

Risk of Infection Using Peripherally Inserted Central and Umbilical Catheters in Preterm Neonates

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abstract

OBJECTIVE: To compare the rates of catheter-associated bloodstream infection (CABSI) in preterm infants born at <30 weeks' gestation who received a peripherally inserted central catheter (PICC) versus an umbilical venous catheter (UVC) immediately after birth as their primary venous access.

METHODS: This retrospective matched cohort study examined data from infants born at <30 weeks' gestation and admitted between January 2010 and December 2013 to neonatal units in the Canadian Neonatal Network. Eligible infants who received a PICC on the first day after birth (day 1) were matched with 2 additional groups of infants, those who received a UVC on day 1 and those who received a UVC on day 1 that was then changed for a PICC after 4 days or more. The primary outcome was number of infants with CABSI per 1000 catheter days, which was compared between the 3 groups using multivariable analyses.

RESULTS: Data from 540 eligible infants were reviewed (180 per group). There was no significant difference in infants with CABSI/1000 catheter days between the 3 groups (9.3 vs 7.8 vs 8.2/1000 catheter days, respectively; $P > .05$) despite lower rates of late onset sepsis in the group of infants who received only a UVC.

CONCLUSIONS: There was no significant difference in the incidence of CABSI between very preterm neonates who received a PICC, UVC, or UVC followed by PICC as the primary mode of venous access after birth. A prospective randomized controlled trial is justified to further guide practice regarding primary venous access and reduction of infection.

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Dr Shalabi developed the study protocol, data collection sheet, and initial manuscript; Dr Adel reviewed and edited the study protocol and manuscript; Mr Yoon reviewed the collected data and did the statistical analysis; Drs Aziz and Lee contributed to study design, reviewed results, and edited the manuscript; Dr Shah conceived the idea, reviewed and edited the study protocol, supervised study analyses, and reviewed and edited the manuscript; and all authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: A umbilical venous catheter (UVC) is a commonly used venous access for newborn infants. Infection rate increases with prolonged use of UVC. Peripherally inserted central catheters (PICCs) are increasingly used after an initial short period of UVC with the assumption that they decrease the risk of infection.

WHAT THIS STUDY ADDS: The incidence of catheter-associated bloodstream infection in very preterm neonates appears unrelated to whether they receive a PICC, UVC, or UVC followed by PICC as the primary mode of venous access after birth.

Venous access is essential in the management of preterm infants especially for providing parenteral nutrition and medications¹⁻⁴ and thus, secure venous access is crucial in their management.⁵ Very preterm neonates who receive nutrition via a central catheter have been reported to have significantly higher weight gain, shorter hospital stay, and lower rates of infection compared with infants with multiple peripheral points of venous access.^{6,7}

Umbilical venous catheters (UVCs) are frequently the first choice for vascular access in very low birth weight infants because they provide easy and fast access.⁸ However, use of UVCs is associated with an increased rate of late onset sepsis (LOS) after a median period of 5 days,^{9,10} and an alternative access point is usually needed after UVC removal. In addition, UVCs are associated with short and longer term complications including misplacement, extravasation, and thrombosis.¹¹ The most commonly used alternative mode of venous access is peripherally inserted central catheters (PICCs).¹²⁻²⁰ These catheters provide prolonged central venous access, are considered cost effective,^{21,22} and have a longer indwelling time before the risk of LOS increases.²³ The risk of LOS associated with PICCs has been reported to increase after an indwelling time of 35 days,²⁴ compared with 7 days with UVCs.²⁵ The majority of neonatal units use UVCs for primary access followed by placement of PICCs after 5 to 7 days in infants who need ongoing central access.^{26,27} However, on the basis of LOS data and complications associated with UVC, some neonatal units have opted to use PICCs for primary access and do not use UVCs if possible. It is unclear which strategy is better in the management of very preterm infants.

Our study objective was to compare the risk of catheter-associated bloodstream infection (CABSI) in

infants who had a UVC as the primary venous access immediately after birth compared with infants who had a PICC as their primary venous access.

METHODS

Study Population

In this retrospective matched cohort study, we used data from the Canadian Neonatal Network (CNN) database. In 2010, the CNN database included data from 29 of the 30 tertiary-level NICUs in Canada, comprising 95% of tertiary-level NICU admissions in Canada. Data were abstracted from infant medical records according to standardized definitions²⁸ and electronically transmitted to the CNN coordinating center as previously described.²⁹ Gestational age was defined by strict criteria, prioritizing menstrual dating confirmed by early ultrasound.

Eligibility Criteria

The study included data from preterm infants born at less than 30 weeks' gestational age and admitted to CNN NICUs between January 1, 2010, and December 31, 2013, who received either a UVC or PICC on the first day after birth (day 1) as their venous access. Infants who had a major congenital anomaly, were moribund on admission (palliative care planned at birth), had early onset sepsis, or did not receive a central catheter on day 1 were excluded.

Exposure

The analysis examined 3 groups of infants. The PICC group included infants who received a PICC on day 1 and never received a UVC. The UVC group included infants who received a UVC on day 1 and did not receive any other central venous access. The UVC + PICC group included infants who received a UVC on day 1 that remained in place for a minimum of 4 days followed by placement of a PICC. Because we expected a small number of infants in the PICC group, we first identified eligible infants

for that group. Once the infants in the PICC group were identified, the UVC and UVC + PICC groups were formed by randomly selecting infants from the pool of eligible infants by matching 1:1 for gestational age in weeks, gender, and birth weight \pm 100 g.

Outcomes and Variables

Our primary outcome was CABSI, which was defined as presence of bacteria or fungus in 1 or more blood cultures obtained from a symptomatic infant after 2 days of placement of a central catheter or within a 48-hour period after catheter removal. To remain pragmatic, we did not mandate the need for 2 blood cultures or a blood culture to be drawn from the catheter for diagnosis of CABSI. We did not include cultures from the catheter tip in the definition of CABSI. Patients with multiple episodes of infections were counted once. A patient was identified as having a second episode of infection only after 7 days of treatment with the appropriate antibiotic for the previous episode. A patient who had a UVC removed and a PICC inserted on the same day and then developed an infection within 2 days was counted as CABSI associated with UVC and not PICC. Incidence was calculated per 1000 catheter days and as raw incidence. Secondary outcomes included rate of any LOS (defined as presence of bacteria or fungus in 1 or more blood cultures from a symptomatic infant).

The following variables were collected: gender, birth weight, gestational age and small for gestational age, Apgar score, and the need for mechanical ventilation on day 1 after birth, Score for Neonatal Acute Physiology, version II (SNAP-II) score,³⁰ duration of mechanical ventilation, duration of continuous positive airway pressure, and duration of UVC and PICC.

Statistical Analysis

The characteristics of the study population were summarized by

using descriptive statistical methods. Infant characteristics were compared between the 3 central venous access groups by using the χ^2 test for categorical variables, and Student's *t* test or the Mann–Whitney *U* test for continuous variables. To assess the association between the type of venous access and neonatal outcomes and NICU resource use, the rates of adverse neonatal outcomes were compared in the 3 venous access groups by using the χ^2 test for categorical variables and the Mann–Whitney *U* test for continuous variables. To compare the incidence rates (number of infants with CABSIs or LOS per 1000 catheter days) between the 3 groups, Poisson regression models were fitted with a generalized estimating equation to account for the correlation within matched cohorts in the 3 groups. Possible confounders, whose significant differences between the groups were identified in univariate analysis, were adjusted for in the regression models.

Ethics

Data collection was approved by the local research ethics board or quality improvement committees at each center as appropriate, and this study was approved by the Executive Committee and the Research Ethics Board of Mount Sinai Hospital, Toronto, Ontario, Canada.

RESULTS

During the study period, 7919 infants born at <30 weeks' gestational age were admitted to NICUs participating in the CNN. The inclusion of infants in each of the 3 groups is described in Fig 1. A total of 180 infants were eligible for the PICC group and were matched with similar infants in the UVC group and UVC + PICC group for a total of 540 patients in the study (Fig 1). The characteristics of the infants in the 3 groups are shown in Table 1. As would be expected after matching, there were no differences

between the 3 groups in the matched items of gestational age, birth weight, and gender. However, the 3 groups revealed a statistically significant difference in SNAP-II score and mechanical ventilation on day 1 (Table 1).

The total central catheter duration was the longest in the UVC + PICC group followed by the PICC group and then the UVC group. The number of infants with CABSIs per 1000 catheter days revealed no statistically significant difference between the 3 groups (Table 2). Considering the occurrence of multiple episodes of infection in some patients, we analyzed CABSIs episodes per 1000 catheter days, which also revealed no significant difference between the groups. The rates of LOS were lowest in the UVC group with no difference between the PICC and UVC + PICC groups (Table 2).

Multivariate analyses (Poisson regression models with generalized estimating equation) were conducted to adjust for differences in SNAP-II score and mechanical ventilation on day 1. Consistent with the univariate analyses, there was no significant difference in CABSIs in the

multivariate analyses (Table 3). However, in the multivariate analyses, there was an increase in episodes of LOS per 1000 catheter days in the PICC group compared with infants in the UVC + PICC group.

DISCUSSION

In this retrospective population-based matched cohort study, we identified that there was no statistically significant difference in the CABSIs rate when a UVC or PICC was used as the primary vascular access immediately after birth in preterm neonates born at <30 weeks' gestation. Multivariate analyses revealed a higher incidence of infants with LOS per 1000 catheter days in the PICC group versus the UVC + PICC group; however, this may be reflective of total catheter days.

To our knowledge, this is the first study to compare UVCs and PICCs when used as primary access from immediately after birth. Previous studies have compared either PICCs or UVCs versus peripheral intravenous access.^{2,6} But, to our knowledge, no study has compared PICCs versus UVCs and their association with CABSIs

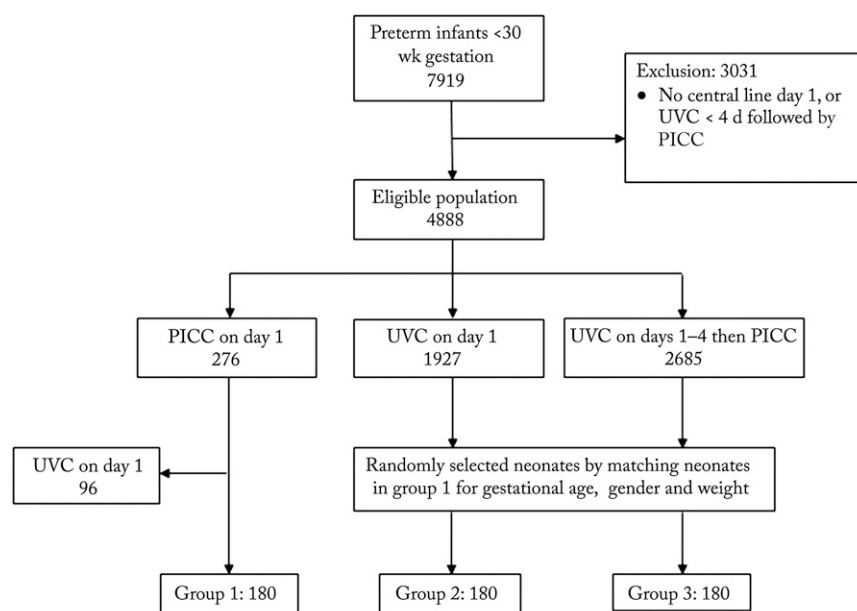


FIGURE 1 Patient selection flowchart.

TABLE 1 Demographic Characteristics of the 3 Study Groups

| Characteristics | PICC Group (n = 180) | UVC Group (n = 180) | UVC + PICC Group (n = 180) | P | | |
|---|-------------------------|------------------------|-------------------------------|--------------------|---------------------------|--------------------------|
| | | | | PICC Versus UVC | PICC Versus UVC + PICC | UVC Versus UVC + PICC |
| Gestational age, mean (SD), wk | 27.2 (1.5) | 27.2 (1.5) | 27.2 (1.5) | .99 | .99 | .99 |
| Birth weight, mean (SD), g | 1019 (244) | 1023 (250) | 1023 (243) | .88 | .88 | .99 |
| Boy, n (%) | 106 (59) | 106 (59) | 106 (59) | .99 | .99 | .99 |
| Small for gestational age, n (%) | 22 (12) | 18 (10) | 16 (9) | .50 | .30 | .72 |
| Apgar at 5 min < 7, n (%) | 54 (31) | 67 (39) | 53 (30) | .18 | .82 | .12 |
| SNAP-II score >20, n (%) | 26 (20) | 55 (40) | 49 (32) | <.01 | .03 | .17 |
| Mechanical ventilation on day 1, n (%) | 89 (49) | 116 (64) | 126 (70) | <.01 | <.01 | .26 |
| Duration of mechanical ventilation, median (IQR), d | 2 (0–10) | 2 (0–6) | 5 (1–13.5) | .34 | .02 | <.01 |
| Duration of CPAP, median (IQR), d | 7 (1–18) | 10 (1–29) | 18 (5–29) | .05 | <.01 | <.01 |
| Duration of UVC, median (IQR), d | NA | 8 (6–10) | 7 (5–9) | NA | NA | <.01 |
| Duration of PICC, median (IQR), d | 13 (9–19) | NA | 13 (8–22) | NA | 0.49 | NA |

CPAP, continuous positive airway pressure; IQR, interquartile range; NA, not applicable.

or LOS. Individual studies have revealed an increased risk of infection when a UVC is used for more than 5 to 7 days and when a PICC is used for >35 days^{24–26}; however, a head-to-head comparison is lacking. Butler-O'Hara et al³¹ compared prolonged UVC use to the current practice of combined use of a UVC followed by a PICC after 5 to 7 days if access is still required. The authors concluded that PICCs and UVCs have the same rate of sepsis in the first few days after birth, but that a PICC was less likely to be infected after 7 days of indwelling.³¹

The portal for entry of an infectious organism with either a UVC or PICC is the catheter hub. Microorganisms are introduced predominantly through the hub during routine use or at the time of catheter insertion. After the first 14 days, intraluminal colonization is the most important

source of infection.³² However, it remains to be elucidated why an average of 7 days of indwelling in UVCs or 35 days of indwelling in PICCs is required for an infection to enter the blood stream. Despite an equal number of patients in each group, the catheter days were significantly higher in both the PICC groups compared with the UVC alone group. This is probably a reflection of the clinical practice of removing UVCs by 5 to 7 days after birth, whereas PICCs are removed mostly when not needed or when complications occur. Whether this difference in the timeline of infection has something to do with the size of catheter, lack of proper sterile technique in the high-pressure situation of placing UVCs during resuscitation, or proximity of the umbilicus to the thigh, groin, and genital areas (which are believed to be highly colonized with

microorganisms) or not remains to be proven. Further experimental studies assessing the colonization patterns of both UVCs and PICCs may be needed to understand the pathophysiology. In addition, use of a UVC can lead to serious complications including thrombosis, embolization, hemorrhage, arrhythmias, effusions, cardiac tamponade, portal vein thrombosis, portal hypertension, severe liver injury, venobiliary fistula, hepatic hematoma, abscess, and sepsis, whereas PICC use is also associated with many of these complications except for liver-related complications. Thus, information is needed as to which of them is “lesser” evil.

The strengths of our study include the selection of a cohort from a population-based data set, careful matching so as not to dilute the cohort with those in whom central access is

TABLE 2 Univariate Analyses of Outcomes Between the 3 Study Groups

| Outcome | PICC Group (n = 180) | UVC Group (n = 180) | UVC + PICC Group (n = 180) | P | | |
|---|-------------------------|------------------------|-------------------------------|--------------------|---------------------------|--------------------------|
| | | | | PICC Versus UVC | PICC Versus UVC + PICC | UVC Versus UVC + PICC |
| Catheter days | 3012 | 1532 | 4515 | NA | NA | NA |
| Number of infants who had CABSIs, n (%) | 28 (15) | 12 (7) | 37 (21) | <.01 | .22 | <.01 |
| Infants with CABSIs/1000 catheter days | 9.3 | 7.8 | 8.2 | .60 | .55 | .89 |
| Number of CABSIs episodes | 37 | 12 | 45 | NA | NA | NA |
| Episodes of CABSIs/1000 catheter days | 12.3 | 7.8 | 10.0 | .18 | .37 | .45 |
| Number of infants with LOS, n (%) | 40 (22) | 21 (12) | 42 (23) | <.01 | .80 | <.01 |
| Infants with LOS/1000 catheter days | 13.3 | 13.7 | 9.3 | .89 | .05 | .12 |
| LOS episodes | 49 | 22 | 59 | NA | NA | NA |
| LOS episodes/1000 catheter days | 16.3 | 14.4 | 13.1 | .60 | .29 | .72 |

NA, not applicable.

TABLE 3 Multivariate Analyses of Incidence of CABSIs and LOS Between the 3 Study Groups

| Outcome | Comparisons | Adjusted Incident Rate Ratio (95% CI) ^a | P |
|--|------------------------|--|------|
| Infants with CABSIs per 1000 catheter days | PICC versus UVC + PICC | 1.33 (0.83–2.15) | .23 |
| | UVC versus UVC + PICC | 1.13 (0.59–2.16) | .71 |
| | PICC versus UVC | 1.18 (0.59–2.34) | .64 |
| Infants with LOS per 1000 catheter days | PICC versus UVC + PICC | 1.73 (1.15–2.60) | <.01 |
| | UVC versus UVC + PICC | 1.63 (0.97–2.76) | .06 |
| | PICC versus UVC | 1.06 (0.64–1.75) | .82 |

CI, confidence interval.

^a Adjusted for SNAP-II score >20, mechanical ventilation on day 1.

not an issue, careful and meticulous data collection, and robust analyses. However, we must acknowledge the limitations of our study. First, we do not have documentation of the reasons for the choice of 1 mode of central access over the other. Placement of a PICC on the first day after birth may reflect an inability to obtain access with a UVC or it could be a unit policy. Second, some patients had multiple episodes of infection while the PICC was in situ. This reflects practice variations because in some cases a PICC is not removed after the first episode of infection and we do not have data on the reasoning behind such an occurrence. Whether this would have made any impact on our primary outcome or not could not be answered from our data, and as such only a head-to-head randomized trial would solve this dilemma. Third, there were center variations in number of neonates contributing to each group, which may have affected outcome. In addition, our wider quality improvement effort, Evidence-based Practice Identification and Quality Improvement was ongoing at this time and many centers participated and implemented activities to reduce CABSIs; however, this would have affected reduction in primary outcome in all groups equally. Finally, the retrospective design of this study may have introduced residual confounding.

CONCLUSIONS

This study indicates that among preterm neonates born at <30 weeks' gestation, the type of primary central vascular access, whether it was a UVC

or PICC, was not associated with any difference in the incidence of CABSIs. To clarify which mode of primary access is better for reducing CABSIs as well as other short and long-term complications, a well-designed, adequately powered, randomized clinical trial will be needed. Such a trial may need to be a multicenter undertaking because consent would need to be obtained prenatally or immediately after birth with availability of skilled personnel who can place a PICC quickly and easily.

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ABBREVIATIONS

CABSIs: catheter-associated bloodstream infection
 CNN: Canadian Neonatal Network
 LOS: late onset sepsis
 PICC: peripherally inserted central catheter
 SNAP-II: Score for Neonatal Acute Physiology, version II
 UVC: umbilical venous catheter

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PEAK CONFLICT: *The Appalachian Trail, a 2,160 mile hiking trail that extends from Georgia to Maine, runs through Vermont. Each year, while hiking a segment of the Trail, my wife and I meet a few through-hikers – someone hiking the entire trail. As most journey south to north, they are all excited about completing their trek atop Maine's highest peak, Mount Katahdin in Baxter State Park. In years past, the reasons why a through-hiker would not get to summit Mount Katahdin included running out of time, energy, or money. Now, however, it may be that they do not have a permit or that the trail will end elsewhere.*

As reported in The New York Times (U.S.: August 29, 2015), officials charged with conserving Baxter State Park are increasingly at odds with hikers and the Appalachian Trail Conservancy. State Park officials claim that there are too many park visitors and too many hikers are summiting Mount Katahdin. Through-hikers on the Appalachian Trail make up a modest number of the hikers, but according to park officials, they consume more resources than others using the park. With the release of the film "A Walk in the Woods", officials expect a surge in interest similar to the surge in interest in the Pacific Crest Trail after the release of last year's movie "Wild." While the Appalachian Trail Conservancy states the park can handle more through-hikers, park officials are considering requiring permits for through-hikers or simply moving the terminus for the Appalachian Trail. The conflict reached a boiling point last July when an ultramarathon runner summited Mount Katahdin, setting a record for completing the entire trail in the shortest amount of time. He celebrated by popping a bottle of champagne. The park, which has strict rules about drinking, littering, and the number of people that can be in a hiking party, fined the runner for several infractions. The fines led to a social media storm and a legal appeal.

I am not sure how the conflict will resolve. I do know, however, that if I hiked to Maine all the way from Georgia, I would want to gaze out from atop the highest peak in Maine and exult in my accomplishment.

Noted by WVR, MD

Risk of Infection Using Peripherally Inserted Central and Umbilical Catheters in Preterm Neonates

Mohamed Shalabi, Mohamed Adel, Eugene Yoon, Khalid Aziz, Shoo Lee, Prakesh S. Shah and on behalf of the Canadian Neonatal Network

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