The Risk of Bloodstream Infection Associated with Peripherally Inserted Central Catheters Compared with Central Venous Catheters in Adults: A Systematic Review and Meta-Analysis

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The Risk of Bloodstream Infection Associated with Peripherally Inserted Central Catheters Compared with Central Venous Catheters in Adults: A Systematic Review and Meta-Analysis

Vineet Chopra, MD, MSc; John C. O’Horo, MD; Mary A. M. Rogers, PhD; Dennis G. Maki, MD, MS; Nasia Safdar, MD, PhD

Background. Peripherally inserted central catheters (PICCs) are associated with central line–associated bloodstream infection (CLABSI). The magnitude of this risk relative to central venous catheters (CVCs) is unknown.

Objective. To compare risk of CLABSI between PICCs and CVCs.

Methods. MEDLINE, CinAHL, Scopus, EmBASE, and Cochrane CENTRAL were searched. Full-text studies comparing the risk of CLABSI between PICCs and CVCs were included. Studies involving adults 18 years of age or older who underwent insertion of a PICC or a CVC and reported CLABSI were included in our analysis. Studies were evaluated using the Downs and Black scale for risk of bias. Random effects meta-analyses were used to generate summary estimates of CLABSI risk in patients with PICCs versus CVCs.

Results. Of 1,185 studies identified, 23 studies involving 57,250 patients met eligibility criteria. Twenty of 23 eligible studies reported the total number of CLABSI episodes in patients with PICCs and CVCs. Pooled meta-analyses of these studies revealed that PICCs were associated with a lower risk of CLABSI than were CVCs (relative risk [RR], 0.62; 95% confidence interval [CI], 0.40–0.94). Statistical heterogeneity prompted subgroup analysis, which demonstrated that CLABSI reduction was greatest in outpatients (RR [95% CI], 0.22 [0.18–0.27]) compared with hospitalized patients who received PICCs (RR [95% CI], 0.73 [0.54–0.98]). Thirteen of the included 23 studies reported CLABSI per catheter-day. Within these studies, PICC-related CLABSI occurred as frequently as CLABSI from CVCs (incidence rate ratio [95% CI], 0.91 [0.46–1.79]).

Limitations. Only 1 randomized trial met inclusion criteria. CLABSI definition and infection prevention strategies were variably reported. Few studies reported infections by catheter-days.

Conclusions. Although PICCs are associated with a lower risk of CLABSI than CVCs in outpatients, hospitalized patients may be just as likely to experience CLABSI with PICCs as with CVCs. Consideration of risks and benefits before PICC use in inpatient settings is warranted.

The use of peripherally inserted central catheters (PICCs) has grown in contemporary medical practice. Multiple reasons, including ease of insertion, numerous uses (eg, medication administration and venous access), perceived safety, and cost-effectiveness compared with other central venous catheters (CVCs), account for this popularity. Furthermore, the proliferation of nursing-led PICC teams has made their use convenient and accessible in many settings.

Despite these salient benefits, PICCs are also associated with central line–associated bloodstream infection (CLABSI), a healthcare-acquired complication that prolongs hospitalization and increases cost and mortality. Although CLABSI prevention has been a topic of national importance, ambiguity regarding the risk of PICC-related CLABSI exists. Although some evidence suggests that PICCs are associated with a lower risk of CLABSI than other devices, other data support the contrary viewpoint. As the use of PICCs expands to include vulnerable populations, including those that are...
hospitalized and critically ill, determining the risk of CLABSI posed by PICCs relative to other CVCs is important for both cost and patient safety. Additionally, quantifying this risk will serve to inform clinicians when choices regarding vascular access and device selection are confronted. For these reasons, we performed a systematic review and meta-analysis of the literature. Our goal was to better understand the risk of CLABSI in patients who received PICCs compared with those who received other CVCs.

**METHODS**

**Literature Search**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) in conducting this meta-analysis.12 With the assistance of a medical research librarian, we performed serial literature searches for English and non-English articles. MEDLINE (via PubMed), CinAHL, Scopus, EmBASE, and Cochrane CENTRAL registry were
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<td>Duerksen et al 1999</td>
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<td>Chemotherapy, antibiotics, blood products, venous access</td>
<td>Tunneled and nontunneled catheters and ports</td>
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<td>NR</td>
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<td>Tunneled and nontunneled catheters</td>
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<tr>
<td>Worth et al 2009</td>
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<td>Zhao et al 2012</td>
<td>Retrospective cohort</td>
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<td>Tunneled catheters, nontunneled catheters, and ports</td>
<td>Interventional radiology</td>
<td>NR</td>
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Note: CDC, Centers for Disease Control and Prevention; CLABSI, central line-associated bloodstream infection; CVC, central venous catheter; CVP, central venous pressure; ICU, intensive care unit; IV, intravenous; NR, not reported; PICC, peripherally inserted central catheter; TPN, total parenteral nutrition.
Definition of Variables and Outcomes

A CVC was defined as any central venous access device inserted into the internal jugular, subclavian, or femoral vein that terminated in the inferior vena cava or right atrium. PICCs were defined as catheters inserted in the basilic, cephalic, or brachial veins of the upper extremities with tips that terminated in the superior vena cava or right atrium; because midlines and prolines do not terminate in this position, they were not included. Venous access obtained through the external jugular vein and long-term dialysis catheters were not included. We specifically excluded dialysis catheters, because methods of infection prevention and risk factors associated with CLABSI are clinically dissimilar in this subset. Inpatient studies were defined as those in which patients remained hospitalized during the study; conversely, studies classified as outpatient were those that only involved nonhospitalized patients. Studies that featured patients who received PICCs and CVCs, 2 measures were calculated. In studies that reported the numbers of infections in patients who received PICCs and CVCs, 2 measures were calculated. First, the relative risk (RR) of CLABSI by catheter type was determined as the ratio of cumulative risks (ie, proportion of patients with PICC-related CLABSI divided by the proportion of patients with CVC-associated CLABSI). When studies reported number of infections per catheter-days, incidence rate ratios (IRRs) of CLABSI were calculated (PICC-associated CLABSI per catheter-days divided by CVC-associated CLABSI per catheter-days). For both RR and IRR, analyses were conducted such that values less than 1.0 were indicative of a lower risk of CLABSI with PICCs than with CVCs.

The empirical continuity correction, a pseudo-Bayesian approach, was used for studies that reported zero events in either the treatment or control groups. As described by Sweeting et al,17 this correction is based on the pooled effect size from the studies with the events (ie, previous evidence) and is less biased than the typical 0.5 continuity correction. All meta-analyses were performed using a DerSimonian-Laird random effects model for both RR and IRR.
Figure 2. Forest plot showing relative risk of central line–associated bloodstream infection episodes with peripherally inserted central catheter (PICC) versus central venous catheter (CVC), by patient type. CI, confidence interval.

effects model. We explored heterogeneity between studies using Cochrane’s Q test and the I² statistic, classifying heterogeneity as low, moderate, or high on the basis of an I² statistic of 25%, 50%, and 75% according to the method suggested by Higgins et al.18 Publication bias for studies was assessed by visual inspection of funnel plots and Peter’s test, with P < .10 indicative of publication bias.

A priori, we specified several additional analyses. To determine whether patient population (inpatient, outpatient, or both), patient type (patients with cancer, critically ill patients, or patients receiving total parenteral nutrition [TPN]), PICC inserter (nurse, interventional radiologist, or physician), use of ultrasound during PICC insertion, or CLABSI definition affected our conclusions, results were stratified by subgroups. Sensitivity analyses by study characteristics were performed to test the robustness of our findings. Statistical analysis was performed using Cochrane Database’s Review Manager 5.1.0 and STATA MP version 11 (Stata). Statistical tests were 2-tailed with P < .05 considered statistically significant.

RESULTS

After the removal of duplicate entries, 1,185 unique articles were identified by our electronic search (Figure 1). Of these, 1,136 were excluded on the basis of abstract information; an additional 26 studies were excluded after full text review. Therefore, 23 unique studies involving 57,250 patients reporting the occurrence of CLABSI in patients with PICCs compared with CVCs were included in the systematic review.7-11,13,19-33

Among the 23 included studies, 12 were retrospective,9,11,13,19,20,22,24,26,27,32-34 10 prospective,7,8,21,23,25,28-31,35 and 1 was a randomized controlled trial (Table 1).10 Study populations were diverse and included 10 studies that involved predominantly hospitalized patients,7,9-11,14,19,24,26,27,29,34 9 with both inpatients and outpatients,13,21,23,28,30-33 and 3 involving only outpatients.8,22,25 One study did not clearly report the location of patients during treatment or device insertion.20 Within each of these populations, unique subsets were identified. For instance, hospitalized patients included critically ill patients,9,24,26,34 patients with cancer,11,20,27,28,30,31,33,35 and neurosurgical patients.34 Studies involving both inpatients and outpatients included general medical patients,12,24,26,28,30,31,33,35 and neurosurgical patients.34 Studies also varied considerably with respect to inclusion criteria: for instance, 1 study enrolled all patients who received central venous access within a specific...
time frame, whereas 6 studies restricted inclusion to patients who received TPN. No studies reported patients who received both a PICC and a CVC.

In the 20 included studies that reported numbers of CLABSI episodes in patients who received PICCs, the unweighted incidence of PICC-related CLABSI among hospitalized patients was 5.2% (76 of 1,473) versus 5.8% (76 of 1,302) in those that received CVCs. Among outpatients, the risk of CLABSI was 0.5% in patients who received PICCs (117 of 25,822) versus 2.1% (418 of 19,715) in those that received CVCs. The largest retrospective study within the systematic review had the most episodes of CLABSI in either device group.

Infection Prevention Techniques and Surveillance Strategies

Infection prevention techniques were reported variably within the included studies. For example, 1 study exclusively reported using evidence-based bundled practices, whereas others specifically reported weekly or 3-day dressing changes. Notably, the majority of included studies did not report the method of infection prevention used. With respect to CLABSI definitions, 3 studies did not report a precise definition for CLABSI, 15 used clinical findings in conjunction with culture data, and 1 used the National Nosocomial Infection Surveillance (NNIS) definition, and 4 used the more rigorous CDC/NHSN or the NNIS definition. With respect to triggers for microbiological evaluation, 11 reported performing cultures only in the presence of symptoms suggestive of infection, 2,21,22,26,27,36-39 2 studies routinely cultured all catheter tips at the time of removal, and the remainder did not specify what prompted evaluation for CLABSI.

Risk of Study Bias

The median Downs and Black score for included studies was 11.3 (range, 10–14), suggesting average study quality and methodology with little between-study variation (Table 1). Cohen’s interrater statistic for inclusion agreement and quality assessment were 0.84 and 0.80, respectively, indicative of excellent interrater agreement.

Pooled Risk of CLABSI by Infectious Episodes in PICCs versus CVCs

Twenty of the 23 included studies (n = 52,175) reported CLABSI by number of infections per person and were pooled to evaluate the risk of CLABSI in PICCs compared with...
Within these studies, the risk of CLABSI was similar for patients who received PICCs compared with those who received CVCs (IRR [95% CI], 0.91 [0.46–1.79]). Again, a high degree of heterogeneity was observed in the pooled data (I², 87.3%; Cochran’s Q test statistic, 94.80; P < .001). As observed earlier, subgroup analysis by hospitalization status revealed that heterogeneity existed only within studies that include both inpatients and outpatients (I², 96.7%). Studies that involved only hospitalized patients showed no statistical difference in the risk of CLABSI between PICCs and CVCs (RR [95% CI], 0.72 [0.41–1.27]; I² = 0%). Only 1 study included outpatients; this study suggested that PICCs were associated with lower risk of CLABSI than CVCs (IRR [95% CI], 0.72 [0.58–0.88]; Figure 3).

Subgroup, Sensitivity, and Publication Bias Analyses

Because of heterogeneity in the pooled estimate and small numbers of studies involving outpatients, subgroup analyses were restricted to studies involving hospitalized patients (10 studies; n = 2,279; Table 2). Rates of PICC-associated CLABSI relative to CVC-associated CLABSI were similar for patients with cancer, those who were critically ill, and those requiring TPN. Meta-analytical conclusions remained robust to sensitivity testing by study design (Table 3). Visual inspection of funnel plots and Peter’s test did not suggest publication bias (P = .18).

**DISCUSSION**

The prevention of CLABSI is a topic of national importance. Because most CLABSIs occur in intensive care unit (ICU) settings, much of this discourse has focused on the critically ill, for whom significant strides have been made. With the advent of interventions that include unit-based safety approaches, a technical checklist of best practices, and enhanced measurement and feedback of infection rates, significant decreases in CLABSI rates have been realized in ICUs across the United States. Furthermore, several large-scale initiatives have reported statewide elimination of CLABSI in ICUs. However, not all CVCs are equivalent with respect to the associated risk of CLABSI, and shifts in patterns of CVC use from ICU to non-ICU settings may impact this progress. Thus, evidence that is both device- and context-specific is needed to inform CLABSI risk and prevention.

In this systematic review and meta-analyses comparing risk of CLABSI between PICCs and CVCs, we found a 10-fold greater risk of CLABSI among hospitalized patients (5.2%) than among outpatients who received PICCs (0.5%). Additionally, hospitalized patients who underwent PICC placement experienced CLABSI rates that statistically paralleled that associated with CVCs. Conversely, outpatients experienced a lower percentage of CLABSI events with PICCs (0.5%) than with CVCs (2.1%). These findings underscore the role of patient and device factors in the development of CLABSI.
CLABSI and suggest caution when placing PICCs in hospitalized patients for inappropriate indications.

Why might PICCs pose a differential risk of infection in the inpatient setting than in the outpatient setting? CLABSIs are thought to occur by extraluminal migration of bacteria from the skin entry site, forming a critical mass at the catheter tip. Because PICCs are longer in length, and bacteria have farther to travel, lower rates of CLABSI are theoretically expected. However, a considerable proportion of CLABSIs are also caused by hub manipulation, with bacteria migrating intra- rather than extraluminally. This latter route of infection is most implicated with long-term CVCs. PICCs straddle the line between short- and long-term devices, such that both intra- and extraluminal routes become relevant in CLABSI related to these devices. More frequent hub manipulation in inpatient settings than in outpatient settings may explain the increased risk of PICC-related CLABSI among hospitalized patients.

Our study has important limitations. First, we were only able to compare infections by catheter-days in 13 of the included 23 studies, a limitation that reflects the paucity of reporting of CLABSIs by catheter-days in the available literature. Second, our analyses were based on unadjusted data of rates of infection; failure to include patient- or device-level characteristics may influence our conclusions. Although the use of sensitivity and subgroup analyses helps address this problem, our findings should be interpreted with caution in this regard. Third, because the included studies did not specifically report on the use of antimicrobial catheters or practices to prevent CLABSI (eg, bundle use, site disinfection, and line-maintenance practices), we were not able to adequately address the impact of factors such as technology or infection prevention methods on PICC-related bloodstream infections.

Despite these limitations, our study also has important strengths. First, to our knowledge, this is the largest systematic review and meta-analyses specifically examining the risk of CLABSI in PICCs compared with other CVCs. Because our study specifically isolates CLABSI outcomes and characteristics associated with this event, it uniquely adds to the literature regarding PICC safety. Second, we separately analyzed CLABSI based on risk per patient, as well as CLABSI episodes per catheter-days. In doing so, we were able to assess not only CLABSI risk by exposure for groups of patients but also how CLABSI rates vary based on time-at-risk due to catheter placement. Indeed, these analyses showed that hospitalized patients who received PICCs experienced CLABSI at rates that were no different than those associated with other CVCs. In an era of escalating inpatient PICC use, this finding is timely and calls for scrutiny regarding the necessity and appropriateness of PICC insertion. Third, our study is strengthened by the inclusion of unpublished study data obtained by direct author contact.

Our findings have important implications for clinicians and policy makers. First, our study reemphasizes how the prevention of PICC-related CLABSI in hospitalized patients should be approached with the same drive, intensity, and strategic insights that have driven down CLABSI rates in ICUs. Specifically, greater use of insertion and maintenance checklists, development of appropriateness guidelines to ensure suitable placement, and timely removal of PICCs to prevent idle catheter-days are in need of greater attention in non-ICU settings. Second, because homogenous care teams are increasingly difficult to assemble in these areas, studies that specifically assess the role of novel technologies and practices, such as chlorhexidine-impregnated site dressings or antimicrobial PICCs, are needed in the battle against CLABSI in non-ICU settings. These technological approaches may provide important layers of reinforcement against CLABSI in non-ICU settings, especially as the use of PICCs increases in these areas. Third, because the risk of CLABSI associated with CVCs and PICCs appears to be similar in hospitalized patients, expansion of practices and campaigns such as hub decontamination and “scrub the hub” should specifically be targeted toward PICCs. Finally, we note that PICCs continue to appear safe in outpatient settings when used in healthier, ambulatory populations for appropriate indications. Continued efforts to educate patients on catheter care, including aseptic access, flushing techniques, and early recognition of warning signs, are important to maintain this course.

In conclusion, when placed in hospitalized patients, PICCs are associated with a risk of CLABSI that mirrors that of
CVCs. Policy and procedural oversight regarding PICC insertion and maintenance in these settings is warranted. Future studies investigating pathogenesis, insertion practice, and comparative effectiveness of prevention strategies for PICC-related CLABSI in non-ICU settings are necessary to improve patient safety.

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Potential conflicts of interest. All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

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