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Construction of a Risk Prediction Model for Central Venous Catheter–Associated Thrombosis in Pediatric Patients with Severe Traumatic Brain Injury

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***A*bstract:** *Objective:* To develop and validate a risk prediction model for catheter-related thrombosis (CRT) in pediatric patients with severe traumatic brain injury (sTBI). *Methods:* Using convenience sampling, 216 pediatric patients with sTBI admitted to the Surgical Intensive Care Unit of Kunming Children's Hospital between June 2022 and May 2025 were enrolled and randomly divided into a training set of 151 cases and a validation set of 65 cases. Influencing factors were identified through univariate analysis and logistic regression analysis to construct the prediction model. The model's discrimination and calibration were evaluated by the area under the receiver operating characteristic (ROC) curve (AUC) and the Hosmer–Lemeshow goodness-of-fit test. *Results:* Univariate analysis showed that admission GCS score, CVC insertion site, D-dimer level, and duration of mechanical ventilation were risk factors for CRT in children with sTBI ($P < 0.05$). The logistic regression equation was constructed as follows: Logit(P) = 2.74 – 1.95 × GCS score + 0.25 × D-dimer (μg/mL) + 0.02 × duration of mechanical ventilation (h). Based on this model, the AUC was 0.87 in the training set and 0.88 in the validation set. The Hosmer–Lemeshow goodness-of-fit test indicated good agreement between the model's calibration curve and the ideal curve. *Conclusion:* The developed prediction model demonstrates good predictive performance and can serve as a reference for the early clinical identification of CRT risk in pediatric patients with sTBI.

Keywords: Severe traumatic brain injury; Central venous catheter-related thrombosis; Children; Prediction model; Influencing factors

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1. Introduction

The main causes of traumatic brain injury (TBI) in children are falls, traffic accidents, and blows, with a global incidence rate of approximately (47–280)/100,000. TBI is one of the leading causes of death and disability among

children worldwide [1, 2]. With the improvement of living standards and the development of urban transportation, the number of children with TBI has significantly increased, and the severity of trauma has been increasing [3]. Children with severe traumatic brain injury (sTBI) often face life-threatening issues such as hypovolemia and increased intracranial pressure, urgently requiring vasoactive drugs, blood transfusions, hypertonic solutions, and other treatments. Therefore, the central venous catheter (CVC) serves as a crucial lifesaving access route. However, research has shown that CVC is a significant risk factor for venous thromboembolism in pediatric patients [4]. Additionally, the incidence of central venous device-related thromboses (CRT) has been increasing in recent years [5]. Current studies indicate that the CRT incidence rate among hospitalized children is as high as 25.7%–43.53% [6–9]. Currently, there are no reports on CRT risk prediction models for children with sTBI. Therefore, this study aims to construct a CRT prediction model for children with sTBI to assist in the early identification of CRT patients.

2. Objects and methods

2.1. Subjects

Children with sTBI admitted to the surgical intensive care unit (SICU) of Kunming Children's Hospital from June 2022 to May 2025 were selected to construct the prediction model.

The sample size calculation in this study followed the clinical prediction model sample size calculation formula EPV (events per variable) [10]. Through literature review and expert panel meetings, it was determined that there were 5 predictive variables. Considering a 10% loss to follow-up rate, the total sample size was determined to be at least approximately 216 cases. Patients were randomly split into a training set (151 cases) and a validation set (65 cases) at a 7:3 ratio.

The children were divided into CRT and non-CRT groups. This study was approved by the Medical Ethics Committee of Kunming Children's Hospital (2023-03-264-K01).

2.1.1. Inclusion criteria

(1) Children diagnosed with severe or extremely severe traumatic brain injury.

(2) Children aged < 18 years.

(3) Admission to the hospital within 24 hours of injury, with a hospital stay ≥ 3 days and CVC indwelling time ≥ 72 hours.

(4) Doppler ultrasonography performed before catheterization to confirm no thrombosis in the catheterized vein.

2.1.2. Exclusion criteria

(1) History of venous thromboembolism.

(2) Coagulation dysfunction or thrombocytopenia before trauma.

(3) Incomplete medical records.

2.1.3. CRT diagnosis criteria

(1) Clinicians or nurses with 3 or more years of experience perform vascular ultrasound screening. Detection of thrombus in the blood vessels of the limb with the catheter indicates CRT.

(2) During routine catheter maintenance by nurses, if there is no blood return when withdrawing the catheter,

infusion is not smooth, or tissue plasminogen activator is required, it indicates the occurrence of CRT.

2.2. Determination of predictive variables

The clinical data collected in this study was determined through expert consultation:

(1) A risk factor item pool for CRT was formed through literature review and research group discussion.

(2) Inclusion criteria for experts: having a professional title of associate professor or above; engaged in pediatric critical care or intravenous therapy nursing for more than 10 years; voluntarily participating in this consultation. Five experts were included in this study for consultation.

(3) After two rounds of expert consultation, the items were revised to determine the predictive variables.

Finally, the clinical data of the patients included:

(1) General information: age, gender, weight, whether surgery was performed, whether there were multiple injuries, and Glasgow Coma Scale (GCS) score at admission for sTBI patients.

(2) Catheter factors: CVC model, CVC type, catheter insertion site.

(3) Laboratory indicators 24 hours after CVC placement: activated partial thromboplastin time (APTT), prothrombin time (PT), D-dimer (D-d), fibrinogen concentration (FIB), white blood cell count, platelet count, C-reactive protein, cholesterol concentration, lactic acid level (Lac).

(4) Treatment factors: duration of mechanical ventilation, whether blood products, vasoactive drugs, parenteral nutrition, hypertonic fluids, anticoagulants, two or more antibiotics, or early rehabilitation were used.

2.3. Data collection

Data was collected by a trained member of the research team and verified by another team member to ensure authenticity and accuracy. If any issues were found during the collection process, adjustments were made promptly after discussion within the research team.

2.4. Statistical methods

Statistical analysis was performed using SPSS 25.0 software and R 4.5.1. Qualitative data were described using frequency and proportion, and univariate analysis was conducted using the χ^2 test. Quantitative data conforming to a normal distribution were described using mean ± standard deviation, and comparisons between groups were made using the t-test. Quantitative data not conforming to a normal distribution were described using median (quartiles) [M(P25, P75)], and comparisons between groups were made using the Mann-Whitney U test. Variables with statistical significance were included in Logistic regression analysis. A nomogram prediction model was established using R 4.5.1 software. The area under the receiver operating characteristic (ROC) curve (AUC) and the Hosmer-Lemeshow goodness-of-fit test were used to evaluate the model's discrimination and calibration, respectively. The model was internally validated using the Bootstrap method with 500 repetitions. Statistical significance was set at $P < 0.05$.

3. Results

3.1. General information of children with sTBI

Among the 151 children with sTBI in the training set, 38 developed CRT and 113 did not, resulting in an incidence rate of 25.17%. In the validation set of 65 children with sTBI, 17 developed CRT and 48 did not, yielding an incidence rate of 26.15%. None of the children in the CRT group exhibited clinical symptoms in this study.

3.2. Univariate analysis of CRT occurrence in children with sTBI

In the univariate analysis of CRT occurrence in children with severe traumatic brain injury (sTBI), significant differences were observed in GCS score, catheter insertion site, D-dimer concentration, and duration of mechanical ventilation, with statistical significance ($P < 0.05$). No statistically significant differences were found in age, gender, weight, surgery, multiple trauma, CVC model, CVC type, APTT, PT, FIB, white blood cell count, platelet count, C-reactive protein concentration, cholesterol concentration, Lac level, use of blood products, use of vasoactive drugs, use of parenteral nutrition, use of hyperosmolar solution, use of anticoagulants, use of two or more antibiotics, and implementation of early rehabilitation ($P > 0.05$), as shown in **Table 1**.

Table 1. Univariate analysis of CRT occurrence in children with sTBI

Variable	CRT group	Non-CRT group	Statistic	P-value
Age [months, M (Q1, Q3)]	57.5 (10.5, 75)	30 (18, 66)	-1.89	0.06
Gender				
Male	20	74	2.00	0.16
Female	18	39		
Weight [kg, M (Q1, Q3)]	18 (8.5, 19.75)	14 (10, 19)	-0.74	0.46
Surgery				
Yes	18	45	0.67	0.41
No	20	68		
Multiple trauma				
Yes	16	48	0.02	0.97
No	22	65		
GCS [score, M (Q1, Q3)]	3 (3, 4)	6 (5, 7)	-0.842	< 0.001
CVC Size				
18G	3	12	-1.67	0.10
20G	7	36		
4F	28	65		
CVC Type				
Single-lumen	12	47	1.20	0.27
Double-lumen	26	66		
Insertion site				
Jugular vein	14	79	13.15	< 0.001
Femoral vein	24	34		
APTT [s, M (Q1, Q3)]	37.2 (29, 40.9)	36.2 (34, 40.1)	-0.33	0.74
PT [s, M (Q1, Q3)]	14.7 (14, 15.93)	14.4 (13.6, 15.3)	-0.57	0.12
D-dimer [μg/mL, M (Q1, Q3)]	18 (15.25, 22)	7 (2.76, 9)	-8.66	< 0.001
FIB [g/L, M (Q1, Q3)]	2.99 (1.57, 3.26)	2.53 (1.65, 3.11)	-1.17	0.24

Table 1 (Continued)

Variable	CRT group	Non-CRT group	Statistic	P-value
WBC [×10⁹/L, M (Q1, Q3)]	11.85 (9.54, 18.42)	10.77 (7.34, 13.9)	-1.84	0.07
Platelet [×10⁹/L, M (Q1, Q3)]	254 (182, 315)	260 (213, 315)	-0.82	0.41
CRP [mg/L, M (Q1, Q3)]	11.18 (1.47, 49.73)	9.37 (1.49, 31.98)	-0.40	0.69
Cholesterol [mg/dL, M (Q1, Q3)]	3.46 (2.6, 4.46)	3.31 (3.01, 4)	-0.10	0.92
Lac [mmol/L, M (Q1, Q3)]	1.59 (1.4, 2)	1.3 (0.6, 2.2)	-1.76	0.08
MV Duration [h, M (Q1, Q3)]	96 (60, 148.5)	24 (1, 60)	-6.04	< 0.001
Blood product use				
Yes	31	94	0.52	0.82
No	7	19		
Vasoactive drug use				
Yes	31	90	0.67	0.80
No	7	23		
Parenteral nutrition use				
Yes	4	8	0.11	0.74
No	34	105		
Hypertonic fluid use				
Yes	24	56	2.11	0.15
No	14	57		
Anticoagulant use				
Yes	9	18	1.17	0.28
No	29	95		
≥ 2 Antibiotic use				
Yes	10	20	1.33	0.25
No	28	93		
Early rehabilitation				
Yes	13	44	0.27	0.60
No	25	69		

3.3. Logistic regression analysis of CRT occurrence in children with sTBI

Variables with statistical significance in the univariate analysis were included as independent variables in the logistic regression analysis. Whether CRT occurs was set as the dependent variable (yes=1, no=0). The independent variables were assigned as follows: catheter insertion site (femoral vein=1, jugular vein=0), GCS score, D-dimer concentration, and duration of mechanical ventilation were entered as original values. The results showed that GCS score, D-dimer concentration, and duration of mechanical ventilation were influencing factors for CRT occurrence in children with sTBI ($P < 0.05$), as shown in **Table 2**.

Table 2. Logistic regression analysis of CRT occurrence in children with sTBI

	Regression coefficient	Standard error	Wald χ^2 value	Degrees of freedom	P-value	OR	95% CI
GCS score	-1.95	0.55	12.40	1	< 0.001	0.14	[0.05, 0.42]
Catheter insertion site	2.85	1.57	3.28	1	0.07	7.17	[0.79, 11.25]
D-dimer level	0.25	0.11	5.50	1	0.02	1.28	[1.04, 1.57]
Mechanical ventilation duration	0.02	0.01	4.18	1	0.04	1.02	[1.00, 1.04]

3.4. Construction of a prediction model for CRT occurrence in children with sTBI

Based on the results of the logistic regression analysis, a prediction model was constructed. The logistic regression equation is: Logit(P) = 2.74 - 1.95 × GCS score + 0.25 × D-dimer (ug/mL) + 0.02 × duration of mechanical ventilation (h). A nomogram was created based on this equation, as shown in **Figure 1**.

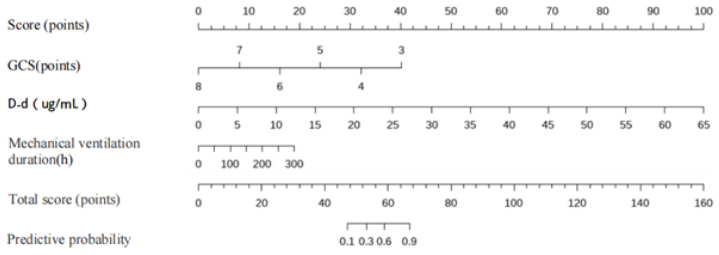

Figure 1. Nomogram for predicting CRT in children with sTBI

3.5. Evaluation and validation of the prediction model for CRT in children with sTBI

The AUC of the ROC curve for the constructed model was 0.87 [95% CI (0.80, 0.93)], as shown in **Figure 2**. The sensitivity was 81.6%, the specificity was 84.1%, the maximum Youden index was 0.66, and the corresponding cut-off value was -0.58. Internal validation was performed using the Bootstrap method repeated 500 times to evaluate the discrimination and calibration of the model. The AUC of the ROC curve was 0.86 [95% CI (0.81, 0.92)], the sensitivity was 82.5%, and the specificity was 79.2%. The calibration curve showed good agreement with the prediction curve, as seen in **Figure 3**. The Hosmer-Lemeshow goodness-of-fit test showed χ^2=4.79, P = 0.78. Validation was performed using a validation set of 65 children with sTBI, where the AUC of the ROC curve was 0.88 [95% CI (0.80, 0.94)], the sensitivity was 88.2%, and the specificity was 79.2%.

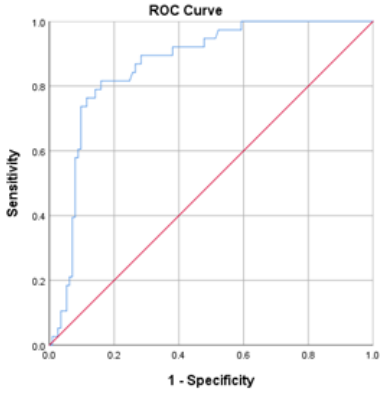

Figure 2. RC en with sTBI

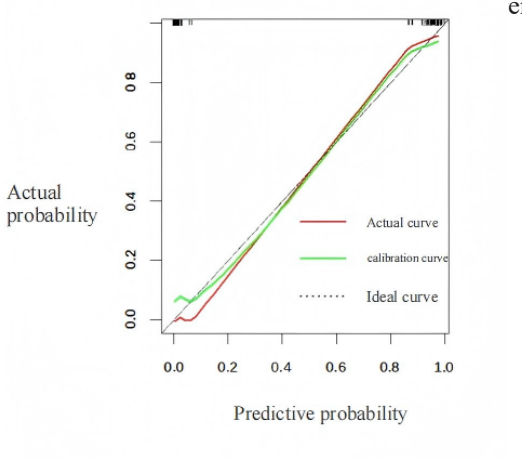

Figure 3. Calibration curve of the CRT prediction model for children with sTBI

4. Discussion

4.1. High incidence of CRT in children with sTBI

Critically ill children have potential life-threatening factors, and the placement of CVCs further increases the incidence of CRT during treatment. In this study, the incidence of CRT in children with sTBI was 25.17%, which is higher than the 9.85% incidence of CRT in general critically ill children reported by Li *et al.* [12]. Severe brain injury leads to post-traumatic hypercoagulability of the blood, which is already a strong inducer of thrombosis. Guidelines indicate that the treatment of sTBI includes surgical procedures, the use of mechanical ventilation, blood products, vasoactive agents, and intravenous infusion of high-concentration electrolyte solutions [13]. Studies have shown that these treatment factors increase the risk of venous thromboembolism [4]. CVC catheters are widely recognized as important risk factors for venous thromboembolism in pediatric trauma patients, and each additional risk factor triples the chance of thrombosis [14, 15]. Therefore, early identification of CRT risk and prevention are particularly important in children with sTBI.

4.2. GCS is an important predictor of CRT in children with sTBI

A GCS score of ≤ 8 in children with traumatic brain injury is considered sTBI. These children often experience the most severe condition within 24-72 hours after injury, which can lead to diffuse brain swelling. The resulting increase in intracranial pressure can further damage cerebral perfusion, causing more cerebral ischemia, swelling, cerebral hernia, and death [16]. Multiple studies have reported a significant correlation between a GCS score of ≤ 8 and increased risk of thrombosis, with lower GCS scores associated with higher thrombotic risk [17, 18]. This is consistent with the findings of this study. Therefore, timely assessment of GCS scores is crucial during condition observation.

4.3. D-dimer is an important predictor of CRT in children with sTBI

D-dimer is the terminal product of cross-linked fibrin. Elevated concentrations represent coagulation activation and secondary fibrinolysis in the body, reflecting a hypercoagulable state. D-dimer has high sensitivity but low specificity [19]. The results of this study show that D-dimer is a risk factor for CRT in children with sTBI, and higher concentrations are more likely to lead to CRT, consistent with previous studies on thrombotic risk [20]. Therefore, medical staff should routinely screen children's coagulation function after admission. For children with

high or continuously rising D-dimer concentrations, they should be alert to the occurrence of CRT.

4.4. Duration of mechanical ventilation is an important predictor of CRT in children with sTBI

The duration of mechanical ventilation itself does not directly cause thrombosis. However, due to consciousness disorders, respiratory abnormalities, surgery, and other reasons after sTBI, mechanical ventilation is often required. Factors such as long-term sedation therapy, restraint, or immobilization during mechanical ventilation can significantly slow down blood flow in the body. The longer the duration of mechanical ventilation, the longer the blood stasis time, and the higher the risk of CRT. In previous studies, mechanical ventilation has also been identified as one of the influencing factors for thrombosis in children with moderate to severe TBI [21].

The AUC for the training set in this study was 0.87, and the AUC for the validation set was 0.88, indicating good discrimination in predicting CRT. The calibration curve of the model demonstrated good fit, and the decision curve showed a good benefit rate. Therefore, the model has high efficacy and certain clinical practical value. However, there are some limitations in this study. Firstly, the sample size is limited, and multi-center studies are needed. Secondly, the study tracked whether CRT occurred during the children's stay in the ICU, but failed to continue tracking some children who were transferred to general wards with CVC, which may lead to missed cases.

5. Conclusion

In summary, this study explored the risk factors for CRT in children with sTBI, including GCS score at admission, catheter location, D-dimer concentration 24 hours after CVC placement, and duration of mechanical ventilation. Additionally, a clinical prediction model for CRT in children with sTBI was constructed using GCS score, D-dimer concentration, and duration of mechanical ventilation, and the reliability of the model was verified. This model can guide clinical healthcare professionals in early identification of CRT risk in children with sTBI and further improve the quality management of central venous access.

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Disclosure statement

The authors declare no conflict of interest.

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