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Case Study

Management of acute appendicitis in the COVID era: a case study

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Key Learning Points

Mr Bruce George

This paper has highlighted the continuing challenge of optimum management of acute appendicitis. The covid-19 pandemic has forced surgeons to re-evaluate the "risk-benefit" equation when faced with a patient with suspected acute appendicitis.

Key learning points from this paper include:

- Patients with acute uncomplicated appendicitis without a faecolith may be reasonably managed non-surgically with antibiotics.
- Conversely patients with complicated appendicitis or with a faecolith are better treated by appendicectomy. Delayed appendicectomy is associated with increased morbidity.
- A non-surgical approach to appendicitis is crucially dependent on an accurate diagnosis usually be CT scanning.
- Non-surgical treatment of acute appendicitis has an approximately 20% of recurrence within 1 year.
- In situations where surgery is high risk, such as during the covid-19 pandemic or during non-covid times such as pregnancy or major medical co-morbidity, a detailed risk-benefit discussion is required to decide between medical and surgical treatments.

Abstract

Acute appendicitis is a common surgical presentation usually managed with laparoscopic appendicectomy. There has been long-standing debate as to whether conservative management of acute appendicitis could provide a superior alternative to surgical management. COVID-19 infection emerged in December 2019 and was labelled as a pandemic by the World Health Organisation in March 2020. Re-structuring as a result of the pandemic forced rapid changes in guidelines from recommending surgical management to advocating for medical management in all cases of uncomplicated acute appendicitis. The patient; a 43 year-old male, had a delayed presentation of complicated acute appendicitis as a result of anxiety about being in a clinical environment during the pandemic. This was successfully managed with surgery and a 4-day inpatient stay. This case report evaluates the best approach for the treatment of acute appendicitis, evaluates whether a change in management was appropriate in the case of a pandemic and details how to avoid more cases of delayed and complex presentation as a result of COVID-19.

Introduction

Acute appendicitis is the most common general surgical emergency[1]. There is some debate surrounding the best management for acute appendicitis, with some groups doubting the superiority of antibiotic management[2], while other groups and recent guidelines advocate for conservative care[3,4] based on large cohort and randomized controlled trials that have suggested short-term outcomes equivalent to surgery[5,6]. Current guidelines in the UK recommend emergency laparoscopic appendicectomy if acute appendicitis is suspected[7].

COVID-19 infection emerged from Wuhan, China in December 2019 and has rapidly spread around the world. COVID-19 has caused major disruption to health services globally. Surgery is among the many services impacted by restructuring to provide surge capacity. In the UK all elective surgery was suspended for at least three months from the 15th April 2020[8]. Additionally, there was a push to manage surgical emergencies, such as appendicitis, non-operatively due to safety concerns regarding general anaesthesia in patients with occult COVID-19 infection and the risks of aerosol generating procedures (especially intubation, extubation and laparoscopy[9]) to staff[10]. Many groups have hypothesised that the disruption and delay to surgical services due to this pandemic is likely to have unprecedented effects on outcomes[11]. There is evidence that this pandemic has caused delay of presentations in the case of appendicitis[12] and that these delays have resulted in worse post-operative outcomes after laparoscopic appendicectomy[13]. Delay due to an overwhelmed system

is compounded with the widespread publicity of the 'Stay at home' policy and the population's fear of the current hospital environment meaning yet further delays to presentation compared to a routine healthcare scenario.

Here we will consider a patient admitted with a late presentation of complicated appendicitis. In this case anxiety due to the COVID-19 pandemic led the patient to delay their presentation to hospital, thus potentially leading to a more complicated condition and a longer overall hospital stay.

Case History

A 43-year-old gentleman self-presented to A&E with 5-day history of fever, anorexia and lower abdominal pain radiating to the right iliac fossa (RIF). He is otherwise fit and well with history of uveitis for which he takes prednisolone eye drops. He has no known allergies, drinks 14 units per week, and stopped smoking one year ago before which he smoked 5-10 cigarettes per day. Mr C lives at home with his wife and works as a computer system administrator.

On examination Mr C was ambulatory and comfortable with a BMI of 32.14. His observations were stable with no fever at the time of examination. His abdomen was tender in the RIF, left upper quadrant (LUQ), right upper quadrant (RUQ), with voluntary guarding but no peritonism or rigidity. On admission, his bloods showed raised white cell count (WCC) (13) and C-reactive protein (CRP) (314) but were otherwise unremarkable. A Computed Tomography (CT) of his abdomen and pelvis showed acute appendicitis complicated by perforation, so he was admitted in preparation for an emergency laparoscopic appendicectomy.

The operative findings confirmed a complicated appendicitis with a phlegmon, abscess in RIF (with localised frank pus), thickened inflamed mesentery, a very inflamed, perforated appendix with an unhealthy appearance to the base and some reactionary fluid in the pelvis. There was a decision to leave a slightly longer stump due to the unhealthy base and perform appendicectomy with 2 endoloops on the stump and 1 endoloop on the mesoappendix. The removal of the appendix was followed by a copious lavage with 3 litres of saline. A RIF drain was left in situ, anchored and wounds closed.

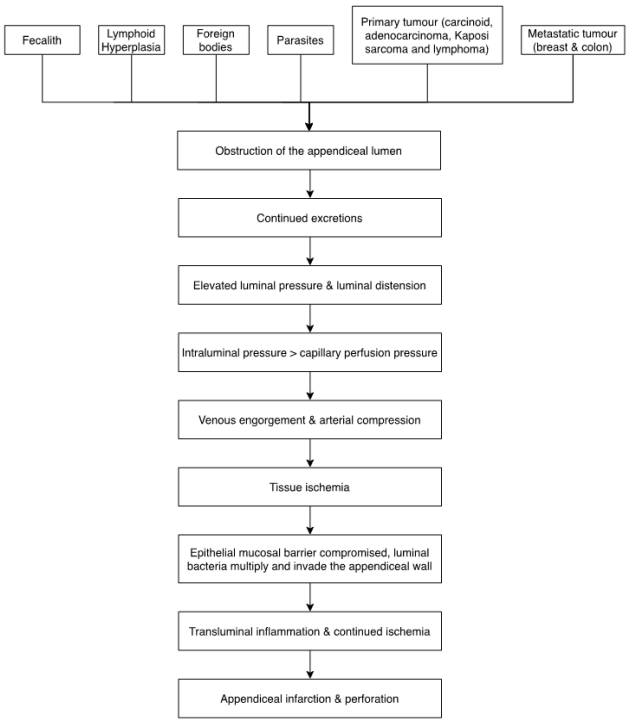

Figure 1: Pathophysiology of acute appendicitis. Adapted from Birnbaum et al, 2000[15].

Post operatively the patient was given a 5-day course of co-amoxiclav, starting with 48 hours intravenously and then converted to oral. The patient had moderate post-operative pain managed with morphine for the first day following surgery and then codeine and paracetamol for the subsequent 2 days. On the third post-operative day his bloods had improved with WCC of 10 and CRP of 176 and the patient was discharged with oral antibiotics and advice to mobilise at home avoiding over-exertion.

Aetiology & Standard Management of Appendicitis

The exact aetiology of appendicitis is poorly understood, though in most cases it is believed to be caused by obstruction of the lumen[14] as a result of a variety of different causes. The sequence of pathological progression[15] can be seen in Figure 1. However, it is important to note that some studies report that uncomplicated and complicated appendicitis are differing entities and that many cases of acute appendicitis will resolve spontaneously and not follow this entire progression[16]. Uncomplicated appendicitis could perhaps be likened to other uncomplicated intraabdominal inflammations such as uncomplicated diverticulitis, in which non-operative management with antibiotics are a mainstay of treatment[17]. However, it must be noted that appendicectomy is a relatively safe procedure, with lower complication rates than emergency colorectal surgery, for example, the risk of stump leakage is not equivalent to the risk of anastamotic leakage. Perhaps this explains why the antibiotic treatment of appendicitis remains a poorly explored and controversial topic[16].

Since the definition of the surgical appendicectomy by McBurney, surgical removal of the appendix has been the treatment of choice for acute appendicitis[18] due to its good outcomes[15,19]. Thus, before the current pandemic, surgical intervention for all cases of acute appendicitis was the gold standard. Figure 2 shows the pre-COVID treatment algorithm for appendicitis. Whilst surgical appendicectomy is a successful treatment modality, complications are inherent to operative treatment. The most common complications are wound infection, ileus caused by intraabdominal adhesions and intraabdominal abscess formation. These vary in frequency between open and laparoscopic appendicectomy[20,21]. The overall complication rates for open and laparoscopic appendicectomy are 11.1% and 8.7% respectively, with an overall mortality rate of less than 0.5%[22].

Conservative vs Surgical treatment of appendicitis

Following the declaration of the new coronavirus disease (COVID-19) as a pandemic by the World Health Organisation on March 11 2020[23], the Royal College of Surgeons of England published their first 'General Surgery Guidance on COVID-19' in which they advocated for a conservative approach to uncomplicated appendicitis[24]. Figure 3 illustrates the changes to the existing treatment algorithm based on this new guidance. As a direct result of this change in guidelines, the normal practice in the UK of early laparoscopic appendicectomy for adult acute appendicitis immediately changed to over half of patients being conservatively managed and of those having an operation, the majority having an open procedure[25]. In a study conducted from January to March 2020, 54% of

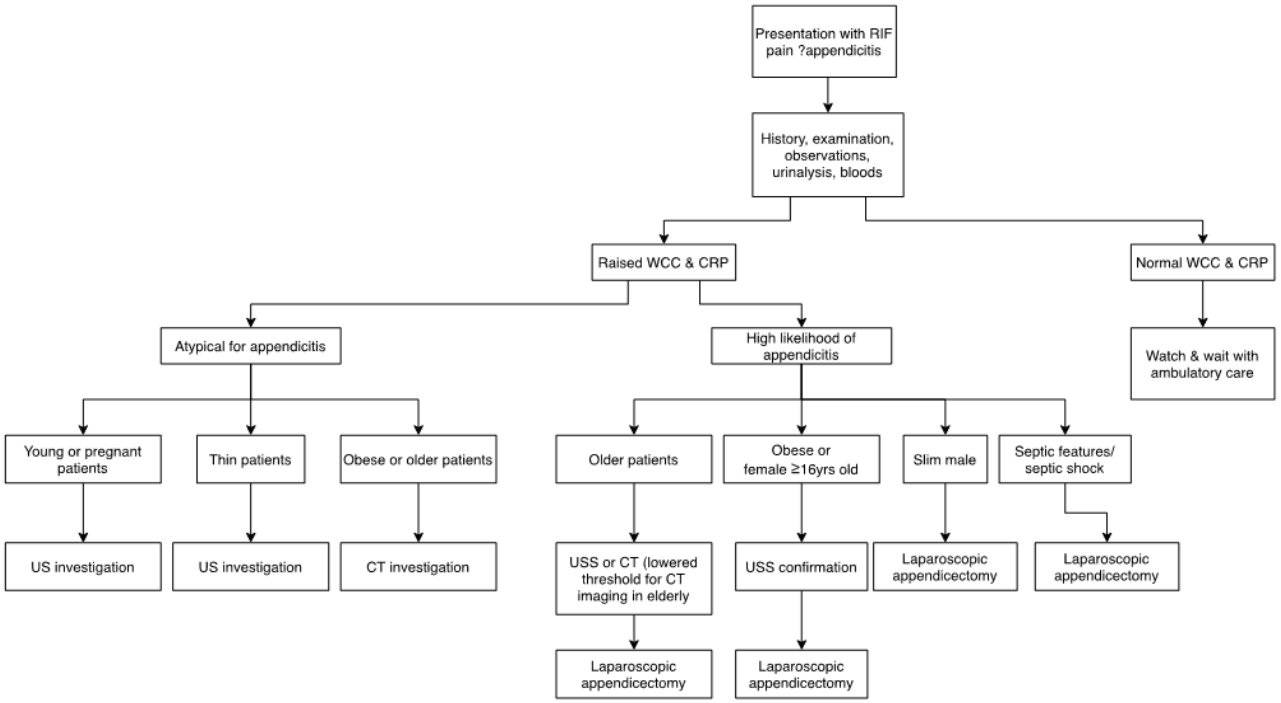

Figure 2: Pre-COVID-19 treatment algorithm for acute appendicitis. Synthesised from RCS general surgery commissioning guide[7].

patients with acute appendicitis were initially managed conservatively. By the third week of lockdown conservative management peaked at 64%[25]. The evidence for the efficacy of conservative management of appendicitis is debateable and often of low to moderate quality[2] due to the difficulty of performing a clinical trial with high methodological quality for this subject. Table 1 details outcomes from major clinical trials comparing conservative with surgical management of appendicitis.

These trials have a number of inherent limitations, some of which have been outlined in Table 1. Crucially, the defined primary endpoints of the individual trials varied, for example including treatment efficacy (with varying definitions), recurrence rates or complication rates, making comparison of their outcomes difficult. Further, conclusions are made difficult by the high crossover rates from the antibiotic to the surgery groups, this results in the presence of an unreported bias in complication rates in the surgery group[26]. Additionally, more men than women were included in the studies overall. This is important because the differential diagnosis of right lower quadrant pain in women is more diverse than in men because of gynaecological causes. This may mean that in a female cohort, negative appendicectomy rates and the rate of antibiotic treatable diseases are higher[2]. Furthermore, there was little consistency in the diagnostic methods used in the different studies, perhaps a standard of randomisation after appendicitis has been proven using USS or CT could form more clear inclusion and diagnostic criteria. The fact that it is difficult to compare complications in the surgical vs conservative group was not addressed. This inherent difficulty is due to the fact that not all complications can occur in both groups. For example, wound infections can only occur in post-operative patients. A number of these studies assumed some advantage of conservative treatment over surgery and thus had non-inferiority designs. This in itself may not be the case, so perhaps an intention-to-treat design may be better suited in this instance[26]. Although, as previously stated, this has resulted in unreported bias in complications from the surgery group due to a high number of crossovers. Thus, the data all need to be analysed with these limitations in mind.

Although the use of antibiotics in these studies led to a supposed trend of decreased complications with no associated prolongation of hospital stay, there is compelling evidence that the use of antibiotics has disadvantages[17]. These include delayed appendicectomy in patients who fail to resolve on antibiotics. Delayed appendicectomy has been associated with higher complication rates and should be avoided if possible[27]. Of note, in opposition to this, a recent meta-analysis found that antibiotic treatment is in fact not associated with a higher incidence of complications than appendicectomy. In particular, secondary appendicectomy does not lead to more surgical complications[28]. Varadhan and colleagues found that there was a 20% chance of recurrence of appendicitis after conservative treatment within one year[26]. Of these recurrences, 20% presented with a perforated or gangrenous appendix, the question is what failure rate we find acceptable in 'normal' times and should this change in the context of protecting our patients and workforce during a pandemic? Further, with antibiotic therapy, for obvious reasons, there is no opportunity to perform histopathological examination of the appendix. This means that other extra-appendiceal pathologies and pathologies of the appendix itself may be missed, some examples of this include inflammatory (e.g. appendiceal diverticulitis, Crohn´s disease) and neoplastic changes. It is crucial not to miss neoplastic changes because they may require ongoing treatments. The most common neoplastic change that has been found to present as appendicitis, is a carcinoid tumour and these are found in about 1% of the appendicectomies for acute appendicitis. In the majority of cases its diagnosis is rarely expected prior to histological examination[29–31]. The long-term effects of widespread antibiotic treatment, such as drug resistance both in the individual patient and the population at large[32] are poorly considered in the literature. Finally, quality of life plays an important role when comparing two differential treatment

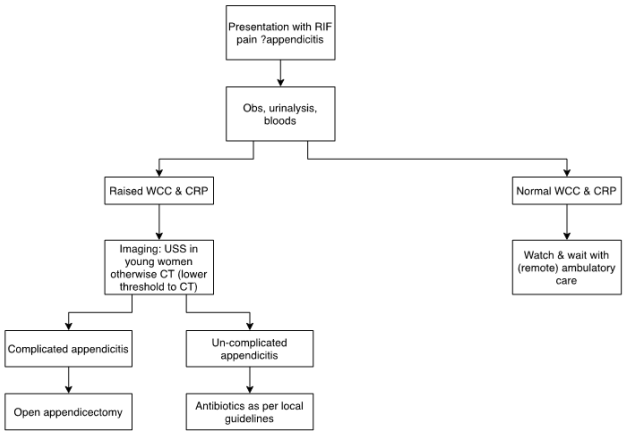

Figure 3: New acute appendicitis treatment algorithm.

approaches. This is especially relevant when choosing between a medical and surgical treatment. For many people, the process of surgery and associated anaesthesia, even when considering 'routine' operations, is considered stressful.

For such patients, surgery may have a potentially higher impact on quality of life than a drug therapy, even in the absence of surgical complications. Conversely, there may be other patients who rate their quality of life lower following conservative treatment due to the risk of recurrent appendicitis. There have been a number of studies showing that patient preferences on the choice of treatment for appendicitis differ in relation to socioeconomic factors and past medical history[33,34]. Listening to patient preference will certainly affect quality of life[35], however assessment of patient preferences and quality of life is rarely addressed in studies.

In light of the aforementioned disadvantages, without the context of a pandemic, it is clear that although antibiotics may be used as primary treatment for select patients with uncomplicated appendicitis, this therapeutic approach is unlikely to supersede appendicectomy.

Changes in the treatment modality related to the COVID-19 health crisis

The key consideration is whether the context of the COVID-19 pandemic shifts the balance enough to justify a change in management in spite of the conflicting and unclear evidence of its superior efficacy. In order to evaluate whether this is the case, we must address the reasons for limiting surgical care in the context of a pandemic. Firstly, it must be noted that appendicitis presents a unique pathology for two main reasons; the non-surgical alternative of medical management by antibiotic therapy alone has been evaluated to be safe in the literature[28] and further, due to the high prevalence within the population, any change to the standard treatment would have major implications and provide tangible differences in the surgical cohort within this pandemic context.

Indications for conservative in preference to surgical management in the context of the pandemic include; acute appendicitis with occult COVID-19 infection, consideration of surge capacity in hospitals and staff safety concerns. Research into surgery with occult COVID infection has reported high mortality rates even following minor procedures[38]. Of note, in our current knowledge, there are no arguments indicating that COVID-19 positive patients respond differently to antibiotic therapy[35]. Thus, avoidance of surgery in these patients is a viable option and is important not only because it reduces risk to the patient themselves, but also reduces the risk of exposing theatre staff, particularly in case of inadvertent release of pneumoperitoneum during laparoscopy[39]. Additionally, there was a lack of personal protective equipment (PPE) for surgical teams at the start of the pandemic which compounds the risk to staff[40]. A further consideration is the turn-around time for a COVID swab result. At the beginning of the pandemic a result would take between 24-72hrs, now we have a turn-around time of 1hour. This means that initially, all patients had to be treated as positive whereas now we can operate on patients with more confidence after a negative swab. In relation to changing management to avoid the saturation of hospitals in a crisis setting, it can be noted that the literature shows the main limitation of exclusively medical treatment is the risk of recurrent appendicitis, thus, this treatment option represents an alternative choice to reduce hospital overload in the short-term in this context of health crisis.

To allow medical treatment to be safely chosen, a number of factors must be addressed. Firstly; to which patients can non-surgical management be proposed? In the studies included, old age was not associated with worse outcomes following medical management[6]. Data concerning co-morbidities is limited due to the fact that a majority of patients with uncomplicated acute appendicitis are young and without associated severe disease. It is crucial for common sense to prevail before proposing non-surgical treatment to patients with high-risk features in their history (for example, patients who are immunosuppressed or patients with mechanical heart valves). Importantly, in one study 400 pregnant women treated medically for non-complicated appendicitis had higher risk of severe sepsis, septic shock and thromboembolic events than pregnant women who had undergone appendicectomy[41]. Thus, medical management should be carefully selected for those in early pregnancy with uncomplicated appendicitis, with close monitoring by obstetric and surgical teams, and discussion with the patient regarding options and risks of various management methods should occur. Finally, the only criteria on imaging studies that was statistically significantly associated with failure of medical treatment and progression to a more complicated form of appendicitis was the presence of endo-appendicular faecolith[6]. Thus, this finding should, whenever possible, lead to the preference of surgery.

Risk of failure of treatment, classed as either primary failure of treatment <24hrs (ranging from 5-20% of patients) or a longer-term recurrence (ranging from 60-84% of patients), has been noted in all the studies reviewed (Table 1). The patient should be clearly informed of this fact, additionally, adequate follow-up is essential to integrate this low but not negligible risk into the overall therapeutic management plan.

If appendicectomy has been chosen, there are some novel considerations that must be made in the context of this pandemic. CT scanning has been recommended for definitive diagnosis of acute appendicitis in order to more accurately exclude perforation or other pathology presenting with RIF pain[45]. Further, to minimise aerosol generation, open surgery has been recommended over laparoscopic surgery if surgery is absolutely required [40,42–45].

Conclusions

The COVID-19 pandemic has markedly altered the standard of surgical management of acute appendicitis in the UK, with conservative management being favoured for a number of reasons. Based on the data presented in

Study	Participants	Initial failure rate of antibiotics <24hrs	Failure rate of antibiotics at 1yr after initial success	Overall recurrence free success rate at 1 yr	Limitations
Eriksson, 1995	40	5%	35%	60%	- Failed to fully describe their methods of randomisation
Styrud, 2006	252	12%	14%	76%	- Female patients excluded - Primary end-point unclear - Unclear reporting of complication number - Under-powered RCT(36)
Hansson, 2009	260	9%	12%	78%	- 52.5% of patients in the antibiotic group crossed over to the surgery group - Unclear calculation of effectiveness(37) - Loss of patients to follow-up not addressed and makes results prone to bias - Poor randomisation technique based on birth date
Turhan, 2009	290	18%	10%	75%	- Performed US & CT only in the antibiotic treatment group after randomisation and didn't use as diagnostic standard
Malik, 2009	80	5%	10%	85%	- Article since retracted due to significant overlap with other published articles
Vons, 2011	239	12%	29%	63%	- Only oral abx used: patients with abdominal illness do not absorb abx as well as patients without abdominal illness however dosing was not adjusted accordingly.
Park 2014	119	8%	13%	84%	- Non-randomized protocol - Inconsistent imaging method used for diagnosis
Salminen, 2015	530	6%	23%	73%	- Was not able to show non-inferiority of abx relative to surgery
Allievi, 2017	462	20%	21%	63%	- Cross-over between groups - Long-term equivalence of surgical/medical groups after ~1yr - Non-standardized inclusion criteria & indications to imaging - Unclear definition of 'uncomplicated appendicitis'

Table 1: Outcomes from major clinical trials comparing conservative with surgical management of appendicitis.

this report, in the setting of the covid-19 pandemic, non-operative management of acute appendicitis appears to be an effective first-line treatment with a minority of patients requiring second-line surgical intervention. In the case of our patient, he might have benefitted from clearer advice from the medical community and Public Health officers about the detrimental effect of delaying medical attention. His case was managed surgically due to the complex presentation found on imaging early on in his admission, and this supports early imaging in the management of patients presenting with a possible appendicitis. The disruption due to COVID has certainly led to change in the clinical context of uncomplicated appendicitis and perhaps this will persist beyond this acute pandemic scenario, however, in order for this to happen safely, more research of a higher quality is required to fully understand the risks and benefits of this change in management.

Conflicts of interest
None.

Funding
None.

Consent
The patient has consented to the publication of this case study.

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