

## ORIGINAL ARTICLE

# Catheter related bloodstream infection following PICC removal in preterm infants

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**Objective:** Describe the incidence of catheter-related blood stream infection (CRBSI), following removal of peripherally inserted central venous catheters (PICC) in preterm infants.

**Study Design:** A retrospective cohort study of infants <29 weeks gestational age with a PICC revealed 101 PICCs placed (2159 PICC days). Patients were hospitalized in a level III Neonatal Intensive Care Unit (NICU) between January 2002 and December 2003.  $\chi^2$  analysis was performed.

**Results:** One infection was detected after the removal of a PICC (1 per 202 days). Ten infants had a CRBSI attributed to a PICC (1 per 216 PICC days). CRBSI during indwelling PICC was associated with increased risk for sepsis evaluation after PICC removal ( $P < 0.05$ ).

**Conclusions:** The incidence of CRBSI in the 48 h following PICC removal was not different than the incidence of CRBSI while a PICC was in-dwelling. There was no evidence from this study to support antibacterial prophylaxis before PICC removal.

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**Keywords:** peripherally inserted central venous catheter; catheter-related bloodstream infection; prematurity

## Introduction

Peripherally inserted central venous catheters (PICC lines) are widely used and thought to be valuable in the management of extremely premature infants.<sup>1</sup> The presence of an indwelling PICC line increases the risk for systemic bacterial infections, termed catheter-related blood stream infections (CRBSI). CRBSIs are an important cause of morbidity and mortality in premature infants.<sup>2</sup> The Centers for Disease Control and Prevention define CRBSI as any bloodstream infection (BSI) that occurs although a central venous catheter is in place and up to 48 h after its removal.<sup>2</sup>

The majority of CRBSIs seen in infants are caused by coagulase negative *Staphylococci*.<sup>3</sup> Several efforts have been undertaken to prevent CRBSIs with antibiotic prophylaxis but have either been inconclusive or controversial.<sup>4–6</sup> PICC lines are prone to colonization with infectious agents that may inhabit a thrombus at the catheter tip. There is to date no evidence which supports the practice of administering antibiotics through the PICC line just before removal of the PICC line to avoid septic dissemination. The generation of antibiotic-resistant bacteria will remain a concern without an evidence-driven strategy for the use of vancomycin.

The incidence of CRBSI within 48 h after PICC line removal has not been examined. The purpose of this cohort study was to examine the incidence of CRBSI after PICC removal and to identify risk factors associated with CRBSI and clinical deteriorations leading to sepsis evaluations within 48 h of PICC removal.

## Methods

The objective of this retrospective review was the identification of the incidence of CRBSI in premature infants treated with the assistance of a PICC line and focusing on the 48 h following PICC removal. Identification of patient characteristics and treatment modalities that may modulate CRBSI was also undertaken.

Eligible patients were consecutive outborn infants transferred to the level III NICU at Cardinal Glennon Children's Hospital in the calendar years 2002 to 2003 with gestational age less than 29 completed weeks. Infants were ineligible if they did not have a PICC placed during their NICU hospitalization or if they died before the PICC removal.

Insertion of PICC lines was performed as described.<sup>7</sup> Silicone, single lumen PICC lines were placed under sterile technique, using gown and sterile gloves, after assessing the best possible peripheral blood vessel. All lines were placed percutaneously and monitored by a dedicated team of neonatal nurse practitioners. Povidone iodine was used as the topical antiseptic in all cases. No topical antibiotics were used. No antibiotic prophylaxis was administered for PICC placement. PICC insertion sites and hubs were kept under sterile occlusive dressings. Three-way stopcocks connecting IV

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administration sets to PICCs were changed every 72 h, or 24 h if the PICC was used for TPN infusion. Heparin was used during periods of continuous infusion (1 U/ml) and periods of intermittent infusions (30 U/ml every 8 h). The sites were monitored daily. Dressings were changed if the line position was altered, if leakage or bleeding were noted under the occlusive dressing, or if the occlusive dressing became loose. Dressing changes were performed under sterile conditions. No blood products were administered through the PICCs. There were no changes in PICC insertion or maintenance practice during this study period.

Data for collection were prospectively identified and included total days of indwelling PICC, days of antibiotics through PICC, days of TPN through PICC, BSI within 48 h of PICC removal, gestational age of infants and their birth weight, method and location of PICC placement, infections noted during the period of indwelling PICC, sepsis evaluations within 48 h of PICC removal and catheter tip culture results. Sepsis evaluations were defined as complete blood count and blood culture. If a sepsis evaluation was undertaken, empiric antibiotic therapy was initiated and continued until blood culture showed no growth for at least 48 h. The Centers for Disease Control and Prevention define CRBSI as any BSI that occurs while a central venous catheter is in place and up to 48 h after its removal.<sup>2</sup> PICC manipulation was defined as dressing change, changing the internal position of the line, or managing a cracked hub.

Bacterial infections during the period of indwelling PICC were tabulated as well as their etiologic agents. Only culture proven bacterial infections treated with antibiotics were included in the primary analysis. Decisions to treat with antibiotics were made by the attending of record caring for the infant.

Statistics were performed with SPSS software (12.0 version, Chicago, IL, USA).  $\chi^2$  analysis was performed to compare outcome frequencies between defined groups. This research was reviewed by the St Louis University Institutional Review Board. Informed consent was exempted.

## Results

During the 2002 to 2003 calendar years, 177 infants who met the criteria for review were admitted to the level III NICU at Cardinal Glennon Children's Hospital. There were 31 deaths before discharge from the nursery (17.5%); 146 infants survived to discharge, and 108 (74%) infants had at least one PICC placed. Two infants died before PICC removal. Thirteen PICC lines were excluded because antibiotics were administered through the line just before removal as prophylaxis against CRBSI. There were no sepsis evaluations following PICC removal for this group. Four infants had more than one PICC placed during their NICU stay. In all, 101 PICC lines were reviewed during the study period (2159 PICC days).

Descriptive information is shown in Table 1. The average birth weight of infants with PICC lines in this study was 824 g; 25% of

**Table 1** Descriptive statistics of PICC lines placed during study period

	Percentiles		
	Mean	25th	75th
Birth weight of patient (g)	824	640	947
Duration of PICC (days)	21.4	11	25
Number of days after birth when PICC placed	12.4	5	9
Number of days of TPN through PICC	16.1	7	20
Number of days of antibiotics through PICC	7.6	2	13
Number of days with intermittent infusion through PICC	4.3	1	6
Number of days with no antibiotics before removal	7.2	2	12
Previous central venous catheter	63/101 (62.4%)		
Concurrent central venous catheter	21/101 (20.8%)		
PICC placed below umbilicus	15/101 (14.9%)		
PICC placed during day shift	67/101 (66.3%)		
Antibiotics given through PICC	83/101 (82.2%)		
Corticosteroids during in-dwelling PICC	42/101 (41.6%)		
BSI detected before PICC	3/101 (3%)		
Other infection during in-dwelling PICC	30/101 (29.7%)		
Manipulated	33/101 (32.7%)		

Abbreviations: BSI, blood stream infection; PICC, peripherally inserted central venous catheters; TPN, total parental nutrition.

infants weighed less than 640 g at birth, and 75% of lines were placed by 9 days after birth. The average duration of indwelling PICC was 21 days (range 5 to 91 days); 75% of lines had an indwelling duration of less than 25 days. Total parental nutrition (TPN) and lipid infused through 99 PICC lines (98%) with an average of 16.1 days infusion.

Many of the PICC lines had antibiotic infusions (83 of 101 lines). 17 PICC lines had antibiotic infusions within 72 h of removal. Three out of those 17 had a sepsis evaluation within 48 h of removal. Approximately 33% of the PICC lines were manipulated. Infusing any antibiotics in the 72 h preceding PICC removal was not associated with less sepsis evaluations within 48 h of PICC removal.

A single infant had a CRBSI identified within 48 h of PICC removal. This infant was born at 28 weeks gestation weighing 970 g. An umbilical venous catheter had been placed shortly after birth and was removed after PICC position was confirmed. There was no evidence of BSI before PICC placement. A PICC was placed 7 days after birth and remained in-dwelling for 9 days. A sepsis evaluation was performed 36 to 48 h after PICC removal as a response to rapidly developing respiratory failure, hemodynamic instability and acidosis following a single episode of feeding intolerance. Further evaluation revealed NEC with pneumoperitoneum. A blood culture taken at that time grew oxacillin-sensitive *Staphylococcus aureus* within 24 h.

There were six sepsis evaluations within 48 h of PICC removal. The reasons for these sepsis evaluations were as follows: respiratory

failure (four), apnea (one) and feeding intolerance (one). The history of a CRBSI noted during PICC life was associated with more frequent sepsis evaluations within 48 h of PICC removal (Table 2). None of the other factors evaluated was associated with sepsis evaluations performed more frequently following PICC removal.

There were nine CRBSI noted during the period of indwelling PICC (1 per 239 PICC days). The rate of CRBSI noted within 48 h

of PICC removal was nearly identical (1 per 202 days). If the days following catheter removal were not counted as PICC days, the overall CRBSI rate was 1 per 216 days. The infectious agents isolated were coagulase negative *Staphylococcus* (three), oxacillin-sensitive *aureus*, (three), oxacillin-resistant *aureus* (two), *Escherichia coli* (one) and *Candida* (one). A birth weight of less than 641 g (the lower quartile of birth weight) was associated with increased risk of CRBSI during the period of indwelling PICC (Table 3), but not with CRBSI detected within 48 h of PICC removal. None of the other factors evaluated was associated with CRBSI during the period of in-dwelling PICC.

Culture proven bacterial infections other than BSI occurred in approximately 30% of cases before PICC removal. Most infections were positive tracheal aspirate cultures with a clinical diagnosis of pneumonia or tracheitis (25/30 infections). The etiologic agents were *aureus*, coagulase negative *Staphylococcus*, *coli* and *Candida*. Of note, five infants with pneumonia/tracheitis and CRBSI in this study grew the same bacteria from both tracheal aspirate and blood cultures. These organisms were not subtyped. However, other infections were not associated with CRBSI during the period of in-dwelling PICC.

## Discussion

PICC removal appears to have no increased risk of infection. In this study, the rate of CRBSI related to PICC lines for infants less than 29 completed weeks gestation at birth was 1 per 233 days. The 2002 Centers for Disease Control Morbidity and Mortality Report titled 'Guidelines for the Prevention of Intravascular Catheter-Related Infections' indicated the rate of CRBSI was 1 per 91 days of central venous catheter in preterm infants.<sup>2</sup> Personal communications have revealed that despite a lack of evidence, some practitioners elect to use antibiotic prophylaxis before PICC removal to prevent CRBSI. The rate of CRBSI detected after PICC

**Table 2** Association with sepsis evaluation within 48 h of PICC removal

Factor	Number with sepsis evaluations (%)	$\chi^2$	P-value
<i>Birth weight</i>			
<750 g	2/45 (4.4%)	0.33	>0.05
>750 g	4/56 (7.1%)		
<i>Birth weight</i>			
<640 g	1/25 (4%)	0.22	>0.05
>640 g	5/76 (6.6%)		
<i>PICC hepllocked</i>			
>3 days before removal	2/45 (4.4%)	0.33	>0.05
<3 days before removal	4/56 (7.1%)		
PICC manipulated before removal	2/33 (6.1%)	0.01	>0.05
Not manipulated	4/68 (5.9%)		
Steroids given before PICC removal	2/42 (4.8%)	0.18	>0.05
None given before PICC removal	4/59 (6.8%)		
<i>In-dwelling PICC</i>			
>25 days	1/27 (3.7%)	0.33	>0.05
<25 days	5/74 (6.8%)		
No antibiotics given within 24 h of PICC removal	4/88 (4.5%)	2.38	>0.05
Antibiotics given within 24 h of PICC removal	2/13 (15.4%)		
No antibiotics given >72 h before PICC removal	3/76 (3.9%)	2.18	>0.05
Antibiotics given within 72 h of PICC removal	3/25 (12%)		
<i>Infections</i>			
BSI before PICC placement	0/3 (0%)	0.2	>0.05
No BSI before PICC placement	6/98 (6.1%)		
CRBSI during in-dwelling PICC	2/9 (22.2%)	4.69	<0.05
No CRBSI during in-dwelling PICC	4/92 (4.3%)		
Other infection during in-dwelling PICC	3/30 (10%)	1.26	>0.05
No other infection during in-dwelling PICC	3/71 (4.2%)		

Abbreviations: BSI, blood stream infection; CRBSI, catheter-related blood stream infection; PICC, peripherally inserted central venous catheters.

**Table 3** Association with CRBSI noted during period of in-dwelling PICC

Factor	$\chi^2$	P-value
Birth weight<750 g	0.48	>0.05
Birth weight<640 g	5.03	<0.05
Steroids given before PICC removal	1.53	>0.05
PICC life>25 days	1.23	>0.05
Manipulation of PICC before removal	0.62	>0.05
<i>Infection</i>		
BSI noted before PICC placement	2.27	>0.05
Other infection during in-dwelling PICC	3.16	>0.05

Abbreviations: BSI, blood stream infection; CRBSI, catheter-related blood stream infection; PICC, peripherally inserted central venous catheters.

line removal was equivalent to the overall rate of CRBSI in this study.

More sepsis evaluations occurred after PICC removal for patients with a history of a previous CRBSI. The reason for this is unclear. The majority of the sepsis evaluations occurred in response to a clinical respiratory event. The infant with a CRBSI detected within 48 h of PICC removal did not have a CRBSI suspected or detected during the period of indwelling PICC. Need for increased respiratory support, apnea and feeding intolerance have been identified in a previous study as clinical indicators of late onset sepsis for infants born prematurely.<sup>8</sup>

In a review of the available literature, CRBSI rate ranges from 1 per 54 days to 1 per 1100 days.<sup>6</sup> These studies evaluated infants with higher birth weights, averaging greater than 1000 g. Birth weight less than 640 g was associated with increased incidence of CRBSI related to PICC line in this study. This finding is consistent with the observation that birth weight is inversely related to the incidence of any BSI.<sup>2</sup>

Previous studies<sup>9,10</sup> have shown an increased incidence of CRBSI with increasing catheter in-dwelling duration. After a 2000 internal review of PICC management, our NICU changed its policy to include increased surveillance for aseptic technique during placement and management of PICC lines. This change in policy has resulted in a greatly decreased CRBSI rate attributed to PICCs. This may explain why we did not see an increased CRBSI rate for PICC lines in-dwelling greater than 25 days.

Being born very small was associated with coexistent infections, perhaps owing to longer duration of mechanical ventilation. Coexistent infection has been shown to be independently related to CRBSI in adult populations.<sup>11</sup> Cases of CRBSI with a coexistent infection had the same bacteria type isolated from blood culture and tracheal aspirate culture. Colonization with opportunistic agents may have contributed to CRBSI in this group of infants.

Some cases of CRBSI were not included in this study because of infant mortality before PICC removal. The retrospective design of this study may not answer the question of whether the incidence of sepsis evaluations after PICC removal warrants intervention. The threshold for sepsis evaluation in this patient population was not prospectively standardized, but there was a consistent approach to initiating sepsis evaluations across practitioners. The majority of sepsis evaluations occurred following changes in ventilation or oxygenation as determined by capillary blood gas and pulse oximetry. Another limitation of this study is that the rate of an unusual event may be mis-estimated. Small numbers in the subgroups may have altered the impact of particular factors.

This study shows that the risk of CRBSI noted after the PICC removal is no greater than the risk of CRBSI during the period of indwelling PICC in this patient population. Antibiotic prophylaxis against CRBSI following PICC removal cannot be recommended based on this study. A large prospective trial with standardized indications for sepsis evaluation may provide more accurate information about the incidence of CRBSI following PICC removal.

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