Original Article

Risk factors for central venous catheter-related thrombosis in hospitalized children: a single-center a retrospective cohort study

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Background: This study aimed to explore the risk factors of catheter-related thrombosis (CRT) in children in Southwest China who underwent central venous catheter (CVC) insertion.

Methods: An observational cohort study was conducted at a single tertiary center in southwest China between November 2019 and February 2020. All patients who received a CVC were enrolled and Doppler-ultrasound examination was performed weekly until CVC removal. All patients in this study were hospitalized and were observed and followed up in this hospital. Patient demographics, medication, biochemical indexes, catheter maintenance practice, activities after CVC placement data were analyzed. The Kaplan-Meier method was used to calculate the incidence of CRT, and the Cox regression model was used to analyze the factors influencing CRT.

Results: A total of 594 children were included in the study, and the median indwelling time was 10 days, with the shortest being 1 day and the longest 60 days. The overall incidence of CRT was 26.60% (158/594), the 15-day cumulative incidence rate was 30.81%, and the 45-day cumulative incidence rate was 46.27%. After 45 days, the incidence of CRT further increased. Age <12 months [hazard ratio (HR), 1.654; 95% confidence interval (CI): 1.171–2.338], use of 20% mannitol or glycerol fructose (HR, 1.593; 95% CI: 1.058–2.398), CVC placement by a pediatric intensive care unit (PICU) doctor (HR, 1.921; 95% CI: 1.347–2.740), placement length ≥9 cm (HR, 1.633; 95% CI: 1.142–2.336), and D-dimer >1.5 mg/L (HR, 1.451; 95% CI: 1.044–2.015) were risk factors for CRT. Limb exercises (HR, 0.660; 95% CI: 0.469–0.929) after placement was a protective factor for CRT.

Conclusions: The incidence of CRT was higher in children with CVCs, and the key duration of CRT monitoring should be within 15 and 45 days after placement. Patients with age <12 months, using 20% mannitol or glycerol fructose, insertion length ≥9 cm, D-dimer >1.5 mg/L before placement are more likely to happen CVC-CRT than other patient, and it is necessary to be highly vigilant and take preventive measures.

Keywords: Central venous catheter (CVC); catheter-related thrombosis (CRT); children; risk factors

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Introduction

A central venous catheter (CVC) is widely used in pediatric clinical practice, especially in critically ill patients (1). CVC use can prevent and reduce the pain and difficulty of repeated puncture, protect peripheral blood vessels, and provide rapid access for infusion, blood transfusion, and central venous pressure monitoring. Catheter-related thrombosis (CRT) is the most common complication of CVC (2). The incidence of CRT varies greatly among different races, ages, diseases, and medical institutions, with an incidence ranging from 2–81% in children with CVCs in different unit (3-7), and 20–66% in Chinese children with CVCs without prophylaxis (8,9). CRT can lead to loss of catheter function, obstruction of treatment, prolonged hospitalization, pain, physical disability, and even death (10,11).Current studies (12-15) have shown that the risk factors for CRT in children with CVC include age (infancy and adolescence), underlying diseases (such as severe infection, surgery, tumor, kidney disease, congenital heart disease), catheter factors, iatrogenic factors (such as operation, infusion, drug use), catheterization site, and so on.

However, most current above studies of CRT have involved small populations concentrated in one type of care unit (16-19), a single type of disease. Most studies have focused on peripheral central catheter-related thrombus, not central catheter-related thrombus (20-22). At present, the risk factors for CVC-CRT in hospitalized children are still not well identified (16,23), and there is no consensus on the risk factors for CRT in children.

Therefore, this study investigated the risk factors for the occurrence of CRT in hospitalized children in different units with CVC placement to provide a reference for further assessment of the risks of CRT and take interventions to prevent CRT. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-529/rc).

Methods

Study setting, design, and data collection

This was a retrospective cohort study conducted between November 2019 and February 2020 at Children's Hospital of Chongqing Medical University, a tertiary care pediatric hospital and medical center for chronic and complex pediatric diseases. All patients who received a CVC in this hospital were included and weekly Doppler ultrasound was conducted until the catheter was removed to monitor whether CVC-CRT occurred.

Data were collected through an electronic medical record system. According to the risk factors of CRT reported in previous studies and clinical experience of the investigators, the following data were selected as potential risk factors for CRT collection, including general demographic characteristics, main diagnosis (whether suffering from hematological system diseases, kidney disease, congenital heart disease, severe infection, use of respirator, etc.), medication status (20% mannitol, glycerol fructose, furosemide, hormones, blood products, anticoagulants, etc.), catheterization information (catheterization operator, insertion length, catheterization position, catheter type, etc.), blood test results (blood coagulation before and after catheterization and routine blood test), limb exercise after catheter insertion, whether the patient received special treatment [surgery, ventilator, blood purification, intensive care unit (ICU) admission, etc.], caregiver's educational level, and CRT information (whether and when it occurred).

Patient selection

All the patients were hospitalized in our medical center and the CVC inserted during hospitalization. The indication for CVC placement was established on the basis of the patient's clinical assessment and informed consent was taken from all the patients' parents. This study was approved by the Theoretical Committee of the Children's Hospital of Chongqing Medical University (No. 296 of 2021). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Patient inclusion criteria were: (I) children successfully underwent CVC puncture and catheterization at our medical center; (II) children had no history of thrombosis; and (III) the parents signed informed consent when children were hospitalized. The exclusion criteria were: (I) children with incomplete research data; and (II) children with the CVC not removed when discharged or transferred.

Follow-up strategy and determination of CRT

After CVC placement, all children in the study underwent weekly evaluation by the same investigators (Mingping Fan and Ting Wang), including physical examination and Doppler ultrasound scan. The physical examination including general physical examination, the cannulated site.

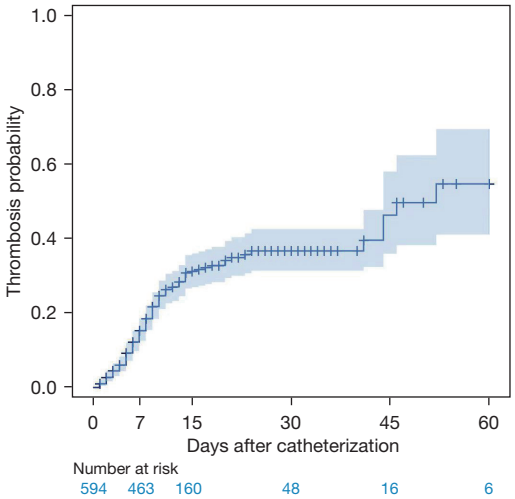

Figure 1 CRT in children with CVCs. CRT, catheter-related thrombosis; CVC, central venous catheter.

CVC-CRT physical symptoms included local pain, swelling, redness and blueish-purple skin, elevated skin temperature, and loss of catheter function. CRT was diagnosed by ultrasound with the presence of an intraluminal thrombosis, incomplete compressibility in two-dimensional mode, or a vascular filling defect with residual flow in color-Doppler mode.

In our study, CRT was defined as the presence of ultrasound image features, including asymptomatic and symptomatic CRT. Because not all CRT cases require removal of the catheter and to be able to perform time-to-event analysis, the time to CRT was defined as the time from CVC placement to the first identification of thrombosis.

All patients with CVC were hospitalized. Once patients were discharged or CVC removed, the follow-up finished.

Sample size calculation

The sample size was calculated according to the 10 events per independent variable (EVP) rule for multifactorial analysis, where the ratio of the number of categories with a relatively small composition of outcome events to the independent variable is greater than 10. Based on previous literature (24), the incidence of CRT in multifactorial analysis was assumed to be 40%, with the number of influencing factors ranging from 5–15, thus a minimum of 150 children with CRT and 375 children with CVCs were required, for a total of 525 cases.

Statistical analysis

Enumeration data is described using the number and rate of cases. The Kaplan-Meier method was used to calculate the cumulative incidence of thrombosis and draw survival curves. The factors to be compared by using the log-rank test. Multivariate Cox regression model was used to explore the influencing factors of thrombosis. Hazard ratio (HR) and its confidence interval (CI) indicated the risk. The factors with $P<0.05$ in univariate Cox regression analysis were included in the multivariate analysis, and the Cox regression models (models 1–4) were constructed for general information, medication, catheterization information, and blood test results before catheterization, respectively. Finally, variables with $P<0.05$ in models 1–4 were included in the full model. All statistical analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Children's demographics and clinical characteristics

The study comprised a total of 594 children with CVCs, including 317 males (53.37%) and 277 females (46.63%), the median age was 11.83 months, and the median number of CVC insertion days was 10 days, with the shortest being 1 day and the longest 60 days. A total of 158 cases (26.60%) developed CRT.

The peak period for CRT occurred within 15 days of CVC placement. The cumulative incidence of CRT within 15 days was 30.81%, with the incidence slowing between 15–45 days. The cumulative incidence of CRT within 45 days was 46.27%. After 45 days, the incidence of CRT further increased, as shown in *Figure 1*.

CRT univariate analysis

Compared with the control group, age <12 months, use of 20% mannitol or glycerol fructose, use of furosemide, pediatric intensive care unit (PICU) personnel for catheterization, catheterization length ≥9 cm, fibrinogen ≤1.7 g/L, activated partial prothrombin time >32 s, and D-dimer >1.5 g/L were associated with a higher incidence of CRT, while the patients who underwent limb movement training after catheter insertion had a lower incidence than the control group, HR (95% CI) was 0.639 (0.457, 0.894), $P=0.009<0.05$. See *Table 1* for details.

Table 1 Univariate analysis of thrombosis group and no thrombosis group

Variables	Total (n=594)	No thrombosis group (n=436)	Thrombosis group (n=158)	HR (95% CI)	P
General information					
Age (months)					0.005
<12	299 (50.3)	200 (66.9)	99 (33.1)	1.588 (1.150, 2.193)	
≥12	295 (49.7)	236 (80.0)	59 (20.0)	1.0 (reference)	
Gender					0.747
Male	317 (53.4)	233 (73.5)	84 (26.5)	0.950 (0.695, 1.298)	
Female	277 (46.6)	203 (73.3)	74 (26.7)	1.0 (reference)	
Blood purification					0.293
Yes	108 (18.2)	72 (66.7)	36 (33.3)	1.222 (0.841, 1.777)	
No	486 (81.8)	364 (74.9)	122 (25.1)	1.0 (reference)	
On a ventilator					0.073
Yes	402 (67.7)	282 (70.1)	120 (29.9)	1.397 (0.969, 2.015)	
No	192 (32.3)	154 (80.2)	38 (19.8)	1.0 (reference)	
Limb movement training					0.009
Yes	248 (41.8)	198 (79.8)	50 (20.2)	0.639 (0.457, 0.894)	
No	346 (58.2)	238 (68.8)	108 (31.2)	1.0 (reference)	
Related medications					
20% mannitol or glycerol fructose					<0.001
Yes	93 (15.7)	53 (57.0)	40 (43.0)	2.103 (1.467, 3.014)	
No	501 (84.3)	383 (76.4)	118 (23.6)	1.0 (reference)	
Furosemide					0.015
Yes	347 (58.4)	237 (68.3)	110 (31.7)	1.527 (1.087, 2.144)	
No	247 (41.6)	199 (80.6)	48 (19.4)	1.0 (reference)	
Heparin sodium					0.097
Yes	522 (87.9)	376 (72.0)	146 (28.0)	1.647 (0.913, 2.969)	
No	72 (12.1)	60 (83.3)	12 (16.7)	1.0 (reference)	
Hemostatic					0.295
Yes	512 (86.2)	379 (74.0)	133 (26.0)	0.796 (0.519, 1.221)	
No	82 (13.8)	57 (69.5)	25 (30.5)	1.0 (reference)	
Hormones					0.928
Yes	155 (26.1)	112 (72.3)	43 (27.7)	1.016 (0.715, 1.445)	
No	439 (73.9)	324 (73.8)	115 (26.2)	1.0 (reference)	

Table 1 *(continued)*

Table 1 *(continued)*

Variables	Total (n=594)	No thrombosis group (n=436)	Thrombosis group (n=158)	HR (95% CI)	P
Problems related to catheter insertion					
Catheter placing position					
Neck	472 (79.4)	359 (76.2)	113 (23.8)	0.778 (0.287, 2.111)	0.622
Stock	108 (18.2)	67 (62.0)	41 (38.0)	1.403 (0.501, 3.923)	0.519
Subclavian	14 (2.4)	10 (71.4)	4 (28.6)	1.0 (reference)	
Catheter placing personnel					<0.001
PICU personnel	193 (32.5)	108 (56.0)	85 (44.0)	2.900 (2.120, 3.966)	
Operating room anesthetist	401 (67.5)	328 (81.8)	73 (18.2)	1.0 (reference)	
Successful one-time catheterization					0.779
Yes	591 (99.5)	434 (73.4)	157 (26.6)	0.754 (0.106, 5.388)	
No	3 (0.5)	2 (66.7)	1 (33.3)	1.0 (reference)	
Insertion length (cm)					<0.001
≥9	157 (26.4)	95 (60.5)	62 (39.5)	2.088 (1.517, 2.875)	
<9	437 (73.6)	341 (78.0)	96 (22.0)	1.0 (reference)	
Hemagglutination term before catheter insertion					
Prothrombin time					0.148
>12 s	279 (47.0)	191 (68.5)	88 (31.5)	1.263 (0.921, 1.732)	
≤12 s	315 (53.0)	245 (77.8)	70 (22.2)	1.0 (reference)	
Thrombin time					0.22
>17 s	430 (72.4)	324 (75.3)	106 (24.7)	0.812 (0.583, 1.133)	
≤17 s	164 (27.6)	112 (68.3)	52 (31.7)	1.0 (reference)	
Fibrinogen					0.041
≤1.7 g/L	211 (35.5)	141 (66.8)	70 (33.2)	0.720 (0.526, 0.986)	
>1.7 g/L	383 (64.5)	295 (77.0)	88 (23.0)	1.0 (reference)	
Activated partial prothrombin time					0.003
>32 s	267 (44.9)	173 (64.8)	94 (35.2)	1.632 (1.185, 2.246)	
≤32 s	327 (55.1)	263 (80.4)	64 (19.6)	1.0 (reference)	
D-dimer					<0.001
>1.5 g/L	271 (45.6)	174 (64.2)	97 (35.8)	1.872 (1.358, 2.581)	
≤1.5 g/L	323 (54.4)	262 (81.1)	61 (18.9)	1.0 (reference)	

Data are presented as n (%) if stated otherwise. HR, hazard ratio; CI, confidence interval; PICU, pediatric intensive care unit.

CRT incidence

A summary of the incidence of CRT in children with different characteristics is presented in *Table 2* and *Figure 2*. Except for the catheter operator and 20% mannitol or glycerol fructose, there was no significant difference in the incidence of CRT within 0–7 days after insertion in children with different characteristics. The incidence of CRT in children with 20% mannitol or glycerol fructose, catheterization by PICU personnel, and catheterization

Table 2 Cumulative incidence of thrombosis in children after 7, 15, 30, 45, and 60 days of PICC insertion

Variables	Cumulative incidence of thrombosis (%)					Log-rank test	
	7 days after catheterization	15 days after catheterization	30 days after catheterization	45 days after catheterization	60 days after catheterization	χ^2	P
Overall	15.27	30.81	36.68	46.27	54.67	–	–
Age (months)						8.254	0.004
<12	15.88	38.68	46.34	56.27	56.27		
≥12	14.66	20.87	24.58	32.96	56.01		
Limb movement training						7.142	0.008
Yes	12.58	22.23	29.34	38.17	38.17		
No	17.18	36.36	41.32	51.25	67.50		
20% mannitol or glycerol fructose						20.026	<0.001
Yes	27.02	48.40	50.46	70.28	85.14		
No	13.16	27.61	34.48	38.57	43.30		
Furosemide						6.212	0.013
Yes	16.28	34.69	42.57	54.44	64.50		
No	13.84	24.34	25.60	25.60	25.60		
Catheter placing personnel						50.018	<0.001
PICU personnel	26.28	49.52	57.20	75.54	75.54		
Operating room anesthetist	10.38	21.51	26.15	26.15	41.97		
Insertion length (cm)						21.85	<0.001
≥9	23.85	45.30	53.33	62.66	81.33		
<9	12.32	25.89	30.54	39.66	39.66		
Fibrinogen						4.328	0.037
≤1.7 g/L	16.12	37.29	42.59	53.61	59.41		
>1.7 g/L	14.82	26.77	33.01	40.46	50.38		
Activated partial prothrombin time						9.433	0.002
>32 s	17.48	38.61	45.18	53.62	58.77		
≤32 s	13.48	22.66	27.51	37.87	50.30		
D-dimer						15.543	<0.001
>1.5 mg/L	20.11	39.88	46.91	55.89	55.89		
≤1.5 mg/L	11.35	21.78	25.76	35.04	58.24		

PICC, peripherally inserted central catheter; PICU, pediatric intensive care unit.

length ≥9 cm were 48.40%, 49.52%, and 45.30% respectively, which were significantly higher than those in the control group (27.61%, 21.51%, and 25.89%, respectively, all P<0.05), as shown in *Figure 2C*,*2E*,*2F*.

Risk factors of CRT

The influencing factors of CRT in children is presented in *Table 3*. Children's age younger than 12 months (HR,

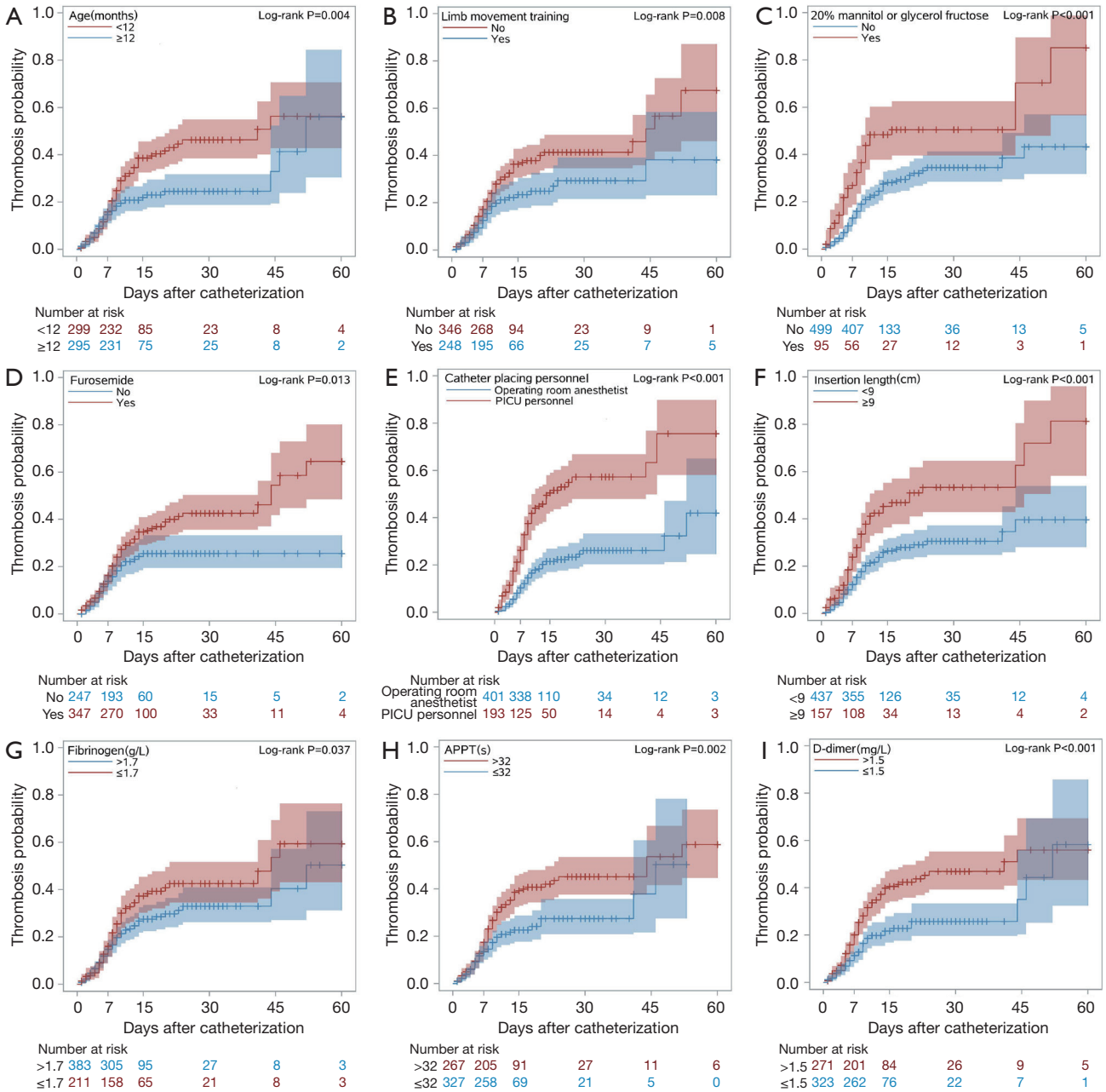

Figure 2 Kaplan-Meier survival curves of CRT in children with different characteristics. (A) Age; (B) limb movement training; (C) 20% mannitol or glycerol fructose; (D) furosemide; (E) catheter placing personnel; (F) the insertion length of PICC; (G) fibrinogen; (H) activated partial prothrombin time; (I) D-dimer. PICU, pediatric intensive care unit; PICC, peripherally inserted central catheter; APPT, activated partial prothrombin time; CRT, catheter-related thrombosis.

1.417; 95% CI: 1.012–1.985) and limb movement training after catheterization (HR, 0.632; 95% CI: 0.449–0.889) were the influencing factors of thrombosis. In terms of relevant medication use, after adjusting for age and sex, the use of 20% mannitol or glycerol fructose (HR, 2.384; 95% CI: 1.646–3.453) was a risk factor for thrombosis. Regarding catheterization, after adjusting for age and gender, catheterization performed by PICU personnel (HR, 2.373; 95% CI: 1.695–3.322) and insertion length ≥9 cm (HR, 1.671; 95% CI: 1.180–2.366) were risk factors for thrombosis.

Table 3 Influencing factors of thrombosis after PICC insertion in children

Variables	β	Standard error	χ^2	HR (95% CI)	P
Model 1 (general)					
Age (<12 *vs.* ≥12 months)	0.349	0.172	4.116	1.417 (1.012, 1.985)	0.042
Gender (male *vs.* female)	−0.060	0.160	0.142	0.942 (0.689, 1.288)	0.706
On ventilator (yes *vs.* no)	0.307	0.196	2.458	1.359 (0.926, 1.995)	0.117
Limb movement training (yes *vs.* no)	−0.459	0.174	6.932	0.632 (0.449, 0.889)	0.008
Model 2[a]					
20% mannitol or glycerol fructose (yes *vs.* no)	0.869	0.189	21.151	2.384 (1.646, 3.453)	<0.001
Furosemide (yes *vs.* no)	0.175	0.187	0.883	1.192 (0.826, 1.719)	0.347
Heparin sodium (yes *vs.* no)	0.224	0.316	0.500	1.251 (0.673, 2.325)	0.479
Model 3[a]					
Catheter placing personnel (PICU *vs.* operating room)	0.864	0.172	25.352	2.373 (1.695, 3.322)	<0.001
Insertion length (≥9 *vs.* <9 cm)	0.513	0.177	8.370	1.671 (1.180, 2.366)	0.004
Model 4 (hemagglutination term before catheterization)[a]					
Fibrinogen (≤1.7 *vs.* >1.7 g/L)	0.073	0.174	0.178	1.076 (0.765, 1.515)	0.673
Activated partial prothrombin time (>32 *vs.* ≤32 s)	0.167	0.195	0.738	1.182 (0.807, 1.732)	0.390
D-dimer (>1.5 *vs.* ≤1.5 mg/L)	0.507	0.175	8.380	1.661 (1.178, 2.341)	0.004
Full model					
Age (<12 *vs.* ≥12 months)	0.503	0.176	8.143	1.654 (1.171, 2.338)	0.004
Limb movement training (yes *vs.* no)	−0.415	0.174	5.669	0.660 (0.469, 0.929)	0.017
20% mannitol or glycerol fructose (yes *vs.* no)	0.465	0.209	4.971	1.593 (1.058, 2.398)	0.026
Catheter placing personnel (PICU *vs.* operating room)	0.653	0.181	13.009	1.921 (1.347, 2.740)	<0.001
Insertion length (≥9 *vs.* <9 cm)	0.491	0.183	7.220	1.633 (1.142, 2.336)	0.007
D-dimer (>1.5 *vs.* ≤1.5 mg/L)	0.372	0.168	4.924	1.451 (1.044, 2.015)	0.026

[a], corrected for age and gender. PICC, peripherally inserted central catheter; HR, hazard ratio; CI, confidence interval; PICU, pediatric intensive care unit.

D-dimer >1.5 mg/L (HR, 1.661; 95% CI: 1.178–2.341) was a risk factor for thrombosis in terms of blood coagulation before catheterization. In the full model, the risk factors for thrombosis were as follows: age younger than 12 months, use of 20% mannitol or glycerol fructose, the catheter placed by PICU personnel, insertion length ≥9 cm, and D-dimer >1.5 mg/L, while limb movement training was a protective factor for thrombosis.

Discussion

The incidence of CRT

CRT is the formation of venous thrombosis in the deep vein where the guiding catheter is located or in the venous drainage area adjacent to it and is the most common complication after CVC insertion. The incidence of CRT varies greatly among different races, ages, diseases, and medical institutions, with an incidence ranging from 2–67% (6). The incidence of CVC-CRT in this study was 26.60%, which was consistent with previous studies (3,24). Tian *et al.* (8) reported that CRT occurred in 20–58% of children with CVCs without preventive measures. The lower incidence in this study may have been related to the adoption of preventive measures, the attention paid by medical staff, the selection of research subjects, and the method of thrombus examination and judgment.

Clinically, CRT can be divided into symptomatic CRT and asymptomatic CRT. Among them, the most common is asymptomatic CRT, which is often difficult to detect but has less serious consequences, while symptomatic thrombosis may lead to serious consequences and even death. The incidence rate of symptomatic thrombosis in this study was 4.71% (28 cases), which was consistent with the incidence of symptomatic thrombosis (5% of patients) reported by Kamphuisen and Lee (25). Patients with symptomatic thrombosis should be actively treated and great importance given to timely removal of the catheter (11) to prevent limb disability caused by further deterioration of thrombosis and even death due to pulmonary embolism caused by thrombosis shedding. For asymptomatic thrombosis, dysfunction or blockage of the CVC may occur clinically. It is necessary to take appropriate intervention measures after comprehensive evaluation based on the patient's condition, treatment status, and severity of thrombosis, including continued catheter use, increased observation, thrombolysis to maintain smooth infusion, and switching to peripheral venous infusion after catheter removal.

The peak of CRT is within 15 and 45 days after CVC placement

Jones *et al.* (26) reported that 70% of CRT occurred within 7 days of CVC placement, while Kou *et al.* (27) reported that the high-risk period of CRT occurred more than 14 days after catheterization. However, this study showed that peak CRT occurrence was within 15 and 45 days after CVC insertion, and the incidence of CRT was lower 15–45 days after catheterization, which might have been related to factors such as the indwelling time of the CVC for research subjects, research statistical methods, and management measures after catheterization. At present, there is no unified opinion in China and abroad on the high-risk period for CRT after CVC use (28). In clinical diagnosis and treatment, the key observation period for CRT after CVC placement should be extended from 1 week to at least half a month after catheterization or even longer. For patients who have been undergoing long time catheterization, it is important to monitor the risk of thrombosis more than 45 days after CVC insertion. The illness of children with CVC more than 45 days may be more serious than other children with CVC. At the same time, indwelling catheter time is too long, the catheter is easier between vascular thrombosis. In clinical practice, CVC catheter indwelling for more than 45 days should be avoided as much as possible. When necessary, adequate evaluation can be conducted to consider the advantages and disadvantages of removing the existing CVC catheter. For patients who continue to indwelling CVC catheter more harm than good, other intravenous access should be established in time.

Risk factors for CRT

The basis of CVC-CRT formation includes vascular intimal injury, blood stasis, and blood hypercoagulability. Domestic and foreign studies have shown that the occurrence of CRT in children with CVCs may be related to the following risk factors: age of the child [it is more likely to occur in the neonatal period and above 11 years old (6)], medical conditions and diseases (29) (such as infection, surgery, trauma, tumor, kidney disease, blood hypercoagulability, and obesity, etc.), catheter factors [the larger the catheter diameter, the more prone to thrombosis (30)], the site of catheterization, iatrogenic factors (such as catheter insertion operation, flushing and sealing, infusion of nutrition, hyperpermeable liquid, and whether or not anticoagulant is used). At present, there is no unified consensus on the above risk factors, and disputes still exist over more risk factors (31).

In this study, CVC insertion was performed by qualified PICU catheterization doctors or anesthesiologists. The study found that the incidence rate of CRT in children undergoing catheterization by PICU doctors was significantly higher than by an anesthesiologist, suggesting that operation factors such as catheterization personnel directly affected the occurrence of CRT after catheterization. Since the seniority of the specific operator could not be traced back in this study, it was not possible to distinguish in detail which elements of the catheterization personnel affected the outcome of thrombosis. At the same time, because the specific condition or critical degree score of the children was not collected in this study, we were unable to compare whether there was a difference in the severity of the disease and the degree of activity limitation during hospitalization between the PICU group and the anesthesiologist's group, and this needs to be further clarified and explored in subsequent studies. A study has found that compared with general pediatric patients with CVCs, PICU children are more prone to develop CRT (32). In the management of CVC catheterization, it is of great significance to strengthen training (33), assessment, effect evaluation, and tracking management of the catheterization operators (28,34), and to strictly control the catheterization

procedure, which greatly affects the occurrence of CRT in the later stage.

For children with CVCs, patients who used mannitol, glycerol fructose, and dehydrating agents for an extended period were more prone to mural thrombus due to the blood thickening caused by dehydrating agents. Because of thin blood vessels in children under 1 year old, there is little space between the catheter and vessel wall and blood flow is easily blocked, which is more likely to cause mural thrombus. When the length of the CVC catheter ≥9 cm, children are more prone to develop thrombosis, which may be related to the depth of the insertion position and the blood flow velocity. In this study, we found that fibrinogen ≤1.7 g/L, activated partial thromboplastin time >32 s, and D-dimer >1.5 mg/L were more likely to be associated with thrombosis. Fibrinogen, activated partial prothrombin time, and D-dimer are important markers reflecting the function of coagulation and fibrinolysis. When D-dimer is too high, the blood is often in a hypercoagulable state and more likely to lead to thrombosis, and thus high vigilance is required. Timely assessment of the risk of thrombosis and undertaking of targeted preventive measures to prevent thrombosis are particularly important (29). As shown in this study, limb movement training at the catheterization site can reduce the occurrence of thrombosis and is a protective factor.

Discussion on measures to prevent CRT in children with CVCs

A number of studies (10,32,35) have shown that the occurrence of CRT is unavoidable, but the incidence of thrombosis can be reduced by taking active preventive measures, such as strengthening limb movement training after catheterization, strengthening the training of catheterization operators, selecting the appropriate catheter (30,36), standardizing the CVC flushing and sealing operation, preventing the use of anticoagulants in high-risk patients (37), and adopting interstitial limb pneumatic therapy after catheterization. The specific methods and frequencies of physical training such as limb activities, the specific requirements of CVC tube flushing and sealing operation, and the specific implementation methods of various interventions need to be further refined. At present, a recognized risk assessment scale for evaluating the occurrence of CRT in children with CVCs is lacking (28) in China and abroad (38), which needs further research and development. In clinical practice, it is necessary to take appropriate layered preventive measures based on the patient's CRT risk assessment level and the characteristics of risk factors in order to reduce the burden of clinical work (39), improve clinical efficiency, and reduce the occurrence of CVC-CRT under the condition of ensuring the safety of patients. At the same time, in clinical settings, peripheral intravenous infusion channels need to be retained as much as possible based on the patient's situation so as to minimize the use of CVCs catheters and reduce the potential for developing CRT.

Conclusions

In this retrospective cohort study, we found that the incidence of CRT in children was high and the peak period was within 15 days of CVC insertion. There were 5 factors associated with the occurrence of CRT, including the age of the children, diuretics, CVC insertion length, blood coagulation function, and functional exercise. The discovery of these factors is helpful for clinicians in making predictions based on the situation of the child and taking targeted measures to reduce the risk of CRT and ensure patient safety. Further confirmation of the risk factors for CVC-CRT is needed through multicenter large-sample studies.

Limitations of this study

Our study had several limitations related to the retrospective design. First, the extrapolation of results is limited to a certain extent, and the data mainly represent the Chongqing area or areas with a similar level of medical care. Second, this study was retrospective and incomplete with respect to influencing factors. Given the hazards of CRT in children with CVCs, future studies should consider multicenter prospective studies that include a broader sample size and consider more comprehensive influencing factors.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-529/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Theoretical Committee of the Children's Hospital of Chongqing Medical University (No. 296 of 2021). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was taken from all the patients' parents.

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