Cardiology in the Young

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Analysis of risk factors for prolonged stay in the intensive care unit after cardiac surgery in children with pneumonia

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Original Article

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Abstract

Aim: Preoperative pneumonia in children with CHD may lead to longer stays in the ICU after surgery. However, research on the associated risk factors is limited. This study aims to evaluate the pre-, intra-, and postoperative risk factors contributing to extended ICU stays in these children. *Methods:* This retrospective cohort study collected data from 496 children with CHD complicated by preoperative pneumonia who underwent cardiac surgery following medical treatment at a single centre from 2017 to 2022. We compared the clinical outcomes of patients with varying ICU stays and utilised multivariate logistic regression analysis and multiple linear regression analyses to evaluate the risk factors for prolonged ICU stays. *Results:* The median ICU stay for the 496 children was 7 days. Bacterial infection, severe pneumonia, and Risk Adjustment for Congenital Heart Surgery-1 were independent risk factors for prolonged ICU stays following cardiac surgery ($P < 0.05$). *Conclusion:* CHD complicated by pneumonia presents a significant treatment challenge. Better identification of the risk factors associated with long-term postoperative ICU stays in these children, along with timely diagnosis and treatment of respiratory infections in high-risk populations, can effectively reduce ICU stays and improve resource utilisation.

Introduction

CHD is the most common congenital malformation in infants and young children.[1] Haemodynamically significant CHD is a well-known high-risk factor for severe pulmonary infection.[2]. Viruses and bacteria are the most common pathogens responsible for hospital-acquired pulmonary infectious diseases.[3] For children with CHD, pneumonia is prone to recurrence, is difficult to control after infection, and has a high mortality rate.[4] Therefore, research into such children is of great significance.

The reported mortality rate of children with CHD complicated by pneumonia is 11.9–56%, often due to uncontrolled heart failure during conservative treatment.[5,6]. Surgery in infants with CHD and pneumonia is typically postponed until the pneumonia is fully treated. However, some infants die of respiratory and cardiac failure before surgical treatment can be administered. With the advancements in surgical techniques, myocardial protection methods, general anaesthesia, and intensive care management, the effectiveness of paediatric cardiac surgery has significantly improved. The current approach promotes early surgery.[7]

A considerable number of children with CHD and preoperative pneumonia require longer stays in the ICU after surgery, which poses a significant challenge to intensive care providers. Prolonged hospitalisation also brings a substantial economic burden to hospitals. However, few studies have investigated the risk factors associated with prolonged ICU stays in these children.[8] In addition, differences in endpoint definitions (i.e., ICU stays) can make comparing these studies challenging. In some studies, the postoperative ICU stays after CHD surgery were relatively long. For instance, in the study by Shi et al., the median ICU stay was 7 days,[8] while in the study by Manrique et al., the median ICU stay was 9.5 days.[9] Recognising these gaps, this study conducted a single-centre review of the pre-, intra-, and postoperative risk factors in children with CHD complicated by pneumonia, focussing on those with postoperative ICU stays ≥7 days (representing the 50th percentile in this study).

Materials and methods

Ethical statement

This study was approved by the Medical Ethics Committee of Beijing Children's Hospital (No. 2023-E-079-R). This retrospective analysis was conducted at the Beijing Children's Hospital,

affiliated with the Capital Medical University in China. Due to the retrospective nature of this study, the Institutional Review Committee waived the need for informed consent.

Study population

This study included 496 children with CHD and preoperative pneumonia who underwent cardiac surgical correction between 2017 and 2022. Most children were initially hospitalised for pneumonia. The criteria for ICU discharge were as follows: stable cardiac and pulmonary function, sufficient oxygen support through nasal catheters, and no severe infection indicator abnormalities (body temperature, white blood cell, C-reactive protein, etc.). The median ICU stay for all patients was 7 days (range, 1–111 days). The patients were divided into two groups: the short-term group included 296 children who stayed in the ICU for less than 7 days, and the long-term group included 200 children who were in the ICU for 7 days or more. The diagnosis of pneumonia was based on abnormalities such as cough, fever, shortness of breath (respiratory rate >50/min for infants aged 3–12 months), wet rales or wheezing detected by auscultation during chest examination, and spots or plaque infiltration on chest radiographs before admission or within 72 h after admission.[8] The diagnosis of severe community-acquired pneumonia was based on the diagnostic criteria proposed in the clinical practice guidelines of the Pediatric Infectious Disease Society and the American Infectious Disease Society.[9]

Procedural details

The assessment of pre-, intra-, and postoperative risk factors was based on the completeness of previously published analyses, clinical judgements, and data collection.[6,8,10]

Preoperative risk factors included age, sex, weight, chromosomal abnormalities, premature birth, malnutrition, pulmonary hypertension, tracheal stenosis, bacterial infection, viral infection, severe pneumonia, and bronchopulmonary dysplasia. Intraoperative risk factors assessed included congenital heart surgery risk (Risk Adjustment for Congenital Heart Surgery-1 grade)[11] and cardiopulmonary bypass. Postoperative risk factors included delayed sternal closure (the sternum remained open in the operating room or was reopened in the ICU), extracorporeal membrane oxygenation assistance, and failure to extubate. Pulmonary hypertension was defined as an average pressure of greater than 20 mmHg in the pulmonary artery.[12]

According to the guidelines of the Centers for Disease Control and Prevention, sputum samples were collected using the sterile negative-pressure suction method. Samples collected within 24 h of admission were tested for common respiratory virus antigens using direct immunofluorescence assays. Each sample was immersed in 1 mL of sterile physiological saline, after which 0.1 mL of this solution was inoculated into a culture dish. The samples were then incubated at 37 °C for 24 h, colonies were isolated and counted, and a microbial detector was used for bacterial identification. The positive cut-off point for quantitative cultivation of pathogenic bacteria was $\geq 10^6$ CFU/mL.[13]

Statistical analysis

Continuous variables were expressed as the medians with interquartile ranges, and categorical variables were expressed as numbers and percentage (%). Before analysis, the normal distribution of all continuous variables was evaluated. As most variables exhibited a non-normal distribution, we conducted nonparametric univariate analysis using the Kruskal–Wallis test and the Mann–Whitney *U* test. For qualitative variables, the chi-square test was performed. Statistical significance was defined as $p < 0.05$.

A logistic regression model was used for multivariate analysis. The Wald forward selection method was utilised, with an entry probability of 0.1 and an exit probability of 0.05. Severe illness was defined as a postoperative ICU stay of ≥7 days. The predictive variables included in the model were age, sex, body weight, cardiopulmonary bypass, delayed chest closure, viral infection, bacterial infection, severe pneumonia, pulmonary hypertension, tracheal stenosis, and CHD score. The results of multivariate analysis are expressed as the relative risk and 95% confidence interval. Multivariable linear regression analysis was also applied to assess the prognostic value of risk factors for ICU stays, expressed as linear regression coefficient (β). All statistical tests were two-tailed, and the significance level was set at $P < 0.05$. Data were analysed using the SPSS version 24.0 (IBM Corp., Armonk, NY, USA) statistical software package.

Results

Baseline characteristics

There were no significant differences in gender between the groups. The average age and weight values of the long-term ICU stay group were significantly lower than those of the short-term ICU stay group ($p < 0.01$). Half of the children in the long-term ICU stay group were under 3 months old and weighed less than 5 kg. The Risk Adjustment for Congenital Heart Surgery-1 grade revealed no significant differences between the groups ($p = 0.76$). However, significant differences were observed between the two groups in terms of cardiopulmonary bypass time, blockage time, hospitalisation time, ventilator time, pneumonia severity, pulmonary arterial hypertension, and extubation failure. There were no significant differences in proportion of cardiopulmonary bypass surgery, delayed chest closure, tracheal stenosis, premature birth, malnutrition, bronchopulmonary dysplasia, chromosomal abnormalities, or extracorporeal membrane oxygenation support. During the study period, the in-hospital mortality rates in the long-term and short-term ICU admission groups were similar and were 8.5% and 4.1%, respectively ($p = 0.39$). The main causes of death were severe infections and multiple organ system failure (Table 1).

Differences in bacterial infection were observed between the groups. The positive rate of bacterial infection culture in the long-term group was significantly higher than that in the short-term group ($p < 0.01$). In the long-term group, *Klebsiella pneumoniae* was the most common gram-negative bacteria, while *Staphylococcus aureus* was the most common gram-positive bacteria. In the short-term group, *Haemophilus influenzae* was the most common gram-negative bacteria, while *S. aureus* was the most common gram-positive bacteria. Viral infections showed no difference between the groups ($p = 0.37$), with respiratory syncytial virus being the most frequently identified. Additionally, there was no significant difference in the incidence of mixed infections between the groups ($p = 0.28$; Table 2, Figure 1).

Risk factor analysis

Univariate analysis

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Table 1. Baseline clinical characteristics

	<7 days ($n = 296$)	≥7 days ($n = 200$)	Total ($n = 496$)	p value
Sex (male)	162 (54.7%)	110 (55%)	27 (54.8%)	0.95
Age(mo),IQR	5 (2-9)	3 (1-6)		<0.01
<3mo	103 (34.8%)	110 (55.0%)	213 (42.9%)	
3-6mo	89 (30.1%)	48 (24.0%)	137 (29.2%)	
6-12mo	55 (18.6%)	26 (13.0%)	91 (18.3%)	
>12mo	49 (16.6%)	16 (8.0%)	65 (13.1%)	
Body weight(kg),IQR	6 (4.7–7.9)	4.8 (4–6.2)		<0.01
<5kg	101 (34.1%)	115 (57.5%)	216 (43.5%)	
>5kg	195 (65.9%)	85 (42.5%)	280 (56.5%)	
ICU time(day),IQR	3 (2-5)	10 (8-17)	7 (3-10)	<0.01
hospital stay(day),IQR	15 (12-20)	24 (19-30)	18 (14-25)	<0.01
Postoperative mechanical ventilation(h),IQR	28.5 (17-52)	142 (78-218)	52 (24-120)	<0.01
Cardiopulmonary bypass	258 (87.2%)	175 (87.5%)	433 (87.3%)	0.912
Cardiopulmonary bypass time (min),IQR	69 (62-86)	83 (69-112)	73 (66-93)	<0.01
Aortic crossclamp time (min),IQR	44 (37-52)	48 (42-70)	45 (40-59)	<0.01
RACHS-1	2 (1-5)	2 (1-5)	2 (1-5)	0.76
Severe pneumonia	70 (23.6%)	84 (42%)	154 (31%)	<0.01
Pulmonary arterial hypertension	209 (70.6%)	169 (84.5%)	378 (76.2%)	<0.01
Delayed chest closure	7 (2.4%)	13 (6.5%)	20 (4%)	0.22
Tracheal stenosis	40 (13.5%)	42 (21%)	82 (16.5%)	0.03
Ventilator extubation failure	1 (0.3%)	18 (9%)	19 (3.8%)	<0.01
Premature delivery	37 (12.5%)	32 (16%)	69 (13.9%)	0.27
Malnutrition	49 (16.6%)	40 (20%)	89 (17.9%)	0.33
Bronchopulmonary dysplasia	3 (1%)	4 (2%)	7 (1.4%)	0.6
Chromosome abnormalities	7 (2.4%)	5 (2.5%)	12 (2.4%)	1
ECMO	1 (0.3%)	5 (2.5%)	6 (1.2%)	0.08
Death	12 (4.1%)	17 (8.5%)	29 (5.8%)	0.39

RACHS-1 = Risk Adjustment for Congenital Heart Surgery-1; ECMO = extracorporeal membrane oxygenation; IQR = interquartile range.

Table 2. Bacterial, viral, and mixed infections in two groups of patients

	<7 days ($n = 296$)	≥7 days ($n = 200$)	Total ($n = 496$)	p value
Bacterium	73(24.7%)	106(53%)	179(36.1%)	<0.01
Gram negative bacteria				
Haemophilus influenzae	9 (3%)	5 (2.5%)	14 (2.8%)	
Acinetobacter baumannii	5 (1.7%)	16 (8%)	21 (4.2%)	
Klebsiella pneumoniae	6 (2%)	22 (11%)	28 (5.6%)	
Gram positive bacteria				
Staphylococcus aureus	17 (5.7%)	17 (8.5%)	34 (6.9%)	
Streptococcus pneumoniae	5 (1.7%)	2 (1%)	7 (1.4%)	
Pseudomonas aeruginosa	7 (2.4%)	10 (5%)	17 (3.4%)	

(*Continued*)

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Table 2. (*Continued*)

	<7 days ($n = 296$)	≥7 days ($n = 200$)	Total ($n = 496$)	p value
Virus	28 (9.5%)	23 (11.5%)	51 (10.2%)	0.37
Respiratory syncytial virus	21 (7.1%)	16 (8%)	37 (7.5%)	
Influenza A virus	2 (0.7%)	2 (1%)	4 (0.8%)	
Parainfluenza virus	2 (0.7%)	2 (1%)	4 (0.8%)	
Adenovirus	1 (0.3%)	0	1 (0.3%)	
Mixed infection	13 (4.4%)	13 (6.5%)	26 (5.2%)	0.28

Table 3. Multivariate logistic regression analysis of the influence of perioperative risk factors on prolongation of ICU length of stay over 7 days

	p value	OR	−95% CI	+95% CI
Sex	0.99	0.99	0.66	1.51
Age	0.66	1.04	0.99	1.08
Body weight	0.001	0.76	0.65	0.88
Cardiopulmonary bypass	0.45	0.78	0.4	1.5
Delayed chest closure	0.69	1.23	0.44	3.5
Virus	0.78	1.1	0.58	2.1
Bacterium	0.001	2.86	1.88	4.36
severe pneumonia	0.001	2.11	1.34	3.32
Pulmonary arterial hypertension	0.32	1.32	0.76	2.29
Tracheal stenosis	0.334	1.3	0.76	2.25
RACHS-1	0.001	2.04	1.44	2.88

RACHS-1 = Risk Adjustment for Congenital Heart Surgery-1.

Demographic data and preoperative, intraoperative, and postoperative variables were used as potential risk factors for prolonged ICU stay in the univariate analysis. Patients in the long-term ICU stay group were significantly younger, had lower body weights, longer cardiopulmonary bypass and blockage times, a higher incidence of severe pneumonia and pulmonary hypertension, and a higher risk of extubation failure. However, there was no significant correlation between sex distribution and prolonged ICU stay.

Multivariate analysis

Multivariate logistics regression analysis showed that low body weight ($p = 0.001$), bacterial infection ($p = 0.001$), severe pneumonia ($p = 0.001$), and Risk Adjustment for Congenital Heart Surgery-1 ($p = 0.001$) were independent risk factors for prolonged stay in ICU after cardiac surgery in children with pneumonia (Table 3). Multivariate linear regression analysis showed that bacterial infection ($p = 0.001$), severe pneumonia ($p = 0.04$), and Risk Adjustment for Congenital Heart Surgery-1 ($p = 0.001$) were risk factors for longer ICU stays (Table 4).

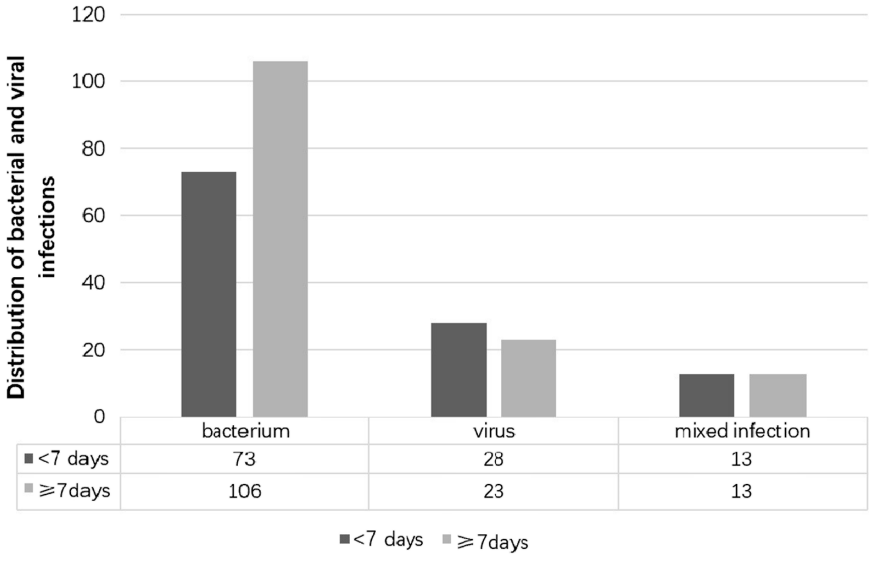

Figure 1. Distribution of bacterial and viral infections.

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Table 4. Linear regression regression analysis of the influence of perioperative risk factors on prolongation of ICU

	p value	*β*	−95% CI	+95% CI
Sex	0.61	0.51	−3.73	6.32
Age	0.94	0.01	−0.12	0.13
Body weight	0.57	−0.06	−0.65	0.36
Cardiopulmonary bypass	0.51	−0.03	−3.12	1.55
Delayed chest closure	0.06	0.08	−0.17	7.5
Virus	0.22	−0.05	−3.97	0.91
Bacterium	0.001	0.2	2.08	5.21
severe pneumonia	0.04	0.09	0.05	3.38
Pulmonary arterial hypertension	0.17	0.07	−0.58	3.25
Tracheal stenosis	0.05	0.09	0.15	4.17
RACHS-1	0.001	0.16	0.85	3.29

RACHS-1 = Risk Adjustment for Congenital Heart Surgery-1.

Discussion

Zhang et al.[14] reported that patients with severe pneumonia and concomitant CHD have higher mortality rates. Furthermore, community-acquired pneumonia has significant fatal consequences in children with various CHDs.[15] Moreover, CHD increases the risk of severe community-acquired pneumonia. These findings emphasise the need for preventive measures against pneumonia in children with chronic disease, particularly CHD. However, the impact of CHD on disease severity varies among different age groups, with CHD emerging as a crucial predictor of severity in paediatric patients under 2 years of age. Thus, in most cases, CHD is recommended to be surgically treated within 2 years of birth.[16]

Children with CHD and pneumonia may undergo one of the two treatment strategies: (1) medication and corrective surgical intervention during the same hospitalisation period or (2) medical management, discharge, and elective surgical repair. Many physicians in developing countries choose the second strategy. Concerns about employing cardiopulmonary bypass in critically ill infants with active pulmonary infections arise from concerns regarding the exacerbating lung inflammation and increasing potential infections due to immune suppression.[17] In this context, components such as complements, kinins, endotoxins, proinflammatory cytokines, and tumour necrosis factors are believed to mediate lung injury and alter cellular and humoral immune responses, thereby exacerbating pneumonia symptoms. Consequently, pulmonary complications often occur in young children and lead to delayed recovery after cardiac surgery.

Most centres in developing countries have relatively limited human and material resources, preventing the adoption of proactive policies to promptly treat heart defects in young infants. Typically, limited resources are allocated to patients who are more likely to achieve better outcomes. In line with these considerations, we have adopted a policy of early surgical correction because we believe that, in cases of haemodynamically significant CHD combined with pneumonia, long-term attempts to completely resolve preoperative respiratory infections will not be successful.

Our study showed that the long-term ICU stay group mainly comprised young, low-weight infants, with significant differences in ICU stays among the different weight groups. Furthermore, low body weight was shown to be an important predictor of prolonged ICU stay in our multivariate logistics regression analysis, which is consistent with previous studies.[18,19] Specifically, we found that the number of infants aged under 3 months and weighing less than 5 kg who stayed in the long-term group was significantly higher than that of older and heavier children. This may be attributed to an underdeveloped immune system[20] and immature respiratory system, which make the infant more susceptible to this serious disease.

Most children with severe pneumonia complicated by CHD have left-to-right shunts. Specifically, 95% of the cases in this group exhibit left-to-right shunts, including those associated with ventricular septal defects, patent ductus arteriosus, atrial septal defects, right pulmonary arteries that originated from the aorta, and other similar conditions. Meanwhile, the remaining 5% consisted of cases with right-to-left shunts or vascular rings. Due to the presence of shunts at the atrial, ventricular, or great artery levels, these children are prone to pulmonary circulation congestion, pulmonary capillary exudation, and varying degrees of oedema in the alveolar interstitium and airway mucosa, which can lead to secondary bacterial infection. It is worth noting that the increase in pulmonary blood flow is also conducive to bacterial growth. Furthermore, these children often encounter early disease onset, incomplete lung development, and a heightened susceptibility to immune dysfunction, especially in cases with chromosomal abnormalities. In clinical practice, many children with CHD are prone to recurrent pneumonia and are more likely to develop severe pneumonia. However, due to the frequent incidence of refractory heart failure and pulmonary arterial hypertension in these children, the treatment effectiveness rate tends to be low. Therefore, timely adjustment and selection of sensitive antibacterial drugs based on clinical efficacy and drug sensitivity results can effectively improve the success rate in children with severe pneumonia and CHD while also improving cardiopulmonary function. Ultimately, when the general condition of the child improves and surgery becomes tolerable, timely intervention should be carried out to achieve treatment during a single hospitalisation period.

Early and repeated sputum cultures and pathogen susceptibility tests after admission are helpful for the rational and effective use of antibiotics in clinical practice. Notably, the main pathogens in these children are viruses and bacteria. Given that viral infection is usually transmitted from the upper respiratory tract and that viruses grow and reproduce in living cells, upper respiratory tract specimens can reflect lower respiratory tract viral antigens. In this group of patients (CHD combined with pneumonia), the total positivity rate of bacterial infections, mainly *S. aureus* and *K. pneumoniae*, was 36.1%. Moreover, the bacterial infection rate in the long-term ICU stay group showed significant differences compared to the short-term ICU stay group. Furthermore, gram-negative bacteria are the most common microorganisms, which is in line with other studies (42–65%).[21]

Among the participants in this study, the total positive rate of viral infection (mainly respiratory syncytial virus) was 10.2%, with no statistical difference between the two groups. Respiratory syncytial virus is a common pathogen that causes community-acquired pneumonia in children in the Chinese population.[22] Additionally, this virus is the most common viral pathogen in children with severe community-acquired pneumonia.[23] In our

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study, respiratory syncytial virus accounted for 7.5% of the cases, with no significant difference between the two groups. Notably, respiratory syncytial virus infection has been previously reported as a risk factor for CHD-related death.[24] Therefore, for the majority of children infected with respiratory syncytial virus, we found that antipyretic and symptomatic treatments were administered for respiratory symptoms. After the pneumonia was cured, the patients were discharged for recovery and underwent elective surgical treatment. Hence, the proportion of children infected with the virus was relatively small in this study. These findings are consistent with those of Medrano et al.[25], who evaluated the epidemiological behaviour of acute respiratory infections in 167 children under 2 years of age with CHD and haemodynamic responses. At the community level, most childhood pneumonia cases are caused by respiratory syncytial virus (approximately 29% of all pneumonia cases).[26] Additionally, it is worth noting that the mortality rate caused by viral pathogens in children with pneumonia is very low, with only 6.6% of deaths attributed to respiratory syncytial and influenza viruses. In this context, most mild-to-moderate pneumonia cases in children are caused by viruses, whereas the most severe and fatal cases are caused by bacterial infections.

Jenkins et al. published the Risk Adjustment for Congenital Heart Surgery-1 in 2002, which was one of the earliest standardised risk adjusted methods for CHD surgery.[11] Higher Risk Adjustment for Congenital Heart Surgery-1 classification was associated with longer ICU stays.[27] In this study, multivariate logistics regression analysis and multiple linear analysis revealed that a higher Risk Adjustment for Congenital Heart Surgery-1 grade was an independent risk factor for prolonging hospitalisation time in the ICU.

In this study, the two groups showed significant difference in pulmonary hypertension. The determination of pulmonary hypertension in this group of children mainly relied on echocardiography,[28] although it was not an independent risk factor for longer ICU stay. However, there were significant differences in both the average and total length of ICU stay between the two groups.

Combining multivariate logistics regression analysis and multiple linear regression analysis, our results indicate that bacterial infections, severe preoperative pneumonia, and Risk Adjustment for Congenital Heart Surgery-1 can prolong the ICU duration in children with CHD and pneumonia. Better identification of the risk factors associated with long-term postoperative ICU stays in these children, along with timely diagnosis and treatment of respiratory infections in high-risk populations, can effectively shorten ICU stays and improve resource utilisation.

This study has some limitations. First, it was a single-centre, small-scale case study, which may hinder the application of the current results to other institutions. Second, this was a retrospective study that may introduce potential misclassification bias. This study is a preliminary systematic evaluation of the impact of perioperative variables on the duration of ICU stay in children with CHD complicated by pneumonia. Larger prospective multicentre studies are necessary to further investigate this important clinical issue.

Data availability statement. The data used to support the findings of this study are available from the corresponding author upon request.

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Author contributions. Nan Ding contributed to all aspects of this study, including study concept and design, data acquisition, statistical analysis and interpretation, and drafting and revising the manuscript. Lei Shen, Zhiqiang Li, Jian Guo, Xiaofeng Li, and Hanlu Yi contributed to data acquisition and ethical issues. All authors have approved the final article.

Competing interests. None.

Ethical standard. This study was approved by the Medical Ethics Committee of Beijing Children's Hospital (No. 2023-E-079-R).

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