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Postoperative cardiopulmonary complications in children with preoperative Omicron SARS-CoV-2 variants infection: a single-center retrospective cohort study

Yan-Yifang Xu^{1†}, Zhen-Zhen Dai^{2†}, Han Zhou^{2†}, Hai Li^{2*} and Yi Du^{1*}

Abstract

Objective The purpose of this study was to investigate: (1) the incidence of cardiopulmonary complications within 30 days after surgery in pediatric patients with preoperative Omicron variants infection, (2) the mortality, and (3) their possible risk factors.

Methods This retrospective study included a consecutive patient cohort who underwent elective non-cardiac surgery for any indication in the Pediatric Department of our hospital between November 2022 and February 2023. Cardiopulmonary complications and mortality within 30 days after surgery were compared between patients with pre-operative SARS-CoV-2 infection (Omicron variants infected group) and those without infection (the uninfected group) within 90-day before the surgery. The study evaluated the demographic data and related clinical factors of complications by analyzing their clinical records.

Results Our study included 502 patients, of which 194 (38.65%) had a pre-operative Omicron variants diagnosis. The mean duration between definite Omicron variants infection and surgery was 31.28 ± 10.19 days. In our study, the incidence of pulmonary complications was 1.59% (8/502 patients), no cardiac complication or mortality was found in the 30-day postoperative follow-up. The Omicron variants infected group had a significantly higher incidence of complications (7/194, 3.61%) compared to the uninfected group (1/308, 0.32%) ($p = 0.006$). After adjusted for other factors, it was found that the Omicron variants infection within 4 weeks before surgery (OR = 17.84, 95% CI: 1.25–255.35, $p = 0.034$), higher BMI (OR = 1.26, 95% CI: 1.02–1.55, $p = 0.034$), ASA physical status grade III–V (OR = 17.35, 95% CI: 1.19–253.80, $p = 0.037$), and abnormal preoperative chest radiograph (OR = 60.07, 95% CI: 1.92–1878.21, $p = 0.020$) were independent risk factors for postoperative pulmonary complications in patients within 30 days after the surgery.

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Conclusions Omicron infection may heighten the risk of pulmonary complications in children undergoing elective non-cardiac surgery. It is advisable to schedule elective surgery at least 4 weeks after infection of Omicron variants.

Keywords SARS-CoV-2, Omicron variants, Postoperative cardiopulmonary complications, Anesthesia, Pediatric

Introduction

With the global pandemic of SARS-CoV-2 brought in March 2020 [1], several variants of the virus have emerged, including alpha, beta, and delta versions. In November 2021, the Omicron variants were first discovered in South Africa. From December 2022 to January 2023, 105 428 SARS-CoV-2 sequences were shared through Global Initiative of Sharing All Influenza Data (GISAID) and 98.4% of sequences were the Omicron variants of concern (COVID-19 Weekly Epidemiological Update). In China, BA.5 and its descendant lineages BA.5.2 and BE.7 were dominant Omicron variants of concern at that time [2, 3]. Fortunately, the clinical manifestations of infection by Omicron variants were milder than previous versions [4, 5]. For children, pulmonary symptoms of Omicron variants were less severe than that in adults partially due to the better regeneration potential of juvenile alveolar epithelium [6]. According previous researches [7–10], the cardiopulmonary complications included postoperative unplanned retention of tracheal catheter ventilator support, intubation after extubation, new-onset pulmonary infection, pleural effusion, atelectasis, acute respiratory distress syndrome (ARDS), myocarditis, arrhythmia, myocardial ischemia, and circulatory instability necessitating vasoactive drug support. However, the impact of preoperative Omicron variants infection on postoperative cardiopulmonary complications in children undergoing elective surgery is still unclear. More clinical data are warranted to demonstrate this. We performed the retrospective study to investigate: (1) the incidence of cardiopulmonary complications within 30 days after surgery in pediatric patients with preoperative Omicron variants infection, (2) the mortality, and (3) their possible risk factors.

Patients and methods

After approval by the institutional review board (IRB), we reviewed a consecutive patient cohort who was treated with elective surgery for any indication in the Pediatric Department of our hospital from November 2022 to February 2023.

The inclusion criteria were as follows: (1) patients younger than 18 years old; (2) patients from pediatric surgery departments, including pediatric orthopedics, general surgery, urology, and neurosurgery, underwent surgery in an operating theatre under general anesthesia; (3) patients with the definite Omicron variants test result within 90 days preoperatively (reverse transcription-polymerase chain reaction of nasopharyngeal swab

or rapid antigen test); (4) patients with complete medical data with perioperative operation.

The exclusion criteria were as follows: (1) patients underwent multiple operations while in hospital; (2) patients underwent either enteroscopy or ultrasound-guided puncture biopsy using intravenous anesthesia only because of the short duration of anesthesia required and the simplicity of the operation; (3) patients with preoperative oxygen dependence and/or preoperative respiratory support; (4) patients had persistent symptoms related to Omicron variants preoperatively; (5) follow-up was lost within 30-day after surgery. Patients with persistent symptoms related to Omicron variants preoperatively was defined as the respiratory symptoms like cough, nasal discharge, sore throat, dyspnea and asthma, fever of $\geq 37.3^{\circ}\text{C}$, and gastrointestinal symptom like diarrhea, nausea and vomiting.

During the Omicron variants epidemic, the medical records of inpatients was required to record completely and accurately whether they have a history of Omicron variants infection, including symptoms (fever, frequent coughing, diarrhea, pain, rash), related examinations (reverse transcription-polymerase chain reaction (RT-PCR) of nasopharyngeal swab or rapid antigen test) and infection time. Fever is defined as having a temperature above the normal range ($\geq 37.3^{\circ}\text{C}$, axillary) due to an increase in the body's temperature set point [11]. Diarrhea is the condition of having at least three loose, liquid, or watery bowel movements each day [12]. Based on the definite Omicron variants test result within 90 days preoperatively, patients included were divided into two groups: the Omicron variants infected group and the uninfected group.

The following information was collected for each patient: age; sex; Omicron variants infection symptoms; surgery departments (pediatric orthopedics, general surgery, urology, and neurosurgery); preoperative American Society of Anesthesiologists (ASA) physical status; grade of surgery (Grades 1, 2, 3, and 4) according to International Classification of Diseases Clinical Modification of 9th Revision Operations and Procedures [ICD-9-CM-3]; preoperative chest radiograph (normal or abnormal) and electrocardiograph (ECG, normal or abnormal); preoperative respiratory support; the presence of 30-day postoperative cardiopulmonary complications; and presence of 30-day postoperative mortality.

Consistent with previous research [8], age was categorized as 0–4 weeks, 5–52 weeks, 1–9 years, and 10–17 years. And ASA physical status was classified as grades

1–2 or grades 3–5. Preoperative chest radiograph was classified by radiology reports as normal and abnormal condition (pneumonia, part pulmonary atelectasis, and mediastinal tumor). Time from the diagnosis of Omicron variants infection to the surgery was collected as a categorical factor and analyzed by weeks. We defined postoperative cardiopulmonary complications as the following conditions including postoperative unplanned retention of tracheal catheter ventilator support, intubation after extubation, pulmonary infection, pleural effusion, atelectasis, arrhythmia, myocardial ischemia, and circulatory instability necessitating vasoactive drug support, according to previous researches [7–10].

Statistical analysis

The Fisher exact test or Wilcoxon test was used for categorical variables and the t-test or analysis of variance (ANOVA) for continuous variables. Risk factors for the presence of 30-day postoperative cardiopulmonary complications and postoperative transferring to ICU were evaluated by multivariate logistic regression models, and odds ratios (ORs) with their 95% CIs were obtained. Statistical tests were considered significant at $p < 0.05$. Analysis was performed with the statistical software Stata/SE for Windows (version 15.0; StataCorp LLC).

Results

A total of 502 patients were included in our study: 312 boys and 190 girls (Fig. 1). The mean age was 6.56 ± 4.53 years old, ranging from 10 days to 18 years old. They were divided into two groups: the Omicron variants infection group (194 patients) and the uninfected group (308 patients). The mean interval between the definite Omicron variants infection and surgery was 31.28 ± 10.19 days. In the Omicron variants infection group, 10/194 (5.39%) were asymptomatic, and 166/194 (85.57%) patients had cough with fever at the time of infection. The other symptoms were leg or head pain accompanied by cough with fever (4/194, 2.06%), diarrhea accompanied by cough with fever (9/194, 4.64%), rash accompanied by cough with fever (1/194, 0.52%), and only diarrhea (3/194, 1.55%). One patient (1/194, 0.52%) with Omicron variants infection forgot his symptoms. All symptoms of patients with Omicron variants infection disappeared before surgery. The overall pulmonary complication rate was 1.59% (8/502 patients) and no cardiac complication or mortality in 30-day postoperative follow-up.

Patient and surgical characteristics are shown in Table 1. In our study, there were only one patient with ASA grade IV and no patient with ASA grade V. There were no significant differences in sex, age, surgery department, ASA physical status, grade of surgery, preoperative chest radiograph, preoperative ECG, and postoperative transfer to ICU between the Omicron variants infection group and the uninfected group. However, the incidence

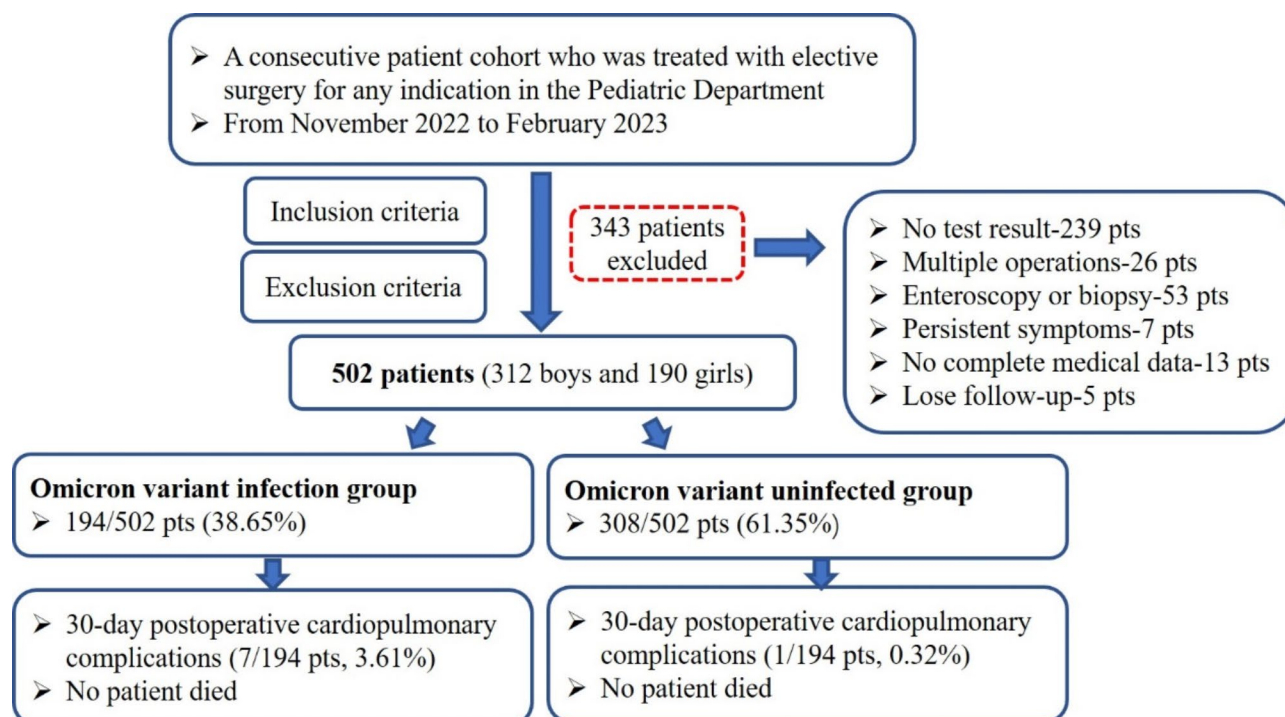


Fig. 1 The flow chart of the study

Table 1 Patient characteristics stratified by the Omicron variant infection condition

Characteristics	N (%) or Mean (Range)			P
	All Patients (n = 502)	Uninfected (n = 308)	Infected (n = 194)	
Age stratification				0.380
0–4 weeks	3 (0.60)	2 (0.65)	1 (0.52)	
5–52 weeks	52 (10.36)	30 (9.74)	22 (11.34)	
1–9 y	297 (59.16)	191 (62.01)	106 (54.64)	
10–18 y	150 (29.88)	85 (27.60)	65 (33.51)	
Sex (female)	190 (37.85)	112 (36.36)	78 (40.21)	0.387
BMI	18.07 ± 3.73 (17.76–18.52)	18.13 ± 3.73 (17.70–18.56)	17.99 ± 3.74 (17.46–18.52)	0.685
Surgery department				0.407
Pediatric orthopedics	193 (38.45)	119 (38.64)	74 (38.14)	
Pediatric surgery	137 (27.29)	86 (27.92)	51 (26.29)	
Pediatric urology	102 (20.32)	56 (18.18)	46 (23.71)	
Pediatric neurosurgery	70 (13.94)	47 (15.26)	23 (11.86)	
ASA physical status				0.150
Grades I–II	452 (90.40)	272 (88.89)	180 (92.78)	
Grades III–V	48 (9.60)	34 (11.11)	14 (7.22)	
Grade of surgery (Grade 1–4)	2.90 ± 0.84 (1–4)	2.94 ± 0.83 (1–4)	2.84 ± 0.85 (1–4)	0.190
Preoperative chest radiograph				0.204
Normal	473 (97.93)	288 (98.63)	185 (96.86)	
Abnormal	10 (2.07)	4 (1.37)	6 (3.14)	
Preoperative electrocardiograph				0.068
Normal	481 (95.82)	291 (94.48)	190 (97.94)	
Abnormal	21 (4.18)	17 (5.52)	4 (2.06)	
Postoperative transfer to ICU	53 (10.56)	36 (11.69)	17 (8.76)	0.299
30-day postoperative cardiopulmonary complications				0.006
No	494 (98.41)	307 (99.68)	187 (96.39)	
Yes	8 (1.59)	1 (0.32)	7 (3.61)	

Bold values are statistically significant $P < 0.05$

BMI indicates Body Mass Index

ASA indicates American Society of Anaesthesiologists

of complications in the Omicron variants infection group (7/194, 3.61%) was significantly higher than that in the uninfected group (1/308, 0.32%) ($p = 0.006$, Table 1). The shortest interval from diagnosis of Omicron variant infection to surgery was 14 days in patients with 30-day postoperative cardiopulmonary complications. The mean interval of between diagnosis of Omicron variants infection and surgery was 24.00 ± 11.17 days in patients with 30-day postoperative cardiopulmonary complications, and 85.7% of postoperative complications occurred within 4 weeks of Omicron variant infection. When we analyzed the correlation between the time from Omicron variants infection diagnosis to surgery and the 30-day postoperative pulmonary complications by weeks, we found that 4 weeks was the critical time point. When stratified by the time from Omicron variants infection diagnosis to surgery as 4 weeks, 30-day postoperative pulmonary complication rates were as follows: 75% (6/8 patients) within 4 weeks and 12% (1/8 patients) more than 4 weeks ($p < 0.001$, Table 2). The postoperative pulmonary complications included pneumonia diagnosed with a chest radiograph or computerized tomography

(CT) in 6 patients and unexpected postoperative ventilation (concomitant postoperative pneumonia) in 2 patients. In our research, there were no cardiac complications, and all these patients with pneumonia recovered and were discharged after routine symptomatic treatment.

Compared with patients without 30-day postoperative pulmonary complication, patients with complications had higher ASA physical status grade (III–V) (75.00% vs. 8.54%, $p < 0.001$), higher grade of surgery (mean grade: 3.50 ± 0.53 vs. 2.89 ± 0.84 , $p = 0.048$), higher abnormal preoperative chest radiograph (50.00% vs. 1.26%, $p < 0.001$) and Omicron variants infection within 4 weeks before surgery (75.00% vs. 14.37%, $p < 0.001$) in univariate analysis (Tables 2 and 3). While adjusted other factors, the Omicron variants infection within 4 weeks before surgery (OR = 17.84, 95% CI: 1.25–255.35, $p = 0.034$), higher BMI (OR = 1.26, 95% CI: 1.02–1.55, $p = 0.034$), ASA physical status grade III–V (OR = 17.35, 95% CI: 1.19–253.80, $p = 0.037$), and abnormal preoperative chest radiograph (OR = 60.07, 95% CI: 1.92–1878.21, $p = 0.020$) were the

Table 2 Patient characteristics stratified by the occurrence of 30-day postoperative cardiopulmonary complications

Variable	N (%) or Mean (Range)		P
	No complication (n = 494)	complications (n = 8)	
Age			0.112
0–4 weeks	3 (0.61)	0 (0)	
5–52 weeks	50 (10.12)	2 (25.00)	
1–9 y	295 (59.72)	2 (25.00)	
10–18 y	146 (29.55)	4 (50.00)	
Sex (female)	188 (38.06)	2 (25.00)	0.716
BMI	18.04 ± 3.69 (17.71–18.37)	20.03 ± 5.71 (15.26–24.79)	0.359
Surgery department			0.033
Pediatric orthopedics	192 (38.87)	1 (12.50)	
Pediatric surgery	133 (26.92)	4 (50.00)	
Pediatric urology	102 (20.65)	0 (0)	
Pediatric neurosurgery	67 (13.56)	3 (37.50)	
ASA physical status			< 0.001
Grades I–II	450 (91.46)	2 (25.00)	
Grades III–V	42 (8.54)	6 (75.00)	
Grade of surgery (Grade 1–4)	2.89 ± 0.84 (1–4)	3.5 ± 0.53 (3–4)	0.015
Preoperative chest radiograph			< 0.001
Normal	469 (98.74)	4 (50.00)	
Abnormal	6 (1.26)	4 (50.00)	
Preoperative electrocardiograph			1.000
Normal	473 (95.75)	8 (100)	
Abnormal	21 (4.25)	0 (0)	
The time from Omicron variants infection diagnosis to surgery			< 0.001
No diagnosis	307 (62.15)	1 (12.5)	
0–4 weeks	71 (14.37)	6 (75.00)	
≥ 4 weeks	116 (23.48)	1 (12.50)	

Bold values are statistically significant $P < 0.05$

BMI indicates Body Mass Index

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independent risk factors for the 30-day postoperative pulmonary complication in patients (Table 3).

Discussion

Our research showed that during the Omicron variants pandemic period, the postoperative pulmonary complications of pediatric patients undergoing non-cardiac surgery were significantly associated with preoperative infection of Omicron variants, ASA physical status grade III–V, higher BMI, and abnormal preoperative chest radiograph, and that most of the patients with complications were infected within 4 weeks preoperatively. Pneumonia was the only clinical manifestation of the complications observed in present research. No cardiac complications or mortality was found within 30 days after surgery in either infection or non-infection group.

The incidence of postoperative complications (3.61%) in the patients infected by Omicron variants in our study was relatively lower than other studies special on pediatric infected by other SARS-CoV-2 variants [8, 10, 13–15]. Pneumonia was the only complication observed in our study and all these patients had cough, fever, and related

imaging (X-ray or CT) findings, which only required symptomatic treatment. Among them, two cases result in unplanned transferred to PICU without extubation. No cardiac complications or mortality was found within 30 days after surgery in either infection or non-infection group. The reduction in virulence of Omicron variants may be one of the most important reasons for the mild complication in our study [16]. An international, multi-center, observational study showed that during general anesthesia, pediatric patients could suffer mild hypoxemia and complications after infection of SARS-CoV-2, but all had no severe sequelae [8, 9].

By now, there was no established guideline for how soon an infected child should undergo elective surgery. Several international cohort studies [7, 17] on general population suggested that elective surgery should be delayed at least 7 weeks after SARS-CoV-2 infection, and even longer if there were persistent symptoms of lung infection. However, in one of the international cohort studies [7], no significant increase of pulmonary complications or mortality was found for the pediatric patients infected by SARS-CoV-2. The author admitted that

Table 3 Unadjusted and adjusted model for 30-day postoperative cardiopulmonary complications in all patients. Values are odds ratio (OR) (95% CI)

Variable	Unadjusted		Adjusted	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.00 (0.86–1.17)	0.988	0.90 (0.69–1.19)	0.465
Sex				
Male	Reference	-	Reference	-
Female	0.54 (0.11–2.72)	0.457	0.63 (0.06–6.94)	0.703
BMI	1.11 (0.97–1.27)	0.140	1.26 (1.02–1.55)	0.034
Surgery department				
Pediatric orthopedics	Reference	-	Reference	-
Pediatric surgery	5.77 (0.64–52.24)	0.119	0.94 (0.04–20.58)	0.971
Pediatric urology	NA	-	NA	-
Pediatric neurosurgery	8.60 (0.88–84.07)	0.064	2.35 (0.08–70.35)	0.621
ASA physical status				
Grades I-II	Reference	-	Reference	-
Grades III-V	32.14 (6.29–164.26)	< 0.001	17.35 (1.19–253.80)	0.037
Grade of surgery	3.15 (1.01–9.84)	0.048	1.22 (0.22–6.65)	0.818
Preoperative chest radiograph				
Normal	Reference	-	Reference	-
Abnormal	78.17 (15.74–388.27)	< 0.001	60.07 (1.92–1878.21)	0.020
Preoperative electrocardiograph	NA	-	NA	-
Pre-operative SARS-CoV-2 by timing of pre-operative diagnosis				
No diagnosis	Reference	-	Reference	-
0–4 weeks	25.94 (3.07–218.90)	0.003	17.84 (1.25–255.35)	0.034
≥4 weeks	2.65 (0.16–42.66)	0.493	10.35 (0.42–254.85)	0.153

Bold values are statistically significant $P < 0.05$

ASA indicates American Society of Anaesthesiologists

BMI indicates Body Mass Index

CI indicates confidence interval

patients with rarity of persistent symptoms of infection may be one reason of negative results. The study's data calculation may also be controversial [13]. Nielson C et al. [14] found that infection of SARS-CoV-2 in pediatric patients could increase risk of postoperative pulmonary complications (5.5% vs. 1.4%, $p < 0.05$), but the complications had no correlation with time of infection or persistent infectious symptoms preoperatively. Another matched cohort study [10] for pediatric patients undergoing surgery within 7 days of infection of SARS-CoV-2 had similar results (26% vs. 1%, $p < 0.01$). Even though the surgery was performed 42 days after infection, there were more complications of myocardial damage within 30 days after surgery than in uninfected children. According our study, non-cardiac elective surgery should be scheduled 4 weeks after infection to reduce the incidence of complications.

We found that pediatric patients with higher BMI or abnormal preoperative chest radiograph were more likely to suffer postoperative pulmonary complication. Obesity had been identified as a significant risk factor for more severe cases of SARS-CoV-2, particularly among younger individuals [18, 19]. Sewell M et al. found that abnormal BMI was identified as one of risk factors associated with

adverse perioperative outcomes for SARS-CoV-2 positive patients, but their subjects were adult patients who underwent emergency instrumented spinal surgery [20]. In Watanabe M et al. study [18], the mean age of their patients was 64.15 ± 15.69 years old, which was significantly older than that of our study. They introduced a new index, visceral fat, and founded that increased visceral accumulation of fat was associated with worse SARS-CoV-2 severity. More postoperative pulmonary complication might be due to a greater oxygen consumption for overweight people and restricted respiratory capacity by reducing resting lung volumes [21]. The abnormal preoperative chest radiograph also showed an affected lung, which may decrease the pulmonary regulatory capacity. We need to treat young patients with higher BMI or abnormal preoperative chest radiograph carefully before elective surgery to reduce the occurrence of postoperative complications as much as possible.

Geng-Ramos G et al. [22] found that the cycle time (Ct), the number of polymerase chain reaction (PCR) cycles for SARS-CoV-2 test, increased significantly by 28 days of infection indicating lower viral load and perhaps lower transmissibility. They recommended that elective surgery should be delayed for a minimum of 4 weeks

from the initial positive test, allowing time to reduce transmissibility of virus and minimize anesthesia risks in asymptomatic pediatric patients. However, they did not show exactly what the risk for postoperative complication in pediatric patients undergoing elective surgery was. A multidisciplinary consensus statement on behalf of the Association of Anaesthetists [23–25] have recommended against elective surgery within 7 weeks of infection for general population mainly on the consideration that infected patients were infectious and could infect hospital staff and other patients in the perioperative period. Our study indicated that pediatric patients undergoing elective non-cardiac surgery within 4 weeks of infection would have higher risk of pulmonary complications than those non-infected. Therefore, we recommended that elective non-cardiac surgery should be delayed minimal 4 weeks for pediatric patients even for asymptomatic ones.

In our study, higher infection rates were founded than other studies due to super transmissibility of Omicron variants and all patients who we chose performed antigen or PCR testing before elective surgery. Our study also had some limitations. Firstly, this study was a single center retrospective research, but our institution is a regional pediatric medical center, and the results could be representative of pediatric people in our region. Secondly, emergency surgery was not included because the patients do not routinely perform antigen or PCR testing for Omicron variants before emergency surgery. Thirdly, cardiac surgery was also not included because most of the cardiac surgery were performed under cardiopulmonary bypass which may have an impact on the evaluation of postoperative complications. In future study, we will do some research special for the pediatric patients infected by Omicron variants undergoing cardiac surgery. As we know, this study was the first one that investigated the postoperative complication for pediatric patients undergoing elective non-cardiac surgery after Omicron variants infection.

Conclusions

Omicron infection could increase pulmonary complications after elective non-cardiac surgery in children. It is recommended that surgery be scheduled 4 weeks after infection to reduce the incidence of complications.

Abbreviations

GISAID	Global Initiative of Sharing All Influenza Data
IRB	Institutional review board
RT-PCR	Reverse transcription-polymerase chain reaction
ASA	American Society of Anesthesiologists
ECG	Electrocardiography
ARDS	Acute respiratory distress syndrome
ANOVA	Analysis of variance
ORs	Odds ratios

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Not applicable.

Author contributions

Prof Hai Li and Prof Yi Du conceptualized and designed the study, supervised data collection, drafted the initial manuscript, and critically reviewed and revised the manuscript. Drs Yan-Yifang Xu, Zhen-Zhen Dai, and Han Zhou designed the data collection instruments, collected data, carried out the initial analyses, drafted the initial manuscript, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data availability

The datasets analyzed in this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study received approval from the Institutional Review Board/Ethics Committee of Xin-Hua Hospital (Reference number: XHEC-C-2023-010-1). The study was conducted according to the ethical principles stated in the Declaration of Helsinki.

Competing interests

No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

Consent to participate

Written informed consent was obtained from the parents.

Article summary

It is advisable to schedule elective surgery at least 4 weeks after Omicron variants infection because of its higher postoperative pulmonary complications in pediatric.

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