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Major Article

Surgical outcomes inchildren with perioperative SARS-CoV-2 diagnosis

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III

Key Words:
SARS-CoV-2
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Objective: To understand whether perioperative SARS-CoV-2 infection increases risk of pulmonary complications in children.
Methods: A retrospective cohort study of children who underwent surgery with perioperative SARS-CoV-2 infection at a children's hospital from March 1, 2020, to June 30, 2021. Uninfected, age-matched control patients who underwent the same procedure as infected patients over the past ten years were included in the study in a 3:1 ratio to infected patients. Primary outcomes were 7- and 30-day mortality. Secondary outcomes were development of pulmonary complications, readmission, length of hospital or ICU stay, and oxygen administration in post-anesthesia care unit (PACU).
Results: Our study included 73 patients who underwent surgery with perioperative diagnosis of SARS-CoV-2, and 218 control patient undergoing similar procedures. One total mortality event was observed within 7 days in an uninfected control patient, and none occurred in infected patients. Perioperative SARS-CoV-2 infection was associated with increased risk for pulmonary complications in univariate analysis. Infection was not associated with any of our other secondary outcomes. Symptomatic SARS-CoV-2 infection and timing of diagnosis was not associated with development of pulmonary complications among infected patients.
Conclusions: Children with perioperative SARS-CoV-2 infection may be at increased risk for development of pulmonary complications. Larger studies should be performed to confirm our results.

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has drastically restricted surgical practices in the United States. Many elective surgeries were delayed or cancelled due to safety precautions, workforce shortages and resource limitations.[1,2] Widespread institutional implementation of preoperative COVID-19 screening has been successful in identifying infected patients and determining appropriate surgical plans.[3,4] Decreasing new COVID-19 case counts and increased vaccination rate could potentially loosen COVID-19 screening protocols for surgical patients in the future.

Retrospective studies have found that adult surgical patients with SARS-CoV-2 infection are at higher risk for postoperative pulmonary complications and mortality.[5–8] However, the risk for pediatric patients with SARS-CoV-2 infection undergoing surgery is not well understood, though several studies have sought to understand this question.[9–12] Our study was completed in the United States where vaccinations recently became available for children 5 years or older, leaving a portion of the pediatric population vulnerable to infection while approval for younger children is considered.[13] Globally, this issue is exaggerated as children of all ages remain with limited immunization access due to inequitable vaccine distribution.[14] Given the increased vulnerability of children to infection, our study sought to understand the risk of perioperative infection on surgical outcomes in children. Improved understanding of trends within pediatric patients with SARS-CoV-2 infection will help inform individual clinical decision making between families and providers and guide institutional decisions to continue preoperative testing and establish protocols for infected children needing surgery.

METHODS

Study design

We performed a retrospective observational cohort study of patients testing positive for SARS-CoV-2 infection and undergoing surgery at Primary Children's Hospital (PCH) in Salt Lake City, Utah from March 1, 2020, to June 30, 2021. Eligible patients were

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identified from ongoing hospital records at PCH intended to track the care of all patients who tested positive for SARS-CoV-2. Desired outcomes and patient data were gathered from electronic health records and stored in a password-protected RedCAP database. This study was deemed exempt for written consent and was approved by the Institutional Review Board at the University of Utah in Salt Lake City, Utah. The authors adhered to STROBE guidelines in the design and execution of this study.

Participants

Eligible patients were identified by a hospital tracking system established to follow all patients who tested positive for SARS-CoV-2. All patients 18 years or younger who underwent surgery and tested positive for SARS-CoV-2 infection within 7 days before or 7 days after their procedure were included in the study as infected patients. Our selected time period of 7 days before surgery is consistent with previous studies.[10] Surgery was defined as any procedure requiring anesthesia and performed in an operative suite. Patients were included regardless of procedure, indication, and urgency of the surgery, and were excluded if they had a positive test prior to 7 days before surgery. If an individual patient underwent multiple surgeries within 7 days of SARS-CoV-2 diagnosis, then only the initial surgery following a positive test was considered in the study.

Current procedural terminology (CPT) codes were used to search for control patients who underwent similar procedures to infected patients from January 1, 2010, to June 30, 2021. Control patients were included in a 3:1 ratio to infected patients and were defined as patients who underwent the same or similar surgical procedures as infected patients and either tested negative for SARS-CoV-2 or underwent surgery prior to the SARS-CoV-2 pandemic. Control patients were age-matched to infected patients and were included if they underwent surgery when they were within 2 years of the age of infected patients at the time of surgery. Patients were selected at random from the lists generated by the CPT query. Occasionally, the selected control patient was not an appropriate match (eg, incorrectly coded procedure). In these instances, consecutive patients from the originally selected patients were then screened for inclusion in the study. Only patient age and identification numbers were known to the researchers at the time of selection to minimize the risk of bias.

Procedures

SARS-CoV-2 diagnosis was based on viral RNA detection by quantitative RT-PCR. In patients with inconclusive results, repeat testing was performed and their COVID status was based on the second test. Timing of SARS-CoV-2 diagnosis was recorded as greater than 3 days prior to surgery, less than 3 days prior to surgery, or after surgery. Patients who tested positive for SARS-CoV-2 were categorized as either symptomatic or asymptomatic. The following specific symptoms of infection were also recorded: abdominal pain, dyspnea, cough, diarrhea, fatigue, fever >38°C, hemoptysis, nausea or vomiting, sputum, and other. Symptomatic patients were categorized as having 1, 2, or 3 or more of the listed symptoms.

Age, sex, race and ethnicity, and insurance provider were included as demographic variables. Insurance provider was recorded as commercial, Medicaid, self-pay, or other. Vital signs included in the study were weight, height, systolic blood pressure, respiratory rate, and heart rate as recorded immediately before surgery. Cigarette smoke exposure, asthma, cancer, kidney disease, heart disease, and immunocompromised were included as comorbidities. Patients were categorized as having zero, one, or two or more comorbidities. Preoperative respiratory support was recorded as either none or oxygen only, noninvasive (CPAP or BiPAP), or invasive (extracorporeal membrane oxygenation or ventilator support). Chest x-ray and computed tomography (CT) studies were recorded as either performed or not performed immediately prior to surgery, and whether any abnormalities were noted. American Society of Anesthesiologists (ASA) physical status at the time of surgery was also recorded and analyzed as grades 1-2 against grades 3-5. Characteristics of the procedures were recorded and included surgical specialty, urgency of surgery (emergent or elective), surgical complications (infection or bleeding), and depth of anesthetic administration (local, regional, or general). Emergent surgery was defined as a procedure that was not scheduled in advance.

Outcomes

The primary outcome of our study is 7- and 30-day mortality. Our secondary outcomes included development of pulmonary complications, readmission, length of hospital or ICU stay, and oxygen administration in postanesthesia care unit (PACU) were included as additional secondary outcomes. Pulmonary complications were defined as pneumonia, unexpected postoperative ventilation, and acute respiratory distress syndrome. Unexpected postoperative ventilation included any episode of non-invasive ventilation, invasive ventilation, extracorporeal membrane oxygenation following surgery or intubation, or failure to be extubated after surgery.

Statistical analysis

Stata version 16.1 for Windows was used for statistical analysis. Differences in continuous data between groups were tested using Student's t test. Fisher's exact text or chi-square test were used to test for differences in categorical data between groups. Fisher's exact test was used as a more conservative measure of significance in instances where the minimum expected cell frequency did not exceed one.[15] Due to a low number of events observed, a multivariable logistic regression model was not included in our analysis to avoid overfitting.

RESULTS

A total of 73 patients tested positive for SARS-CoV-2 infection and underwent surgery within 7 days before or after their diagnosis from March 1, 2020, to June 30, 2021 at Primary Children's Hospital. Uninfected age-matched controls were screened and included in a 3:1 ratio and underwent similar procedures from January 1, 2010, to June 30, 2021 for a total of 291 patients in our study (Fig 1). Demographic data describing pre-operative patient characteristics are outlined in Table 1. One hundred sixty-eight (58%) patients were male with an average age of 8.9 years old (interquartile range 4-13) at the time of surgery. Two (0.7%) of the patients were American/Alaskan Native, 1 (0.3%) was Asian, 3 (1%) were Black or African American, 5 (1.7%) were Native Hawaiian/Pacific Islander, 51 (17.5%) were Hispanic/Latinex, and 217 (74.6%) were white. Race and ethnicity data

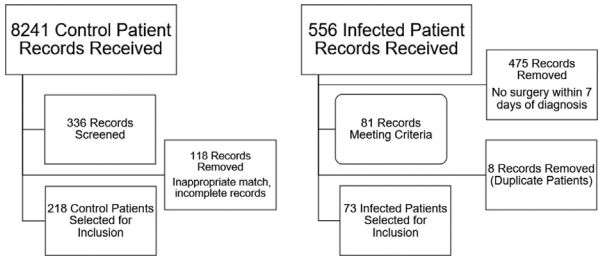


Fig 1. Flow diagram demonstrating number of patient records screened and included in the study for control patients and patients infected with SARS-CoV-2.

Table 1
Comparison* of demographic information, comorbidities, and preoperative assessments between patients testing positive or negative for SARS-CoV-2, and between patients with or without postoperative pulmonary complications

	COVID status				Pulmonary complications		
	Positive	Negative			Yes	No	
Sex			*P* = .18	Sex			*P* = .46
Male	47	121		Male	5	163	
Female	26	97		Female	2	121	
Age†	8.8 (4-13)	8.9 (4-13)	*P* = .87	Age†	8.4 (1-12)	8.9 (4-13)	*P* = .79
Race/Ethnicity			*P* = .05	Race/Ethnicity			*P* = .75
America/Alaska Native	0	2		America/Alaska Native	0	2	
Asian	0	1		Asian	0	1	
Black/African American	2	1		Black/African American	0	3	
Native Hawaiian/Pacific Islander	0	5		Native Hawaiian/Pacific Islander	0	5	
Hispanic/Latinex	20	31		Hispanic/Latinex	3	48	
White	47	170		White	4	213	
Unknown	4	8		Unknown	0	12	
Insurance provider type			p=0.02	Insurance Provider Type			p=0.88
Commercial	49	155		Commercial	5	199	
Medicaid	14	54		Medicaid	1	67	
Self-Pay	10	7		Self-Pay	1	16	
Other	0	1		Other	0	1	
Unknown	0	1		Unknown	0	1	
Comorbidites			*P* = .47	Comorbidites			*P* = .76
0	46	137		0	4	179	
1	16	37		1	2	51	
2 or more	11	44		2 or more	1	54	
Specific comorbidities				Specific comorbidities			
Cigarette smoke exposure	9	15		Cigarette smoke exposure	0	24	
Asthma	1	11		Asthma	0	12	
Cancer	10	34		Cancer	0	44	
Kidney disease	0	3		Kidney disease	0	3	
Heart disease	4	13		Heart disease	1	16	
Immunocompromised	7	30		Immunocompromised	0	37	
Other	9	24		Other	3	30	
Pre-op respiratory support			*P* = .73	Pre-op respiratory support			*P* = .33
None or oxygen only	71	208		None or oxygen only	6	273	
Noninvasive	0	1		Noninvasive	0	1	
Invasive	2	9		Invasive	1	10	
Pre-op vitals‡				Pre-op vitals‡			
Systolic blood pressure	109.8 (14.7)	109.9 (14.6)	*P* =0.97	Systolic blood pressure	111.1 (29.3)	109.8 (14.1)	*P* = .81
Respiratory rate	22.1 (5.2)	22.3 (6.4)	*P* = .81	Respiratory rate	24.6 (7)	22.2 (6.1)	*P* = .30
Heart rate	101.9 (21.7)	99 (21.5)	*P* = .33	Heart rate	106 (19.1)	99.6 (21.6)	*P* = .44
Hemoglobin‡	12.9 (2.5)	13.5 (8.3)	*P* = .62	Hemoglobin‡	13.5 (1.5)	13.3 (7.2)	*P* = .94
Missing	29	118		Missing	0	147	
WBC count‡	10.2 (5.4)	11.8 (6.6)	*P* = .19	WBC count‡	15.5 (7.3)	11.1 (6.2)	*P* = .09
Missing	33	121		Missing	1	153	
ASA status			*P* = .08	ASA status			*P* = .01
1 or 2	23	98		1 or 2	1	120	
3 to 5	48	118		3 to 5	5	161	
Missing	2	2		Missing	1	3	
Preoperative chest x-ray			*P* = .74	Preoperative chest x-ray			*P* = .52
Not performed	60	184		Not performed	5	239	
Yes: normal	8	24		Yes: normal	1	31	
Yes: abnormal	5	10		Yes: abnormal	1	14	
Preoperative chest CT			*P* = .17	Preoperative chest CT			*P* = .14
Not performed	69	210		Not performed	6	273	
Performed: normal	1	4		Performed: normal	1	4	
Performed: abnormal	3	4		Performed: abnormal	0	7	

*Measures of significance for categorical data determined using Chi-square test and measure of significance for continuous data determined using Student's t test.
†Age presented as group averages with interquartile range in parentheses.
‡Continuous data presented as group averages with standard deviation in parentheses.

was missing for 12 (4.1%) patients. Two hundred five (69.7%) patients had commercial insurance coverage, and 23.4% and 5.8% of patients were covered by Medicaid and self-pay, respectively. Insurance provider information was missing for 1 patient (0.3%), and 1 patient was covered by other means. One hundred eighty-three (62.9%) patients did not have any comorbidities associated with severe COVID-19 disease. Fifty-three (18.2%) of patients had one comorbidity, and 55 (18.9%) patients had 2 or more comorbidities associated with severe disease. Forty-four (15.1%) patients had a cancer diagnosis, the most common comorbidity in our cohort. Fifteen (4.6%) patients were on invasive ventilation prior to surgery, 2 (0.6%) were on noninvasive ventilation, and the remaining 306 (94.7%) either did not require ventilation or were on oxygen nasal cannula only.

Baseline vitals (blood pressure, respiratory rate, and heart rate) and labs (hemoglobin and white blood cell count), and preoperative imaging (x ray and CT) were not significantly different between infected and control patients, or patients who developed pulmonary complications compared to those who did not (Table 1). ASA physical

Table 2
Comparison* of surgery characteristics between patients testing positive or negative for SARS-CoV-2, and between patients with or without postoperative pulmonary complications

	COVID status			Pulmonary complications		
	Positive	Negative		Yes	No	
Urgency of surgery			$P = .1$	Urgency of surgery		$P = .32$
Elective	11	58		Elective	0	69
Emergency	62	157		Emergency	7	212
Missing	0	1		Missing	0	1
Specialty			$P = .88$	Specialty		$P = .01$
Cardiac	1	2		Cardiac	0	3
GI and general	31	91		GI and general	4	118
Head and neck	7	22		Head and neck	0	29
Neurosurgery	3	6		Neurosurgery	2	7
Ophthalmology	1	3		Ophthalmology	0	4
Orthopedics	19	60		Orthopedics	1	78
Plastics/Reconstructive	0	0		Plastics/Reconstructive	0	0
Urology	1	7		Urology	0	8
Other	10	27		Other	0	37

*Measures of significance determined using Chi-square test.

status was not different between patients with or without SARS-CoV-2 infection. However, patients with ASA Status 3 to 5 were found more frequently among those who developed pulmonary complications compared to those who did not (71% vs 11%, $P = .01$). Characteristics of each procedure (urgency of surgery and specialty) were not significantly different between infected and control patients, though specialty of the procedure was correlated with development of pulmonary complications (Table 2). Urgency of surgery did not impact development of pulmonary complications. The majority of procedures were emergent or unplanned (75%), and gastrointestinal and general surgery was the most represented specialty (42% of procedures). All patients underwent general anesthesia for all procedures in our study.

One 7-day mortality event, and therefore one 30-day mortality event, was observed in our cohort of control patients. This event was observed following an exploratory laparotomy for necrotic small bowel which led to worsening hemorrhagic shock and mortality. No 7- or 30-day day mortality events were observed in infected patients.

Pulmonary complications occurred after 4 procedures performed on infected patients, and pulmonary complications occurred following 3 procedures performed on control patients (Summary in Table 3). The most common pulmonary complication was unexpected failure to be extubated following surgery, occurring in 5 of the 7 episodes. In the remaining 2 episodes, one child required resuscitation and reintubation in the 24 hours following surgery, and the other child returned to the hospital in worsening respiratory distress requiring BiPAP support within 12 hours of surgery.

Pulmonary complications occurred more frequently in infected patients compared to uninfected control patients (5.5% vs 1.4%, respectively; $P < .05$; Fig 2A). Infected and control patients were admitted to the hospital floor and ICU following surgery at similar rates, and length of stay in the hospital or ICU was similar between the 2 groups (Fig 2B). Oxygen was provided in the PACU to patients

Table 3
Summary of patients who developed postoperative pulmonary complications

Enounter #	SARS-CoV-2 status	Patient age	Specialty and procedure	Complication
1	Positive	1	Neurosurgery ventricuoperitoneal shunt revision	Code blue requiring resuscitation and intubation
2	Positive	10	General surgery laparascopic appendectomy	Developing postoperative respiratory failure requiring BiPAP
3	Positive	11	Neurosurgery epidural hematoma evacuation	Could not be extubated
4	Positive	11	General surgery Exploratory laparotomy	Could not be extubated
5	Negative	11	Orthopaedics Internal fixation humeral fracture	Could not be extubated
6	Negative	1	General surgery Exploratory laparotomy	Could not be extubated
7	Negative	15	General surgery Exploratory laparotomy	Could not be extubated

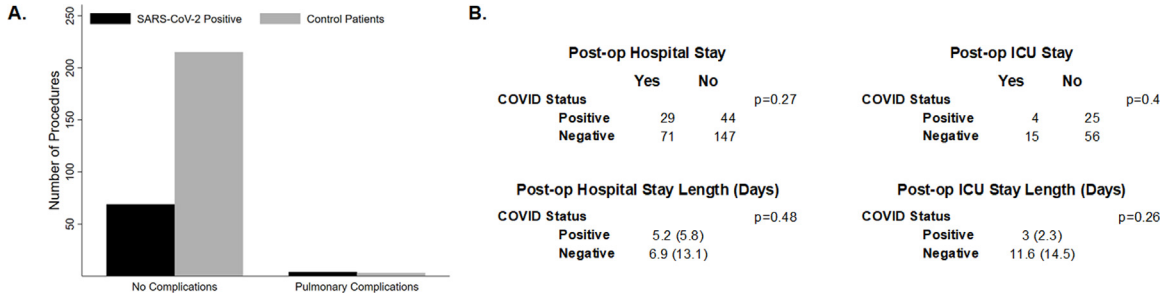
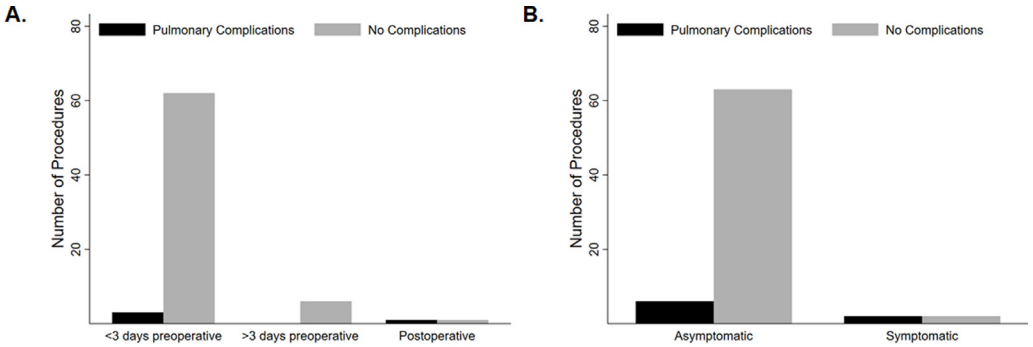


Fig 2. Postoperative outcomes in patients testing positive for SARS-CoV-2. (A) Pulmonary complications in patients with SARS-CoV-2 infection compared to patients without infection. (B) Comparison of hospital and ICU admission, and length of stay in days for patients who tested positive for SARS-CoV-2 and patients without infection. Length of stay is presented as the average length of stay with standard deviation in parenthesis.



C. Specific COVID-19 Symptoms

Abdominal pain	1
Dyspnea	1
Cough	1
Diarrhea	1
Fatigue	3
Fever >38 C	5
Hemoptysis	-
Nausea or Vomiting	3
Sputum	-
Other	5

Fig 3. Pulmonary complications in patients who tested positive for SARS-CoV-2 by timing of diagnosis (A) and presence of symptoms of SARS-CoV-2 infection (B). Specific reported symptoms of SARS-CoV-2 infection are shown in C.

at similar rates between infected and control patients (4.2% vs 5.7%, respectively; P = .62). Infected patients required readmission or emergency room visits at similar rates to control patients (5.5% vs 2.3%, respectively; P = .17).

Timing of SARS-CoV-2 diagnosis was not associated with development of pulmonary complications (Fig 3A). Symptoms were present in 50% of infected patients who developed pulmonary complications compared to 8.7% of infected patients who did not develop pulmonary complications, though this difference did not reach statistical significance (P = .06 by Fisher's exact test; Fig 3B). Three (37.5%) of the symptomatic patients reported one symptom of COVID-19, and 5 (62.5%) of the symptomatic patients reported ≥3 symptoms. Specific reported symptoms are outlined in Figure 3C.

DISCUSSION

Our study aimed to understand whether pediatric patients who test positive for SARS-CoV-2 within one week of surgery are at increased risk for poor outcomes. We did observe one mortality event in our group of control patients, and no mortality events in the infected group of patients. Postoperative pulmonary complications were observed in 4 of 73 patients who tested positive for SARS-CoV-2 compared to 3 of 218 procedures performed on patients without SARS-CoV-2 diagnosis. In patients with SARS-CoV-2, we found that those with symptoms were not more likely to develop pulmonary complications, though the number of symptomatic patients in our study was low. SARS-CoV-2 diagnosis was not associated with reoperation, readmission, length of postoperative hospital or ICU stay, or PACU oxygen administration compared to uninfected control patients.

The largest study on this topic measured mortality events in 393 infected patients and included contemporaneous comparative data for 207 infected patients to over 13,000 uninfected control patients.[10] These authors concluded no increase in 30-day mortality or pulmonary complications among children with perioperative infection. Mehl et al and Nepegodiev[9,12] also concluded children with perioperative infection were not at increased risk for complications. These 2 studies did not include matched controls and were based solely on observed postoperative complication rates among infected children. Kavanagh et al[16] did not identify any pulmonary complications in infected children who underwent surgery in a 2-month time frame. However, Saynhalath et al[11] concluded increased risk for pulmonary complications in infected children in a study which included matched controls. Our present study fortifies Saynhalath's conclusions, helping to clarify the risks and benefits to proceeding with surgery in infected children.

Other groups have acknowledged the potential risks to patient and staff of surgery in children with perioperative SARS-CoV-2 infection. Basnet et al[17] advocated for conservative management of acute appendicitis in infected children as a safer alternative for treatment. A case report described spinal anesthesia as a safe alternative to general tracheal anesthesia in certain contexts of pediatric surgery to avoid the risks of infection to staff and pulmonary injury to patients.[18] However, Matava determined that endotracheal intubation may be performed safely on infected patients with proper precautions.[19]

Our results are meaningful in the context of an ever-evolving pandemic to assess the risk to pediatric patients undergoing surgery with perioperative SARS-CoV-2 infection. As vaccine hesitancy and new variants drive new waves of infections, children younger than 5 years old in the United States are currently left without the protection of an approved vaccine.[20,21] Furthermore, infected children may present with asymptomatic infection and otherwise go undetected.[22] In this context, our study supports maintaining preoperative SARS-CoV-2 testing to allow families and providers to make informed, shared decisions about the risks and benefits of proceeding with surgery. Certainly, in some instances, surgery cannot be delayed. However, our data demonstrate increased, but small, risk for some patients who undergo surgery with perioperative infection. Other studies support delaying surgery in infected patients until infection is likely cleared.[10,23] These data may be important to share with families as they weigh whether to proceed with surgery if delaying surgery is an option.

Limitations to our study exist. First, the rate of pulmonary complications was low at 5.5% and 1.4% in the infected and control groups, respectively, making it difficult to determine whether a true difference exists. The low number of patients in our study also raises the likelihood that we may miss or understate a difference between infected and uninfected patients, should one exist. We sought to overcome the low number of patients in our study design by including 3 control patients for every infected patient. Our patient population in our study was taken from a single institution serving the Rocky Mountain region, perhaps biasing our results. Further studies incorporating data from multiple institutions should be completed to expand the external validity of our study. Another limitation of our study is possible undetected infection in surgical patients, especially prior to widespread testing during the early phases of the pandemic. It is also possible that some infected patients were overlooked by falsely testing negative for SARS-CoV-2 infection. Methods for confirming infection in all patients were uniform (laboratory testing), so any false negative test is not attributable to differences in diagnostic technique.

When interpreting our data, one must also consider the constantly evolving nature of the pandemic. Our study includes patients that were infected during the early virus strains and concluded during the early stages of the delta wave and does not include data for the omicron wave. Children and infants appear to have been affected more by the omicron variant in our geographic region, as the hospitalization rates for infants in the state of Utah age 0-1 years old increased 4-fold on January 30, 2022, compared to November 2020.[24] Therefore, it is possible that our data may understate or overstate the effect of SARS-CoV-2 infection on surgical outcomes depending on the current and local landscape of the pandemic. Further studies should be completed to help clarify this question as the pandemic evolves.

CONCLUSIONS

Despite the limitations, we conclude that children with perioperative SARS-CoV-2 infection may be at higher risk for postoperative pulmonary complications compared to uninfected children. Further multi-institutional studies on this topic should be conducted to gain a better understanding of the effects of SARS-CoV-2 on children undergoing surgery. The identified risk in our study should be considered in the clinical decision making for individual pediatric patients requiring surgery. On a larger scale, as the SARS-CoV-2 pandemic evolves, institutions should consider these results as they consider whether to continue preoperative testing and other safety protocols.

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