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## Frequency of Peripherally Inserted Central Catheter Complications in Children

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### Abstract

This study examined the frequency and types of complications with PICCs placed in immunocompetent pediatric patients for parenteral antimicrobial therapy. It also sought to determine risk factors associated with those complications. Complications occurred at a frequency of 19.3/1000 PICC days, and greater than 30% of PICCs developed at least one complication. Risk factors for complication include double lumen PICCs, PICCs placed in the femoral vein, younger age, and greater number of daily doses.

### Keywords

PICC; antibiotics; pediatric; catheter-related infections; anti-bacterial agents; parenteral infusions; child

### Introduction

Prolonged antimicrobial therapy is often indicated for children with severe infections (e.g. endocarditis, osteomyelitis, and complicated pneumonia), and the decision to administer parenteral versus oral therapy is often complex. However, because of concerns regarding antimicrobial resistance among orally administered antibiotics for certain pathogens, the perception of superior efficacy for parenteral therapy, and the increased availability of outpatient-based administration, prolonged parenteral therapy is increasingly common. Peripherally inserted central venous catheters (PICCs) account for the majority of central catheters used in otherwise healthy children for this purpose. In some populations, PICC complication rates of 20–50% have been observed<sup>1,2</sup>; however, complication rates for PICCs used primarily for antimicrobial therapy in otherwise healthy children have not been fully established.

In this study, we sought to determine the frequency and types of PICC complications occurring among immunocompetent pediatric patients receiving parenteral antimicrobials in

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both the inpatient and outpatient settings. We also sought to determine risk factors associated with the occurrence of PICC complications.

## Materials and Methods

Medical records of all hospitalized individuals < 21 years of age with PICCs placed between January 1, 2008 and December 31, 2008 at our institution were reviewed. Billing codes for PICC placement were used to identify potential children. Patients whose primary indication for PICC placement was antimicrobial administration were considered for inclusion. Catheters placed in children in the neonatal intensive care unit, those with congenital or acquired immunodeficiency syndromes, and children with PICCs placed for indications other than antimicrobial administration (e.g., parenteral nutrition or frequent blood sampling) were excluded. Patients with cystic fibrosis were included in the study if no underlying primary/secondary immunodeficiencies were identified.

Vanderbilt University Medical Center employs a fully integrated electronic medical records system (StarPanel) that includes all inpatient and outpatient encounters; emergency department visits; clinical communications made by telephone, fax, or letter to patients, families, and providers; laboratory data, including microbiologic cultures; and procedural notes. All Vanderbilt University Medical Center providers use StarPanel exclusively for medical documentation. Data extracted included demographic information (gender, race, age, weight), indication for PICC placement, PICC characteristics (size, location, duration of therapy), and all medically attended PICC complications. We defined a medically attended PICC complication as any event that prompted an unscheduled assessment by a healthcare provider in the outpatient, emergency department, or inpatient settings and was determined to be related to the PICC. Catheter complications included central line-associated bloodstream infections (CLABSI), line displacement, line occlusion (defined as a PICC failing to draw and/or flush), line fracture or leakage, localized infection, and localized pain or swelling at the site of the PICC. All data were entered into the Vanderbilt Research Electronic Data capture (REDCap) system to preserve data integrity<sup>3</sup>.

Poisson regression was used to estimate incidence rate ratios (accounting for total PICC days) and identify characteristics associated with PICC complications. Factors with a  $p < 0.2$  in univariate analyses were considered for inclusion in the multivariable model. To reduce potential model overfitting, we removed covariates with a  $p < 0.2$  from the full model if, after removal, effect estimates were essentially unchanged. We also repeated the final model after restricting to those with severe complications, which was defined as any PICC-related complication requiring PICC removal, replacement, or change in antibiotic therapy. Finally, a multivariable Cox regression model (using the same covariates from the primary analysis) was constructed to estimate hazard ratios for time to first complication. Analyses were conducted using Stata 10.1 (StataCorp LP, College Station, TX). This study was approved by the Vanderbilt Institutional Review Board.

## Results

Of 1,280 PICCs placed, 610 (48%) met study criteria and were included. The most common reasons for exclusion included PICCs placed for chemotherapy, total parenteral nutrition, or for frequent blood draws. Among the included children, median age at PICC placement was 3.2 years; 73.8% were Caucasian, 14.9% were African-American, and 7.4% were Hispanic. The most common indications for PICC placement were cystic fibrosis-related pneumonia (18.9%), skin and soft tissue infection (14.6%), osteoarticular infections (13.6%), bacteremia/fungemia (11.4%), and CNS infection (8.7%). Overall, there were 207 PICC complications during 10,712 total PICC days (19.3 complications per 1000 PICC days). One

hundred seventy-one PICCs were associated with at least one complication; 22 PICCs were associated with 2 complications, and 7 experienced 3 complications. The median day of first complication was 7 days (IQR 3–15 days); subjects with PICC-associated infections experienced complications later than did those with mechanical/thrombotic complications (19 days vs. 6 days,  $p < 0.001$ ). Overall, 77/207 (38%) complications occurred following discharge from the hospital. The most common complication was occlusion ( $n = 71$ , 34.3%), with 52.1% of patients requiring TPA, 4.2% replacement, and 5.6% removal; no repair was necessary in 27 patients (38%). More importantly, 19 children with PICC-related complications experienced a catheter-associated infection that required modification of antibiotic therapy or PICC removal (9.1% of those experiencing a complication, 3% of the total). Overall, 64/207 children (31.0%) experienced a complication that required PICC replacement or removal. Thus, a total of 83 children experienced a severe complication, defined as infection, removal, or replacement of the catheter.

Univariate analyses to assess factors associated with a PICC complication are displayed in Table 1. In comparison to infants <1 year of age (30.7 complications/1000 PICC days) and children 1–4 years of age (27.3/1000 PICC days), older children were less likely to experience a complication (5–10 years, 11.6/1000 PICC days; >10 years, 8.5/1000 PICC days). Double lumen PICCs had higher rates of complication (30.8/1000) than single lumen PICCs (17.2/1000), as did those with smaller gauge. Patients with PICCs in place for <14 days and those receiving greater than 4 daily doses of antimicrobials also experienced higher complication rates (Table 1). In multivariate analysis, increased age, presence of a double lumen catheter, more than four daily antimicrobial doses, and PICC duration of more than 14 days remained statistically significant (see Table, Supplemental Digital Content 1). Results were similar when restricting the analysis to those with severe complications (see Table, Supplemental Digital Content 2), and when analyzing the time to first complication using Cox regression (see Table, Supplemental Digital Content 3).

## Discussion

In this study, greater than 30% of all PICCs placed for antimicrobial administration were associated with a medically attended complication. Complications included thrombosis, leakage, PICC fracture, and infection, which required manipulation of the line, PICC replacement, or line removal. Double lumen PICCs, younger children, PICCs in place for a shorter period, and those receiving a greater number of daily doses had the highest rates of complications in both univariate and multivariate models.

Our data are consistent with those from other investigators, with complication rates ranging from 29–41% depending on the type of catheter, the population, and the indication for use<sup>4–6</sup>. The rate of complication in this cohort, 16.1/1000 PICC days, is similar to that of Levy et al, who describe a rate of 11.9/1000 PICC days<sup>12</sup>. Our study adds to the previous literature by determining additional risk factors for complications, including the type of line (double lumen vs. single lumen) and the number of daily antibiotic doses. The latter finding may be a function of increased line access events, leading to an increased risk of secondary infection when line care is suboptimal. Others have demonstrated that PICCs in place for greater than 21 days in the general pediatric population<sup>7</sup> and greater than 35 days in neonates<sup>8,9</sup> were more likely to experience infection and greater duration of lines was associated with increased breakage or leakage<sup>1,10</sup>. Paradoxically, our study found that PICCs in place for shorter durations were more likely, overall, to experience a complication in our study; however, PICC-related infections occurred much later, consistent with previous data. Therefore, careful attention must be paid to the overall duration of PICC access, the number of antibiotics prescribed, and the location of the PICC, with early transition to oral antimicrobial therapy when clinically feasible.

We also found that younger patients were more likely to experience higher rates of PICC-related complications, a finding that remained highly significant in multivariate models adjusting for potential confounders. Higher complication rates in younger patients have also been documented in previous studies<sup>5,7,8</sup>, though one study has shown higher rates of complications in older populations<sup>12</sup>. This creates a clinical challenge since younger children often receive prolonged parenteral antibiotics for invasive bacterial infections due to erratic absorption of oral antimicrobials (neonates) or noncompliance (toddlers). However, given the complication rates observed in this study and others, the superiority of parenteral therapy should be systematically evaluated. This has occurred for some infections, such as urinary tract infections in young children, where Hoberman et al clearly demonstrated the non-inferiority of oral cefixime to parenteral ceftriaxone in children <2 years of age<sup>11</sup>.

While our study provides important data regarding pediatric PICCs, there are limitations that should be discussed. Our data represent only one institution during the course of one year; therefore, we cannot over-generalize these findings to the rest of the US. However, as a tertiary, academic medical center, many similarities exist between our institution and other children's hospitals, including case mix, demographics, and indications for PICC placement. As a result, these data are likely to be applicable for all PICC lines, and not merely those placed for outpatient parenteral antimicrobial therapy. Also, data were collected in a retrospective manner; therefore, it is possible that not all complications were captured. Our role as the primary children's hospital for the area makes this unlikely since pediatric PICC care is exclusively performed by our institution and our home health partners. Our study did not control for certain confounding risk factors such as severity of illness or indication for double lumen catheters. It is possible that sicker children received double lumen catheters and thus were at higher risk for complications; however, our multivariate model included adjustment for overall indication by disease. Studies with differing results for risk factors indicate that there may be more confounding factors contributing to these risks that need to be explored further<sup>12</sup>.

PICC utilization in children continues to increase, thus it is critically important to recognize both the overall risk of complications and the risk factors contributing to these adverse events. Our data, taken with the contributions of others to the field, reinforce that best practice guidelines are urgently needed for pediatrics PICCs. These guidelines should recognize the independent roles that age, PICC type (single vs. double lumen), and number of daily doses play in modifying risk of PICC complications. These guidelines should also incorporate elements known to be important in central venous catheter care, such as CVL bundles, limiting access, and line care technique.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

## Unadjusted Rates and Risk Factors for PICC Complication

Covariate	No. of Patients	No. of Complications	Complication rate (per 1000 PICC days)	Incidence rate ratio (95% CI)
<b>Race</b>				
White	450	153	19.1	Reference
Black	91	30	16.4	0.85 (0.58–1.27)
Hispanic	45	8	15.3	0.80 (0.39–1.62)
Other/Unknown	24	16	39.2	2.04 (1.22–3.41)
<b>Sex</b>				
Male	273	92	21.7	Reference
Female	337	115	17.7	0.82 (0.62–1.07)
<b>Age at PICC Placement</b>				
<1 year	223	99	30.7	Reference
1–4 years	114	53	27.3	0.89 (0.64–1.25)
5–10 years	103	27	11.6	0.38 (0.25–0.58)
>10 years	170	28	8.5	0.28 (0.18–0.43)
<b>Reason for PICC</b>				
Osteoarticular Infection	83	39	16.1	Reference
CNS device infection	27	15	28.7	1.78 (0.98–3.23)
Bacteremia/Fungemia	69	37	32.2	2.00 (1.27–3.14)
Meningitis	53	15	18.4	1.14 (0.63–2.07)
Endocarditis	14	13	31.1	1.93 (1.03–3.62)
Complicated Pneumonia	46	9	16.3	1.01 (0.49–2.09)
Skin/Soft Tissue Infection	89	20	15.9	0.99 (0.58–1.70)
Cystic Fibrosis	115	19	10.2	0.63 (0.37–1.10)
GI Disease	37	17	27.6	1.72 (0.97–3.03)
Urinary Tract Disease	33	7	23.7	1.47 (0.66–3.29)
Other	44	16	20.1	1.25 (0.70–2.24)
<b>Previous PICC</b>				
No	356	108	19.4	Reference
Yes	254	99	19.1	0.98 (0.75–1.29)
<b>Type of PICC</b>				
Single Lumen	527	157	17.2	Reference
Double Lumen	83	50	30.8	1.84 (1.34–2.53)
<b>Location of PICC</b>				
Non-femoral	603	199	18.6	Reference
Femoral	7	8	37.9	2.00 (0.99–4.06)
<b>Gauge of PICC</b>				
>18 gauge	316	74	11.7	Reference

Covariate	No. of Patients	No. of Complications	Complication rate (per 1000 PICC days)	Incidence rate ratio (95% CI)
≤18 gauge	294	133	30.0	2.55 (1.92–3.39)
<b>No. of Daily Doses</b>				
≤4	370	104	16.2	Reference
> 4	240	103	23.6	1.45 (1.10–1.90)
<b>PICC Duration</b>				
≤14 days	300	80	30.2	Reference
> 14 days	310	127	15.6	0.52 (0.39–0.68)

Complication rates calculated by dividing the total number of complications by the total PICC duration (days) for each row. Incidence rate ratios estimated using Poisson regression.