Journal of Anesthesia (2024) 38:125–135
https://doi.org/10.1007/s00540-023-03272-7

REVIEW ARTICLE

Postoperative outcomes of pediatric patients with perioperative COVID-19 infection: a systematic review and meta-analysis of observational studies

Tianqing Gong[1] · Qinghua Huang[1] · Qianqian Zhang[1] · Yu Cui[1]

Received: 30 May 2023 / Accepted: 5 October 2023 / Published online: 28 October 2023

Abstract

Objective To quantify the risk of adverse postoperative outcomes in pediatric patients with COVID-19 infection.

Methods We searched PubMed, Embase, Cochrane Library from December 2019 to 21 April 2023. Observational cohort studies that reported postoperative early mortality and pulmonary complications of pediatric patients with confirmed COVID-19-positive compared with COVID-19-negative were eligible for inclusion. We excluded pediatric patients underwent organ transplantation or cardiac surgery. Reviews, case reports, letters, and editorials were also excluded. We used the Newcastle–Ottawa Scale to assess the methodological quality and risk of bias for each included study. The primary outcome was postoperative early mortality, defined as mortality within 30 days after surgery or during hospitalization. The random-effects model was performed to assess the pooled estimates, which were expressed as risk ratio (RR) or mean difference (MD) with 95% confidence intervals (CI).

Results 9 studies involving 23,031 pediatric patients were included, and all studies were rated as high quality. Compared with pediatric patients without COVID-19, pediatric patients with COVID-19 showed a significantly increased risk of postoperative pulmonary complications (PPCs) (RR = 4.24; 95% CI 2.08–8.64). No clear evidence was found for differences in postoperative early mortality (RR = 0.84; 95% CI 0.34–2.06), postoperative intensive care unit (ICU) admission (RR = 0.80; 95% CI 0.39–1.68), and length of hospital stay (MD = 0.35, 95% CI -1.81–2.51) between pediatric patients with and without COVID-19.

Conclusion Perioperative COVID-19 infection was strongly associated with increased risk of PPCs, but it did not increase the risk of postoperative early mortality, the rate of postoperative ICU admission, and the length of hospital stay in pediatric patients. Our preplanned sensitivity analyses confirmed the robustness of our study findings.

Keywords COVID-19 · Pediatric · Postoperative outcome · Mortality

Introduction

Coronavirus Disease 2019 (COVID-19) is a highly contagious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has rapidly swept worldwide since its outbreak in December 2019. The disease has presented an unprecedented challenge to global healthcare systems regarding the perioperative care of patients. Multiple studies have reported that adults with perioperative COVID-19 infection have a higher risk of mortality and postoperative pulmonary complications (PPCs) such as pneumonia, acute respiratory distress syndrome (ARDS), or unexpected postoperative ventilation [1–6]. According to the American Society of Anesthesiologists and Anesthesia Patient Safety Foundation Joint Statement, elective surgery should be delayed for 7 weeks after a SARS-CoV-2 infection, while emergent surgery should weigh the risk of postoperative complications with the urgency of the procedure [7].

However, children seem less affected by COVID-19 and rarely experience severe symptoms compared to adults [8, 9]. Additionally, the data suggest that children with

✉ Yu Cui
cuiyu19831001@163.com

[1] Department of Anesthesiology, Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, No. 1617, Riyue Avenue, Qingyang District, Chengdu 611731, China

COVID-19 infection have less severe postoperative complications and mortality than adult patients [10, 11]. Thus, routinely postponing surgeries may confer additional risk to children in some cases. For example, delaying elective inguinal hernia repair may increase the risk of incarceration [12] and delay diagnosis in the emergency department [13].

A complete understanding of the impact of COVID-19 infection on postoperative outcomes for pediatric patients can assist managers in making perioperative management decisions and help clinicians and families weigh the risk of undergoing surgery in the setting of infection against the risk of delaying the procedure. Therefore, to solve this problem, we performed a systematic review and meta-analysis of observational studies to quantify the risk of adverse postoperative outcomes in pediatric patients with COVID-19 infection.

Methods

This study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. The protocol was registered in the International Prospective Register of Systematic Reviews (registration number: CRD42023415519).

Search strategy

We searched PubMed, Embase, Cochrane Library from December 2019 to 21 April 2023 with the search terms: ("Pediatric*" or "Child*") and ("COVID-19" or "SARS-CoV-2") and ("Postoperative Complication*" or "Postanesthesia outcome*" or "Mortality"). The details of search strategy were listed in Online Resource 1. References of included articles and relevant reviews or meta-analyses were manually searched to find additional studies. There were no language restrictions.

Selection criteria

Two reviewers (Q.Z. and Q.H.) independently performed an initial eligibility screen of titles and abstracts of all retrieved articles. The full texts of potentially eligible articles were then retrieved and assessed. In cases of disagreement, a third reviewer (T.G.) was consulted. We included observational cohort studies that reported postoperative early mortality and pulmonary complications of pediatric patients with confirmed COVID-19-positive compared with COVID-19-negative. Studies in which pediatric patients underwent organ transplantation or cardiac surgery were excluded. Additionally, reviews, case reports, letters, and editorials were excluded.

Data extraction

Two reviewers (Q.Z. and Q.H.) independently extracted data from the included studies using a standardized extraction form. In cases of disagreement, a third reviewer (T.G.) was consulted. Only data from the most recent study or the one with the largest sample size was extracted when a study was reported twice or more. The following data were extracted: author and publication year, location of the study, study design, data collection period, sample size, characteristics of participants, diagnostic criteria of COVID-19 infection, anesthesia and surgical details, and duration of follow-up. The primary outcome was postoperative early mortality, defined as mortality within 30 days after surgery or during hospitalization. Secondary outcomes were PPCs, postoperative intensive care unit (ICU) admission, and length of hospital stay.

Quality assessment

Two reviewers (Q.Z. and Q.H.) independently used the Newcastle–Ottawa Scale (NOS) to assess the methodological quality and risk of bias for each included study [15]. Studies were judged on three perspectives: selection (range 0–4), comparability (range 0–2), and outcome (range 0–3). The total score ranges from 0 to 9, and the high-quality study was defined as NOS scores greater than 5 [16, 17]. (Online Resource 2).

Data synthesis and analysis

We analyzed data in accordance with the recommended methods in the Cochrane Handbook [18]. The strength of the relation between COVID-19 infection and postoperative mortality or pulmonary complications was expressed as risk ratio (RR) with 95% confidence intervals (CI). For continuous outcomes, we selected mean difference (MD) as effect measure. Statistical significance was assessed by the Z test, and $P < 0.05$ was considered significant. Heterogeneity between studies was assessed using the Cochrane Q statistic and the inconsistency index (I^2) statistic. We combined the effect measures across studies using the random-effects model, considering anticipated clinical heterogeneity among included studies, such as the diagnosis criteria for COVID-19, the definition of PPCs, and the length of follow-up. To explore possible sources of heterogeneity, we had planned subgroup analyses for factors that could potentially affect outcomes: country status (developing or developed country), risk of bias (low or high), and time of diagnosing COVID-19 (within or over 7 days before the procedure). To evaluate the robustness of the pooled results, sensitivity analyses were performed by omitting each study individually and recalculating the pooled estimates for the remaining studies. Publication bias was assessed by funnel plot and Egger test. All analyses were performed by Review Manager (RevMan Version 5.3).

Results

Study selection and characteristics

Of the 6065 studies identified, 5537 studies were eligible for initial title and abstract screening. Of these, 70 studies were eligible for full-text review. Since one study was reported twice [19, 20], the most recent version was included [20]. Ultimately, 9 studies involving 23,031 pediatric patients met the criteria and were subsequently quantitatively analyzed (Fig. 1) [20–28].

Characteristics of the included studies were shown in Online Resource 3. Of the 9 studies included, 5 were from the USA, 1 from India, 1 from Indonesia, and 2 were international multi-center studies. There were 2 prospective cohort studies, and 7 retrospective cohort studies with or without matched controls. 7 studies used laboratory diagnosis as the standard for diagnosing COVID-19, while 2 studies used laboratory or clinical diagnosis (symptoms, history, physical examination, laboratory or imaging findings were consistent with the disease). 2 studies divided COVID-19-positive patients into several groups according to the time of diagnosing COVID-19. We have undertaken a careful data extraction process in light of the heterogeneity issues. Specifically, we just extracted the data of which the time to COVID-19 diagnosis was 7 days [22] and 2 weeks [27] before procedure, respectively. Thus, the time of diagnosing COVID-19 ranged from 21 days before to 21 days after the procedure in included studies. All studies reported short-term outcomes: 5 studies had a follow-up of 30 days, 1 study had 7 days, 1 study had a perioperative period, and 2 studies had a hospital stay. There were some variations among studies in the definition of PPCs, which were composed of several following complications: laryngospasm, bronchospasm, hypoxaemia, postoperative respiratory support, ARDS, or

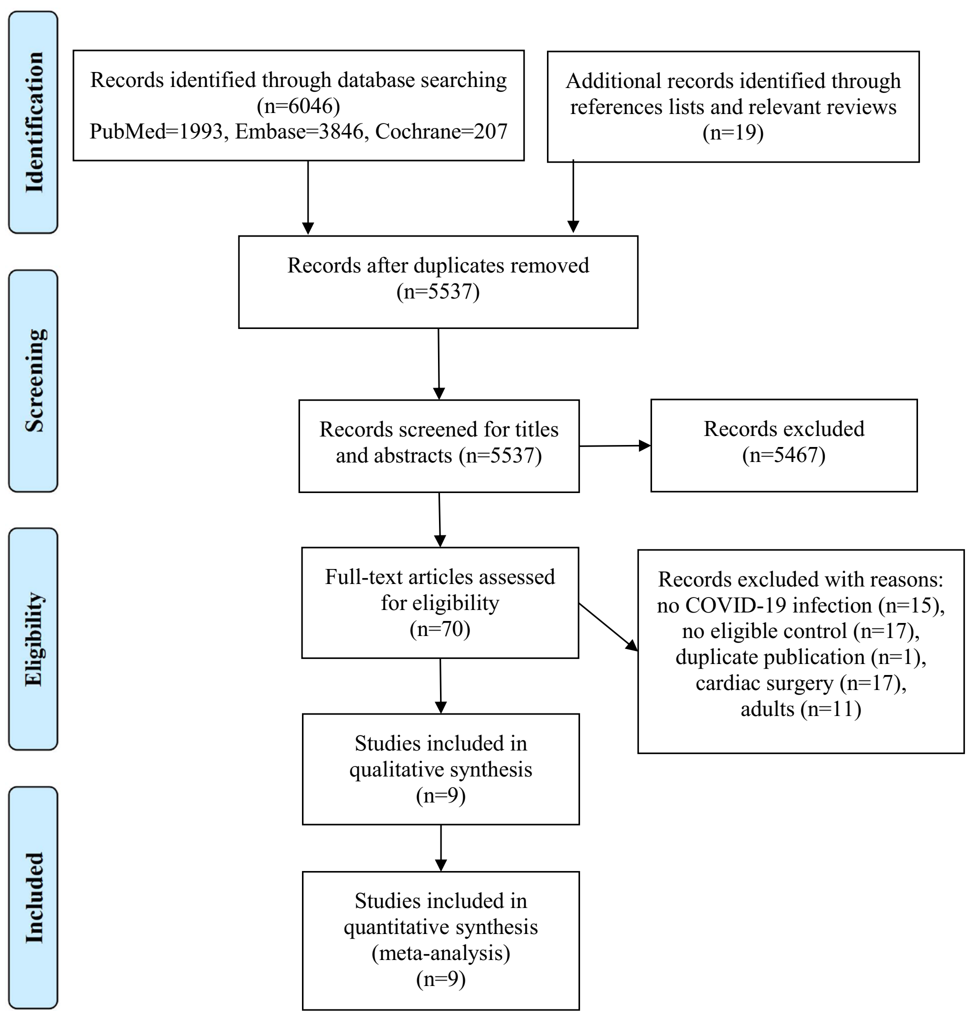

Fig. 1 Study selection flow diagram

pneumonia. According to the Newcastle–Ottawa Scale, all studies were rated as high quality (Online Resource 4).

Characteristics of the included patients were summarised in Table 1. A total of 23,031 pediatric patients underwent surgical procedures, including 650 (2.8%) COVID-19-positive patients and 22,381 (97.2%) COVID-19-negative patients.

Postoperative early mortality

Across all of the 9 included studies, the overall postoperative early mortality in COVID-19-positive pediatric patients was 0.46% (3/650) compared with 0.76% (169/22381) in COVID-19-negative pediatric patients. There was no significant difference in postoperative early mortality between the two groups (RR = 0.84; 95% CI 0.34–2.06; $P = 0.70$), and without significant heterogeneity ($I^2 = 0\%$; $P = 0.52$) (Fig. 2).

PPCs

The overall incidence of PPCs in COVID-19-positive pediatric patients was 6.5% (39/596) compared with 1.8% (379/21599) in COVID-19-negative pediatric patients, which from 6 included studies [20–24, 27]. The most common PPC in COVID-19-positive pediatric patients was postoperative respiratory support, with incidence rates ranging from 1.4% to 20.6%, followed by hypoxaemia (2.0% to 3.6%), and then bronchospasm (2.0%) and laryngospasm (1.2% to 2.0%) (Online Resource 5). Pooled results revealed that pediatric patients with COVID-19 showed a significantly increased risk of PPCs (RR = 4.24; 95% CI 2.08–8.64; $P < 0.01$), and without significant heterogeneity ($I^2 = 43\%$; $P = 0.12$) (Fig. 3). For further analysis, pooled results from 3 studies [20, 23, 24] revealed that COVID-19-positive pediatric patients with preoperative symptoms had significantly higher rates of PPCs than asymptomatic patients (RR = 2.86; 95% CI 1.23–6.62; $P = 0.01$), without significant heterogeneity ($I^2 = 38\%$; $P = 0.2$) (Fig. 4).

Postoperative ICU admission

4 studies [20–22, 26] reported the rate of postoperative ICU admission. Our analysis revealed that the incidence of postoperative ICU admission was similar between pediatric patients with and without COVID-19 (RR = 0.80; 95% CI 0.39–1.68; $P = 0.56$), and without significant heterogeneity ($I^2 = 33\%$; $P = 0.21$) (Fig. 5).

Length of hospital stay

6 studies [20–23, 25, 26] reported the length of hospital stay. There was no significant difference in the length of hospital stay between pediatric patients with and without COVID-19 (MD = 0.35, 95% CI -1.81–2.51; $P = 0.75$). Heterogeneity among these studies was significant ($I^2 = 60\%$; $P = 0.03$) (Fig. 6). Subgroup analyses were not performed due to the small number of studies in each subgroup. Further sensitivity analyses were performed by omitting each study individually and recalculating the pooled estimates for the remaining studies. These data showed that the heterogeneity was not significant ($I^2 = 37\%$; $P = 0.18$) only when the study by Geng-Ramos et al. [22] was excluded; this exclusion did not change the results (MD = -0.44, 95% CI -2.08–1.21; $P = 0.60$) (Online Resource 6).

Sensitivity analyses

In sensitivity analyses, all of the pooled estimates were not significantly different when each study was omitted individually, suggesting that no study significantly affected the pooled estimates and highlighting the robustness of our findings (Online Resource 7–9).

Publication bias

Because there were fewer than 10 studies, it was inappropriate to conduct the funnel plot and Egger test.

Discussion

To the best of our knowledge, this report is the first systematic review and meta-analysis evaluating the association between perioperative COVID-19 infection and postoperative short-term outcomes in pediatric patients. Data from 23,031 pediatric patients indicated that the perioperative COVID-19 infection status did not increase the risk of postoperative early mortality, the rate of postoperative ICU admission, and the length of hospital stay. However, COVID-19-positive pediatric patients had about 4 times higher risk of PPCs compared with COVID-19-negative counterparts. Although there were differences among studies in the diagnosis criteria for COVID-19, the definition of PPCs and the length of follow-up, our results were robust to sensitivity analyses.

Many previous studies in adults have reported that COVID-19-positive patients have a much higher risk of PPCs and early mortality than their COVID-19-negative counterparts, with a range of postoperative early mortality from 16 to 20.5% in COVID-19-positive patients [2, 3, 5, 6]. An international study at 235 hospitals included 1128 adult patients which from the COVIDSurg Collaborative demonstrated that the incidence of PPCs and 30-day mortality in COVID-19-positive patients were 51.2% and 23.8%, respectively, and perioperative COVID-19 infection was associated with high mortality [1]. At the same time, these

Table 1 Characteristics of included patients

Study	Patient number	Patients with COVID, n (%)	male, n (%)	Age (year), mean ± SD[a], median (IQR[b]) or n (%)	Comorbidity, n (%)	General anesthesia, n (%)	Endotracheal intubation, n (%)	Emergent procedure, n (%)	Most common procedures, n (%)	NOS[d] score and methodological quality
Saynhalath et al. [21]	150	51 (34%)	79 (52.7%)	COVID + : 10 (4–15); COVID-: 11 (5–14)	NR[c]	150 (100%)	COVID + : 45 (88.2%); COVID-: 70 (70.7%)	118 (78.7%)	General surgery: 24 (47.1%); orthopedic surgery: 11 (21.6%); interventional radiology: 8 (15.7%)	7, high
Geng-Ramos et al. [22]	261	34 (13%)	143 (54.8%)	7.3 ± 5.8	NR	236 (90.4%)	COVID + : 20 (59.6%); COVID-: 123 (54.2%)	44 (13%)	NR	8, high
Cronin et al. [23]	105	35 (33.3%)	54 (51.4%)	3.7 (1–6)	COVID + : 15 (42.9%); COVID-: 20 (28.6%)	105 (100%)	NR	NR	NR	8, high
Peterson et al. [24]	7896	329 (4.2%)	4614 (58.4%)	1–4y: 2388 (30%); 13–18y: 3793 (48%)	NR	7896 (100%)	COVID + : 232 (70%); COVID-: 4241 (56%)	COVID + : 146 (44%); COVID-: 734 (10%)	NR	6, high
Prajapati et al. [25]	312	9 (2.9%)	210 (67.3%)	2.5 (0.5–7)	NR	NR	NR	216 (69.2%)	Abdominal surgery: 169 (54.2%); urological surgery: 54 (17.3%); thoracic surgery: 38 (12.2%)	6, high
Giwangkancana et al. [26]	73	24 (32.9%)	36 (49.3%)	1–2y: 19 (26%); > 12y: 30 (41%)	COVID + : 6 (25%); COVID-: 12 (24.5%)	66 (90.4%)	59 (80.8%)	COVID + : 20 (83.3%)	COVID + : neurosurgery 9 (37.5%), general surgery 8 (33.3%)	6, high

Table 1 (continued)

Study	Patient number	Patients with COVID, n (%)	male, n (%)	Age (year), mean ± SD[a], median (IQR[b]) or n (%)	Comorbidity, n (%)	General anesthesia, n (%)	Endotracheal intubation, n (%)	Emergent procedure, n (%)	Most common procedures, n (%)	NOS[d] score and methodological quality
Glasbey [27]	13,492	74 (0.5%)	8609 (63.8%)	5–9y: 3042 (22.5%); 10–17y: 5578 (41.3%)	COVID + : 4 (5.4%); COVID-: 473 (3.5%)	NR	NR	COVID + : 56 (75.7%); COVID-: 4907 (36.6%)	Orthopaedics: 2664 (19.7%); general surgery: 2052 (15.2%); urology: 1946 (14.4%); Head & Neck surgery:1889 (14%)	6, high
Price et al. [28]	451	21 (4.7%)	269 (59.6%)	< 1y: 141 (31.3%); 3–11y: 123 (27.3%); 12–19y: 107 (23.7%)	NR	NR	NR	139 (27.5%)	General surgery: 194 (38.4%); cardiothoracic: 106 (21%); orthopedic: 70 (13.9%)	7, high
Nielson et al. [20]	291	73 (25%)	168 (57.7%)	8.9 (4–13)	COVID + : 27 (37%); COVID-: 81 (37.2%)	291 (100%)	NR	219 (75.3%)	Gastrointestinal and general surgery: 122 (41.9%); Orthopedics: 79 (27.1%)	8, high

[a]Standard deviation; [b]Interquartile range; [c]Not report; [d]Newcastle–OttawaScale

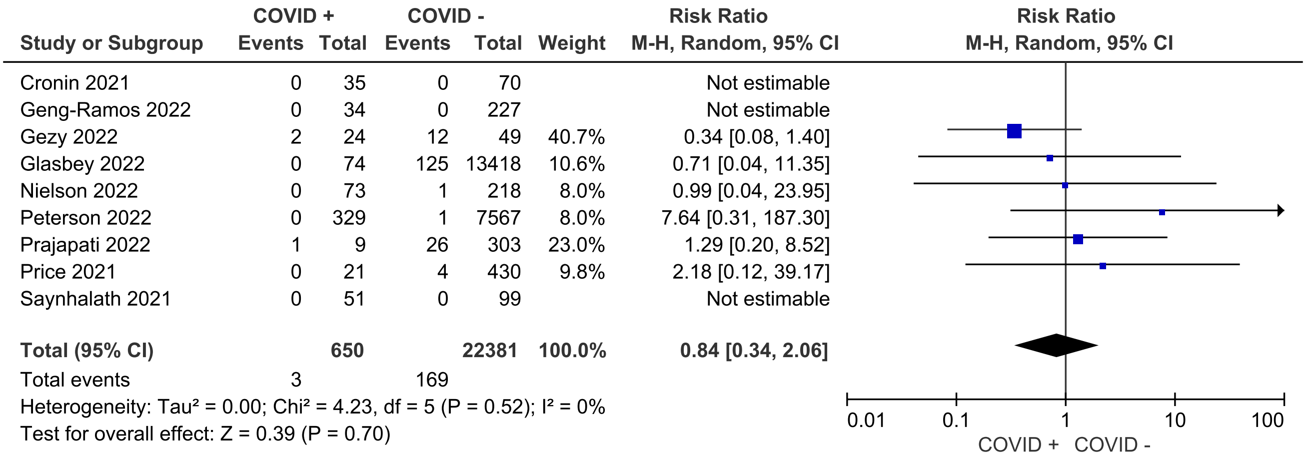

Fig. 2 Impact of COVID-19 infection on postoperative early mortality in pediatric patients

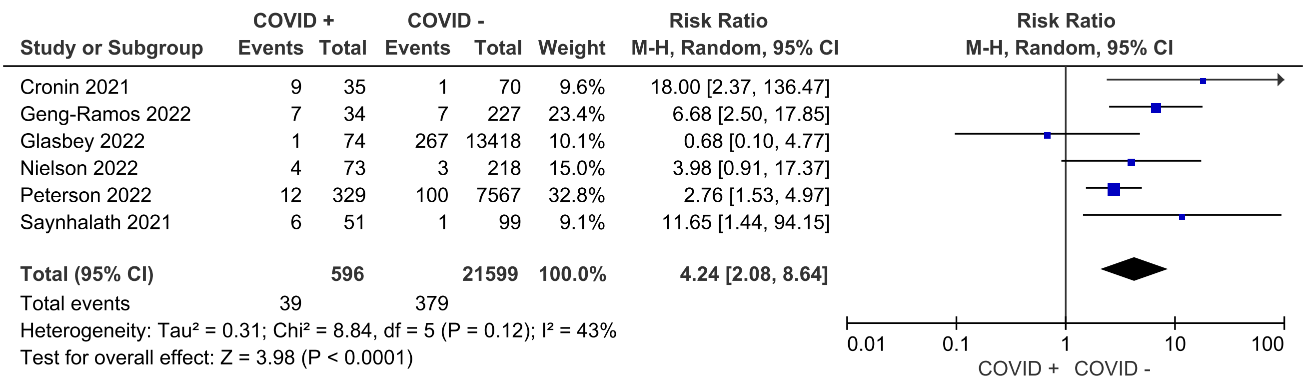

Fig. 3 Impact of COVID-19 infection on postoperative pulmonary complications in pediatric patients

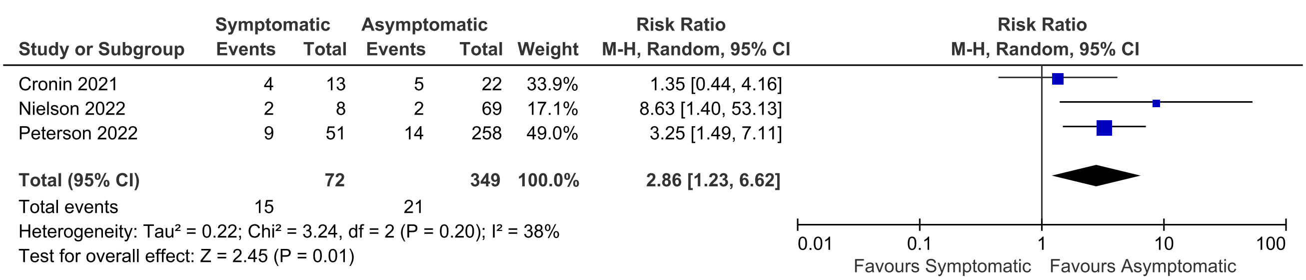

Fig. 4 Impact of preoperative symptoms on postoperative pulmonary complications in COVID-19-positive pediatric patients

postoperative outcomes in patients with COVID-19 infection were substantially worse than pre-pandemic baseline rates of PPCs and mortality [29]. However, our meta-analysis results demonstrated that perioperative COVID-19 infection did not increase the risk of postoperative early mortality in pediatric patients, with a very low postoperative early mortality of 0.46% compared with adults (16% to 23.8%). Although COVID-19 infection in pediatric patients was associated with a higher risk of PPCs with an incidence rate of 6.5%, which was much lower than that in adults (51.2%). Consistent with previous studies [10, 11], a possible explanation for these favorable outcomes is that pediatric patients typically experience a milder disease course and better prognosis of COVID-19 than adults [30–34]. Younger children tend to have many viral infections, and repeated viral exposure may support the immune system when it responds to SARS-CoV-2 [31]. The immune system undergoes substantial changes from birth to adulthood, which are considered

Study or Subgroup	COVID + Events	COVID + Total	COVID - Events	COVID - Total	Weight	Risk Ratio M-H, Random, 95% CI
Geng-Ramos 2022	2	34	11	227	19.0%	1.21 [0.28, 5.24]
Gezy 2022	7	24	28	49	46.5%	0.51 [0.26, 1.00]
Nielson 2022	4	73	15	218	29.1%	0.80 [0.27, 2.32]
Saynhalath 2021	2	51	0	99	5.5%	9.62 [0.47, 196.60]
Total (95% CI)		**182**		**593**	**100.0%**	**0.80 [0.39, 1.68]**
Total events	15		54			

Heterogeneity: Tau² = 0.19; Chi² = 4.48, df = 3 (P = 0.21); I² = 33%
Test for overall effect: Z = 0.58 (P = 0.56)

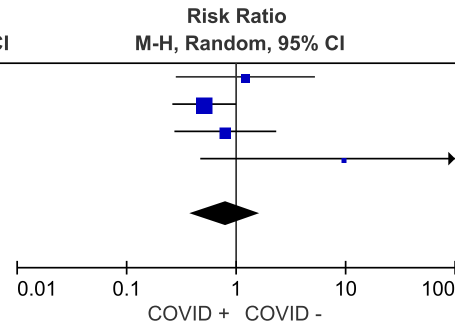

Fig. 5 Impact of COVID-19 infection on postoperative ICU admission in pediatric patients

Study or Subgroup	COVID + Mean	COVID + SD	COVID + Total	COVID - Mean	COVID - SD	COVID - Total	Weight	Mean Difference IV, Random, 95% CI
Cronin 2021	10.8	18.2	35	6.8	15.9	70	7.3%	4.00 [-3.09, 11.09]
Geng-Ramos 2022	11	18.4	34	3.2	10.6	227	8.6%	7.80 [1.46, 14.14]
Gezy 2022	11.9	13.4	24	10.8	10.3	49	9.2%	1.10 [-4.99, 7.19]
Nielson 2022	5.2	5.8	73	6.9	13.1	218	25.1%	-1.70 [-3.89, 0.49]
Prajapati 2022	7.1	4.4	9	9.4	8	303	20.4%	-2.30 [-5.31, 0.71]
Saynhalath 2021	2.7	4.6	51	2.1	3.8	99	29.3%	0.60 [-0.87, 2.07]
Total (95% CI)			**226**			**966**	**100.0%**	**0.35 [-1.81, 2.51]**

Heterogeneity: Tau² = 3.58; Chi² = 12.36, df = 5 (P = 0.03); I² = 60%
Test for overall effect: Z = 0.31 (P = 0.75)

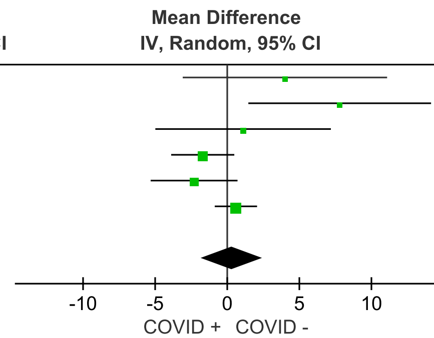

Fig. 6 Impact of COVID-19 infection on length of hospital stay (days) in pediatric patients

alongside the risks of different types of infection [35]. Additionally, the SARS-CoV-2 S protein binds to the angiotensin converting enzyme 2 (ACE2) receptor, and children may be protected against SARS-CoV-2 because this enzyme is less mature at a younger age [36].

The study from the COVIDSurg Collaborative reported that 51.2% of COVID-19-positive adult patients had at least one PPC: 40.4% had pneumonia, 21.3% had unexpected ventilation, and 14.4% had ARDS [1]. In our study, the overall incidence of PPCs was reported to be only 6.5% in COVID-19-positive pediatric patients, in which postoperative respiratory support was the most common PPC (1.4% to 20.6%), followed by hypoxaemia (2.0% to 3.6%), and then bronchospasm (2.0%) and laryngospasm (1.2% to 2.0%). The explanation for these differences in PPCs between adults and pediatrics is still unclear. Ground-glass opacities and consolidation involved both lungs and multiple lobes in a predominant peripheral distribution were the primary findings on CT scans in adult patients [37]. Although peribronchial distribution was uncommonly seen in both populations, it was relatively more frequent in the pediatric group. In addition, bronchial wall thickening was also more prevalent in the pediatric group [38]. These differences in distribution of the coronavirus infection along the respiratory epithelium between the two populations may explain the different PPCs results.

Perioperative respiratory complications are some of the most common events in the general pediatric population, with incidence varying from 0.1% to 3% [39]. Recent upper respiratory infections (URI), which result in airway inflammation and sensitivity, is the most common cause of surgical cancellation in pediatric patients. The risk of perioperative respiratory adverse events (PRAEs) in children with recent URI ranged from 25% to 34.3%, with the most common of PRAEs being oxygen desaturation and severe cough [40–43]. A large prospective cohort study reported that URI was associated with an increased risk for PRAEs only when symptoms were present (RR = 2.05) or less than 2 weeks before the procedure (RR = 2.34) [43]. It appears that the high risk for PRAEs was limited to the first 2 weeks after a URI, and thus rescheduling a pediatric patient at least 2–3 weeks after URI seems to be a safe approach [42, 43]. In our study, the incidence of PPCs in symptomatic COVID-19-positive pediatric patients was 20.8%, with the most common complications of postoperative respiratory support, while a previous study by Reiter et al. [44] reported an incidence rate of 30.8%. Symptomatic COVID-19-positive pediatric patients were more likely to experience PPCs, which had a 2.8-fold increased risk compared with asymptomatic patients. Interestingly, the risk of PPCs in symptomatic COVID-19-positive pediatric patients was similar to the published risk of PRAEs in children with recent URI;

however, the constitution of PPCs were weighted toward less severe events such as oxygen desaturation in patients with URI compared with relatively serious events such as postoperative respiratory support in patients with COVID-19. Further, we may form a risk assessment of the presence or absence of symptoms and the time of diagnosing COVID-19 to determine whether to defer surgery in pediatric patients. We also suggest that the perioperative decision-making logic for pediatric patients with COVID-19 be similar to that for patients with recent URI.

Adult studies found that the increased risk of 30-day postoperative complications and mortality persisted for up to 4–6 weeks from the initial diagnosis of COVID-19 [45, 46]. Geng-Ramos et al. investigated the optimal timing of surgery following COVID-19 infection and found that the risk for PPCs was not increased in pediatric patients with an initial diagnosis of COVID-19 more than 7 days prior to anesthesia compared to the negative cohort [22]. Another study demonstrated that proceeding with elective surgery in children after the diagnosis of mild COVID-19 infection as few as 14 days did not increase the incidence of PPCs compared to waiting at least 28 days [47]. In our meta-analysis, 6 included studies reported the rate of PPCs, in which the time of diagnosing COVID-19 ranged from 14 days before to 7 days after the procedure. Together, these data demonstrated that the increased risk of PPCs persisted for at least 14 days from the initial diagnosis of COVID-19 compared with COVID-19-negative pediatric patients.

To date, there is insufficient evidence to inform guidelines on postponing surgery and optimizing preoperative management for pediatric patients with COVID-19. In the current study, although COVID-19 infection did not increase the risk of postoperative early mortality in pediatric patients, it was associated with a higher risk of PPCs which persisted for at least 14 days from the initial diagnosis. Therefore, similar to recommendations for pediatric patients with symptomatic URI, our data suggest that, where possible, anesthesia and elective surgery should be delayed for at least 2 weeks following symptomatic COVID-19 infection in pediatric patients to decrease the risks of PPCs. Shared decision-making by anesthesiologists, surgeons and patients should seriously weigh the increased risks associated with COVID-19 infection against the risks of delaying surgery in individual patients undergoing emergency or urgent surgery.

The present study has some limitations. First, evidence from observational studies should be interpreted cautiously since these studies are prone to selection and recall biases. Second, there were some expected differences between included studies in the diagnosis criteria for COVID-19, the definitions of PPCs, the types of surgery and anesthesia, and the follow-up duration. Such clinical differences and uncertainty contributed to the heterogeneity in our meta-analysis and limited the generalizability of our results. Third, we did not conduct a grey literature search, which could lead to under- or overestimation of the effect size. Fourth, we did not conduct an estimation of publication bias because of the small number of studies included in our meta-analysis, thus publication bias cannot be ruled out. Fifth, we excluded studies of patients undergoing organ transplantation or cardiac surgery because the postoperative management strategy for these patients was significantly different from other patients, and we planned to review these studies separately. Finally, the incidence, severity, and variant strains of COVID-19 have varied over time and regions, which limited the generalizability of our results. Limitations notwithstanding, our meta-analysis with large sample size was able to show a robust association between perioperative COVID-19 infection and postoperative short-term outcomes in pediatric patients, which may help guide decision-making and inform guidelines in the pediatric population.

Conclusion

This systematic review and meta-analysis showed that perioperative COVID-19 infection was strongly associated with an increased risk of PPCs. However, it did not increase the risk of postoperative early mortality, the rate of postoperative ICU admission, and the length of hospital stay in pediatric patients. Moving forward, more well-designed prospective studies with long-term follow-ups are needed to investigate the optimal timing of surgery following COVID-19 infection in pediatric patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00540-023-03272-7.

Author contributions Conceptualization, methodology, formal analysis were performed by TG. Investigation and data curation were performed by QH and QZ. Supervision, writing-review and editing were performed by YC. The first draft of the manuscript was written by TG and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding All phases of this study were supported by Science & Technology Department of Sichuan Province (No. 2023NSFSC1626).

Declarations

Conflict of interest None.

References

1. Nepogodiev D, Bhangu A, Glasbey JC, Li E, Omar OM, Simoes JF, Abbott TE, Alser O, Arnaud AP, Bankhead-Kendall BK, Breen KA. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet. 2020;396(10243):27–38.

2. Doglietto F, Vezzoli M, Gheza F, Lussardi GL, Domenicucci M, Vecchiarelli L, Zanin L, Saraceno G, Signorini L, Panciani PP, Castelli F, Maroldi R, Rasulo FA, Benvenuti MR, Portolani N, Bonardelli S, Milano G, Casiraghi A, Calza S, Fontanella MM. Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (COVID-19) in Italy. JAMA Surg. 2020;155(8):691–702.
3. Knisely A, Zhou ZN, Wu J, Huang Y, Holcomb K, Melamed A, Advincula AP, Lalwani A, Khoury-Collado F, Tergas AI, Clair CMS. Perioperative morbidity and mortality of patients with COVID-19 who undergo urgent and emergent surgical procedures. Ann Surg. 2021;273(1):34–40.
4. Yates MT, Balmforth D, Lopez-Marco A, Uppal R, Oo AY. Outcomes of patients diagnosed with COVID-19 in the early postoperative period following cardiac surgery. Interact Cardiovasc Thorac Surg. 2020;31(4):483–5.
5. Jonker PK, Van der Plas WY, Steinkamp PJ, Poelstra R, Emous M, Van der Meij W, Thunnissen F, Bierman WF, Struys MM, de Reuver PR, de Vries JPP. Perioperative SARS-CoV-2 infections increase mortality, pulmonary complications, and thromboembolic events: a Dutch, multicenter, matched-cohort clinical study. Surgery. 2021;169(2):264–74.
6. Lei S, Jiang F, Su W, Chen C, Chen J, Mei W, Zhan LY, Jia Y, Zhang L, Liu D, Xia ZY. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020;21:100331.
7. American Society of Anesthesiologists and Anesthesia Patient Safety Foundation Joint Statement on Elective Surgery and Anesthesia for Patients after COVID-19 Infection. https://www.apsf.org/news-updates/asa-and-apsf-joint-statement-on-elective-surgery-and-anesthesia-for-patients-after-covid-19-infection/.
8. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. JAMA. 2020;323(13):1239–42.
9. Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. JAMA. 2020;323(23):2427–9.
10. Mehl SC, Loera JM, Shah SR, Vogel AM, Fallon SC, Glover CD, Monson LA, Enochs JA, Hollier LH, Lopez ME. Favorable postoperative outcomes for children with COVID-19 infection undergoing surgical intervention: experience at a free-standing children's hospital. J Pediatr Surg. 2021;56(11):2078–85.
11. Nepogodiev D. Favourable perioperative outcomes for children with SARS-CoV-2. Br J Surg. 2020;107(13):e644–5.
12. Masoudian P, Sullivan KJ, Mohamed H, Nasr A. Optimal timing for inguinal hernia repair in premature infants: a systematic review and meta-analysis. J Pediatr Surg. 2019;54(8):1539–45.
13. Hu A, Reiter AJ, Gerardo R, Skertich NJ, Lewit R, Ghani M, Witte A, Kang HS, Richards H, Perry B, Tian Y. Association between COVID-19 related elective surgery cancellations and pediatric inguinal hernia complications: a nationwide multicenter cohort study. Surgery. 2022;172(3):989–96.
14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
15. Wells GA, Shea B, D O'Connell JP, Welch ML, P Tugwell. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
16. Salluh JI, Wang H, Schneider EB, Nagaraja N, Yenokyan G, Damluji A, Serafim RB, Stevens RD. Outcome of delirium in critically ill patients: systematic review and meta-analysis. BMJ. 2015;350:h2538.
17. Damuth E, Mitchell JA, Bartock JL, Roberts BW, Trzeciak S. Long-term survival of critically ill patients treated with prolonged mechanical ventilation: a systematic review and meta-analysis. Lancet Respir Med. 2015;3(7):544–53.
18. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, Thomas J. Updated guidance for trusted systematic reviews: a new edition of the cochrane handbook for systematic reviews of interventions. Cochrane Database Syst Rev. 2019;10:ED000142.
19. Nielson C, Taylor I, Huang Y, Park AH. Surgical outcomes in pediatric patients testing positive for SARS-CoV-2. J Am Coll Surg. 2021;233(5):e153.
20. Nielson C, Suarez D, Taylor IK, Huang Y, Park AH. Surgical outcomes inchildren with perioperative SARS-CoV-2 diagnosis. Am J Infect Control. 2022;50(6):602–7.
21. Saynhalath R, Alex G, Efune PN, Szmuk P, Zhu H, Sanford EL. Anesthetic complications associated with severe acute respiratory syndrome coronavirus 2 in pediatric patients. Anesth Analg. 2021;133(2):483–90.
22. Geng-Ramos G, Nelson J, Lee AC, Deutsch N, Challa C, Pestieau S, Rana MS, Hubbard M, Cronin JA. Postanesthesia complications in pediatric patients with previous SARS-CoV-2 infection: a cohort study. Paediatr Anaesth. 2023;33(1):79–85.
23. Cronin JA, Nelson JH, Farquhar I, Braffett B, Bebu I, Pestieau SR, Geng-Ramos G, Heitmiller E, Deutsch N. Anesthetic outcomes in pediatric patients with COVID-19: a matched cohort study. Paediatr Anaesth. 2021;31(6):733–5.
24. Peterson MB, Gurnaney HG, Disma N, Matava C, Jagannathan N, Stein ML, Liu H, Kovatsis PG, von Ungern-Sternberg BS, Fiadjoe JE, PAWS-COVID-19 Group. Complications associated with paediatric airway management during the COVID-19 pandemic: an international, multicentre, observational study. Anaesthesia. 2022;77(6):649–58.
25. Prajapati S, Choudhury SR, Aditya M, Maheshwari A, Anirudha AJ, Sarin YK. Magnitude of SARS-CoV-2 infection and outcome in paediatric surgical inpatients during the first wave of pandemic at a tertiary care Children's hospital in India. J Trop Pediatr. 2022;68(2):fmac011.
26. Giwangkancana G, Oktaliansah E, Ramlan AAW, Utariani A, Kurniyanta P, Arifin H, Widyastuti Y, Pratiwi A, Syukur R. Perioperative management for emergency surgery in pediatric patients with COVID-19: retrospective observational study. Open Access Emerg Med. 2022;14:515–24.
27. Glasbey J. Peri-operative outcomes of surgery in children with SARS-CoV-2 infection. Anaesthesia. 2022;77(1):108–9.
28. Price JC, Lee JJ, Ing C, Li G, Narula J, Clark MK, Stylianos S, Whittington RA, Levy RJ, Sun LS. Prevalence of SARS-CoV-2 positivity in pediatric surgical patients amid the first wave of the COVID-19 pandemic in New York City. J Neurosurg Anesthesiol. 2022;34(1):132–5.
29. Senanayake KJ. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. Br J Surg. 2016;103(8):971–88.
30. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, Rovida F, Baldanti F, Marseglia GL. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr. 2020;174(9):882–9.
31. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020;109(6):1088–95.
32. Li B, Zhang S, Zhang R, Chen X, Wang Y, Zhu C. Epidemiological and clinical characteristics of COVID-19 in children: a systematic review and meta-analysis. Front Pediatr. 2020;2(8):591132.
33. Bailey LC, Razzaghi H, Burrows EK, Bunnell HT, Camacho PE, Christakis DA, Eckrich D, Kitzmiller M, Lin SM, Magnusen BC, Newland J. Assessment of 135 794 pediatric patients tested for

severe acute respiratory syndrome coronavirus 2 across the United States. JAMA Pediatr. 2021;175(2):176–84.
34. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S. Epidemiology of COVID-19 among children in China. Pediatrics. 2020. https://doi.org/10.1542/peds.2020-0702.
35. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. Proc Biol Sci. 1821;2015(282):20143085.
36. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, Graham BS, McLellan JS. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020;367(6483):1260–3.
37. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, Cui J, Xu W, Yang Y, Fayad ZA, Jacobi A. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology. 2020;295(1):202–7.
38. Chen A, Huang JX, Liao Y, Liu Z, Chen D, Yang C, Yang RM, Wei X. Differences in clinical and imaging presentation of pediatric patients with COVID-19 in comparison with adults. Radiol Cardiothorac Imaging. 2020;2(2):e200117.
39. Egbuta C, Mason KP. Recognizing risks and optimizing perioperative care to reduce respiratory complications in the pediatric patient. J Clin Med. 2020;9(6):1942.
40. Zhang S, Ding S, Cai M, Bai J, Zhang M, Huang Y, Zheng J. Impact of upper respiratory tract infections on perioperative outcomes of children undergoing therapeutic cardiac catheterisation. Acta Anaesthesiol Scand. 2018;62(7):915–23.
41. Lee LK, Bernardo M, Grogan TR, Elashoff DA, Ren W. Perioperative respiratory adverse event risk assessment in children with upper respiratory tract infection: validation of the COLDS score. Paediatr Anaesth. 2018;28(11):1007–14.
42. von Ungern-Sternberg BS, Boda K, Schwab C, Sims C, Johnson C, Habre W. Laryngeal mask airway is associated with an increased incidence of adverse respiratory events in children with recent upper respiratory tract infections. Anesthesiology. 2007;107(5):714–9.
43. von Ungern-Sternberg BS, Boda K, Chambers NA, Rebmann C, Johnson C, Sly PD, Habre W. Risk assessment for respiratory complications in paediatric anaesthesia: a prospective cohort study. Lancet. 2010;376(9743):773–83.
44. Reiter AJ, Ingram MC, Raval MV, Garcia E, Hill M, Aranda A, Chandler NM, Gonzalez R, Born K, Mack S, Lamoshi A. Postoperative respiratory complications in SARS-CoV-2 positive pediatric patients across 20 United States hospitals: a cohort study. J Pediatr Surg. 2022. (**In press**)
45. Lobo D, Devys JM. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. Anaesthesia. 2022;77(1):110.
46. Leventoğlu ÖKKEŞ. Delaying surgery for patients with a previous SARS-CoV-2 infection. Br J Surg. 2020;107(12):e601–2.
47. Lee DR, Banik GL, Giordano T, Kazahaya K, Lin EE. Early elective surgery in children with mild COVID-19 does not increase pulmonary complications: a retrospective cohort study. Paediatr Anaesth. 2022;32(10):1172–4.