Catheter Dwell Time and CLABSIs in Neonates With PICCs: A Multicenter Cohort Study

WHAT’S KNOWN ON THIS SUBJECT: Peripherally inserted central catheters (PICCs) are essential to deliver life-saving treatment to neonates. Longer PICC dwell times may increase the risk of central line–associated bloodstream infections (CLABSIs) in neonates, but previous studies have yielded inconsistent results, likely due to different study designs, analytic methods, and small sample sizes.

WHAT THIS STUDY ADDS: The risk of CLABSIs increases during the 2 weeks after PICC insertion and remains elevated for the catheter duration. These data support daily review of PICC necessity, optimization of catheter maintenance practices, and consideration of novel strategies to prevent CLABSIs.

abstract

OBJECTIVE: To determine whether the daily risk of central line–associated bloodstream infections (CLABSIs) increases over the dwell time of peripherally inserted central catheters (PICCs) in high-risk neonates.

METHODS: Multicenter retrospective cohort including NICU patients with a PICC inserted between January 2005 and June 2010. We calculated incidence rates and used Poisson regression models to assess the risk of developing CLABSI as a function of PICC dwell time.

RESULTS: A total of 4797 PICCs placed in 3967 neonates were included; 149 CLABSIs occurred over 89,946 catheter-days (incidence rate 1.66 per 1000 catheter-days). In unadjusted analysis, PICCs with a dwell time of 8 to 13 days, 14 to 22 days, and ≥23 days each had an increased risk of infection compared with PICCs in place for ≤7 days (P < .05). In adjusted analysis, the average predicted daily risk of CLABSIs after PICC insertion increased during the first 2 weeks after PICC insertion and remained elevated for the dwell time of the catheter. There was an increased risk of CLABSIs in neonates with concurrent PICCs (adjusted incidence rate ratio 2.04, 1.12–3.71). The incidence of Gram-negative CLABSIs was greater in PICCs with dwell times >50 days (incidence rate ratio 5.26, 2.40–10.66).

CONCLUSIONS: The risk of CLABSIs increased during the 2 weeks after PICC insertion and then remained elevated until PICC removal. Clinicians should review PICC necessity daily, optimize catheter maintenance practices, and investigate novel CLABSI prevention strategies in PICCs with prolonged dwell times. Pediatrics 2013;132:e1609–e1615

AUTHORS: Aaron M. Milstone, MD, MHS,a Nicholas G. Reich, PhD,b Sonali Advani, MBBS, MPH,a Guoshu Yuan, MS,c Kristina Bryant, MD,a Susan E. Coffin, MD, MPH,a W. Charles Huskins, MD, MSc,a Robyn Livingston, MD,d Lisa Saiman, MD, MPH,a,b P. Brian Smith, MD, MPH,a,b and Xiaoyan Song, MBBS, PhDi

aDivision of Pediatric Infectious Diseases, Johns Hopkins University, Baltimore, Maryland; bDivision of Biostatistics and Epidemiology, University of Massachusetts, Amherst, Massachusetts; cDivision of Pediatric Infectious Diseases, University of Louisville, Louisville, Kentucky; dUniversity of Pennsylvania, Philadelphia, Pennsylvania; eDivision of Pediatric Infectious Diseases, Mayo Medical School, Rochester, Minnesota; fDivision of Pediatric Infectious Diseases, University of Missouri-Kansas City, Kansas City, Missouri; gDivision of Pediatric Infectious Diseases, Columbia University Medical Center, New York, New York; hDivision of Neonatology, Duke University, Durham, North Carolina; and iDivision of Pediatric Infectious Diseases, George Washington University, Washington, District of Columbia

KEY WORDS infection, catheter-related infections, NICU, central venous catheters, peripheral venous catheterization

ABBREVIATIONS

aIRR—adjusted incidence rate ratio
bCI—confidence interval
cCLABSI—central line–associated bloodstream infection
dIP—infection preventionist
eIRR—incidence rate ratio
fNHSN—National Healthcare Safety Network
gPICC—peripherally inserted central catheter

Dr Milstone conceptualized and designed the study, oversaw data collection at 1 site, participated in the analyses, and drafted the initial manuscript; Dr Reich designed and oversaw the analyses, and reviewed and revised the manuscript; Dr Advani coordinated data collection, participated in the analyses, and reviewed and revised the manuscript; Mr Yuan performed the primary data analyses and critically reviewed the manuscript; Drs Bryant, Coffin, Huskins, Livingston, Saiman, Smith, and Song supervised data collection at 1 site and critically reviewed the manuscript; and all authors approved the final manuscript as submitted. (Continued on last page)
Intravenous access is essential to provide fluids, medications, and nutrition to many hospitalized patients. Peripherally inserted central catheters (PICCs) are frequently used to provide life-saving intravenous access for neonates. PICCs can be placed at the bedside without general anesthesia and can remain in place for days to weeks. However, infectious and noninfectious complications occur, including central line–associated bloodstream infections (CLABSIs).1,2

In the NICU, CLABSIs are the most common health care–associated infection and are a significant cause of morbidity and mortality in high-risk neonates.3–5 National campaigns and collaborative efforts have reduced CLABSIs in NICUs, but infection rates have not fallen to zero.6–9 These successes have in large part relied on a widespread awareness that catheter maintenance practices are essential to prevent CLABSI, especially as catheters often remain in place for prolonged periods.

Many studies have suggested that the longer a catheter remains in place, the greater the risk of a catheter complication, including CLABSIs.1,2,10–14 The cumulative risk of CLABSI increases the longer a PICC remains in place, but it is unknown whether the daily risk of CLABSIs increases over the dwell time of the catheter.15 A recent study of neonates suggested that for PICCs that remained indwelling for >35 days, the risk of CLABSIs increased by 33% per additional day the catheter was in place.11 These findings are plausible, because intra-luminal catheter colonization and biofilm formation are associated with CLABSIs, and both are associated with increased catheter dwell time.16 If confirmed, these data could challenge the common practice of keeping PICCs in place until signs or symptoms of a complication necessitate their removal. Our objective was to perform a multicenter study to determine if the risk of CLABSIs in neonates with PICCs increases over catheter dwell time and identify a threshold beyond which time the daily risk of CLABSIs increases.

METHODS

Setting and Participants

We performed a multicenter retrospective cohort study of neonates who had a PICC inserted in the NICU. Institutions were recruited to participate if they had access to an electronic medical record or other electronic database that contained catheter insertion and removal dates and catheter type. Mayo Eugenio Litta Children’s Hospital (Rochester, MN), Children’s Hospital of Philadelphia (Philadelphia, PA), Duke University Medical Center (Durham, NC), Morgan Stanley Children’s Hospital of New York-Presbyterian at Columbia University Medical Center (New York City, NY), Children’s National Medical Center (Washington, DC), Kosair Children’s Hospital (Louisville, KY), Children’s Mercy Hospital and Clinics (Kansas City, MO), and Johns Hopkins Children’s Center (Baltimore, MD) provided data. A child was included if he or she had a PICC inserted between January 1, 2005, and June 30, 2010. Not all sites provided data for the entire study period. This study was approved by each site’s institutional review board with a waiver of informed consent.

Data Collection

Each institution collected data on patient demographics, catheter characteristics, and positive blood cultures by querying administrative and laboratory databases. Race, ethnicity, gender, date of birth, date of hospital admission, date of hospital discharge, date of NICU admission, date of NICU discharge, gestational age, and birth weight were extracted from hospital databases and medical records when available. Collected catheter characteristics included catheter insertion and removal dates, insertion location, and number of lumens when available. The primary exposure was PICC dwell time, defined as days from PICC insertion until either PICC removal or the date of CLABSI, whichever was earlier.

The outcome of interest was PICC-associated CLABSI. Each participating institution had trained infection preventionists (IPs) who performed prospective surveillance to monitor positive blood cultures in patients with indwelling catheters, by using laboratory databases and infection surveillance support systems. CLABSIs were identified prospectively by IPs at each site and defined using criteria from the Centers for Disease Control and Prevention’s National Healthcare Safety Network’s (NHSN) surveillance definitions.17 A list of all CLABSIs in the NICU of participating hospitals was obtained from the site’s IP. The NHSN CLABSI definition changed in 2008 to include “two or more blood cultures drawn on separate occasions” for common skin commensal bacteria (ie, coagulase-negative staphylococci)17; therefore, additional microbiology data were collected and reviewed by study investigators for CLABSIs occurring before 2008. Ten (21%) of 49 CLABSIs occurring before 2008 were not included because they did not meet the NHSN criteria of having ≥2 blood cultures drawn on separate occasions. A PICC-associated CLABSI was defined as a CLABSI in a patient with a PICC.1,11

Statistical Analysis

Descriptive analyses were performed to characterize the patient population with reporting of median values, quartiles, and percentages. Because some sites were not able to obtain gestational age, number of catheter lumens, and PICC insertion site, these
variables were not included in the analysis. The unit of analysis was a PICC. We excluded from the analysis PICCs that were placed and removed on the same day. For patients with multiple PICCs placed during their NICU hospitalization, all PICCs were included. For patients with >1 PICC in place at the same time (concurrent PICCs), both PICCs were included while accounting for correlated observations at the patient level by using a robust variance estimator. One site was not reliably able to capture PICC insertion and removal dates, so data from that site were not included. Data for concurrent non-PICC central catheters (ie, tunneled-catheters, umbilical catheters) were not available. For patients who had a CLABSI and simultaneous PICCs (3 patients), the CLABSI was randomly attributed to 1 of the 2 PICCs and a sensitivity analysis was performed and found no change in the results when these CLABSIs were attributed to the other PICC. If multiple CLABSIs were associated with the same PICC, only the first CLABSI was included and at-risk time was censored at the time of the first CLABSI. Subsequent CLABSIs in the same patient with a different PICC were included.

The risk of CLABSI over PICC dwell time was estimated by calculating incidence rates per 10-day intervals from PICC insertion and by using Poisson regression models to estimate unadjusted and adjusted incidence rate ratios (IRRs and aIRRs). Catheter dwell time was categorized into quartiles for the unadjusted models, but an adjusted model was developed while accounting for patient-level clustering with a robust variance estimator. Sensitivity analyses included omitting the site with highest rates, including calendar year of PICC placement, only including the first PICC for each child, using a hierarchical model to account for patient-level clustering, and using a robust variance estimator to account for hospital-level clustering. Data were maintained in Microsoft Excel 2007 (Bellevue, WA) and analyzed by using Stata 11.0 (Stata Corp, College Station, TX). Restricted cubic splines and the predicted model graphic were generated by using the postrcspline package for Stata.18

**RESULTS**

Of the 4899 identified PICCs, 4797 PICCs were eligible for analysis. Seventy-three PICCs were excluded because they were inserted and removed on the same day, 22 had missing insertion or removal dates, and 7 were duplicate entries. Of the 3967 neonates who had ≥1 PICCs, the median birth weight was 2000 g (quartiles 1030, 2991) and the median age at PICC insertion was 5 days (quartiles 2, 13) (Table 1). Most patients were boys (57.1%) and Caucasian (53.4%).

The total observation time was 89 946 catheter days. The median PICC dwell time was 14 days (quartiles 7, 23), and 25% of PICCs remained in place for ≥23 days. The distribution of PICC dwell time is shown in Fig 1. The distribution of PICC dwell time was similar at each site (Supplemental Fig 4).

There were 149 CLABSIs from 4797 PICCs (3.1%). Of the 143 neonates with a CLABSI, 54% were boys, 54% were Caucasian, and the median birth weight was 1032 g. The median time from PICC insertion to CLABSI was 18 days (range 1–166 days). The incidence of PICC-associated CLABSIs was 1.66 per 1000 catheter-days (95% confidence interval [CI] 1.40–1.94). The highest incidence of CLABSIs was observed in PICCs with dwell times >50 days (Table 2 and Supplemental Table 5). The most commonly identified organisms were coagulase-negative staphylococci (32.2%) and *Staphylococcus aureus* (20.1%), as shown in Table 3. Gram-positive organisms were most commonly recovered in the first 40 days after catheter insertion (Fig 2). There was an increase in the incidence of Gram-negative CLABSIs in PICCs with dwell times ≥50 days compared with PICCs with dwell times ≤50 days (IRR 5.26, 95% CI 2.40–10.66).

In unadjusted analyses, neonates with higher birth weight were at reduced risk for CLABSIs (Table 4). There was not...
a statistically significant difference in the risk of CLABSIs in neonates with or without concurrent PICCs (P = .06) or those with or without a CLABSI from a previous PICC (P = .05). PICCs with a dwell time of 8 to 13 days, 14 to 22 days, and ≥23 days each had an increased risk of infection compared with PICCs in place for ≤7 days (P < .05). In multivariable analyses, for every 100-g increase in birth weight there was a 3% reduction in the risk of CLABSIs (aIRR 0.97, 0.95–0.99). Neonates with a concurrent PICC were twice as likely to develop a CLABSI (aIRR 2.04, 1.12–3.71). There was not an increased risk of CLABSIs in neonates with a CLABSI from a previous PICC (aIRR 1.66, 95% CI 0.69–3.98).

Figure 3 illustrates the complex and nonlinear relationship between catheter dwell time and risk of CLABSIs in neonates with PICCs. We found evidence that the predicted risk of CLABSIs increases steadily until ~2 weeks after PICC insertion and then remains elevated until catheter removal. Beyond a 50-day dwell time, limited data and widening CIs make it difficult to predict the trajectory of the risk of CLABSIs, and there is no clear inflection point after which the daily risk of CLABSIs increases. To account for a change in catheter care practices over time, we performed a secondary analysis to include calendar year in our regression model and observed the same association between the predicted daily risk of infection and PICC dwell time.

Based on the observation from Fig 3 that the predicted risk of CLABSIs remains elevated beyond 14 days after PICC insertion, we sought to estimate the number of catheter days that would need to be eliminated to prevent 1 CLABSI. The observed incidence of CLABSIs in PICCs indwelling for >2 weeks was 2.43 per 1000 catheter-days among catheter days that occurred beyond 14 days from insertion (95% CI 1.96–2.98). To prevent 1 CLABSI, 412 catheter days (95% CI 335–510) that occur >14 days after PICC insertion would need to be eliminated.

### DISCUSSION

These data confirm that the daily risk of infection is higher in PICCs that have been in place for >2 weeks as compared with those that have been in place for <2 weeks. However, we found no evidence that the daily risk of infection changes after the 2-week time point. CLABSIs are the most common health care–associated infection in NICUs. Many studies have identified risk factors for CLABSIs in neonates, but this is the first multicenter study to examine the association between PICC dwell time and CLABSIs. Frequently, PICCs remain in place for prolonged periods in the NICU. The decision about whether to remove a functioning PICC must take into account the ongoing daily risk of infection and potential complications associated with PICC replacement.

This study is a major advance over previous single-center studies that have evaluated the relationship between catheter dwell time and CLABSIs. Previous studies have treated time as a categorical or continuous variable to assess risk of CLABSIs over catheter dwell time and have found differing results. Our data demonstrate a nonlinear association of catheter dwell time with CLABSIs and explain differences reported in the literature. Our large sample size enabled a more robust estimate of the risk of CLABSIs over the entire catheter dwell time.

Sengupta et al accounted for the nonlinear association of PICC dwell time and CLABSIs and suggested that for lines in place for >35 days, the daily risk of CLABSIs increased by 33%.
remain in place for 2 weeks. Therefore, clinicians should continue to re-
view the need for a PICC on a daily basis, consider removal, and optimize 
practices to maintain the catheter to prevent infection. In addition, future 
udies are needed to determine if additional interventions, such as anti-
biotic or antiseptic locks, should be con-
idered in neonates with prolonged 
PICC dwell times to further reduce the 
isk of infection.

In neonates and children, central line 
insertion and maintenance care prac-
tices may be especially im-
portant in children with prolonged 
catheter dwell times. A previous study 
in neonates demonstrated that most 
catheter-related bloodstream infections 
are caused by intraluminal catheter 
contamination. Catheter maintenance 
practices, including hand hygiene be-
fore contact with the catheter and 
ough scrubbing of the catheter 
ub, may help to prevent intraluminal 
catheter contamination and subse-
quently infection. Ensuring compliance 
with basic PICC insertion and main-
tenance practices should be the first step 
in a program to reduce and prevent 
CLABSIs. In addition to PICC main-
tenance practices, clinicians should 
actively discuss the ongoing need for 
a catheter, recognizing the significant 
daily risk of infection. Our data suggest 
that 1 CLABSI can be prevented by 
eliminating 412 catheter days in PICCs 
that remain in place for >14 days. That 
number may seem high, but if 200 neo-
nates on a unit have a PICC in place for 
>14 days each year, reducing PICC dura-
tion by 2 days per patient would prevent 1 
CLABSI. Such targets are important for 
quality improvement initiatives aimed 
at reducing CLABSIs in the NICU.

Our study confirms previous observa-
tions that the organisms causing 
CLABSIs and bacteremia causing 
change over catheter dwell time. Smith 
et al found that median time to de-
velop Gram-positive bacteremia was 8 
days after catheter insertion, whereas 
the median time to develop Gram-
negative bacteria was 13.5 days after 
catheter insertion. Sengupta et al found 
that coagulase-negative staphy-
lococci were the predominant organ-
ism (55.6%) within the first 2 weeks 
after PICC insertion, whereas Gram-
negative bacteria were the dominant 
pathogens (58.3%) after the first 2 
weeks. Our data showed a 3.5-fold in-
crease in the incidence of Gram-
negative CLABSIs in PICCs with a dwell 
time >50 days.

Several considerations should be made 
when interpreting our findings. This 
was a retrospective study that relied 
on available databases from multiple 
centers. Because of unique data re-
ources at each site, we were unable to 
capture and adjust for known con-
founders of CLABSIs, including receipt 
of parenteral nutrition, gestational age, 
and severity of illness. Follow-up data 
were limited to a neonate’s hospital or 
NICU stay, so an event that occurred 
after NICU discharge would not have 
been captured; however, we previously 
found that >90% of children had 
their PICCs removed before NICU dis-
charge. We captured and adjusted for 
their PICCs removed before NICU dis-
charge; however, we previously 
found that >90% of children had 
their PICCs removed before NICU dis-
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actively discuss the ongoing need for 
a catheter, recognizing the significant 
daily risk of infection. Our data suggest 
that 1 CLABSI can be prevented by 

TABLE 3 Pathogens Causing CLABSIs in 
Neonates With PICCs

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>48 (32.2)</td>
</tr>
<tr>
<td>Staphylococcus aureus*</td>
<td>30 (20.1)</td>
</tr>
<tr>
<td>Candida spp</td>
<td>15 (8.7)</td>
</tr>
<tr>
<td>Enterococcus spp</td>
<td>12 (6.1)</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>12 (6.1)</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>8 (4.5)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>8 (5.4)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>6 (4.0)</td>
</tr>
<tr>
<td>Other organisms</td>
<td>5 (3.3)</td>
</tr>
<tr>
<td>Serratia spp</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>3 (2.0)</td>
</tr>
</tbody>
</table>

* Five isolates were methicillin-resistant Staphylococcus aureus.

per day. This study reported 21 events, 
only 3 of which occurred in PICCs with 
dwell times >40 days. In the current 
study, 23 CLABSIs (15%) occurred in 
PICCs with dwell times >40 days. De-
spite the larger sample size, the wid-
ening 95% CIs in Fig 3 illustrate the 
uncertainty in the predicted daily risk 
of CLABSIs in PICCs with a prolonged 
dwell time. Given this uncertainty, 
making any definitive projections 
about the risk over prolonged dwell 
times remains challenging. These data 
explain and confirm previous studies 
that have found an increased risk of 
CLABSIs in PICCs with longer dwell time. 
Although these data did not identify 
a second phase during which the daily 
isk of infection again increases, poss-
ibly due to being underpowered, the 
findings do verify that the risk of 
CLABSIs remains elevated in PICCs that 
remain in place for >2 weeks. There-

FIGURE 2 Incidence of CLABSIs during 10-day time intervals after PICC insertion for Gram-positive bacteria, Gram-
negative bacteria, and Candida spp.
remains possible. Each site had and implemented different infection prevention practices during the course of the study. We accounted for these temporal and hospital characteristics in our statistical models, which may have affected the power to detect a change in daily CLABSI risk beyond 14 days of PICC dwell time. Because not all sites provided data for the entire study period, we were not able to assess change in risk of CLABSI over time, but the association between daily CLABSI risk and PICC dwell time remained after adjusting for temporal trends. As practices have changed over time and as national collaboratives have shown reductions in rates, our findings are informative but should be confirmed with contemporary data. Finally, previous research has identified variability in how different practitioners apply NHSN criteria for CLABSI. This variability has not been associated with catheter dwell time and should not affect the interpretation of these data.

CONCLUSIONS
PICCs are essential to the care of hospitalized neonates, and CLABSIs are a potentially devastating complication. Our data confirm that the risk of CLABSIs in PICCs increases over the first 2 weeks after insertion and then remains elevated. Health care workers should continue to review the need for a PICC on a daily basis, remove if possible, and optimize practices to maintain the catheter to prevent infection. Future studies are needed to determine if additional interventions are warranted in neonates with prolonged PICC dwell times to further reduce the risk of infection.

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Address correspondence to Aaron M. Milstone, MD, MHS, JHU Department of Pediatric Infectious Diseases, 200 North Wolfe St, Rubenstein 3141, Baltimore, MD 21287. E-mail: amilsto1@jhmi.edu

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