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Patient and Process Outcomes among Pediatric Patients Undergoing Appendectomy during the COVID-19 Pandemic: An International Retrospective Cohort Study

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ABSTRACT

Background: COVID-19 forced healthcare systems to make unprecedented changes in clinical care processes. The authors hypothesized that the COVID-19 pandemic adversely impacted timely access to care, perioperative processes, and clinical outcomes for pediatric patients undergoing primary appendectomy.

Methods: A retrospective, international, multicenter study was conducted using matched cohorts within participating centers of the international *PE*diatric *A*nesthesia *CO*VID-19 *C*ollaborative (PEACOC). Patients younger than 18 yr old were matched using age, American Society of Anesthesiologists Physical Status, and sex. The primary outcome was the difference in hospital length of stay of patients undergoing primary appendectomy during a 2-month period early in the COVID-19 pandemic (April to May 2020) compared with prepandemic (April to May 2019). Secondary outcomes included time to appendectomy and the incidence of complicated appendicitis.

Results: A total of 3,351 cases from 28 institutions were available with 1,684 cases in the prepandemic cohort matched to 1,618 in the pandemic cohort. Hospital length of stay was statistically significantly different between the two groups: 29 h (interquartile range: 18 to 79) in the pandemic cohort *versus* 28 h (interquartile range: 18 to 67) in the prepandemic cohort (adjusted coefficient, 1 [95% CI, 0.39 to 1.61]; $P < 0.001$), but this difference was small. Eight centers demonstrated a statistically significantly longer hospital length of stay in the pandemic period than in the prepandemic period, while 13 were shorter and 7 did not observe a statistically significant difference. During the pandemic period, there was a greater occurrence of complicated appendicitis, prepandemic 313 (18.6%) *versus* pandemic 389 (24.1%), an absolute difference of 5.5% (adjusted odds ratio, 1.32 [95% CI, 1.1 to 1.59]; $P = 0.003$). Preoperative SARS-CoV-2 testing was associated with significantly longer time-to-appendectomy, 720 min (interquartile range: 430 to 1,112) with testing *versus* 414 min (interquartile range: 231 to 770) without testing, adjusted coefficient, 306 min (95% CI, 241 to 371; $P < 0.001$), and longer hospital length of stay, 31 h (interquartile range: 20 to 83) with testing *versus* 24 h (interquartile range: 14 to 68) without testing, adjusted coefficient, 7.0 (95% CI, 2.7 to 11.3; $P = 0.002$).

Conclusions: For children undergoing appendectomy, the COVID-19 pandemic did not significantly impact hospital length of stay.

(Anesthesiology 2023; 139:35–48)

EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- The COVID-19 pandemic caused challenges in access to clinical care and alterations in clinical process for operative and nonoperative care
- It remains unknown whether common pediatric procedures, such as appendectomy for operative management of acute appendicitis, demonstrated differences in length of stay, time to surgery, or clinical outcomes during the early stages of the pandemic

What This Article Tells Us That Is New

- A total of 1,618 pediatric patients across 28 institutions undergoing appendectomy from April to May 2020 were age, sex, and American Society of Anesthesiologists Physical Status matched to 1,684 similar patients treated in April to May 2019
- Overall, hospital length of stay was similar, demonstrating an average of 29 h during the pandemic cohort *versus* 28 h prepandemic cohort

This article is featured in "This Month in Anesthesiology," page A1. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has a visual abstract available in the online version. This work was presented in part at the Canadian Anesthesiologist Society Annual Conference, Halifax, Nova Scotia,

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The COVID-19 pandemic has forced healthcare systems to make unprecedented changes in clinical care pathways and processes to accommodate changes in patient volumes and to protect healthcare professionals from infection.[1] Similarly, health agencies and institutions implemented policies regarding the use of personal protective equipment and preoperative testing for SARS-CoV-2 in patients.[2–6] Despite the lesser burden of COVID-19 among pediatric patients, the global ramp-down of elective surgical cases and the implementation of preoperative testing were extended to many pediatric centers.[7–10] Although intended to identify infected patients and protect other patients and the healthcare workforce, these processes may have led to delays in patient care, resulting in greater morbidity and mortality among patients requiring emergent surgeries, including appendectomy for appendicitis. Appendicitis is one of the most common diseases requiring emergency surgery worldwide.[11] Race, insurance status, and lower rates of outpatient healthcare utilization have been shown to be associated with greater occurrence of complicated appendicitis during COVID-19 in children.[7,8,12–14]

We hypothesized that hospital length of stay would be longer during the COVID-19 pandemic along with longer access to care times, longer perioperative processes, and more negative clinical outcomes for pediatric patients undergoing primary appendectomy. To assess this impact, we compared perioperative care processes and patient outcomes in children undergoing appendectomy during the COVID-19 pandemic (April to May 2020) with those from a prepandemic period (April to May 2019). Centers from members of the international *PE*diatric *A*nesthesia *CO*VID-19 *C*ollaborative (PEACOC) participated in the study.

Our primary aim was to determine the difference in hospital length of stay between pediatric patients undergoing primary appendectomy during a 2-month period early during the COVID-19 pandemic (April to May 2020), compared with matched cohorts during the same 2-month period the previous year (April to May 2019).

Materials and Methods

Study Design and Population

This study was approved by the Institutional Review Board at Boston Children's Hospital (IRB-P00035907; Boston, Massachusetts). Each individual center also obtained separate institutional review board approval or waiver as per

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their local institutional policies. Because this was a retrospective study, the requirements for written informed consent and assent were waived by each center's institutional review board. We designed this retrospective, observational, multicenter study using matched cohorts from participating *PE*diatric *A*nesthesia *CO*VID-19 *C*ollaborative member institutions. Eligibility criteria included data from patients younger than 18 yr of age undergoing primary appendectomy for acute appendicitis. Patients who underwent appendectomy during the study periods were identified and data abstracted from each institution's electronic medical record. Exact matching was performed manually at each study center. Exact matching criteria included patient age (< 1, 1 to 2, 3 to 5, 6 to 11, 12 to 18 yr), American Society of Anesthesiologists (ASA) Physical Status classifications (ASA Physical Status 1 to 2, 3 to 4, and 5), and sex (male, female).[15,16] To minimize sampling bias, we included all pediatric patients undergoing primary appendectomy during both study periods and allowed one-to-many matching to increase the sample size and include all cases. In addition, we minimized differential measurement bias by recording data elements that are commonly used throughout the clinical course of all cases. Each center used a common data dictionary to abstract data from their electronic health record systems (Supplemental Digital Content 1, https://links.lww.com/ALN/D120, and Supplemental Digital Content 2, https://links.lww.com/ALN/D121). All data were entered into a secure, central REDCap database maintained at Boston Children's Hospital.[17] Data were reviewed for missingness or errors. Two investigators, CTM and AFS, reviewed all data entries and contacted each center to verify and validate data as needed.

Study Definitions

The exposure variables were the period of appendectomy (April to May 2019 *vs.* April to May 2020) and COVID-19 test result. Measured potential confounding factors that were examined included age, weight, sex, race, ethnicity, ASA Physical Status, emergent procedure, and insurance type. Our primary outcome was hospital length of stay, measured in hours. We chose hospital length of stay as a surrogate measure that encompasses the impact of timely access to care, perioperative processes, and patient-centered outcomes. Secondary outcomes were time to appendectomy (time to intervention), total operative time, time from operating room entry to intubation, total anesthesia time, postanesthesia care unit (PACU) length of stay, length of time of symptoms before presentation, occurrence of severe postoperative pain, pathology of appendicitis, surgical complexity of appendectomy, need for second procedure, occurrence of postoperative stroke, renal failure requiring renal replacement therapy, respiratory failure, need for inotropic therapy, cardiac arrest, and mortality. No variables were analyzed as effect modifiers. In addition, we compared the primary and secondary outcomes between patients from the 2020 cohort who had a positive SARS-CoV-2 test or were *patients under investigation versus* those with a negative SARS-CoV-2 test during the pandemic period. We used the rate of SARS-CoV2 positive tests or patients under investigation as a marker of COVID-19 burden at each center. Outcome definitions are highlighted in appendix 2 and detailed in the study protocol (Supplemental Digital Content 2, https://links.lww.com/ALN/D121) and statistical analysis plan (Supplemental Digital Content 3, https://links.lww.com/ALN/D122). The Statistical Analysis Plan was written and filed with a private entity (institutional review board) before data were accessed. We used the National Surgical Quality Improvement Program Pediatric definition to categorize primary appendectomy as simple *versus* complicated.[18] Simple appendicitis was defined as surgical findings of appendicitis without clinical evidence of perforation or purulent fluid associated with perforation, and complicated appendicitis was defined as perforated appendicitis with clinical evidence of perforation or purulent fluid associated with perforation (appendix 2). Excluded were patients older than 18 yr, or those where appendectomy was performed as part another procedure (*e.g.*, Ladd procedure, interval appendectomy).

Further, we aimed to assess the influence of SARS-CoV-2 polymerase chain reaction test positivity or patients under investigation on primary and secondary outcomes during the pandemic year compared with those with a negative test or no SARS-CoV-2 polymerase chain reaction test.

Statistical Analysis

No statistical power calculation was conducted before the study. All continuous data are presented as medians and interquartile ranges, and all categorical data are presented as frequencies and percentages. Comparisons of all patient characteristics between April to May 2019 *versus* April to May 2020 were performed using the absolute standardized mean difference as a measure of balance between the two comparison groups. Standardized mean difference values less than 0.10 were considered as reflecting good balance between the two groups on a given explanatory variable. Because good balance was determined for all baseline confounding factors between the two cohorts based on the standardized mean difference, all data were included in the analyses of outcomes. We did not perform any imputation because missing data were only observed for ethnicity, with 2% missing observation (n = 67 of 3,302). The distribution of nonmissing observations is provided in Supplemental Digital Content 4 (https://links.lww.com/ALN/D123). For both pathology of appendicitis and surgical complexity of appendectomy, logistic regression was implemented with dichotomization of complicated *versus* normal or simple.

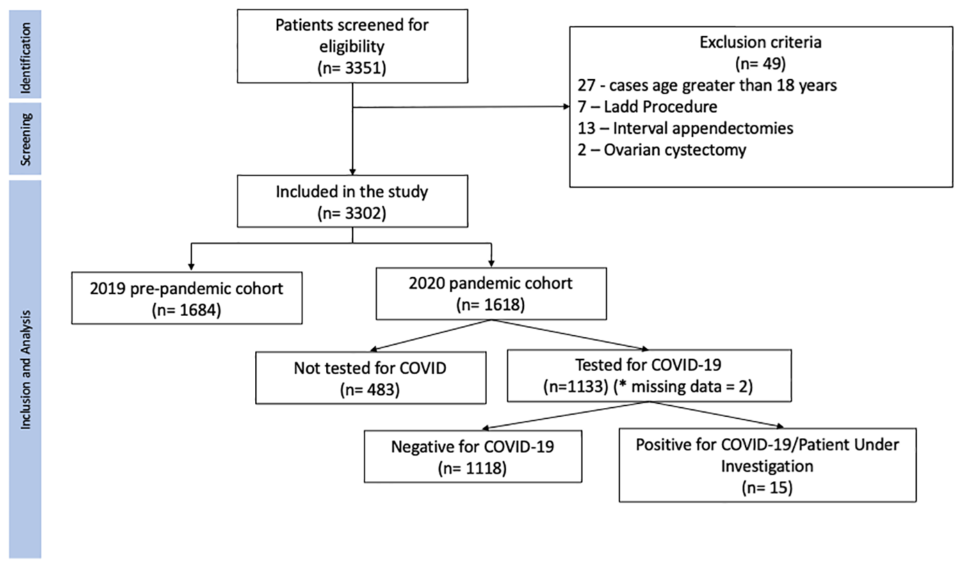

Fig. 1. Study flow chart.

For continuous outcomes, including the primary outcome of hospital length of stay, data were summarized as medians and interquartile ranges due to departure from normality as determined by the Shapiro–Wilk test. Statistical comparisons for continuous outcomes were performed using mixed-effect median regression modeling with a random effect for the matched set. Conditional logistic regression was implemented to assess binary outcomes, with a conditional specification for matched set. Median regression was performed using quantile regression on the 50th percentile (median) to compare the median of the distribution for the continuous outcomes between the time-period groups.[19] Binary outcomes were expressed as frequencies and percentages, and conditional logistic regression was implemented with the matched set incorporated as a random effect in the model. Centers were incorporated into the model as a random effect. Analyses comparing pandemic *versus* prepandemic time periods were also performed stratified by center and geographical region. Results were summarized as adjusted coefficients or odds ratios with corresponding 95% CIs and *P* values, where the term "adjusted" refers to the results from conditional regression accounting for the matched set as a random effect in each model. Forest plots were constructed to visualize the results regarding key outcomes, by center and by region. Centers were compared based on outcome findings using the Wilcoxon rank sum test for continuous variables and Fisher exact test for categorical or binary data. *Post hoc* exploratory analysis using mixed-effects median regression was performed to assess the associations between-center volume (per 100 patients), SARS-CoV-2 testing, and outcomes. Subgroup analyses of SARS-CoV-2 testing status in 2020 according to SARS-CoV-2 positivity or patients under investigation status were performed using the same regression techniques.

All statistical analyses were performed using Stata (version 16.1, StataCorp LLC., College Station, Texas). A two-tailed $P < 0.05$ was considered statistically significant for the primary outcome. For all secondary outcomes using a Bonferroni correction for multiple tests (0.05 divided by 16) we determined a two-tailed $P < 0.0031$ as statistically significant.[20] The study is reported using the Strengthening the Reporting of Observational Studies in Epidemiology statement: guidelines for reporting observational studies.[21]

Sensitivity Analyses

In addition to the primary analysis, we performed preplanned sensitivity analyses to look at hospital length of stay after excluding outlier centers. We defined outliers as centers experiencing an increase or decrease greater than 12 h in hospital length of stay, the primary outcome.

In response to peer review, additional *post hoc* sensitivity analyses were performed on all patients without including a random effect of matched set to avoid matching bias.

Results

Study Population and Patient Characteristics

Of the 3,351 patients identified as undergoing appendectomy, 3,302 were included in the study with 1,684 patients in the prepandemic cohort and 1,618 in the pandemic cohort, and 49 patients met exclusion criteria (fig. 1). Twenty-eight

Table 1. Patient Characteristics during the Prepandemic Period *vs.* the Pandemic Period

Variable	April to May 2019 (n = 1,684)	April to May 2020 (n = 1,618)	Standardized Mean Difference
Age, yr	10.5 ± 3.7	10.6 ± 3.7	0.02
Weight, kg	44.2 ± 20.3	44.6 ± 20.6	0.02
Sex, n (%)			
Male	1011 (60)	979 (60.5)	0.01
Female	673 (40)	638 (39.4)	0.01
Unspecified	0 (0)	1 (0.1)	0.04
Race, n (%)			
White	1009 (59.9)	939 (58)	0.04
Black	96 (5.7)	97 (6)	0.01
Asian	49 (2.9)	55 (3.4)	0.03
Alaska	9 (0.5)	7 (0.4)	0.02
Hawaii	5 (0.3)	5 (0.3)	< 0.01
Other	441 (26.2)	436 (27)	0.002
Ethnicity	n = 1647	n = 1588	
Hispanic, n (%)	583 (35.4)	560 (35.3)	< 0.01
Non-Hispanic, n (%)	922 (56)	898 (56.6)	0.01
Other, n (%)	142 (8.6)	130 (8.2)	0.02
ASA Physical Status, n (%)			
I	882 (52.4)	839 (51.9)	0.01
II	726 (43.1)	709 (43.8)	0.01
III	74 (4.4)	68 (4.2)	< 0.01
IV	1 (0.1)	2 (0.1)	0.02
V	1 (0.1)	0 (0)	0.03
Emergent, n (%)	1058/1667 (63.5)	1078/1602 (67.3)	0.08
Insurance type, n (%)			
Public	893 (53)	793 (49)	0.08
Private	696 (41.3)	704 (43.5)	0.04
Self-Pay	52 (3.1)	38 (2.4)	0.05
COVID-19 tested, n (%)	Not available	1,135 (70.2)	—

Continuous data are presented as mean ± SD and categorical data are presented as n (%). Sample sizes are presented for variables with missing data. An absolute standardized mean difference value less than 0.10 is considered as representing good balance between the two groups.

institutions contributed data for the study (Supplemental Digital Content 5, https://links.lww.com/ALN/D124).[22] We used all cases in the analysis, regardless of matching status. In the full dataset, we had a total of n = 3,302 primary appendectomies, and 86 cases (2.6%) did not have at least one valid match. Baseline characteristics of the participants are shown in table 1. All variables had a standardized mean difference less than 0.10 between the study groups, indicating good balance between the two study groups (table 1). The mean age was 11 yr in the prepandemic cohort *versus* 11 yr in the pandemic cohort. Three patients (0.27%) were confirmed SARS-CoV-2 positive and 12 were managed as patients under investigation.

Outcomes

There was greater, albeit not clinically significant, hospital length of stay from a median of 28 h in the prepandemic cohort to 29 h in the pandemic group (adjusted coefficient, 1 h [95% CI, 0.39 to 1.61]; $P < 0.001$; table 2 and fig. 2). Individual centers had differing hospital length of stay changes from the prepandemic to the pandemic period (fig. 2). Eight centers demonstrated a statistically significantly longer hospital length of stay in the pandemic period compared with the prepandemic period, while 13 demonstrated a shorter hospital length of stay during the pandemic period (fig. 2) and 7 did not observe a statistically significant difference. Two regions demonstrated a statistically significantly longer hospital length of stay in the pandemic period than in the prepandemic period, three regions demonstrated a shorter hospital length of stay during the pandemic period, and one region did not observe a statistically significant difference (fig. 3).

Time to appendectomy was greater in the pandemic period, 648 min (interquartile range: 357 to 1006) *versus* the prepandemic period, 540 min (interquartile range: 305 to 840) (adjusted coefficient, 108 min [95% CI, 106 to 110]; $P <$ 0.001; table 2 and Supplemental Digital Content 6, https://links.lww.com/ALN/D125). Patient care processes such as total operative time, total anesthesia time, and PACU length of stay changed from the prepandemic to the pandemic period across individual institutions (table 2, Supplemental Digital Content 6, https://links.lww.com/ALN/D125) and geographical regions (Supplemental Digital Content 7,

Table 2. Comparison of Outcomes during the Prepandemic Period *vs.* the Pandemic Period

Outcome Variable	April to May 2019 (n = 1,684)	April to May 2020 (n = 1,618)	Adjusted Coefficient or Odds Ratio (2020 vs. 2019)	95% CI	*P* Value
Primary outcome					
Hospital length of stay, h	28 (18–67)	29 (18–79)	1	(0.39 to 1.61)	0.001*
Secondary outcomes					
Time to appendectomy, min	540 (305–840)	648 (357–1006)	108	(106 to 110)	< 0.001*
Total operative time, min	41 (32–56)	43 (31–57)	2	(0.6 to 3.4)	0.006
Time from operating room entrance to intubation, min	8 (6–10)	8 (6–11)	0	(–1 to 1)	0.999
Total anesthesia time, min	81 (65–99)	85 (68–108)	4	(3.7 to 4.3)	< 0.001*
Postanesthesia care unit length of stay, min	64 (42–90)	60 (42–88)	–4	(–4.5 to –3.5)	< 0.001*
Length of symptoms before presentation, days	1 (1–2)	1 (1–2)	0	(–0.2 to 0.2)	0.999
Severe postoperative pain, n (%)	236 (14%)	284 (17.6%)	1.36	(1.1 to 1.68)	0.004
Pathology of appendicitis, n (%)					
Normal	71/1683 (4.2%)	33/1617 (2%)			
Simple	1284/1683 (76.3%)	1206/1617 (74.6%)			
Complicated	308/1683 (18.3%)	368/117 (22.8%)	1.28	(1.06 to 1.54)	0.010
Other	20/1683 (1.2%)	10/1617 (0.6%)			
Surgical complexity of appendectomy, n (%)					
Normal	12/1683 (0.7%)	4/1617 (0.3%)			
Simple	1345/1683 (79.9%)	1201/1617 (74.3%)			
Complicated	313/1683(18.6%)	389/1617 (24.1%)	1.32	(1.1 to 1.59)	0.003*
Other	14 (0.8%)	23/1617 (1.4%)			
Need for second procedure	34 (2%)	50 (3.1%)	1.63	(1.01 to 2.66)	0.049
Occurrence of postoperative stroke	1 (0.06%)	1 (0.06%)	1	(0.06 to 16)	0.999
Occurrence of postoperative renal failure requiring renal replacement therapy	4 (0.24%)	2 (0.12%)	0.52	(0.1 to 2.84)	0.45
Postoperative respiratory failure	12 (0.71%)	15 (0.93%)	1.23	(0.52 to 2.92)	0.642
Postoperative need for inotropic therapy	4 (0.24%)	10 (0.62%)	2.33	(0.59 to 9.16)	0.224
Cardiac arrest	1 (0.06%)	0 (0%)	Cannot estimate		
Mortality	2 (0.12%)	1 (0.06%)	0.52	(0.04 to 5.74)	0.594

Because the two groups were balanced on all characteristics, statistical comparisons were performed using median regression or conditional logistic regression while accounting for matched sets.

*Statistically significant at threshold $P < 0.0031$ after Bonferroni correction.

https://links.lww.com/ALN/D126). During the pandemic period, there were more patients presenting with complicated appendicitis, prepandemic 18.6% *versus* pandemic 24.1%, absolute difference of 5.5% (adjusted odds ratio, 1.32 [95% CI, 1.1 to 1.59]; $P = 0.003$).

Table 3 shows the outcomes of patients presenting within the pandemic cohort. During the study period, 15 patients received a positive SARS-CoV-2 test result or were patients under investigation during the pandemic and overall had a greater and clinically significant hospital length of stay than patients who tested negative or patients who were not tested (hospital length of stay 34 h [interquartile range: 30 to 96], 31 h [interquartile range: 20 to 83], and 24 h [interquartile range: 14 to 68], respectively; adjusted coefficient, 3 h [95% CI, 1.7 to 4.3]; $P < 0.001$). Preoperative SARS-CoV-2 testing was associated with significantly longer hospital length of stay (31 h [interquartile range: 20 to 83] with testing *versus* 24 h [interquartile range: 14 to 68] without testing; adjusted coefficient, 7 [95% CI, 2.7 to 11.3]; $P = 0.002$). In addition, patients testing positive for SARS-CoV-2 had a greater and clinically significant median time to intervention of 1,165 min (interquartile range: 763 to 1,468) compared with 718 min (interquartile range: 425 to 1,104) for those testing negative for SARS-CoV-2 and 414 min (interquartile range: 231 to 770) for those not requiring a SARS-CoV-2 test (adjusted odds coefficient, 447 min [95% CI, 332 to 562]; $P < 0.001$; table 3). Preoperative SARS-CoV-2 testing was associated with significantly longer time to appendectomy (720 min [interquartile range: 430 to 1112] with testing *versus* 414 min [interquartile range: 231 to 770] without testing; adjusted coefficient, 306 [95% CI, 241 to 371]; $P < 0.001$).

Supplemental Digital Content 8 (https://links.lww.com/ALN/D127) shows the characteristics of institutions with longer or shorter process measures in prepandemic *versus* pandemic time periods (*post hoc* analysis). Supplemental Digital Content 9 (https://links.lww.com/ALN/D128) reports the association of center volumes, proportion of SARS-CoV-2–tested patients ,and SARS-CoV-2 positive

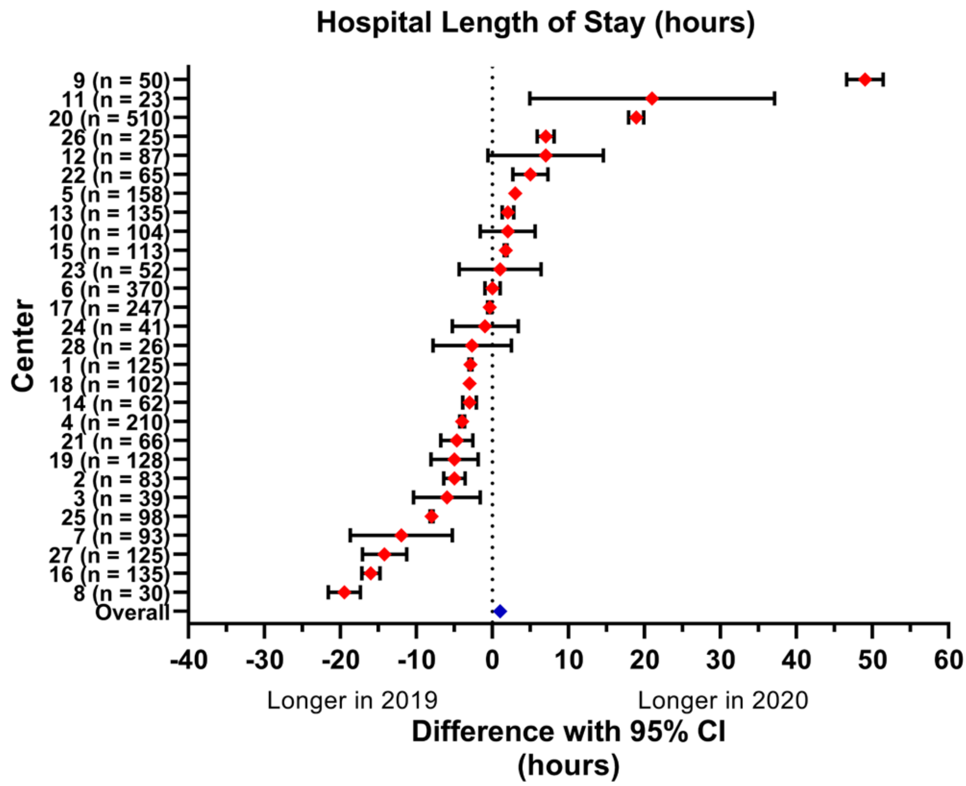

Fig. 2. Primary outcome of hospital length of stay difference prepandemic *versus* pandemic period, stratified by individual center. Pediatric patients undergoing primary appendectomy for acute appendicitis during the COVID-19 pandemic (April to May 2020) were compared with matched cohorts during the same 2-month period the previous year (April to May 2019). Overall, a statistically significant, but clinically insignificant difference was observed: 29 h (interquartile range: 18 to 79) in the pandemic cohort *versus* 28 h (interquartile range: 18 to 67) in the prepandemic cohort (adjusted coefficient, 1 [95% CI, 0.39 to 1.61]; $P < 0.001$).

results with study outcomes. For each center, the case volume of every additional 100 patients at a center was associated with a decrease of 0.41 days in hospital length of stay (adjusted coefficient, –0.41 days [95% CI, –0.42 to –0.41]). Centers with a higher volume of cases, more patients undergoing testing, and higher rate of SARS-CoV-2 testing were associated with longer time to appendectomy. For every additional 100 patients tested for SARS-CoV-2 at a given center, we estimate that this was associated with an increased median time to appendectomy of 96 min (95% CI, increase of 95.7 to 96.3). In other words, when more patients are tested for SARS-CoV-2 at a given center, this was associated with a longer time to appendectomy.

In 2020, a 1% increase in the rate of SARS-CoV-2 test positivity was associated with an increase in time to appendectomy by 17.4 h (95% CI, 15.2 to 19.5 h). A higher SARS-CoV-2 test positivity rate in a center was associated with longer time to appendectomy.

Sensitivity Analysis

In preplanned sensitivity analysis evaluating hospital length of stay after excluding outlier centers (difference in hospital length of stay from prepandemic to pandemic time period of more than 12 h), the median hospital length of stay in prepandemic was 27 h (interquartile range: 18 to 56) and the median hospital length of stay in pandemic was 26 h (interquartile range: 17 to 69; adjusted coefficient, –1 [95% CI, –3.6 to 1.6]; $P = 0.456$). Therefore, with outliers removed, there was no statistically or clinically significant difference in prepandemic *versus* pandemic hospital length of stay. *Post hoc* sensitivity analysis performed in response to peer review performed without including a random effect of matched set to avoid matching bias did not demonstrate any differences in the primary outcome of median hospital length of stay, with a median of 28 h (interquartile range: 18 to 67) in the prepandemic cohort to 29 h (interquartile range: 18 to 79) in the pandemic group (adjusted coefficient, 1 h [95% CI, –1.8 to 3.8]; $P = 0.49$).

Discussion

Among children undergoing emergency appendectomy, the COVID-19 pandemic did not impact processes and patient-centered outcomes when compared with the prepandemic period. Specifically, our study shows that the

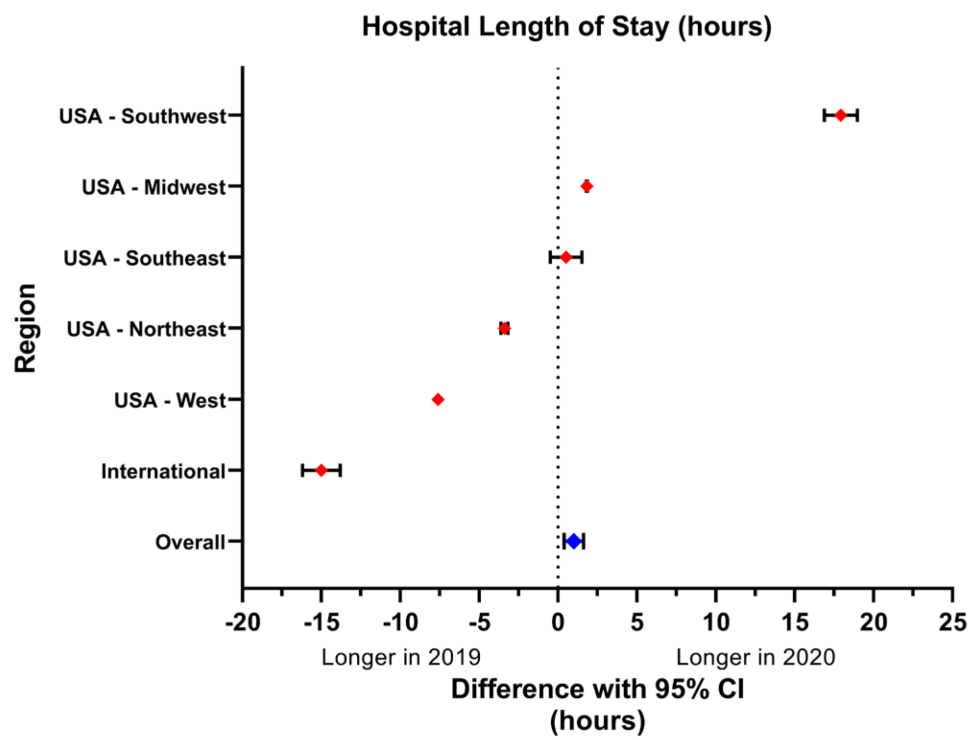

Fig. 3. Primary outcome of hospital length of stay difference prepandemic *versus* pandemic period, stratified by geographic region. Pediatric patients undergoing primary appendectomy for acute appendicitis during the COVID-19 pandemic (April to May 2020), were compared with matched cohorts during the same 2-month period the previous year (April to May 2019). Centers were grouped by geographical region to evaluate any geographic association with changes in hospital length of stay.

pandemic was not associated with a clinically significant greater hospital length of stay, or a clinically significant delayed access to surgical care, complicated appendicitis, and severe postoperative pain. However, children undergoing SARS-CoV-2 testing in the pandemic period, especially those patients testing positive for SARS-CoV-2, experienced greater hospital length of stay and time to appendectomy than those either not tested or with a negative SARS-CoV-2 test.

The impact of the pandemic on patient care has been reported among pediatric patients presenting for nonsurgical care[10,23–29]; we evaluated this impact among children presenting for a common surgical emergency across an international consortium of pediatric centers. Although the primary outcome, hospital length of stay, showed a statistically significant increase of 1 h, this increase is not clinically significant. The changes in hospital length of stay varied across centers and geographic regions. In a sensitivity analysis looking at hospital length of stay after removal of outliers and controlling for matching bias, there was no difference in hospital length of stay between the two cohorts.

Although hospital length of stay was not clinically significantly different prepandemic *versus* pandemic, we did observe statistically and clinically significant differences in processes of care associated with SARS-CoV-2 testing. These findings may reflect the different phases of the pandemic that influenced local hospital policies during the study period. The rolling implementation of preoperative SARS-CoV-2 testing, delays associated with the duration of SARS-CoV-2 testing, and safety practices such as operating room "settle time" and a "clearance period" before other personnel entered the room may have influenced workflows and processes, including time to intervention, operative time, anesthesia time, and turnover times.[30] A higher burden of SARS-CoV-2 testing and positive tests may have played a significant role in delaying time to appendectomy in these patients. However, very few patients tested positive.

Our study was performed in what can be defined as the early phase of the pandemic, April to May 2020, when institutions were still adjusting to the pandemic. A survey conducted in June 2020 of 98 participating institutions from 31 countries reported an estimated 2-h increase in the time to diagnosis and another 2-h increase in time to intervention in patients presenting for emergency surgery.[31] Changes in the perioperative workflow may have included delays in access to diagnostic imaging and delays related to processing of preoperative testing. It is possible that, as the pandemic progressed, these workflow processes impacted time to intervention among our study population. Most patients in our study underwent preoperative

Table 3. Analysis of Outcomes by SARS-CoV-2 Status in the Pandemic Cohort

Variable	No SARS-CoV-2 Test (n = 483)	SARS-CoV-2 Test Negative (n = 1,118)	SARS-CoV-2 Positive/Patient under Investigation (n = 15)	Adjusted Coefficient or Odds Ratio (COVID-19 Positive *vs.* Negative)	95% CI	*P* Value
Primary outcome						
Hospital length of stay, h	24 (13.5 to 68.4)	31 (20 to 83.2)	34 (30 to 96)	3	(1.7 to 4.3)	< 0.001*
Secondary outcomes						
Time to appendectomy, min	414 (231 to 770)	718 (425 to 1104)	1165 (763 to 1468)	447	(332 to 562)	< 0.001*
Total operative time, min	43 (32 to 55)	42 (31 to 57)	45 (36 to 66)	3	(2.4 to 3.6)	< 0.001*
Time from operating room entrance to intubation, min	9 (7 to 11)	8 (6 to 10)	12 (8 to 15)	3	(0.4 to 5.6)	0.023
Total anesthesia time, min	86 (71 to 106)	84 (65 to 108)	137 (105 to 169)	60	(44 to 76)	< 0.001*
Postanesthesia care unit length of stay, min	63 (41 to 92)	59 (42 to 85)	25 (0 to 55)	–34	(–43 to –25)	< 0.001*
Length of symptoms before presentation, days	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)	0	(–0.03 to 0.03)	0.999
Severe postoperative pain	59 (12.2%)	221 (19.8%)	4 (26.7%)	1.47	(0.46 to 4.66)	0.512
Pathology of appendicitis						
Normal	14/482 (2.9%)	18 (1.6%)	1 (6.7%)			
Simple	353/482 (73.2%)	841 (75.2%)	10 (66.7%)			
Complicated	113/482 (23.4%)	251 (22.5%)	4 (26.7%)	1.25	(0.4 to 4)	0.698
Other	2/482 (0.4%)	8 (0.7%)	0 (0%)			
Surgical complexity of appendectomy						
Normal	2 (0.4%)	2/1,117 (0.2%)	0 (0%)			
Simple	371 (76.8%)	819/1,117 (73.3%)	9 (60%)			
Complicated	101 (20.9%)	282/1,117 (25.3%)	6 (40%)	1.97	(0.7 to 5.6)	0.201
Other	9 (1.9%)	14/1,117 (1.3%)	0 (0%)			
Need for second procedure	21 (4.4%)	29 (2.6%)	0 (0%)	Cannot estimate		
Occurrence of postoperative stroke	1 (0.2%)	0 (0%)	0 (0%)	Cannot estimate		
Occurrence of postoperative renal failure requiring renal replacement therapy	0 (0%)	2 (0.2%)	0 (0%)	Cannot estimate		
Postoperative respiratory failure	6 (1.2%)	9 (0.8%)	0 (0%)	Cannot estimate		
Postoperative need for inotropic therapy	7 (1.5%)	3 (0.3%)	0 (0%)	Cannot estimate		
Cardiac arrest	0 (0%)	0 (0%)	0 (0%)	Cannot estimate		
Mortality	0 (0%)	1 (0.1%)	0 (0%)	Cannot estimate		

Because the two groups were balanced on all characteristics, statistical comparisons were performed using median regression or conditional logistic regression while accounting for matched sets.

*Statistically significant at threshold $P < 0.0031$ after Bonferroni correction.

SARS-CoV-2 testing. Our study reports a low incidence of 0.27% positivity rate among children tested for SARS-CoV-2 before emergent appendectomy during the period April to May 2020. However, this incidence may have changed based on the "wave" of the pandemic and emergence of new variants.

Our study observed an increase in complicated appendicitis. The observed increase in time to intervention may be associated with the more complicated cases of appendicitis encountered. The overall incidence of COVID-19 was low in our study population, and so unlikely that COVID-19 itself had a direct impact on the complexity of acute appendicitis. The pandemic has also been associated with late and more severe presentations among populations with acute gastrointestinal diseases, including acute cholecystitis in adults.[28] Our study did not observe an increased time to diagnosis across the prepandemic period *versus* pandemic period or in patients who underwent SARS-CoV-2 testing. Although reports confirm hesitancy in accessing healthcare among adults, data for this phenomenon are lacking for children.[28] Further, our study demonstrates similar access-to-care times for appendectomies during the pandemic period April to May 2020 and prepandemic period April to May 2019. Our study does not report on patients that underwent nonoperative management; however, during the pandemic, a very low proportion (3.9%) of surgeons are reported to have considered this option for acute appendicitis in children.[32] We observed that very few patients undergoing appendectomy were SARS-CoV-2 positive and none required preoperative oxygen or postoperative respiratory support.

The COVID-19 pandemic cohort undergoing preoperative testing and especially those testing positive or patients under investigation was associated with significantly longer hospital length of stay, time to intervention, and higher rate of complicated appendectomy while anesthesia times, operative times, and PACU length of stay were shorter. Despite a small number of patients testing SARS-CoV-2 positive or patients under investigation, these findings may indicate the influence of process changes on patient outcomes. The delays in accessing care can be explained by delayed presentation to hospitals due to pandemic-related avoidance of medical care.[25] However, in our study, SARS-CoV-2 testing was associated with statistically and clinically significant increased time to intervention and hospital length of stay.

Centers with a higher volume of cases, more patients undergoing testing, and higher rate of SARS-CoV-2 testing experienced significantly longer time to appendectomy (time to intervention; Supplemental Digital Content 4, https://links.lww.com/ALN/D123). In other words, when more patients were tested for SARS-CoV-2, this was associated with longer times to appendectomy. The challenges of processing a larger number of nasal swabs with molecular testing may have played a significant role at the centers with a greater burden of COVID-19.

Our study has several limitations. We were unable to determine the prevalence of COVID-19 in the general community at each location, therefore unable to provide data on how overall prevalence may have affected the primary and secondary outcomes. Across centers, there was variation in the timing of elective surgery shutdowns and of universal testing of surgical patients. Even during the study period, the status of each location was rapidly evolving. However, the impact of the pandemic may have still affected clinical and workforce processes implemented at that time. The strengths of our study include the focus on a common global pathologic process, acute appendicitis, with standardized management and definition of outcomes within and across institutions. We also included data from a wide geographical area that allowed for both a global view of the impact of the pandemic and a more focused view of the changes at each individual institution, including a wide range of institution patient volumes. Different public health measures implemented in a variety of geographical areas included school closures, stay-at-home orders, and centralization of pediatric care to tertiary institutions; these could also have impacted volume and time from diagnosis to definitive treatment.

In summary, we studied the impact of the pandemic on pediatric perioperative care in a large, multicenter, international cohort and observed that children undergoing emergent primary appendectomy during the COVID-19 pandemic did not experience clinically significant longer hospital length of stay. There was a statistically significant increase in time to appendectomy (108 min, $P < 0.001$) in the pandemic cohort compared with the prepandemic cohort. In addition, children testing positive for SARS-CoV-2 or managed as patients under investigation had greater hospital length of stay, time to appendectomy, and total anesthesia time than those testing negative for SARS-CoV-2. SARS-CoV-2 testing was associated with longer processes of care, especially among those testing positive or patients under investigation despite low numbers and requires consideration during the ongoing COVID-19 pandemic and future pandemics.

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Competing Interests

The authors declare no competing interests.

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Supplemental Digital Content

Supplemental Digital Content 1. *PE*diatric *A*nesthesia *CO*VID-19 *C*ollaborative data dictionary, https://links.lww.com/ALN/D120

Supplemental Digital Content 2. Study Protocol, https://links.lww.com/ALN/D121

Supplemental Digital Content 3. Statistical Analysis Protocol, https://links.lww.com/ALN/D122

Supplemental Digital Content 4. Non-missing observations, https://links.lww.com/ALN/D123

Supplemental Digital Content 5. List of Participating Institutions, https://links.lww.com/ALN/D124

Supplemental Digital Content 6. Secondary Outcomes by institution, https://links.lww.com/ALN/D125

Supplemental Digital Content 7. Secondary Outcomes according to geographical region, https://links.lww.com/ALN/D126

Supplemental Digital Content 8, Comparison of centers, https://links.lww.com/ALN/D127

Supplemental Digital Content 9. Centers and outcomes, https://links.lww.com/ALN/D128

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Appendix 2. Study Metrics and Outcome Definitions

Metric	Definition
Hospital length of stay	Time from arrival at the hospital to discharge from the hospital
Time to appendectomy	Time from arrival at the hospital to entrance in the operating room
Time from operating room entrance to intubation	Time from arrival at the operating room to the anesthesia intubation event timestamp
Total operative time	Time elapsed between Incision and Surgery Stop events
Total anesthesia time	Time elapsed between Anesthesia Start and Anesthesia Stop events
PACU length of stay	Time from arrival at the PACU after surgery to discharge from PACU
Length of symptoms before presentation	Number of days that patient reported symptoms consistent with appendicitis, such as nausea, vomiting, or right-lower quadrant abdominal pain, before presentation to the hospital
Severe postoperative pain	The highest pain score documented in the patient's medical record between PACU arrival and hospital discharge exceeded 7 of 10 on the numeric rating scale, FLACC (face, legs, activity, cry, and consolability), Neonatal/Infant Pain Scale, or ≥ 8 on the Wong-Baker Faces scale
Complicated appendicitis	Perforated appendicitis with clinical evidence of perforation or purulent fluid associated with perforation
Normal appendix	Pathology report for the surgical specimen from the appendectomy states the appendix is normal and lacks evidence of perforation or appendicitis
Need for a second procedure within the index hospitalization	The patient required a subsequent procedure in an operating or interventional procedure room (not a bedside procedure) during the index hospitalization, including but not limited to reoperation, washout, or drain placement
Postoperative stroke	A new stroke was identified between PACU discharge and hospital discharge
Postoperative renal failure requiring renal replacement therapy	Patient required new initiation of renal replacement therapy after leaving the operating room. This includes but is not limited to intermittent hemodialysis, continuous renal replacement therapy, and continuous venovenous hemofiltration
Postoperative respiratory failure	The patient required supplemental oxygen or positive pressure ventilation after PACU discharge or when taken to the intensive care unit after leaving the operating room.
Postoperative need for inotropic therapy	The patient required one or more inotropic or vasopressor agents after leaving the operating room and before hospital discharge

PACU, postanesthesia care unit.