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Concurrent SARS-COV-19 and acute appendicitis: Management and outcomes across United States children's hospitals

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ABSTRACT

Background: Nonoperative management of acute appendicitis is a safe and effective alternative to appendectomy, though rates of treatment failure and disease recurrence are significant. The purpose of this study was to determine whether COVID-19–positive children with acute appendicitis were more likely to undergo nonoperative management when compared to COVID-19–negative peers and to compare clinical outcomes and healthcare use for these groups.

Methods: A retrospective cohort study of children <18 years with acute appendicitis across 45 US Children's Hospitals during the first 12 months of the COVID-19 pandemic was performed. Operative management was defined as appendectomy or percutaneous drain placement, whereas nonoperative management was defined as admission with antibiotics alone. Multivariable hierarchical logistic regression using an exact matched cohort was used to determine the association between COVID-19 positivity and nonoperative management. The secondary outcomes included intensive care unit admission, mechanical ventilation, length of stay, nonoperative management failure rates, and hospital variation in nonoperative management.

Results: Of 17,481 children in the cohort, 581 (3.3%) were positive for COVID-19. The odds of nonoperative management was significantly higher in the COVID-19–positive group (adjusted odds ratio [95% confidence interval]: 13.4 [10.7–16.8], $P < .001$). Patients positive for COVID-19 had increased odds of intensive care unit admission (adjusted odds ratio [95% confidence interval]: 3.78 [2.01–7.12], $P < .001$) and longer length of stay (median 2 days vs 1 day, $P < .001$). Hospital rates of nonoperative management ranged from 0% to 100% for COVID-19–positive patients and 0% to 42% for COVID-19–negative patients.

Conclusion: Children with concurrent acute appendicitis and COVID-19 positivity are significantly more likely to undergo nonoperative management. Both groups experience infrequent nonoperative management failure rates and rare intensive care unit admissions. Marked hospital variability in nonoperative management practices was demonstrated.

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Introduction

Nonoperative management (NOM) with antibiotics is a safe and effective alternative to appendectomy for acute appendicitis in adults and children.^{1–5} The key disadvantage of NOM is its potential for treatment failure; rates of disease recurrence after NOM requiring subsequent operation have been reported as high as 25% to 40% at 1 year.^{6–8} Many providers and caregivers are willing to accept the perioperative risks of appendectomy for the greater likelihood of definitive treatment, and operative management remains the most common treatment for acute appendicitis in the US.^{6,7,9}

However, the COVID-19 pandemic brought renewed attention to this management decision, especially for patients who were found to be concurrently positive for severe acute respiratory syndrome coronavirus 2 (hereafter, “COVID-19–positive”).^{10–15} Foremost, the impact of COVID-19 infection on the risk of anesthetic and surgical complications due to pulmonary and immune system compromise was unknown.^{12,16} Second, avoiding or delaying surgery was believed to enhance provider and staff safety by minimizing their risks of COVID-19 exposure from aerosol-generating procedures.^{11,17,18} Finally, NOM offered an opportunity to spare hospital resources in some settings, an important consideration when hospital and operating room capacities were limited.^{6,19–21} The American College of Surgeons released COVID-19 Emergency General Surgery triage guidelines emphasizing that surgeons should consider NOM as a first-line treatment recommendation for acute appendicitis while also

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factoring in patient preferences and local resources (eg, hospital staff, bed, and supply availability).²¹

Despite these recommendations and theoretical advantages of NOM for COVID-19–positive patients, information about subsequent practice patterns during the pandemic is lacking, especially for the pediatric population.^{12,15,22,23} There are single institution studies and small case series describing the preferential use of NOM for COVID-19–positive children,^{14,24,25} but no multicenter studies have been reported. It is unknown how pediatric patients with concurrent appendicitis and COVID-19 positivity were managed across the US and to what extent patient outcomes and healthcare use were impacted.

The purpose of this study was to determine whether COVID-19–positive children with acute appendicitis presenting to US children's hospitals were more likely to undergo NOM when compared to COVID-19–negative peers. Second, we aimed to compare key healthcare use outcomes in these groups, including length of stay (LOS), readmissions for failure of NOM, and intensive care use. We hypothesized that COVID-19–positive patients were more likely to undergo NOM, but we anticipated that both groups had acceptable outcomes and similar overall healthcare use.

Methods

This study was approved by the Institutional Review Board at our institution, and the requirement for informed consent was waived because patient-level data were deidentified. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline.

Study design and data source

A retrospective matched cohort study was performed using the Pediatric Health Information System (PHIS). The PHIS is an administrative database that contains inpatient, emergency department (ED), ambulatory surgery, and observation encounter-level data from >40 not-for-profits, tertiary care pediatric hospitals in the US affiliated with the Children's Hospital Association (Lenexa, KS). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS database are managed by Truven Health Analytics (Ann Arbor, MI). Data are subjected to reliability and validity checks before being included in the database.

Inclusion criteria

We included all children aged <18 years with a primary diagnosis of acute appendicitis based on the *International Classification of Diseases, Tenth Edition* (ICD-10) codes (included in [Supplementary Table S1](#)). Patients who were treated during the first 12 months of the COVID-19 pandemic, between April 1, 2020 and March 31, 2021, were included. Data from 45 Children's Hospitals were updated through July 31, 2021 and therefore allowed for adequate 90-day follow-up. Data from 1 hospital were excluded due to known operating room closures during this period. The COVID-19 infection status was based on the previously validated ICD-10 code U07.1.^{26,27} Appendectomy and drainage procedures were identified through ICD-10 and Current Procedural Terminology codes ([Supplementary Table S1](#)).

Outcomes

Our primary outcome was NOM, defined as patients with acute appendicitis who were admitted to an observation or inpatient bed,

received a pharmacy charge for parenteral antibiotics, and did not undergo an appendectomy or drainage procedure during their index admission. Specifically, parenteral administration of an antibiotic within any of the following therapeutic categories was needed to fit NOM criteria: aminoglycoside/penicillin, cephalosporin/macrolide, tetracycline/fluoroquinolone, and miscellaneous antibiotic/sulfa. Patients who underwent percutaneous drain placement during their index admission were included in operative management group. Our secondary outcomes included an intensive care unit (ICU) admission, mechanical ventilation, index admission LOS, and failure of NOM. Failure of NOM was defined as readmission through the ED for an appendectomy or percutaneous drain placement within 90 days after discharge from NOM. Patients who returned to the hospital for operative management on an elective basis (ie, for an interval appendectomy) were not considered to have NOM failure.

Covariates

Demographic and clinical data pertaining to all included patients were extracted from the database and included age, sex, race, ethnicity, presence of complex chronic conditions, primary insurance payor, ZIP Code-based median household income, geographic census region, and urban versus rural residence. Race was self-reported and based on the following US Census groups: White, Black or African American, American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander. Ethnicity was self-reported as Hispanic/Latino or Not Hispanic/Latinx. Patients were subsequently grouped as Non-Hispanic White, Non-Hispanic Black, Hispanic/Latinx, and Other. Primary insurance payor based on the index hospitalization was grouped as Private, Public, or Other/Self-Pay. Appendiceal perforation status was determined based on ICD-10 codes specifying perforation or abscess ([Supplementary Table S1](#)). The presence of a complex chronic condition is a binary variable provided by PHIS and indicates chronic disease in at least 1 of the following categories: cardiovascular, respiratory, neuromuscular, renal, gastrointestinal, hematologic or immunologic, metabolic, other congenital or genetic, and malignancy.²⁸

Statistical approach

Statistical analysis was performed using R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). An exact-matched cohort analysis was used to assess the independent association between COVID-19 positivity and NOM. The exact matching approach was chosen because it is an ideal method for ensuring patients are paired on key confounding variables of interest.^{29,30} It is most useful when the resulting proportion of unmatched, discarded patients is small in order to preserve statistical power.^{29,30} Two exact matching variables were chosen based on previous research and expert clinical experience regarding factors most likely to influence the likelihood of NOM: perforation status and treating hospital.^{31,32} The balance of all remaining variables was assessed using standardized mean differences (SMD).^{29,30} The variables with absolute SMDs >0.1 were included as covariates in the subsequent multivariable conditional regressions. This analysis was performed using the MatchIt package in R.³³

Univariate analyses were performed using Fisher exact or Pearson χ^2 statistic for discrete variables and Wilcoxon rank sum tests for the continuous variables, when appropriate. Hierarchical multivariable conditional regression models were developed using the exact-matched cohort to determine the association between COVID-19 positivity and our primary and secondary outcomes. Separate models were developed for each outcome—logistic regression was used for categorical outcomes, and Poisson regression was used for LOS. As above, covariates not used for matching

Table 1
Demographic and clinical characteristics of the matched cohort

	COVID-19 negative (n = 16,404)	COVID-19 positive (n = 581)	P value*	Absolute SMD
Age, median (IQR), y	11.0 (8.0–14.0)	11.0 (8.0–14.0)	.5	0.03
Sex, n (%)			> .9	0.003
Female patients	6,496 (40%)	231 (40%)		
Male patients	9,908 (60%)	350 (60%)		
Race/Ethnicity, n (%)			< .001	
Non-Hispanic White	7,282 (44%)	153 (26%)		0.41
Non-Hispanic Black	1,055 (6.4%)	30 (5.2%)		0.06
Hispanic/Latino	6,711 (41%)	360 (62%)		0.43
Other	1,356 (8.3%)	38 (6.5%)		0.07
Insurance, n (%)			< .001	
Private	6,929 (42%)	179 (31%)		0.25
Public	8,527 (52%)	353 (61%)		0.18
Other/self-pay	948 (5.8%)	49 (8.4%)		0.09
ZIP Code median household income quartile, n (%)			< .001	
1 (<\$34,714)	4,154 (25%)	189 (33%)		0.15
2 (\$34,714–\$44,085)	4,064 (25%)	161 (28%)		0.07
3 (\$44,086–\$57,271)	4,049 (25%)	126 (22%)		0.07
4 (>\$57,271)	4,137 (25%)	105 (18%)		0.19
Residential Location, n (%)			.9	0.01
Rural	1,676 (10%)	58 (10.0%)		
Urban	14,728 (90%)	523 (90%)		
Perforated appendicitis, n (%)	5,486 (33%)	205 (35%)	.4	0.00
Complex chronic condition, n (%)	783 (4.8%)	34 (5.9%)	.2	0.05
Census region, n (%)			.003	
Northeast	1,517 (9.2%)	32 (5.5%)		0.16
Midwest	3,256 (20%)	106 (18%)		0.04
South	7,465 (46%)	269 (46%)		0.02
West	4,166 (25%)	174 (30%)		0.10

SMD, standardized mean difference.

* Wilcoxon rank sum test; Pearson's χ^2 analysis.

were included in the multivariable models if their absolute SMDs were >0.1. The treating hospital was included as a random effect within all models to account for potential clustering within hospitals. Multicollinearity of variables was assessed using the variance inflation factor.³⁴ Model discrimination was assessed using the area under the receiver operating characteristic curve.³⁵ Overall model performance and calibration was assessed using Brier Scores and Hosmer-Lemeshow tests for logistic regression models.^{35,36} Pearson and deviance χ^2 analysis statistics were used to assess goodness-of-fit for the Poisson regression models.³⁷ Our multivariable models included race/ethnicity, insurance, ZIP Code-based median household income quartile, and census region as covariates.

To evaluate for hospital variation in NOM, we calculated each hospital's rate of NOM for COVID-19–positive and COVID-19–negative patients and generated ranges. To test for an association between NOM rates for COVID-19–positive patients and NOM rates for COVID-19–negative patients at each hospital, we used Pearson's correlation coefficient. We plotted overall rates of NOM on a per-month basis for COVID-19–positive and COVID-19–negative groups to assess trends over time.

Sensitivity analysis

A sensitivity analysis was prespecified to examine the subgroup of patients with non-perforated appendicitis. This sensitivity analysis was performed because the optimal treatment strategy for patients with perforated appendicitis (ie, NOM versus immediate or delayed operation, with or without percutaneous drainage) remains controversial and may be affected by additional clinical features not accounted for in PHIS, such as abscess size.^{4,31,38} The same statistical methods described above were applied to our subgroup of nonperforated cases.

Results

During the first 12 months of the COVID-19 pandemic, a total of 17,481 children were treated for acute appendicitis in 45 US children's hospitals. Of these patients, 581 (3.3%) were concurrently COVID-19–positive. After exact-matching on treating hospital and perforation status, 100% (581/581) of the COVID-19–positive patients were matched, and 97.0% (16,404/16,900) of the COVID-19–negative patients were matched, leaving 496 unmatched COVID-19–negative patients who were thus discarded from the analyses.

When comparing COVID-19–positive and COVID-19–negative patients after matching, there were no significant differences with respect to age, sex, urban versus rural residence, appendiceal perforation status, or the presence of complex chronic conditions (Table 1). However, COVID-19–positive patients were more likely to be Hispanic/Latinx (62% vs 41%, $P < .001$), have public insurance (61% vs 52%, $P < .001$), live in a ZIP Code within the lowest median household income quartile (33% vs 25%, $P < .001$), and live in the West region (30% vs 25%, $P < .001$) compared to COVID-19–negative patients (Table 1).

Perioperative outcomes for COVID-19–positive patients treated with operative versus NOM are presented in Table 2. COVID-19–positive patients who underwent operative management were more likely to have abscess or perforation (42% vs 19%, $P < .001$) compared to COVID-19–positive patients treated with NOM. There were no significant differences in the presence of appendicolith, index hospitalization LOS, ICU admission, or mechanical ventilation between the operative versus NOM groups of COVID-19–positive patients ($P > .05$). Of the 416 COVID-19–positive patients who underwent operative management, 29 (7.0%) included a drain placement.

Univariate analysis of the matched cohort

The univariate analysis between COVID-19–positive and COVID-19–negative patients is shown in Table 3. The COVID-

Table II
Perioperative outcomes for COVID-19–positive patients with operative vs nonoperative management of acute appendicitis

	Operative Management (n = 416)	Nonoperative Management (n = 165)	P value*
Appendicolith, n (%)	44 (11%)	21 (13%)	.5
Perforated, n (%)	173 (42%)	32 (19%)	< .001
Drain, n (%)	29 (7.0%)	0 (0%)	< .001
Length of stay, median (IQR)	2.00 (1.00–4.25)	2.00 (1.00–3.00)	.7
ICU admission, n (%)	9 (2.2%)	3 (1.8%)	.9
Mechanical ventilation, n (%)	3 (0.7%)	0 (0%)	.6

ICU, intensive care unit.

* Pearson's χ^2 analysis; Wilcoxon rank sum test; Fisher exact test.**Table III**
Univariate analysis of the effect of COVID-19 positivity on nonoperative management and healthcare use for patients with acute appendicitis

	COVID-19 Negative (n = 16,404)	COVID-19 Positive (n = 581)	Absolute Difference*	95% CI*	P value†
Nonoperative management, n (%)	706 (4.3%)	165 (28.4%)	24.1%	+20%, +28%	< .001
ICU admission, n (%)	104 (0.6%)	12 (2.1%)	1.4%	+0.18%, +2.7%	< .001
Mechanical ventilation, n (%)	30 (0.2%)	3 (0.5%)	0.33%	+0.34%, +1.0%	.10
Length of stay, median (IQR)	1.00 (1.00–3.00)	2.00 (1.00–4.00)	0.63	+0.36, +0.90	< .001
Failure of nonoperative management, n (%)	41 (5.8%)	11 (6.7%)	0.86%	3.7%, –5.4%	.70

ICU, intensive care unit.

* Two sample test for equality of proportions; Welch 2-sample *t* test.† Pearson's χ^2 analysis; Fisher exact test; Wilcoxon rank sum test.

19–positive patients had higher rates of NOM compared to their COVID-19–negative peers (28.4% vs 4.3%, absolute difference [AD] [95% CI]: +24.1% [+20% to +28%], $P < .001$). The COVID-19–positive patients also had higher rates of ICU admission compared to their COVID-19–negative peers (2.1% vs 0.6% AD [95% CI]: +1.4% [+0.18% to +2.7%], $P < .001$). There were no significant differences in rates of mechanical ventilation between COVID-19–positive and COVID-19–negative patients (0.5% vs 0.2%, AD [95% CI]: +0.33% [+0.34% to +1.0%], $P = .10$). The median index hospital admission LOS was significantly longer for the COVID-19–positive group (2.0 days vs 1.0 days, AD [95% CI]: +0.63 [+0.36 to +0.90], $P < .001$). The rates of NOM failure were not significantly different between COVID-19–positive and COVID-19–negative patients (6.7% vs 5.8%, AD [95% CI]: +0.86% [+0.36 to +0.90], $P = .70$).

Hierarchical multivariable logistic regression

The results of our multivariable analyses assessing the impact of COVID-19 positivity on primary and secondary outcomes are shown in [Table IV](#). The adjusted odds of receiving NOM were significantly higher in the COVID-19–positive group compared to the COVID-19–negative group (adjusted odds ratio [aOR] [95% CI]: 13.4 [10.7–16.8], $P < .001$). The adjusted odds of ICU admission were significantly higher in the COVID-19–positive group (aOR [95% CI]: 3.78 [2.01–7.12], $P < .001$); however, there were no significant differences in the odds of mechanical ventilation (aOR [95% CI]: 3.14 [0.94–10.5], $P = .06$). Patients who were COVID-19–positive did not have an increased odds of failing NOM compared to COVID-19–negative patients (aOR [95% CI]: 1.15 [0.55–2.41], $P = .7$). The full models for all outcomes are included in [Supplementary Table S2](#). Our sensitivity analysis of patients with nonperforated appendicitis revealed the same trends for all outcomes ([Supplementary Tables S3 and S4](#)).

Temporal trends and hospital variability

When considering total NOM rates across all hospitals, there was no evident change during the first year of the pandemic for COVID-19–negative patients—NOM rates for COVID-19–negative patients remained approximately 5% throughout the study period ([Figure 1](#)). In contrast, for COVID-19–positive patients, there was an increase in NOM rates during the first 4 months of the pandemic, followed by a gradual decrease after August 2020 ([Figure 1](#)). There was marked variability in management practices at the hospital level; the average rates of NOM over the course of 1 year ranged from 0% to 100% for COVID-19–positive patients and 0% to 42% for COVID-19–negative patients ([Figure 2](#)). There was a significant association between each hospital's rate of NOM for COVID-19–positive patients and their rate of NOM for COVID-19–negative patients (Pearson $r[43] = 0.34$, $P = .02$).

Discussion

This study is the first to describe the in-hospital and short-term outcomes for pediatric patients with concurrent COVID-19 infection and acute appendicitis across US children's hospitals, and it has three notable and novel findings. First, COVID-19–positive children were significantly more likely to undergo NOM compared to COVID-19–negative peers. Second, outcomes were acceptable for both groups, with low rates of NOM failure at 90 days and rare ICU admissions. Third, there was substantial hospital variability with regard to the adoption of NOM during this time. Our findings have important implications for patient safety, healthcare resource use, and shared decision-making with families.

At the start of the pandemic, there were natural concerns about the safety of endotracheal intubation and surgery for COVID-19–positive patients.^{16,18} An early report from the Lancet's "COV-IDSurg" Collaborative demonstrated dramatically increased morbidity and mortality in 1,128 patients with perioperative

Table IV

Multivariable hierarchical conditional regression analyses showing the effect of COVID-19 positivity on nonoperative management and healthcare use for patients with acute appendicitis

	Adjusted* OR [†] or IRR [‡]	95% CI	P value
Nonoperative management	13.4	10.7–16.8	< .001
ICU admission	3.78	2.01–7.12	< .001
Mechanical ventilation	3.14	0.94–10.5	.064
Length of stay	1.18	1.13–1.24	< .001
Failure of nonoperative management	1.15	0.55–2.41	.7

ICU, intensive care unit; IRR, incident rate ratios; OR, odds ratio.

* Final models included covariate adjustment for race/ethnicity, insurance payor, ZIP Code based median household income quartile, and census region, with hospital as a random effect.

† Adjusted OR are reported for binary categorical variables: nonoperative management, ICU admission, mechanical ventilation, and failure of nonoperative management.

‡ Adjusted IRR are reported for length of stay.

Trends in Non-Operative Management of Acute Appendicitis During the First Year of the COVID-19 Pandemic

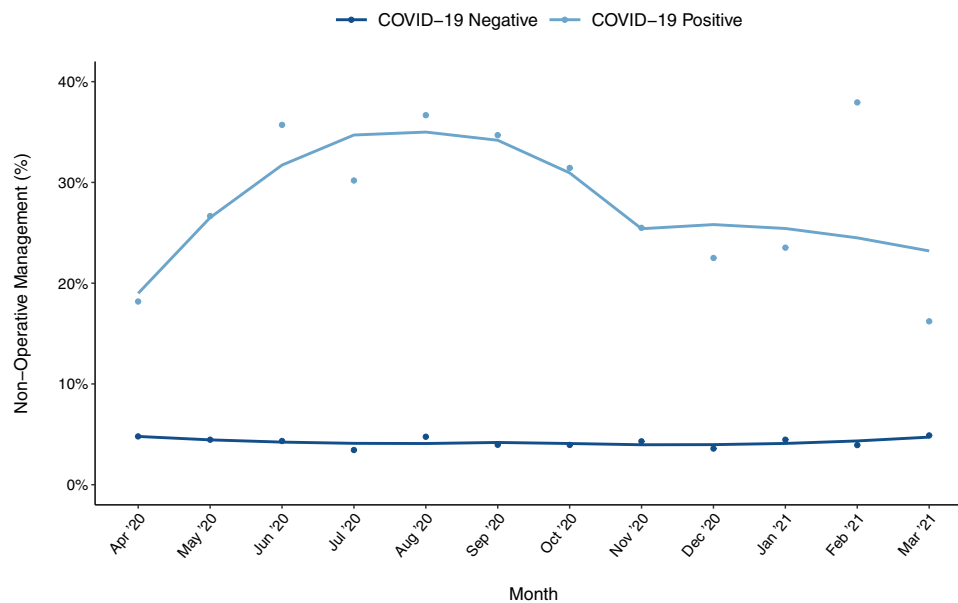


Figure 1. Trends in nonoperative management of acute appendicitis during the first year of the COVID-19 pandemic across 45 tertiary care pediatric hospitals in the US. Monthly rates of nonoperative management for COVID-19–negative patients are represented in dark blue; monthly rates of nonoperative management of COVID-19–positive patients are represented in light blue.

COVID-19 infection—30-day mortality was 23.8%, and pulmonary complications occurred in 51.2%.¹⁶ Multiple subsequent studies confirmed a strong association between perioperative COVID-19 infection and serious postoperative complications.^{39–41} These early data, combined with efforts to protect hospital staff from operating room exposures, likely influenced many providers to shift toward more frequent NOM for acute appendicitis.^{12,15,23}

Importantly, the abovementioned studies concerning postoperative complications were focused on adults,^{27,39–41} and emerging data specific to children with perioperative COVID-19 infections has yielded better results.^{42–44} Nepogodiev et al used the same “COVIDSurg” prospective cohort to study 88 children with COVID-19 positivity; in contrast to the poor outcomes seen in adults, they found 0% mortality and only 13% postoperative pulmonary complications (eg, pneumonia, unexpected postoperative mechanical ventilation, and/or acute respiratory distress syndrome) in children.⁴⁵ Saynhalath et al reviewed 51 cases of surgical patients with COVID-19 positivity and found similar results—11.8% suffered pulmonary complications, with rare severe morbidity and 0% mortality.⁴³ Mehl et al

described infrequent (7%) postoperative complications and 0% mortality for COVID-19–positive children who underwent surgery at their institution.⁴² Our findings from a large, multicenter US cohort provide additional reassurance on this matter—of the 416 COVID-19–positive children who underwent operative management for acute appendicitis, 9 (2.1%) required ICU admission, 3 (0.7%) required postoperative mechanical ventilation, and no patients died. Our data supports the perspective that children with COVID-19 positivity have a relatively small increased risk of postoperative complications, and therefore delays in surgery may be unnecessary from a patient safety perspective.^{42,44,45}

Less than 6% of all patients treated with NOM in our cohort returned to the hospital for appendectomy within 90 days, a short-term failure rate in line with previously published, prepandemic studies.⁴⁶ Some authors have expressed concern that children with concurrent COVID-19 infection may experience exaggerated inflammatory responses to appendicitis that can impact their disease severity and likelihood of treatment success.^{12,47} For example, Emile et al reported high failure rates of NOM (43%) for the 7

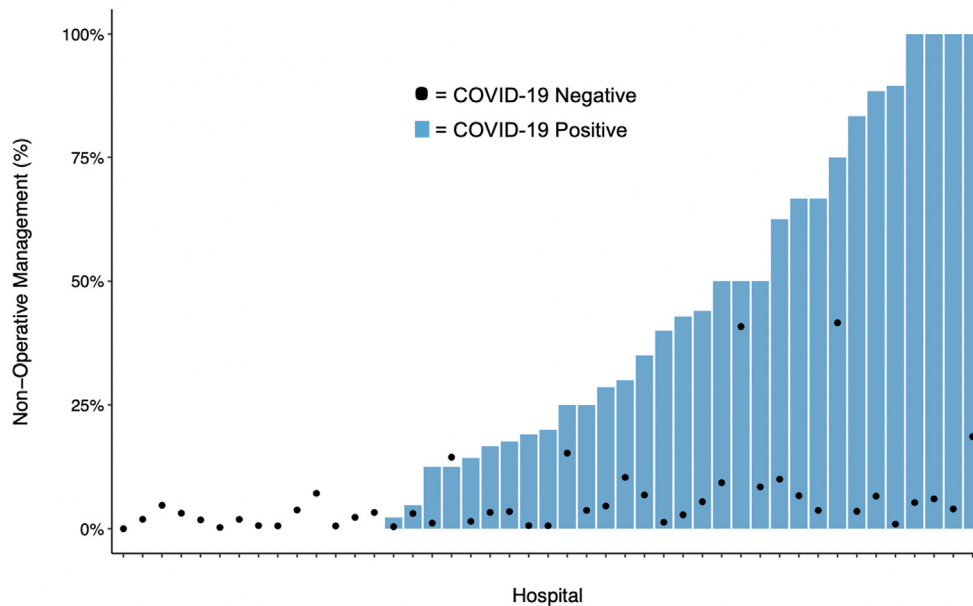


Figure 2. Hospital variability in nonoperative management of acute appendicitis, during the first year of the COVID-19 pandemic. Each tick on the x-axis represents 1 hospital. The light blue bars represent each hospital's rate of nonoperative management for COVID-19–positive patients. The black dots represent the same hospital's rate of nonoperative management for COVID-19–negative patients.

COVID-19–positive children included in their meta-analysis.^{12,47} They proposed that COVID-19–positive patients may respond differently to antibiotic therapy and, therefore, may be more likely to fail NOM.¹² Fortunately, data from our present study suggest otherwise; COVID-19–positive children were not more likely to fail NOM when compared to COVID-19–negative peers. We believe these findings of our large cohort are important to fully inform the shared decision-making process of providers and families when choosing between surgery and antibiotics.^{2,9}

In addition to safety and efficacy concerns, efficient resource use became an essential objective during the pandemic. To preserve hospital bed space and free up healthcare personnel, strategies were proposed to delay elective surgeries and pursue nonoperative therapies when possible.^{21,23} Yet, finding the optimal resource strategy for acute appendicitis is complex because the potential advantages offered by NOM are dependent on patients' disease severity and odds of NOM success.^{20,48,49} Because many children can be discharged soon after their appendectomy, they may require shorter LOS compared to patients managed with NOM, especially for early, uncomplicated cases.⁴⁸ At the start of the pandemic, it was unknown whether patients with COVID-19 positivity would require longer durations of antibiotic therapy, significant ICU resources, or fail NOM more frequently when compared to COVID-19–negative peers. We found that patients who were COVID-19 positive had only slightly longer LOS (with a mean difference of <1 day), rare ICU admissions, and equally low failure rates of NOM. Based on our data, both NOM and operative management appear to be reasonable and comparable strategies from a healthcare use perspective, regardless of COVID-19 status.

We anticipated that the rates of NOM would be highest at the start of the pandemic and decline over time as data about patient safety and infection control emerged. Our hypothesis was supported by data for the COVID-19–positive group, as there was an early increase in NOM rates followed by a slow downtrend after August 2020. Interestingly, however, there was no such trend when looking at the COVID-19–negative cohort, whose rates of NOM

hovered around 5% for the duration of this study period. The overall adoption of NOM across the tertiary care pediatric US hospitals included in our study was considerably lower than NOM rates previously published in systematic reviews focusing on acute appendicitis management during the pandemic.^{12,15} Whether the infrequent adoption of NOM reflects the strong preferences of providers, patients, and/or institutions warrants further investigation.

We found substantial variability when comparing individual hospitals' rates of NOM during this timeframe. Some hospitals performed 100% NOM, whereas many others continued to treat most of their patients with surgery. The marked variability seen in our study implies that the use of NOM remains controversial and highly dependent on institutional practices. Our findings mirror the huge variation of management strategies seen on the global scale for both adults and children with appendicitis during the pandemic.^{12,15} Based on their meta-analysis, Emile et al reported that the range of NOM rates during the early pandemic was 7.8% to 100%.^{12,15} Geographic differences have been demonstrated as well, with the median rate of NOM in Western countries (US, United Kingdom, and Ireland) found to be 54.2% versus 29.3% in Eastern countries (India, China, and Nepal).¹²

There were several limitations to this study. First, although PHIS is subject to quality assurance audits, misclassification and other coding errors related to diagnoses and therapeutic procedures are possible. However, we suspect that our main outcome—whether a patient underwent appendectomy—has acceptable coding reliability. Second, we only included patients who were admitted to observation and/or inpatient status and, therefore, we excluded those who may have received antibiotics in the ED and were discharged without an observation period. We suspect the total number of these instances to be low and, therefore, unlikely to bias our results. Finally, because we could only measure readmissions to the index hospital, we were unable to capture the proportion of patients who were readmitted to another hospital. This may have led to an

underestimation of NOM failure. We expect that children who were COVID-19–positive and COVID-19–negative were equally likely to return to their index hospital, and, therefore, this potential underestimation is likely nondifferential between the 2 cohorts.

In conclusion, our study provides crucial information for providers and caregivers as they make shared decisions about operative versus NOM for children with acute appendicitis. Both COVID-19–positive and COVID-19–negative children experienced low NOM failure rates, rare ICU admissions, and short LOS. Substantial variation in NOM rates was demonstrated between hospitals. The implementation of evidence-based practice changes, including NOM for acute appendicitis, still faces significant barriers to adoption across the US despite the COVID-19 pandemic.

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Conflict of interest/Disclosure

The authors have no conflicts of interests or disclosures to report.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.surg.2022.12.004>.

References

- Svensson JF, Patkova B, Almström M, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. *Ann Surg*. 2015;261:67–71.
- Minnecci PC, Mahida JB, Lodwick DL, et al. Effectiveness of patient choice in nonoperative vs surgical management of pediatric uncomplicated acute appendicitis. *JAMA Surg*. 2016;151:408–415.
- Tanaka Y, Uchida H, Kawashima H, et al. Long-term outcomes of operative versus nonoperative treatment for uncomplicated appendicitis. *J Pediatr Surg*. 2015;50:1893–1897.
- López JJ, Deans KJ, Minnecci PC. Nonoperative management of appendicitis in children. *Curr Opin Pediatr*. 2017;29:358–362.
- Salminen P, Paajanen H, Rautio T, et al. Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis: the APPAC randomized clinical trial. *JAMA*. 2015;313:2340–2348.
- Flum DR, Davidson GH, Monsell SE, et al. A randomized trial comparing antibiotics with appendectomy for appendicitis. *N Engl J Med*. 2020;383:1907–1919.
- Gonzalez DO, Deans KJ, Minnecci PC. Role of non-operative management in pediatric appendicitis. *Semin Pediatr Surg*. 2016;25:204–207.
- CODA Collaborative, Flum DR, Davidson GH, et al. A randomized trial comparing antibiotics with appendectomy for appendicitis. *N Engl J Med*. 2020;383:1907–1919.
- Hanson AL, Crosby RD, Basson MD. Patient preferences for surgery or antibiotics for the treatment of acute appendicitis. *JAMA Surg*. 2018;153:471–478.
- Antakia R, Xanthis A, Georgiades F, et al. Acute appendicitis management during the COVID-19 pandemic: a prospective cohort study from a large UK centre. *Int J Surg*. 2021;86:32–37.
- Dexter F, Parra MC, Brown JR, et al. Perioperative COVID-19 defense: an evidence-based approach for optimization of infection control and operating room management. *Anesth Analg*. 2020;131:37–42.
- Emile SH, Hamid HKS, Khan SM, et al. Rate of application and outcome of non-operative management of acute appendicitis in the setting of COVID-19: systematic review and meta-analysis. *J Gastrointest Surg*. 2021;25:1905–1915.
- Javanmard-Emamghissi H, Boyd-Carson H, Hollyman M, et al. The management of adult appendicitis during the COVID-19 pandemic: an interim analysis of a UK cohort study. *Tech Coloproctol*. 2021;25:401–411.
- Jones BA, Slater BJ. Non-operative management of acute appendicitis in a pediatric patient with concomitant COVID-19 infection. *J Pediatr Surg Case Rep*. 2020;59:101512.
- Köhler F, Müller S, Hendricks A, et al. Changes in appendicitis treatment during the COVID-19 pandemic - A systematic review and meta-analysis. *Int J Surg*. 2021;95:106148.
- COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet*. 2020;396:27–38.
- Dhillon RS, Rowin WA, Humphries RS, et al. Aerosolisation during tracheal intubation and extubation in an operating theatre setting. *Anaesthesia*. 2021;76:182–188.
- Myles PS, Maswime S. Mitigating the risks of surgery during the COVID-19 pandemic. *Lancet*. 2020;396:2–3.
- Wu JX, Sacks GD, Dawes AJ, et al. The cost-effectiveness of nonoperative management versus laparoscopic appendectomy for the treatment of acute, uncomplicated appendicitis in children. *J Pediatr Surg*. 2017;52:1135–1140.
- Isani MA, Jackson J, Barry WE, et al. Non-operative management is more cost-effective than immediate operation in perforated appendicitis patients with seven or more days of symptoms. *J Surg Res*. 2019;240:70–79.
- The American College of Surgeons. COVID-19 guidelines for triage of emergency general surgery patients; 2020. <https://www.facs.org/covid-19/clinical-guidance/elective-case/emergency-surgery>. Accessed March 5, 2022.
- El Boghdady M, Ewalds-Kvist BM. Laparoscopic surgery and the debate on its safety during COVID-19 pandemic: a systematic review of recommendations. *Surgeon*. 2021;19:e29–e39.
- Collard M, Lakkis Z, Loriau J, et al. Antibiotics alone as an alternative to appendectomy for uncomplicated acute appendicitis in adults: changes in treatment modalities related to the COVID-19 health crisis. *J Visc Surg*. 2020;157:S33–S42.
- Kvasnovsky CL, Shi Y, Rich BS, et al. Limiting hospital resources for acute appendicitis in children: lessons learned from the U.S. epicenter of the COVID-19 pandemic. *J Pediatr Surg*. 2021;56:900–904.
- Fisher JC, Tomita SS, Ginsburg HB, et al. Increase in pediatric perforated appendicitis in the New York City metropolitan region at the epicenter of the COVID-19 outbreak. *Ann Surg*. 2021;273:410–415.
- Kadri SS, Gundrum J, Warner S, et al. Uptake and accuracy of the diagnosis code for COVID-19 among US hospitalizations. *JAMA*. 2020;324:2553–2554.
- Centers for Disease Control and Prevention. ICD-10-CM official coding and reporting guidelines: April 1, 2020 through September 30, 2020. <https://www.cdc.gov/nchs/icd/icd10cm.htm>. Accessed March 9, 2022.
- Feudtner C, Feinstein JA, Zhong W, et al. Pediatric complex chronic conditions classification system version 2: updated for ICD-10 and complex medical technology dependence and transplantation. *BMC Pediatr*. 2014;14:199.
- Stuart EA. Matching methods for causal inference: a review and a look forward. *Stat Sci*. 2010;25:1–21.
- Burden A, Roche N, Miglio C, et al. An evaluation of exact matching and propensity score methods as applied in a comparative effectiveness study of inhaled corticosteroids in asthma. *Pragmat Obs Res*. 2017;8:15–30.
- Zavras N, Vaos G. Management of complicated acute appendicitis in children: still an existing controversy. *World J Gastrointest Surg*. 2020;12:129–137.
- Boland PA, Donlon NE, Kelly ME, et al. Current opinions and practices for the management of acute appendicitis: an international survey. *Ir J Med Sci*. 2021;190:749–754.
- Ho D, Imai K, King G, et al. MatchIt: nonparametric preprocessing for parametric causal inference. *J Stat Softw*. 2011;42:1–28.
- Fox J, Monette G. Generalized collinearity diagnostics. *J Am Stat Assoc*. 1992;87:178–183.
- Steyerberg EW, Vickers AJ, Cook NR, et al. Assessing the performance of prediction models: a framework for traditional and novel measures. *Epidemiology*. 2010;21:128–138.
- Huang Y, Li W, Macheret F, et al. A tutorial on calibration measurements and calibration models for clinical prediction models. *J Am Med Assoc*. 2020;27:621–633.
- Michael JM, Ian S. A comprehensive methodology for the fitting of predictive accident models. *Accid Anal Prev*. 1996;28:281–296.
- Nimmagadda N, Matsushima K, Piccinini A, et al. Complicated appendicitis: immediate operation or trial of nonoperative management? *Am J Surg*. 2019;217:713–717.
- Doglietto F, Vezzoli M, Gheza F, et al. Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (COVID-19) in Italy. *JAMA Surg*. 2020;155:691–702.
- Knisely A, Zhou ZN, Wu J, et al. Perioperative morbidity and mortality of patients with COVID-19 who undergo urgent and emergent surgical procedures. *Ann Surg*. 2021;273:34–40.
- Jonker PKC, van der Plas WY, Steinkamp PJ, et al. Perioperative SARS-CoV-2 infections increase mortality, pulmonary complications, and thromboembolic events: a Dutch, multicenter, matched-cohort clinical study. *Surgery*. 2021;169:264–274.

42. Mehl SC, Loera JM, Shah SR, et al. Favorable postoperative outcomes for children with COVID-19 infection undergoing surgical intervention: experience at a free-standing children's hospital. *J Pediatr Surg.* 2021;56:2078–2085.
43. Saynalath R, Alex G, Efun PN, et al. Anesthetic complications associated with severe acute respiratory syndrome coronavirus 2 in pediatric patients. *Anesth Analg.* 2021;133:483–490.
44. Glasbey J. Peri-operative outcomes of surgery in children with SARS-CoV-2 infection. *Anaesthesia.* 2022;77:108–109.
45. Nepogodiev D. Favourable perioperative outcomes for children with SARS-CoV-2. *Br J Surg.* 2020;107:e644–e645.
46. Huang L, Yin Y, Yang L, et al. Comparison of antibiotic therapy and appendectomy for acute uncomplicated appendicitis in children: a meta-analysis. *JAMA Pediatr.* 2017;171:426–434.
47. Malhotra A, Sturgill M, Whitley-Williams P, et al. Pediatric COVID-19 and appendicitis: a gut reaction to SARS-CoV-2? *Pediatr Infect Dis J.* 2021;40:e49–e55.
48. Kashyap MV, Reisen B, Hornick MA, et al. Same-day discharge after laparoscopic appendectomy for non-perforated appendicitis is safe and cost effective. *Pediatr Surg Int.* 2021;37:859–863.
49. Mudri M, Coriolano K, Bütter A. Cost analysis of nonoperative management of acute appendicitis in children. *J Pediatr Surg.* 2017;52:791–794.