EVALUATION OF APPENDICITIS MANAGEMENT DURING EARLY COVID-19 PANDEMIC AND LITERATURE REVIEW

Lim RZM[1], Lee EP[1], Tan HCL[1], Tan JH[1], Pang SL[1], Lee KZ[1], Diya VD[1], and Tuan Mat TNA[1].
[1] Department of Surgery, Hospital Sultanah Aminah, 8000 Johor Bahru, Johor, Malaysia

Correspondence:
Raymond Zhun Ming Lim
Department of Surgery, Hospital Sultanah Aminah,
Jalan Persiaran Abu Bakar Sultan,
80100 Johor Bahru, Johor, Malaysia
Tel: +60 7-225 7000
Email: raymondlzm@gmail.com

Abstract

Purpose: Numerous guidelines have been proposed in managing surgical emergencies during COVID-19 pandemic. Literature on the implications of these adjustments during this pandemic remained limited. This review aims to examine the implications of these critical adjustments with focus on appendicitis management.

Method: This is a single-centre retrospective observational study in a Malaysian tertiary state surgical centre and review of recent guidelines and literature. Patients with appendicitis from March to May 2020 were included and medical records were reviewed and analysed.

Results: Of the 173 appendicitis patients, 117 (67.6%) were operated and 56 (32.4%) were conservatively treated. Those screened for SARS-CoV-2 pre-operatively showed longer wait for operation (3.0 vs 2.0 days, *p*=0.001) and a longer hospital stay (4.5 vs 4.0 days, *p*=0.005). One-third of patients screened (36.6%) were expedited for surgery on clinical suspicion of complicated appendicitis and 42.1% progressed from acute to complicated appendicitis while waiting for screening result. All patients screened were COVID-19 negative. Delay due to SARS-CoV-2 screening did not result in worse outcome for appendicitis patients.

Conclusion: With the increase in incidence and rise of COVID-19 cases, routine screening by questionnaire, physical examination and naso-oropharyngeal swab may be considered to detect asymptomatic carrier, especially in regions with high infection. Regular reassessment with low threshold to expedite the surgery is necessary, to ensure satisfactory surgical outcome.

Keywords: Appendicitis, Pandemic, SARS-CoV-2, COVID-19, Screening

Introduction

To date, more than 11 million confirmed cases of Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been reported, and it accounts for more than five million deaths globally (1). The impact of COVID-19 pandemic on all levels of society has been evident, including the healthcare system and have resulted in various changes to the surgical management in hospitals (2).

Appendicitis remains one of the commonest surgical emergencies worldwide, and timely appendicectomy is recommended as the treatment of choice. Considering the risks during this ongoing pandemic, various surgical bodies and organizations have issued guidance for surgical services in the endeavour to maintain the service while upholding the safety of both patients and healthcare workers. While outpatient laparoscopic appendicectomy was proposed as the standard of care (3), few bodies have considered the risk of laparoscopic surgeries during this pandemic and advised for trial of non-operative management (4, 5). Non-operative management, however, has also been associated with high failure rates, longer hospital stays and complications (6).

While various guidelines have surfaced, the literature on the implications of these adjustments during COVID-19 pandemic remain scarce. The rise in COVID-19 incidence recently calls for a revision of previous guidelines. Hence, this study aims to provide information by presenting our experience with the adjustments made during this ongoing pandemic, especially in a resource limited setting. The rationale and impact of compulsory SARS-CoV-2 screening prior to the operation will also be discussed in this paper.

Materials and Methods

Inclusion, exclusion criteria and definitions

Ethical approval was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR ID-20-1081-55074). In this retrospective study, records of all patients aged 13 years and above treated for appendicitis at the surgical unit of Hospital Sultanah Aminah, Johor Bahru, Malaysia – the state tertiary hospital, were reviewed. Those with appendicular masses or appendicular tumours confirmed by histopathological examination (HPE) were not included in this study. To present the impact on the management of appendicitis during this pandemic, we included patients diagnosed with appendicitis from March – May 2020, during the initial peak of COVID-19 pandemic in this region. The surgical registry, operative notes, and follow up notes of patients included were reviewed. For the purpose of this study, simple non-perforated appendicitis is termed acute appendicitis, whereas suppurative and perforated appendicitis are termed complicated appendicitis.

Relevant clinical data was reviewed and recorded into the case report form. We analysed the basic demographics, duration of stay and post-operative outcome including post-operative complications and readmission rates. For statistical analysis, we used IBM® SPSS® version 23. Discrete variables were expressed as counts (percentage) and continuous variables as means ± standard deviation (SD) or median with interquartile range (IQR) depending on normality. Frequency comparisons between acute and complicated appendicitis groups were done using Chi-Square or Fisher's Exact Test where applicable. We also used Independent t-tests for continuous data with normal distribution while Mann–Whitney U was used for non-normal data. A p-value of less than 0.05 was considered statistically significant.

Standard of care for appendicitis patients in our centre before covid-19 pandemic

Prior to the COVID-19 pandemic, the standard of care for those diagnosed clinically as acute appendicitis was timely appendicectomy, either via laparoscopy or open approach, with a single dose of antibiotic prior to the start of the operation. In contrast, those diagnosed with complicated appendicitis, based on clinical judgment or less commonly with radiological evidence, were started on intravenous antibiotics followed by open appendicectomy. The choice of antibiotics in our centre were amoxicillin with clavulanic acid. The diagnoses of acute appendicitis or complicated appendicitis were typically based on the overall clinical history, physical examination and basic full blood examination with leucocytes count. The use of imaging either by ultrasound or computed tomography (CT) were reserved for those with clinical diagnostic uncertainty or those with considerable operative risks due to our resource-limited setting.

Both acute appendicitis and complicated appendicitis patients were typically discharged on the day after the operation unless there are complications such as ileus, surgical site infection, or drainage to be managed post-operatively. Less frequently, a small fraction of those with uncertain diagnosis or those who responded with antibiotics with pain resolving while waiting for operation, may be discharged with oral antibiotics to be completed within a week. The patients who were discharged post-surgery will be followed up at the surgical outpatient clinic two months upon discharge. The HPE result will be reviewed at follow-up.

Standard of care for appendicitis patients in our centre during covid-19 pandemic

During COVID-19 pandemic, few adjustments have been made with regards to the management of patients requiring emergency surgeries in our centre:

i. All patients were screened from clinical history to rule out any risk of being infected with SARS-CoV-2, including recent contact with confirmed or suspected cases. They were examined for any suspicious physical signs and chest radiograph was performed. If suspected, further investigations and testing ensued, and patients were admitted to a designated isolation ward.

ii. Non-operative management of acute or simple appendicitis were encouraged in patients with mild symptoms and low septic parameters. Patients will be admitted for one to three days, observed for response to non-operative management and subjected to prompt appendicectomy if symptoms persisted or worsened.

iii. When operative management was decided, open appendicectomy instead of laparoscopic approach was utilized.

iv. For those who have not been tested for SARS-CoV-2, operation was carried out with the team wearing full personal protective equipment (PPE) in the operation theatre.

v. To reduce the congestion at surgical follow-up clinics, the HPE result of the patients who underwent appendicectomy will be informed by phone calls within two months post-operatively. A check of the patients' overall condition and if there was presence of any post-operative complications throughout the two months' duration will be done during the call.

Compulsory testing was implemented in the middle of the study period from 16th April 2020. All acute appendicitis patients whom surgery is not immediately required, a compulsory laboratory test to rule out SARS-CoV-2 was required. An exception to this was when there were reasonable clinical grounds to suspect a progression to

complicated appendicitis. In such cases, surgery was expedited without waiting for the availability of SARS-CoV-2 test result (Figure 1). For those awaiting the test result, serial examination was done twice a day or more to assess the need to expedite surgery.

An algorithm describing the management of patients with appendicitis is demonstrated in Figure 1. In our centre, the laboratory test used during this study was the detection of SAR-CoV-2 RNA by reverse-transcription polymerase chain reaction (RT-PCR) from the upper respiratory tract using nasopharyngeal and oropharyngeal swabs. Rapid test to detect the antigen was not used due to its unavailability during the time of this study; Rapid test is less sensitive and has a lower negative predictive value (7), especially in places with low prevalence. If screening test was negative, laparoscopic approach was not taken in consideration of the possible false negative and the window period where SARS-CoV-2 might not be detectable by the screening test. There remained a concern of the theoretical risk of spread during laparoscopic procedure then.

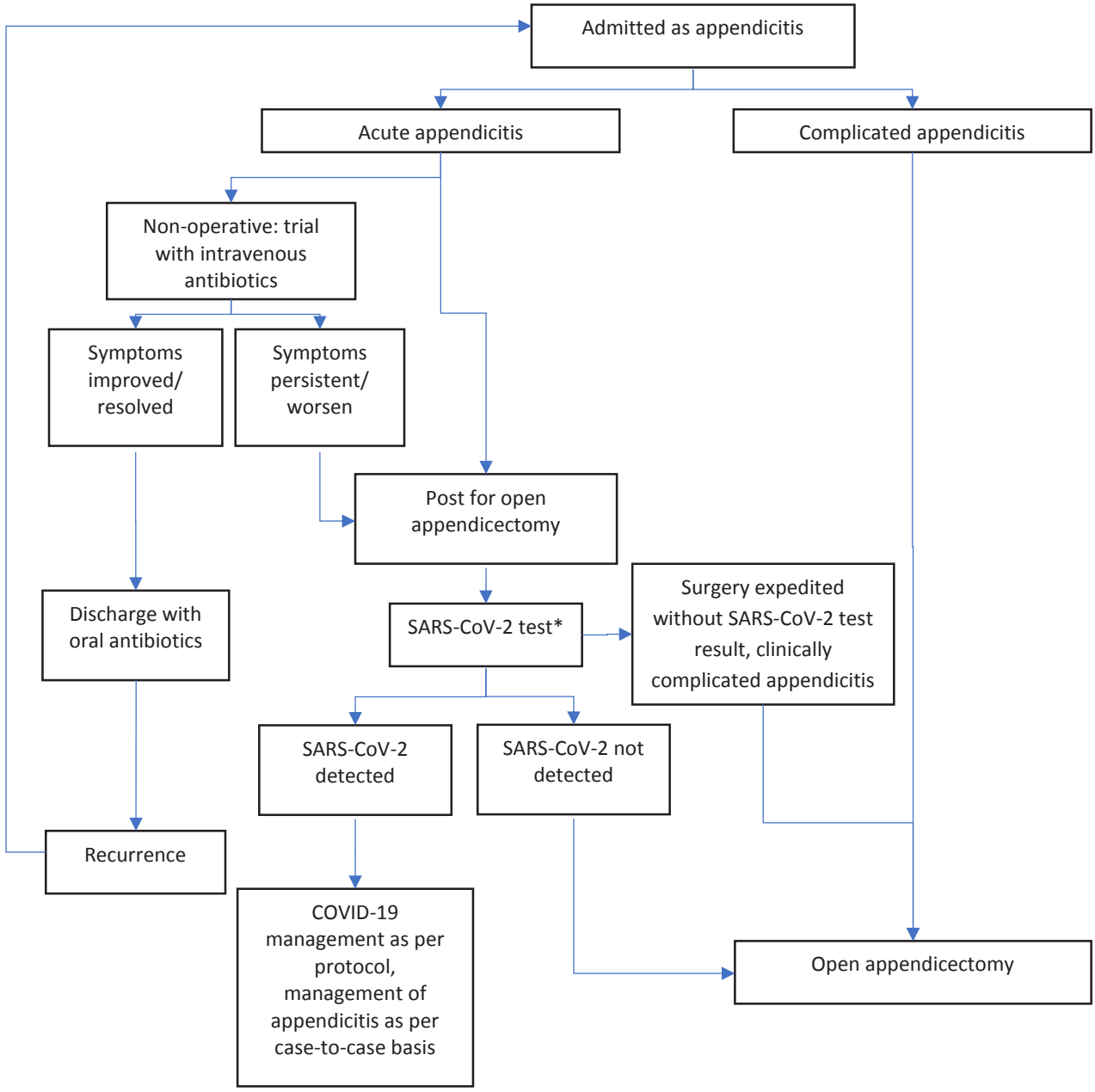

Figure 1: Algorithm of the management of acute appendicitis after the implementation of compulsory SAR-CoV-19 laboratory testing since 16th of April. COVID-19, Coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. *Detection of SAR-CoV-2 RNA by reverse-transcription polymerase chain reaction (RT-PCR) from the upper respiratory tract using nasopharyngeal and oropharyngeal swab.

Results

Subject descriptions

In this study, there were 173 patients who were admitted for appendicitis from 1st of March to 31st May 2020, of which 56 (32.4%) of them were diagnosed clinically as acute appendicitis and treated with antibiotics, whereas 117 (67.6%) were operated. Among those operated, 10/117 (8.5%) were white appendix, with no appendicitis related pathology found intra-operatively. Two out of the 56 subjects who were treated conservatively were found upon follow-up to be readmitted again to our centre for persistent symptoms and were later operated for acute appendicitis. The mean follow-up for the patients operated were two-months from discharge.

Those operated and confirmed to have appendix-related pathology by histopathological examination were included for analyses. More than half of the remaining 107 patients operated (59.8%) were complicated appendicitis (Table 1). Complicated appendicitis was associated with male gender and older age group. Acute appendicitis patients were associated with longer waiting time for operation with median waiting time of 3 days [interquartile range (IQR), 2 days], compared to those with perforated appendicitis (median, 2 days; IQR, 2 days). Those with complicated appendicitis were seven times more likely to be readmitted compared to the acute appendicitis group (p-value=0.046). Complicated appendicitis was also more likely to have post-operative complications, though not statistically significant.

Table 1: Subject descriptions of all acute appendicitis patients, excluding those who were found to have no appendix-related pathology (N=163). Only those who were operated and confirmed to have appendix-related pathology by histopathological examination were included for analyses (N=107).

		Non-operated appendicitis *N=56*	Operated appendicitis, *N*=107			
	***N* (%)**		Acute, *n*=43 (40.2)	Complicated, *n*=64 (59.8)	OR (95% CI)[a]	*p*†
Age, *years* Median (IQR)		31.9 (19.2)	20.4 (9.6)	26.5 (24.0)	NA	**0.013***
Gender						
Male	81 (49.7)	24 (42.9)	15 (34.9)	42 (65.6)	3.57 (1.58-8.00)	**0.002****
Female	82 (50.3)	32 (57.1)	28 (65.1)	22 (34.4)		
Ethnicity						
Malay	106 (65.0)	41 (73.2)	24 (55.8)	41 (64.1)		
Chinese	12 (7.4)	4 (7.1)	3 (7.0)	5 (7.8)	NA	0.072**
Indian	18 (11.0)	6 (10.7)	9 (20.9)	3 (4.7)		
Others	27 (16.6)	5 (8.9)	7 (16.3)	15 (23.4)		
Period in relation to implementation of compulsory testing						
Before	84 (51.5)	29 (51.8)	23 (53.5)	32 (50.0)	0.87 (0.40-1.89	0.723**
After	79 (48.5)	27 (48.2)	20 (46.5)	32 (50.0)		
White cell count, *x10^9/L* Mean (SD)		11.4 (4.4)	12.6 (6.0)	15.1 (5.1)	NA	0.061***
Waiting time for those operated, *days* Median (IQR)		NA	3.0 (2.0)	2.0 (2.0)	NA	**0.004***
Length of stay, *days* Median (IQR)		3.0 (2.0)	4.0 (2.0)	4 (2.0)	NA	0.403*
Post-operative complications (*n*=73)[f]						
Yes	16 (21.9)	NA	3 (11.1) *-SSSI, n=2 -DSSI, n=1*	13 (28.3) *-SSSI, n=6 -DSSI, n=1 -Others/ non-specified, n=6*	3.15 (0.81-12.3)	0.087**
No	57 (78.1)		24 (88.9)	33 (71.7)		
Readmission (*n*=88)[f]						
Yes	13 (14.8)	2 (13.3)	1 (3.7)	10 (21.7)	7.22 (0.87-59.97)	**0.046****
No	75 (85.2)	13 (86.7)	26 (96.3)	36 (78.3)		

†Statistical tests were conducted only for those operated; ‡number varies in this variable due to lost to follow up. *Mann-Whitney U test; **Chi-square; ***Independent sample t-test; ****Fisher's exact test. IQR, Interquartile range; OR, Odds Ratio; CI, Confidence interval; SSSI, Superficial surgical site infection; DSSI, Deep surgical site infection.

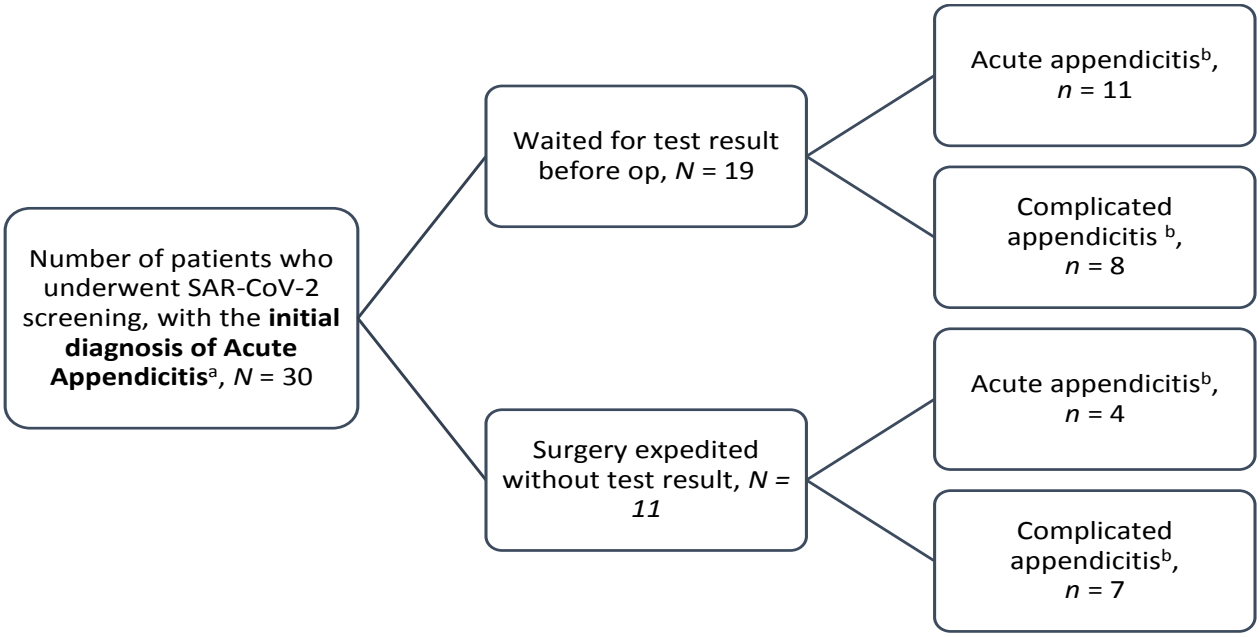

Figure 2: Patients who were initially diagnosed as acute appendicitis and underwent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) screening and the implications of waiting for test during the period when SARS-CoV-2 screening test was mandatory for non-urgent emergency surgery. [a]the initial diagnosis is clinical, based on history and examination; [b]final diagnosis based on Histopathological Examination (HPE) and intra-operative findings.

Outcome comparing the two-duration studied

After 16th April, SARS-CoV-2 screening became mandatory for all non-urgent operations including acute appendicitis patients. As illustrated in Figure 2 there were 30 patients whom the screening tests were ordered, of which only 19 had waited for the test prior to operation, among which, 8 progressed from clinical acute appendicitis to complicated appendicitis (Table 2).

The remaining 11 out of the 30 patients tested were expedited for surgery without waiting for the test result in anticipation of progression to complicated appendicitis. Among these, seven did progress from acute to complicated appendicitis. As imaging was not routinely used due to resource limitations, the initial diagnosis was made based on the clinical diagnosis using history, physical examination and basic full blood examination.

Notably, none of the 30 patients screened had SARS-CoV-2 in our centre. The RT-PCR test of SARS-CoV-2 generally takes seven hours to process, excluding the time taken to request for the test and time taken for the designated team to carry out the nasopharyngeal and oropharyngeal swab. Unless it is of absolute necessity, the test is only conducted during office hours. Considering the above factors, the test results generally take about a day to be ready hence an expectedly longer waiting time for those whose results were required prior to operation (p-value=0.001) and consequently longer hospital stay (p-value=0.005) (Table 3).

There is, however, essentially no difference of post-op complications (OR, 1.05; 95% CI, 0.22-4.99) and readmission rates (OR, 1.18; 95% CI, 0.18-7.75) between those who waited for SARS-CoV-2 result and those with whom surgery was withheld for SARS-CoV-2 screening (p-value=1.00).

Discussion

Since the start of this COVID-19 pandemic, surgical services have been affected worldwide. Appendicitis, being one of the commonest surgical emergencies, may reasonably reflect the implications of the ongoing pandemic on surgical emergencies in many centres. In accordance with the recommendations by international surgical services (4, 5), adjustments were made to ensure the continuance of surgical services in the face of this pandemic.

Operative vs antibiotics treatment during COVID-19 pandemic

One of the most apparent change is the high ratio of acute appendicitis patients who were treated conservatively compared to those operated, (acute appendicitis conservatively treated: acute appendicitis operated=56:43). Up to a-third of patients were reported to have failed antibiotics treatment and more than a quarter required subsequent appendicectomy within a year from the initial presentation (6, 8). Outcome of surgical management was also superior when rate of post-intervention complications and length of hospital were compared to those treated with antibiotics alone (6). Among fifteen patients followed up in the present study, two (13.3%) of those treated conservatively required appendicectomy within two months from initial presentation.

Table 2: Outcome of all operated appendicitis patients before and after implementation of compulsory SARS-CoV-2 screening test (N=107)

N (%)	Before implementation of Compulsory SARS-CoV-2 screening test 01/03/2020-15/04/2020 (6 weeks)				After implementation of Compulsory SARS-CoV-2 screening test 16/04/2020-31/05/2020 (6 weeks)			
	Operated, *n* = 55				Operated, *n* = 52			
	Acute appendicitis, *n* = 23	Complicated appendicitis, *n* = 32	OR (95%CI)	*p*	Acute appendicitis, *n* = 20	Complicated appendicitis *n* = 32	OR (95%CI)	*p*
Waiting time for Operation, *days*[a]	2 (2)	2 (2)	-	0.070[b]	3 (1)	2 (2)	-	**0.032***
Length of stay, *days*[a]	4 (3)	4 (2)	-	0.596[b]	4 (2)	4 (2)	-	0.550*
Post Operative Complications[b]								
yes	2 (13.3)	6 (24.0)	2.05 (0.36-11.80)	0.686[c]	1 (8.3)	7 (33.3)	5.50 (0.59-51.62)	0.206**
no	13 (86.7)	19 (76.0)			11 (91.7)	14 (66.7)		
Readmission[b]								
yes	1 (6.7)	5 (20.0)	3.50 (0.37-33.31)	0.381[c]	0 (0.0)	5 (23.8)	-	0.133**
no	14 (93.3)	20 (80.0)			12 (100.0)	16 (76.2)		

[a]median (Interquartile range, IQR); [b]the total number here is less because of the lost to follow up; *Mann-Whitney U test is used to calculate the p-value; **p calculated using Fisher's exact test. OR, Odds Ratio; CI, Confidence Interval.

Table 3: The outcome of patients operated after implementation of compulsory test, comparing those who had waited for the SARS-CoV-2 screening test result and those who did not (N=52)

	Surgery done without SARS-CoV-2 result, *n* = 33	Surgery withheld for SARS-CoV-2 screening, *n* = 19	OR (95%CI)	*p*
Waiting time for Op, *days* †	2 (2)	3 (1)	-	**0.001***
Length of Stay, *days* †	4 (1)	4.5 (2)	-	**0.005***
Post Operative Complications, *n* (%)				
Yes	5 (15.2)	3 (15.8)	1.05 (0.22-4.99)	1.000**
No	28 (84.8)	16 (84.2)		
Readmission rate, *n* (%)				
Yes	3 (9.1)	2 (10.5)	1.18 (0.18-7.75)	1.000**
No	30 (90.9)	17 (89.5)		

†median (Interquartile range, IQR); *Mann-Whitney U test is used to calculate the p-value; **p calculated using Fisher's exact test. OR, Odds Ratio; CI, Confidence Interval.

The authors of the present study concur with other authors that surgery is still the preferred treatment with excellent outcome in this pandemic (9, 10). It may be reasonable, however, to consider conservative approach with trial of antibiotics in patients who have mild symptoms, normal septic parameters with no clinical evidence of complicated appendicitis. This is an agreement with the recent interim analysis of the UK Cohort study, which proposed that non-operative management may be safe and effective for the management of acute appendicitis in the short term (11). The use of Alvarado score and CT scan findings have been proposed as a guide to the management of acute appendicitis patients (12). The feasibility of such approach is in question however, considering the infrequent use of CT scan in our centre with limited resources. Moreover, while Alvarado score has been associated with high sensitivity, it has poor specificity (13).

During the peak of the COVID-19 pandemic, only open appendicectomy were performed, consistent with the guidelines from various bodies including American College of Surgeons and Royal College of Obstetricians & Gynaecologists (14, 15). While there is a theoretical risk of virus diffusion during laparoscopic surgery (16), other authors have questioned if the evidence of such fear is sufficient to justify exclusion of patients from laparoscopic surgery and its advantages over open surgeries (17).

The rationale of compulsory screening test for emergency surgeries

While SARS-CoV-2 screening among patients undergoing elective surgeries is recommended (5, 18), the rationale for mandatory screening for patients must be weighed cautiously against the risks of delaying the surgery. The waiting time for appendicectomy depends on the availability of operation room resources and availability of surgeons. Prior to the implementation of compulsory SARS-CoV-2 screening, the median time of waiting for operation for acute appendicitis patients was two days (Table 2 and Table 3) whereas those who waited for the screening test, waited a day longer, before the operation.

The decision for laboratory test prior to non-urgent surgeries since 16th of April 2020 was based on the consensus between the anaesthesiology and surgical department at the peak of the pandemic locally. The rationale was to minimize the risk of exposure of the operating team to SARS-CoV-2 and to reduce the wastage of PPE that was scarce. Hence, those who were screened negative, were operated on with the team wearing basic PPE, as per any other surgeries prior to the COVID-19 pandemic.

Delays of up to 48 hours has not been associated with increased rate of complex appendicitis (19). However, an appendicectomy carried out after 48 hours, has been significantly associated with surgical site infections and other complications, with no increase in the rate of perforation. Therefore, it is evident that the morbidity is directly related to the delay of surgery in the management of appendicitis.

While our study did not reveal a statistical difference in rates of complications and readmissions among those who had waited for the screening test to be available, there was a longer waiting time and extended hospital stay among those who waited for the screening test to be made available prior to operation (Table 3). As shown in Figure 2, half (15 patients) of the 30 patients who had the initial diagnosis of acute appendicitis that underwent screening test were identified to have complicated appendicitis. Notably, appendicectomy was expedited in 11 of them based on worsening clinical signs, and seven of them indeed have complicated appendicitis. There was no significant difference in post-op complications and readmission rate among those who had waited for screening and those who did not (Table 3). Such observation may be attributed by the low threshold to expedite the surgeries in any clinical suspicion of complicated appendicitis.

The decision to expedite the surgery required regular assessment and careful clinical judgment, especially in the setting of limited radiological resources. This study showed that it is reasonable to use clinical judgment to decide on when to expedite the surgery without waiting for the availability of COVID-19 test result (Figure 1). If the patient is clinically stable, not septic and unlikely to have complicated appendicitis clinically, it may be reasonable to wait for the SARS-CoV-2 screening test result prior to operation. The delay in the availability of the SARS-CoV-2 screening results must not be a cause for the delay in those indicated for surgery.

It must be kept in mind that with the ongoing pandemic, there was also a significant proportion of patients who had an unusual delay in the presentation of non-traumatic abdominal emergencies, as reported by almost half of the surgeons in Italy (20). Such delay may result in disease progression even before presentation to hospital and a further delay by operative management must be avoided. While the use of rapid test to detect the SARS-CoV-2 antigen may be a potential answer to address the long waiting time for operation, the availability, cost and lower sensitivity and negative predictive value in places low prevalence must be borne in mind (7). In places where COVID-19 are prevalent, it is sensible to implement screening test for those not requiring surgery urgently, for the safety of the medical staffs, while considering the need for regular clinical assessment to prevent adverse outcome resulting by the delayed surgery. Multitier screening using questions, examination and radiograph besides RT-PCR test are useful in proper assessment to exclude COVID-19 infection.

Limitations and strengths

There were several limitations to our study mainly due to its single centre retrospective design. Besides the small sample and lost to follow ups, data collected retrospectively in this study was dependent on the availability and accuracy of the records available. Moreover, in view of

the limitations of resources and cost-effective approach, we could not confirm the diagnosis of acute appendicitis among those who had been managed conservatively during this pandemic which contributed to almost a-third of the subjects, since no imaging or operation was done. Notably, none of our patients screened were found to have SARS-CoV-2, and hence we were not able to present on the outcome of acute appendicitis patients with COVID-19.

Nevertheless, this study presents the experience of local management of appendicitis in a resource-limited setting of a regional tertiary state hospital. This data provides information and aid in management of other surgical conditions requiring emergency operations during this pandemic. Implementations of changes to our surgical department in response to COVID-19 pandemic is published elsewhere (21).

Conclusion

This study presents the local experience in the approach of acute appendicitis management, one of the commonest surgical emergencies. While COVID-19 screening increases the waiting time for operation and overall length of hospital stay, the delay did not increase the complication rate. Our clinical flow care during the first wave of local cases appeared to yield reasonably good outcome. Pre-operative screening prior to operation for non-emergency operations may be considered. A high index of suspicion for complicated appendicitis and a low threshold to expedite the surgery is necessary to prevent delay and morbidity. Considerations must also be made in alignment to local policies and capacity, with steps taken in the endeavour for resumption of surgical services.

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Competing interests

The authors declare there is no conflict of interest, and no funding was received for this review.

Ethical Clearance

Ethical approval was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR ID-20-1081-55074).

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