Do COVID-19 Pandemic-Related Behavior Changes Affect Perioperative Respiratory Adverse Events in Children Undergoing Cardiac Interventional Catheterization?

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Research

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Abstract

Background: The Novel Coronavirus Disease (COVID-19) pandemic-related behavior changes could affect the perioperative respiratory adverse events in children with congenital heart disease (CHD). This study was designed to compare the incidence of perioperative respiratory adverse events (PRAEs) in children with and without upper respiratory infection (URI) undergoing the cardiac catheterization before and during COVID-19 pandemic.

Methods COVID-19 was outbreak in January 2020 in China. 260 pediatric patients scheduled for elective therapeutic cardiac catheterization were included from January 2019 to March 2021 and 154 were completed during the pandemic. Recent URI was diagnosed by the attending anesthesiologist owing to different PRAEs incidence in non-URI and URI children. The overall incidence of PRAEs (laryngospasm, bronchospasm, coughing, airway secretion, airway obstruction, and oxygen desaturation) in non-URI and URI children undergoing the elective cardiac catheterization were compared before and during the COVID-19 pandemic. Logistic regression model was fitted to identify the potential risk factors associated with PRAEs.

Results: Of 564 children enrolled, 359 completed the study and was analyzed finally. URI incidence decreased substantially during the COVID-19 pandemic (14% *vs.* 41%, $P<0.001$). Meanwhile, the overall PRAEs also significantly declined no matter whether or not the child had recent URI (22.3% *vs.* 42.3%, $P=0.001$ for non-URI and 29.2% *vs.* 58.7%, $P=0.012$ for URI respectively). Post-operative agitation in non-URI children occurred less frequently during the pandemic than before (2.3% *vs.* 16.2%, $P=0.001$). Behaviors before the COVID-19 pandemic (odd ratio=2.84, 95%CI 1.76 to 4.58) and recent URI (odd ratio =1.79, 95%CI 1.09 to 2.92) were associated with the PRAEs.

Conclusions: COVID-19 pandemic-related behavior changes were associated with the reduction of PRAEs in non-URI and URI children undergoing elective therapeutic cardiac catheterization.

Introduction

It has been more than 18 months since the first case of the novel coronavirus disease (COVID-19) was reported on Dec.1 2019, this disease has yet not been fully controlled [1, 2]. Covid-19 transmission can result in severe respiratory disease which can lead to hospitalization and death as such there have been widespread, but shifts in routine behavior in the public such as social distancing, less time outdoors, mask wearing, and increased attention to hygiene all in an effort to reduce transmission [3–8]. While the disease has been brought under control after 76 days in China, the behavioral changes still remained [9]. It was reported that the disease spectrum at Respiratory Department and Infection Department in children hospital in China have dramatically changed due to the reduction of pediatric upper respiratory infections (URI), which may be attributed to COVID-19 pandemic-related behavior changes [4, 10]. The effects of COVID-19 pandemic-related behavior changes on our clinical practice and patient outcomes are still unknown.

Determining the optimal timing to deliver anesthesia to children with URI can be a challenging issue involving both anesthesiologist and parents [11, 12]. Presence of URIs in children undergoing general anesthesia significantly increase peri-operative respiratory adverse events (PRAEs), and may also increase length of hospital stay, cost and suffering, and even death [13–16]. Postponement of surgery because of sudden URI may disturb both the surgical, guardian's and children' schedules, potentially even missing the optional surgical time window since children usually experience 7-8 times URI each year and it is better to delay 4-6 weeks for URI children scheduled for general anesthesia to reduce PRAEs [17].

This is particularly true for children with congenital heart disease (CHD) since they are more vulnerable to URI compared to otherwise healthy children [18, 19]. Furthermore, the incidence and severity of post-operative respiratory complications significantly increase in CHD children undergoing open heart surgery [20]. The lengths of stay (LOS) in the hospital and cardiac intensive care unit (ICU) are also significantly 2~3 times longer in URI children than non-URI [20]. Therefore, open heart surgery in URI children should be postponed whenever possible.

Compared to open heart surgery, therapeutic cardiac catheterization is relatively less invasive and has a lower incidence of life-threatening events [21, 22]. However, our previous study showed that the incidence of overall PRAEs for children with less 2 weeks URI undergoing cardiac catheterization is still very high, about 66.3% compared to 46.6% in non-URI children [12]. Along with the ongoing of COVID-19 pandemic related behavior changes, whether these behavior changes can affect the incidence of PAREs in non-URI and URI children undergoing the cardiac interventional catheterization is still unknown. Thus, our aim at present study was to primarily investigate the incidence of PRAEs in non-URI children decreased during COVID-19 pandemic. The secondary endpoint was to examine whether the overall PRAEs were also decreased in URI children, and whether URI and/or COVID-19 pandemic were the potential risk factors for PRAEs.

Materials And Methods

Pediatric patients

Included data were extracted from our database as previous studies described. Children scheduled for elective cardiac transcatheter occlusion under general anesthesia for ventricular septal defects (VSD), atrial septal defects (ASD), and/or patent ductus arteriosus (PDA) were recruited into the study from 20th February 2019 to 19th March 2021 at the Shanghai Children's Medical Center & National Children's Medical Center, a tertiary hospital affiliated to Shanghai Jiao Tong University. Exclusion criteria included parents' refusal to sign the informed consent; the American Society of Anesthesiologists physical status score ≥ ; evidence of a recent lower respiratory tract infection (such as pneumonia and bronchitis) within the past 2 weeks; unavailable medical history (parents or legal guardian cannot recall the medical history clearly); known hypersensitivity to anesthetics; recent participation in other clinical studies; medical history of hepatic or nephritic disease or complex cyanotic heart disease; premedication (e.g.,

dexmedetomidine, salbutamol and midazolam); and endotracheal tube in exchange for LMA due to dissatisfactory ventilation.

Anesthesia Management

After children entered the operating room, routine monitoring including electrocardiography, noninvasive blood pressure monitoring, and pulse oxygen saturation measurement were conducted. Anesthetics such as propofol (3-4 $mg \cdot kg^{-1}$) and sufentanil (0.1-0.2 $\mu g \cdot kg^{-1}$) were used for the induction of anesthesia and were administered through the peripheral vein. Appropriate LMA was inserted while the child was unconscious. Sevoflurane 1-1.2 MAC with the mixture of oxygen and air (50:50) was inhaled to maintain the depth of anesthesia depending on the heart rate and blood pressure. Crystalloid fluid was infused following the 4-2-1 rule. The LMAs were removed while the children were still anaesthetized (regular breathing, end-tidal sevoflurane level: 0.8 MAC). The anesthesiologist in charge was blinded to the patient's URI history.

Protocol

All CHD children were divided into two groups, the COVID-19 period spanning March 2020 to March 2021 and non-pandemic period considered from February 2019 to January 2020 due to January 23rd being the date when Wuhan declared strict anti-pandemic measures which would cause changes in behavior.

Before surgery, the parents or legal guardians of all children were visited by a senior resident anesthesiologist with at least three years anesthesia experience and the parents/guardians were asked to fill out a questionnaire form. The questionnaire included questions concerning patient's demographic information (age, sex, weight, and height), type of CHD, history of asthma and passive smoking, presence of URI symptoms, and the exact time of URI occurrence. Patient who presented with any two of the following URI symptoms, as confirmed by the parent or legal guardian, over the last the two weeks were considered to have a history of URI: nasal congestion, rhinorrhea, dry or moist cough, sore throat, sneezing, or fever >38°C.

PRAEs (laryngospasm, bronchospasm, coughing, airway secretion, airway obstruction, and oxygen desaturation) as well as details of anesthesia management were recorded. Adverse respiratory events were defined as any episode of perioperative airway obstruction (snoring or requirement of intervention with a decrease in SpO_2 after inhalation of room air; interventions included repositioning/neck roll, jaw thrust/ chin lift, and oral airway), laryngospasm (partial or complete airway obstruction associated with muscle rigidity of the abdominal and chest walls), bronchospasm (increased respiratory effort, especially during expiration; wheezing on auscultation), oxygen desaturation less than 95% (for ≥10s), breath holding (≥15s), severe coughing (a series of pronounced, persistent, severe coughs lasting more than 10s), and increased airway/oral secretion (≥one suction). Intraoperative observation and postoperative visit were completed by a researcher in our study team who was also the qualified anesthesiologist. If a

laryngospasm occurred, children were treated with positive airway pressure combined with increased anesthetic levels; some patients required the administration of succinylcholine. In cases where bronchospasm occurred, children were treated with nebulized albuterol using a metered-dose inhaler.

Statistical analysis

According to our previous studies[12, 23], the incidence of PRAEs in CHD children without recent URI was 37.7% (95%CI 35.3–40.2%) during the non-COVID-19 pandemic period. We assumed the incidence of PRAEs in the same population decreased by a half in 2020 (COVID-19 period). 114 children in each period were required with a power of 90% and a significance level of 0.05. Accounting for the 10% dropouts of samples, 125 patients per group were required.

Normality testing was conducted using the Shapiro-Wilk test. Numerous variables were presented as mean and standard deviation (SD), and categorical data as absolute numbers and percentages. Differences between groups were determined using the Student's t-test for numerous variables and the χ^2 test or Fisher exact test for categorical variables. Logistic regression model measured the association between behavior changes during the pandemic and PRAEs. The results were presented as odds ratios (OR) and 95% confidence intervals (CI). For all tests, a two-sided value of *P* value <0.05 was considered significant. Statistical analyses were performed using IBM SPSS statistics for Windows, Version 26.0 (IBM corp., Armonk, NY, USA).

Results

Of total 564 pediatric patients we recruited, 364 were eligible for inclusion into this observational study. Finally, 359 children with complete records were analyzed, 260 before and 154 during the COVID-19 pandemic respectively. STROBE flow diagram was showed in the Figure 1. During the CPVID-19 pandemic, only 15.6% (95% CI 12.7–18.5%) children were diagnosed as recent URI, significantly lower than before (vs. 36.6%, 95% CI 33.2–40.0%, *P*<0.001). The demographical characteristics were comparable before and during COVID-19 period (Table 1), except for the passive smoking which occurred less frequently during the pandemic.

Table 1

Characteristics of all children. Data were shown as mean ± SD or *n* (%). † was considered as statistically significant.

	non-URI		*P* value	URI		*P* value
	2019	2020		2019	2020	
	n=130	*n*=130		*n*=75	*n*=24	
age, year	3.1 (2.2, 5.2)	3.3 (2.1, 6.4)	0.219	2.7 (2.1, 4.4)	3.6 (2.3, 6.0)	0.076
gender, *n*			0.900			0.919
M	56 (43)	57 (44)		29 (38.7)	9 (37.5)	
F	74 (57)	73 (56)		46 (61.3)	15 (62.5)	
height, cm	97 (88, 110)	100 (87, 121)	0.174	95 (88, 106)	100 (90, 125)	0.172
weight, kg	15 (12, 19)	16 (12, 23)	0.078	14 (12, 18)	15 (13, 22)	0.127
tobacco exposure, *n*	44 (33.8)	12 (9.2)	<0.001†	30 (40.0)	2 (8.3)	0.004†
history of asthma, *n*	2 (1.5)	1 (0.8)	1.000	1 (1.3)	0 (0)	NA
history of allergy, *n*	12 (9.2)	12 (9.2)	1.000	19 (25.3)	3 (12.5)	0.188
history of hay fever, *n*	10 (7.7)	6 (4.6)	0.302	8 (10.7)	4 (16.7)	0.477
snoring, *n*	38 (29.2)	13 (10.0)	<0.001†	35 (46.7)	9 (37.5)	0.432

Table 2
Incidence of peri-operative respiratory adverse events and post-operative adverse events. Data were shown as *n* (%). † was considered as statistically significant. NA. not applicable

	non-URI		*P* value	URI		*P* value
	2019	2020		2019	2020	
	n=130	*n*=130		*n*=75	*n*=24	
PRAEs, *n*						
severe cough	2 (1.5)	1 (0.8)	1.000	0 (0)	0 (0)	NA
breath holding	0 (0)	1 (0.8)	NA	0 (0)	0 (0)	NA
laryngospasm	5 (3.8)	0 (0)	NA	3 (4.0)	1 (2.4)	1.000
airway obstruction	28 (21.5)	16 (12.3)	0.047†	34 (45.3)	18 (25.0)	0.077
desaturation	48 (36.9)	20 (15.4)	<0.001†	37 (49.3)	4 (16.7)	0.005†
any of above	55 (42.3)	29 (22.3)	0.001†	44 (58.7)	7 (29.2)	0.012†
Others, *n*						
agitation	21 (16.2)	3 (2.3)	0.001†	6 (8.0)	0 (0)	NA
vomiting	9 (6.9)	7 (5.4)	0.606	4 (5.3)	1 (4.2)	1.000
copious secretion	8 (6.2)	5 (3.8)	0.393	11 (14.7)	3 (12.5)	1.000
fever	2 (1.5)	1 (0.8)	1.000	2 (2.7)	1 (4.2)	0.569

Table 4
multivariate analysis of factors associated with perioperative respiratory adverse events (PRAEs). Results from logistic regression were presented as mean ± SD, n (%), odds ratio (OR) with 95% confidence interval (95% CI) and Wald test P value. † was considered as statistically significant.

	univariate analysis			**multivariate analysis**	
	PRAEs (*n*=135)	**non-PRAE (*n*=224)**	***P* value**	**OR (95% CI)**	***P* value**
age, year	3.5 ± 2.5	4.2 ± 2.8	0.089		
gender, *n*			0.404		
M	53 (39)	98 (44)			
F	82 (61)	126 (56)			
year, *n*			<0.001†		
2019	99 (73)	106 (47)		2.84 (1.76, 4.58)	<0.001†
2020	36 (27)	118 (53)		Reference	
URI, *n*			0.002†		
non-URI	84 (62)	176 (79)		Reference	
URI	51 (38)	48 (21)		1.79 (1.09, 2.92)	0.020†
tobacco exposure, *n*	43 (32)	45 (20)	0.012†		
history of snoring, *n*	43 (32)	52 (23)	0.072		
history of hay fever, *n*	11 (8)	17 (8)	0.848		
history of asthma, *n*	3 (2)	1 (0.4)	0.151		

The overall volume of cardiac catheterization was similar in 2019 and 2020, with a dramatic decrease in quarter 1 (Q1) 2020 when the COVID-19 breakout began and the Chinese health authorities declared the traffic restriction (Figure 2). The overall incidence of URI and PRAEs before pandemic showed seasonality. Along with the decrease of URI in the consecutive time from Q1 2019 to Q1 2021, the overall incidence of PRAEs also demonstrated a similar trend downwards. During the COVID-19 pandemic, PRAEs in all children decreased by 50% compared with the same period of 2019. In non-URI children, the overall PRAEs decreased from 42.3% (95% CI 38.0–46.6%) to 22.3% (95% CI 18.6–26.0%, *P*=0.001). And in URI children, it decreased from 58.7% (95% CI 53.0–64.4%) to 29.2% (95% CI 19.7–38.7%, *P*=0.012). Difference in perioperative lower SpO_2 was particularly clear before and during the pandemic. Post-

operative agitation in non-URI children during the pandemic occurred less than before (2.3%, 95% CI 1.0–3.6% *vs.*16.2%, 95% CI 13.0–19.4%, *P*=0.001).

The univariate analysis indicated three variables were associated with PRAEs (Table 3). Multivariate analysis identified pandemic-related behavior changes as an independent factor which mitigated the risk of PRAEs (OR 0.33, 95% CI 0.21 to 0.52, *P*<0.001). And recent URI was associated with the increased incidence of PRAEs (OR 1.79, 95%CI 1.09 to 2.92, *P*=0.02).

Discussion

We found that the URI incidence in children undergoing elective cardiac interventional catheterization decreased substantially during the COVID-19 pandemic period. Meanwhile, the overall PRAEs incidence also significantly decreased in non-URI and URI children with CHD, especially the lower SpO_2. This decrease in PRAEs may be seen as a benefit from the behavior changes during the COVID-19 pandemic period and provide a potential pathway to reduce the PRAEs incidence and medical cost and increase safety through behavior changes before surgery.

Unexpectedly, our current study showed that PRAEs were significantly reduced in CHD children with URI and without URI compared to our data before the COVID-19 pandemic breakout. Along with many other studies, our previous studies also demonstrated that recent URI significantly increased PRAEs in children undergoing elective cardiac interventional catheterization and postpone of surgery was thought as an easy and effective way to reduce PRAEs [12, 14, 23]. Although the precise mechanisms remained elusive, multivariate regression analysis indicated that COVID-19 pandemic-related behavior changes were associated with these reductions in PRAEs and these behavior changes might be adopted as an effective strategy of pre-operative preparation for reducing PRAEs in CHD children regardless of URI. Wearing a mask as a non-pharmaceutical intervention is an effective measure to prevent the transmission chain of virus [4]. Wearing facemask offered several benefits, but it did not completely block the occurrence of PRAEs. A combination of interventions will always be required to provide effective protection from airway infection and reduce higher airway sensitivity, and finally reduce PRAEs [10, 24].

Different from our previous study that passive smoking is an independent risk factor associated with PRAEs in URI children [23], our current study showed that the percentages of passive smoking in non-URI and URI children dramatically reduced and passive smoking was not an independent risk factor any more after COVID-19 pandemic breakout, which might relate to social distancing or/and smoking reduction in guardians due to COVID-19 pandemic-related behavior changes. Reduction of tobacco exposure might alleviate airway stimulation and finally reduce PRAEs in CHD children, which further investigation is needed to clarify it.

In addition to PRAEs reduction, post-operative agitation was also alleviated after COVID-19 pandemic breakout. Due to the sharp decrease in operation volume during the COVID pandemic, anesthesiologists and residents were able to give enough care on emergence and post-operative recovery of each patient.

Furthermore, under the “one ward for one child” policy in order to reduce in-hospital transmission, post-operative cry and noise from a crowded place with many people nearby obviously disappeared. PRAEs reduction itself was also a potential cause of agitation alleviation.

Our study also indirectly confirmed the recent report from the region of Taiwan showing a significant decrease in cases of influenza, enterovirus, and all-cause pneumonia during the COVID-19 period, which might be due to the influence of voluntary and policy-related behavior changes including improved personal hygiene, less environmental tobacco exposure, social distancing and school closing, and restrictions on transportation and movement [7]. Although our data demonstrated seasonal changes of URI and PRAEs in the consecutive years of 2018 and 2019 with lowest incidence in Q3, the incidences of URI and PRAEs substantially decreased during the COVID-19 pandemic without significant seasonal changes. After the COVID-19 broke out, there was no difference in the PRAEs incidence between URI and non-URI children (29.2% vs. 22.3%, P=0.466).

Strengths and Limitations

A key strength of our study is that the data was prospectively collected instead of retrospective analysis only since this was a part of our series study[12, 23, 25], which increased the ability to trace the effects of COVID-19 pandemic-related sudden behavior changes on the PRAEs occurrence in children undergoing elective cardiac interventional catheterization. Some limitations in our study should be pointed out. First, COVID-19 is a sudden outbreak of pandemic disease, it is impossible for us to conduct a cohort study or randomized controlled trial to explore its potential effects on PRAEs, we only collected data prospectively and analyze them retrospectively. Second, several voluntary and policy-induced behavior changes have occurred due to COVID-19 pandemic, but the specific or primary behavior change related to PRAEs reduction was not sorted out in current study, which is very important for future changes of pre-operative preparation strategies. Third, the mechanisms of COVID-19 pandemic-related behavior changes induced PRAEs reduction was not explored. Fourth, results drawn from this single-center database may not generalize to patients nationally or in other geographic contexts.

Conclusions

COVID-19 pandemic-related behavior changes can reduce perioperative respiratory adverse events in children undergoing cardiac interventional catheterization no matter with or without URI. Whether and how these behavior changes could be adopted as an effective strategy of pre-operative preparation for reducing PRAEs occurrence is worthy of further investigation.

Abbreviations

COVID-19, The Novel Coronavirus Disease

CHD, congenital heart disease

PRAEs, perioperative respiratory adverse events

URI, upper respiratory infection

LOS, lengths of stay

ICU, intensive care unit

ASD, atrial septal defects

VSD, ventricular septal defects

PDA, patent ductus arteriosus

SD, standard deviation

OR, odds ratios

CI, confidence intervals

Declarations

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None declared

Ethics approval and consent to participate

The prospective study (SCMCIRB-K20170122) was approved by the Institutional Review Board of Shanghai Children's Medical Center, China (Chairperson Prof. Fan Jiang) on 30th June 2017 and was registered with the Chinese Clinical Trial Registry (ChiCTR2000034531).

Authors' contributions

Jijian Zheng and Mazhong Zhang initiated the research, wrote the research proposal, conducted the search. Wei Ji and Kan Zhang initiated the research, wrote the research proposal, conducted the research, performed data entry and analysis, and wrote the manuscript. Mengqi Li, Siyuan Wang and Liping Sun performed data entry and analysis. Yue Huang and Jie Bai contributed to patient recruitment, data input and review of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available in our institution and can be requested from the corresponding author on reasonable request

Consent for publication:

Not applicable

Conflict of interest

None declared

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Table

Table 3 is not available with this version.

Figures

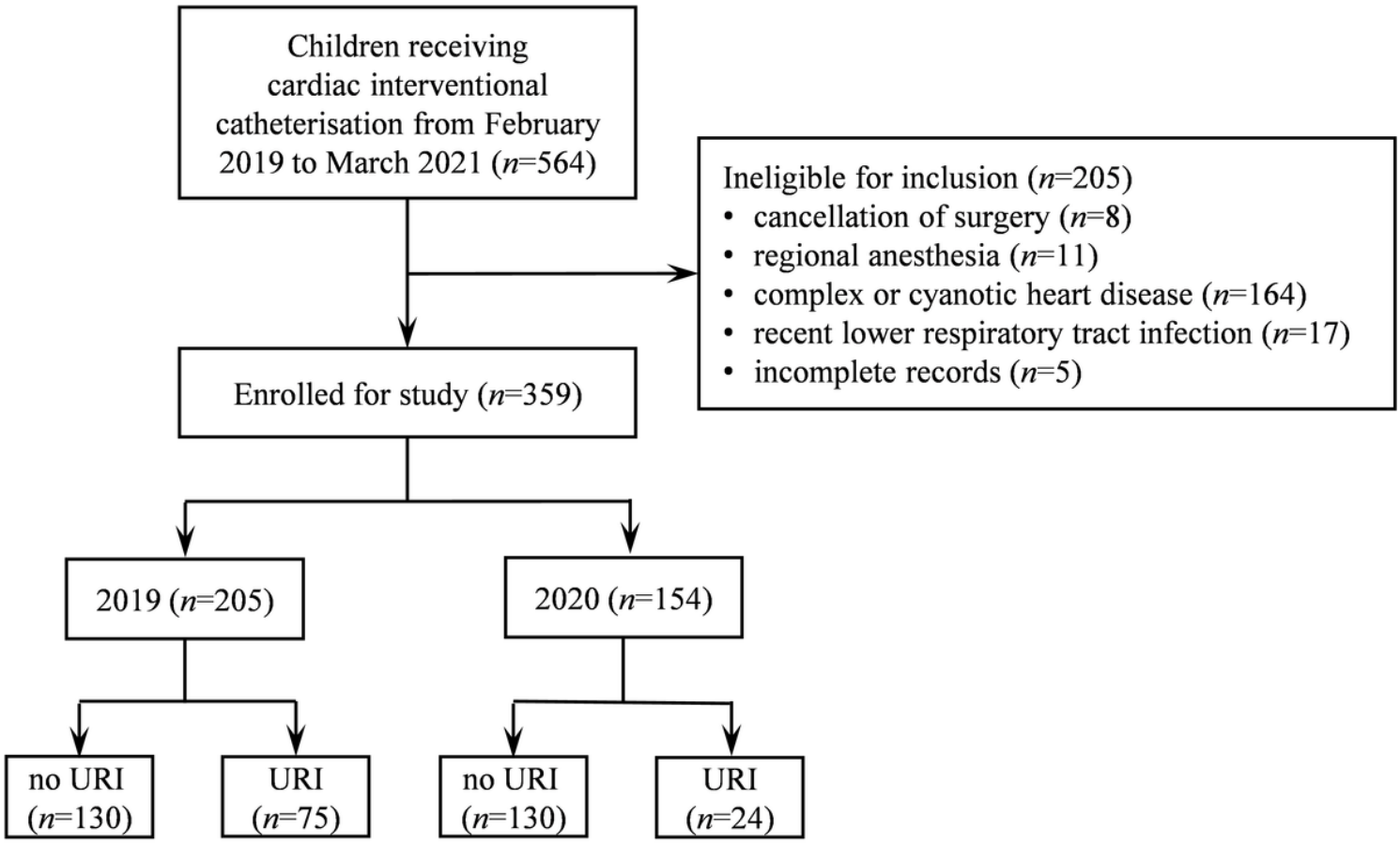

Figure 1

flow diagram.

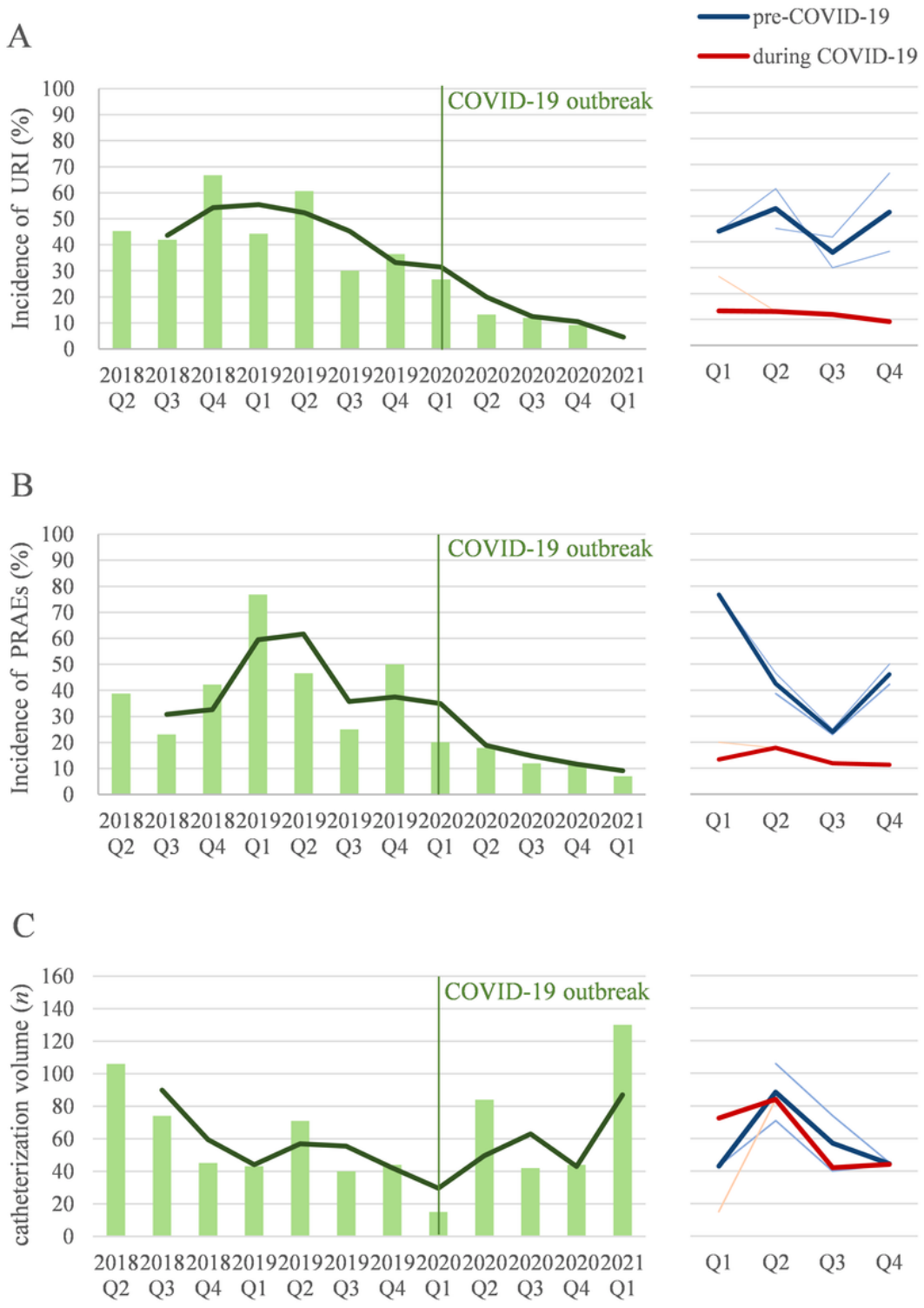

Figure 2

left panels showed a quarterly trend for the incidence of upper respiratory infection (URI, panel A) and perioperative respiratory adverse events (PRAEs, panel B), and the total surgery volume (panel C) from 2nd quarter (Q2) 2018 to 1st quarter of 2021. Green line as moving average showed the chronological viewing order of incidence and volume. Right panels showed the seasonality of URI, PRAEs and surgical

volume. Bule line was the average line before the pandemic (2018 and 2019), while the red line was the line during the pandemic.

Supplementary Files

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