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ORIGINAL ARTICLE

Risk factors for unplanned removal of central venous catheters in hospitalized children with hematological and oncological disorders

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Abstract

Central venous catheters (CVCs) are essential devices in the treatment of pediatric patients with hematological and oncological disorders; however, the most suitable type of CVC for these patients remains unclear. We retrospectively compared risk factors for unplanned removal of two commonly used CVCs, peripherally inserted central catheters (PICCs) and tunneled CVCs, to propose which is the better device. We followed 89 patients fitted with a tunneled CVC (total 21,395 catheter-days) and 84 fitted with a PICC (total 9177 catheter-days) between January 1, 2013 and December 31, 2015, until catheter removal. Patients with a PICC had a significantly higher 3-month cumulative incidence of catheter occlusion (5.2% vs. 0%, $p = 4.08 \times 10^{-3}$) and total unplanned removals (29.0% vs. 6.9%, $p = 0.0316$) than those with tunneled CVCs. However, the cumulative incidence of central line-associated bloodstream infection did not differ significantly by CVC type. Multivariable analysis identified younger age (< 2 years) [sub-distribution hazard ratio (SHR) 2.29; 95% confidence interval (CI) 1.27–4.14] and PICC (SHR 2.73; 95% CI 1.48–5.02) as independent risk factors for unplanned removal. Thus, our results suggest that tunneled CVCs are preferable in pediatric patients with hematological and oncological disorders requiring long-term, intensive treatment.

Keywords Peripherally inserted central venous catheter · Tunneled central venous catheter · Pediatric · Hematological disorder

Abbreviations

CVCs	Central venous catheters
PICCs	Peripherally inserted central catheters
DVT	Deep vein thrombosis
CLABSI	Central line-associated bloodstream infection
VTE	Venous thromboembolism
SCT	Stem cell transplantation

Introduction

Central venous catheters (CVCs) are essential devices for safe and reliable vascular access in the treatment of pediatric patients with hematological or oncological diseases requiring long-term intensive treatment [1]. CVCs play a fundamental role in the administration of chemotherapeutic agents, transfusion, and parenteral nutrition, as well as painless blood sampling for frequent regular examination. Conversely, catheter-related complications are always highly problematic for clinicians because they result not only in unplanned removal

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and catheter reinsertion, but also in treatment delay, increased mortality, and healthcare costs [2]. Deep vein thrombosis (DVT) and central line-associated bloodstream infections (CLABSI) are two major CVC complications. Immunosuppression related to disease or therapy, thrombocytopenia, and coagulopathy in patients with cancer makes the prevention and management these complications especially important [3].

Peripherally inserted central catheters (PICCs) are non-tunneled CVCs inserted through a peripheral vein in the upper arm. Owing to its ease of insertion and removal, it is more commonly used as an alternative to other types of CVCs for pediatric and adult patients [4]. PICC insertion is less invasive and more cost effective than conventional type CVCs, including tunneled CVCs or implanted ports requiring general anesthesia and surgery in the operating room. Even during removal, PICCs can be easily removed without sedation or local anesthesia. Although PICCs have these advantages, many studies have reported the limited longevity and higher risk of DVT in PICCs compared with other types of CVCs in both adults [4] and children [5].

Therefore, the British Committee for Standards in Hematology guidelines for adults recommended that PICCs are suited as ambulatory or outpatient-based therapy and contraindicated as inpatient therapy for adult patients with hematological disorders [6]. Although some studies reported the acceptability of the long-term use of PICCs for hospitalized children with cancer [7, 8], a prospective observational study [9] on children with various diseases requiring CVC placement showed that PICCs had significantly higher incidences of venous thromboembolism (VTE), CLABSI, and catheter malfunction than tunneled CVCs. This study also showed that patients with leukemia harbor a higher risk of CVC-related VTE. However, no comparative studies have been conducted on PICCs and conventional CVCs in pediatric patients with hematological and oncological disorders.

Here, we performed a retrospective study on PICC longevity compared with that of tunneled CVCs to identify risk factors of unplanned CVC removal and help select the appropriate CVC type in pediatric patients with hematological and malignant diseases.

Materials and methods

Patients

A total of 173 consecutive pediatric patients with hematological or oncological disorders who received placement of initial CVCs (PICC [$n=84$] or tunneled CVC [$n=89$]) at Nagoya University Hospital from January 1, 2013, to December 31, 2015, were retrospectively reviewed. We excluded second or further CVC insertions in this study. The clinical characteristics of patients are summarized in Table 1. This study was approved by the ethics committee of Nagoya University Graduate School of Medicine.

Catheter placement and management

The attending physicians selected the type of catheter based on the patients' clinical conditions. PICCs (Groshong® [Bard Peripheral Vascular, Inc., Tempe, AZ, USA] catheter) were inserted by well-trained pediatricians under clean contaminated condition in the fluoroscopy room. Operators selected any of the major veins of the upper extremities, usually the cephalic or basilica vein. Tunneled CVCs (Hickman® [Bard Peripheral Vascular, Inc.] or Broviac® [Bard Peripheral Vascular, Inc.] catheters) were inserted into one of the internal jugular veins by well-trained pediatric surgeons in the operating room. For both types of catheters, the catheter tip was positioned at the superior vena cava under radiographic guidance.

The management of catheters was uniformly implemented as described below, and no major changes were made to the protocol within the study period. To prevent infection

Table 1 Clinical characteristics

	PICCs	Tunneled CVCs	*p*-value
Total, *n*	84	89	
Catheter life, days, median (range)	88 (5–344)	186 (6–1078)	< 0.001
Age, years, median (range)	6 (0–17)	2 (0–16)	< 0.001
Gender, *n* (%)			
Male	47 (56.0)	54 (60.7)	NS
Female	37 (44.0)	35 (39.3)	NS
Disease, *n* (%)			
Hematological malignancy	37 (44.1)	36 (40.4)	NS
Solid tumor	39 (46.4)	39 (43.8)	NS
Nonmalignant hematological disorder	5 (5.9)	9 (10.1)	NS
PID	3 (3.6)	5 (5.6)	NS
SCT, *n* (%)	8 (9.5)	29 (32.6)	< 0.001

PICC peripherally inserted central catheter, *CVC* central venous catheter, *PID* primary immunodeficiency, *SCT* stem cell transplantation, *NS* not significant

and clotting, we flushed the lumen with saline containing heparin once a day for PICCs and three times a week for tunneled CVCs. For both catheter types, we disinfected the skin around the catheter insertion site and changed the dressing three times a week.

Unplanned catheter removal

The causes of unplanned catheter removal were categorized into self-removal, occlusion, mechanical events (catheter malposition or fracture), CLABSI, or infection without confirmed CLABSI. Confirmed CLABSI was defined as catheter infection with a positive blood culture. Catheters inserted into patients with persistent fever of unknown origin who did not respond to antibiotic therapy were empirically removed, and the cases were categorized as infections without confirmed CLABSI when their blood culture was negative.

Statistical analysis

PICCs and tunneled CVCs were compared using the Mann–Whitney *U* test for continuous variables and Fisher's exact test for categorical variables. Correlations between patients' covariates or factors and unplanned removal were evaluated using univariate and multivariable logistic regression analyses. The cumulative incidence of unplanned catheter removal was calculated using competing risk methods. The Fine–Gray proportional hazards model was used to estimate the sub-distribution hazard ratios of causes of catheter removal in PICCs versus tunneled CVCs. Incidences of complications or removal were calculated per 1000 catheter days. All *p*-values reported are two-sided, and *p*-values <0.05 were considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [10]. Proportionality was evaluated using Schoenfeld residuals, which was attained for all analyses.

We compared the cumulative incidence of unplanned removal of PICCs and tunneled CVCs. Removal at the end of therapy was regarded as censoring. The incidence for each event was calculated per 1000 catheter days.

Results

Patient characteristics

The median age of patients with PICCs was higher than those with tunneled CVCs (6.5 vs. 2.7 years; $p<0.001$). No gender or disease predominance was noted between the two groups. Patients with PICCs were less likely to receive stem cell transplantation (SCT) than those with tunneled CVCs (9.5% vs. 32.6%, $p<0.001$) because patients scheduled for SCT were initially inserted with a tunneled CVC at our institute.

Complications during catheter insertion procedure

Arterial puncture ($n=2$) and arrhythmia ($n=1$) were the complications identified during PICC insertion. However, no complications were found related to tunneled CVC insertion (Table 2).

The incidence of unplanned catheter removal

Unplanned catheter removal was observed in 28 of 84 (33%) patients with PICCs and 33 of 89 (37%) with tunneled CVCs (Table 3). The median catheter life was 88 days with a total of 9177 catheter days for PICCs and 186 days with a total of 21,395 catheter days for tunneled CVCs. The incidence of unplanned removal per 1000 catheter days was 3.05 and 1.54 for PICCs and tunneled CVCs, respectively (Table 4). The 3-month cumulative incidence of unplanned catheter removal of PICCs (29.0%; 95% confidence interval [CI] 19.1–39.6%) was significantly higher than that of tunneled CVCs (6.9%; 2.8–13.5%; $p=0.0316$) (Fig. 1A).

Infection with or without confirmed CLABSI

Among the causes of unplanned removal, infection without confirmed CLABSI was the most common for both catheter

Table 2 Complications during catheter insertion

Type of complications	PICCs $n=84$	Tunneled CVCs $n=89$	*p*-value
Puncture of the arteries, *n* (%)	2 (2)	0 (0)	NS
Arrhythmia, *n* (%)	1 (1)	0 (0)	NS
Air embolization, *n* (%)	0 (0)	0 (0)	NS
Lung injury, *n* (%)	0 (0)	0 (0)	NS
Catheter deviation from vessels, *n* (%)	0 (0)	0 (0)	NS
Nerve injury, *n* (%)	0 (0)	0 (0)	NS

PICC peripherally inserted central catheter, *CVC* central venous catheter, *NS* not significant

Table 3 Causes of catheter removal

	PICCs $n=84$	Tunneled CVCs $n=89$	p-value
Unplanned removal, *n* (%)	28 (33)	33 (37)	NS
Infection with confirmed CLABSI	8 (9.5)	16 (18)	NS
Infection without confirmed CLABSI	3 (3.6)	5 (5.6)	NS
Occlusion	5 (6.0)	0 (0)	0.0253
Mechanical cause	6 (7.1)	11 (12)	NS
Self-removal	5 (6.0)	1 (1.1)	NS
Others	1 (1.2)	0 (0)	NS
Planned removal, *n* (%)	45 (53.6)	48 (54)	NS
Death before catheter removal, *n* (%)	8 (9.5)	2 (2.2)	NS
Under treatment, *n* (%)	3 (3.6)	6 (6.7)	NS

PICC peripherally inserted central catheter, *CVC* central venous catheter, *CLABSI* central line-associated blood stream infection, *NS* not significant

types, with the incidence per 1000 catheter days of 0.87 and 0.56 for PICCs and tunneled CVCs, respectively. The incidence of confirmed CLABSI was also similar between PICCs (0.33 per 1000 catheter days) and CVC (0.42 per 1000 catheter days). The cumulative incidence of infection did not differ significantly between both catheter types ($p=0.664$) (Supplementary Fig. 1A).

Catheter occlusion

The incidence per 1000 catheter days of catheter occlusion was 0.54 and 0.00 for PICCs and tunneled CVCs, respectively. The cumulative incidence of catheter occlusion for PICCs was significantly higher than that for tunneled CVCs ($p=0.0041$) (Supplementary Fig. 1B).

Mechanical events, self-removal, and other causes

The incidence per 1000 catheter days of mechanical events was 0.65 and 0.51 for PICCs and tunneled CVCs, respectively. The cumulative incidence of mechanical events did not vary significantly between both catheter types ($p=0.716$) (Supplementary Fig. 1C). The incidence per 1000 catheter days of self-removal was 0.54 and 0.047 for PICCs and tunneled CVCs, respectively. The incidence of self-removal was extremely low for tunneled CVCs; however, it was one of the major causes of catheter removal for PICCs. Consequently, the cumulative incidence of self-removal for PICCs was significantly higher than that for tunneled CVCs ($p=0.0469$) (Supplementary Fig. 1D). The incidence per 1000 catheter days of other causes was 0.11 and 0.00 for PICCs and tunneled CVCs, respectively. One of the other reasons was discomfort at the catheter insertion site, which was the only case with PICC.

Table 4 Incidence of catheter removal per 1000 catheter days

Causes of unplanned catheter removal	PICCs (9177 catheter days)	Tunneled CVCs (21,395 catheter days)
Infection with confirmed CLABSI	0.33	0.42
Infection without confirmed CLABSI	0.87	0.56
Occlusion	0.54	0
Mechanical cause	0.65	0.51
Self-removal	0.54	0.047
Others	0.11	0
Total unplanned removal	3.05	1.54

PICC peripherally inserted central catheter, *CVC* central venous catheter, *CLABSI* central line-associated blood stream infection

Univariate and multivariable analyses of risk factors for unplanned catheter removal

Univariate and multivariable analyses were performed to identify risk factors for unplanned removal of CVCs (Table 5). Age < 2 years (sub-distribution hazard ratio [SHR] 2.290; 95% CI 1.26–4.16; $p=0.006$) and PICCs (SHR 2.727; 95% CI 1.518–4.9; $p<0.001$) were identified as independent risk factors for unplanned removal, whereas no significant associations were observed among gender, disease, and stem cell transplantation. The cumulative incidence of unplanned catheter removal in younger patients (< 2 years) was significantly higher than those in other patients (3-month cumulative incidence [95% CI] 21.7% [10.6–35.3%] vs. 15.4% [9.7–22.4%]; $p=0.0496$] (Fig. 1B).

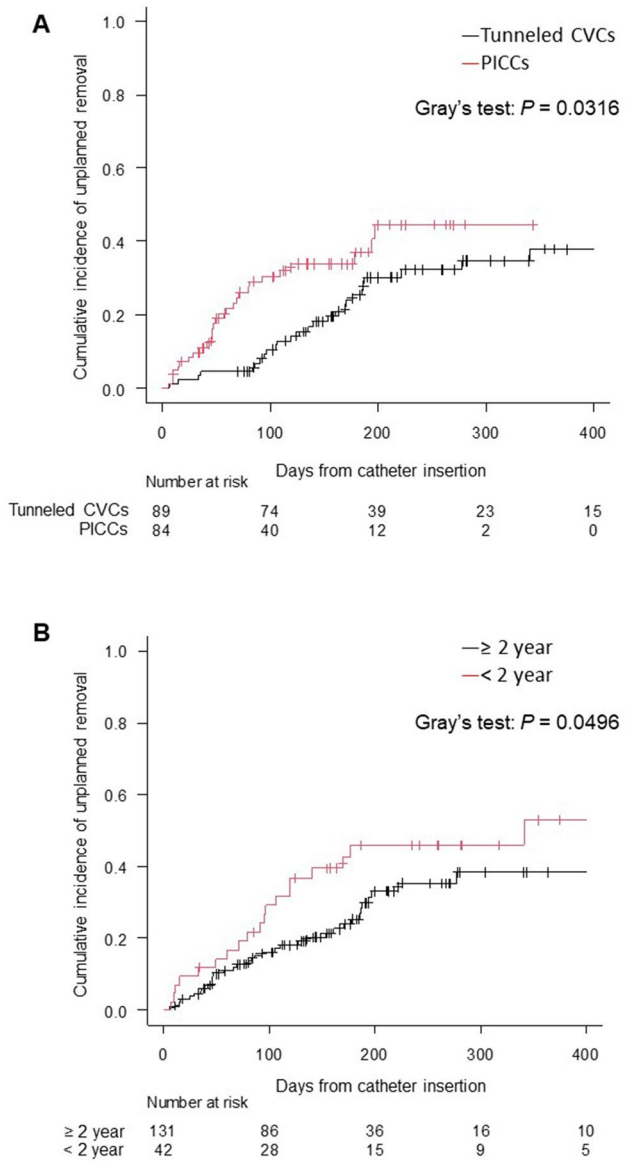

Fig. 1 **A** Comparison of the cumulative incidence of unplanned removal in PICCs vs. tunneled CVCs after insertion. **B** Comparison of unplanned removal by age

Discussion

We performed the first retrospective study that identified risk factors for unplanned removal of CVCs in pediatric patients with hematological and malignant diseases. The multivariable analysis showed that PICCs and a younger age (< 2 years) were independent risk factors for unplanned catheter removal. Although the incidence of planned removal was similar between PICCs and tunneled CVCs (54.0% vs. 53.6%), the median catheter life of PICCs was significantly shorter than that of tunneled CVCs (88 vs. 186 days). To the best of our knowledge, no reports have assessed the effects of children's age on catheter complications. In this study, younger patients with PICCs had a particularly high frequency of unplanned removal (11 of 17, 65%). Notably, 4 of 5 children who self-removed their PICCs were aged < 2 years. These results suggest that the tunneled CVC is more appropriate in the treatment of hematological and malignant diseases, especially in younger children. However, tunneled CVCs require the ligation of the vein used for insertion, making reinsertion using the same vessel difficult.

A meta-analysis of adult patients [4] and a systemic review of pediatric patients [11] have reported a higher risk of VTE with PICCs compared with tunneled CVCs. In particular, a prospective study conducted on pediatric patients with leukemia similarly showed that PICC use had a higher risk of VTE [9]. Although the present cohort included only a few cases of catheter blockage without radiographic confirmation of VTE, catheter removal due to blockage was significantly more common with PICCs than with CVCs. Our observations are consistent with those of previous studies, as CVC occlusion is mostly due to a thrombus [12].

In the present study, no difference was observed in the frequency of CLABSI between PICCs and CVCs in patients with hematological and malignant diseases, which is inconsistent with the findings of previous pediatric studies showing a higher incidence of catheter infection in PICCs, [9, 11] although these studies included a wider range of pediatric diseases and were not limited to those with pediatric hematological and malignant diseases. In adult patients, the frequency of CLABSIs in PICCs and CVCs has been investigated in several cohorts of patients with various diseases, with some reports suggesting a higher risk for PICCs [13], whereas others suggested a higher risk for CVCs [14]. Meanwhile, a systematic review of adult patients with cancer concluded that the occurrence of infection did not differ among catheter types [15]. A larger prospective study should be conducted to determine the catheter type with a lower risk of CLABSI, especially in pediatric patients with hematological and malignant diseases.

In conclusion, this study revealed that PICCs are associated with a higher risk of unplanned catheter removal than tunneled CVCs in children with hematological and malignant diseases. Among the causes of catheter removal, the risk of CLABSI in PICCs was comparable to that in tunneled CVCs; however, the risk of catheter occlusion was significantly higher in PICCs than in tunneled CVCs. Moreover, a younger age (aged < 2 years) was another independent risk factor for unplanned catheter removal. These results suggest that tunneled CVCs is preferable for children, especially younger ones, with hematological and oncological disorders requiring long-term intensive treatment. Future studies are warranted to determine more reliable catheter selection methods.

Table 5 Univariate and multivariable analyses of risk factors for unplanned removal

Related risk factors	Univariate analysis		Multivariable analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Gender				
Female	1			
Male	1.49 (0.87–2.57)	0.15	–	–
Age				
≥ 2 years old	1			
< 2 years old	1.57 (0.92–2.70)	0.10	2.29 (1.27–4.14)	0.006
Device				
Tunneled CVCs	1			
PICCs	2.00 (1.16–3.45)	0.01	2.73 (1.48–5.02)	0.001
Disease				
Hematological malignancy	0.88 (0.52–1.48)	NS	–	–
Solid tumor	0.91 (0.54–1.51)	NS	–	–
Non-malignant hematological disorder	1.59 (0.57–4.46)	NS	–	–
PID	2.09 (0.74–5.85)	0.16	–	–
SCT				
No	1			
Yes	0.64 (0.35–1.19)	0.16	–	–

HR hazard ratio, *CI* confidence interval, *CVC* central venous catheter, *PICC* peripherally inserted central catheter, *PID* primary immunodeficiency, *SCT* stem cell transplantation, *NS* not significant

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12185-022-03346-4.

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Author contributions Drs. MM, MH, YH, and HM conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Drs. TT, CS, AH, MK, EN, NK, AN, NN, SK, and YT conceptualized and designed the study, supervised data collection, assisted in conducting the analyses, and reviewed and revised the manuscript. Drs. TI and MN assisted with data interpretation and critically reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data availability statement The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Conflict of interest The authors have no example conflicts of interest to disclose.

Ethics approval This study was approved by the ethics committee of Nagoya University Graduate School of Medicine. All methods were carried out in accordance with relevant guidelines and regulations.

Consent to participate Written informed consent was obtained from the parents.

Consent to publish Not applicable.

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