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Analysis of Risk Factors for Central Venous Catheter-Associated Thrombosis in Children after Congenital Heart Surgery

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ABSTRACT: **Objective:** To investigate the status and influencing factors of central venous catheter-associated thrombosis in children after congenital heart surgery and to provide evidence for preventive measures. **Methods:** From January 2024 to March 2024, hospitalized children with central venous catheters (CVC) in the Shanghai Grade III Children's Hospital intensive care unit were selected. Catheter-related thrombosis (CRT) was evaluated using bedside ultrasound technology combined with visible thrombus after CVC extraction, dividing the patients into the thrombus and non-thrombus groups. Univariate and LASSO regression analyses were used to analyze the factors influencing CRT in children after congenital heart surgery, and binary logistic regression was used to analyze the risk factors. **Results:** 229 children were included, of which 24 (10.48%) had CRT. Binary logistic regression analysis showed that time of vasoconstrictor use >one day, sedation and analgesia time, and flushing the CVC with saline were the risk factors for CRT in children after congenital heart surgery. **Conclusion:** The incidence of CRT is higher in children after congenital heart surgery. The medical staff can formulate targeted intervention measures based on the corresponding risk factors to reduce the incidence of CRT.

KEYWORDS: Congenital heart surgery; children; central venous catheter; thrombosis; risk factors

1 Introduction

A central venous catheter (CVC) is a catheter whose tip is positioned within the proximal third of the superior vena cava, right atrium, or inferior vena cava [1]. Common sites for CVC insertion include the internal jugular, subclavian, and femoral veins [2]. The use of CVCs can prevent and reduce the pain and difficulty of repeated venous punctures in pediatric patients [3]. In cardiovascular surgery, CVC is used routinely as an important channel for administering various vasoactive agents and for monitoring central venous pressure [4]. Catheter-related thrombosis (CRT) refers to the formation of a thrombus in the deep vein where the catheter is placed or in the adjacent venous drainage area after CVC implantation [5], and CRT is the most common noninfectious complication associated with CVC implantation [6–8]. The Children's Hospital Acquired Thrombosis Consortium has found that 80% of hospital-acquired venous



thromboembolism cases are related to CVC [9]. The incidence of CRT in children with congenital heart defects is 2.00%–22.65% [10–12]. While CRT is mainly asymptomatic, it can also present with symptoms such as inflammation or vascular obstruction [13,14]. Additionally, CRT may cause long-term complications, including post-thrombotic syndrome (PTS), adversely affect the prognosis of children, and can potentially lead to life-threatening conditions such as pulmonary embolism [14–16]. In addition, CRT can increase central venous pressure in children with congenital heart disease, leading to chylous effusions, which may complicate future surgeries and increase overall mortality [17]. Therefore, addressing the occurrence of CRT in children with congenital heart disease is crucial.

Current research has focused chiefly on the occurrence and risk factor analysis of venous thrombosis in children with congenital heart disease. Related studies have found several risk factors for thrombosis in this population, such as young age, history of catheterization, mechanical ventilation, and extracorporeal membrane pulmonary oxygenation (ECMO) [11,18,19]. Additionally, research has found that children with congenital or acquired heart disease undergoing cardiothoracic surgery are particularly prone to thromboembolic events [20]. However, few studies have paid specific attention to the occurrence and influencing factors of CRT in children after congenital heart surgery. This study aimed to investigate the incidence of CRT in children after congenital heart surgery and analyze the influencing factors to provide evidence for nurses to take implement appropriate preventive measures for reducing the incidence of CRT in children after congenital heart surgery.

2 Methods

2.1 Study Design

This study is a single-center, cross-sectional prospective study.

2.2 Study Population

Children with congenital heart disease in the intensive care unit of Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, were selected for this study from January 2024 to March 2024. The inclusion criteria were as follows: (1) age between 28 days and 18 years; (2) CVC retention time ≥ 48 h; and (3) all participants underwent cardiac surgery. The exclusion criteria were as follows: (1) death of the child; (2) withdrawal of treatment by the child or family members; and (3) preoperative history of catheterization, mechanical ventilation, or ECMO. This study was approved by the Ethics Committee of Shanghai Children's Medical Center (SCMCIRB-K2023231-1) with the informed consent obtained from all survey subjects.

2.3 Tool

Based on the pre-systematic literature analysis and expert consultation, the researcher designed clinical data questionnaire, comprising six sections: (1) Patient-related factors, including age, gender, and ICU stays; (2) Disease-related factors, including whether the congenital heart disease staging is cyanotic or not, high-risk comorbidities or complications (common infections, liver function abnormalities, sepsis, organ hemorrhage, low cardiac output syndrome, cardiac arrest, inflammatory bowel disease), vasoactive inotrope score (VIS), pediatric critical illness score (PCIS), Caprini scale score, and nutritional status (that of children < 6 years of age was calculated concerning the World Health Organization growth curve, and that of children ≥ 6 years of age was determined via calculation of body mass index [BMI]); (3) Drug-related factors, including use of parenteral nutrition, mannitol, and blood products, duration of glucocorticoid use, duration of vasoconstrictor use, and duration of sedation and analgesia; (4) Factors related to invasive treatment,

including the use of ECMO, hemodialysis, cardiac catheterization intervention (either for diagnosis or treatment), duration of surgery, duration of extracorporeal circulation and duration of mechanical ventilation; (5) Laboratory test-related factors, including D-dimer concentration, fibrinogen concentration, activated partial thromboplastin time (APTT), prothrombin time (PT), international normalized ratio (INR), fibrin degradation product (FDP), lactic acid value (LAC), and platelet count (PLT); and (6) Catheter-related factors, including catheter type, number of catheter lumens, orientation of the CVC, vein used for CVC, and the type of fluid used for flushing and sealing the CVC.

The vasoactive drug score used in this study was VIS, proposed by Gaies et al. [21] in 2010, and the score was evaluated 24 h after surgery, except for children exposed to ECMO [22]. The PCIS is a scoring system used to assess the severity of diseases in children [23]. The tool includes 11 indicators such as heart rate, respiration, arterial blood oxygen partial pressure, blood pressure, and pH, where lower scores indicate a more serious condition. A lower score indicates a more severe condition [24]. Caprini's thrombosis risk assessment table was put forward by American scholar Caprini [25], including patient-related factors, surgical factors, and clinical laboratory examination. Based on the total score, a higher score indicates a higher risk.

2.4 Data Collection Method

The data were collected by a trained researcher and checked by another researcher. The relevant data in the clinical data questionnaire were obtained by consulting electronic medical records and nursing records. The first ultrasound examination was conducted 48 to 72 h after CVC implantation. Subsequently, it was performed every three days until one of the following conditions arose: CRT, removal of the CVC in the intensive care unit (ICU), or transfer out of the ICU.

CRT was diagnosed by ultrasonography, which suggested the presence of an intravascular thrombus or a thrombus visible to the naked eye on the catheter after the removal of the CVC. After the child's CVC was placed, ultrasound screening was performed by a nurse trained in intensive care ultrasound. In addition, sonographers familiar with the study's objective guide its implementation. When an operator identified a positive case, the sonographers conducted a review to confirm the finding. The ultrasound diagnostic criteria for CRT were as follows [10,13,26,27]: (1) solid echoes were detected within the lumen of the CVC, catheter wall, or placed vein; (2) the lumen of the probe-pressurized vein could not be closed or could not be closed entirely; (3) the Color Doppler did not detect blood flow signals; and (4) the period-phase nature of the blood flow spectra was weakened or disappeared. CRT was judged positive if one of the above conditions was met.

2.5 Statistical Method

SPSS 26.0 and R4.4.0 software were used for data analysis. Quantitative data conforming to normal distribution were presented as mean with standard deviation ($X \pm S$), and Student's *t* test was used for intergroup comparison. Quantitative data not conforming to normal distribution were presented as median with interquartile range (M [P25, P75]), and nonparametric tests were used for intergroup comparisons. Categorical data were expressed as frequency and percentage (%), and the chi-square test was used for intergroup comparisons. For variables that showed statistical significance in the univariate analysis, the minor absolute shrinkage and selection operator (LASSO) regression method was used for dimensionality reduction to screen the factors influencing CRT in children after congenital heart surgery. Then, binary logistic regression analysis was performed on the factors selected by LASSO. The differences were considered statistically significant at $p < 0.05$.

3 Results

3.1 General Information and CRT Status

A total of 229 children were included in this study, with a median age of 23.0 (7.0, 56.5) months, 114 (49.8%) male and 115 (50.2%) female. Twenty-four (10.48%) patients developed CRT. The high incidence time of CRT occurs between 4–7 days after CVC placement. Detailed results are shown in [Table 1](#).

Table 1: Univariate analysis of CRT in children after congenital heart surgery [n = 229, M (P25, P75), number and percentage of cases (%)]

Variable	CRT group (n = 24)	Non-CRT group (n = 205)	Statistic	p value
Age (months)	13.00 (7.50, 56.50)	24.00 (6.50, 56.50)	-0.733 ¹⁾	0.464
Sex			4.753 ²⁾	0.029
Male	17 (70.8)	97 (47.3)		
Female	7 (29.2)	108 (52.7)		
ICU stays (days)	2.00 (2.00, 5.00)	2.00 (2.00, 3.50)	-1.072 ¹⁾	0.284
Diagnosis of high-risk diseases			0.000 ²⁾	1.000
Yes	2 (8.3)	17 (8.3)		
No	22 (91.7)	188 (91.7)		
High-risk complications or comorbidities associated with CRT			3.931 ²⁾	0.047
Yes	13 (54.2)	69 (33.7)		
No	11 (45.8)	136 (66.3)		
Vascular activity drug score	5.00 (5.00, 10.00)	5.00 (5.00, 10.00)	-0.384 ¹⁾	0.701
Pediatric critical illness score	96.00 (92.00, 96.00)	96.00 (92.00, 100.00)	-0.853 ¹⁾	0.394
Caprini scale score	5.00 (5.00, 5.00)	5.00 (5.00, 5.00)	-1.416 ¹⁾	0.157
Nutritional status			0.012 ²⁾	0.913
Normal	17 (70.8)	143 (69.8)		
Abnormal	7 (29.2)	62 (30.2)		
Parenteral nutrition therapy			-	1.000
Yes	0 (0.0)	3 (1.5)		
No	24 (100.0)	202 (98.5)		
Mannitol treatment			-	1.000
Yes	2 (8.3)	3 (1.5)		
No	22 (91.7)	202 (98.5)		
Time of use of glucocorticoid (days)	3.00 (2.00, 4.50)	2.00 (2.00, 3.00)	-1.380 ¹⁾	0.167
Vasoconstrictor use time (days)			11.998 ²⁾	0.001
≤1	9 (37.5)	148 (72.2)		
>1	15 (62.5)	57 (27.8)		
Sedation and analgesia time (days)	2.00 (2.00, 4.75)	1.00 (1.00, 2.00)	-4.606 ¹⁾	<0.001
Blood products			0.000 ²⁾	1.000

(Continued)

Table 1 (continued)

Variable	CRT group (n = 24)	Non-CRT group (n = 205)	Statistic	p value
Yes	19 (79.2)	166 (81.0)		
No	5 (20.8)	39 (19.0)		
Operation duration (hours)	2.50 (2.10, 3.00)	2.33 (1.75, 2.92)	-1.176 ¹⁾	0.239
Duration of extracorporeal circulation (hours)	52.50 (33.50, 87.25)	50.00 (30.50, 71.50)	-0.592 ¹⁾	0.554
Mechanical ventilation time (days)	1.50 (1.00, 2.00)	1.00 (1.00, 1.00)	-2.792 ¹⁾	0.005
Cardiac catheterization			-	0.284
Yes	1 (4.2)	2 (1.0)		
No	23 (95.8)	203 (99.0)		
ECMO			-	0.199
Yes	1 (4.2)	1 (0.5)		
No	23 (95.8)	204 (99.5)		
Hemodialysis			-	1.000
Yes	0 (0.0)	1 (0.5)		
No	24 (100.0)	204 (99.5)		
D-dimer concentration (after CVC placement) (mg/L)	0.36 (0.28, 0.51)	0.36 (0.26, 0.59)	-0.445 ¹⁾	0.657
Fibrinogen concentration (after hospitalization) (g/L)	2.14 (1.74, 2.59)	2.28 (1.94, 2.56)	-0.997 ¹⁾	0.319
Fibrinogen concentration (after CVC placement) (g/L)	3.15 (2.44, 3.45)	3.17 (2.70, 3.61)	-1.143 ¹⁾	0.253
APTT (after hospitalization) (s)	36.25 (33.00, 38.48)	36.40 (33.85, 39.70)	-1.208 ¹⁾	0.227
APTT (after CVC placement) (s)	30.90 (28.78, 32.43)	30.80 (28.85, 33.10)	-0.388 ¹⁾	0.698
PT (after hospitalization) (s)	11.25 (10.65, 12.18)	11.30 (10.80, 12.00)	-0.166 ¹⁾	0.868
PT (after CVC placement) (s)	13.25 (12.48, 13.78)	13.30 (12.60, 14.10)	-0.588 ¹⁾	0.556
INR (after hospitalization)	1.04 (0.99, 1.28)	1.05 (1.01, 1.12)	-0.287 ¹⁾	0.774
INR (after CVC placement)	1.21 (1.13, 1.27)	1.22 (1.16, 1.30)	-0.989 ¹⁾	0.323
FDP (after CVC placement) (µg/mL)	4.40 (2.90, 7.53)	4.00 (2.10, 7.20)	-0.834 ¹⁾	0.404
LAC (mmol/L)	1.80 (1.30, 2.18)	1.80 (1.40, 2.40)	-0.668 ¹⁾	0.504
PLT (after hospitalization) (×10 ⁹ /L)	395.00 (297.25, 470.75)	311.00 (259.50, 364.50)	-2.491 ¹⁾	0.013
PLT (after CVC placement) (×10 ⁹ /L)	249.00 (190.50, 330.75)	228.00 (190.00, 273.00)	-1.438 ¹⁾	0.150
Number of catheter lumens			3.153 ²⁾	0.076
Single cavity	18 (75.0)	115 (56.1)		
Dual chamber	6 (25.0)	90 (43.9)		
Orientation of CVC			1.363 ²⁾	0.243

(Continued)

Table 1 (continued)

Variable	CRT group (n = 24)	Non-CRT group (n = 205)	Statistic	p value
Left side of Patient's body	16 (66.7)	111 (54.1)		
Right side of Patient's body	8 (33.3)	94 (45.9)		
Vein used for CVC			1.564 ²⁾	0.211
Internal jugular vein	7 (29.2)	87 (42.4)		
Femoral vein	17 (70.8)	118 (57.6)		
Type of fluid used for flushing and sealing CVC			42.873 ²⁾	<0.001
Heparin	1 (4.2)	147 (71.7)		
Saline	23 (95.8)	58 (28.3)		

Note: APTT, activated partial thromboplastin time; CRT, catheter-related thrombosis; ECMO, extracorporeal membrane oxygenation; FDP, fibrin degradation products; LAC, lactic acid value; INR, international normalized ratio; PLT, platelet count; PT, prothrombin time; 1) Z-value; 2) χ^2 -value.

3.2 Univariate Analysis of CRT in Children after Congenital Heart Surgery

There were statistically significant differences ($p < 0.05$) between the CRT group and the non-CRT group in terms of gender, presence of high-risk comorbidities or complications, duration of vasoconstrictor use, duration of sedation and analgesia, duration of mechanical ventilation, PLT (after hospitalization), and the type of fluid used for flushing and sealing CVC. The detailed results are shown in [Table 1](#).

3.3 LASSO Regression of CRT in Children after Congenital Heart Surgery

Seven variables with statistical significance in the univariate analysis were input to LASSO regression dimensionality reduction to extract the most important predictors and avoid overfitting. The LASSO model's best parameter (lambda) was selected by minimum criteria using fivefold cross-validation. The minimum lambda value was selected as the standard error (SE) of the optimal value of the model ([Figs. 1 and 2](#)). LASSO regression results showed that gender, time of vasoconstrictor use, sedation and analgesia time, PLT (after hospitalization), and the type of fluid used for flushing and sealing CVC were essential factors affecting the development of CRT in children.

3.4 Binary Logistic Regression Analysis of CRT in Children after Congenital Heart Surgery

Binary logistic regression analysis was carried out with CRT as the dependent variable, and the five risk factors were screened out by LASSO regression as the independent variables. The backward method was selected. The assignment of the independent variables is shown in [Table 2](#). The results showed that the time of using vasoconstrictors, sedation and analgesia, and flushing the CVC with normal saline were the independent risk factors for CRT ($p < 0.05$). The detailed results are shown in [Table 3](#).

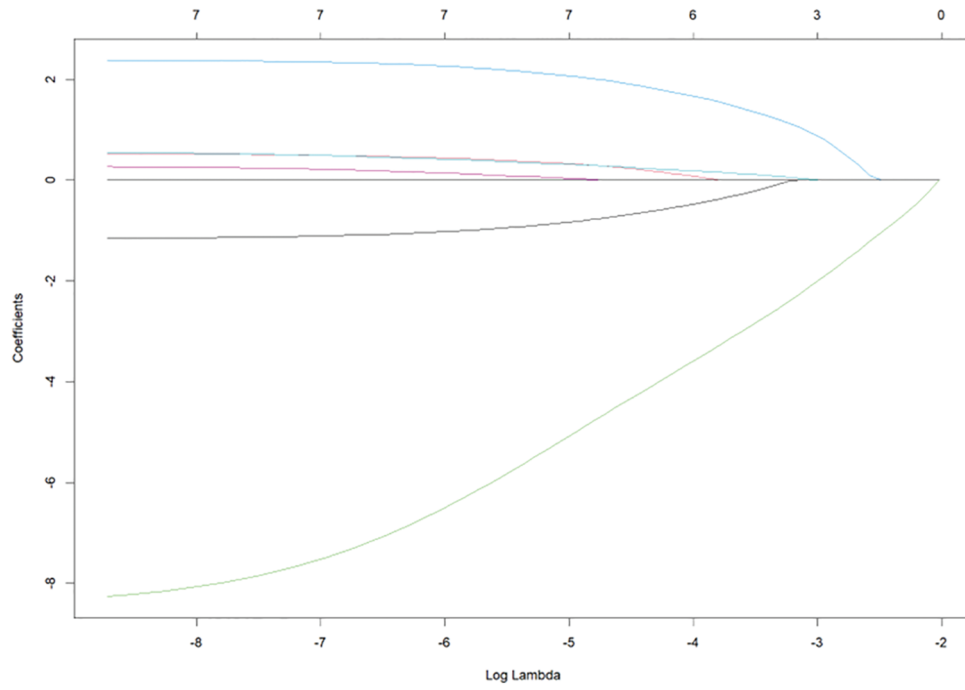


Figure 1: Optimal parameter (λ) selection in the least absolute shrinkage and selection operator (LASSO) model

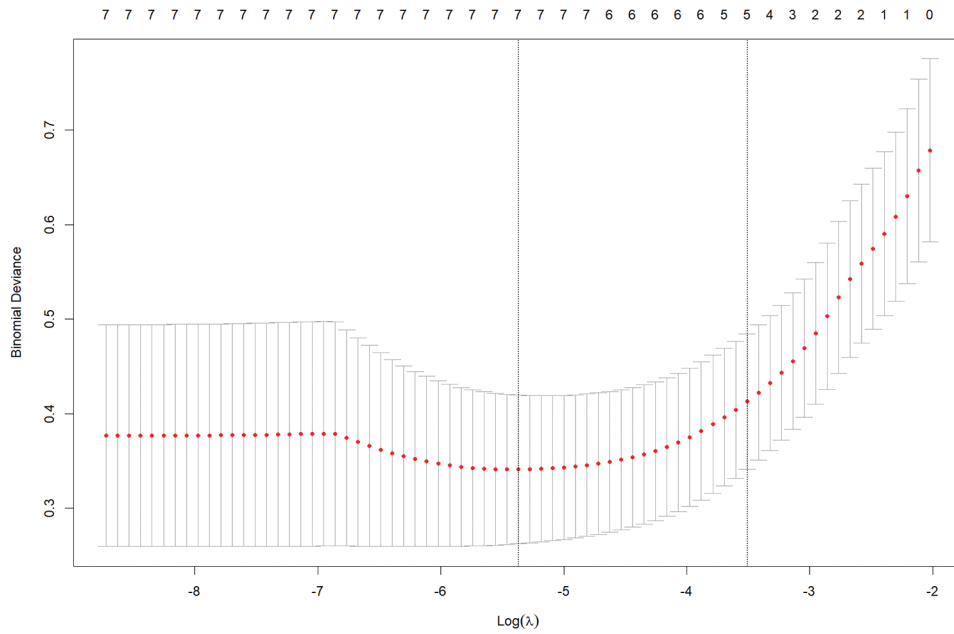


Figure 2: Distribution of the minor absolute shrinkage and selection operator (LASSO) coefficients for seven factors

Table 2: Independent variable assignment

Independent variable	Assignment method
Gender	Male = 1; female = 2
Time of vasoconstrictor use	$\leq 1 = 1$; $>1 = 2$
Sedation and analgesia time	Substitute the original values into the statistical model
PLT (after hospitalization)	Substitute the original values into the statistical model
Type of fluid used for flushing and sealing CVC	Heparin = 1; saline = 2

Note: PLT, platelet count.

Table 3: Results of multivariate analysis

Variable	B value	Standard error	Wald χ^2	p value	OR value	95% CI
Gender	1.204	0.655	3.384	0.066	3.334	0.924–12.027
Time of vasoconstrictor use	-2.719	0.822	10.952	0.001	0.006	0.013–0.330
Sedation and analgesia time	0.564	0.235	5.758	0.016	1.758	1.109–2.788
PLT (after hospitalization)	0.005	0.003	2.891	0.089	1.005	0.999–1.011
Type of fluid used for flushing and sealing CVC	-7.438	2.069	12.930	<0.001	0.001	0.000–0.034

Note: CI, confidence interval; OR, odds ratio; PLT, platelet count.

4 Discussion

4.1 Higher Incidence of CRT in Children after Congenital Heart Surgery

In this study, 24 out of the 229 children after congenital heart surgery (10.48%) developed CRT, which is higher than the incidence of CRT in children with heart disease reported by DiPietro et al. [11] (2.0%). The reasons for this may be as follows. Children with congenital heart disease are generally young, their coagulation system is not fully developed, and the concentration of anticoagulant proteins in their bodies is lower than that in adults. Insufficient liver perfusion secondary to impaired cardiac function can also affect the synthesis of anticoagulant substances. In addition, during intraoperative extracorporeal circulation, thrombin production increases, and the blood exhibits a hypercoagulable state [28]. Although venography is the gold standard for detecting venous thrombosis, this examination is invasive and has limited practical application in clinical practice. For this reason, previous studies have utilized imaging methods such as ultrasound to detect venous thrombosis [29–31]. According to guidelines, ultrasound can be effectively used as a screening tool for venous thrombosis, and research has shown that it has a sensitivity of 88% and a specificity of 98%, indicating high detection accuracy [32]. In some cases, ultrasound examinations are performed only when there is a clinical suspicion of thrombosis, relying on the healthcare clinical judgment, which can result in missed diagnoses [29]. However, CRT is mainly asymptomatic, this study directly used Doppler ultrasound to evaluate and reduce omissions. It has been found that 8%–18% of children with CRT may develop post-thrombotic syndrome [33], which affects prognosis. Therefore, early identification of CRT risk and appropriate prevention measures are essential.

4.2 Longer Duration of Vasoconstrictor Use Is Associated with a Higher Risk of CRT in Children after Congenital Heart Surgery

This study showed that the use of vasoconstrictor drugs for a long time was a risk factor for CRT in children after congenital heart surgery, and the use of vasoconstrictor drugs has been reported as a risk factor for CRT in previous studies [34]. The vasoconstrictor drugs in this study were mainly epinephrine and norepinephrine, which can stimulate α receptors and cause systemic vasoconstriction, thereby narrowing the lumen, slowing down blood flow rate, and promoting CRT when platelets gather under the damaged endothelial tissue [35,36]. With the long-term use of such drugs, blood vessels continue to shrink, reducing blood flow and further promoting thrombosis. It has been found that vasoconstrictor drugs can reduce the activity of coagulation factor Xa in plasma, thereby reducing the effect of low-molecular-weight heparin sodium on preventing thrombosis [37]. However, other studies have shown no correlation between norepinephrine dose and anti-factor Xa activity in patients using low-molecular-weight heparin [38], and more high-quality studies are needed to explore the relationship between the two further. It is also worth noting that prolonged vasoconstrictor use typically indicates a more severe shock state, potentially reflecting more severe underlying heart disease or a more complex surgical procedure. Nursing staff should closely monitor the reaction after medication for children exposed to vasoconstrictor drugs to maintain good blood circulation. When the child's circulation is stable, the staff should inform the doctor promptly to adjust the treatment plan and gradually reduce the use of vasoconstrictor drugs.

4.3 Longer Duration of Sedation and Analgesia Is Associated with a Higher Risk of CRT in Children after Congenital Heart Surgery

The present study showed that long duration of sedation and analgesia was a risk factor for CRT in children after congenital heart surgery, consistent with previous findings [10]. Sedative analgesics are needed early after surgery in children with congenital heart disease to reduce oxygen consumption, reduce the functional burden of various organs, and promote cardiac function and body recovery [39,40]. During sedation and analgesia, the child is in a state of immobilization and blood flow is slowed down. There is blood stasis in the vein, and increased platelet adhesion and aggregation in the intima of blood vessels favors thrombosis. Longer duration of sedation and analgesia is associated with a higher risk of CRT. While deep sedation may cause circulatory depression [41], children with prolonged bed rest and little or no physical activity are at an increased risk of thrombosis. Therefore, for children under long-term sedation and analgesic drugs, nurses need to control the pump speed and drug dosage strictly, as well as regularly assess the sedation and analgesia levels of the children. Then, according to the changes in the child's condition, nurses must inform the doctor to adjust the drug dose promptly. If the patient's condition permits, passive movement such as limb abduction and internal rotation should be performed appropriately.

4.4 Flushing and Sealing CVC with Heparin Reduces the Risk of CRT in Children after Congenital Heart Surgery

This study showed that children after congenital heart surgery who received heparin to flush the CVC had a lower risk of CRT. First, heparin is an anticoagulant with remarkable effects in preventing and treating thrombotic diseases [42]. However, excessive use of heparin can prolong blood clotting time, leading to an increased risk of bleeding. In addition, heparin induces thrombocytopenia, which leads to a decrease in platelet count and further elevating bleeding risk [43]. Children undergoing congenital heart surgery typically require extracorporeal circulation necessitating heparin before and after the surgery procedure. The dosage of heparin significantly affects coagulation function [44], making the concentration and dosage of heparin crucial. Unfortunately, in the absence of high-quality evidence, the existing guidelines and expert

consensus recommend using normal saline to flush and seal CVC and do not recommend the routine use of CVC flushing and sealing fluids containing anticoagulants to prevent CRT [45]. “Expert Consensus on Central Venous Catheter Flushing and Sealing” points out that for patients with hypercoagulable blood, it is recommended first to use regular saline flushing and then use heparin saline sealing. Further high-quality studies are needed to explore the effects of different doses and concentrations of heparin on the formation of CRT.

However, some limitations should be acknowledged. First, the study was a single-center cross-sectional survey with a limited sample size. Second, the study monitored whether the children experienced CRT during ICU stays, which resulted in missed positive cases.

5 Conclusions

The incidence of CRT in children after congenital heart surgery is high, and it is affected by the duration of use of vasoconstrictor drugs, sedation and analgesia time, and flushing the CVC with saline. In the future, well-designed randomized controlled trials will be necessary to validate these results. Clinical staff should combine these risk factors to build a systematic and targeted CRT prevention program for children after congenital heart surgery and actively implement nursing preventive measures to reduce the risk of CRT.

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Availability of Data and Materials: The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval: This study was approved by the Ethics Committee of Shanghai Children’s Medical Center (SCMCIRB-K2023231-1) with the informed consent obtained from all survey subjects.

Conflicts of Interest: The authors declare no conflicts of interest to report regarding the present study.

Nomenclature

APTT	Activated partial thromboplastin time
BMI	Body mass index
CI	Confidence interval
CRT	Catheter-related thrombosis
CVC	Central venous catheter
ECMO	Extracorporeal membrane pulmonary oxygenation
FDP	Fibrin degradation product
ICU	Intensive-care unit
INR	International normalized ratio
LAC	Lactic acid value
LASSO	Least absolute shrinkage and selection operator
OR	Odds ratio
PCIS	Pediatric critical illness score

PLT	Platelet count
PT	Prothrombin time
SE	Standard error
VIS	Vasoactive inotrope score

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