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

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Abstract

Objective

Central venous catheters (CVCs) have been essential devices for the treatment of children with hematological and oncological disorders. Only few studies investigated the complications and selections of different types of CVCs in these pediatric patients. This study aimed to compare risk factors for unplanned removal of two commonly used CVCs, i.e., peripherally inserted central catheters (PICCs) and tunneled CVCs, and propose better device selection for the patient.

Methods

This retrospective, single center cohort analysis was conducted on pediatric patients with hematological and oncological disorders inserted with either a PICC or a tunneled CVC.

Results

Between January 1, 2013, and December 31, 2015, 89 patients inserted with tunneled CVCs (total 21,395 catheter-days) and 84 with PICCs (total 9,177 catheter-days) were followed up until the catheter removal. The median duration of catheterization was 88 days in PICCs and 186 days in tunneled CVCs ($p = 1.24\times10^{-9}$). PICCs at the 3-month cumulative incidence of catheter occlusion (5.2% vs. 0%, $p = 4.08\times10^{-3}$) and total unplanned removal (29.0% vs 7.0%, $p = 0.0316$) were significantly higher, whereas no significant difference was observed in the cumulative incidence of central line-associated bloodstream infection (11.8% vs. 2.3%, $p = 0.664$). Multivariable analysis identified younger age (<2 years) (subdistribution hazard ratio [SHR], 2.29; 95% confidence interval [CI], 1.27–4.14) and PICCs (SHR, 2.73; 95% CI, 1.48–5.02) were independent risk factors for unplanned removal.

Conclusion

Our results suggest that tunnel CVCs would be a preferred device for children with hematological and oncological disorders requiring long-term, intensive treatment.

Introduction

Central venous catheters (CVC) are essential devices for a safe and reliable vascular access when treating 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 in not only unplanned removal and catheter reinsertion but also treatment delay, increased mortality, and healthcare costs [2]. Deep vein thrombosis (DVT) and central line-associated bloodstream infection (CLABSI) are two major CVC complications. The presence of immunosuppression related to disease or therapy, thrombocytopenia, and coagulopathy in patients with cancer makes it more important to prevent and manage these complications [3].

Peripherally inserted central catheters (PICCs) are non-tunneled CVCs inserted through a peripheral vein of the upper arm. Owing to its ease of insertion and removal, it is more commonly used as alternative devices of other types of CVCs for pediatric and adult patients [4]. PICC insertion is less invasive and more cost-effective than that of conventional type of 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 of PICCs as compared with other types of CVCs in both adults and [4] children [5].

Therefore, the British Committee for Standards in Haematology (BCSH) guideline in adults recommended that PICCs are suited as ambulatory or outpatient-based therapy contraindicated as an inpatient therapy for adult patients with hematological disorders. Although some studies reported the acceptability of long-term use of PICCs for hospitalized children with cancer, [6, 7] the prospective observational study on children with various diseases requiring CVC placement showed that PICCs had significantly higher incidences of venous thromboembolism (VTE), CLABSI, and catheter malfunction than those of tunneled CVCs. This study also showed that patients with leukemia harbor higher risk of CVC-related VTE [8]. 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 in comparison with tunneled CVCs to identify risk factors of unplanned CVC removal for appropriately selecting the CVC type in pediatric patients with hematological and malignant diseases.

Material And Methods

Patients

A total of 173 consecutive children with hematological or oncological disorders who received placement of their 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 more CVC insertions according to 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.

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

Catheter placement

The attending physicians selected the types of catheter based on their patients' clinical conditions. PICCs (Groshong® [Bard Peripheral Vascular, Inc., Tempe, 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., Tempe, USA] or Broviac® [Bard Peripheral Vascular, Inc., Tempe, USA] catheters) were inserted into one of the internal jugular veins by well-trained pediatric surgeons in the operating room. The catheter tip was positioned at the superior vena cava under the radiographic guidance in both types of catheters.

Unplanned catheter removal

The causes of unplanned catheter removal were categorized into self-removal, occlusion, mechanical events (catheter malposition or fracture), CLABSI, and infection without confirmed CLABSI. Confirmed CLABSI was defined as catheter infection with positive blood culture. Catheters inserted to patients with persistent fever of unknown origin who did not respond to antibiotic therapy were empirically removed and categorized as infection 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. Cumulative incidence of unplanned catheter removal was calculated using competing risk methods. Fine-Gray proportional hazards model was used to estimate the subdistribution hazard ratios on causes of catheter removal with PICCs versus tunneled CVCs. Incidences of complications or removal were calculated per 1,000 catheter days. All *p*-values reported are two-sided, and *p*-values of < 0.05 were considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University). [9] Proportionality was evaluated using Schoenfeld residuals, met for all analyses.

We compare cumulative incidence of unplanned removal of PICCs and tunneled CVCs, and removal at the end of therapy was regarded as censoring. The incidence for each event was calculated per 1,000 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 SCT than those with tunneled CVCs (9.5% vs. 32.6%, $p < 0.001$) because patients scheduled for SCT were initially inserted with tunneled CVC in our institute.

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 2). The median catheter life was 88 days with a total of 9,177 catheter days for PICCs and 186 days with a total of 21,395 catheter days for tunneled CVCs, respectively. The incidence of unplanned removal per 1,000 catheter days was 3.05 and 1.54 for PICCs and tunneled CVCs, respectively (Table 3). The cumulative incidence of unplanned catheter removal of PICCs was significantly higher than that of tunneled CVCs at (3-month cumulative incidence, 29.0%; 95% confidence interval [CI], 19.1–39.6% vs. 6.9%; 2.8–13.5%; $p = 0.0316$) (Fig. 1A).

Table 2
Cause 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, peripheral inserted central catheter

CVC, central venous catheter

CLABSI, central line-associated blood stream infection

NS, not significant

Table 3. Incidence of catheter removal per 1000 catheter days

Causes of unplanned catheter removal	PICCs (9,177 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, peripheral inserted central catheter
CVC, central venous catheter
CLABSI, central line-associated blood stream infection

Infection with or without confirmed CLABSI

Among the causes of unplanned removal, infection without confirmed CLABSI was the most common for both types of catheter, with the incidence per 1,000 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 1,000 catheter days) and CVC (0.42 per 1,000 catheter days). The cumulative incidence of infection was not significantly different between both types of catheters ($p = 0.664$) (**Supplementary Fig. 1A**).

Catheter occlusion

The incidence per 1,000 catheter days of catheter occlusion was 0.54 and 0 for PICCs and for 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 reasons

The incidence per 1,000 catheter days of mechanical events was 0.65 and 0.51 for PICCs and tunneled CVCs, respectively. The cumulative incidence of mechanical events was not significantly different between both types of catheters ($p = 0.716$) (**Supplementary Fig. 1C**). The incidence per 1,000 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, as it was one of the major causes of catheter removal for PICCs. 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 1,000 catheter days of other reasons was 0.11 and 0 for PICCs and tunneled CVCs, respectively. One of the other reasons was discomfort at the catheter insertion site, the only case with PICC.

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 4**). Age < 2 years (subdistribution 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; $p < 0.001$) are 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 patients with younger age (< 2 years) was significantly higher than those of other patients (3-month cumulative incidence [95%], 21.7% [10.6–35.3%] vs. 15.4% [9.7–22.4%]; $p = 0.0496$] (Fig. 1B).

Table 4. Univariate and multivariable analysis of risk factors for unplanned removal

Related risk factors		Univariate analysis			Multivariable analysis		
		SHR (95% CI)		*P*-value	SHR	(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	-	-	-

SHR, subdistribution hazard ratio
CI, confidence interval
CVC, central venous catheter
PICC, peripheral inserted central catheter
PID, primary immunodeficiency
SCT, stem cell transplantation
NS, not significant

Discussion

Here, we performed the first retrospective study that identifies risk factors for unplanned removal of CVCs in pediatric patients with hematological and malignant diseases. In multivariable analysis, PICCs and younger age (< 2 years) are found as 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 aged < 2 years. These results suggest that the tunneled CVC is a more appropriate device for the treatment of hematological and malignant diseases, especially in younger children.

A meta-analysis of adult patients [4] and a systemic review of pediatric patients [10] have reported a higher risk of VTE with PICCs as compared to tunneled CVCs. In particular, a prospective study was conducted on pediatric patients with leukemia and similarly showed that PICCs were at a higher risk of VTE [8]. A limitation of this study is that only a few cases with catheter occlusion did not receive radiological confirmation of VTE. However, in this cohort, catheter removal due to occlusion was significantly more common in PICCs than that in CVCs; our observations are consistent with those of previous studies, as CVC occlusion is mostly due to a thrombus [11].

In this study, no difference was observed in the frequency of CLABSI between PICCs and CVCs in patients with hematological and malignant diseases, a result inconsistent with that of previous pediatric studies with the higher incidence of catheter infection in PICCs, [8, 10] although these studies included a wide range of pediatric diseases and 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 reports suggesting a higher risk for PICCs [12] and other reports suggesting a higher risk for CVCs [13]. Meanwhile, a systematic review of adult patients with cancer concluded that the occurrence of infection did not differ between catheter types [14]. A larger prospective study should be conducted to determine which catheter type has a lower risk of CLABSI, especially in pediatric patients with hematological and malignant diseases. In conclusion, this study revealed that PICCs is associated with a higher risk of unplanned catheter removal than tunneled CVCs in children with hematological or malignant diseases. Among the causes of catheter removal, the risk of CLABSI according to PICCs was comparable to tunneled CVCs; however, the risk of catheter occlusion was significantly higher than that of tunneled CVCs. Moreover, young age (aged < 2 years) was another independent risk factor for unplanned catheter removal. These results suggest that tunneled CVCs would be a preferred device for children, especially with younger age, with hematological and oncological disorders requiring long-term and intensive treatment. Future studies are warranted to determine more reliable catheter selection methods.

Abbreviations

Abbreviation	Full term
CVCs	Central venous catheters
PICCs	Peripherally inserted central catheters
DVT	Deep vein thrombosis
CLABSI	Central line-associated bloodstream infection
VTE	Venous thromboembolism

Declarations

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Conflict of Interest Disclosures: The other authors have no example conflicts of interest to disclose.

Data Availability Statements:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Code Availability: Not applicable

Author Contributions:

Drs Miyagishima, Hamada, Hirayama, and Muramatsu conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.

Drs Tainaka, Shirota, Hinoki, Kamei, Nishikawa, Kawashima, Narita, Nishio, Kojima, and Takahashi conceptualized and designed the study, supervised data collection, assisted in conducting the analyses, and reviewed and revised the manuscript.

Drs Imaizumi and Nakatochi 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.

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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Figures

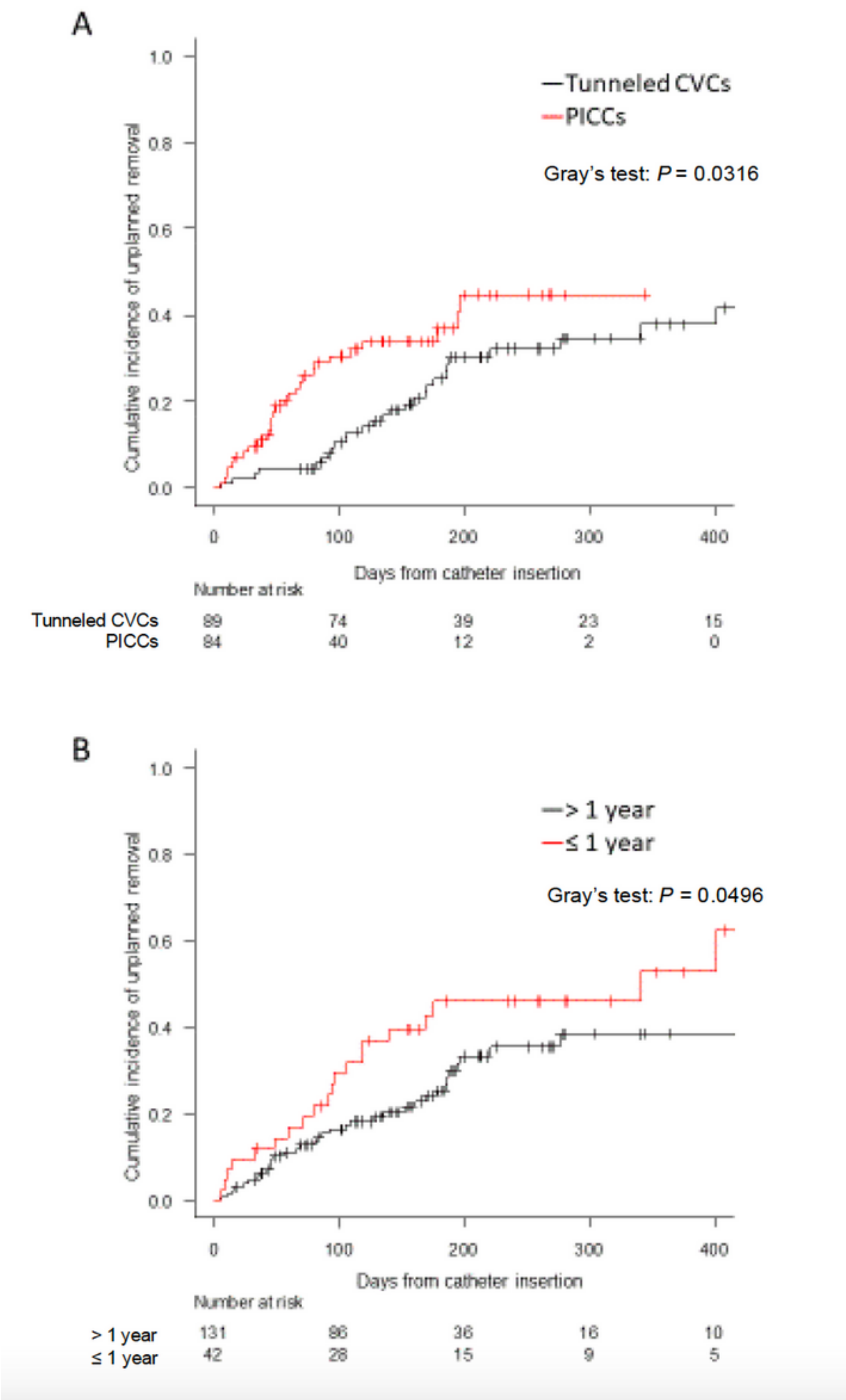

Figure 1

(A) Comparison of cumulative incidence of unplanned removal in PICCs vs. tunneled CVCs after the insertion. (B) Comparison of unplanned removal by age.

Supplementary Files

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