Nosocomial catheter-related bloodstream infections in a pediatric intensive care unit: Risk and rates associated with various intravascular technologies*

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LEARNING OBJECTIVES

On completion of this article, the reader should be able to:

1. Identify factors associated with catheter-related bloodstream infections in the pediatric intensive care unit.
2. Recall that the use of extracorporeal life support is associated with a greater than tenfold increase in developing a bloodstream infection in the pediatric intensive care unit.
3. Recall that the use of multiple catheters is associated with an increased infection risk.

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Objective: **Nosocomial bloodstream infections are associated with increased patient morbidity, mortality, and hospital costs. More than 90% of these infections are related to the use of intravascular catheter devices. This study was done to assess the risk and rates of catheter related-bloodstream infections (CR-BSI) associated with different intravascular technologies in a pediatric intensive care unit population.**

Design: **Retrospective cohort study.**

Setting: **A 16-bed pediatric intensive care unit in a tertiary children's hospital.**

Study Population: **All admissions between July 1997 and December 1999 requiring placement of an intravascular access device for care were examined. Patients with CR-BSI were identified through ongoing surveillance using Centers for Disease Control/National Nosocomial Infections Surveillance System definitions for bloodstream infection.**

Interventions: **None.**

Measurements and Main Results: **Of the 2,728 admissions during the review period, 1,043 (38.3%) required placement of an intravascular access device. Bivariate analysis revealed that patients who required intravascular cannulae for extracorporeal life support had a 10-fold increased risk of developing a CR-BSI, and patients requiring vascular access for renal replacement therapy demonstrated a 4-fold increase in the risk of developing CR-BSI compared with the referent group. There was a significant increase in the CR-BSI rate associated with the use of more intravascular access devices per patient admission. Multivariate logistic regression identified the use of extracorporeal life support therapy and the total duration of use of intravascular access devices as significant independent predictors of CR-BSI when controlling for other predictors.**

Conclusion: **The use of extracorporeal life support therapy, the presence of multiple intravascular access devices, and the total duration of intravascular access device use were associated with an increase in the rate and risk of developing CR-BSI in our pediatric intensive care unit population. Larger, prospective studies may help elucidate additional factors responsible for these observations. (Pediatr Crit Care Med 2003; 4:432–436)**

KEY WORDS: nosocomial; catheter; bloodstream infections; pediatric intensive care; risk; rate

An estimated 200,000–400,000 nosocomial bloodstream infections (BSIs) occur annually in the United States, and >90% are associated with the use of intravascular catheter devices (1). These infections vary in occurrence from 2.1 BSIs per 1000 central catheter days in respiratory intensive care units (ICUs) to 30.2 per 1000 central catheter days in burn ICUs (2). Catheter related BSIs (CR-BSIs) are associated with increased morbidity, mortality, and medical costs (3–7).

Previous studies, involving adult populations, have reported an increased risk of infection in patients receiving hemodialysis or extracorporeal life support (ECLS) higher than that observed in patients with central vascular catheters

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inserted for other indications (8–10). Several factors have been described in the adult population as playing a role in the occurrence of nosocomial CR-BSI. These factors include prolonged catheterization, poor aseptic insertion technique, emergent catheter placement, size of catheter, number of lumens, type of catheter material, location of catheter, and frequency of catheter manipulations (catheter factors) (11). Other factors include presence of an infusion therapy team, use of sterile barrier precautions, type of insertion site dressing, and frequency of system entry (hospital factors). Patient-related factors have also been identified, which include age, granulocytopenia, immune suppression, and severity of underlying disease.

Certain risk factors for pediatric nosocomial infections, as a whole, have been described (12); however, no assessment of the risk of CR-BSI related to the use of various intravascular technologies has been reported at the present time in the pediatric population. This study was performed to estimate the risk and rates of CR-BSI associated with the utilization of various intravascular technologies and the presence of multiple catheters in a critically ill pediatric population. We hypothesized that the use of ECLS and renal replacement therapy (RRT) technologies would be associated with increased occurrence of CR-BSI.

MATERIALS AND METHODS

This was a retrospective cohort study approved by the University of Michigan Medical Center's Institutional Review Board. The study population consisted of all patients admitted to our pediatric ICU (PICU) who required use of central intravascular catheters for medical management. The study population was identified retrospectively by examining quality assurance data that had been collected prospectively at all PICU admissions at our institution. The quality assurance data include information related to intravascular access devices such as the number, type, and duration of device use, operative status, use of total parenteral nutrition, and length of PICU stay before the onset of bloodstream infection. Admissions to the PICU included new admissions, readmissions, and transfers. Patients >18 yrs of age and cardiac patients not receiving ECLS, who would otherwise be housed in our cardiac surgery ICU, were excluded.

Patients with CR-BSI were identified through active surveillance by the hospital's Infection Control and Epidemiology Unit, using Centers for Disease Control's National Nosocomial Infections Surveillance System definitions for blood stream infection. Each case of CR-BSI represented a new episode of suspected CR-BSI in those patients utilizing intravascular access devices during their stay in the PICU. To document CR-BSI, blood samples sent for culture were drawn from the patient's central vascular catheter at the discretion of the physicians caring for each patient. Catheter segments were not routinely sent for culture, as it is not part of routine surveillance practice at our institution. Our Critical Care Support Service database of patient admissions requiring placement of an intravascular access device over a 30-month period from July 1, 1997, to December 31, 1999, were matched to the Infection Control and Epidemiology records for the same period.

Data on all catheter types were routinely recorded as part of the Critical Care Support Service quality assurance monitoring. A subgroup of intravascular access devices, including nontunneled central venous catheters, peripherally inserted central venous catheters, and umbilical vascular catheters, were used for reference comparison (referent group) of risk and rates between intravascular access device types. The referent group was chosen as a convenience cohort, the composition of which was reflective of the catheter insertion frequencies in our PICU. The catheters had similar infection rates and were comprised of nontunneled central venous catheters (93%), peripherally inserted central venous catheters (6%), and umbilical catheters (1%). The similarity in infection rates from surveillance data in the PICU made the group an homogeneous sample ideal as a reference group in our study. Arterial catheters were excluded from our analysis.

Definitions

For the purpose of this study, specific definitions were made *a priori*.

Catheter Types. Tunneled catheters were defined as surgically implanted, cuffed, and tunneled central venous catheters used to provide vascular access for prolonged intravenous therapy. RRT catheters were defined as dual or triple-lumen catheters placed percutaneously or surgically for intermittent hemodialysis or continuous veno-venous hemofiltration. ECLS catheters were placed percutaneously or surgically for either veno-venous or veno-arterial ECLS.

ICU-Associated Infection. An infection in a National Nosocomial Infections Surveillance System ICU patient that was not present or incubating at the patient's admission to the ICU but became apparent during the ICU stay or within 48 hrs after transfer from the ICU (13).

CR-BSI. CR-BSI was defined as a primary bloodstream infection in a patient with an intravascular access device that was used within the 48-hr period before the onset of infection (13). Infections that developed within 24 hrs of PICU admission were not considered CR-BSI acquired during the PICU admission. Definitions of catheter-associated infections as used in this study were as follows: ECLS-associated infections were infections occurring in patients receiving ECLS, regardless of the other types of indwelling intravascular catheters. RRT-associated infections were those occurring in patients receiving RRT through an RRT catheter described above (excludes patients receiving ECLS because a separate dialysis catheter placement is not required in this setting). Tunneled catheter–associated infections were those occurring in patients with tunneled catheters only.

Statistical Analyses

Descriptive analyses were performed to characterize the patient population, reporting mean values with standard deviations, and median values with ranges. Chi-square test for equal proportions was used for all bivariate comparisons of the risk and crude rates of CR-BSI associated with the different types and numbers of intravascular access devices examined in this study. A p value $\leq .05$ was considered statistically significant. Independent predictors identified in the bivariate analysis were included in a multivariate logistic regression model to identify final predictors for CR-BSI while controlling for each covariate. Interaction between the candidate predictors was examined, and no interaction of statistical significance was found. All analyses were conducted using a commercially available statistical software package (SPSS version 10.0 for the PC, SPSS, Chicago, IL).

RESULTS

A total of 2,728 admissions to the PICU were identified during the 30-month period of study from July 1, 1997, to December 31, 1999. A total of 1,043 admissions (38.3%) involved use of intravascular access devices for patient care and constituted the study population. The mean age of the population was 6.7 yrs (median, 4.1 yrs; range, 0–18 yrs). Five hundred thirty-eight admissions (52%) were associated with patients who had an operative procedure performed, and 440 admissions (42%) were associated with patients requiring mechanical ventilation during their PICU stay. Table 1 describes the use of intravascular access devices in the study population.

A total of 44 cases of CR-BSI were identified, and Table 2 shows the bivariate associations between the use of the intravascular access devices and the risk and rates of CR-BSI. As shown, patients

receiving ECLS (92 admissions) and RRT (171 admissions) had 10- and- 4-fold increased risk, respectively, of developing a CR-BSI as compared with the referent group of patients.

The rate and risk (as estimated by the risk ratio) of acquiring CR-BSI increases with the number of intravascular access devices utilized per patient admission, as shown in Table 3. During a PICU admission, the use of two intravascular devices at any time was associated with a 5.5-fold increase in the risk of developing a CR-BSI, and a 12-fold increase in risk was associated with the use of three or more intravascular devices. Rates of CR-BSI expressed per 1000 device days were 4.0, 12.1, and 20.1 in association with the utilization of one, two, or three or more intravascular access devices, respectively.

Table 4 depicts a full multivariate logistic regression model of CR-BSI, which incorporates factors identified in the bivariate analyses and controls for potential confounding effects of additional factors. In this model, only ECLS use and total duration of intravascular access device use were observed to be statistically associated with CR-BSI.

DISCUSSION

This study highlights certain important observations regarding the use of specific central intravascular access devices. During a single PICU admission, higher risk and rates of CR-BSI are associated with the use of ECLS therapy, the use of multiple central intravascular access devices, and the duration of use of such access devices.

The Centers for Disease Control's National Nosocomial Infections Surveillance System has reported a national PICU pooled mean CR-BSI rate of 7.7 per 1000 catheter days (3.9–11.9) for the period January 1995 through April 2000 (14). Singh-Naz et al. (12) also reported a rate of 16.8 per 1000 catheter days at a single tertiary PICU. In our study, we have observed rates ranging from 3.3 to 22.1 CR-BSI per 1000 device days, the higher rates being in patients receiving ECLS and the lower rates in the referent group of patients with catheters other than ECLS, RRT, and tunneled catheters.

Adult patients receiving ECLS have been reported to have an increased rate of BSI. Rates as high as 90.9 cases per 1000 ECLS days after 31–40 days of ECLS have been reported (8). Several factors have been postulated to contribute to increased risk of nosocomial infection in ECLS patients, including the presence of multiple indwelling vascular catheters, presence of an open chest, undergoing major operative procedures before or while receiving ECLS (15, 16), and leukopenia (17). ECLS patients often have multiple other vascular catheters, and the individual contribution of these other catheters to the prevalence of CR-BSI is difficult to ascertain.

Our study is consistent with previous reports that have associated longer duration of intravascular catheter use with higher CR-BSI rates (19–22). Reasons for this finding include operator characteristics and catheter, patient, and hospital

Table 1. Intravascular access device use in the study population

Device	No. of Admissions with Device (%)	Duration of Device Use, Days	
		Mean ± SD (Median)	Range
ECLS	92 (9)	7 ± 5 (6)	1–29
RRT	171 (16)	6 ± 7 (3)	1–55
Tunneled	284 (27)	7 ± 12 (4)	1–109
Referent group	779 (75)	6 ± 6 (4)	1–55

ECLS, extracorporeal life support; RRT, renal replacement therapy.

Table 2. Risk and rate of catheter related-bloodstream infections (CR-BSI) by intravascular access device type

Device Type	Patient Admissions, n	Device Days	Crude CR-BSI Risk (%)	RR (95% CI)	CR-BSI Rate per 1000 Device Days
ECLS	92	679	15/92 (16.3)	9.8[a] (2.3–41.3)	22.1[a]
RRT	171	829	11/171 (6.4)	3.9[a] (1.1–15)	13.3[a]
Tunneled	237	1743	9/237 (3.8)	2.3 (0.8–6.7)	5.2
Referent group	543	2765	9/543 (1.7)	—	3.3

RR, risk ratio; CI, confidence interval; ECLS, extracorporeal life support; RRT, renal replacement therapy.

[a] $p < .05$; Pearson's chi-square test for bivariate comparisons.

Table 3. Risk and rate of catheter related-bloodstream infections (CR-BSI) by number of intravascular access devices

No. of Devices	Patients, n	Device Days	Crude CR-BSI Risk (%)	RR (95% CI)	Rate of CR-BSI per 1000 Device Days
1	786	4025	16/786 (2.0)	—	4.0
2	233	2147	26/233 (11.2)	5.5[a] (1.3–23.0)	12.1[a]
≥3	24	298	6/24 (25.0)	12.4[a] (3.0–50.1)	20.1[a]

RR, risk ratio; CI, confidence interval.

[a] $p < .05$; Pearson's chi-square test for bivariate comparisons.

Table 4. Multivariate logistic regression model of factors associated with catheter related-bloodstream infections

Variable	Beta Coefficient	*p* Value	Adjusted Odds Ratio	95% Confidence Interval
Age, yrs	0.030	.304	1.030	0.973–1.090
CVC duration, days	0.104	<.001[a]	1.110	1.070–1.151
Tunneled	0.060	.905	1.061	0.397–2.835
RRT	0.846	.077	2.330	0.914–5.940
ECLS	1.013	.047[a]	2.753	1.013–7.487
Mechanical ventilation	0.192	.705	1.212	0.448–3.280
Hyperalimentation	0.165	.707	1.180	0.498–2.797

CVC, central venous catheter; RRT, renal replacement therapy; ECLS, extracorporeal life support.

[a] $p < .05$.

factors mentioned previously. The formation of a biofilm as a host reaction to the presence of a catheter is known to occur within 24 hrs of catheter insertion. The extent of biofilm formation and colonization is known to increase with longer duration of catheter use (23).

The association of CR-BSI with use of RRT therapy, in unadjusted bivariate analyses, was not observed to be a predictor of CR-BSI in the multivariate analysis ($p = .07$). We cannot exclude limited sample size as being the reason for this observation, as there were only 11 cases of CR-BSI associated with the use of RRT catheters. As in our study, Souweine et al. (18) also failed to observe any difference in the rates of catheter-related bacteremia when comparing BSI rates between central venous catheters and dialysis catheters; of 381 hemodialysis catheters inserted in 170 patients, only three patients developed CR-BSI.

We found no difference in the rate of CR-BSI in our patients with tunneled catheters compared with the referent group. Broviac catheters, a type of tunneled catheter, are associated with a low prevalence of bacteremia, a characteristic thought to be related to the use of a subcutaneous tunnel before entering the vein. The presence of a Dacron cuff is believed to promote formation of fibrous adhesions, which in turn stabilize the catheter and form an effective seal against contaminating bacteria that may colonize the catheter and subsequently cause bacteremia (24).

Similar to a recent single-center PICU study by Yogaraj et al. (25), we demonstrated an increase in the risk of developing BSI with the use of multiple central intravascular access devices during a PICU admission. Our study went further to assess the relationship between the use of intravascular technologies like ECLS and RRT and the risk of developing CR-BSI. Critically ill patients, as in this study, are prone to the development of multiple system organ dysfunction, often necessitating the placement of multiple vascular catheters.

Potential shortcomings of this study should be noted. Appropriate risk adjustment of the results, based on an assessment of multiple patient diagnoses and severity of illness, could not be fully done. Although the Pediatric Risk of Mortality (PRISM) III score is routinely utilized in our PICU currently, it was not available for a significant portion of the study period because of the logistic reasons such as transition from PRISM to PRISM III. The association of PRISM score with increased prevalence of CR-BSI has been previously suggested (26). However, in the study by Yogaraj et al. (25), severity of illness, as measured by the PRISM score, underlying illnesses, and medications, was not associated with increased risk of nosocomial bloodstream infection.

PRISM is calculated based on information available during the first 24 hrs of admission into the PICU. The placement of catheters for ECLS and RRT may occur several days after admission in a subset of patients who fail to improve. Furthermore, ECLS patients treated at our center are sometimes placed on this technology at a referring center before transfer or in the operating room before PICU admission. It is quite possible that the use of ECLS, RRT therapy, and multiple catheters are associated with patient severity of illness. Yeh et al. (27) reported the use of the Therapeutic Intervention Scoring System, which utilizes intensity of care provided, to correlate to severity of illness in a pediatric population. Grouping simply by intravascular technology use (ECLS, RRT, etc.) would have major advantages in terms of simplicity of measurement and comparison of CR-BSI rates between centers. However, future studies should investigate the potential effect of using this pediatric-specific severity of illness mortality prediction score on the occurrence of CR-BSI in the different intravascular device groups examined in this report.

Previously published studies have identified several methods in the diagnosis of CR-BSI, pioneered by Maki et al. (28). These include quantitative cultures of both surfaces of the catheter segment and *in situ* cultures. Our study did not routinely obtain semiquantitative culture of the intracutaneous segment of vascular catheters; however, we did perform blood cultures with catheters *in situ*. The presence of a positive culture result via this method without culturing the catheter itself could arguably manifest catheter colonization in some of our patients and lead to higher rates of CR-BSI as reported in this study. The patients in our report, however, had clinical manifestations of bacteremia and no other apparent source of bloodstream infection, as determined by our Infection Control and Epidemiology personnel who utilized the Centers for Disease Control's National Nosocomial Infections Surveillance System criteria to identify patients with CR-BSI. Removal of intravascular access devices in patients with a presumptive diagnosis of CR-BSI is problematic in pediatric patients because of limited venous access. Also, ECLS catheters can only be removed when this therapy is discontinued, as the patients are heparinized.

The use of extracorporeal life support therapy, the presence of multiple intravascular access devices, and the total duration of intravascular access device use were associated with an increase in the rate and risk of developing catheter related-bloodstream infections in our pediatric intensive care unit population.

Catheter- and patient-related factors could confound the relationship between our significant independent predictors (duration of catheter use and ECLS use) and the risk of developing CR-BSI. These factors have been associated with CR-BSI in previous studies (11). As stated earlier in the introduction, catheter factors include a spectrum from catheter material, which may promote thrombogenesis and adherence of organisms, to the technique and location of catheter insertion, and patient-related factors include immunosuppression, severity of underlying disease, age, and granulocytopenia.

The authors were restricted to the data contained in the databases, which, although prospectively gathered, were used primarily for quality assurance purposes. The authors advocate for the conduct of an adequately powered prospective study with adjustment for these factors in critically ill children.

In conclusion, this study has highlighted the seemingly obvious contention that the risk and rates of CR-BSI are increased with the use of multiple intravascular access devices in the critically ill pediatric population. As hypothesized, the use of intravascular technologies, specifically

ECLS, was associated with increased risk and rates of CR-BSI in our study population. The duration of use of intravascular access devices and ECLS use were predictive of increased risk of developing CR-BSI. The results of this study will need to be confirmed in larger prospective studies that control for several factors, including patient diagnosis, severity of illness, presence of multiple catheters, duration of catheter use, and the use of various intravascular technologies. Furthermore, potential confounding factors for the development of CR-BSI, including immunosuppression and granulocytopenia, will also need to be adjusted for. Comparison of pediatric CR-BSI rates for bench-marking purposes between hospitals should consider types and numbers of intravascular technologies utilized.

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