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Peripherally inserted central catheter–associated bloodstream infection: Risk factors and the role of antibiotic-impregnated catheters for prevention

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Background: Antimicrobial-impregnated (AIP) peripherally inserted central catheters (PICCs) may lower risk of central line–associated bloodstream infection (CLABSI) compared with nonantimicrobial-impregnated (NAIP) catheters. We sought to assess risk factors for CLABSI with a focus on the effect of AIP PICCs.

Methods: CLABSI rate was determined among patients who received PICCs from July 2009 through June 2012 using a retrospective study design. A nested case-control study matched for operators (interventional radiology [IR], infectious diseases [IDs], and the nurse venous access team [VAT]) was conducted to assess risks for PICC CLABSI.

Results: Eighty-nine PICC CLABSIs (1.66%) occurred among 5,372 PICC placements a mean of 32 days after placement. Higher infection risk (1.75) was observed for IR-placed PICCs compared with ID-placed PICCs ($P = .02$). In addition, higher infection risk (4.22) was observed for IR-placed PICCS compared with VAT-placed PICCs ($P = .0008$). IR-placed NAIP catheters, as indicated by multivariate analysis, revealed a 5.45-fold greater CLABSI risk compared with AIP catheters ($P < .0005$). Other risk factors included chemotherapy, placement of a tunneled catheter, leukemia, and AIDS.

Conclusions: PICC CLABSIs were highest among patients receiving NAIP catheters in this large study. Highest risk occurred with placement of a tunneled catheter, AIDS, leukemia, and if the indication for PICC was chemotherapy. Our study suggests that the AIP PICC should be considered in all patients receiving PICCs.

BACKGROUND

The use of central venous catheters has increased substantially, and the association between type of catheter and risk of central line–associated bloodstream infection (CLABSI) has been studied previously.[1-5] Some have reported lower risk of CLABSI associated with peripherally inserted central catheters (PICCs); however, a recent systematic review and meta-analyses on the risk of CLABSI showed a 10-fold increase in risk among hospitalized patients (5.2%) compared with outpatients (0.5%).[6] CLABSIs are one of the most serious complications of PICC use and are associated with increased morbidity and mortality rates. The reported incidence of PICC CLABSI has ranged from 1.0-7.71 per 1,000 catheter days, with an estimated mortality risk of 12%-36%.[7,8] According to the Centers for Disease Control and Prevention (CDC), an estimated 30,100 CLABSI cases occur in US intensive care units annually,[9] with roughly 250,000 across care settings.[10,11] Coating or impregnating the external and internal surfaces of the catheters with antimicrobial agents may help reduce risk of bloodstream infection (BSI),[12] but current recommendations are that PICCs with antimicrobial agents impregnated on their surfaces or intercalated into their polymers should not be used except in high-risk settings. Several studies have investigated the risk factors for PICC-associated BSI in high-risk populations.[6,13] Review of these studies has indicated several limitations, including small population size, male participants only, use of nonantibiotic-impregnated (NAIP) catheters, or failure to use chlorhexidine-impregnated dressings.[13]

The purpose of our study was to assess risk factors for PICC CLABSI using case controls in our large and diverse patient population. We were particularly interested in assessing the role of antibiotic-impregnated (AIP) catheters versus NAIP PICCs and whether differing insertion operators (interventional radiology [IR], infectious diseases

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[ID], and the nurse venous access team [VAT]) might have different risks for PICC-associated BSI.

METHODS

Study site

The Medical University of South Carolina (MUSC) is a 700-bed tertiary academic medical center located in Charleston, South Carolina. There is a separate pediatric hospital, but pediatric patients were not included in this study. The medical center provides all types of medical and surgical subspecialty services for inpatient and outpatient care in South Carolina and neighboring states. Services include active solid organ and bone marrow transplant programs, as well as an infusion center for chemotherapy, long-term antibiotics, and other long-term medications.

PICC insertion procedures

Approximately 1,200 PICC lines are inserted annually at MUSC by IR and ID physicians or nurse VATs. All physician team members were appropriately trained and credentialed by the hospital credentialing committee for PICC placement. All VAT nurses were trained and credentialed according to MUSC nursing credentialing requirements. Both IR and ID perform PICC insertions under fluoroscopy guidance, with insertion within the radiology suite (IR), dedicated PICC suite (ID), or at the bedside (ID and VAT). ID is the only team to tunnel PICCs for selected patients, including morbidly obese patients; patients with cystic fibrosis; and patients receiving long-term total parenteral nutrition (TPN), long-term inotropes, and chemotherapy.

MUSC adopted the Institute for Healthcare Improvement central line insertion bundle for infection prevention in 2009 and developed and implemented a central line care maintenance bundle for infection prevention in 2010. This bundle includes daily assessment for line necessity, as well as ensuring timely dressing changes and scrubbing the hub with chlorhexidine or alcohol. A chlorhexidine-impregnated sponge disc is used for every PICC dressing unless there is a documented allergy. The bundles were implemented by all teams simultaneously with hospital infection control guidance.

Two different PICCs were placed during the study: the Bard PowerPICC (Bard Access Systems Inc, Salt Lake City, UT) and the Cook Spectrum, which is coated with minocycline and rifampin (Cook Medical Inc, Bloomington, IN). Most PICCs placed by ID and VAT were the Cook product, selected owing to its reported anti-infectious properties. IR preferred the Bard product because of its ease of insertion.

Study design and study population

A retrospective cohort study design was used to determine the rate of BSI among patients who received a PICC from July 1, 2009, to June 30, 2012, with a nested case-control study to identify risk factors for BSI. We compared patients who had development of PICC CLABSI with randomly selected control subjects without PICC CLABSI in a 1:3 ratio matched by operator (IR, ID, or VAT).

Data collection and statistical analysis

The infection control nurses identified all infected central venous lines using the surveillance definition from the National Healthcare Safety Network.[14] We determined which CLABSI were owing to PICCs and obtained details on the infecting organisms from the microbiology laboratory. Potential risk factors for PICC-related complications were identified through published evidence.[13] The Charlson comorbidity score[15] was used for weighting comorbid conditions and comparing patient populations. Demographic data, clinical characteristics, outcomes (death), PICC type (rifampin/minocycline impregnated [AIP] vs NAIP), indication for PICC, and operator types were recorded from hospital charts. Time to infection in days was calculated from the date of first positive blood culture and the date of PICC insertion. The follow-up period was 6 months from the date of PICC line insertion or until the PICC was removed, whichever was longer. The analysis included patients who were discharged with PICCs. Patients who were seen at outside hospitals for care while they had a PICC line were excluded. The overall and between-groups (operators and whether an antimicrobial-coated catheter was used) PICC CLABSI rates were determined. Proportions were compared by use of χ^2 analysis. Risk factors for PICC CLABSI were assessed by univariate and multivariate logistic regression analysis (EpiInfo v7; CDC, Atlanta, GA). Multivariate analysis included variables significant in univariate analysis *P* values ($\leq$.05).

RESULTS

A total of 5,372 PICCs were placed over the study period: 2,770 (51.6%) were NAIP catheters, and 2,602 were AIP catheters. IR placed 2,572 (47.9%) of the study PICCs and ID placed 1,896 (35.3%) PICCs, whereas 904 (16.8%) were placed by the VAT. Seventy-five (1.39%) NAIP catheters of 5,372 PICCs placed became infected over the study period (95% confidence interval [CI], 1.08-1.71). Fourteen (0.26%) AIP catheters of 5,372 PICCs placed became infected over the study period (95% CI, 0.12-0.39). Overall, 89 PICC CLABSIs occurred, for a rate of 1.66%. The PICC CLABSI rate was 2.33%, 1.32%, and 0.55% for IR, ID, and VAT placements, respectively. With IR, a 1.75-fold increased risk of PICC CLABSI compared with ID (95% CI, 1.10-2.82; $P = .02$) was found, whereas a 4.22 higher risk was found compared with VAT (95% CI, 1.69-10.55; $P = .0008$). There was no difference in risk between ID and VAT operators.

Etiologic agents of PICC CLABSI in our study (Table 1) were similar to those reported in other studies.[1,2] There were fewer gram-positive coccal bacteremias (21.1% vs 43.4%) and more *Candida* bacteremias (31.6% vs 18.8%) among patients with AIP catheters than in those with NAIP catheters; however, these differences were not statistically significant, not surprising given the limited number of infections and variety of etiologic agents.

The characteristics of patients included in the case-control population are shown in Table 2. IR placed only NAIP catheters, whereas ID and VAT placed mostly AIP catheters. Significant differences occurred between AIP and NAIP catheter types (Table 2) in both indications for placement and patient risk factors. Having AIP catheters showed a significant association with receiving antibiotics, tunneled catheters, chronic obstructive pulmonary disease, and solid tumors, whereas NAIP catheters were more associated with TPN. Despite differences in patient populations, the Charlson comorbidity weighting score was not significantly different.

Table 3 shows patient characteristics by PICC CLABSI versus non-CLABSI in the case-control group. Female sex and having an AIP catheter showed a protective effect. However, having a catheter placed for chemotherapy, leukemia, or AIDS or having a tunneled catheter placed resulted in an increased risk. A higher Charlson score was predictive of PICC CLABSI. In the multivariate logistic regression analysis (Table 4), significant risks for PICC CLABSI included NAIP PICCs, chemotherapy, tunneled PICC placement, leukemia, and AIDS.

DISCUSSION

Our study examines the role of antimicrobial PICCs in prevention of PICC CLABSI. The PICC CLABSI rate of 1.66% is consistent with findings of similar studies with rates ranging between 0 and 3.13 per 1,000 PICC-days.[16-22] This study shows that NAIP catheters, tunneled

Table 1
Microbiology of peripherally inserted central catheter–associated bloodstream infections by type of catheter

	Total n (%)	Nonantimicrobial PICC	Antimicrobial PICC	*P* value*
Infected PICC	89 (1.66)	75 (84.3)	14 (15.7)	
Number of pathogens isolated	104	85	19	
Gram-positive organisms	41 (39.4)	37 (43.5)	4 (21.1)	.12
Coagulase-negative staphylococci	9 (8.7)	8 (9.4)	1 (5.3)	
Vancomycin-susceptible *Enterococcus* species	12 (11.5)	9 (10.6)	3 (15.8)	
Vancomycin-resistant *Enterococcus* species	7 (6.7)	7 (8.2)	0	
MRSA	5 (4.8)	5 (5.9)	0	
MSSA	3 (2.9)	3 (3.5)	0	
Other gram positives	5 (4.8)	5 (5.9)	0	
Gram-negative organisms	39 (37.5)	31 (36.5)	8 (42.1)	.84
Enterobacter species	5 (4.8)	5 (5.9)	0	
Escherichia coli	10 (9.6)	8 (9.4)	2 (10.5)	
Klebsiella species	12 (11.5)	9 (10.6)	3 (15.8)	
Pseudomonas aeruginosa	4 (3.8)	4 (4.7)	0	
Other gram negatives	8 (7.7)	5 (5.9)	3 (15.8)	
Candida species	22 (21.2)	16 (18.8)	6 (31.6)	.36
Candida albicans	8 (7.7)	8 (9.4)	0	
Non-albicans species	14 (2.9)	8 (9.4)	6 (31.6)	
Acid-fast bacteria	2 (1.9)	1 (1.2)	1 (5.3)	1.00
Rapidly growing mycobacteria	2 (1.9)	1 (1.2)	1 (5.3)	
Polymicrobial	14 (13.5)	10 (11.8)	4 (21.1)	.48

MRSA, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-sensitive *S aureus*; *PICC*, peripherally inserted central catheter.
*$P \leq .05$ is considered significant.

Table 2
Patient characteristics of those included in the case-control study, stratified by type of catheter

	Antimicrobial catheter, n = 93 (%)	Nonantimicrobial catheter, n = 263 (%)	*P* value*
Race (AA)	37 (39.8)	98 (37.3)	.76
Sex (F)	44 (47.3)	146 (55.5)	.21
Age (mean y)	59	55	.17
Insertion team			
ID	75 (80.6)	24 (9.1)	<.0001
IR	0	237 (90.1)	NA
VAT	18 (19.4)	2 (0.8)	<.0001
Indication for PICC			
Antimicrobials	63 (67.7)	88 (33.5)	<.0001
Chemotherapy	5 (5.38)	28 (10.6)	.19
Total parenteral nutrition	12 (12.9)	62 (23.6)	.042
Tunneled catheter	12 (12.9)	8 (3.0)	.001
Comorbid conditions			
Myocardial infarction	8 (8.60)	45 (17.1)	.07
Congestive heart failure	9 (9.7)	36 (13.7)	.41
Peripheral vascular disease	1 (1.1)	5 (1.9)	.95
Cerebral vascular accident	9 (9.7)	21 (8.0)	.77
Dementia	1 (1.2)	4 (1.5)	.84
Chronic obstructive pulmonary disease	9 (9.7)	8 (1.5)	.021
Connective tissue disease	3 (3.2)	10 (3.8)	.95
Peptic ulcer disease	2 (2.2)	7 (2.7)	.91
Diabetes	20 (21.5)	74 (28.1)	.27
Chronic kidney disease	15 (16.1)	46 (17.5)	.89
Hemiplegia	1 (1.1)	7 (2.7)	.63
Leukemia	2 (2.2)	21 (8.0)	.085
Lymphoma	1 (1.1)	6 (2.3)	.78
Liver disease	7 (7.5)	13 (4.9)	.50
Solid tumor	20 (21.5)	24 (9.1)	.0033
AIDS	2 (2.2)	7 (2.7)	.91
Charlson score (mean)	2.01	2.36	.17

AA, African American; *F*, female; *ID*, infectious diseases; *IR*, interventional radiology; *NA*, not applicable; *PICC*, peripherally inserted central catheter; *VAT*, nurse venous access team.
*$P \leq .05$ is considered significant.

PICCs, PICCs used for chemotherapy, and PICCs for AIDS and leukemia were significant risk factors for PICC CLABSI.

Patient populations were different between NAIP and AIP groups, which was not surprising given that this was not a randomized trial; however, the Charslon comorbidity scores were not significantly different between the patient populations, which offers some support for our contention that there were no meaningful differences. Additional support was provided by the fact that the increased odds ratio for PICC CLABSI among patients with NAIP catheters remained highly significant in the final multivariate analysis.

The impact of AIP central venous catheters of various types on the incidence of BSI has been studied extensively. In vitro evidence has shown that the minocycline and rifampin combination may be better than the chlorhexidine gluconate and silver sulfadiazine combination against gram-positive and gram-negative bacteria and *Candida albicans*.[23] A higher protective activity of extended-spectrum AIP

Table 3
Patient characteristics (demographic and clinical) by PICC CLABSI

	Overall, n = 356 (%)	PICC CLABSI, n = 89 (%)	No PICC CLABSI, n = 267 (%)	*P* value*
Race (AA)	135 (37.9)	37 (41.6)	98 (36.7)	.41
Sex (F)	190 (53.4)	39 (43.8)	151 (56.6)	.04
Age (mean years)	56	54.9	56.8	.35
Type of catheter				
Nonantimicrobial catheter	263 (73.9)	75 (84.3)	188 (70.4)	.01
Antimicrobial catheter	93 (26.1)	14 (15.7)	79 (29.6)	
Insertion Team				
ID	99 (27.8)	24 (27.0)	75 (28.1)	.84
IR	237 (66.6)	60 (67.4)	177 (66.3)	1.0
VAT	20 (5.6)	5 (5.6)	15 (5.6)	1.0
Indication for PICC				
Antimicrobials	151 (42.4)	35 (39.3)	116 (43.4)	.50
Chemotherapy	33 (9.3)	20 (22.5)	13 (4.9)	<.0001
Total parenteral nutrition	74 (20.8)	16 (18.0)	58 (21.7)	.45
Tunneled catheter	20 (5.6)	12 (13.5)	8 (3.0)	.0002
Comorbid conditions				
Myocardial infarction	53 (14.9)	11 (12.4)	42 (15.7)	.44
Congestive heart failure	45 (12.6)	9 (10.1)	36 (13.5)	.41
Peripheral vascular disease	6 (1.7)	1 (1.1)	5 (1.9)	.63
Cerebral vascular accident	30 (8.4)	9 (10.1)	21 (7.9)	.51
Dementia	5 (1.4)	1 (1.1)	4 (1.5)	.79
Chronic obstructive pulmonary disease	17 (4.8)	1 (1.1)	16 (6.0)	.06
Connective tissue disease	13 (3.7)	4 (4.5)	9 (3.4)	.63
Peptic ulcer disease	9 (2.5)	1 (1.1)	8 (3.0)	.33
Diabetes	94 (26.4)	17 (19.1)	77 (28.8)	.072
Chronic kidney disease	61 (17.1)	19 (21.3)	42 (15.7)	.22
Hemiplegia	8 (2.2)	2 (2.2)	6 (2.2)	1.0
Leukemia	23 (6.5)	16 (18.0)	7 (2.6)	<.0001
Lymphoma	7 (1.97)	0	7 (2.6)	NA
Liver disease	20 (5.6)	5 (5.6)	15 (5.6)	1.00
Solid tumor	44 (12.4)	16 (18.0)	28 (10.5)	.06
AIDS	9 (2.5)	7 (7.9)	2 (0.75)	.0002
Charlson Score (mean)	2.28	2.75	2.10	.01

AA, African American; *CLABSI*, central line–associated bloodstream infection; *F*, female; *ID*, infectious diseases; *IR*, interventional radiology; *NA*, not applicable; *PICC*, peripherally inserted central catheter; *VAT*, nurse venous access team.
*$P \le .05$ is considered significant.

catheters against resistant pathogens compared with traditional antimicrobial catheters has also been reported.[24]

Tunneled cuffed catheters have been shown to have lower infection rates than nontunneled catheters.[19] The use of tunneled PICCs to lower infection rates was based on these studies and is unique to ID at our center. However, unexpectedly, a higher risk of CLABSI with the use of tunneled PICCs was found in our study. We believe that the significance of this difference is suspect because of the small number of tunneled catheters (n = 20) combined with widely divergent indications (morbid obesity, TPN for short gut, chemotherapy, axillary access required [usually in patients with chronic illnesses and multiple serious illnesses, etc]). TPN, chemotherapy, admission to the oncology ward, and active cancer have been shown to be independent risk factors for sepsis.[25-29] Our study supports chemotherapy and hematologic malignancy as risk factors for CLABSIs. Of note, a recent study showed a significantly lower rate of CLABSI among patients with hematologic malignancies who had a PICC (1.23/1,000 catheter days) compared with other types of catheters (5.3/1,000 catheter days).[27]

Table 4
Significant risk factors for PICC BSI by univariate and multivariate analysis

	Odds ratio	95% CI	*P* value*
Univariate analysis			
Sex (M)	1.67	1.03-2.71	.04
Nonantibiotic PICC	3.46	1.65-7.25	.001
Indication chemotherapy	5.66	2.68-11.96	<.001
Tunneled PICC	4.47	1.81-11.0	.001
Charlson score	1.15	1.03-1.28	.01
Leukemia	8.25	3.27-20.83	<.001
Multivariate analysis			
Nonantibiotic PICC	5.45	2.10-14.18	.0005
Indication chemotherapy	2.64	1.02-6.84	.05
Tunneled PICC	9.35	2.94-29.79	.0002
Leukemia	4.57	1.48-14.13	.008
AIDS	11.76	1.81-76.37	.01

BSI, bloodstream infection; *CI*, confidence interval; *M*, male; *PICC*, peripherally inserted central catheter.
*$P \le .05$ is considered significant.

Our multivariate analysis also indicates that AIDS is an independent risk factor for PICC CLABSI. Previous studies have shown an increased rate of infectious complications in AIDS patients,[30-33] although lower rates have also been reported.[33]

Our study has important strengths, including being 1 of 2 large studies of PICC CLABSIs to date (the other study was reported in the abstract only).[34] Moreover, all study participants benefited from the insertion of PICCs under the universal infection prevention methods and line maintenance bundle.

This study had limitations including the possibility of missed PICC infection events because of a patient's care taking place at another facility. This is expected to be minimal, however, with close collaborations with home health agencies and patients' follow-up care at MUSC. The retrospective nature of the data could affect the inference that was based on the available data. In addition, our study was not randomized, resulting in differences in patient populations receiving the 2 different types of PICC.

To our knowledge, this is the first study that directly compares the rates of infection among different operator groups, one of which was the ID division, which is unique in the literature. Although differences were noted in favor of ID and VAT versus IR in univariate analysis, those differences were not confirmed in multivariate analysis.

Current CDC and Infectious Disease Society guidelines suggest that AIP catheters be used only in settings of increased PICC CLABSI that do not respond to other preventative strategies.[12] The weight of evidence of this and other studies, especially the recent meta-analysis of Kramer et al[5] supports the universal use of AIP catheters rather than limiting their use to high-risk settings. It is unfortunate that there is only 1 small randomized controlled but underpowered trial[35] to support this point. Whether it will ever be feasible to do such a study, which would require several years and significant funding from a noncommercial source, remains to be seen.

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