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Risk of Catheter-Related Bloodstream Infection With Peripherally Inserted Central Venous Catheters Used in Hospitalized Patients*

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Background: **Peripherally inserted central venous catheters (PICCs) are now widely used for intermediate and long-term access in current-day health care, especially in the inpatient setting, where they are increasingly supplanting conventional central venous catheters (CVCs) placed percutaneously into the internal jugular, subclavian, or femoral veins. Data on the risk of PICC-related bloodstream infection (BSI) with PICCs used in hospitalized patients are limited.**
Study objectives: **To determine the risk of PICC-related BSI in hospitalized patients.**
Study design: **Prospective cohort study using data from two randomized trials assessing the efficacy of chlorhexidine-impregnated sponge dressing and chlorhexidine for cutaneous antisepsis.**
Methods: **PICCs inserted into the antecubital vein in two randomized trials during from 1998 to 2000 were prospectively studied; most patients were in an ICU. PICC-related BSI was confirmed in each case by demonstrating concordance between isolates colonizing the PICC at the time of removal and from blood cultures by restriction-fragment DNA subtyping.**
Results: **Overall, 115 patients had 251 PICCs placed. Mean duration of catheterization was 11.3 days (total, 2,832 PICC-days); 42% of the patients were in an ICU at some time, 62% had urinary catheters, and 49% had received mechanical ventilation. Six PICC-related BSIs were identified (2.4%), four with coagulase-negative staphylococcus, one with *Staphylococcus aureus*, and one with *Klebsiella pneumoniae*, a rate of 2.1 per 1,000 catheter-days.**
Conclusion: **This prospective study shows that PICCs used in high-risk hospitalized patients are associated with a rate of catheter-related BSI similar to conventional CVCs placed in the internal jugular or subclavian veins (2 to 5 per 1,000 catheter-days), much higher than with PICCs used exclusively in the outpatient setting (approximately 0.4 per 1,000 catheter-days), and higher than with cuffed and tunneled Hickman-like CVCs (approximately 1 per 1,000 catheter-days). A randomized trial of PICCs and conventional CVCs in hospitalized patients requiring central access is needed. Our data raise the question of whether the growing trend in many hospital hematology and oncology services to switch from use of cuffed and tunneled CVCs to PICCs is justified, particularly since PICCs are more vulnerable to thrombosis and dislodgment, and are less useful for drawing blood specimens. Moreover, PICCs are not advisable in patients with renal failure and impending need for dialysis, in whom preservation of upper-extremity veins is needed for fistula or graft implantation.** ***(CHEST 2005; 128:489–495)***

Key words: bacteremia; bloodstream infection; catheter-related bloodstream infection; cross-infection; intravascular catheters; nosocomial bacteremia; nosocomial infection; peripherally inserted central catheters

Abbreviations: BSI = bloodstream infection; CI = confidence interval; PFGE = pulsed-field gel electrophoresis; PICC = peripherally inserted central catheter; TPN = total parenteral nutrition

Safe and reliable vascular access is an essential element of modern-day health care. In recent years, the use of peripherally inserted central catheters (PICCs) for intermediate and long-term venous access has steadily grown, initially for outpatient IV therapy, recently for hospitalized patients needing

prolonged central access. Data from Medtech Insight (Newport Beach, CA), a company that collects data on all types of medical products and devices, show sales of 942,000 PICCs in US health centers. Reported rates of PICC-related bloodstream infection (BSI) have ranged from 0.4 to 0.8 per 1,000 catheter-days[1–6] However, most of the previously reported studies were retrospective, and nearly all were conducted in the outpatient setting. Thus, the risk of PICC-related BSI in hospitalized patients is unclear. We report a prospective study undertaken to determine the risk of PICC-related BSI in a university hospital with PICCs used exclusively in hospitalized patients and perform a systematic review to estimate rates of PICC-related BSI in hospitalized patients.

Materials and Methods

Patients participating in two randomized trials during from 1998 to 2000, one study[7] evaluating the efficacy of a novel chlorhexidine-gluconate impregnated sponge dressing, and the other study[8] evaluating 1% tincture of chlorhexidine for prevention of catheter-related infection, formed the study population. Data were collected prospectively on study patients with newly inserted PICCs, including demographic features, underlying diseases, severity of illness according to APACHE (acute physiology and chronic health evaluation) II score,[9] reason for placement of the catheter, service, antibiotic use, length of hospital stay, number of days each catheter was in place, presence of other invasive devices (urinary catheters and endotracheal tubes), and all clinical and laboratory data pertaining to infection.

Microbiological Methods

At catheter removal, skin of the insertion site was cultured quantitatively as previously described.[10] For each catheter, two 5-cm segments, a proximal intracutaneous segment, and the tip (both transported in a sterile container) were cultured semiquantitatively, and each hub and fluid from the most distal injection port of each lumen were cultured quantitatively, as previously described.[10]

Microorganisms were identified according to standard criteria.[11] When catheter-associated BSI occurred, isolates recovered from the insertion site, catheter segments, infusate, or hubs, and blood cultures that appeared similar phenotypically were subtyped by pulsed-field gel electrophoresis (PFGE) after digestion of genomic DNA with restriction endonucleases,[12] using a computerized system for determining the relatedness of isolates (Gel Doc 2000; Bio Rad Laboratories; Hercules, CA).

Definitions

Catheter-tip colonization was defined as a positive semiquantitative culture finding of an intravascular catheter segment (> 15 cfu) and is considered synonymous with local infection of the catheter.[10] *Catheter-related BSI* was defined as isolation of the same strain from the catheter segment, a hub, or infusate, and from one or more blood cultures, as proven by restriction-fragment subtyping with no other identifiable source for the BSI.[10]

Systematic Review of the Literature

We performed a computerized search of PUBMED (including MEDLINE) using the following key words: "peripherally inserted central catheter," "PICC," "infection," "prospective," and "risk," and combinations of these search terms. Reference lists of articles were searched to identify additional articles. Studies were included if all or most of the study population was hospitalized, catheter-related BSI was defined explicitly, and sufficient data were provided to calculate rates of infection. We restricted our search to PICCs in inpatients since the focus of this article was to determine rates of PICC-related BSI in hospitalized patients.

Statistical Analysis

The cumulative incidence of PICC-related BSI was calculated separately for adults and neonatal populations, by combining the results of several studies using standard formulas for combining proportions in which the weighted average and variance are

Table 1—*Features of the Study Population

Features	Data
Patients, No.	115
Age, yr	62 ± 19
Gender, %	
Male	55
Female	45
Host risk factors, %	
Surgery	10
Insulin-dependent diabetes mellitus	23
Malignancy	20
Transplant	20
Open wound	17
Therapeutic risk factors, %	
Urinary catheters	62
Mechanical ventilation	49
Prior antibiotics	71
Mean laboratory values	
Albumin, g/L	23
Hematocrit, g/L	300
APACHE II score, mean±SD	12.6 ± 7.0
Duration of catheterization, d, mean±SD	11.3 ± 19.8
Reason for removal, %	
No longer needed	41
Patient died	12
Suspected catheter-related BSI	7
Not stated	40

*Data are presented as mean ± SD or %.

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Table 2—*Microbiology of PICC-Related BSI*

Pathogens	No.
Coagulase-negative staphylococci	4
S aureus	1
K pneumoniae	1

calculated.[13] All statistical analyses were performed using Statacorp 2003 (Stata Statistical Software; College Station, TX).

Results

A total of 251 PICCs inserted in 115 patients were studied prospectively over a mean duration of catheterization of 11.3 days (total, 2,832 PICC-days). Most catheters were used in patients highly vulnerable to nosocomial infection, as shown by high APACHE II scores (mean score, 12.6), multiple invasive medical devices, and hypoalbuminemia (Table 1); 42% of the study patients were in an ICU for some time in their hospital stay.

Fifty-two PICCs (20.7%) were colonized at removal. Six PICC-related BSIs (2.4%) were confirmed, all showing concordance between cultures obtained from an infected PICC and blood cultures (Table 2). A representative PFGE is shown in Figure 1. BSIs were caused by coagulase-negative staphylococci,[4] *Staphylococcus aureus*,[1] and *Klebsiella pneumoniae*,[1] at a rate of 2.1 per 1,000 catheter-days.

Recognizing that the database is comprised of patients who were participating in two randomized trials of novel strategies for prevention of CVC-related BSI, and both strategies were found to reduce the incidence of catheter colonization and CVC-related BSI,[7,8] the rate of PICC-related BSI was calculated for the pooled control groups of both trials (150 PICCs, 1,673 PICC-days). All six PICC-related BSIs occurred in control PICCs, which had a rate of PICC-related BSI of 3.5 per 1,000 PICC-days (3.9%); 40 PICCs were colonized (26.6%).

Results of Literature Review

Our literature review identified 33 studies that have addressed the risk of PICC-related BSI in hospitalized patients; 19 were performed in neonates and 14 in adults. These studies are summarized in Table 3.[14–46] The cumulative incidence of PICC-related BSI was 2.1 per 1,000 PICC-days (95% confidence interval [CI], 1.7 to 2.5) overall. In adults and children, the rate was 1.9 per 1,000 PICC-days (95% CI, 1.4 to 2.6); in neonates, the rate was 2.20 per 1,000 PICC-days (95% CI, 1.7 to 2.3). The risk of PICC-related BSI per 100 PICCs was 3.2 (95% CI, 1.9 to 4.5) overall, 2.5 (95% CI, 0.5 to 4.5) in adults and children, and 3.8 (95% CI, 1.9 to 5.6) in neonates, including very low birth weight neonates. Five of the studies included only adult ICU patients. Eleven studies were retrospective, and 22 were prospective. The rate of PICC-related BSI when the analyses were restricted to prospective studies was 1.3 (95% CI, 1.0 to 1.7) per 1,000 days and 2.5 (95% CI, 0.9 to 3.4) per 100 PICCs.

Discussion and Literature Review

Numerous prior reports[1–6] of clinical experience with PICC lines have suggested that PICCs pose a much lower risk of catheter-related BSI than conventional nontunneled, noncuffed CVCs placed percutaneously in the internal jugular or subclavian veins, perhaps because of less dense bacterial colonization on the midarm as compared to the sites used for conventional CVCs, the neck, upper chest, or groin.[47] However, the vast majority of the prior published studies[1–6] of PICC-related BSI were retrospective, and PICCs were used exclusively or primarily in the outpatient setting. Thus, whether

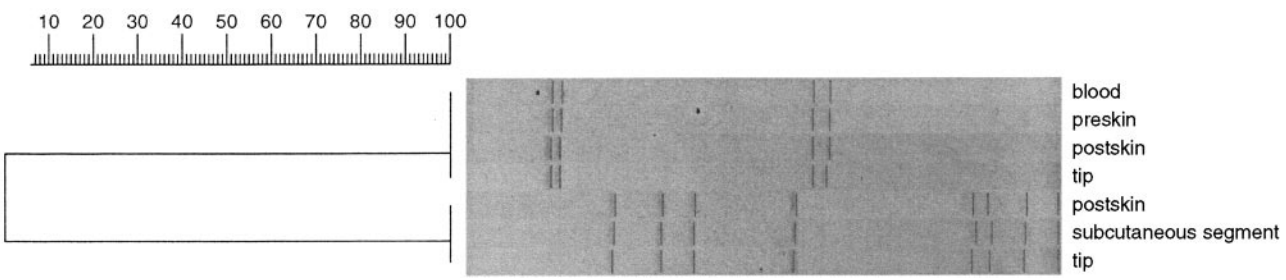

Figure 1. PFGE of isolates of coagulase-negative staphylococci recovered from cultures of a PICC that caused PICC-related BSI. Coagulase-negative staphylococcus were recovered from multiple sites; one recovered from the skin of the insertion site at catheter removal and from the catheter tip shows 100% restriction fragment polymorphism identity with the strain recovered from blood cultures. Presumed epidemiology: skin, catheter, blood, extraluminally.

Table 3—*Studies of PICC-Related BSI in Hospitalized Patients

Source	Type of Study	PICCs, No.	BSIs, No.	PICC-Days, No.	Hospital Population	PICC-Related BSI	
						Per 100 PICCs	Per 1,000 PICC-Days
Sketch et al[14]	Prospective	70	0	7,280	Coronary care unit	0	0
Abi-Nader[15]	Prospective	92	1	878	Adults in an ICU	1.1	1.1
Lam et al[16]	Retrospective	135	3	1,890	Adults	2.2	1.6
Chait et al[17]	Retrospective	137	5	1,245	Children	3.6	2.1
Alhimyary et al[18]	Retrospective	135	0	1,381	Adults receiving TPN	0.0	0.0
Ng et al[19]	Prospective	89	1	635	Adults in an ICU	1.1	1.6
Yeung et al[20]	Prospective	111	12	1,869	Children receiving TPN	10.8	6.4
Cowl et al[21]	RCT	51	2	490	Adults	3.9	4.0
Griffiths and Philpot[22]	Prospective	29	2	435	Adults in an ICU	6.8	4.5
Chlebicki and Teo[23]	Retrospective	94	3	1,598	Adults	3.2	1.9
Giuffrida et al[24]	Prospective	472	0	2,360	Adults in an ICU	0	0
Harter et al[25]	Prospective	65	1	455	Adults with hematologic malignancy	1.5	2.2
Funk et al[26]	Prospective	167	4	789	Adults receiving general medical service	2.4	1.2
Ogura et al[27]	Retrospective	52	9	1,375	Pregnant women	17.3	6.5
Kamala et al[28]	Prospective	31	1	288	Neonates receiving TPN	3.2	3.5
Chathas et al[29]	Retrospective	481	6	6,206	Neonate	1.2	1.0
Reynolds[30]	Retrospective	17	1	165	Neonate	5.8	6.0
Dolcourt and Bose[31]	Prospective	18	0	446	Neonate	0	0
Foo et al[32]	Retrospective	68	13	775	Very low birth weight neonates	19.1	16.7
Durand et al[33]	Prospective	53	4	1,325	Neonate	7.5	3.0
Golombek et al[34]	Prospective	57	4	792	Neonate	7.1	5.1
Harms et al[35]	Prospective	148	2	2,220	Neonate	1.35	0.9
Klein and Rudd[36]	Prospective	34	4	1,088	Neonate	11.7	3.6
Leick-rude[37]	Prospective	283	0	1,162	Neonate	0	0
Loeff et al[38]	Retrospective	58	4	1,298	Neonate	6.9	3.0
Nakamura et al[39]	Prospective	40	0	440	Neonate	0	0
Rudin and Nars[40]	Prospective	283	0	1,983	Neonate	0	0
Sherman et al[41]	Prospective	55	1	1,199	Neonate	1.8	0.8
Shulman et al[42]	Prospective	29	2	704	Neonate	6.8	2.8
Maki et al[43]	RCT	43	8	860	Neonate	18.6	0.9
Cairns et al[44]	Retrospective	61	19	915	Very low birth weight neonates	31.1	2.0
Aggarwal and Downe[45]	Retrospective	44	3	256	Neonates	6.8	11.7
Neubauer[46]	Prospective	535	4	12,305	Neonate	0.7	0.3
Pooled rate							
All studies						3.2 (1.9–4.5)	2.1 (1.7–2.5)
Prospective studies						2.1 (0.9–3.4)	1.3 (1.0–1.7)
Adults and older children						2.5 (0.5–4.5)	1.9 (1.4–2.6)
Neonates						3.8 (1.9–5.6)	2.2 (1.7–2.3)

*Data in parentheses indicate 95% confidence intervals. RCT = randomized clinical trials.

PICCs are safer than conventional CVCs in hospitalized patients has been unclear.

In our rigorous prospective study of PICCs used solely in the inpatient setting in a high-risk patient population, we found a rate of PICC-related BSI (overall, 2.4%; 2.1 per 1,000 PICC-days; in control catheters in the database, 3.9%; 3.5 per 1,000 PICC-days) to be considerably higher than a pooled rate based on numerous retrospective reports of PICCs used in outpatients (0.4 per 1,000 days), but comparable to rates of BSI found in prospective studies of conventional CVCs placed percutaneously in the internal jugular, subclavian, or femoral veins in inpatients (approximately 2.3 per 1,000 days).[6]

We found overall pooled rates of PICC-related BSI of 2.1 per 1,000 PICC-days in our literature review encompassing ICU settings, general inpatient settings, and neonatal ICUs. This is comparable to the rates reported in our current study.

Other studies[14,15,19,22,24] of PICC used exclusively in the adult ICU setting have found rates of PICC-related BSI ranging from 0 to 4.5 per 100 catheter-days. The discrepant results can be explained in part by different patient populations, including differences in severity of illness, the duration of catheter implantation, and extent of catheter manipulation in these studies.

In the general adult inpatient setting, rates of PICC-related BSI reported in the literature have ranged from 0 to 6.5 per 1,000 PICC-days (Table 3). In a retrospective analysis of 135 PICCS inserted in inpatients by Lam et al,[16] most of the patients were hospitalized in a general medical or surgical service; unfortunately, few PICCS were cultured at removal. The rate of reported PICC-related BSI was 2.3% (1.6 per 1,000 catheter-days). Chait et al[17] reported a rate of PICC-related BSI of 2.1 per 1,000 catheter-days in a retrospective study of PICCs used in children; however, PICCs were removed only if bacteremia failed to respond to antimicrobial therapy. Another retrospective study[21] in adult inpatients had no PICC-related infections; however, the catheters were used exclusively for total parenteral nutrition (TPN) and were not routinely cultured.

In a prospective study of 111 PICCs used for TPN in hospitalized children, Yeung et al[20] reported a rate of BSI of 6.4 per 1,000 catheter-days; however, again, catheters were not cultured. In a study of 51 PICCs in adult inpatients in which every PICC with suspected infection was cultured, Cowl et al[21] found a rate of 4.9 BSIs per 1,000 catheter-days; granulocytopenic patients and organ transplant recipients were excluded from this study. A high incidence of PICC-related BSI was reported in a small retrospective study[27] of pregnant women (6.5 per 1,000 PICC-days); univariate analysis found preterm labor to be associated with PICC-related BSI. Harter et al[25] performed a prospective study to determine the rate of PICC-related BSI in adult patients with hematologic malignancy, and found a rate of 2.2 per 1,000 catheter-days.

Two randomized controlled trials, one comparing conventional CVCs to PICCs in adults[21] and the other comparing PICCs to peripheral IV catheters in neonates,[48] have been reported. Janes et al[48] reported a 34% rate of PICC-associated sepsis in their randomized trial of PICCs vs peripheral IV catheters in 63 very low birth weight neonates; however, catheters were not routinely cultured at removal. Moreover, rates of catheter-related BSI were not reported, and we did not include the data from this study in our calculation of rates of PICC-related BSI.

Low birth weight and very low birth weight neonates in neonatal ICUs are a population at exceedingly high risk of catheter-related BSI, as our summary of the literature suggests, with a rate of PICC-related BSI of 2.20 per 1,000 catheter-days. Life-threatening complications beyond infection, such as cardiac tamponade, pleural effusion, and ventricular tachycardia, have also been well described in the neonatal population.

In many of the studies included in our literature review, catheters were not routinely cultured at removal. Moreover, molecular subtyping to corroborate the origin of every PICC-associated BSI was not performed in any of these studies. However, the definitions used for PICC-related infection were generally commensurate with those recommended by the Centers for Disease Control and Prevention for diagnosis of vascular catheter-related BSI.[49] The risk of PICC-related BSI in hospitalized patients in our center is similar to the results of Cowl et al,[21] which we feel reflects the prospective nature of our study in which every PICC was cultured at removal, including the implanted catheter, hubs, and infusate, and DNA subtyping was employed in every case when the patient had positive blood cultures and possible PICC-related BSI.

Our data and the previous studies suggest that PICCs used for intermediate access in inpatients are associated with a risk of catheter-related BSI higher than that reported with cuffed and tunneled Hickman-like CVCs (approximately one per 1,000 catheter-days),[6] and raise the question whether the growing trend in many hospital hematology and oncology services to switch from the use of cuffed and tunneled CVCs to PICCs is justified, particularly since PICCs are more vulnerable to thrombosis and dislodgment[50–53] and are less useful for drawing blood specimens. Moreover, because of a high incidence of thrombosis, PICCs are not advisable in patients with renal failure who may require hemodialysis in the future, since preservation of upper-extremity veins is essential for later fistulas or grafts.[54]

Our rate of PICC-related BSI (2.1 to 3.5 per 1,000 catheter-days) is quite similar to that reported with prospectively studied, short-term, noncuffed CVCs placed percutaneously in the internal jugular or subclavian veins (2.3 per 1,000 CVC-days).[6] As such, the assumption that PICCs are safer than conventional CVCs with regard to the risk of infection is in question and should be assessed by a larger, adequately powered randomized trial that assesses peripheral vein thrombophlebitis, PICC-related thrombosis, and premature dislodgment, as well as catheter-related BSI.

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