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Prospective Cohort Study

Acute appendicitis management during the COVID-19 pandemic: A prospective cohort study from a large UK centre

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ABSTRACT

Background: During the Covid-19 pandemic, non-operative management for acute appendicitis (AA) was implemented in the UK. The aim of this study was to determine the efficacy and outcomes of conservative versus surgical management of AA during the pandemic.
Materials & Methods: We conducted an observational study in a tertiary referral centre. Data was collected from all patients (≥16 years) with a diagnosis of AA between November 1, 2019 to March 10, 2020 (pre-COVID period) and March 10, 2020 to July 5, 2020 (COVID period).
Results: A total of 116 patients in the pre-COVID period were included versus 91 in the COVID period. 43.1% (n = 50) of patients pre-COVID were classified as ASA 2 compared to 26.4% (n = 24) during the COVID period (p-value = 0.042). 72.5% (n = 66) of the patients during the COVID period scored as high risk using the Alvarado score compared to 24.1% (n = 28) in the pre-COVID period (p-value<0.001). We observed a significant increase in radiological evaluation, 69.8% versus 87.5% of patients had a CT in the pre-COVID and COVID periods respectively (p-value = 0.008). 94.9% of patients were managed operatively in the pre-COVID period compared to 60.4% in the COVID period (p-value<0.001). We observed more open appendicectomies (37.3% versus 0.9%; p-value<0.001) during the COVID period compared to the pre-COVID period. More abscess formation and free fluid were found intraoperatively in the COVID period (p-value = 0.021 and 0.023 respectively). Re-attendance rate due to appendicitis-related issues was significantly higher in the COVID period (p = 0.027).
Conclusion: Radiological diagnosis of AA was more frequent during the COVID period. More conservative management for AA was employed during the COVID-19 pandemic, and for those managed operatively an open approach was preferred. Intra-operative findings were suggestive of delayed presentation during the COVID period without this affecting the length of hospital stay.

1. Introduction

Acute appendicitis (AA) is the most common general surgery emergency worldwide [1]. Decision making in patients with a clinical suspicion of appendicitis remains a prominent challenge [2–4]. A global debate exists regarding the use of antibiotics versus operative techniques to manage appendicitis and the future of appendicitis treatment [5]. At present UK institutes remain reluctant to change their traditional approach of index operative management of right iliac fossa (RIF) pain with exploratory laparoscopy, with or without appendicectomy in the absence of other differential diagnosis, with surgery as the gold standard for AA rather than conservative antibiotic therapy [5]. The antibiotic-first strategy has been found to be safe and effective in selected patients with uncomplicated acute appendicitis, however the risk of recurrence is estimated to be up to 39% after 5 years [6]. A 2019 meta-analysis including 20 studies (7 prospective RCTs, 8 prospective

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cohort studies, 4 retrospective cohort studies and 1 quasi-randomized study) investigated outcomes in non-operative management with antibiotics in appendicitis with a moderate quality of evidence when regarding complications and treatment efficacy [7]. Overall, antibiotic therapy achieved a significantly lower post-intervention complication rate including postoperative abscesses, surgical site infection, incisional hernias and other general operative complications at 5 years compared to index event surgery [7]. However, there was a lower complication-free treatment success rate and a non-significantly higher rate of complicated appendicitis with delayed surgery in patients receiving initial antibiotic therapy [7].

During the onset of the Covid-19 pandemic, a contingency care plan was made across the UK and non-operative management was employed for acute surgical conditions such as appendicitis as per expert guidance due to concerns of spreading the infection during aerosol generating procedures (AGP) [8]. Therefore, an antibiotic-first appendicitis pathway was accepted nationally in the UK for the first time presenting a unique period for investigation. This study undertook a retrospective review of cases of appendicitis presenting to a UK tertiary referral centre in the period prior to, and a prospective review during, the Covid-19 driven change in practice. Data analysis aimed not only to explore the outcomes of a change in appendicitis management, but also to reflect on lessons learned during this period which can be applied to future appendicitis pathways and patient care.

2. Materials and methods

2.1. Study design and population

This prospective observational cohort study was conducted in a single UK University tertiary referral centre and was registered locally as a clinical audit. Patients included in this study were adults (≥16 years) with a diagnosis of acute appendicitis made clinically and/or radiologically in our hospital. Patients presented sequentially to the emergency department, and subsequently were referred to the emergency surgical service for further management. The data collection periods were between November 1, 2019 and March 10, 2020 ('the pre-COVID period') and March 10, 2020 to July 5, 2020 ('COVID period'). The start of the COVID period was determined as the day of our hospital pandemic policy introduction, following the identification of the first SARS-CoV-2 positive patient at our site.

2.2. Definitions and data collection

Data were collected retrospectively for the pre-COVID period and prospectively during the COVID pandemic using the electronic patient record (HYPERSPACE® Epic 2014 Version IU1, Epic Systems Corporation, Verona, WI, USA). Data collected included patient demographics, radiology reports, timings of consultations, operative records, post-operative care, post-operative complications, re-operation rate, length of hospital stay (LOS), histology results, re-attendance to hospital and mortality within 90 days of the initial presentation. All patients participating in this study were followed-up for 90 days following their initial presentation, either in person or via telephone clinics.

Study participants were scored using the Alvarado score [9], Appendicitis inflammatory response (AIR) score [10], the Adult appendicitis score (AAS) [11], American Society of Anaesthesiologists (ASA) physical status classification [12] and Rockwood Clinical Frailty Scale [13] based on their initial presentation history and investigations, as previously described in the literature. Conservative management was determined as the use of antibiotics only (i.e. an intervention was not offered at initial consultation). Interventional radiology (IR) guided drain insertion refers to CT or ultrasound (US) guided insertion of an intra-abdominal drain. Time to theatre was calculated in hours from the admission time to the start of the operation. Operative time was calculated in minutes from skin incision to the end of skin closure. Time of day when the procedure was performed was determined by the start time of the operation, with those starting after 17:00 until the following day at 08:00 classified to have been performed out of hours.

Operative details were recorded based on the operating surgeon's documentation. Conversion from a laparoscopic to open approach was determined as additional incisions performed either in the right iliac fossa or midline laparotomy. The level of the surgeon was determined based on the years of practice post-qualification (Junior Trainee; Senior Trainee; Consultant). Critical care admission was determined if the patient was cared for in a Level 2 (high dependency unit) or a Level 3 care (intensive care unit) setting. Re-attendance referred to any patient re-presenting following their initial admission. This study has been reported in line with the STROCSS criteria [14].

2.3. Statistical analysis

Descriptive data were reported as mean [Standard deviation (SD) and range] or number/total (%) as appropriate. For some data, proportions were reported as the number of patients/total patients due to missing data in certain data collection points. When comparing nominal data, Chi-squared or Fisher's exact test was used. For continuous, not normally distributed data the Mann–Whitney *U* test was used. A p-value of <0.05 was regarded as the level of statistical significance, noted as * in the main text of this article. Data analysis was performed using JASP (version 0.13.1, University of Amsterdam, The Netherlands) and Prism (GraphPad, version 7.04, San Diego, CA, USA).

3. Results

3.1. Patient demographics

A total of 207 patients were identified as part of this study between the two periods. In the pre-COVID period there was a total of 116 patients, with 65 (56%) being female. A total of 91 patients were included in the COVID period, of which 44 (51.6%) were female (p-value = 0.326; Table 1). The mean age was 40.3 years (range 17–85) and 38.2 years (range 16–94) in the pre-COVID and COVID periods respectively (p-value = 0.221). The mean BMI was 27.4 kg/m^2 (range 17.2–44.1) in the pre-COVID and 27.3 kg/m^2 (range 18–57.7) in the COVID period. 69.8% of the pre-COVID cohort and 60.4% in the COVID cohort had no underlying co-morbidities (p-value = 0.185). Most participants in both groups were never smokers, 82.8% in pre-COVID and 74.7% in the COVID period (p-value 0.188). During the pre-COVID period 43.1% (n = 50) of patients were classified as ASA 2 compared to 26.4% (n = 24) during the COVID period (p-value = 0.042*; Table 1).

3.2. Appendicitis risk scoring

72.5% (n = 66) of the patients presenting during the COVID period were considered high risk for appendicitis with the Alvarado score, in comparison to 24.1% (n = 28) in the pre-COVID period (p-value<0.001*). Using the AIR score 9 (9.9%) patients in the COVID period and 19 (16.4%) patients in the pre-COVID period were considered high risk (p-value = 0.266). While using the AAS, 24 (26.4%) patients in the COVID and 23 (19.8%) in the pre-COVID period scored to the high risk category (p-value = 0.194; Table 1).

3.3. Imaging for appendicitis

In the pre-COVID period, 28 (24.1%) patients had an US as part of their investigations in comparison to 15 (16.5%) during the COVID period (p-value = 0.0227). In the pre-COVID period 24 out of 65 (39.6%) females had an US scan to exclude alternate pathology compared to 4 out of 51 (7.8%) male patients (p-value<0.001*). While in the COVID period, 9 out of 44 (20.5%) females had an US scan compared to 6 out of 47 (12.8%) males (p-value = 0.402). From the 116

Table 1
Patient demographics, investigations and initial management plan.

	Pre-COVID (n = 116)		COVID (n = 91)		
	Mean (±SD)	**Range**	**Mean (+SD)**	**Range**	**p-value**
Age (years)	40.3 (±15.7)	17–85	38.2 (±16.7)	16–94	0.221†
Body Mass Index (Kg/m^2)	27.4 (±4.9)	17.2–44.1	27.3 (±6.9)	18–57.7	0.261†
Self-reported duration of symptoms (hours)	47.2 (±45.6)	3–288	68.9 (±88.7)	5–506	0.238†
Length of hospital stay (days)	3.4 (±2.8)	1–15	5.1 (±8.3)	0–60	0.158†
Gender					0.326*
Male	51 (44.0%)		47 (48.4%)		
Female	65 (56%)		44 (51.6%)		
Comorbidities					
None	81 (69.8%)		55 (60.4%)		0.185*
Hypertension	8 (6.9%)		8 (8.8%)		0.613*
Diabetes Mellitus	6 (5.2%)		4 (4.4%)		0.999*
Ischaemic Heart Disease	4 (3.4%)		5 (5.5%)		0.510*
Airways disease	14 (12.1%)		10 (11%)		0.831*
Vascular disease	3 (2.6%)		0 (0%)		0.257*
Immunosuppressed	5 (4.3%)		1 (1.1%)		0.233*
Smoking status					0.302‡
Current	14 (12.1%)		14 (15.4%)		
Former	6 (5.2%)		9 (9.9%)		
Never	96 (82.8%)		68 (74.7%)		
Rockwood Frailty Scale Score					0.188‡
Not frail	115 (99.1%)		89 (97.8%)		
Pre-frail	1 (0.9%)		0 (0%)		
Frail	0 (0%)		2 (2.2%)		
ASA					0.042‡
1	63 (54.3%)		63 (69.2%)		
2	50 (43.1%)		24 (26.4%)		
3	3 (2.6%)		4 (4.4%)		
Alvarado Score					<0.001‡
Low Risk	47 (40.5%)		8 (8.8%)		
Intermediate Risk	41 (35.4%)		17 (18.7%)		
High Risk	28 (24.1%)		66 (72.5%)		
AIR Score					0.266‡
Low Risk	37 (31.9%)		26 (28.6%)		
Intermediate Risk	60 (51.7%)		56 (61.5%)		
High Risk	19 (16.4%)		9 (9.9%)		
Adult Appendicitis Score					0.194‡
Low Risk	32 (27.6%)		16 (17.6%)		
Intermediate Risk	61 (52.6%)		51 (56.0%)		
High Risk	23 (19.8%)		24 (26.4%)		
Imaging modality					
None	13 (11.2%)		5 (5.5%)		0.214*
Ultrasound	28 (24.1%)		15 (16.5%)		0.227*
CT	81 (69.8%)		78 (85.7%)		0.008*
Faecolith present	23/81 (28.4%)		27/78 (34.6%)		0.495*
Free fluid present	33/81 (40.7%)		43/77 (55.8%)		0.079*
Appendix diameter ≥7 mm	60/63 (95.2%)		60/64 (93.8%)		0.999*
Initial management plan					<0.001‡
IR drainage	0 (0%)		3 (3.3%)		
Operated	110 (94.9%)		55 (60.4%)		
Conservative	6 (5.2%)		33 (36.3%)		
Failed conservative and operated	0 (0%)		4/33 (12.1%)		0.999*
Admission SARS-CoV-2 Swabs collected	–		72 (79.1%)		

†: Mann-Whitney test; *: Fisher's exact test; ‡: Chi-squared test.

patients in the pre-COVID period, 81 (69.8%) had a CT of their abdomen to aid in diagnosis compared to 78 (87.5%) out of 91 patients during the COVID period (p-value = 0.008*) (Table 1). A small proportion of patients, 11.2% (n = 13) and 5.5% (n = 5) in the pre-COVID and COVID period respectively, did not undergo any radiological investigations (p-value = 0.214). 4 (3.4%) patients and 6 (6.6%) had both a CT and an US as part of their investigations in the pre-COVID and COVID period, respectively (p-value = 0.224). From those who underwent a CT scan in the pre-COVID period, 23 (28.4%) out of 81 patients a faecolith was identified, 33 (40.7%) out of the 81 patients had free fluid, and for the 60 out of 63 (95.2%) where the CT reported the appendix diameter this was ≥7 mm. Whilst for patients who had a CT scan during the COVID period, in 27 (34.6%) out of the 78 patients a faecolith was present, 43 (55.8%) out of 77 had free fluid identified and in 60 (93.8%) out of 64 had an appendix diameter reported as ≥7 mm. When each of these findings were compared between each period, no statistically significant difference was observed (Table 1) and no gender differences were observed (p-value = 0.369).

3.4. Management across both periods

The vast majority of patients, 94.9% (n = 110), presenting in the pre-COVID period were offered operative management as their initial management plan, in comparison to 60.4% (n = 55) for the COVID period. Three (3.3%) patients presenting during the COVID period were managed with IR drain insertion whilst this wasn't offered as an initial management in the pre-COVID period (Table 1). Conservative treatment as an initial management plan was offered to 5.2% (n = 6) of patients in the pre-COVID period compared to 36.3% (n = 33) during the COVID period (p-value<0.001*). 4 out of the 33 (12.1%) patients from the COVID period required an operation after a period of conservative management, whilst none from the 6 patients managed conservatively during the pre-COVID period required an operation (p-value = 0.999). From the patients presenting during the COVID period 72 (79.1%) were screened with a nasal swab to detect SARS-CoV-2 on admission.

3.5. Operative management

For those patients that had undergone an operation (n = 110 during the pre-COVID period and n = 59 during the COVID period) the mean time from admission to theatre was 22.7 h (range 1–119.5) in the pre-COVID period compared to 17.5 h (range 1–68.5) in the COVID period (p-value = 0.029*; Table 2). Mean operative time was 88.9 min (range 23–221) in the pre-COVID period and 81.8 min (range 41–160) during the COVID period (p-value = 0.095). Majority of patients during the pre-COVID period, 109 out of 110 (99.1%) had laparoscopic appendicectomy with 8 (7.3%) of them requiring a conversion to an open approach. For the remaining patient who underwent laparoscopy in the pre-COVID period, the appendix was not resected due to other pathology (ovarian cyst rupture) identified intra-operatively with a macroscopically normal appendix. During the COVID period, 22 patients (37.3%) had an open appendicectomy (p-value=<0.001*) and only one patient (1.7%) from the COVID period required a conversion to open from a laparoscopic approach (p-value = 0.452).

The majority of operations were performed within hours, 64.6% compared to 66.1% in the pre-COVID and COVID periods, respectively (p-value = 0.867; Table 2). The operating surgeon was an SPR in 51.8% of cases in the pre-COVID and 52.5% in the COVID period with the assisting surgeon being an SHO in 60.9% of cases during the pre-COVID and 49.1% during the COVID period. Consultant surgeons were the operating surgeons in 20.9% of cases in the pre-COVID and 11.9% of cases in the COVID period (p-value = 0.265).

A perforated appendix was found intra-operatively in 20% (n = 22) during the pre-COVID period and 20.3% (n = 12) during the COVID period (p-value = 1.000; Table 2). During the procedure, appendicular abscess was noted in 19 cases (17.3%) during the pre-COVID period versus 20 (33.9%) during the COVID period (p-value = 0.021*). Serous fluid was present in 44 cases (40%) and in 35 cases (59.3%) during the pre-COVID and COVID periods respectively (p-value = 0.023*). Faecal contamination was present in 6.4% (n = 7) and 3.4% (n = 2) of cases during pre-COVID and COVID respectively (p-value = 0.497).

Table 2
Operated patients' intra-operative and post-operative details.

	Pre-COVID (n = 110)		COVID (n = 59)		
Intra-operative data					
	Mean (±SD)	Range	Mean (+SD)	Range	p-value
Time from admission to theatre (hours)	22.7 (±17.8)	1–119.5	17.5 (±12.9)	1–68.5	0.029†
Operative time (min)	88.9 (±32.3)	23–221	81.8 (±26.3)	41–160	0.095†
Operative Approach for appendicectomy					<0.001‡
Open	1 (0.9%)		22 (37.3%)		
Laparoscopic	101 (91.8%)		36 (61.0%)		
Laparoscopic converted to open	8 (7.3%)		1 (1.7%)		0.452*
Time of day procedure performed					0.867*
Within office hours (8:00–17:00)	71 (64.6%)		39 (66.1%)		
Out of hours (17:00–8:00)	39 (35.4%)		20 (33.9%)		
Level of operating surgeon					0.265‡
Consultant (≥15 years post-qualification)	23 (20.9%)		7 (11.9%)		
SPR (6–14 years post-qualification)	57 (51.8%)		31 (52.5%)		
SHO (1–5 years post-qualification)	30 (27.3%)		21 (35.6%)		
Level of assisting surgeon					0.219‡
Consultant (≥15 years post-qualification)	3 (2.7%)		4 (6.8%)		
SPR (6–14 years post-qualification)	40 (36.4%)		26 (44.1%)		
SHO (1–5 years post-qualification)	67 (60.9%)		29 (49.1%)		
Operative findings					
Perforated appendix	22 (20.0%)		12 (20.3%)		0.999*
Abscess formation	19 (17.3%)		20 (33.9%)		0.021*
Serous fluid	44 (40.0%)		35 (59.3%)		0.023*
Faecal contamination	7 (6.4%)		2 (3.4%)		0.497*
Appendicular stump closure					<0.001‡
Endoloop	96/109 (88.1%)		34 (57.6%)		
Stapled	8/109 (7.3%)		6 (10.2%)		
Sutured	5/109 (4.6%)		19 (32.2%)		
Drain at time of surgery	19 (17.3%)		7 (11.9%)		0.503*
Post-operative data					
Post-operative complications					
Intra-abdominal collection	6 (5.5%)		6 (10.2%)		0.346*
Ileus	5 (4.6%)		7 (11.8%)		0.114*
HAP	3 (2.7%)		1 (1.7%)		0.999*
Post-operative critical care admission	0 (0%)		1 (1.1%)		0.658‡
Return to theatre	0 (0%)		0 (0%)		
Histology results					0.993‡
Appendicitis	103/109 (94.5%)		56 (94.9%)		
Malignancy	2/109 (1.8%)		1 (1.7%)		
Normal	4/109 (3.7%)		2 (3.4%)		

†: Mann-Whitney test; *: Fisher's exact test; ‡: Chi-squared test.

Endoloops were used for appendicular stump closure in 96 out of 109 cases (88.1%) in the pre-COVID period and in 34 out of 59 (57.6%) in the COVID period (p-value<0.001). Only in 5 cases (4.6%) during the pre-COVID period the appendix stump was sutured compared to19 (32.2%) during the COVID period (p-value<0.001*; Table 2). A drain was left at the end of the operation in 17.3% (n = 19) of cases and 11.9% (n = 7) of cases during the pre-COVID and COVID period, respectively (p-value = 0.503).

Post-operatively none of the operated patients required re-operation. Only 1 patient required critical care admission post-operatively during the COVID period (1.1%) and none during the pre-COVID period (p-value = 0.658; Table 2). Post-operative intra-abdominal collection was found in 5.5% (n = 6) of patients and 10.2% (n = 6) during the pre-COVID and COVID period, respectively (p-value = 0.346). 11.8% (n = 7) of patients during the COVID and 4.6% (n = 5) patients during the pre-COVID period developed ileus post-operatively (p-value = 0.114). Three patients during the pre-COVID and one patient during the COVID period developed a hospital acquired pneumonia (HAP) post-operatively (p-value = 0.999). None of these patients with HAP tested positive for SARS-CoV-2 nucleic acids on screening post-operatively. We observed no wound infections, cardiac events or venous thromboembolism events for any of the patients within the two time periods.

In the vast majority of cases in both time periods (94.5% Vs 94.9%, pre-COVID versus COVID), histology confirmed the diagnosis of acute appendicitis. In 2 out of 109 (1.8%) patients during the pre-COVID period and one (1.7%) patient during the COVID period, a malignancy was noted on histology. In addition, four patients (3.7%) in the pre-COVID and two patients (3.4%) in the COVID period had a normal appendix on histology (p-value = 0.993).

3.6. Follow-up and outcomes

The mean LOS was 3.4 days (range 1–15) in the pre-COVID period compared to 5.1 days (range 0–60) in the COVID period (p-value = 0.158; Table 1). Overall, 24 patients re-attended within 3 months following their initial diagnosis and management plan. From the pre-COVID period, there were 8 (6.9%) patients compared to 16 from the COVID period (p-value 0.027*; Table 3). From these patients, 7 out of 8 (87.5%) for the pre-COVID period and 12 out 16 (75%) for the COVID period their re-attendance was related to their appendicitis diagnosis (p-value = 0.631). An IR drain was inserted in 1 of these 16 (6.3%) patients re-presenting from the COVID group for a postop collection. No IR drain was required for those re-attending from the pre-COVID period (p-value = 0.999).

We observed 3 mortalities during the COVID period (2.2%) compared to none during the pre-COVID period (p-value = 0.109). The first patient was a 94-year old male (with ischaemic heart disease (IHD), heart failure and atrial fibrillation) who presented in sepsis with perforated appendicitis, was deemed palliative and passed away within four days of his admission. The second patient was a 85-year old male (with Parkinson's disease, IHD and coronary artery bypass graft) with perforated appendicitis who deteriorated despite maximal conservative treatment with broad-spectrum antibiotics and IR drainage of a RIF abscess and passed away 37 days into his admission. The third patient was a 68-year old female who passed away with sepsis secondary to relapsed acute myeloid leukaemia >90 days following her diagnosis of appendicitis.

Table 3
Patient outcomes.

	Pre-COVID (n = 116)	COVID (n = 91)	p-value
Re-attendance within 3 months	8 (6.9%)	16 (17.6%)	0.027[a]
Appendicitis related	7/8 (87.5%)	12/16 (75.0%)	0.631[a]
IR drain insertion	0 (0%)	1/16 (6.3%)	0.999[a]
Mortality within 90 days	0 (0%)	2 (2.2%)	0.109‡

[a] Fisher's exact test; ‡: Chi-squared test.

4. Discussion

Concerns over infection spread, self-isolation/social distancing, shortage of personal protective equipments (PPE) and overwhelmed hospital resources have led to marked changes in clinical practice during the COVID-19 pandemic [15]. This included the management of AA, specifically concerns about laparoscopy being an AGP. There are significant clinical and financial costs incurred secondary to negative appendicectomy during the treatment of suspected AA [16]. Therefore it is crucial to avoid such unnecessary morbidity and mortality especially during a health crisis/pandemic by ensuring getting the correct diagnosis, prompt appropriate management and minimising the re-attendance risk.

4.1. Imaging-confirmed diagnosis of appendicitis

Our local practice is to confirm the diagnosis of AA particularly in clinically equivocal cases with imaging prior to proceeding to surgery as this has been reported in the literature to be associated with lower rates of negative appendicectomy [17]. This explains our low rate of negative appendicectomy of 4.5% when it has reported to be as high as 20% in some centres [1]. Sensitivity and specificity of ultrasound do not exceed that of physical examination and patients often require further imaging [18]. The use of CT imaging has significantly increased during the pandemic. At the start of the Covid-19 pandemic, finding a reliable test to help diagnose COVID-19 positive patients was paramount and CT-thorax was one of the first readily available tests, which could explain this significant increase [19–21]. In the UK, for patients presenting with acute abdominal pain, guidance during the pandemic was to include imaging of the thorax as a diagnostic test for Covid-19. This has led to an increased use of CT scanning worldwide and also in our centre as stated above.

4.2. Laparoscopic versus open appendicectomy

In order to minimise exposure from AGP, open surgery was preferred in the beginning of the pandemic without this affecting the operative time in our cohort. Regardless of the operative approach, significantly more abscess formation and free fluid were found during COVID versus pre-COVID times. This could be explained by patients presenting late to the hospital due to fear during the COVID pandemic or delayed surgery after failed conservative treatment, as higher rates of perforation and abscess formation are known to be associated with delayed surgery [22] with reported relative risk for appendicular perforation up to 9% per day delay with a 8% increased risk of postoperative abscess [23]. At the start of the Covid-19 pandemic, laparoscopic surgery was labelled as a potential AGP and national guidance advocated the use of open surgery for both patients and staff protection till more evidence became available. Hence in the UK many hospitals reverted back to open surgery.

4.3. Operative versus conservative management of appendicitis

More patients were treated conservatively during COVID, however no significant difference was observed in LOS between both groups. However, we noted a significantly shorter interval from admission to theatre during the COVID period. This could be due to more CT scans being performed in that period. Patients with confirmed AA with faecolith and/or free fluid were considered high risk and hence were offered surgery. Appendicolith has been reported as an independent prognostic risk factor for treatment failure associated with perforation more often than with uncomplicated appendicitis [24]. Patients without evidence of faecolith or other complicated features were offered non-operative treatment.

Antibiotic therapy failed in four patients, who represented with recurrent AA within 90 days of their initial presentation. Two more patients also represented with AA more than 90 days from their initial presentation and all six underwent laparoscopic appendicectomy, bringing the total failure rate of conservative management up to 15.38% (6 out of the initially conservatively managed 39 patients). Although this did not reach statistical significance, this could be due to the relatively small number of patients included in our study. Of the 33 conservatively-managed patients, 12 patients are awaiting interval appendicectomy, 15 were discharged with no further routine follow up, three are awaiting further investigations prior to definite treatment and the three mortalities previously discussed.

Re-attendance rate due to appendicitis-related issues was significantly higher in the COVID period. However, of the 16 patients who re-attended at the time, six returned for a planned follow up in the surgical assessment unit to ensure adequate clinical improvement. A seventh patient re-attended with a non-appendicitis catheter-related problem. One can argue that more conservative management carried out during the COVID period has put more load on services as these patients need regular senior review with or without repeat blood tests and imaging to identify early treatment failure and the need for prompt appendicectomy, which did not have happened pre-COVID.

The main limitation of our study is the relative small size of our cohort and a short follow up period of 90 days. Although this is not a randomized study, the risk of bias is minimal as the data from the COVID period were collected prospectively and checked by multiple investigators. Also there was a noticeable gradual return to our normal practice i.e. laparoscopic appendicectomy for all patients with confirmed AA during the last week of our study, which could be explained by our improved testing capability and subsequently quicker case turnover. An additional factor to be considered is that some patients in our cohort chose to attend our centre rather than going to their local hospital, for reasons that are not well documented.

Our study showed that there is a role for open surgery when needed with comparable outcomes and complication rates to laparoscopy. Wearing PPE did not seem to affect the total operative time irrespective of the operative approach. We still believe that operative management should be the management of choice of AA particularly with imaging-confirmed presence of appendicolith [25]. Open surgery and conservative treatment were useful in selected situations e.g. during the pandemic, however on balance we have decided to continue with laparoscopic surgery during any further surges in COVID-19 cases. With the current rising number of COVID-19 cases, the lessons learned during the first wave of this pandemic have made us better equipped to manage acute surgical emergencies more efficiently.

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Author contribution

Ramez Antakia: study design, Data collection, Cross checking Data, Data analysis, Writing & Manuscript revision.

-**Athanasios Xanthis**: Data collection, Cross checking Data & Writing

-**Fanourios Georgiades**: Data collection, Cross checking Data, Data analysis & Writing

-**Victoria Hudson, James Ashcroft, Siobhan Rooney, Aminder A Singh**: Data collection

-**John R O'Neill, Nicola Fearnhead, Richard H Hardwick, R**

Justin Davies, John MH Bennett: Manuscript revision

Ethical approval was given, by whom and the relevant Judgement's reference number

Ethical approval was given and the study was registered locally with the "Clinical Audit & Research Department" at Addenbrooke's Hospital (Cambridge University Hospitals NHS Foundation Trust), project ID: PRN8996.

Research registration unique identifying number (UIN)

Please enter the name of the registry, the hyperlink to the registration and the unique identifying number of the study. You can register your research at http://www.researchregistry.com to obtain your UIN if you have not already registered your study. This is mandatory for human studies only.

1. Name of the registry: www.clinicaltrials.gov
2. Unique Identifying number or registration ID: **NCT04615728**
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.clinicaltrials.gov/ct2/show/NCT04615728?cond=Acute+Appendicitis&cntry=GB&draw=2&rank=1

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. Please note that providing a guarantor is compulsory.

Mr Ramez Antakia.

The data that support the findings of this study are available from the corresponding author, RA, upon reasonable request.

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