Effect of Catheter Dwell Time on Risk of Central Line–Associated Bloodstream Infection in Infants

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abstract

BACKGROUND AND OBJECTIVE: Central venous catheters in the NICU are associated with significant morbidity and mortality because of the risk of central line–associated bloodstream infections (CLABSIs). The purpose of this study was to determine the effect of catheter dwell time on risk of CLABSI.

METHODS: Retrospective cohort study of 13 327 infants with 15 567 catheters (93% peripherally inserted central catheters [PICCs], 7% tunneled catheters) and 256 088 catheter days cared for in 141 NICUs. CLABSI was defined using National Health Surveillance Network criteria. We defined dwell time as the number of days from line insertion until either line removal or day of CLABSI. We generated survival curves for each week of dwell time and estimated hazard ratios for CLABSI at each week by using a Cox proportional hazards frailty model. We controlled for postmenstrual age and year, included facility as a random effect, and generated separate models by line type.

RESULTS: Median postmenstrual age was 29 weeks (interquartile range 26–33). The overall incidence of CLABSI was 0.93 per 1000 catheter days. Increased dwell time was not associated with increased risk of CLABSI for PICCs. For tunneled catheters, infection incidence was significantly higher in weeks 7 and 9 compared with week 1.

CONCLUSIONS: Clinicians should not routinely replace uninfected PICCs for fear of infection but should consider removing tunneled catheters before week 7 if no longer needed. Additional studies are needed to determine what daily maintenance practices may be associated with decreased risk of infection, especially for tunneled catheters.

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WHAT'S KNOWN ON THIS SUBJECT: Central catheters are life-saving interventions for infants in the NICU but are associated with central line–associated bloodstream infections (CLABSIs). Previous studies have provided conflicting results on the impact of catheter dwell time on risk of CLABSI.

WHAT THIS STUDY ADDS: Dwell time was not associated with increased risk of CLABSI for peripherally inserted central catheters, but the risk of CLABSI for tunneled catheters increased at week 7. These data support removal of tunneled catheters as soon as no longer necessary.

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The use of central catheters is common in the NICU and is critical for survival. These catheters provide stable intravascular access for the administration of intravenous fluids, parenteral nutrition, and medications. Peripherally inserted central catheters (PICCs) are particularly useful for ensuring long-term vascular access and can be placed at the bedside by trained providers without a surgical procedure. Tunneled catheters, such as Broviacs, require a surgical procedure but can remain in place longer. Although life-saving, central catheters are associated with increased risk of neonatal central line–associated bloodstream infection (CLABSI).[1–3] Infants in the NICU, particularly those of low birth weight, are at significantly higher risk for CLABSI compared with adults and older children.[4] Because infants with CLABSIs are more likely to die than those without infections, development of strategies aimed at preventing these infections is crucial.

The optimal dwell time (the number of days between catheter insertion and removal) for central lines in infants is unknown. Longer dwell time provides a cumulatively higher number of opportunities for exposure to bacteria (accessing of the line), but it is unclear whether the daily risk of infection increases over time. Several studies have suggested a link between catheter dwell time and risk for CLABSI,[3,5–7] although others have reported no increased risk of CLABSI with increased dwell time.[8,9] Clinicians generally attempt to limit dwell time whenever possible; however, the risks of infection must be weighed against the risks of frequently replacing catheters, including PICCs. Knowledge of the optimal dwell time for central lines would be useful to clinical neonatologists and lead to safer care of infants. Using data from the National Central Line Associated Blood Stream Infection Prevention Project (NCLABSI), which represents the largest registry to date assembled for neonatal central lines, we sought to test the hypothesis that longer dwell times are associated with higher incidence of CLABSI.

METHODS

Data Source

This was a retrospective cohort study of infants with PICCs or tunneled catheters obtained from the NCLABSI from September 2011 to August 2013. Of note, tunneled catheters were referred to as "Broviacs" on the data collection form, because this is the trade name with which most clinicians are familiar. The NCLABSI enrolled infants from 141 NICUs in 13 states (Kentucky, Illinois, Oregon, California, Colorado, Florida, Hawaii, Massachusetts, Michigan, North Carolina, New Jersey, South Carolina, and Wisconsin). State leaders (recognized clinical leaders, neonatologists, and neonatal nurses, who led the development of statewide neonatal collaboratives within their states) recruited teams at the individual sites to report on central line placement, removal, and infections as part of a quality improvement initiative that sought to reduce CLABSIs by 75%. As part of the initiative, participating sites adopted a central catheter insertion and maintenance bundle, which included hygiene for insertion, daily assessment of line need, a recommendation to remove central lines when infants achieved 120 mL/kg per day of enteral feedings, and techniques for sterile dressing changes and catheter access. Antibiotic practices were not standardized between the sites. Central lines inserted and removed within the first 2 days were excluded from analysis. When required by the participating institutions, the local institutional review boards reviewed the project and provided permission to conduct this investigation.

Definitions

We defined CLABSI according to National Health Surveillance Network criteria.[10] Briefly, infants with CLABSI had a positive blood culture for a recognized pathogen that was not related to an infection at another site. Diagnosis of CLABSI due to commensal organisms (including diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci, viridans group streptococci, *Aerococcus* spp., and *Micrococcus* spp.) required systemic signs and symptoms of infection and isolation of the same organism from ≥2 blood cultures drawn on separate occasions. Positive blood cultures occurring within 2 days of line placement were considered to be related to insertion and were excluded. If a single catheter had multiple associated positive blood cultures (this occurred on 12 occasions), only the first positive blood culture was included in the analysis. If a CLABSI occurred in the presence of multiple catheters (this occurred on 3 occasions), the CLABSI was attributed to both catheters. We defined dwell time as the number of days from line insertion until either line removal or day of CLABSI. The day of line insertion was defined as line day 1; weeks of dwell time were categorized into 7-day periods starting on line day 3 (week 1 = line days 3–9, week 2 = line days 10–16, etc).

Statistical Analysis

Descriptive statistics were reported as medians with interquartile ranges (IQRs) or percentages where appropriate. We compared the incidence of CLABSI and dwell time according to line type by using Fisher's exact test and the Wilcoxon rank-sum test, respectively. We calculated Spearman's rank correlation coefficient to determine the effect of median dwell time per center on incidence of infection. We estimated hazard ratios for CLABSI

for weeks 2 to 10 relative to week 1 by using a Cox proportional hazards frailty model. We controlled for postmenstrual age (PMA) and year of catheter insertion (September 2011–August 2012 vs September 2012–August 2013), included facility as a random effect, and generated separate models by line type. We calculated the incidence of CLABSI at each facility as the number of CLABSIs per 1000 catheter days reported per facility. We analyzed data in Stata 13 (Stata Corp, College Station, TX). P values $< .05$ were considered to be statistically significant.

RESULTS

A total of 13 327 infants with 15 567 catheters and 256 088 catheter days were included in the study. The majority of catheters were PICCs (14 451/15 567; 93%). Median PMA was 29 weeks (IQR 26–33). Median dwell time was shorter for PICCs than for tunneled catheters (11 days vs 25 days, $P < .001$; Table 1). Dwell time was >10 weeks for 87 PICCs (2 of which were infected) and 124 tunneled catheters (8 of which were infected).

The incidence of CLABSI was 2.4 times as high for tunneled catheters (39/1116; 3.5%) as for PICCs (199/14 451; 1.4%; $P < .001$). The overall incidence of CLABSI was 0.93 per 1000 catheter days. Incidence of CLABSI varied widely across facilities (Fig 1); 66 (47%) of the 141 NICUs reported an incidence of 0. The median center incidence of CLABSI was 0.35 per 1000 catheter days. The highest incidence reported was 60.6 per 1000 catheter days in a facility that reported only 2 catheters, both of which became infected. On a center level, increased median dwell time was not associated with increased overall center infection rate ($P = .88$).

Compared with the risk of CLABSI in week 1, no other week was associated with increased risk of CLABSI for PICCs (Table 2). For tunneled catheters, infection incidence was significantly higher in weeks 7 and 9 compared with week 1. There was no significant effect of catheter insertion year on CLABSI for PICCs or tunneled catheters ($P = .35$ and $P = .08$, respectively). When compared with adjusted term infants (those born at ≥37 weeks PMA), premature infants born at 26 to 29 weeks PMA and <26 weeks PMA with PICCs had a significantly higher risk of CLABSI (Table 3). Premature infants with tunneled catheters were not at significantly higher risk of CLABSI.

DISCUSSION

To our knowledge, this study is the largest analysis to date of the effect of dwell time on risk of infection in neonatal central lines. Knowledge of a critical time point beyond which the risk of infection increases would be of crucial benefit for clinicians, who could then replace catheters before this critical time point. In our cohort of infants across multiple states, longer PICC dwell time was not associated with increased risk of infection. These findings are consistent with those of 2 previous single-center studies.[8,9] The incidence of infection was higher in these previous studies (8.8% and 4.1%) than in the current study (1.5%). Differences in infection incidence may have been caused by differences in the definition of catheter-associated infection. In the study by Smith et al,[9] multivariable logistic regression analysis revealed that increased dwell time was associated with decreased risk of infection. We postulate that the significant maturational changes in the immune system that occur in the early neonatal period, particularly in premature infants, may lead to decreased risk of infection as the infant ages with the central line in place. Increased enteral feeds and decreased acuity of illness over time may also lead to fewer times the line is accessed and therefore less frequent opportunities to introduce infection. Finally, maturation of the gastrointestinal system in older infants may lead to less translocation of bacteria and decreased risk for infection.

Several other previous studies have reported results in disagreement with our findings regarding PICCs. A large multicenter cohort study of 6215 very low birth weight infants cared for at Neonatal Research Network centers found that longer overall percutaneous central line dwell time was associated with increased risk of late-onset sepsis.[3] However, the specific timing of late-onset infections in relationship to catheter dwell time was not available. In this previous study, a late-onset infection occurring on day 14 of catheter placement in a patient whose catheter was in place for 35 days would appropriately appear to be associated with longer catheter dwell time, when in fact the infection should have been attributed to the second week of catheterization.

A single-center study of 2210 central lines in 1124 infants reported that CLABSI risk increased for up to 7 days of dwell time for PICCs but not afterward.[5] We chose not to examine the risk of infection within the first week of PICC placement because the results probably would not lead to change in clinical management. Clinicians choose to insert PICCs

TABLE 1 Catheter Dwell Time

Dwell Time, d	PICCs, Median (IQR)	Tunneled Catheters, Median (IQR)	*P*
Overall	11 (7–18)	24.5 (14–45)	<.001
September 2011–August 2012	11 (7–18)	25 (14–48)	
September 2012–August 2013	10 (7–18)	24 (13–42)	

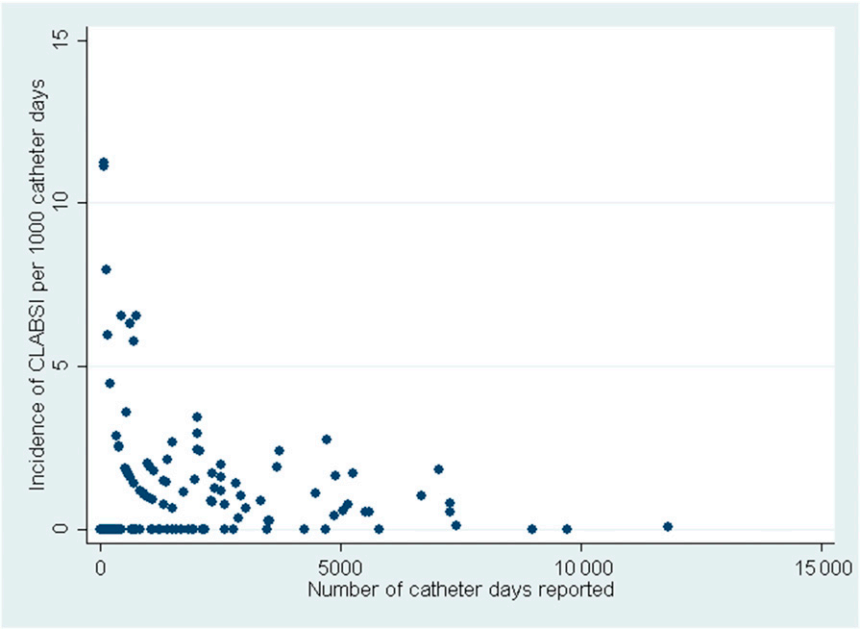

FIGURE 1
Incidence of CLABSI per 1000 catheter days by unit size (number of catheter days reported). Graph excludes 1 site with incidence of CLABSI of 60.6 per 1000 catheter days.

with the general expectation that they will be in place for at least 1 week. Knowing that infection is more likely to occur on day 5 of dwell time compared with day 3 would not lead clinicians to replace a PICC within the first week. The finding that the risk of CLABSI is not increased after 7 days is in agreement with the findings of our study. Another single-center study of 683 infants with 683 PICCs suggested that CLABSI risk was increased after day 35; however, the sample size was small, and the incidence of infection was higher than the current study (2.01 per 1000 catheter days).[7]

Milstone et al[6] analyzed 4797 PICCs placed in 3967 infants in a multicenter cohort study. The authors found that predicted risk of CLABSI increased for the first 2 weeks after PICC insertion and then remained elevated until catheter removal. The incidence of infection (3.11%, or 1.66 per 1000 catheter days) was higher than that of the current study. The previous study may also have contained a different population of infants; median birth weight of study infants was 2000 g. Although we do not have information about birth weight in our cohort, the median PMA was 29 weeks, which probably represents a more premature, smaller population. In addition, our cohort represents a population of infants in NICUs that had implemented specific catheter maintenance interventions to prevent CLABSI, which may account for the lower infection risk. Finally, the difference in results may reflect the different analytic approaches used in the 2 studies.

TABLE 2 Effect of Dwell Time on CLABSI

Week of Dwell Time	PICCs, *N*	CLABSI, *N* (%)	PICCs, HR[a] (95% CI)	Tunneled Catheters, *N*	CLABSI, *N* (%)	Tunneled Catheters, HR[a] (95% CI)
1	14 451	82 (0.6)	Reference	1116	5 (0.4)	Reference
2	8250	56 (0.7)	1.2 (0.9–1.7)	969	5 (0.5)	1.3 (0.4–4.4)
3	4061	31 (0.8)	1.3 (0.8–1.9)	748	3 (0.4)	1.0 (0.2–4.4)
4	2209	5 (0.2)	0.4 (0.1–0.9)	580	2 (0.3)	0.9 (0.2–4.7)
5	1290	7 (0.5)	0.9 (0.4–1.9)	452	3 (0.7)	1.8 (0.4–7.6)
6	765	7 (0.9)	1.5 (0.7–3.2)	355	4 (1.1)	3.2 (0.8–12.0)
7	453	4 (0.9)	1.4 (0.5–4.0)	280	4 (1.4)	4.0 (1.1–15.4)
8	278	3 (1.1)	1.6 (0.5–5.2)	228	1 (0.4)	1.3 (0.1–11.4)
9	183	2 (1.1)	1.5 (0.4–6.3)	178	3 (1.7)	4.7 (1.1–20.3)
10	125	0		151	1 (0.7)	2.0 (0.2–17.7)

CI, confidence interval; HR, hazard ratio.
[a] HRs are adjusted for PMA, year of catheter insertion, and site.

To our knowledge, the current study is the largest analysis of the relationship between dwell time and CLABSI in infants with tunneled catheters. Several previous studies have reported a similar risk of CLABSI in infants with surgical lines compared with infants with PICCs.[1,11,12] Brodie et al[13] previously reported an increased risk of CLABSI among neonates with Broviacs (n = 54) in a multicenter study of 1354 infants. However, this study did not address duration of catheter use. In our study of 1116 tunneled catheters in 1037 infants, we noted a significantly higher risk of CLABSI at weeks 7 and 9 relative to week 1. This finding is in agreement with a smaller study by Beck-Sague et al[14] of 376 infants (36 with tunneled catheters) that showed an association between prolonged tunneled catheter use and increased risk of sepsis.

Surgically placed catheters in the NICU are unique in their role, placement, and care. Infants with complex gastrointestinal surgical conditions often have tunneled catheters placed with the expectation of needing prolonged intravenous nutrition before adequate enteral feeding is achieved. Replacing surgical catheters is riskier than replacing PICC lines because of the potential need for

TABLE 3 Effect of PMA on CLABSI

PMA, wk	PICCs, *N*	PICCs, HR[a] (95% CI)	Tunneled Catheters, *N*	Tunneled Catheters, HR[a] (95% CI)
≥37	1835	Reference	314	Reference
34–36	1340	1.0 (0.3–3.8)	193	0.6 (0.1–2.8)
30–33	3315	1.3 (0.4–3.6)	130	0.3 (0.04–3.0)
26–29	5251	3.9 (1.6–9.7)	203	1.5 (0.5–5.0)
<26	2707	6.1 (2.5–15.2)	274	1.3 (0.4–3.8)

Sample sizes indicate number of patients with each type of catheter at each PMA. CI, confidence interval; HR, hazard ratio.
[a] HRs are adjusted for line week, year of catheter insertion, and site.

general anesthesia and likelihood of severely limited options for access. For this reason, clinicians may decide to leave tunneled catheters in place longer than PICCs, even if the catheter is no longer necessary, out of concern that the infant may need future access to meet nutritional needs. Tunneled catheters, even when heparin-locked, need regular flushing to maintain patency and may be used as a source for blood sampling. These practices may elevate the risk for infection in tunneled catheters with prolonged dwell times. Our report demonstrates a risk for tunneled catheter infection that is 2.4 times that of PICC lines and that increases after the sixth week of dwell time. Our data suggest that although there may be compelling reasons to leave a tunneled catheter in place, daily consideration should be given to the necessity of a tunneled catheter weighed against the increased risk for infection that develops in the sixth week of dwell time.

The finding that dwell time affected infection rates for tunneled catheters but not PICC lines may be influenced by several factors. First, our quality initiative was based on central line maintenance bundle recommendations that did not address some of the unique elements of tunneled catheters. Addressing the distinctive practice issues and concerns involving tunneled catheters is probably critical to reducing the risk of infection from these catheters. Although the recommendations encouraged PICC removal when infants achieved 120 mL/kg per day of enteral feedings, and a reduction in PICC dwell time was noted over the course of the initiative, we did not see a similar reduction in dwell time for tunneled catheters. Furthermore, we did not specifically address practices related to using tunneled catheters for blood sampling, nor did we make recommendations regarding optimal flushing and entry into these catheters.

We found significant variation in the incidence of CLABSI between facilities. This finding is in agreement with previous studies that have shown differences in infection risk across NICUs.[1,15,16] Despite the size of the data set, given the small number of infections at each center, we are not able to examine the association between dwell time and CLABSI risk within single centers. At the collaborative level, however, there is no relationship between the risk for infection and dwell time. This would imply that some centers have incorporated maintenance line care practices that protect against infection even with longer dwell times. It is for this reason that we used a frailty model that included facility as a random effect. These findings should encourage the vigorous pursuit of identification and adherence to all best central line maintenance practices. We postulate that variation in staff training and central catheter maintenance practices, environment of care, antibiotic practices, and hand hygiene procedures may be important contributors to the susceptibility of central lines to infection. Although all facilities in this analysis were participants in the quality improvement initiative, some factors were immutable (architecture of the unit and environment of care) or not measured (antibiotic practices). Additional studies are needed to examine what maintenance bundle elements and other factors have the greatest impact on infection prevention.

The strengths of our study include the large sample size of infants and catheters, inclusion of both PICCs and tunneled catheters, and multicenter design. In addition, our choice of the Cox proportional hazards model for analysis allowed us to attempt to identify a critical time point at which infection rate would increase without preselecting a hypothesized turning point a priori. We were also able to compare infection risk week by week and provide more evidence for increased risk of infection in smaller infants with PICCs, which is in agreement with the findings of previous studies.[5,6,9]

Our study is limited by its retrospective nature and self-reporting by centers. We attempted to minimize the data burden placed on centers and did not request information on some known risk factors for CLABSI, such as severity of illness, presence of necrotizing enterocolitis or short bowel syndrome, and birth weight. We also have no information about catheter positioning, the use of ultrasound guidance for placing catheters, or distribution of organisms causing CLABSI.

CONCLUSIONS

Central venous catheters provide a means to administer crucial medications and nutrition to sick infants in the NICU, but they are associated with an increased risk of

infection. Replacing catheters unnecessarily is dangerous. Our data indicate that clinicians should not routinely replace uninfected PICCs for fear of infection. However, serious consideration should be given to removing tunneled catheters that are no longer necessary before week 7, given our finding of increased infection risk at that point. Our finding of a lack of association for PICC line infections with dwell time suggests that clinicians should focus their efforts to reduce CLABSI on both proper line maintenance and timely central line removal when the line is no longer needed. Additional studies should focus on identifying and describing individual central line maintenance practices that may decrease the risk of infection.

ABBREVIATIONS

CLABSI: central line–associated bloodstream infection
IQR: interquartile range
NCLABSI: National Central Line Associated Blood Stream Infection Prevention Project
PICC: peripherally inserted central catheter
PMA: postmenstrual age

Dr Greenberg assisted in study design, performed the data analysis, and drafted the initial manuscript; Mr Cochran developed and coordinated data collection systems, as National Central Line Associated Blood Stream Infection Prevention Project (NCLABSI) program manager he fielded daily questions from teams and identified opportunities to improve the NCLABSI action plan and data collection system, and he assisted in drafting the initial manuscript; Dr Smith supervised the data analysis and critically reviewed the manuscript; Ms Edson, senior director of clinical quality at Health Research & Educational Trust (HRET), was vital in conceptualizing this project, provided support from HRET for data collection and analysis, regularly reviewed results and identified opportunities for improvements in practice presented on monthly webinar calls, assisted in drafting the manuscript, and critically reviewed the manuscript; Drs Schulman, Lee, Govindaswami, Pantoja, Hardy, Curran, Lin, Kuo, Noguchi, Ittmann, Duncan, Gupta, Picarillo, Karna, Cohen, Giuliano, Carroll, Guzman-Cottrill, Walker, Garland, and Ellsbury, Ms Page, and Ms Ancona were responsible for developing and executing the NCLABSI project within their state, recruited centers to the project, allocated funding received by the state group from HRET to support the project, provided daily support to centers with questions about the project, held regular state calls, webinars, and face-to-face learning sessions to support the implementation of the NCLABSI bundles, and critically reviewed the manuscript; Dr Laughon provided statistical and data support during the design and the execution of the project and critically reviewed the manuscript; Dr McCaffrey conceptualized and designed the study and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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SHORT AND LONG: *Recently, I was in a small group learning session with 16 medical students. Most of the women and men wore their hair casually and in no particular style that I could recognize. However, two of the men had distinctive hairstyles. The hair just above their ears was cut quite close while the hair on top of their heads was long. One of the two men had combed the hair over and styled it with gel, while another had used some gel to give the hair on top a bit of height. I had to smile. When I was a young child getting a haircut, my father would tell the barber "short on the sides, longer on top." When in the United States Army, we used to tell the barber "two and two" which meant cut the hair very close for the two inches above the ear and then leave the hair on top two inches long.*

As reported in The New York Times *(Men's Style: September 6, 2015), the haircut is now called the disconnected undercut and is widely popular among both the famous and not-so-famous. While athletes such as David Beckham, and musicians such as Justin Bieber, have helped popularize the style, the most famous person with a disconnected undercut may be the actress Ruby Rose who stars in "Orange Is the New Black." The name of the haircut comes from the fact that the transition from short to long hair is sudden or disconnected without a transition. While in the military, there was not much discretion about what one could do with the two inches of long hair left on top of the head; nowadays, stylists can do more intricate cuts and even cut in such a way that a man can have a discrete topknot. As for me, my days of "two and two" are long gone. Even if I wanted such a cut, there just is not enough hair to make it happen.*

Noted by WVR, MD