendixes. Although this could be partly a secondary phenomenon during the inflammatory process, a typical viral illness with symptoms of gastroenteritis could probably trigger an acute appendicitis after a few days [6].

3. Pathophysiology

The obstruction of the appendicular lumen causes inflammation, increased intraluminal pressure and ultimately ischemia. Subsequently, the appendix enlarges and incites inflammatory changes in the surrounding tissues, such as the pericecal fat

DOI: http://dx.doi.org/10.5772/intechopen.97295

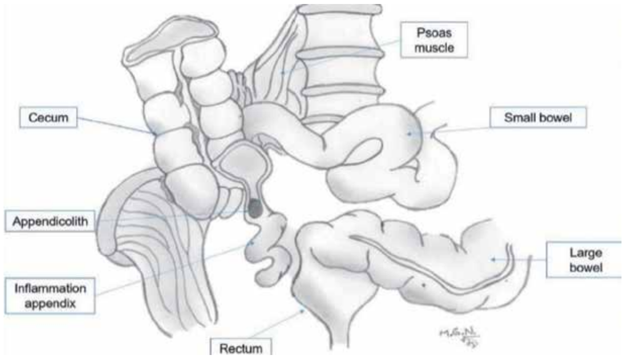

Figure 1.
Showing the anatomy of the cecal appendix and the fecalith obstructing the lumen.

and the peritoneum. Rapid distention of the appendix occurs due to its small luminal capacity, and intraluminal pressures can reach 50 to 65 mm Hg (**Figure 1**) [7]. This appendicular condition leads to an enlargement of the cecum, the cecal content is stored and does not advance towards the right colon. The presence of fecal load within a large cecum can be identified on plain abdominal radiography as a specific sign of acute appendicitis [7]. Once the luminal pressure exceeds 85 mm Hg, thrombosis of the venules draining the appendix occurs, and in the setting of continuous arteriolar flow, vascular congestion and congestion of the appendix develop [5, 7]. Lymphatic and venous drainage is impaired and ischemia develops. The mucosa becomes hypoxic and begins to ulcerate, resulting in compromise of the mucosal barrier and leading to invasion of the appendicular wall by intraluminal bacteria. Most bacteria are gram-negative, mainly *Escherichia coli* (76%), followed by *Enterococcus* (30%), *Bacteroides* (24%), and *Pseudomonas* (20%) [8].

The inflammation spreads to the serosa, parietal peritoneum, and adjacent organs and as a result, visceral afferent nerve fibers entering the spinal cord at T8-T10 are stimulated, causing epigastric and periumbilical pain referred by the corresponding dermatomes. At this stage, somatic pain replaces early referred pain, and patients generally experience a shift at the site of maximum pain towards the right lower

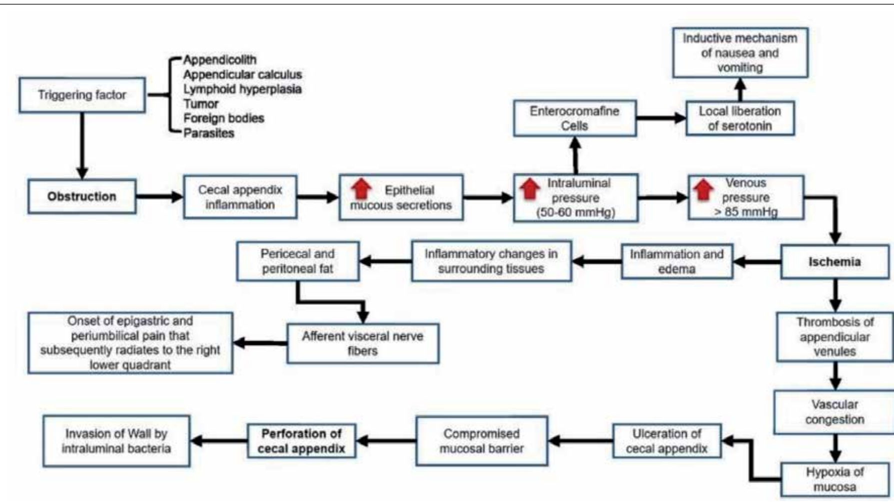

Table 1.
Pathophysiology of appendicitis.

quadrant. If this continues, arterial blood flow is eventually compromised and a heart attack occurs, resulting in gangrene and perforation (**Table 1**) [9].

4. Classification of appendicitis

After a few hours, sometimes less than 24 hours or a little longer, the appendix is observed, (describing it from the inside out) with a large accumulation of mucus in which a significant variety of bacteria, especially anaerobes, are immersed. Being usual inhabitants in normal conditions, they find the ideal means to proliferate. The mucous lining, following the natural history of the disease, responds with the migration of specific inflammatory cells in response to the situation. Therefore, arterial and venous circulation also alter their dynamics and the flow slows down, causing what that observed when the disease is in the initial phase, simple acute appendicitis. There may or may not be a generally small amount of peri-appendicular fluid, rich in bacteria, but transparent in appearance. As time passes, from 24 to 36 hours after symptoms begin and in an average of 3.2 days, that process worsens and the name of the following stages basically obeys the appearance of the structure. Thus, if the appendix is seen intact, with or without a large fecalith inside, but with a blackish coloration of its wall and dark purulent fluid in its environment, it is gangrenous (**Figure 2**) [10].

The most advanced phase is labeled as abscess appendicitis when the evolution time has been days or sometimes weeks, with a tendency for pus to spread to the entire peritoneal cavity. The appendix is usually ruptured or destroyed, and there is a great liquefaction of periappendicular tissue with a quantity of liquid greater than 10 ml, sometimes reaching more than two liters, depending on the age of the child (**Figure 3**) [10].

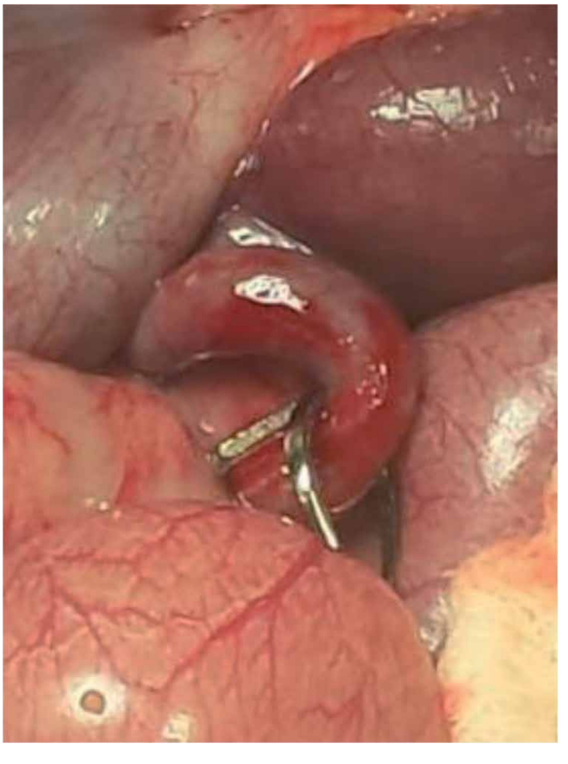

Figure 2.
Appendix in gangrenous phase with dilated bowel loops.

Figure 3.
Appendix with fecalith.

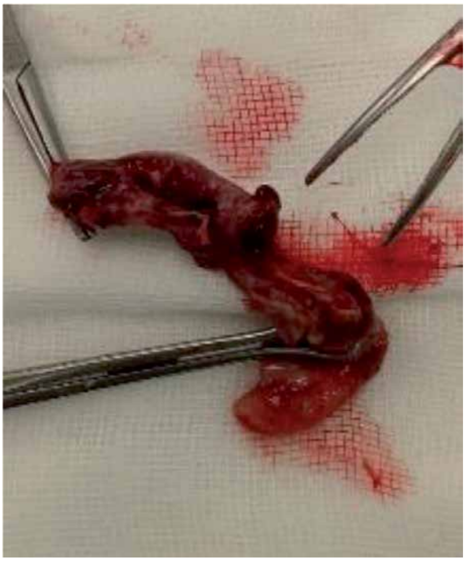

Figure 4.
Appendix with perforation in the middle third.

In all cases clinical behavior is unpredictable, although it can be stated with certainty that the patient's condition will worsen as the hours go by. Although this category obeys somewhat arbitrary rules, in accord with our experience, we believe there is a strong relationship with the response of each phase to the antimicrobial management schemes that are established, and in the same sense, it coincides with the prognosis. A concern of some academics is when the cecal appendix is perforated. According to a study published by the National Institute of Pediatrics of Mexico, micro-perforations can be observed even in the earliest stage of the disease, so that for each stage we add the perforated phase at the margin if it is minimally or grotesquely broken or destroyed (**Figures 3** and **4**) [11].

According to the findings found during surgery, appendicitis is initially staged as simple or uncomplicated and complicated; this staging sets the course for postoperative treatment. Simple and gangrenous appendicitises are considered uncomplicated and have a good prognosis; perforated and abscessed appendicitises are classified as complicated (**Table 2**) [11].

Simple appendicitis
• Inflammation, erythema • Inflammatory fluid • No inflammation • Gangrenated (change of gray or black color in the wall of the appendix, without evidence of complicated appendicitis)
Complicated appendicitis
• Extraluminal appendicolith • Visible perforation in the cecal appendix • Well-formed abscesses • Diffuse pus

Table 2.
Classification of appendicitis.

5. Clinical picture

The symptoms and signs that accompany the disease are typically three, which almost always appear in this order: pain of sudden onset, progressive intensity and periumbilical location, as the appendix is innervated by the splanchnic nerves that emerge of the lower thoracic ganglia, ganglion 10, one of the structures that conducts the painful stimulus to the dorsal nerve root along the dorsal spinothalamic tract. With the appearance of pain and the vagal stimulus, vomiting, anorexia and occasionally diarrhea are added. At the end of the process fever appears, which almost never exceeds 38.5° C, and when it does, the disease has been treated with antibiotics and is in advanced stage, or is not appendicitis. These symptoms can occur in less than 50% of patients and be nonspecific in children under 5 years of age. Children under 3 years of age have perforated appendicitis in more than 80% of cases compared to 20% of children between 10 and 17 years of age [12].

The complementary support resources to prepare the diagnosis in a timely manner, hematic cytology and the radiological study, are almost always useful, but above all is the skill of the surgeon, with the subtlety that a good physical exam requires, who collects the most important data: right quadrant muscle stiffness in the location of the appendix and exquisite pain located around no more than three square centimeters on the same anatomical site. This rule is not carved in stone. If the order is different, it has the same usefulness and validity. Palpation of the lower left quadrant and referred pain in the lower right quadrant, the obturator sign (internal rotation of the right lower limb) and the psoas sign may be nonspecific for appendicitis and only rebound has a greater clinical correlation with appendicitis [12]. With regard to digital rectal examination, we are convinced that it does not provide data to substitute for a good physical study of McBurney's point, so we do not recommend performing it. For a child, the maneuver, in addition to being unnecessary and annoying, requires the informed consent of the parents. The abdominal maneuvers and signs referred to in the literature are useful and should be sought [12].

The support provided by cytology is important, since the increase in the leukocyte count has been mentioned as having a significant relationship of 60–90% with perforated appendicitis. It is advisable to carry out the band count, since in our experience, they are almost always very high, even without leukocytosis. If more than 15,000 are found, it may not be appendicitis or it is complicated. Finally, the total leukocyte count, absolute neutrophils and C-reactive protein have been shown to have a greater sensitivity and specificity for appendicitis when the three are used in addition to the clinical history and evaluation of the patient [12].

6. Diagnosis

There are difficulties in the diagnosis of acute appendicitis, mainly in young children, which has led to the development of tools that have been useful in the clinical evaluation of these patients. The most frequently used instruments have been the Alvarado Scale (**Table 3**), the Pediatric Appendicitis Scale (PAS) (**Table 4**) and the Inflammatory Response Scale for Appendicitis (AIR). The last scale differs from the first two in that it incorporates C-reactive protein as a predictive value [13]. These three scales evaluate variables such as: vomiting, nausea, anorexia, pain in the lower right quadrant, pain migration, muscle stiffness, temperature, polymorphonuclear leukocytes, leukocytes, and the concentration of C-reactive protein. Macco et al. compared the three scales mentioned above and determined that the Inflammatory Response Scale for Appendicitis has greater discriminatory power and surpasses the other two in predicting acute appendicitis in children [13].

Regarding the radiological study, it should be emphasized that the projection is in a vertical position, since what is intended is that a small air-fluid level appears in the right iliac fossa and eventually a concretion (**Figure 5A, B**). Several findings are mentioned that, alone or together, can help and are: effacement of the preperitoneal line, the shadow of the psoas muscle and of the sacroiliac joint, scoliosis, bird's nest sign and ground glass. When in doubt, the next resource is pelvic us, with high sensitivity and specificity. We believe that criteria such as Alvarado's do not replace the above [14].

Migration of pain	1
Anorexia	1
Nausea / Vomiting	1
Rebound pain	1
Increase in temperature(>37.3°C)	1
Leukocytosis (>10,000/mL)	2
Polymorphonuclear neutrophilia (>75%)	1
Righy lower quadrant tenderness	2
Total	10

From Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med 1986; 15(5):558.

Table 3.
Alvarado score.

Migration of pain	1
Anorexia	1
Nausea / Vomiting	1
Right lower quadrant tenderness	2
Cough/hopping/percussion tenderness in right lower quadrant	2
Increase in temperature	1
Leukocytes >10,000/mL	1
Polymorphonuclear neutrophilia >75%	1
Total	10

From Samuel M. Pediatric appendicitis score. J Pediatr Surg 2002;37(6):878.

Table 4.
Pediatric appendicitis score.

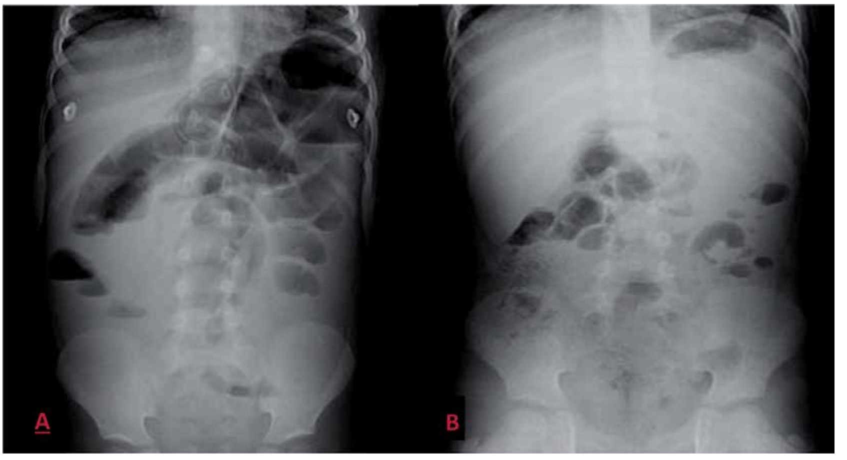

Figure 5.
A. a 4-year-old boy with abdominal pain and decreased consistency of bowel movements. Standing abdominal X-ray, air levels in the right iliac fossa and large dilatation of the proximal bowel loops. **B.** *8-year-old female with pain in the right iliac fossa and fever. Standing abdominal X-ray shows water level in the right iliac fossa.*

Despite the enormous frequency with which it occurs, it is still one of the entities that presents the greatest difficulties for its identification, especially in the early phase, when recognition is essential. Symptomatic progression in children over 12 years of age is practically the same as it appears at later ages. However, there are three circumstances that the clinician frequently encounters: the young child, the child who was inappropriately given antibiotics, and the child with profound psychomotor retardation [14].

7. Treatment

7.1 Surgical treatment

There is controversy regarding the ideal time to perform an appendectomy; if it should be done immediately upon admission to the emergency service or the next morning, if the admission was during the night. Several studies report no difference between the time of surgery, since it does not change between finding an appendix in a gangrenous or perforated phase, the days of hospital stay or the development of postoperative complications [15]. Our group performs most of the procedures the next morning; upon arrival we begin intravenous hydration and antibiotic therapy as well as analgesic and antipyretic therapies [14].

Secondly, we perform an open or laparoscopic surgical procedure. Regarding the open approach, we always recommend a McBurney incision, unlike adult surgeons, at least in our country, who access through a paramedian or median right infraumbilical incision. We are convinced that the oblique incision on the problem offers the opportunity to resolve the situation in 100% of cases. We learned after a few setbacks, that other injuries such as the right transrectal paramedian in most cases, does not help to resolve the situation no matter how serious it is, as McBurney's does. The golden rules we have established for that purpose are all related to neat and orderly technique. Never do we allow even a finger to enter the peritoneal cavity without justification. Everything is within the reach of some instrument. The stump is preserved with a knot and hidden as with a tobacco bag [14, 15].

Patience is the other ingredient, which consists in carrying out a cleaning of such magnitude in the inflamed space, that only the inaccessible residual material

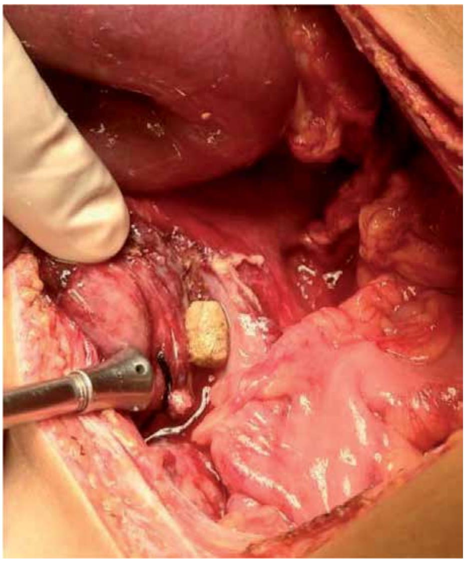

Figure 6.
Free appendicolith in a child with complicated appendicitis

or material that cannot be removed remains. If the previous step is satisfactorily completed, the possibility of not placing drains is considered; we suggest its use almost exclusively if we leave unremoved liquid or solid material to be liquefied. Therefore, it is very feasible that complying with these premises in the first three phases of the disease, the simple, the gangrenous and the suppurative, will not contribute to measures such as drains in most cases. It is almost always required to leave the cavity drained in case there is a missing appendicolith (**Figure 6**) or if it has been destroyed during the maneuvers. Based on what we have learned, we are convinced that almost always, in the first two phases of the disease, the time we dedicate to solving the problem does not require an investment of more than 30–40 minutes [14–16].

7.2 Medical treatment

Both complicated appendicitis and secondary peritonitis have sequelae outside the peritoneal cavity and can result in systemic disease. When diagnosis, and therefore treatment, is delayed, morbidity and mortality increase considerably. Some series report that between 30% and 40% of patients present with complicated appendicitis, although the course of the disease and the prognosis vary widely depending on various factors [16–18].

Both cell injury and some bacterial proteins activate a cellular and humoral response, with recruitment of phagocytic cells and the release of inflammatory substances. These substances induce a local cascade through the activation of receptors in inflammatory and endothelial cells that produce chemo-attractant substances (IL-8 and MPC-1), cytosines (TNF-α, IL-1β, and IL-6) and factors growth (TFGβ, IGF-1, and PDGF) [19].

If the body's regulatory mechanisms fail to control the infection or primary injury, the release of pro-inflammatory mediators predominates and a systemic inflammatory response syndrome (SIRS) develops. If this pro-inflammatory response is excessive and persists, it can progress to organ dysfunction, multisystem compromise, cardiovascular failure, and even death [20].

Respirations rate ≥22 resp/min
Altered mental state
Systolic pressure ≤100 mmHg.
(qSOFA) adapted by Singer et al. [21].

Table 5.
qSOFA criteria.

Age group	Beats/min Tachycardia / Bradycardia		Respirations/ min	Leukocyte count 10^3/mm^3	Systolic pressure mmHg
Newborn	>180	<100	>50	>34	<59
Neonate	>180	<100	>40	>19.5 o < 5	<79
Infant	>180	<90	>34	>17.5 o < 5	<75
Preschool	>140	NA	>22	>15.5 o < 6	<74
School age	>130	NA	>18	>13.5 o < 4.5	<83
Adolescent and young adult	>110	NA	>14	>11.5 o < 4.5	<90

Table 6.
Vital signs and laboratory variables by age.

In 2016, the last update of the definition of sepsis was carried out, emphasizing that there is no validated diagnostic test criterion and no process to operationalize the definitions of sepsis and septic shock. The qSOFA scale (**Table 5**) has been used to identify adult patients with suspected infection who may have prolonged stays in the ICU or die in hospital [21]. An acute change in the qSOFA scale score of 2 points or more has a high predictive value for in-hospital mortality [21].

The definition of sepsis in the pediatric patient is made more difficult by age-specific vital signs and their enormous physiological reserve, so the severity of their condition is often masked [22].

In children, we continue using the criteria of the 2005 Pediatric Sepsis Consensus Congress (CCSP), in which the Systemic Inflammatory Response Syndrome (SIRS) data are categorized by age group (**Table 6**) [22].

SIRS is a generalized inflammatory response that may or may not be associated with an infection. It is characterized by the presence of two or more of the following criteria, one of which must be an abnormal temperature or an alteration in the leukocyte count (**Table 6**) [22].

Sepsis is defined as an organic dysfunction caused by an unbalanced response of the host to a life-threatening infection, and can be significantly amplified by endogenous factors [21]. Septic shock refers to sepsis with cardiovascular dysfunction that persists despite the administration of crystalloids within one hour (> 40 mL/kg) (**Table 7**) [21].

Septic shock is defined as the subset with cardiovascular dysfunction that includes at least one of the following data:

- Hypotension
- Dependence on the administration of vasoactive drugs to maintain normal blood pressure.

Severe sepsis
• ≥ 2 SIRS criteria for age.
• Suspected or proven invasive infection.
• Cardiovascular dysfunction, acute respiratory distress syndrome (ARDS), or ≥ 2 non-cardiovascular organ system dysfunctions.

Table 7.
Criteria for severe sepsis.

- Two or more of the following signs of inadequate tissue perfusion:
    - Prolonged capillary filling.
    - Oliguria.
    - Metabolic acidosis.
    - Elevated blood lactate. The American College of Critical Care Medicine recommends the use of the following parameters to identify septic shock: • Hypothermia or hyperthermia. • Altered mental state. • Abnormal capillary filling (either in "flash" or > 2 seconds).

The American College of Critical Care Medicine recommends the use of the following parameters to identify septic shock:

- Hypothermia or hyperthermia.
- Altered mental state.
- Abnormal capillary filling (either in "flash" or > 2 seconds).

The International Consensus on Pediatric Sepsis developed criteria for organ dysfunction based on various scoring systems, considering a balance of specificity, sensitivity, and wide availability of laboratory tests [22].

Organ dysfunction criteria include the following:

- Cardiovascular: Hypotension or dependence on vasoactive drugs to maintain blood pressure, or two of the following: metabolic acidosis, elevated arterial lactate, oliguria, or prolonged capillary filling.
- Respiratory: arterial oxygen pressure/inspired oxygen fraction (PaO_2/FiO_2) <300, arterial carbon dioxide pressure ($PaCO_2$) > 65 Torr or 20 mmHg above the initial $PaCO_2$, need>50% FiO_2 to maintain the oxygen saturation ≥ 92%, or need for non-selective mechanical ventilation.
- Neurological: Glasgow Coma score ≤ 11 points or acute changes in alertness.
- Hematologic: Platelet count <80,000/microL or a 50% decrease from the highest value recorded in the past 3 days, or disseminated intravascular coagulation (DIC), a consumptive coagulopathy diagnosed by

clinical findings of hemorrhage and microthrombi and abnormalities including thrombocytopenia, prolonged clotting times (PT and aPTT), and evidence of fibrinolysis (low fibrinogen with high fibrin breakdown products).

- Renal: serum creatinine ≥2 times the upper limit of normal for age or double baseline creatinine increase.

- Hepatic: total bilirubin ≥4 mg/dL (not applicable in newborns) or ALT>2 times the upper limit of normal for age.

Studies carried out to date support the use of a standardized scoring system for organ dysfunction on the SIRS criteria in children; Efforts are currently underway to update the definition and clinical criteria for sepsis in pediatrics [22].

7.3 Antibiotic therapy

The selection of an antimicrobial therapy must take into consideration three fundamental aspects: the adequate use of antimicrobial prophylaxis, the clinical conditions of the patient to choose an empirical initial regimen, and to adjust the antimicrobial therapy based on the findings during the surgical event [23]. Highlighting this last consideration, the selection of antimicrobial treatment is based on the usual microbiota, however, in the context of a complicated picture of appendicitis with perforation, the germs involved may present some modification [23].

The use of antimicrobials for pre-surgical prophylaxis should be focused on maintaining coverage primarily on the bacteria that are part of the skin microbiota (*S. epidermidis*, *S. aureus*), and in the specific context of appendicitis, coverage on microorganisms typical of the integral intestinal microbiota must be maintained (without evidence of perforation), such as Gram-negative bacilli (*E. coli* and *K. pneumoniae*), as well as for anaerobic agents (*B. fragilis*) [24].

Multiple bacteria are involved in the microbiology of surgical site infection. The isolates isolated in about 50% of cases are gram positive cocci, *Staphylococcus aureus*, and coagulase-negative Staphylococcus. One third of the isolates correspond to gram negative bacilli such as *Escherichia coli*, *Pseudomonas aeruginosa*, and Enterobacter spp [24].

The greatest change in the microbiology of surgical site infection is due to the emergence of methicillin-resistant *Staphylococcus aureus*, especially of community acquisition, with a dramatic increase, occupying up to 40% of all strains in developing countries. Gram negative bacilli have also shown increased resistance with the indiscriminate use of broad-spectrum antibiotics [25].

The establishment of a pre-surgical antibiotic prophylaxis guide is important, since this procedure is usually not regulated in most institutions, creating confusion among physicians, an increase in hospital bacterial resistance as well as a waste of supplies [26].

The route of administration is intravenous, as it produces a rapid, reliable and predictable effect in serum and tissues [27]. Successful prophylaxis requires that the antimicrobial be delivered to the surgical site before contamination occurs and that it reaches its minimum inhibitory concentrations (MIC) from the moment of incision and throughout the surgical procedure. In general, the administration of the antimicrobial is recommended 60 minutes before the surgical incision (except in fluoroquinolones and vancomycin, which must be 120 minutes before the surgical event) [28].

To ensure that serum and tissue antimicrobial concentrations are achieved, both pharmacokinetics and pharmacodynamics must be considered. In the case of the pediatric population, the dose is standardized according to the weight of the patient, which is ideal, since in certain conditions the concentrations may not be adequate. For example, obese patients have alterations in pharmacokinetics because lipophilic drugs (e.g., vancomycin) reach lower concentrations and hydrophilic drugs can be excessive (e.g., amikacin) [29].

Administration of a second intraoperative dose of the antimicrobial is required to ensure optimal serum and tissue concentration, if the duration of the procedure exceeds two half-lives of the antimicrobial or there is excessive loss of blood. The interval is defined by the preoperative dose and not by the start of the procedure [30].

Appendicitis is divided into uncomplicated and complicated, the latter including perforated appendicitis, peritonitis or abscess formation. Approximately 80% of appendicitises are uncomplicated. All patients with clinical suspicion of appendicitis, even when not complicated, should receive preoperative intravenous antimicrobials to prevent surgical site infection [31].

The most frequently involved microorganisms are aerobic and anaerobic enteric gram negatives. The most common aerobic is *Escherichia coli* and the anaerobic is *Bacteroides fragilis*. *Streptococci*, *Staphylococcus spp*., *Enterococcus spp*. Much less frequently *P. aeruginosa* has been reported. The mean surgical site infections reported by the NHSN ranged from 1.15% to 3.47% according to risk. The rate of superficial and deep incisional infections was lower in laparoscopic versus open appendectomy; however, the organ-space infection rate was higher for laparoscopic appendectomy [32].

Recommendations:

- Uncomplicated appendicitis:
- A single dose of cephalothin + metronidazole.
- In patients allergic to beta-lactams, clindamycin + gentamicin or a fluroquinolone is recommended.
- The duration of prophylaxis should be less than 24 hours.
- Complicated appendicitis:
- ceftriaxone or cefotaxime + metronidazole with a duration of less than 5 days and complete outpatient treatment for 7 days with amoxicillin/clavulanate.

Current recommendations stipulate that children receive intravenous antibiotics after appendectomy until they tolerate a regular diet and are afebrile. Children who persist with fever or a WBC count greater than 12,000 cell/mm3 and/or cannot tolerate a regular diet five to seven days after surgery require imaging studies to look for an abdominal or pelvic abscess [33]. In the immediate postoperative period, based on a meta-analysis of 45 studies, initial treatment with intravenous antibiotics significantly reduces wound infection and intra-abdominal abscess formation [34].

Piperacillin may be used with tazobactam as recommended by the American Association for Pediatric Surgery for perforated appendicitis [35]. However, it is important to note that in perforated appendicitis, the microorganisms involved remain covered with the use of third-generation cephalosporins such as ceftriaxone or cefotaxime, adding metronidazole and ampicillin to the coverage of *Enterococcus spp*. antimicrobial pressure on *Pseudomonas spp*., with the use of Piperacillin with Tazobactam [36].

In retrospective series, single antibiotic therapy (piperacillin/tazobactam, cefoxitin, or ceftriaxone) appears to be as effective as multiple antibiotic therapy (ampicillin, gentamicin, and metronidazole) in preventing complications of perforated appendicitis, measured by duration of hospital stay, readmission rates and profitability [36].

In a prospective randomized controlled trial of 98 children with perforated appendicitis, metronidazole (30 mg/kg as a single daily dose) and ceftriaxone (50 mg/kg as a single daily dose) were as effective as standard multiple daily doses of ampicillin, gentamicin and clindamycin, to prevent abscesses or wound infections and is a reasonable alternative to piperacillin/tazobactam [36], observed that metronidazole and ceftriaxone once daily was equivalent to ertapenem alone or in combination with cefoxitin in terms of abscesses or other postoperative complications. The length of hospitalization was similar between the groups, however, patients who received the simplified regimen incurred significantly lower antibiotic charges [37]. Studied more than 7,000 children with complicated appendicitis, defined as treatment failure upon readmission of a child within 30 days of the appendectomy, and observed complications in about 6% of patients with complicated appendicitis and in patients receiving extended-spectrum antibiotics [38]. Therefore, the benefits of extended-spectrum antibiotics are unclear. More clinical trials are needed to determine the optimal antibiotic regimen [37].

8. Complications

Some authors have pointed out that the frequency of perforated appendicitis is similar in children as in adults [1]. Samiksha et al., mention that perforated appendicitis occurs more frequently in the pediatric age group and up to 60% in those under 5 years of age, reaching up to 86% in children under one year of age, and therefore, the risk of perforation is directly related to age [1]. The poor ability of young children to communicate clearly can result in a misinterpretation of their symptoms and thus delay the diagnosis, as well as the suspicion of other causes of abdominal pain such as respiratory or gastrointestinal infection as the main diagnosis and not suspecting appendicitis [1].

Perforated appendicitis increases morbidity and intra-abdominal abscesses are the most significant complication. The presence of postoperative abscesses is found between 0% and 4% of cases of uncomplicated appendicitis and their incidence increases from 12–20% in the cases of perforated appendicitis [1].

Another complication is undoubtedly residual cavitary abscesses. The proposal of many textbooks, including Sabinston and Schwartz, who stated that all abscesses should be approached surgically, was a proposal that we rejected. In meticulous clinical observations we found that a laparotomy on an already intervened abdomen is more harmful than beneficial, and after many cases, we find that all of them are susceptible to disappear with antibiotic treatment [14]. Something that still interests us is to know the relationship between this complication and the subsequent presence of another even more serious complication: intestinal obstruction due to fibrous bands with severe ischemia or perforation of a section of the small intestine, were those with the highest mortality due to appendicitis, apart from pneumonia, which was frequently fatal when associated with appendicitis [16].

9. Special conditions

Another area of this topic is related to the management of three different entities: appendicitis in young children, appendicitis modified by inappropriate use of antibiotics and appendicitis in children with psychomotor retardation and suffering severe neurological damage.

The first item is, according to our experience, the most frequent cause of abusive laparotomies in children who undergo emergency surgery. These patients have a totally different course from that seen in older children. It is usual that they begin with generalized severe symptoms, diarrhea, fever and vomiting. Data that change with the passing of the hours, and what were diarrheal evacuations, become a presumed picture of intestinal obstruction, not only from the clinical point of view but especially from the perspective of a vertical X-ray. That progression has led, in our experience, to abusive surgical intervention. To dispel doubts, the correct measure is the pelvic sonogram. Another rarely mentioned complication is the appearance of liver hollow fibers, which are a consequence of the migration via portal of bacterial boluses that lodge in the liver and that require long hospitalizations. Finally, the most serious of all and that has been a consequence of our having had patients who lost their lives, is the postoperative presence of associated pneumonia [14–16].

The second refers to those patients who have previously received antimicrobial treatment. Children with appendicitis without having received at least one antimicrobial were almost never admitted to our hospital unit. We learned that when we carried out the clinical study, we frequently found them asymptomatic. If these children come from the outpatient clinic, we study them more thoroughly, and if they have been hospitalized and were given antibiotics, we almost always take them to the operating room [14–16].

The third item is related to the child who suffers from psychomotor retardation and neurological deterioration. In this section, we are talking particularly about those children who suffer from infantile cerebral palsy and myelomeningocele and less frequently children with trisomy 21. Primarily these children are almost always over 6 years of age and the problem is that the parents do not capture disease manifestations beyond local infections and the urinary tract, and secondly because constipation is almost a rule in them. In these cases, we never operated in the initial stages of the disease and they always harbored a considerable amount of pus, due to the delay in diagnosis [14–16].

In recent months, with the COVID-19 pandemic secondary to the SARS CoV-2 virus, there is a delay in the diagnosis of acute appendicitis in children. Therefore, a perforated appendix was found in almost 39% of these cases in surgery, which significantly increases morbidity, produces complications such as pelvic abscesses, intestinal obstruction and sepsis, and prolongs hospitalization [38].

10. Recommendations

Based on the experience of the group, we recommend starting clear liquid diet for children operated on for uncomplicated appendicitis in the mediate postoperative period, early ambulation and considering discharge to home from12 to 24 hours later. Under certain conditions, such as careful selection of patients and application of state-of-the-art anesthetic-operative procedures, the operation can be performed with a short-stay surgery program within the safety margins that the quality of the procedures require.

Conflict of interest

The authors declare no conflict of interest.

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Chapter 5

Mimickers of Acute Appendicitis

Esam Amer

Abstract

Acute appendicitis (AA) is a common surgical diagnosis in patients presenting to the Emergency Department with acute abdominal pain. A wide variety of other clinical conditions can present with a very similar presentation to acute appendicitis and therefore it can be occasionally challenging to make the correct diagnosis. In this review paper, the focus is to shed some light on the differential diagnosis of acute appendicitis which includes a variety of gastrointestinal, vascular, urological, and gynaecological conditions. In the emergency setting there are three main imaging modalities to evaluate patients presenting with abdominal pain, this includes computed tomography (CT), ultrasound (US) and magnetic resonance imaging (MRI). The choice of imaging modality for each clinical condition is variable and as such being familiar with those differential diagnoses is vital in deciding what is the best imaging modality for every patient presenting with abdominal pain.

Keywords: acute appendicitis, appendicitis mimics, emergency department, Alvarado score, aortic abdominal aneurysm, inflammatory bowel disease, infectious enterocolitis, diverticulitis, radiation enteritis, neutropenic colitis, Meckel's diverticulitis, mesenteric ischemia, urolithiasis, pyelonephritis, ectopic pregnancy, ovarian torsion, haemorrhagic ovarian cyst, pelvic inflammatory disease, Mittelschmerz

1. Introduction

Although acute appendicitis is one of the most common causes for acute surgical abdomen accounting for 250,000 appendectomies in the United States every year, a large number of other clinical conditions can mimic the presentation of this acute surgical emergency [1]. Those conditions include a variety of gastrointestinal, vascular, genitourinary and gynaecological diseases. It is very important to consider those mimics when assessing patients presenting to the emergency department (ED) with acute right-sided abdominal pain.

The use of imaging modalities such as abdominal and pelvic ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) can be crucial in assessing those equivocal cases with vague nonspecific symptoms. The use of imaging in those circumstances not only aids in ruling in the diagnosis of acute appendicitis but also helps in differentiating other forms of pathology contributing to patient's symptoms.

The most common imaging modality used in patients with right-sided abdominal pain is abdominal and pelvic CT, which has a sensitivity of 97% and a specificity of 98% [2, 3].

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Classical features suggestive of appendicitis on CT include concentric and thickened appendiceal wall, the presence of an appendicolith, fat stranding, mesenteric lymphadenopathy and the presence of surrounding fluid. The presence of other features such as appendiceal wall defect, extraluminal air or localised abscess is more suggestive of a perforated appendix.

Ultrasound abdomen and pelvis is the second most common imaging modality used in patients presenting with acute abdominal pain in whom there is a degree of clinical uncertainty. Ultrasound has a sensitivity of 78% and a specificity of 83% [4]. It is the most preferred imaging modality in pregnancy and paediatric age group due to the inherent risk of radiation associated with computed tomography. Features suggestive of appendicitis on ultrasound include dilated (>6 mm outer diameter) non-compressible appendiceal wall, hyperechoic appendicolith with posterior acoustic shadowing, peri appendiceal fluid collection and mural hyperaemia on colour flow Doppler mode. Although it is the preferred imaging modality in pregnancy, it can be extremely challenging to interpret the images given the distorted abdominal and pelvic viscera especially in the third trimester of pregnancy.

When it comes to the elderly population presenting with acute abdominal pain, choosing the best Imaging modality can be extremely challenging due to the high mortality risk associated with false-negative imaging. The incidence of acute appendicitis in patients older than 50 years of age is only 15% when compared to younger patients where the incidence doubles to 30% [5]. Despite the declining incidence of acute appendicitis with advancing age, there is an increase in mortality rate from 1% in young patients to almost 8% in patients over 65 years of age [5]. This high mortality rate in the elderly age group can be explained by the increased incidences of appendicitis complications such as the development of appendicular abscess and perforation. There is also a considerable decline in the imaging diagnostic accuracy with advancing age as studies have shown that the percentage of patients with positive histological evidence of appendicitis drops from 78% to 64% in patients older than 65 years of age [6]. The use of enhanced CT scan for imaging in the elderly population is superior to ultrasound imaging. The low sensitivity, and negative predictive value along with the increased number of false-negative imaging in patients with complicated appendicitis make the ultrasound modality less preferable when it comes to choosing the best imaging modality. Due to the aforementioned reasons, the Jerusalem guidelines recommend the use of CT with IV contrast in patients older than 60 years old with an Alvarado score ≥ 5 and a negative ultrasound study [7]. This recommendation taking into account the risk of radiation where the number of performed CT scans after a negative ultrasound is reduced by 50% [7, 8]. It is also worth mentioning that the use of ultrasound is very important in screening elderly patients presenting to the Emergency Department with abdominal pain for an aortic abdominal aneurysm which a vascular emergency that can mimic appendicitis. The current recommendation by the UK Royal College of Emergency Medicine (RCEM) is for the Emergency Physician to perform an ultrasound scan on any patient older than 50 years presenting with abdominal pain [9].

The use of magnetic resonance imaging (MRI) depends on accessibility as it differs from one hospital to another. The presence of other more readily accessible imaging modalities such as computed tomography and ultrasound makes the use of magnetic resonance less popular. Features suggestive of appendicitis on MRI include the presence of dilated appendix (>7 mm outer diameter), fat stranding and restricted diffusion.

2. Conditions that mimic appendicitis

2.1 Gastrointestinal diseases

2.1.1 Inflammatory bowel disease (IBD)

Terminal ileitis caused by Crohn's disease and Backwash ileitis associated with Ulcerative colitis both can present with right lower abdominal pain mimicking acute appendicitis. Typical age group is from 15 to 30 years and clinical presentation usually include symptoms of diarrhoea and bloody stool. IBD cannot be diagnosed via a blood test, however routine blood tests checking for pro-inflammatory markers such as raised white cell count (WCC), C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) may aid in supporting the diagnosis and monitoring the disease activity later on.

Although colonoscopy remains the investigation of choice for confirming the diagnosis, the use of radiological imaging is warranted when colonoscopy is not accessible.

As per imaging choice, IBD is best evaluated with either CT or MRI enterography and classical findings include bowel wall thickening of more than 3 mm, mucosal hyperenhancement, fat stranding and engorged vasa recta known as "Comb" sign. Management of IBD includes both surgical and non-surgical treatment depending on the severity, the extent of the disease and the presence of complications.

2.1.2 Infectious enterocolitis

This refers to bowel inflammation caused by bacteria, viruses or parasites. Patients commonly present with abdominal pain, tenesmus and diarrhoea. Stools are often purulent and mixed with mucous and blood. Commonly implicated organisms include *Campylobacter jujni, Salmonella, Shigella, Escherichia coli, Yersinia enterocolittica, cryptosporidium, Norovirus, Rotavirus and Entamoeba histolytica*. Some infections such as tuberculosis and cryptosporidiosis are very important to consider in immunocompromised patients such as those with HIV infection. Routine blood tests looking for raised inflammatory markers along with stool microscopy and culture may help to support the diagnosis and monitor response to antimicrobial therapy. CT features include bowel long-segment circumferential wall thickening with homogenous enhancement and typically with no adjacent fat stranding. Treatment for infectious enterocolitis depends on the causative organisms.

2.1.3 Radiation enteritis

This is an inflammation of the bowel that occurs after radiotherapy. Symptoms include diarrhoea, nausea, vomiting and abdominal pain. Most cases of radiation enteritis resolve spontaneously a few weeks after treatment ends however for some it can extend for months and years after the termination of treatment. CT and MRI findings include bowel wall thickening with luminal narrowing, small bowel obstruction and sometimes the presence of a fistula between the bowel and the bladder or the vagina.

2.1.4 Neutropenic colitis

Also known as Typhlitis is an acute life-threatening condition that affects immunocompromised patients such as patients with HIV disease or those who are on immunosuppressive therapy. The aetiology involves mucosal damage secondary to ischemia and secondary bacterial infection with a predilection for the caecum and ascending colon. Patients may present with abdominal pain, diarrhoea, vomiting and fever. Typhlitis is commonly associated with Neutropenia. Early diagnosis and management are crucial to prevent complications such as perforation and sepsis. Classical CT findings include dilated caecum with circumferential wall thickening, peri-colic fluid collection and pneumatosis. Management includes bowel rest and antibiotic therapy.

2.1.5 Diverticular disease and diverticulitis

This is commonly seen in patients over the age of 40, where small bulging pouches also known as diverticula, form at the weakest portion of the bowel. Diverticulitis is the term used when there is associated inflammation of the diverticula. Symptoms include abdominal pain, vomiting and fever. Risk factors include aging, smoking, low fibre diet, obesity and sedentary life. Laboratory blood tests checking for raised inflammatory markers are useful in making the diagnosis of diverticulitis. Classical features of diverticulitis on CT include bowel wall thickening with infiltration of adjacent mesenteric fat. Managing patients with uncomplicated diverticular disease involves the introduction of low-fibre diet and antibiotics. Surgery is reserved for patients with complications such as perforation, diverticular abscess or fistula formation.

2.1.6 Meckel's diverticulitis

This is caused by congenital anomaly characterised by the presence of the vitelline duct which normally connects the yolk sac to the midgut during the fetal development. It occurs in 2–3% of the general population [10]. Inflammation of Meckel's diverticulum usually caused by enterolith and symptoms include abdominal pain, rectal bleeding and vomiting.

CT findings include the identification of a blind-end tubular structure protruding from the antimesenteric side of the distal ileum, wall thickening, hyperenhancement and fat stranding. Management is surgical resection of the diverticulum.

2.2 Vascular diseases

2.2.1 Abdominal aortic aneurysm (AAA)

This is a life-threatening emergency where there is an abnormal dilatation of the abdominal aorta due to vascular wall weakness. This abnormal dilation (1.5 times its normal diameter or greater than 3 cm) of the aorta is commonly seen involving the infrarenal part of the abdominal aorta. AAA is a fatal condition where mortality is about 80% with leaking aneurysm and only half of the patients survive 30 days post emergency repair [11]. AAA is more common in men and the risk factors implicated in the aetiology are the same factors contributing to atherosclerosis such advancing age, diabetes, hypertension, hypercholesterolemia and smoking history. Clinical presentation of AAA includes a variety of symptoms such as abdominal pain, back pain, groin pain, and a pulsating abdominal mass. Ultrasound aorta remains the gold standard for screening patients for AAA in the emergency setting and the UK Royal College of Emergency Medicine (RCEM) recommends that all emergency physicians are to perform ultrasound aorta in all patients who are over the age of 50 presenting with abdominal pain. Disadvantages for ultrasound include difficult studies due to the patient's body habitus, or the presence of overlying bowel obscuring the visualisation of the aorta. Another downside to the use of ultrasound is its operator dependability and the inability to exclude any aneurysmal leak. CT aortogram is a highly acute study that can confirm the presence and the size of an aneurysm which aids in planning surgery. Management of AAA involves either open repair or endovascular aneurysm repair (EVAR) depending on the fitness of patients for surgery and the morphology of the aneurysm.

2.2.2 Mesenteric ischemia

This refers to small bowel injury secondary to insufficient blood supply which can be acute or chronic. Patients with mesenteric ischemia can present with diarrhoea, rectal bleeding, abdominal pain, especially after eating, and unintentional weight loss due to the fear of eating and vomiting. Risk factors include atrial fibrillation, heart failure and chronic kidney disease. Early CT findings include mesenteric oedema, bowel dilation and wall thickening, mesenteric stranding and the presence of an adjacent solid organ infarction. Treatment depends on the cause of ischemia and as such can be medical or surgical however if it is a late presentation the only treatment is surgical since there is a risk of necrotic bowel.

2.3 Urological diseases

2.3.1 Urolithiasis

Urolithiasis or kidney stone disease can present with a right lower abdominal pain mimicking acute appendicitis. Careful consideration for the presence of obstructive uropathy is very important to prevent kidney injury. CT Urinary system is the gold standard imaging when assessing patients with suspected urolithiasis. CT findings include the identification of a high attenuation calculus within the urinary system with or without hydroureter and hydronephrosis, ureteral wall thickening and adjacent fat stranding.

Ultrasound can be used in patients with ureteric colic to identify any features of hydronephrosis. The only disadvantage of ultrasound imaging is its operator dependability. Conservative treatment is indicated for patients with stones measuring less than 4 mm.

2.3.2 Pyelonephritis

Pyelonephritis or kidney infection is commonly caused by ascending urinary tract infection with the most commonly implicated organism being *Escherichia coli*. It is a clinical diagnosis where history and clinical examination play a major role. Although imaging such as Computed tomography and Ultrasound can be normal in pyelonephritis, both can be particularly useful in assessment for complications such as abscess formation and identifying emphysematous pyelonephritis, which typically occurs in immunosuppressed patients. Typical features of pyelonephritis on Computed tomography include nephromegaly, delayed nephrogram, perinephric fat stranding and enhancement of the collecting system. Ultrasound features of pyelonephritis include nephromegaly and hydronephrosis with the loss of corticomedullary junction. Treatment includes supportive measures and antibiotics.

2.4 Gynaecological and obstetric diseases

2.4.1 Ectopic pregnancy

This medical emergency occurs when pregnancy happens outside the uterus and needs to be excluded in all women of reproductive age who present with abdominal pain. Blood and urine beta-HCG measurement is crucial in making the diagnosis. The absence of an intrauterine gestational sac on transvaginal ultrasound along with a high beta-HCG, intrapelvic fluid and a delayed period should raise the possibility of an ectopic pregnancy. Ultrasound features include the detection of a yolk sac or a live embryo outside the uterus makes the diagnosis. Other features include the detection of a hyperechoic ring around the adnexal gestation sac also known as the "tubal ring" sign. If detected early, methotrexate can be administered to terminate the ectopic pregnancy. Surgical intervention is indicated in the case of methotrexate contraindication, ruptured ectopic or in patients with hemodynamical instability.

2.4.2 Ovarian torsion

Another medical emergency that should be considered in all women of reproductive age presenting with severe abdominal pain. It is caused by twisting of the ovary around its supporting ligaments cutting the blood supply to the ovary and fallopian tube. Ovarian torsion commonly occurs in patients with ongoing gynaecological pathology such as ovarian cysts, tumours, enlarged corpus luteum or in patients who are undergoing ovarian stimulation for assisted fertilisation. Ultrasound is the first line of imaging and features suggestive of torsion include increased ovarian size more than 4 cm in diameter, heterogeneous appearance due to oedema and haemorrhage, and the detection of a cyst or an ovarian mass. Doppler Arterial and venous flow can be helpful when compared to the other non-affected side. Management includes surgical de-torsion of the ovary and debridement of any necrotic tissue.

2.4.3 Haemorrhagic ovarian cyst

This condition occurs when there is a sudden haemorrhage into an ovarian cyst. Ultrasound findings usually depend on how old the haemorrhage is. Most classical feature on ultrasound is a finely septated fishnet pattern caused by the fibrin bands. Management is usually conservative.

2.4.4 Pelvic inflammatory disease (PID)

This refers to the infection of the female reproductive system caused most commonly as a result of untreated ascending sexually transmitted infections. Most commonly implicated organisms are *Chlamydia trachomatis* and *Neisseria gonorrhoea*. Symptoms can be very subtle such as mild abdominal pain with per vaginal discharge. Rarely infection can spread to the liver and other tissues around the liver what is known as Fitz-Hugh-Curtis syndrome or gonococcal perihepatitis. Transvaginal ultrasound features include enlarged heterogenous ovaries, dilated fallopian tubes and adnexal thickening and pelvic fluid collection. CT features of Pelvic inflammatory disease include enlarged ovaries with abnormal enhancement, fluid-filled dilated fallopian tube, pelvic fat stranding, enhancement of the adjacent peritoneum and the presence of a pelvic abscess in severe cases. Treatment is conservative with antibiotics.

2.4.5 Mittelschmerz

This refers to one-sided abdominal pain that is associated with mid-cycle ovulation. Mittelschmerz means "middle pain" in German. If the pain occurs on the right side of the abdomen, it can mimic acute appendicitis. In most cases, mittelschmerz does not warrant any medical treatment.

3. Conclusion

Although the diagnosis of acute appendicitis is essentially clinical, familiarisation with other causes of acute abdominal pain that can mimic appendicitis is equally important especially in females and those with the extremes of age. Here we present a plethora of gastrointestinal, urological, vascular, infectious, and gynaecological conditions that can be similar in presentation to acute appendicitis. The supplementary use of appropriate laboratory tests and radiological imaging can be pivotal where there is clinical uncertainty, not only aiding in confirming the diagnosis of appendicitis or its associated complications but also in identifying other alternative pathology. Routine blood tests that include a full blood count (FBC) and c-reactive protein (CRP) can aid in the diagnosis of acute appendicitis as evidenced by the presence of raised white cell count and CRP. Although raised inflammatory markers can raise the likelihood for clinically suspected acute appendicitis, it is non-specific and less helpful where the clinical presentation is inconclusive and other differential diagnoses are equivocal. A urinalysis also should be considered in all patients with suspected acute appendicitis as part of their workup since it is an important bedside test when assessing for potential renal or urology pathologies such as the presence of blood in urolithiasis or nitrites and leukocytes in urinary tract infection (UTI).

Special consideration is warranted for female patients presenting with abdominal pain as the presence of an underlying gynaecological pathology can potentially complicate the clinical picture and affect the diagnostic accuracy. In this special category of patients, it is particularly important to check the blood or urine samples for beta Human chorionic gonadotrophin hormone (Beta-hCG) in all female patients of childbearing age presenting to the Emergency Department with acute abdominal pain to exclude ectopic pregnancy. Ultrasound remains the first line of imaging in investigating gynaecological pathology (transvaginal ultrasound) and in the paediatric age group due to the inherent risk of radiation associated with CT imaging.

Another special consideration is given to the elderly population where the incidence of acute appendicitis is less common. In assessing elderly patients, it is of a high priority to exclude time-critical conditions such as ruptured abdominal aortic aneurysm and bowel ischemia. The current recommendation by the Royal College of Emergency Medicine in the UK is for the emergency physician to perform an ultrasound aorta in all patients who are older than 50 years presenting with acute abdominal pain to rule out abdominal aortic aneurysm (AAA). A follow up dedicated CT aortogram may be required if the patient is hemodynamically stable to confirm the diagnosis of abdominal aortic aneurysm and to evaluate for any potential leak. Bowel ischemia is another time-critical emergency where there is a compromise to the bowels blood supply. Risk factors for bowel ischemia include diabetes, hypertension, smoking, hypercholesterolemia and atrial fibrillation (AF). It is important to consider the diagnosis of bowel ischemia in all patients who are older than 50 years presenting with a sudden onset of severe abdominal pain along with a raised serum lactate level reflecting organ hypoperfusion. CT abdomen and pelvis with IV contrast or a dedicated CT angiography remains the best imaging technique for all hemodynamically stable patients in whom bowel ischemia is suspected.

As discussed above a variety of clinical conditions can mimic acute appendicitis and familiarisation with those alternative conditions is crucial when deciding what imaging modality will best suit the patient assessment thus increasing the diagnostic accuracy and ensuring optimal care to all patients.

Funding

I have received no financial funding or grants for this paper.

Disclaimer

I declare no conflict of interest.

Dedication

I dedicate this work to my beloved wife and parents who have both supported me throughout my career in emergency medicine. I will always appreciate their love, affection, patience and encouragement.

Abbreviations

AA	Acute appendicitis
AAA	Abdominal aortic aneurysm
US	Ultrasound
CT	Computed tomography
MRI	Magnetic resonance imaging
WCC	White cell count
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate

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Chapter 6

Complicated Appendicitis: A Surgical Controversy Concerning Risk Factors, Diagnostic Algorithm and Therapeutic Management

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Abstract

By surgeon's perspective, complicated appendicitis is defined as perforated appendicitis, periappendicular abscess, gangrenous appendicitis or peritonitis, noted on radiological studies upon hospital admission, operative reports or pathology results of the surgical specimen. Despite that this clinical condition is truly common in everyday surgical routine, its causes and risk factors are still unclear. Some parameters have been associated with complicated appendicitis, like older age, type 2 diabetes, symptoms for longer duration, appendicoliths/fecaliths, delays in surgery after onset of symptoms and after admission. Furthermore, currently, there is no standard diagnostic algorithm for complicated appendicitis. To be specific, radiological findings lack sensitivity, intraoperative assessment may overestimate it while, histopathological examination is regarded as more specific diagnostic method. In addition, the optimal treatment for complicated appendicitis remains controversial between an immediate surgical operation (laparotomy/laparoscopy) or a trial of nonoperative management. Hereby, by reviewing the current literature, we would aim to clarify the risk factors and the diagnostic procedure of complicated appendicitis as well as to compare the operative management with the conservative one according to the type of complicated appendicitis, the success rate and the postoperative complications.

Keywords: Complicated appendicitis, perforated appendicitis, gangrenous appendicitis, appendiceal empyema, risk factors, diagnosis, non-operative management, open appendicectomy, laparoscopic appendicectomy

1. Introduction

1.1 Definition of complicated appendicitis

Acute appendicitis is one of the most well-known acute abdominal disease and the most frequent one for surgical emergencies, with a lifetime risk of 8.6% in males and 6.9% in females, worldwide, ranging from mild acute appendicitis to fecal peritonitis. The term 'appendicitis' is defined as inflammation of the vermiform appendix, the most common surgical cause of abdominal pain in children and adults and can be divided into uncomplicated and complicated one. Definition of the exact type of appendicitis is based on examination of the peritoneum and appendix. It is truly crucial as it can determine the preoperative management (conservative treatment or immediate surgery), intraoperative management (appendectomy only, aspiration, lavage, cecectomy) and postoperative one (hospitalization, antibiotic regimen) as well as the rates of postoperative complications and morbidity. The current standard treatment of choice for patients with appendicitis is the surgical appendicectomy, either laparoscopic or open. Emerging evidence report that a non-operative strategy with antibiotics has recently been considered in some cases of [1–3].

Currently, a well-structured and specific definition of complicated appendicitis among surgeons is strongly necessary but not clear yet. Complicated appendicitis is thought as an inflammatory type with rapidly proceeding perforation, necrosis, or both and subsequent abscess formation. It is about 4–25% of all the cases and one-third of patients, who develop appendicitis, are diagnosed with complicated appendicitis at the time of hospital admission. To be more specific, while uncomplicated appendicitis is described as any phlegmonous and catarrhal stage of appendicitis without periappendicular infection, complicated appendicitis is defined as the presence of appendiceal perforation, gangrene, serious periappendicular inflammation, peritonitis, mass formation (a plastron), intraabdominal or pelvic abscess [1–3].

The rate of perforation varies from 16–20%. Moreover, abscess rates have been reported as 1% in non-complicated appendicitis and as 50% following perforated appendicitis [4]. Referring to complicated appendicitis, we describe an acute inflammation of the peritoneum secondary to infection of the appendix. Purulent peritonitis is defined by the presence of purulent fluid and fecal peritonitis corresponds to the presence of fecal matter in the peritoneal cavity. However, operative description of peritonitis has not been described clearly (in particular, the distinction between regional and general peritonitis remains unclear), and can vary from one surgeon to another, but this description has a direct impact on the preoperative, operative and postoperative management of patients [1–3].

The mortality risk of acute non-complicated appendicitis is less than 0.1%, but the risk rises to 0.6% in gangrenous appendicitis. On the other hand, perforated appendicitis carries a higher mortality rate of around 5% [4].

2. Risk factors associated with complicated appendicitis

Factors associated with the presentation of complicated appendicitis have been inconsistently identified. In general, frequently described, non-modifiable predictors of appendiceal perforation include extremes of age with a higher frequency occurring in younger age groups (40–57%) and in patients older than 50 years (55–70%). Perforation rate is higher among men (18% men versus 13% women) and it is usually accompanied with three or more comorbid illnesses [4, 5].

Appendicoliths (known as fecaliths), a non-modifiable risk factor, is estimated in up to 30% of asymptomatic population, have historically been associated with appendicitis and has been shown to increase the risk of complicated appendicitis [5]. However, they can also be asymptomatic. In current studies, the presence of appendicolith is associated with earlier and higher rates of appendiceal perforation in patients with acute appendicitis. Ishiyama et al. reported an association of appendicoliths that were large and present at the base of the appendix with appendiceal perforation and gangrene [6]. Clinical significance of appendicolith that incidentally discovered in patients without symptoms of appendicitis, remains controversial. On one hand, the presence of fecalith in the appendix lumen is an explicit mechanically obstructive factor related to appendicitis. On the other hand, appendicoliths detected by CT scan without inflammatory signs may be transient without special clinical importance. Pathology appears to be due to appendicolith obstructing the appendiceal lumen leading to infection or inflammation, to intraluminal obstruction, venous and arterial congestion and finally to perforation [5, 6].

An additional proposed association with the development of complicated appendicitis is a longer interval from the onset of symptoms to admission. The time from onset of symptoms to occurrence of complication like, gangrene or perforation, varies from short duration of 1–2 days in children to 3–4 days in adults. Imran et al. proposed the increased odds of perforated appendicitis with greater symptom duration and the presence of an appendicolith [5, 7]. Duration of symptoms, a modifiable risk factor, can possibly determine access to surgical care. Perforation is a major concern when evaluating a patient with symptoms that have lasted more than 24 hours.

Factors like, various laboratory markers or other novel parameters, such as "intraabdominal pressure" and clearly increased levels of inflammatory markers can induce any type of complicated appendicitis [5, 8, 9]. Moreover, diabetes mellitus have also been associated with appendiceal perforation. Delayed diagnosis, and probably a history of diabetic nephropathy, as well as poorer renal function were risk factors for the development of complicated appendicitis in diabetic patients [5].

Finally, the exact role and effect of the anti-platelet drugs on complicated appendicitis is not very clear yet. From our personal experience in our department, we have already investigated an increased association between the usage of oral anti-platelet therapy with perforated and gangrenous appendicitis. Going through the current literature, the effect of anti-platelet drugs on surgical blood loss and perioperative complications has not been studied in depth and the management of surgical patients taking anti-platelet medications is controversial. Chechic et al. study claims that the blood loss is significantly greater in patients with a perforated appendicitis and in patients with an operative time of more than one hour while preoperative use of anti-platelets exists [10].

3. Symptoms of complicated appendicitis

Diagnosis of complicated appendicitis is not always straightforward according to a standard algorithm. Clinical presentation may be atypical. Patients with perforated appendicitis can suffer from significant dehydration and electrolyte abnormalities, especially when fever and vomiting have been present for a long time. The pain usually localizes to the right lower quadrant if the perforation has been walled off by regional intra-abdominal structures but can be diffuse if generalized peritonitis occurs. Complicated appendicitis is usually diagnosed in patients with atypical symptoms (epigastric pain, diarrhea, malaise, lack of anorexia, and history of chronic RLQ pain). It has been demonstrated that a diagnostic approach based mainly on history and clinical examination caused a high percentage of negative appendectomy of between 9.2 and 35%. Other unusual presentations of appendiceal perforation can occur, such as retroperitoneal abscess formation due to perforation of retrocecal appendix or liver abscess formation due to hematogenous spread of infection through the portal venous system [11].

4. Diagnosis

The clinical diagnosis of complicated appendicitis is usually challenging and involves a combination of clinical, laboratory, and radiological findings. Globally, surgeons follow different criteria and algorithms for classifying patients with complicated appendicitis. Definition of the type of appendicitis is critical, as it determines the type of preoperative management (ambulatory surgery or immediate surgery), intraoperative management (aspiration, lavage), subsequent management (hospitalization, postoperative antibiotic therapy) and postoperative morbidity [12].

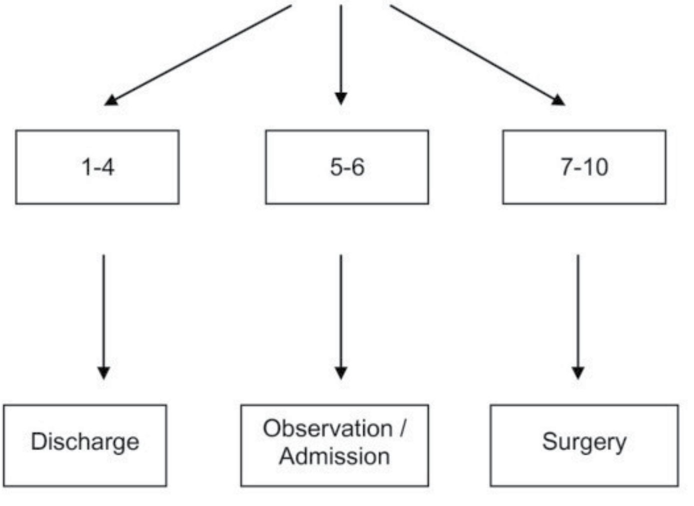
Risk stratification of patients by clinical scoring systems could result in decision-making to reduce hospital admissions, optimize the utility of diagnostic imaging, and reduce negative surgical appendicectomies. Several randomized controlled trials have tried non-operative treatment of uncomplicated appendicitis. Preoperative differential diagnosis of complicated appendicitis from uncomplicated one can be feasible. A false-negative diagnosis of complicated appendicitis may result in severe complications such as abscess or peritonitis, whereas a false-positive diagnosis of uncomplicated appendicitis would result in appendectomy only. The Alvarado (**Table 1**) and AIR scores are standardized diagnostic approaches in evaluating patients with suspected acute appendicitis, using only clinical signs and symptoms and laboratory values. Recently, the appendicitis inflammatory response score (AIR) has been developed and seems to surpass the Alvarado score in terms of accuracy [8, 13]. Gomes et al. report tried to standardize the definition of complicated appendicitis by classifying appendicitis into 5 grades according to the laparoscopic appearance of appendix and peritoneum (**Table 2**) that has been reproducible by further studies. This score classifies appendicitis based on the description of the appendix and the peritoneum into 5 grades. Grades 1 and 2 correspond to uncomplicated appendicitis and grades 3–5 correspond to complicated appendicitis [14].

Many studies have reported that an increase in white blood cells (WBCs) has been the earliest sign of appendiceal inflammation, while increased CRP has been noted in more advanced stages of appendicitis. Older adults tend to have a diminished inflammatory response, resulting in fewer cases of leukocytosis and less remarkable findings on history and physical examination. One reprospective study investigated the changes in mean platelet volume (MPV), platelet distribution width (PDW), and red cell distribution width (RDW) with the diagnosis of acute appendicitis. There are three parameters related to platelets; plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW). MPV is a marker of platelet function and activation, and has been used in diagnosis of inflammatory diseases. WBC elevation and presence of NP support the diagnosis of acute appendicitis [15, 16]. Increased PDW and WBC/neutrophil counts can lead to diagnose cases of acute appendicitis, while MPV and RDW levels were not useful diagnostic markers [17]. Muhammad et al. reported that the diagnostic accuracy of WBCs, INR, TB, and CRP were between 68% and up to 93% indicating that these preoperative laboratory tests were valid for early detection of complicated appendicitis [18].

Diagnosis of complicated appendicitis is still challenging despite the use of ultrasonography, computed tomography scan, and diagnostic laparoscopy. Computed tomography (CT) is generally accepted as the most accurate test for diagnosing acute appendicitis, but its ability to differentiate uncomplicated from complicated one is less satisfactory [19–22]. We have to mention that 17% of appendicoliths were unable to be detected by CT imaging. Despite that CT is regarded as imaging of choice in diagnosing appendicitis because of its increased accuracy and clinical outcomes [23], CT scan has lower sensitivity of identifying complicated appendicitis.

One systematic review and meta-analysis concluded to ten CT features for differentiating complicated appendicitis that include abscess, extraluminal air, appendiceal wall enhancement defect, periappendiceal fat stranding, ileus, periappendiceal fluid collection, ascites, intraluminal air, extraluminal appendicolith, and intraluminal appendicolith. Nine of these features showed higher specificity, but lower sensitivity. To be more specific, periappendiceal fat stranding and

Alvarado score	
Feature	**Score**
Migration of pain	1
Anorexia	1
Nausea	1
Tenderness in right lower quadrant	2
Rebound pain	1
Elevated temperature	1
Leucocytosis	2
Shift of white blood cell count to the left	1
Total	**10**



Predicted number of patients with appendicitis:

- Alvarado score 1-4 - 30%
- Alvarado score 5-6 - 66%
- Alvarado score 7-10 - 93%

Ref: Robert Ohle, Fran O'Reilly, Kirsty K O'Brien, tom Fahey & Borislav D Dimitrov. The Alvarado score for predicting acute appendicitis: A systematic review. BMC medicine 2011, 9:139.

Table 1.
Alvarado score for diagnosis of acute appendicitis.

appendiceal wall enhancement defect showed highest sensitivity, while extraluminal appendicolith, abscess, and extraluminal air showed highest specificity. CT scan findings lack sensitivity in detecting appendiceal perforations. Intraoperative assessment may also overestimate appendiceal perforations by 40% [24, 25]. Current guidelines suggest the conduction of CT scan with intravenous contrast in all elderly patients with an Alvarado score ≥ 5 as it can differentiate uncomplicated appendicitis from complicated one [26].

Laparoscopic grading system of acute appendicitis

- 0 Normal looking appendix
- 1 Hyperemia and edema
- 2 Fibrinous exudate
- 3A Segmental necrosis
- 3B Base necrosis
- 4A Abscess
- 4B Regional peritonitis
- 5 Diffuse peritonitis

Table 2.
Laparoscopic staging system of acute appendicitis [3].

Comparable disappointing results have been reported for ultrasonography, and magnetic resonance imaging (MRI) [27]. Furthermore, there has not been a clinical trial comparing US and CT scanning to suggest that US can be as accurate as CT in the differentiation of complicated and uncomplicated appendicitis.

Imaoka et al. reported that three factors, body temperature ≥ 37.4°C, C-reactive protein ≥4.7 mg/dl, and fluid collection surrounding the appendix on CT, are useful in predicting cases of complicated appendicitis preoperatively and can thus facilitate decisions regarding emergency surgery [28]. Atema et al. reported that the scoring system accurately predicted the complicated appendicitis using a maximum possible score of 22 points based on clinical and CT features and a model was created that included age, body temperature, duration of symptoms, white blood cell count, C-reactive protein level, and presence of extraluminal free air, periappendiceal fluid, and appendicolith [29]. While histopathological diagnosis is regarded as the gold standard, the final report takes many days to become available [30].

To conclude, a total evaluation of the patient and their condition can lead to diagnosis of complicated appendicitis. Naderan et al. concluded that "Bedside evaluation" is a useful, cheap, quick and readily available method for identifying those at risk for developing complicated acute appendicitis [31].

5. Therapy

For over a century, open appendectomy was the only standard treatment of choice for appendicitis. Nowadays, laparoscopic appendectomy has surpassed open appendectomy in everyday usage. A non-operative strategy with antibiotics has recently been favorable in some cases of appendicitis and current evidence suggests that there could be wider applicability depending on its type. Preoperative distinction between uncomplicated and complicated disease is truly crucial to this point before deciding the therapeutic protocol. Cases of complicated appendicitis, which include perforated appendicitis and gangrenous appendicitis, may progress to acute peritonitis, a condition that necessitates emergency surgery regardless of the time of development. In contrast, the short-term risk of perforation in cases of uncomplicated appendicitis, such as catarrhal and cellulitis appendicitis is low, and these cases can be treated conservatively with antibiotics [32].

The optimum management of this disease remains a subject of controversy. Although the role of surgery as primary treatment has recently been questioned, appendectomy remains the treatment of choice. Peritonitis mandates urgent surgery but phlegmon is managed by conservative approach and antibiotic therapy for couple of. The surgery is gold standard treatment for more than a century because of its low incidence of postoperative complications, early recovery and short hospital stay. Nevertheless, surgical treatment exposes the patient to risks due to general anesthesia and other complications such as surgical site infection, adhesions and intestinal obstruction, incisional hernia, infertility in female and pneumonia. Open surgery had been the gold standard until the last 20 years, when laparoscopic approach has currently become the first choice of most surgeons. Laparoscopic appendectomy has already proved of its advantages like less pain, lower wound infection rate and short recovery period. The period between the onset of symptoms and the decision of surgery is truly important as delayed surgery in complicated cases leads to higher risk of postoperative complications.

The goal is to remove any infected material at the time of appendectomy (open or laparoscopic). To be more specific, open appendectomy for perforated appendicitis usually requires a larger incision to provide adequate exposure for drainage of abscesses and enteric contents. Skin closure techniques include primary closure, loose partial closure, and closure with secondary intention. Because of wound infection rates ranging from 30 to 50 percent with primary closure of grossly contaminated wounds, many advocate delayed primary or secondary closure [33]. However, one meta-analysis showed that, compared with primary closure, delayed closure increased the length of hospital stay by 1.6 days without decreasing the wound infection rate [34]. Our preferred technique of skin closure after an open appendectomy is interrupted permanent sutures for patients with complicated appendicitis and the skin is often left open to close secondarily for patients with general peritonitis. Wounds are typically closed after a laparoscopic appendectomy for perforated appendicitis.

Current evidence shows laparoscopic appendectomy to be the most effective surgical treatment, being associated with a lower incidence of wound infection and post-intervention morbidity, shorter hospital stay, and better quality of life scores when compared to open appendectomy [35]. Open and laparoscopic appendectomy have been compared in over 70 randomized trials and analyzed in many systematic reviews. The laparoscopic approach is superior for a lower rate of wound infections, less pain on the first postoperative day and shorter duration of hospitalization. On the other hand, open appendectomy offers a lower rate of intra-abdominal abscesses and a shorter operative duration [36, 37]. However, there is still a controversy about its use in the management of complicated appendicitis. The main guideline from SAGES is that the indications for appendectomy are identical whether performed laparoscopically or open. Moreover, laparoscopic technique provides an additional advantage in patients in whom the diagnosis of appendicitis is uncertain since it offers inspection of the peritoneal cavity especially for women of childbearing age [37, 38]. Furthermore, laparoscopic appendicectomy is better option for obese patients because of the reduction of morbidity-prone incisions [39]. Also, it has been shown that elderly patients who undergo laparoscopic appendectomy, gain shorter hospitalization [40].

Laparoscopy, which leads to less postoperative pain, a shorter hospital stay, and a quicker recovery, represents the standard of care for appendectomy. The most common postoperative complications, such as wound infection, intra-abdominal abscess, and ileus, vary in frequency between open appendectomy (overall complication rate of 11.1%) and laparoscopic approach (8.7%) [35]. We recommend laparoscopic appendectomy as the preferred surgical technique over open appendectomy for both uncomplicated and complicated acute appendicitis, where laparoscopic equipment and expertise are available. Laparoscopy can be recommended for patients with complicated appendicitis even with higher risk categories, like elderly and obese [40]. For high-risk patients, laparoscopy has proven to be safe and feasible and was also associated with decreased rates of mortality, postoperative morbidity, and shorter hospitalization [41]. One randomized controlled trial stated that LA in obese patients was associated with reduced mortality, reduced overall morbidity, and shorter operating times and postoperative length of hospital stay, compared to open technique [42].

An alternative minimal invasive surgical method is single-incision laparoscopy, in which all instruments and the laparoscope are inserted through a multi-channel portal placed at the umbilicus [43]. Miyo et al. study claims that Single-site laparoscopic interval appendectomy (SLIA) for severe complicated appendicitis after conservative treatment to restrict inflammation can be safe, feasible, and less invasive than appendicectomy and offers all the advantages of minimally invasive surgery despite its disadvantage of prolonging the hospital stay [44]. A 2017 systematic review showed that laparoscopic appendectomy, compared with open one, reduced the risk of surgical site infection, length of hospital stay, and time to oral intake without increasing the rate of intra-abdominal abscess [45].

According to peritoneal irrigation, it is reported that there is no advantage over suction alone in complicated appendicitis in both adults and children. The performance of irrigation during laparoscopic appendectomy does not seem to prevent the development of intrabdominal abscess and wound infections. Drains are of no benefit in preventing intra-abdominal abscess and lead to longer length of hospitalization, and there is also low quality evidence of increased 30-day morbidity and mortality rates in patients in the drain group. So, we recommend against the use of drains following appendectomy for complicated appendicitis in adult patients [46, 47].

Although appendectomy has been the treatment of choice for patients with appendicitis, conservative treatment is currently proposed as an alternative. Cases of complicated appendicitis with localized abscesses, however, present a lower risk of progression to acute peritonitis [48]. Before 2000, many surgeons used a triple antibiotic regimen consisting of ampicillin, gentamicin, and clindamycin (triple antibiotics) for the management of perforated appendicitis. Monotherapy with piperacillin/tazobactam for intra-abdominal infections has recently been shown to be equally efficacious as traditional triple therapy [49]. Similarly, cefotaxime, a third-generation cephalosporin, has been shown to be equal to the monotherapy schedule of piperacillin/tazobactam in children with complicated perforated appendicitis when combined with metronidazole [17].

The optimal approach to complicated appendicitis with phlegmon or abscess is a matter of debate. Current evidence shows that surgical treatment of patients presenting with appendiceal phlegmon or abscess is preferable to accompanied with antibiotic oriented treatment in the reduction of the length of hospital stay and need for readmissions. Non-operative management is a reasonable first-line treatment for appendicitis with phlegmon or abscess. Percutaneous drainage as an adjunct to antibiotics, if accessible, could be beneficial, although there is a lack of evidence for its use on a routine basis. Studies suggest that percutaneous drainage of appendiceal abscesses results in fewer complications and shorter overall length of stay than surgical drainage [50].

To conclude, the management of complicated appendicitis depends on the general condition of the patient, the nature of perforation and whether an abscess is present on imaging studies. Septic patients or patients with generalized peritonitis require preoperative resuscitation and emergency appendectomy (open or laparoscopically) as well as drainage and irrigation of the peritoneal cavity. Stable patients with perforated appendicitis with symptoms localized to the right lower quadrant can be treated with immediate appendectomy or initial nonoperative management (includes intravenous antibiotics, intravenous fluids as well as bowel rest). An appendiceal abscess <3 cm can be treated with immediate appendectomy but >3 cm should be treated with intravenous antibiotics and percutaneous drainage first, although appendectomy is required if the abscess is not amenable to drainage. Phlegmon of the right lower quadrant can undergo appendectomy without the need for an ileocecal resection. [50–53]. Non-operative management with antibiotics in combination with percutaneous drainage for complicated appendicitis with a periappendicular abscess, can be a safe and feasible treatment of choice. Operative management of acute appendicitis with phlegmon or abscess is a safe alternative to non-operative management in experienced hands and may be associated with less complications, reduced need for readmissions, and fewer additional interventions than conservative treatment. We believe that the laparoscopic approach can be a treatment of choice for patients with complicated appendicitis with phlegmon or abscess where advanced laparoscopic expertise is available, with a low threshold for conversion [40].

The reported rate of recurrence after non-surgical treatment for perforated appendicitis and phlegmon ranges from 12–24%. Interval appendectomy is recommended for those patients with any recurrent symptoms [40]. Existing studies have shown that laparoscopic appendectomy is superior to open approach in reducing the likelihood of surgical site infection, reducing the need for postoperative analgesics, and providing faster recovery of preoperative functional status.

One postoperative concern related to elderly patients with complicated appendicitis is the need of performing a postoperative colonoscopy. Caecal or appendiceal cancer in patients older than 55–65 years can be present with symptoms of acute appendicitis. An incidence rate of 1.6–36% shows that older patients can suffer from cancer beneath the onset of acute appendicitis. Open appendectomy offers a visual inspection of the bowel. Current guidelines suggest that postoperative colonoscopy in patients older than 65 years can be very useful for the patient follow-up especially, when the patient with the complicated appendicitis has been treated with conservative method or laparoscopic appendectomy [26].

6. Postoperative antibiotic therapy

Currently, there is no standard protocol on the duration of postoperative antibiotic treatment and different antibiotic regimens are used. In patients with complicated acute appendicitis, postoperative broad-spectrum antibiotics are suggested, especially if complete source control has not been achieved. In patients with intra-abdominal infections who had undergone an adequate source control, the outcomes after fixed-duration antibiotic therapy (approximately 3–5 days) are similar to those after a longer course of antibiotics. The meta-analysis by Van den Boom et al., including nine studies with more than 2,000 patients with complicated appendicitis, revealed a statistically significant difference in incidence between the antibiotic treatment of ≤5 vs. > 5 days, but not between ≤3 vs. > 3 days [54, 55].

According to current guidelines, patients should not receive postoperative antibiotic therapy in the absence of peritonitis, patients should receive 48–72 hours of postoperative antibiotic therapy in the presence of regional peritonitis, patients should receive 5 days of postoperative antibiotic therapy in the presence of diffuse peritonitis, and patients should receive 7–10 days of postoperative antibiotic therapy in the presence of fecal peritonitis [56]. Although most surgeons agree that appendicitis with perforation, intra-abdominal abscess, or purulent peritonitis can be defined as complicated one, for which postoperative antibiotic therapy is indicated, there is still a considerable variation in the indications for prolonged antibiotic therapy after appendectomy, and the antibiotic regimen that should be used. One cohort reports that operative surgeons accurately identified patients with complicated appendicitis who did not require post-operative antibiotics. Two days of treatment was associated with reduced complications compared with shorter or longer antibiotic courses [57]. Many studies show that 3 days of postoperative antibiotic treatment is feasible and safe [58]. Three to five days of intravenous antibiotics is recommended for perforated appendicitis after appendectomy. Patients with complicated appendicitis should receive preoperative antibiotics and continue therapy for at least five days. The most common pathogenic organisms isolated after appendectomy are anaerobic and aerobic gram-negative enteric organisms like Bacteroids fragilis and E.Coli and Staphylococcus species [59]. Every patient who responds to initial antibiotic therapy can be discharged with oral therapy to complete a 7 to 10 day course [50–52].

If the surgeon classifies the type of appendicitis as complex, antibiotic prophylaxis should be continued after surgery. This aims to prevent infectious complications, including recurrent intra-abdominal infections. The available guidelines recommend to extend prophylaxis for 3–7 postoperative days [34, 60]. Five days of antibiotics, switched from an intravenous to oral route as early as 48 h after surgery, is common use in many centers. Another strategy, which is gaining ground, consists of 3 days of intravenous antibiotics only. Intravenous regimens most used are cefuroxime or ceftriaxone in combination with metronidazole [9, 58].

7. Postoperative complications

Up to 35% of patients who undergo appendectomy for complicated appendicitis are reported to have post operative complications such as surgical site infections, ileus and bowel obstructions. Some 25–30% of all patients with appendicitis have a complex appendicitis, which is associated with increased risk of postoperative infectious complications. Rogers et al. published a call for a standardized definition of perforated appendicitis. In this study, the postoperative abscess rate after surgery for perforated appendicitis (20.9%) was significantly higher than that published for perforated appendicitis (7.6%), which was lower than published in the 18 most recently published studies (14.4%). Rogers et al. reported that this marked variation in the postoperative abscess rate was due to the lack of a clear definition of perforated appendicitis [61]. Complicated appendicitis has been associated with a significant risk of postoperative septic complications, including wound infections and intra-abdominal abscess formation. Wound dehiscence and fecal fistula are rare but difficult complications of the disease following surgery. Most of the complicated cases require some resuscitation and stabilization with intravenous fluids, and combination of antibiotics before they proceed to surgery. A patient with an appendicular mass is usually treated with antibiotics and observed for development of complications. Of concern is the high complication rate, about 40% of the patients had complicated appendicitis [62]. Complications include wound infection, post op ileus, intra abdominal abscess formation, wound dehiscence, post op intestinal obstruction and rarely enterocutaneous fistula. Surgical site infection (SSI) is one of the commonest postoperative complication seen after appendicectomy, especially for a complicated appendicitis. Surgical-site infection rate was significantly lower in the laparoscopic than in the open group (1.6% vs. 3.2% respectively). The study by Kim et al., showed that untreated acute appendicitis frequently progresses to perforated appendicitis with an increased risk of complications. 23 The time of presentation to the hospital from onset of pain also is a factor to be considered with respect to complications. The more the delay, the higher the incidence of complications. Despite new and better antibiotics, advances in imaging and supportive care, a large number of patients with acute appendicitis develop serious complications and have morbid and prolonged recoveries. Patients with perforated appendicitis often develop an ileus postoperatively regardless of the surgical approach (open versus laparoscopic).

Immediate surgery in patients with long duration of symptoms and phlegmon or abscess formation has been associated with increased morbidity, due to dense adhensions and inflammation. Complications such as postoperative abscess or enterocutaneous fistula may ensue, requiring an ileocolectomy or cecectomy. A 2010 meta-analysis showed that initial nonoperative management of perforated appendicitis with abscess or phlegmon is associated with fewer complications and similar hospitalization and duration of antibiotic therapy in comparison with immediate surgery [50–52]. It is worth to mention that it has been reported that elderly patients with surgical treatment of complicated appendicitis face increases postoperative complications and longer hospitalization as well as lower rates of successful laparoscopic appendicectomy [26].

8. Conclusions

The distinction between complicated and uncomplicated appendicitis and between regional and diffuse peritonitis is the key to the management of appendicitis (ambulatory surgery, need for postoperative antibiotic therapy, duration of antibiotic therapy and information to the patient about the risk of postoperative complications). Complicated appendicitis with gangrene, perforation and abscess form a considerable proportion of all cases of appendicitis. Simple appendicitis has minimal morbidity, whereas complicated cases are associated with postoperative complications. Delay in presentation due to any reason is one of the factors associated with complications. Majority of delayed presentation is seen in children. Most of the cases occur in less than 40 years of age. A combination of history, examination, laboratory tests, and radiological investigations are preferable for the diagnosis. Although diagnosis is clinical, high leukocyte count correlates with complications. Ultrasound is still the investigation of choice for early diagnosis, though CT scan is diagnostic in doubtful cases. Early surgical intervention is the definitive treatment after initial resuscitation. Post operative antibiotics are necessary to avoid infectious complications. Wound infection and paralytic ileus are the common complications following surgery. Overall morbidity is considerable, but mortality is less than 1% and the general overall outcome is good with early intervention.

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Chapter 7

Acute Appendicitis: After Correct Diagnosis Conservative Treatment or Surgery?

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Abstract

Acute appendicitis is the most common surgical disease presented in ED. Ongoing evidence in the literature, in the last 20 years, shows a lot of benefits in favor of conservative treatment. Despite that conservative treatment does not gain the correct position at the daily practice up to day. A large number of parameters related to acute appendicitis, present diversity in their appearance, so the final estimation of the disease may by unclear and the decision for treatment may be incorrect. We analyze these parameters, aiming to clarify their role in correct diagnosis and decision making on appropriate treatment. In the present study a review of the literature is performed, regarding the etiology, pathology, clinical presentation, laboratory, and imaging data of acute appendicitis. The collection and correct estimation of these parameters, is the key for the correct diagnosis of acute appendicitis. Complicated or uncomplicated cases should be diagnosed preoperatively. The next step is the appropriate treatment, conservative or by surgery. At the present time, excluding generalized peritonitis and sepsis, the majority of patients with uncomplicated acute appendicitis and selected complicated cases can by treated successfully by conservative treatment. The majority of patients do not benefit from appendectomy.

Keywords: acute appendicitis, conservative treatment, decision making, laboratory, radiology, peritonitis, appendectomy, complicated, uncomplicated

1. Introduction

According to the literature of the last 20 yrs., the majority of patients with acute appendicitis should be treated conservatively and not by surgery, as they do not benefit from appendectomy and the operation is considered unnecessary. Unfortunately, worldwide surgical treatment of acute appendicitis remain the gold standard treatment of choice; in a recent multi-centric study in 2018 [1], based in a large number of patients with acute appendicitis, more than 95% of patients were treated by surgery, while conservative treatment underwent less than 5% of the patients. Taking into account the recent literature, the percentages for correct treatment, should be: 80–95% conservative treatment and 5–15% surgical treatment.

At the present study we review and analyze the role of many parameters, influencing the clinical presentation of the patient, the correct diagnosis and decision making for the proper treatment. The role of etiology, pathology and anatomy of acute appendicitis is analyzed. In addition the role of predictive markers/factors, inflammatory markers and radiological data, linked with diagnosis-evolution and severity of acute appendicitis is discussed. Emphasis is given in clinical presentation of the patient and the decision making for conservative or surgical treatment.

2. What's the etiology and pathology of acute appendicitis?

At the moment the appendicular inflammation, is quiet obscure and multifactorial. Carr et al. in a review article [2], describes and analyses several etiologies of acute appendicitis; infection, trauma, ischemia, diet factors, genetic factors, foreign bodies, hygiene and type I hypersensitivity may lead to acute appendicitis. The corresponding pathology reports containing a large spectrum of minor or major changes in mucosa, sub-mucosa, appendicular wall and peri-appendicular area, defining the acute appendicitis as catarrhal, suppurate (phlegmonous), gangrenous (necrotizing) or with signs of peri-appendicitis. Theoretical conceptions about the role of fecolith or lymphoid hyperplasia, creating luminal obstruction, today are under-estimating, as there are severe controversies in medical reports; in pathology reports rarely is found lymphoid hyperplasia with luminal obstruction, on the other hand the percentage of fecoliths in acute appendicitis (7–15%), is lower than in autopsies or in general population, studied with modern imaging studies, performed for other medical reasons (up to 30%). So their implication to inflammatory process is unclear with minor importance. Hence the question: what's the real etiologic factor of acute appendicitis? And what's really happens in appendicular wall? This poses some confusion about the conception of surgeon regarding the treatment of acute appendicitis; conservative or by surgery? In this heading, despite the obscure etiology, there are two key points; a) we must exclude secondary appendicitis, due to tumors of the cecum, appendix or peri-appendicular area. As acute appendicitis is a disease of the middle age (3rd and 4th decade of the life), we must be careful, mostly in aged patients (>50 years, or > 65 yrs. old) with acute appendicitis, although this group of patients represent a small percentage (7–15%) of the patients presented [3]. If conservative treatment is decided, after the acute phase, a colonoscopy and CT scan of the lower abdomen must be performed. b) Inflammatory process of the appendix starts initially at the level of mucosa and submucosa, invaded by neutrophils and sometimes by eosinophils. Later, ulcers may appear [2] and the appendicular wall may be invaded by anaerobes, gram negatives and other microbial agents. This evolution explains the use of antibiotics for the regression of inflammation, if conservative treatment is decided. A multi-centric study (APPAC trial), provide level I evidence data, that antibiotic treatment for uncomplicated acute appendicitis is effective and reduce the rate of appendectomies by 75–85% [4]. Following the natural history of acute appendicitis, a self-regression of the inflammation is feasible at 20% of patients [5]. Having in mind that at the beginning of appendicitis the inflammation involves mucosa and sub-mucosa, one should think the use of anti-inflammatory drugs. At the moment, worldwide, there are not reports for the use of such drugs as a part of conservative treatment. The author, in selected patients with acute uncomplicated appendicitis, used a combination of paracetamol and lornoxicam (an analgesic scheme, often used to treat postoperative pain), as the main treatment in a study with more than 100 patients with uncomplicated acute appendicitis [6], with early onset and duration of symptoms. It seems that this kind of treatment combined with antibiotics, offers promptly a clinical and laboratory regression of acute appendicitis. Non-steroidal anti-inflammatory drugs may play an important role in conservative treatment, as such effectiveness is observed in other inflammatory intra-abdominal inflammations; e.g. in acute cholechystitis, (chemical inflammation, without microbial involvement at least at the start of inflammatory process). This is a new field of research, although some parameters must be determined: the kind and time (days) of anti-inflammatory therapy, the effectiveness in cases with early onset of symptoms in acute appendicitis, and their use in purulent appendicitis in combination with antibiotics.

3. What's the role of anatomy of appendix in clinical presentation of acute appendicitis?

RLQ pain and rebound tenderness- aka the classic symptoms of acute appendicitis- accounts at about 40% of patients. In a review study [7], a high percentage of variable position and other anatomic characteristics of the appendix, as the length or orientation, may confuse clinicians. Such cases should be studied by modern imaging studies. One should keep in mind that the position of the appendix is extremely variable; De Souza et al., in a retrospective study of 377 cases [8], describes the most common position of appendix during surgery, as follows: retro-cecal location at 43.5%, sub-cecal at 24.5%, post-ileal at 14.3%, pelvic at 9.3%, para-cecal at 5.8%, pre-ileal at 2.4% and other at 0.27%.

4. Is the diagnosis of acute appendicitis easy?

No. Abdominal pain in the right iliac fossa, do not always correspond to acute appendicitis. Negative appendectomies in bibliography vary from 10 to 45% and especially in females. The percentage of misdiagnosed cases is 10%. Using imaging studies; the percentage of negative appendectomies is still at 10–12% [9]. Correct diagnosis is the most difficult step in evaluation of acute appendicitis; what really happens in the intra-abdominal cavity? By meticulous estimation of clinical and laboratory data and necessary imaging data, this parameter may be evaluated quiet good at the present time. Various scoring systems increase the diagnostic accuracy. The older is a clinical one described by Alvarado since 1986. This score may predict acute appendicitis [10], being a useful diagnostic aid, especially for younger colleagues [11]. The AIR score, incorporates CRP as a variable in the score and is more accurate at predicting appendicitis than Alvarado score in those deemed high risk [12]. At the present time, newer scoring systems are used, combining clinical and imaging features, and they also have an important role to distinguish uncomplicated from complicated cases of acute appendicitis [13]. Score systems can aid in selection of patients for surgical or non-surgical management. Various markers are used in scoring systems using parameters from physical, laboratory and imaging studies; age, body temperature, the duration and time of onset of symptoms, white blood cell count (WBC), CRP level, presence of peri-appendicular fluid, extra-luminal free air and the presence or not of a appendicolith in U/S or CT.

The majority of studies reveal a percentage of complicated appendicitis at 5% and uncomplicated cases at 95% [13]. Other reports present a higher percentage of complicated cases up to 20–25%. Trying to select patients for conservative treatment, may be difficult preoperatively. The best categorization may be done after surgery, combining surgical findings during surgery; appendix status, the effect of inflammation in peri-appendicular areas and peritoneum, and the final pathology report. Even thought, there is heterogeneity in terms used, to describe the type of acute appendicitis. The most often used terms are; simple appendicitis, uncomplicated acute appendicitis, catarrhal appendicitis, purulent appendicitis, complicated acute appendicitis with abscess or phlegmon, dehiscence or rupture of appendicular wall, gangrenous appendicitis, local or diffuse peritonitis, and fecal peritonitis. Laparoscopy offers a correct grading of acute appendicitis [14]. Emphasis is given in complicated cases (grade 3–5) but they represent a small percentage in the total number of patients, with acute appendicitis. Its position for uncomplicated cases (grade 1, 2) is not well determined. Pathology changes and clinical data in ICD-10 system classification, determine 8 types or subtypes of acute appendicitis;

ICD-10: K35 - acute appendicitis.
ICD-10: K35.2 - acute appendicitis with generalized peritonitis.
ICD-10: K35.3 - acute appendicitis with localized peritonitis.
ICD-10: K35.8 - other and unspecified acute appendicitis.
ICD-10: K35.80 - unspecified acute appendicitis.
ICD-10: K35.89 - other acute appendicitis.
ICD-10: K36 Other appendicitis.
ICD-10: K37 Unspecified appendicitis.

5. Are there predictive markers/factors, for the diagnosis, evolution and postoperative complications influencing the course of acute appendicitis?

The history of the disease, clinical examination, WBC, CRP, U/S or CT findings contribute to diagnosis [15] and predict the severity and evolution of acute appendicitis. Postoperative complications are related to the pathology, the contribution of bacteria in inflammation and the type of operation. Early diagnosis in the first 48 h, may be important followed be early management of the disease, and probable for more conservative approach, as antibiotic treatment is a safe and first line therapy for acute appendicitis, with excellent results in uncomplicated cases (patients without diffuse peritonitis), reducing the unnecessary appendectomies [16]. The non-surgical management of uncomplicated appendicitis by the use of antibiotics, predominates as treatment option as it's effective and decreases morbidity [17]. Patient delay for clinical examination and diagnosis is the key factor linked with an increased incidence of complicated acute appendicitis [18]. Today, the use of radiological interventional techniques in combination with antibiotics, extent the spectrum of conservative treatment in many complicated cases of acute appendicitis, as there is possibility for successful treatment-drain of the intra-abdominal abscesses and phlegmon [19], reducing complications compared with surgical treatment [20]. Surgery in such complicated cases is not easy and may lead in right hemi-colectomy due to severe intra-abdominal inflammation during surgery. We consider this effect a catastrophic result of surgery for a benign inflammatory process, in the absence of a local tumor in appendicular and peri-appendicular area.

6. Where should be given attention during clinical examination and estimation of the patient with acute appendicitis?

a. The age and sex of the patient; all reports, mention a disease of the middle age and the majority of patients are between 29 and 40 years old, although the age rage varies from the infantile to older ages. In younger ages exclusion or the presence of septic variables is important, as option treatment must be decided as soon as possible. In older ages, >50 years or 65 yrs. old, the possibility for complicated cases and the presence of an appendicular or peri-appendicular tumor is higher than in the middle age. Elderly patients present a higher mortality, morbidity, higher perforation rate, higher postoperative complication rate, lower diagnostic accuracy and longer delay from symptoms onset and admission [21], the female sex presents a more difficult diagnosis, mainly in reproductive age. Gynecological conditions and acute appendicitis may be studied in emergency by U/S combined with trans-vaginal ultrasound [22], increasing the diagnostic accuracy for acute appendicitis.

b. The past history (start and duration of symptoms) may be false; the patient many times refers a short period of time with symptoms. Acute appendicitis may have atypical clinical presentation (up 30% of the patients), the existence of atypical location of the appendix, and the presence of the disease in advanced ages creates a vague past history, leading in a wrong option treatment.

c. Analyze the features of the pain; complete clinical examination of the abdomen, with emphasis in palpation of the abdomen. We can diagnose the local signs of inflammation or sings of generalized peritonitis. Deep pain, in deep palpation of the right iliac fossa (visceral pain) reveals the local inflammation. Irritation of the peritoneum is expired by rebound (somatic pain). Colic pain may reveal an appendicular fecolith or intestinal obstruction due to severe inflammation-periappendicular inflammatory mass or tumor. Colic pain coexists more times with a permanent local-visceral pain. Sometimes acute appendicitis is manifested with reflex pain in the right hypochondrium, peri-umbilical, epigastria area or left iliac fossa, with no or attenuated local signs in the right lower quadrat. Reflex pain disappear in a short period of time of some hours and finally appear and predominate local signs of visceral pain in the right lower quadrat. We consider that clinical examination of the abdomen is the optimal method for diagnosis and estimation of severity in patients with acute appendicitis, as it's a fast, easy and may be repeated at times. Surgeon's opinion for acute appendicitis, in combination with laboratory and imaging data yield the best outcomes in patients, for the correct diagnosis in acute appendicitis [23].

7. What's the role of inflammatory markers in diagnosis and grading of acute appendicitis?

There are many inflammatory markers that can be used. Increased levels reflect the severity of acute appendicitis. Very high levels may reveal more complicated cases or sepsis [24]. WBC and neutrophil ratio, CRP, procalcitonine and SER are the most often used markers. We recommend the use of WBC and CRP. They are available in most laboratories and the results are taken in a short time. The use of numerous or novel markers is not recommended as they do not improve the diagnostic ability for acute appendicitis [25].

8. What's the role of imaging data in acute appendicitis?

There are three radiologic examinations available; U/S, CT and MRI [26]. U/S dispose a high diagnostic accuracy for acute appendicitis >90% but a high negative predictive value [27] with limited sensitivity, as the no visualization of appendix during U/S is very often observed. If inconclusive data are reported, and clinic-laboratory data support the presence of acute appendicitis, further study with CT (when there is no pregnancy) or MRI is recommended [28]. There are five morphological imaging criteria of appendicitis; a. enlargement (diameter) of the appendix>6 mm, b. thickness of the appendicular wall>2 mm, c. Inflammatory compression of the peri-appendicular adipose tissue, d) abscess formation in the right lower abdomen, e) calcified appendicolith. The three first criteria reveal uncomplicated acute appendicitis. A contrast-enhanced CT is an excellent tool for complicated cases and visualization of appendicular wall dehiscence-rupture.

9. Are there special categories of patients with acute appendicitis influencing option treatment?

a. Pregnancy: Acute appendicitis in pregnancy is a complex situation, and collaboration between obstetrics and surgeons offer the best outcomes for mother and fetus [29]. Severe perforated cases of appendicitis and negative appendectomies may lead to premature delivery [30]. There is need for accurate diagnosis and correct option treatment. Most cases are observed in the second trimester of the pregnancy. CT is contraindicated do to pregnancy. Diagnostic imaging data are obtained by U/S and MRI. MRI yields a high diagnostic rate and accuracy in pregnant and guide further option treatment [31].

b. Gangrene of the appendix (or necrotizing appendicitis); it's a special type of appendicitis. There is need for accurate diagnosis and surgery due to generalized peritonitis and sepsis. Recently appear reports for conservative treatment of level evidence II [32]. It's more often observed in pediatric population and represents a percentage of 12–13% in pathology reports. In adults is a rarer phenomenon with lower percentage. The incidence is not well determined as in pathology reports different terms are used; gangrenous appendicitis, complicated appendicitis, perforated appendicitis, or necrotizing appendicitis and the percentage of this group with complicated cases is 10–25% in different reports [33].

c. Immunosuppressed patients; Surgery is the rule to avoid sepsis and deaths.

10. How and when decision making, is taken for patients with acute appendicitis?

After the clinical examination, collection of inflammatory markers and imaging data. This waiting time for few hours, assure a correct diagnosis, the option treatment and do not influence the pathology report if appendectomy will be decided. As more variables are positive for acute appendicitis, the diagnostic accuracy for acute appendicitis is high. Cases should be categorized for the severity. Uncomplicated cases and selected complicated cases of acute appendicitis should be treated conservatively with benefits for patients. Diffuse peritonitis and the evidence of perforated appendix represent surgical cases.

11. What should contain the conservative management of acute appendicitis?

Admission in the hospital, and active observation according to the needs of the patient. Collection and estimation of inflammatory markers and imaging data. Soft feeding is permitted if there is not nausea, intestinal obstruction or planning for operation. Correction of fluid imbalances due to inflammation. The use of antibiotics is mandatory as is the main therapy in conservative treatment. Antibiotic treatment is performed, according to the instructions for the treatment of intra-abdominal infections [34] and a short scheme of 4 days may be effective, at least in uncomplicated cases. After conservative treatment, an interval time for further intervention tend to be abandoned [35] even more for complicated cases with abscess or phlegmon.

12. Recurrence after conservative treatment

The re-appearance of acute appendicitis after conservative treatment is not easy to be calculated. Most reports mention a percentage of 7–10% with a long period of follow-up [36]. There is a lack of information and heterogeneity about the kind-results of conservative treatment (during the first episode of acute appendicitis). Usually, surgery is followed after a new episode. The pathology report should describe changes of acute appendicitis and not chronic inflammatory changes in mucosa or sub-mucosa, as is the case after appendectomy due to recurrent episodes.

13. Conclusions

Conservative treatment of patients with acute appendicitis is not very popular in surgical community, despite ongoing literature data supporting its role in the majority of patients with uncomplicated and selected cases of complicated acute appendicitis. Uncomplicated cases accounts for the 80–90% of patients with acute appendicitis. At every day's practice, more than 90% of uncomplicated cases undergoing appendectomy and less than 10% are treated conservatively. Conservative treatment should be offered, as an initial approach, to every patient with acute appendicitis. Surgeons should understand that the majority of patients may not need and they do not benefit from appendectomy.

Conflict of interests

The authors declare no conflict of interest.

Abbreviations

RLQ	right lower quadrat
AIR	appendicitis inflammatory response
CRP	C-reactive protein
WBC	white blood cell count
U/S	ultrasounds
CT	computerized tomography
MRI	magnetic resonance imaging
SER	sedimentation erythrocyte rate
ED	emergency department

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Edited by Angelo Guttadauro

Acute appendicitis is a common pediatric abdominal emergency, although it can occur in any age group. The debated role of imaging in diagnosis and diagnostic delays make diagnosis particularly challenging in the elderly. Given the heterogeneity of the population that may be affected by this disease, it is not possible to stipulate a universally valid diagnostic process. As such, an individualized approach guided by age, sex, comorbidities, and clinical manifestations is always necessary. This book reviews the current state of the art in acute appendicitis to help surgeons administer proper and timely treatment.

Published in London, UK

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ISBN 978-1-83968-857-7