ARTICLE

Risk Factors for Peripherally Inserted Central Venous Catheter Complications in Children

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Importance: Peripherally inserted central venous catheters (PICCs) are prone to infectious, thrombotic, and mechanical complications. These complications are associated with morbidity, so data are needed to inform quality improvement efforts.

Objectives: To characterize the epidemiology of and to identify risk factors for complications necessitating removal of PICCs in children.

Design: Cohort study.

Setting: Johns Hopkins Children's Center, Baltimore, Maryland.

Participants: Hospitalized children who had a PICC inserted outside of the neonatal intensive care unit (ICU) from January 1, 2003, through December 31, 2009.

Main Outcome Measures: Complications necessitating PICC removal as recorded by the PICC Team.

Results: During the study period, 2574 PICCs were placed in 1807 children. Complications necessitating catheter removal occurred in 534 PICCs (20.8%) during 46 021 catheter-days (11.6 complications per 1000 catheter-days). These included accidental dislodgement (4.6%), infection (4.3%), occlusion (3.7%), local infiltration (3.0%), leakage (1.5%), breakage (1.4%), phlebitis (1.2%), and thrombosis (0.5%). From 2003 to 2009, complications decreased by 15% per year (incidence rate ratio [IRR], 0.85; 95% CI, 0.81-0.89). In adjusted analysis, all noncentral PICC tip locations—midline (IRR 4.59, 95% CI, 3.69-5.69), midclavicular (2.15; 1.54-2.98), and other (3.26; 1.72-6.15)—compared with central tip location were associated with an increased risk of complications. Pediatric ICU exposure and age younger than 1 year were independently associated with complications necessitating PICC removal.

Conclusions and Relevance: Noncentral PICC tip locations, younger age, and pediatric ICU exposure were independent risk factors for complications necessitating PICC removal. Despite reductions in PICC complications, further efforts are needed to prevent PICC-associated complications in children.

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CENTRAL VENOUS CATHeters provide secure vascular access to facilitate delivery of medications and nutrition to hospitalized children.[1] Peripherally inserted central venous catheters (PICCs) can be conveniently inserted at the bedside without the need for surgical intervention and are commonly used in pediatrics. Despite these advantages, PICCs are prone to infectious, thrombotic, and mechanical complications. These complications are associated with morbidity, so data are needed to inform quality improvement efforts.

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Previous studies[1-3] have identified risk factors for complications of PICCs in children including young age, severity of illness, catheter dwell time, catheter tip location, and catheter insertion site. Identifying modifiable risk factors of complications is especially important as clinicians work to prevent catheter complications. Previous studies[2-15] evaluating modifiable risk factors such as catheter dwell time, catheter insertion site, and catheter tip location have had inconsistent results. Our objective was to determine the association between patient and catheter characteristics and the risk of complications necessitating PICC removal in children.

METHODS

PATIENTS AND SETTING

A cohort was compiled of 1819 children who were admitted to the 175-bed Johns Hopkins Children's Center and had a PICC inserted from January 1, 2003, through December 31, 2009. Children admitted to the 30-bed pediatric intensive care unit (ICU) and the medical/

surgical wards were included, but patients in the neonatal ICU were excluded. The pediatric PICC team placed all PICCs and, as previously described,[2] maintained a database of all children with PICCs. The database contains indications for PICC insertion. Members of the PICC team, who were not masked to patient characteristics, prospectively documented complications necessitating PICC removal, including infectious complications and noninfectious complications (eTable; http://www.jamapeds.com), and reviewed hospital records and contacted home care companies or health care providers to determine PICC disposition and complications following discharge.

DATA COLLECTION

The PICC team prospectively collected age, sex, race, ethnicity, indication for catheter insertion, and other catheter characteristics. Medical records were queried to validate the PICC database. An administrative claims database was queried to extract information regarding ICU admissions, *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes, and length of hospital stay. We defined PICCs as peripherally inserted central venous catheters that were inserted with the intention of terminating at or close to the heart or in one of the great vessels. Exposures were determined prospectively by the PICC team. We considered PICCs as central at the time of placement if they resided in the superior vena cava (SVC), right atrial junction (RAJ), or high inferior vena cava (IVC) or above the level of the diaphragm for lower-extremity catheters and as noncentral if located elsewhere.[16] For PICCs placed in the arm, noncentral tip locations were further categorized as "midline" if the catheter tip extended no further than axilla; as "midclavicular" if the catheter tip extended to the middle of the clavicle on x-ray; and as "other tip location" if the tip extended beyond the middle of the clavicle on x-ray but not into the SVC or if the devices were scalp catheters with tips above the level of the clavicle or lower-extremity PICCs with tips below the IVC.

Catheters were removed after completion of therapy or owing to a complication. The primary outcome, complications necessitating PICC removal, was defined as outlined in the eTable and was divided into secondary outcomes of infectious and noninfectious complications necessitating PICC removal, in recognition that risk factors may vary for different complications. The time at risk for complication was the PICC dwell time, calculated as the number of days from PICC insertion to PICC removal.

After exploratory data analysis, variables were categorized for analysis. Age was not evenly distributed and was categorized into quartiles. The *ICD-9* codes were collected for each patient's hospitalization and categorized into underlying complex chronic medical conditions.[2,17] To account for severity of illness, patients were categorized as those requiring intensive care in the pediatric ICU (PICU) (referred to as having "PICU exposure") and those not requiring intensive care or having "no PICU exposure." The PICC insertion sites were categorized into upper extremity, lower extremity, and head and neck.

STATISTICAL ANALYSIS

Descriptive analyses were performed to characterize the patients and catheter characteristics. We report median values along with the 25th and 75th percentiles for age, PICC duration, and length of stay. Patients whose PICCs were removed in the hospital but who did not have a documented reason for PICC removal in the PICC database or the medical record (n=12, <1%) were not included in the analysis. Patients who transferred to another facility for which outcome data were not available were censored at time of hospital discharge.

Independent predictors of any complication necessitating PICC removal were assessed in bivariable and multivariable analyses using Poisson regression models to estimate incidence rate ratios (IRRs). Covariates determined a priori to be independent predictors of complications and those with $P<.10$ in bivariable analysis were included. Variables were retained in the final model if they were deemed clinically relevant or if they were observed to have a confounding effect on the association between another predictor and risk of complication. A confounding effect was defined as a change in a model coefficient by greater than 10% after removal of a single variable from the model. After exploring the initial data, cubic spline terms were introduced for modeling PICC dwell time to account for a nonlinear association of complications over time.[18,19] Similar multivariable models were used to identify risk factors for infectious complications and noninfectious complications as outcomes. An interaction between catheter dwell time and tip location was explored (1) by including interaction terms explicitly in the full model and (2) by evaluating a graph of the model-estimated complication rates across catheter dwell time for a given catheter tip location, age group, PICU and antibiotic exposure status, site of PICC insertion, and year. The interaction term was not included in the final model because it did not improve model fit on the basis of the Bayesian information criterion (results not shown).[20] Bootstrapping techniques with 1000 replications were used to assess the internal validity of the final model.[21,22] Model fit was confirmed by using the Pearson goodness-of-fit test.

This study was approved by the Johns Hopkins University School of Medicine Institutional Review Board with waiver of informed consent. Data were maintained in Access (Microsoft) and were analyzed using Stata, version 11.0 (StataCorp), and R, version 2.12 (R Foundation for Statistical Computing).[23]

RESULTS

During the study period, 2574 PICCs were placed in 1807 children. More than half of the children were male (55.6%). The median age was 5 years (**Table 1**). Median PICC dwell time was 13 days and median length of hospitalization was 12 days. The PICCs were inserted for administration of antibiotics, total parenteral nutrition, chemotherapy, or intravenous access. Most PICCs (1961, 76.4%) were inserted in the upper extremity. In this cohort, 2152 (83.9%) catheters had a central tip location, and 414 (16.1%) had a noncentral tip location. Children with noncentral PICCs were younger than those with central PICCs (median age, 2 years vs 7 years, $P<.001$).

Most PICCs (1901, 73.8%) were removed electively on completion of therapy, and 139 (5.4%) remained in place at time of patient transfer to an outside facility (**Table 2**). Five hundred thirty-four PICCs (20.8%) were removed owing to a complication during 46 021 catheter-days (incidence rate, 11.6 per 1000 catheter-days), including 422 PICCs removed secondary to noninfectious complications and 112 PICCs removed for infectious complications. Of those removed for infectious complications, 66 (58.9%) met the National Healthcare Safety Network's criteria as a central line–associated bloodstream infection.[24]

The incidence of complications decreased from 17.2 per 1000 catheter-days in the year 2003 to 5.5 per 1000 catheter-days in 2009 (**Table 3**). In parallel, the use of noncentral PICCs decreased from 13.9% in 2003 to 2.8%

Table 1. Characteristics of 1807 Hospitalized Children With Peripherally Inserted Central Venous Catheters[a]

Characteristic	Value
Age, median (IQR)	5 y (10 mo-13 y)
Sex	
Male	1005 (55.6)
Female	802 (44.4)
Race/ethnicity	
White	1017 (56.3)
African American	575 (31.8)
Asian	161 (8.9)
Hispanic	43 (2.4)
Other	11 (0.6)
PICC duration, median (IQR), d	13 (7-21)
Length of hospital stay, median (IQR), d	12 (6-27)
Indication for PICC insertion	
Antibiotics	1352 (52.5)
Total parenteral nutrition	200 (7.8)
Chemotherapy	252 (9.8)
Intravenous access	770 (29.9)
Complex chronic condition[b]	
Neuromuscular	270 (14.9)
Cardiovascular	767 (42.4)
Respiratory	263 (14.6)
Renal	107 (5.9)
Gastrointestinal	121 (6.7)
Hematologic and immunodeficiencies	57 (3.2)
Metabolic	71 (3.9)
Congenital and genetic	101 (5.6)
Malignant neoplasm	198 (11.0)
None	455 (25.2)
Site of PICC insertion	
Upper extremity (basilic, cephalic, brachial)	1961 (76.2)
Lower extremity (saphenous)	132 (5.1)
Head and neck (facial, postauricular, ext jugular)	464 (18.0)
Catheter tip location	
Central	2152 (83.6)
Midline	262 (10.2)
Midclavicular	121 (4.7)
Other	31 (1.2)

Abbreviations: IQR, interquartile range; PICC, peripherally inserted central venous catheter.
[a] Data are given as number (percentage) unless otherwise indicated. A total of 3.3% of the patients were transferred outside the hospital, and their lines were removed elsewhere.
[b] Not all conditions add up to a 100% because many chronic conditions overlap.

Table 2. Disposition of 2574 Peripherally Inserted Central Venous Catheters

Disposition	No. (%)
Removed	
No longer needed	1901 (73.9)
Infectious complications	112 (4.4)
Infection involving PICC	103 (4.0)
Suspected infection involving PICC	9 (0.3)
Noninfectious complications	422 (16.4)
Phlebitis	32 (1.2)
Local infiltration	77 (3.0)
Thrombosis	14 (0.5)
Leakage	38 (1.5)
Occlusion	94 (3.7)
Dislodgement	119 (4.6)
Breakage	36 (1.4)
Other	12 (0.5)
Transferred[a]	139 (5.4)

Abbreviation: PICC, peripherally inserted central venous catheter.
[a] Transferred to another health care facility with PICC, so no further information is available on these patients.

in 2009. Noncentral PICCs were more likely to have complications necessitating removal than central catheters (43.8% vs 16.2%; $P < .001$).

Bivariable analyses of potential risk factors for complications necessitating PICC removal are shown in **Table 4**. All noncentral PICC tip locations—midline (IRR, 5.57; 95% CI, 4.54-6.83), midclavicular (3.62; 2.65-4.95), and other (4.12; 2.20-7.72)—compared with central tip location were associated with an increased risk of complications. Compared with children younger than 1 year, children in older age categories had lower risks of developing complications, with the most significant reduction in risk in those older than 13 years (IRR, 0.35; 95% CI, 0.27-0.44). Pediatric ICU exposure was also associated with a significantly increased risk for complications leading to PICC removal (IRR, 1.71; 95% CI, 1.44-2.03).

After adjusting for other variables including catheter dwell time, age, insertion site, PICU exposure, indication for PICC insertion, and year of PICC insertion, noncentral tip locations were associated with an increased risk of complications compared with central locations (all noncentral tip locations: IRR, 3.58; 95% CI, 2.94-4.34; midline tip location: 4.59; 3.69-5.69; midclavicular tip location: 2.15; 1.54-2.98; and other tip locations: 3.26; 1.72-6.15) (Table 4). Compared with the age group younger than 1 year, all age groups remained important risk factors for complications. After adjusting for other variables, children who had PICU exposure during their hospitalization were at 24% increased risk for developing a complication that necessitated PICC removal (IRR, 1.24; 95% CI, 1.03-1.52). However, site of PICC insertion and clinical indication for PICC insertion were no longer associated with complications in adjusted analyses.

Recognizing that there may be different risk factors for infectious and noninfectious complications necessitating catheter removal, we performed a subanalysis to look at variables associated with each outcome (**Table 5**). After adjusting for catheter dwell time, age, insertion site, tip location, indication for PICC insertion, and year of PICC insertion, ICU exposure was a risk factor for infectious complications but not noninfectious complications. A noncentral tip location was strongly associated with noninfectious complications (IRR, 4.56; 95% CI, 3.67-5.61) but not with infectious complications (0.75; 0.34-1.50).

The **Figure** illustrates the complex and nonlinear interaction of catheter dwell time and risk of complication in PICCs with central and noncentral locations. Peripherally inserted central venous catheters with noncentral locations have a consistently higher risk of noninfectious complication regardless of catheter duration, but this association is not seen for infectious complications.

Table 3. Incidence Rate of Complications by Year

Year	Incidence Rate (per 1000 Catheter-Days)			PICCs Placed, No.	Noncentral PICCs Placed, No. (%)
	Complications	Infectious Complications	Noninfectious Complications		
2003	17.2	2.7	14.5	323	45 (13.9)
2004	17.9	4.1	13.8	380	42 (11.1)
2005	18.0	2.6	15.4	356	34 (9.6)
2006	10.4	1.6	8.8	326	35 (10.7)
2007	9.2	2.2	7.0	380	38 (10.0)
2008	7.3	2.1	5.2	441	29 (6.6)
2009	5.5	1.9	3.6	352	10 (2.8)

Abbreviation: PICC, peripherally inserted central venous catheter.

Table 4. Adjusted and Unadjusted Risk Factors for Peripherally Inserted Central Venous Catheter Complications

Variable	No. (%) (n = 2574)		IRR (95% CI)	*P* Value for IRR	Adjusted IRR (95% CI)[a]	*P* Value for Adjusted IRR
	No Complication (n = 2040)	Complication (n = 534)				
Age, y						
<1	585 (28.7)	255 (47.8)	1 [Reference]		1 [Reference]	
1-7	401 (19.7)	103 (19.3)	0.58 (0.47-0.71)	<.001	0.75 (0.60-0.94)	.01
>7-13	560 (27.5)	77 (14.4)	0.28 (0.21-0.37)	<.001	0.44 (0.33-0.60)	<.001
>13	494 (24.2)	99 (18.5)	0.35 (0.27-0.44)	<.001	0.45 (0.35-0.59)	<.001
Sex						
Male	1073 (52.6)	301 (56.4)	1 [Reference]	.07	1 [Reference]	.94
Female	967 (47.4)	233 (43.6)	0.85 (0.72-1.01)		0.99 (0.83-1.18)	
Site of PICC insertion[b]						
Upper extremity	1592 (78.0)	369 (69.1)	1 [Reference]		1 [Reference]	
Lower extremity	91 (4.5)	52 (9.7)	2.34 (1.75-3.13)	<.001	1.08 (0.79-1.48)	.64
Head and neck	353 (17.3)	111 (20.8)	1.34 (1.09-1.67)	.006	1.11 (0.89-1.39)	.37
Clinical indication for PICC insertion						
Intravenous access	547 (26.8)	223 (41.8)	1 [Reference]		1 [Reference]	
Antibiotics	158 (7.7)	42 (7.9)	0.62 (0.51-0.76)	<.001	0.86 (0.69-1.06)	.15
Total parenteral nutrition	183 (9.0)	69 (12.9)	0.89 (0.64-1.24)	.50	1.21 (0.86-1.69)	.27
Chemotherapy	1152 (56.5)	200 (37.5)	1.08 (0.82-1.42)	.58	0.95 (0.71-1.28)	.74
Catheter tip location						
Central	1803 (88.4)	349 (65.4)	1 [Reference]		1 [Reference]	
Noncentral						
Midline	136 (6.7)	126 (23.6)	5.57 (4.54-6.83)	<.001	4.59 (3.69-5.69)	<.001
Midclavicular	76 (3.7)	45 (8.5)	3.62 (2.65-4.95)	<.001	2.15 (1.54-2.98)	<.001
Other	21 (1.0)	10 (1.9)	4.12 (2.20-7.72)	<.001	3.26 (1.72-6.15)	<.001
PICU exposure						
No	1236 (60.6)	221 (41.4)	1 [Reference]	<.001	1 [Reference]	.03
Yes	804 (39.4)	313 (58.6)	1.71 (1.44-2.03)		1.24 (1.03-1.52)	
Line year	. . .	. . .	0.81 (0.78-0.85)	<.001	0.85 (0.81-0.89)	<.001

Abbreviations: IRR, incidence rate ratio; PICC, peripherally inserted central venous catheter; PICU, pediatric intensive care unit.
[a] Adjusted for catheter dwell time using cubic spline terms.
[b] Insertion sites for PICCs were classified as upper extremity, lower extremity, and head and neck on the basis of where the PICC was inserted.

COMMENT

We report results from a large cohort of hospitalized children with PICCs that will help clinicians provide anticipatory guidance to families when discussing PICC complications and that identify a target for future quality improvement efforts. Although PICCs with a noncentral catheter tip location represented a small percentage (16.1%) of inserted PICCs, these catheters were more than 3 times as likely to be removed secondary to a complication compared with PICCs with a central tip location. Younger children and those with PICU exposure during the current hospitalization were at increased risk of complications. At our institution, PICC complication rates in children decreased from 17.2 per 1000 catheter-days in 2003 to 5.5 per 1000 catheter-days in 2009, but further efforts are needed to prevent infectious and noninfectious complications of PICCs in children.

To our knowledge, our data represent the largest study of children with PICCs to report complications necessitating PICC removal. Our study reports complication rates similar to those of prior studies[2,3,12,15,25-28] that have re-

Table 5. Adjusted Risk Factors for Infectious Complications and Noninfectious Complications

Variable	Infectious Complications		Noninfectious Complications	
	Adjusted IRR (95% CI)[a]	*P* Value	Adjusted IRR (95% CI)[a]	*P* Value
Age, y				
<1	1 [Reference]		1 [Reference]	
1-7	0.89 (0.54-1.48)	.66	0.75 (0.59-0.97)	.03
>7-13	0.56 (0.30-1.56)	.07	0.43 (0.30-0.59)	<.001
>13	0.56 (0.32-0.98)	.04	0.47 (0.35-0.63)	<.001
Site of PICC insertion[b]				
Upper extremity	1 [Reference]		1 [Reference]	
Lower extremity	0.71 (0.32-1.56)	.41	1.21 (0.85-1.70)	.29
Head and neck	0.45 (0.24-0.83)	.01	1.26 (0.99-1.61)	.06
Tip location				
Central	1 [Reference]	.38	1 [Reference]	<.001
Noncentral[c]	0.75 (0.34-1.50)		4.56 (3.67-5.61)	
PICU exposure				
No	1 [Reference]		1 [Reference]	
Yes	2.23 (1.43-3.48)	<.001	1.11 (0.89-1.38)	.35
Line year	0.86 (0.78-0.95)	.003	0.86 (0.82-0.91)	<.001

Abbreviations: IRR, incidence rate ratio; PICC, peripherally inserted central venous catheter; PICU, pediatric intensive care unit.
[a] Adjusted for catheter dwell time using cubic spline terms, sex, and indication for catheter insertion.
[b] Insertion sites for PICCs were classified as upper extremity, lower extremity, and head and neck on the basis of where the PICC was placed.
[c] Catheter tip locations were categorized as noncentral if they did not reside in the superior vena cava, right atrium, or high inferior vena cava or above the level of the diaphragm for lower extremity catheters.

ported rates ranging from 17% to 50%. This large variation in complication rates may be in part explained by differences in types of complications reported (infectious, noninfectious, or both combined) and different populations studied (eg, oncology unit or ICU). In addition, ascertainment of complications can vary by study—for example, our study was unique in that our PICC team followed up children to determine PICC disposition after hospital discharge. This approach identified that 25% of complications necessitating removal occurred after hospital discharge.

The association of catheter-tip location and PICC complications remains unclear from conflicting studies in children. Some pediatric studies[13,15] have found that PICCs placed in noncentral veins provided safe and reliable intravenous access, whereas others[10,14] have suggested that PICCs terminating in noncentral venous locations have higher complication risks. These studies are difficult to compare in part because of inconsistent definitions of central veins. For example, many authors and clinicians consider a PICC to terminate in a central vein if the tip is located in the IVC, SVC, or RAJ.[9,14] Other authors, clinicians, and the Centers for Disease Control and Prevention include the subclavian veins as central veins.[15,24,29] To our knowledge, given the size of our cohort, these are the first pediatric data to compare PICCs with distal tip locations in the IVC, SVC, and RAJ with PICCs in the subclavian veins and other noncentral sites. After adjusting for other important predictors of PICC complications including age, catheter dwell time, PICC insertion site, PICU exposure, and indication for PICC insertion, our data confirmed previous findings that noncentral catheter tip location is associated with increased complication rates.[10,14] In addition, we found that PICCs terminating in any site outside the IVC, SVC, or RAJ, including subclavian veins, had an increased risk of complications necessitating removal. A previous study[15] that found no difference in complication rates between central and noncentral PICCs classified 46% of PICCs terminating in the subclavian vein as central, which may explain our differing results.

Increased complication rates, especially mechanical complications in noncentral PICCs, may result from a combination of factors including turbulence, vessel size, blood flow rate, and endothelial injury.[14] Our data suggest that noncentral catheters were an independent risk factor for noninfectious complications. When a central venous catheter is positioned in the SVC, the tip lies parallel to the vessel wall, so infused solutions dilute rapidly. Peripherally inserted central venous catheters cannot always be advanced to the SVC owing to venospasm, venous valves, and vessel tortuosity.[10] When the catheter tip lies in a noncentral location, the tip may contact the vessel, irritate and disrupt the endothelial cell layer, expose the basement membrane, and trigger coagulation.[30] We observed a parallel in the reduction in PICC complication rates and the decreasing use of noncentral PICCs from 2003 to 2009. Therefore, noncentrally located PICCs should be used with caution owing to their increased risk of complications necessitating catheter removal.

Catheter dwell time has also been suggested as a risk factor for PICC complications with some studies[2,18,19,31] finding longer dwell times associated with complications and others[3] finding shorter dwell times associated with complications. We illustrated the complex interaction of catheter dwell time and risk of complication in PICCs. For example, the risk of infectious complications seemed to increase over the first few weeks then plateau, where the risk of noninfectious complications seemed to decrease over the first few weeks then plateau. We also showed that PICCs with noncentral locations were prone to a consistently

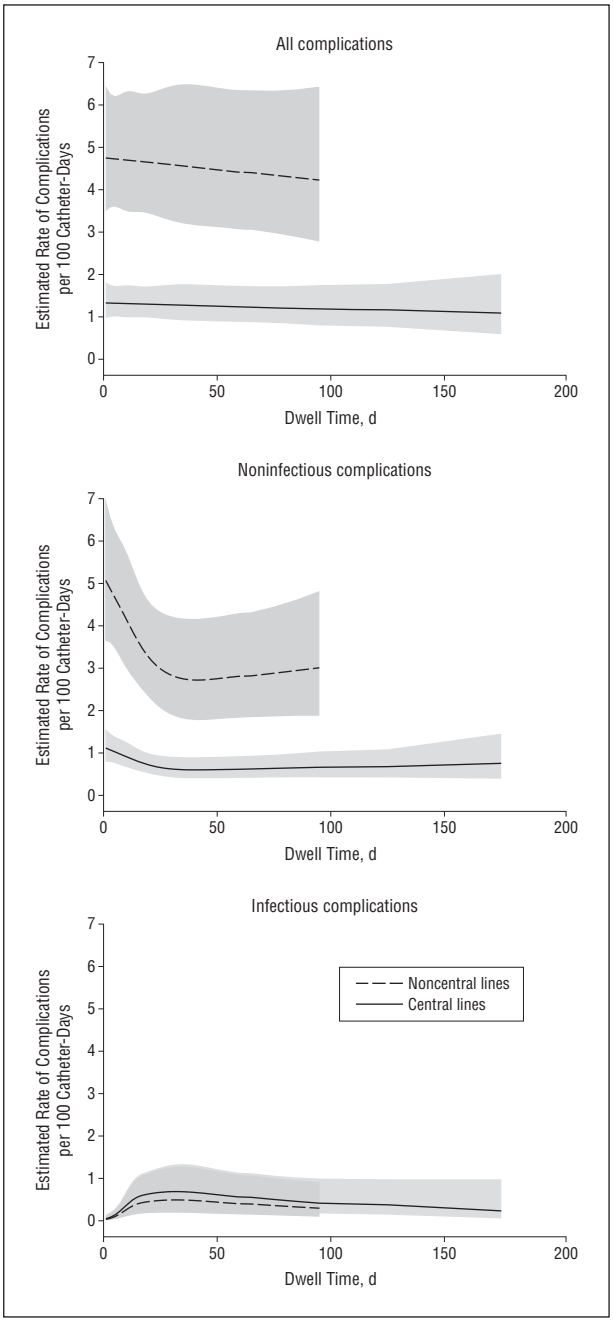

Figure. Predicted complication rates over catheter dwell time for a given catheter tip location, age group, pediatric intensive care unit and antibiotic exposure status, site, and year. Rates for all complications, noninfectious complications, and infectious complications are stratified for peripherally inserted central venous catheters with a central tip location (solid line) and a noncentral tip location (dashed line) with 95% confidence intervals (shading).

higher risk of noninfectious complication regardless of catheter duration but were not prone to higher risk of noninfectious complications. These results may explain differences in associations between catheter dwell time and risk of complications in previous studies. Given that noninfectious complications were 3 times more common than infectious complications, ensuring a central tip location at the RAJ, IVC, or SVC is an appropriate step to prevent PICC complications. However, given the complex association of catheter dwell time with complications, these data do not support the hypothesis that prolonged catheter dwell times are associated with increased PICC complications.

Our data found that younger children were at increased risk of complications requiring PICC removal. Children older than 13 years were at lowest risk for complications, whereas those younger than 1 year were at highest risk, consistent with previous findings[32] that older age may protect against central venous catheter–associated complications. Older children have structurally larger and more stable vessels that may tolerate catheters better. Therefore, age may confound the association between tip location and PICC complication, because advancing PICCs in younger children may be more challenging and this may lead to more unintended noncentral PICCs in this age group. However, after adjusting for age, we still found an increased risk of complication in those PICCs with a noncentral tip location.

Previous studies[2,5,7] have identified insertion site as a risk factor for catheter-associated infection; however, these findings have not been supported by other studies.[4,6,33] In unadjusted analysis of our cohort, PICCs placed in the head and neck and lower extremities were associated with an increased risk for complications necessitating removal; however, after adjusting for other important variables including age, catheter dwell time, ICU exposure, indication for PICC insertion, and tip location, insertion site was no longer a significant risk factor for complications. Younger children were more likely to have complications and were more likely to have PICCs placed in the head and neck and lower extremities (data not shown), which may confound this perceived association.

Several limitations should be considered when interpreting our findings. First, a small percentage of patients (5%) were lost to follow up, mostly due to transfer to other health care facilities. However, for most catheters, prospective follow up by our PICC team reduced missing data and captured entire PICC dwell time including time after discharge. Second, we could document only complications that necessitated line removal; hence, we likely underestimated the risk of complications such as occlusion requiring tissue plasminogen activator administration. In addition, some catheter infections may have been treated with antibiotics while the PICC remained in place, a complication that was not captured. Finally, despite this large cohort, because this is a single-institution study, our findings may not be generalizable to other institutions.

In conclusion, our large cohort and robust adjusted analyses identified noncentral catheter tip location as a modifiable risk factor for complications necessitating PICC removal. Clinicians should be cautious in weighing the risks and benefits of maintaining a noncentral PICC. Quality improvement initiatives should reinforce the importance of inserting PICCs to terminate in the RAJ, IVC, or SVC to reduce the risk of complications. National efforts have dramatically reduced the risk of bloodstream insertions complicating central venous catheters,[34] but further efforts are needed to prevent all complications that lead to additional procedures, patient morbidity, and increased health care costs.

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Author Contributions: Dr Milstone had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Jumani, Advani, Gosey, and Milstone. *Acquisition of data:* Jumani, Advani, Gosey, and Milstone. *Analysis and interpretation of data:* All authors. *Drafting of the manuscript*: Jumani, Advani, and Reich. *Critical revision of the manuscript for important intellectual content:* All authors. *Statistical analysis:* Jumani, Advani, Reich, and Milstone. *Obtained funding:* Milstone. *Administrative, technical, and material support:* Jumani, Advani, Gosey, and Milstone. *Study supervision:* Milstone.
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REFERENCES

1. Bourgeois FC, Lamagna P, Chiang VW. Peripherally inserted central catheters. *Pediatr Emerg Care*. 2011;27(6):556-563.
2. Advani S, Reich NG, Sengupta A, Gosey L, Milstone AM. Central line–associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. *Clin Infect Dis*. 2011;52(9):1108-1115.
3. Barrier A, Williams DJ, Connelly M, Creech CB. Frequency of peripherally inserted central catheter complications in children. *Pediatr Infect Dis J*. 2012;31(5):519-521.
4. Bonventre EV, Lally KP, Chwals WJ, Hardin WD Jr, Atkinson JB. Percutaneous insertion of subclavian venous catheters in infants and children. *Surg Gynecol Obstet*. 1989;169(3):203-205.
5. Goetz AM, Wagener MM, Miller JM, Muder RR. Risk of infection due to central venous catheters: effect of site of placement and catheter type. *Infect Control Hosp Epidemiol*. 1998;19(11):842-845.
6. Lally KP, Brennan LP, Sherman NJ, Grushkin C, Lieberman E, Atkinson JB. Use of a subclavian venous catheter for short- and long-term hemodialysis in children. *J Pediatr Surg*. 1987;22(7):603-605.
7. Merrer J, De Jonghe B, Golliot F, et al; French Catheter Study Group in Intensive Care. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA*. 2001;286(6):700-707.
8. Cadman A, Lawrance JA, Fitzsimmons L, Spencer-Shaw A, Swindell R. To clot or not to clot? that is the question in central venous catheters. *Clin Radiol*. 2004;59(4):349-355.
9. Chait PG, Ingram J, Phillips-Gordon C, Farrell H, Kuhn C. Peripherally inserted central catheters in children. *Radiology*. 1995;197(3):775-778.
10. Colacchio K, Deng Y, Northrup V, Bizzarro MJ. Complications associated with central and noncentral venous catheters in a neonatal intensive care unit. *J Perinatol*. 2012;32(12):941-946.
11. Frey AM. Pediatric peripherally inserted central catheter program report: a summary of 4536 catheter-days. *J Intraven Nurs*. 1995;18(6):280-291.
12. Graham DR, Keldermans MM, Klemm LW, Semenza NJ, Shafer ML. Infectious complications among patients receiving home intravenous therapy with peripheral, central, or peripherally placed central venous catheters. *Am J Med*. 1991;91(3B):95S-100S.
13. Harwood IR, Greene LM, Kozakowski-Koch JA, Rasor JS. New peripherally inserted midline catheter: a better alternative for intravenous antibiotic therapy in patients with cystic fibrosis. *Pediatr Pulmonol*. 1992;12(4):233-239.
14. Racadio JM, Doellman DA, Johnson ND, Bean JA, Jacobs BR. Pediatric peripherally inserted central catheters: complication rates related to catheter tip location. *Pediatrics*. 2001;107(2):E28. doi:10.1542/peds.107.2.e28.
15. Thiagarajan RR, Bratton SL, Gettmann T, Ramamoorthy C. Efficacy of peripherally inserted central venous catheters placed in noncentral veins. *Arch Pediatr Adolesc Med*. 1998;152(5):436-439.
16. Fricke BL, Racadio JM, Duckworth T, Donnelly LF, Tamer RM, Johnson ND. Placement of peripherally inserted central catheters without fluoroscopy in children: initial catheter tip position. *Radiology*. 2005;234(3):887-892.
17. Feudtner C, Christakis DA, Connell FA. Pediatric deaths attributable to complex chronic conditions: a population-based study of Washington State, 1980-1997. *Pediatrics*. 2000;106(1 pt 2):205-209.
18. Milstone AM, Sengupta A. Do prolonged peripherally inserted central venous catheter dwell times increase the risk of bloodstream infection? *Infect Control Hosp Epidemiol*. 2010;31(11):1184-1187.
19. Sengupta A, Lehmann C, Diener-West M, Perl TM, Milstone AM. Catheter duration and risk of CLA-BSI in neonates with PICCs. *Pediatrics*. 2010;125(4):648-653.
20. Schwarz G. Estimating the dimension of a model. *Ann Stat*. 1978;6(2):461-464.
21. Efron BTR. *An Introduction to the Bootstrap*. Boca Raton, FL: Chapman & Hall/CRC; 1993.
22. Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med*. 1996;15(4):361-387.
23. Ihaka R, Gentleman R. R: a language for data analysis and graphics. *J Comput Graph Stat*. 1996;5(3):299-314.
24. Centers for Disease Control and Prevention. Central Line–Associated Bloodstream Infection (CLABSI) Event. http://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf. Published 2012. Accessed August 22, 2012.
25. Matsuzaki A, Suminoe A, Koga Y, Hatano M, Hattori S, Hara T. Long-term use of peripherally inserted central venous catheters for cancer chemotherapy in children. *Support Care Cancer*. 2006;14(2):153-160.
26. Abedin S, Kapoor G. Peripherally inserted central venous catheters are a good option for prolonged venous access in children with cancer. *Pediatr Blood Cancer*. 2008;51(2):251-255.
27. Ng PK, Ault MJ, Ellrodt AG, Maldonado L. Peripherally inserted central catheters in general medicine. *Mayo Clin Proc*. 1997;72(3):225-233.
28. Levy I, Bendet M, Samra Z, Shalit I, Katz J. Infectious complications of peripherally inserted central venous catheters in children. *Pediatr Infect Dis J*. 2010;29(5):426-429.
29. O'Grady NP, Alexander M, Burns LA, et al; Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter–related infections. *Clin Infect Dis*. 2011;52(9):e162-e193.
30. Di Costanzo J, Sastre B, Choux R, et al. Experimental approach to prevention of catheter-related central venous thrombosis. *JPEN J Parenter Enteral Nutr*. 1984;8(3):293-297.
31. Chathas MK, Paton JB, Fisher DE. Percutaneous central venous catheterization: three years' experience in a neonatal intensive care unit. *Am J Dis Child*. 1990;144(11):1246-1250.
32. Ruebner R, Keren R, Coffin S, Chu J, Horn D, Zaoutis TE. Complications of central venous catheters used for the treatment of acute hematogenous osteomyelitis. *Pediatrics*. 2006;117(4):1210-1215.
33. Chwals WJ. Vascular access for home intravenous therapy in children. *JPEN J Parenter Enteral Nutr*. 2006;30(1)(suppl):S65-S69.
34. Miller MR, Griswold M, Harris JM II, et al. Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. *Pediatrics*. 2010;125(2):206-213.