Outcomes of Non-operative Management of Acute Appendicitis in Adults with SARS-COV-2 Infection – A Single Center Retrospective Study

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ABSTRACT

Background: Non-operative management (NOM) of acute appendicitis has regained acceptance with the observed increased morbidity and mortality in SARS-CoV-2 infected patients undergoing surgery.

Objective. This study aimed to determine the outcomes of adult COVID-19 cases with acute appendicitis managed non-operatively at the Philippine General Hospital, a COVID-19 referral center, over a two-year period.

Methods. A retrospective observational study was conducted on adult patients with acute appendicitis, with SARS-CoV-2 infection, admitted from March 2020 to February 2022. Outcomes of NOM, which included treatment failure, readmission, morbidity and mortality rates, were reported.

Results: Twenty-one cases underwent NOM with a mean length of stay (LOS) of 6.8 days with no failure of NOM observed. All cases were either sent home, or transferred to an isolation facility, upon hospital discharge. There were no readmissions, morbidities and mortalities reported at 30- and 60-days after discharge. One case was readmitted after 93 days for ruptured appendicitis that required surgery. The failure rate of NOM within one year was 4.76%.

Conclusion. The study showed that NOM may be safely and effectively applied in patients with uncomplicated acute appendicitis as an alternative to surgery in patients with COVID-19 infection. This approach, however, requires close monitoring and early recognition of treatment failure.

Key words: SARS-CoV-2, Appendicitis, Non-operative management

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Acute appendicitis is one of the most common surgical emergencies in adults. Appendectomy, whether open or laparoscopic, remains to be the gold standard in the treatment of acute appendicitis.[1] Non-operative treatment of acute appendicitis has changed clinical practice, specifically in patients not fit for surgery. Based on the Jerusalem guidelines, NOM of acute appendicitis with initial intravenous antibiotic therapy followed by a stepdown to oral antibiotics as dictated by the patient's clinical condition is recommended.[2] The advantages cited for NOM include fewer complications and shorter LOS.[3] The non-operative approach however still carries safety implications as delaying surgery may increase the risk of perforation, intraabdominal abscess and peritonitis.[4]

With the declaration of the SARS-CoV-2 pandemic in March 2020, the Philippine General Hospital (PGH) was designated to be one of three COVID-19 national referral centers in the country. Consultation of patients requiring operative management continued in the emergency department (ED), despite imposing restrictions to surgery-related admissions and operating room utilization. Poorer surgical outcomes were being observed in patients with COVID-19 undergoing surgery, regardless of the severity of the viral disease. The initial findings of the COVIDSurg Collaborative revealed that patients who were preoperatively diagnosed with SARS-CoV-2 infection, and had surgery within 6 weeks from the diagnosis of SARS-CoV-2 infection had a 9.1% mortality rate as compared to 2.0% mortality rate in those who had surgery after 7 weeks of COVID-19 diagnosis.[5] The postoperative pulmonary complications were also noted to be higher in cases who had surgery within 6 weeks of SARS-CoV-2 infection (r: 26.60 – 29.71%) compared to those who had surgery after 7 weeks (13.12%).[5] These findings were consistent among all types of patient subgroups in terms of age, ASA physical status, urgency of surgery and grade (minor vs

major) of surgery. Patients who remain symptomatic after seven weeks of contracting SARS-CoV-2 infection still had increased mortality rate suggesting the benefit of further delaying surgery, if possible.[5] Non-operative management for uncomplicated appendicitis may be employed. However, NOM requires careful patient selection and exclusion of cases with gangrenous appendicitis, abscess or diffuse peritonitis. Independent predictors of success of NOM also include an imaging-confirmed uncomplicated appendicitis, lower body temperature, lower Alvarado score (<4) and smaller appendix diameter while the presence of appendicolith has been identified as an independent prognostic risk for treatment failure in NOM.[2] NOM for acute appendicitis has proven to be both safe and effective in carefully selected patients. The risks and benefits of foregoing or delaying surgery should be weighed thoroughly.[6]

Objectives

This study aimed to determine the outcomes of adult patients, diagnosed with acute appendicitis, and had positive SARS-CoV-2 infection, who were managed non-operatively. Specific objectives include treatment failure, readmission, morbidity, and mortality rates.

This study also presented a proposed algorithm for NOM of acute appendicitis in adults infected with SARS-CoV-2 to minimize complications and improve outcomes.

METHODS

A retrospective observational study was conducted on adult patients with acute appendicitis, with concomitant SARS-CoV-2 infection as confirmed by a nasopharyngeal swab RT-PCR, who were admitted and managed by the Department of Surgery at the PGH from March 2020 to February 2022. The study was conducted in accordance with the guidelines of Declaration of Helsinki and was approved by the University of the Philippines Manila Research Ethics Board. Using convenience sampling, all records within the specified time frame were retrieved using the Integrated Surgical Information System (ISIS) of the Department of Surgery. Cases included were adult SARS-CoV-2 positive patients with acute appendicitis and those with computed tomography (CT) -confirmed uncomplicated appendicitis. Exclusion criteria for NOM were findings of diffuse peritonitis warranting immediate surgery, CT scan findings of appendiceal perforation or appendicolith or other intraabdominal pathology. The following demographic data were obtained: age, sex and comorbidities.

All SARS-CoV-2 positive patients clinically diagnosed with uncomplicated appendicitis were required to have an abdominal CT scan which guided whether the patient was subjected to NOM or surgery. Abdominal CT scans of the patients were reviewed to confirm the diagnosis of acute appendicitis and the absence of other pathology within the peritoneal cavity. The outcomes relating to the effectiveness of NOM were evaluated during the admission which include treatment failure, readmission, morbidity, mortality rates and LOS.

Criteria prior to home discharge, or transfer to an isolation facility, included the following: clinical improvement of the patient, afebrile for >24 hours, absence of or decreasing abdominal pain and tolerance of regular diet. Failure to meet any of the above criteria will label the case as a treatment failure of non-operative management. The 30-day, 60-day and 365-day outcomes were assessed which included readmission, morbidity and mortality rates using both face-to-face and telephone consultations. Patients were asked for recurrence of symptoms and need for hospitalization or readmission. The obtained data was collected and reviewed, and descriptive analysis of these data was performed.

RESULTS

A total of 62 adult cases of acute appendicitis with SARS-CoV-2 infection were admitted from March 2020 to February 2022. Forty-one patients had immediate surgery due to the presentation of an acute abdomen, or signs of appendiceal rupture, thus failing to meet the criteria for NOM. All patients who had immediate surgery were discharged well, with postoperative ileus (34%) as the most common complication noted. No COVID-19-related complications were noted from the cases that underwent surgery. Only 21 cases underwent NOM.

The mean age of those who underwent NOM was 37 years (range, 19-81 years) (Table 1). On review of records, the NOM group received intravenous cefoxitin based on the antibiogram of PGH with median of 4 days on IV antibiotics (r: 1 – 10 days). Antibiotics were shifted to oral form at the time of discharge, or transfer to an isolation facility, for a total of 7-10 days of antibiotic therapy. The median LOS was 4 days, with a range of 1 to 22 days. The prolonged LOS observed in some cases was due to a need for inpatient isolation due to the inability of patients to have accommodations suitable for home isolation, or absence of, or full, isolation facilities. No failure of

NOM was observed, and the prolonged LOS observed in some cases was not due to complications from NOM of acute appendicitis. All patients were either sent home, or transferred to a COVID-19 isolation facility, once cleared for discharge. There were no recorded readmissions, morbidities and mortalities in all cases at 30- and 60-days post-discharge.

One patient was readmitted 93 days after discharge for recurrence of abdominal pain. The patient underwent an appendectomy via midline laparotomy incision for ruptured appendicitis. At the time of this writing, the remaining 20 cases were still symptom-free. The overall NOM failure rate was 4.76%. (Figure 1)

Table 1. Demographics of adult cases diagnosed with acute appendicitis, with SARS-CoV-2 infection, managed non-operatively at the PGH from March 2020 to February 2022.

	n	%
NOM	21	
Male	13	61.90%
Female	8	38.10%
Comorbidities	6	28.57%
Hypertension	4	19.05%
Diabetes	2	9.52%
	Median	Range
Age	32	19-81

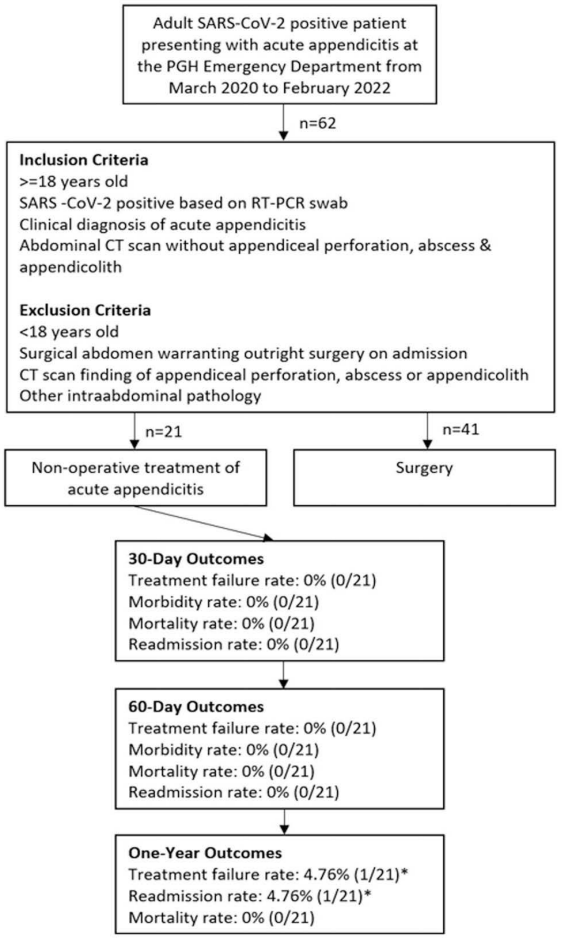

Figure 1. Study flowchart of non-operative management of acute appendicitis in adults with SARS-CoV-2 infection.

DISCUSSION

Acute appendicitis is one of the most common surgical emergencies that is managed primarily with appendectomy, either open or laparoscopic.[7] Although appendectomy is still regarded as the gold standard, there is an increasing global interest in NOM with antibiotic therapy for uncomplicated cases.

The COVID-19 pandemic placed a significant burden on the healthcare system. At the height of the pandemic, patients with COVID-19 inevitably had to be prioritized over other patients. Surgeons had to contend with the reported increased complications seen in patients infected with COVID-19 undergoing surgery.[6]

In this study, all cases of acute appendicitis with SARS-CoV-2 infection with no overt indication for surgery underwent a contrast-enhanced abdominal CT scan to identify the presence of rupture or appendicolith, which may increase the risk of non-operative treatment failure.[8,15] Scoring systems, such as the Alvarado scoring system can be used as an adjunct to assess the severity of acute appendicitis and as an indicator of prognosis. The Alvarado scoring system cannot be reliably used alone to identify patients suitable for non-operative treatment, but it may predict the possibility of treatment failure.[12,13] Although not used in the study, the Alvarado score, and other scoring systems such as the Appendicitis Inflammatory Response, may serve as guides in the diagnosis and treatment selection.[14]

Patients that fit the inclusion criteria for NOM, were administered intravenous cefoxitin, with some variation on the oral antibiotic regimen prescribed upon discharge as the choice was left to the judgment of the primary physician. The APPAC II study demonstrated that oral antibiotics may be as effective as intravenous antibiotics. With oral antibiotic therapy providing an additional advantage of being able to provide home care. In the aforementioned study, it was shown that outpatient NOM of acute appendicitis was found to be noninferior to inpatient NOM. This study suggested that outpatient NOM is safe and effective for uncomplicated acute appendicitis with the potential for reduction in LOS and hospital costs. A wide range (1-22 days) in LOS was noted in our study, which may be explained by the mandatory hospital isolation during the first months of the pandemic. Shorter LOS were recorded when home isolation, or transfer to an isolation facility, were allowed. Use of NOM allowed for shorter LOS, which in turn resulted in faster patient turnover to accommodate more patients. During this period, the patients with a longer hospital stay were often those with severe COVID-19 infection—their long LOS being due to COVID-19 rather than from appendicitis.

The clear benefit of NOM, aside from preventing possible perioperative complications associated with COVID-19, was the more efficient utilization of resources. Due to a decrease in staffing in non-COVID areas as hospital manpower had to be allocated for COVID-related operations, NOM has resulted in earlier discharge, reducing inpatient burden. Even the shorthanded operating rooms benefited from NOM as cases evidently needing surgical intervention were prioritized. The shorter hospital stay seen with NOM also translated to reduced utilization of already limited resources, a critical issue at the height of the pandemic. An interesting proposition, therefore, is the continued employment of NOM for acute appendicitis beyond the pandemic.

For NOM, there was a long-term risk for recurrent appendicitis at 29.8% (outpatient) and 26.2% (inpatient) at 12 months.[8,9] In literature, the rates of treatment failure for NOM vary from 7% to 39%, raising doubts on the overall effectiveness of this modality. All cases were reviewed for signs and symptoms of recurrent appendicitis translating to failure of treatment. Based on the APPAC II trial, "recurrent appendicitis" was diagnosed clinically as determined by a surgeon without predefined clinical criteria, with or without repeat imaging. Patients were under close surveillance for up to a year. Only one (4.76%) patient had treatment failure 93 days after discharge, and was readmitted for ruptured appendicitis for which surgery was performed.

All appendectomies performed in the study were approached through an open technique. At the beginning of the pandemic, there were uncertainties about the safety of performing laparoscopic procedures for both the patient and the operating room personnel in COVID-19 positive patients, hence open procedures were encouraged. However, later systematic reviews showed that laparoscopy can be safely performed in COVID-19 cases with the recommended COVID-19 precautions, and allow for its benefits over open surgery to be realized.[16]

Based on the data gathered, an algorithm for managing acute uncomplicated appendicitis for patients with SARS-CoV-2 infection is proposed. All confirmed hemodynamically stable cases with COVID-19 clinically diagnosed with acute appendicitis with no diffuse peritonitis on physical examination should have an abdominal CT scan. All imaging-confirmed uncomplicated appendicitis cases (e.g. absence of rupture, abscess and appendicolith) may be safely enrolled for NOM (Figure 2).

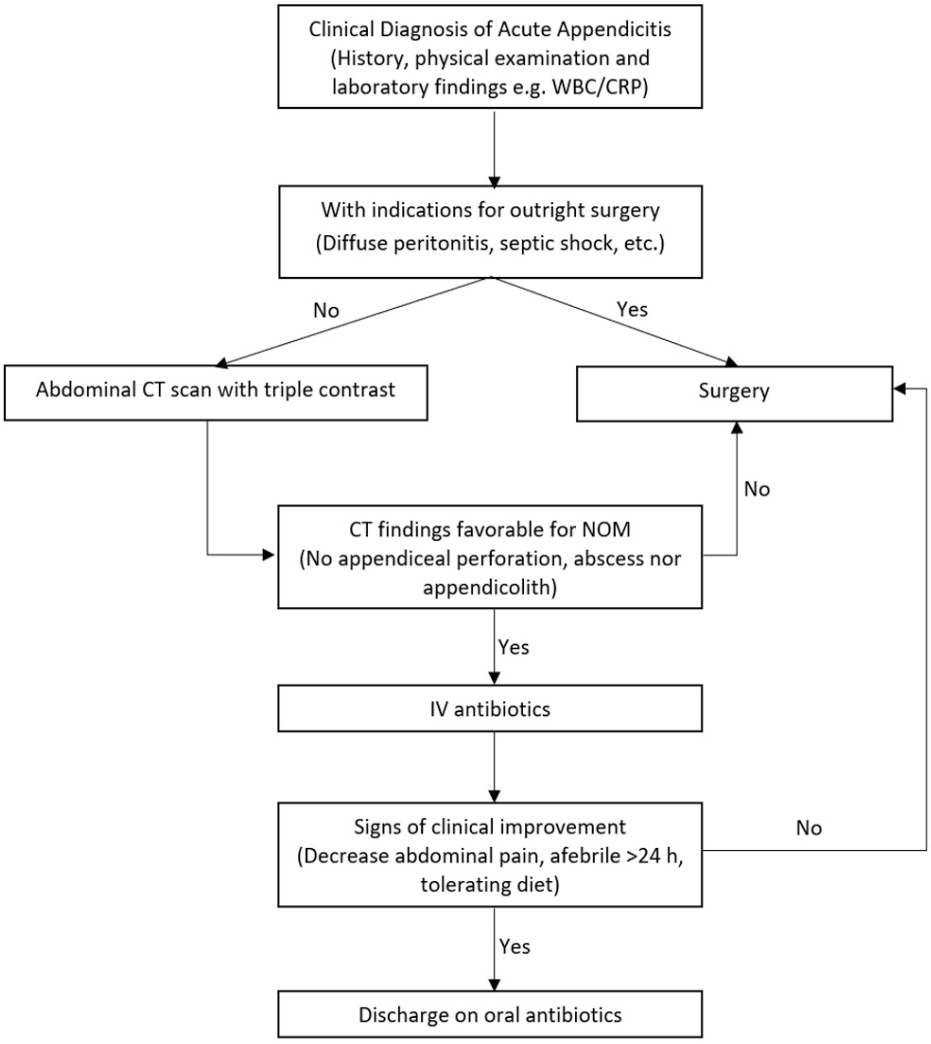

Figure 2. Proposed algorithm for non-operative management of acute appendicitis in patients with SARS-CoV-2 infection.

To date, no guidelines favor NOM for acute appendicitis over surgery. In fact, surgery remains to be the standard of treatment. The treatment failure rate observed in this study is lower as compared to literature. While the pandemic has been declared to be over, this study shows that NOM is still a viable treatment option when faced with similar cases—particularly, those with severe COVID-19 and for those determined to be at high risk for surgery. Furthermore, in the unfortunate event of another health crisis, NOM may be looked into as a means of assisting in the proper allocation of resources.

Limitations of the study include non-randomization of patients into either NOM or surgery. Due to the much-needed immediate response to the pandemic at the time and lack of pre-existing COVID-19-related surgery protocols, modifications of management strategies were based not on clinical guidelines but rather on sound clinical judgement and individual consultant opinion which may have also introduced further bias. Results and the proposed algorithm from the study are also based only on a small sample size and a relatively short follow-up period.

CONCLUSION

Non-operative treatment for uncomplicated appendicitis can be safely and effectively applied after careful patient selection as an alternative to surgical management in COVID-19 cases with acceptable treatment failure, readmission, morbidity and mortality rates. This approach, however, requires

close monitoring and careful clinical re-evaluation for early recognition of treatment failure to prevent complications.

A proposed algorithm of NOM for uncomplicated appendicitis in SARS-CoV-2 positive patients was made, which may be tailored for use in future health crises.

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