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Central Venous Catheter Repair is Associated with an Increased Risk of Bacteremia and Central Line Associated Bloodstream Infection in Pediatric Patients

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Abstract

Background—Repair of broken central venous catheters (CVCs) is common in pediatric patients. We hypothesized that this practice predisposes to bacteremia and CVC-associated bloodstream infections (CLABSI).

Methods—We conducted a retrospective case-crossover study of pediatric patients aged 1 month to 21 years with CVC breakages who underwent a first-time repair at our institution, using repair kits provided by CVC manufacturers. We compared rates of bacteremia and CLABSI (defined by Centers for Disease Control and Prevention criteria) in the 30 days pre-repair (control period) and the 30 days post-repair (exposure period), with adjustment for within-patient correlation using conditional Poisson regression.

Results—The mean pre-repair rate of bacteremia was 9.9 per 1000 catheter days, which increased to 24.5 post-repair, resulting in an adjusted incidence rate ratio (IRR) of 1.87 (95% CI 1.05 – 3.33, p = 0.034). Risk of CLABSI demonstrated a greater than two-fold increase (IRR 2.15, 95% CI 1.02 – 4.53, p = 0.045) when all catheter days were included, and a four-fold increase when days on antibiotics were excluded (IRR 4.07, 95% CI 1.43 – 11.57, p = 0.008).

Conclusions—We found that repair of a broken CVC was associated with a two to four-fold higher risk of developing CLABSI within 30 days of repair in pediatric patients. Further studies are needed to determine interventions to reduce this risk and to better define the relative merits of CVC repair compared with replacement in selected patient populations.

Keywords

central venous catheter; bloodstream infection; line repair; breakage; repair

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INTRODUCTION

Central venous catheters (CVCs) are a mainstay of medical therapy for many critically or chronically ill pediatric patients, allowing prolonged vascular access for the delivery of fluids, parenteral nutrition, or medications. However, use of CVCs is associated with numerous risks including infection, breakage, leakage, occlusion, phlebitis, dislodgement, and malfunction.[1,2,3] Irrespective of the type of CVC, whether tunneled or percutaneously inserted, sterility is of utmost importance whenever a catheter is placed or accessed for use, in order to minimize the risk of central line-associated bloodstream infections (CLABSI).

In addition to CLABSI, another frequent complication of CVC use is breakage of the external portion of the catheter. In pediatric patients, the rates of breakage have been reported from 0.04 to 1.05 per 1000 catheter-days.[4,5] In certain pediatric populations, breakages occur in as many as 8–14% of CVCs placed.[6,7] When a CVC breakage occurs in pediatric patients, catheter repair is commonly attempted, in efforts to avert the risks and costs associated with surgical replacement. Repairs are performed using kits sold by the manufacturers of most CVCs. Two studies reported the efficacy of CVC repair kits in terms of restoring function to the broken catheter, and suggested that repair was cost-effective compared to the alternative of surgery to place a new catheter.[8,9] However, the infectious consequences of repairing a CVC are unknown.

A break in the catheter that breaches the lumen is expected to compromise its sterility. Repair and retention of that catheter might, therefore, predispose the patient to a higher risk of bloodstream infection. Furthermore, anecdotal experience at our institution suggested an increased risk of bloodstream infection following CVC breakage and repair. However, to our knowledge, no studies have been published that examine the relationship between catheter repairs and subsequent risk of bloodstream infection. Thus, we performed a study to evaluate whether the risk of bacteremia and the risk of CLABSI is increased in the period following breakage and repair of a CVC. Identification and assessment of the magnitude of such a risk is important for determining the safest management of patients who experience breakage of their CVC.

METHODS

Study Design, Setting, and Patients

We conducted a retrospective case cross-over study, in which patients served as their own controls,[10] to compare the rates of bacteremia and CLABSI before and after catheter breakage and repair. The exposure period was designated as the 30 days following CVC breakage/repair because it was assumed that the majority of resulting bacterial and fungal infections would occur during that period; the 30 days prior to the repair was the control period. The study design was chosen to minimize any potential confounding from patient age, underlying medical condition, indication for central access, or other factors.

This study was conducted at Seattle Children's Hospital, a 250-bed tertiary referral center. Subjects were identified using billing codes for the catheter repair procedure, with verification by written documentation of the procedure in the medical record. We included subjects aged 1 month to 21 years at the time of a clearly documented first repair procedure performed between 2005–2010, on a CVC that had been in place at least 30 days. The repair could take place in the ambulatory clinic, the emergency department, or an inpatient unit. Approval for this study was obtained from the Seattle Children's Hospital institutional review board.

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Definition of CLABSI

For this study, positive blood cultures were categorized as “bacteremia” or “CLABSI”. Bacteremia consisted of any positive blood culture in a patient with an indwelling CVC. We restricted the definition of CLABSI to those episodes of bacteremia meeting Centers for Disease Control and Prevention (CDC) criteria for CLABSI, which require that at least one of the following set of conditions be met: 1) A recognized pathogen is cultured from one or more blood cultures, and the pathogen is not related to infection at another site. 2) Patient exhibits one or more of the following signs or symptoms: fever >38° Celsius, chills, hypotension, and a common skin contaminant is cultured from 2 or more blood cultures drawn on separate occasions, not related to infection at another site. 3) For patients <1 year of age, the second group of conditions could be applied with the following signs and symptoms also being acceptable: hypothermia <36° Celsius, apnea, or bradycardia.[11]

Catheter Repair Procedures

Two types of repairs were performed during the study period, “glued” and “glue-less”. In the glued repair (Bard Access Systems, Salt Lake City, Utah), the catheter is cut with sterile scissors approximately one inch proximal to the break site, an extension piece is inserted into place, adhesive is applied to tubing, and a plastic sheath slides over the union site to splint the repair. The glue must set for 24 – 48 hours before the catheter may be used again. In the glue-less repair (Gish Biomedical Inc., Rancho Santa Margarita, California), the catheter is cut approximately one inch proximal to the break site, then an extension catheter with an adaptor or connector piece locks into place onto the original catheter end. Following glue-less repair, the catheter may be used immediately. Catheters with multiple prior repairs, occlusion proximal to the break, or an insufficient length of catheter are generally not considered for repair.

Data Collection

Demographic and clinical data were abstracted from the medical records and included age, race, sex, primary diagnosis, immunocompromised state (defined as any transplant recipient, any patient receiving chemotherapy or any immunosuppressive medications including systemic steroids if >2 mg/kg/day, or any patient with a diagnosis of primary immune deficiency), receipt of total parental nutrition, and exposure to antibiotics during the pre- and post-repair period. Additional information about the catheter itself was also collected, including type (peripherally inserted vs. tunneled CVC) and location of catheter, type of repair (glued vs. glue-less), and number of lumens. Data pertaining to positive blood cultures included the organisms identified, associated clinical symptoms, and serious sequelae including death or transfer to an intensive care unit (ICU).

Statistical Analyses

The primary outcome, defined *a priori*, was the within-patient incidence rates of bacteremia for the pre- and post-repair periods. Secondary outcome measures included incidence rates of CLABSI based on CDC criteria, and of CLABSI when the pre- and post-repair periods were restricted to exclude days when antibiotics were used. Associations between baseline risk of bacteremia and CLABSI in the pre-repair period and various recognized risk factors for CLABSI were explored with chi-square analysis using number of bacteremia or CLABSI events because the observation period was identical for all subjects (30 days). The incidences of bacteremia and CLABSI were compared between the pre- and post-repair periods using conditional Poisson regression, to account for the paired data structure and variable catheter days at risk.[12] Additional conditional Poisson regression models were constructed to explore this association restricted to CLABSI meeting CDC criteria, and excluding the catheter-days during which antibiotics were used since patients were

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hypothesized to be at reduced risk of developing CLABSI while receiving antibiotics. To explore whether the effect of catheter break and repair on the risk of CLABSI was modified by demographic or clinical factors, subgroup analyses were performed using conditional Poisson regression within groups characterized by immunocompromise, underlying medical disorder, parenteral nutrition administration, age group, and type of catheter repair. Effect modification was tested by comparing the post- vs. pre-repair incidence rate difference across subgroups using Wilcoxon rank sum test. Two-sided p values <0.05 were considered statistically significant.

Based on an institutional average rate of 3 CLABSI per 1000 catheter-days, we estimated that a minimum sample size of 73 subjects was needed to achieve 80% power to detect a difference of one CLABSI per 1000 catheter-days. We included subjects in reverse chronological order extending from August, 2010 to October, 2005. Analyses were performed using STATA SE 10.1.

RESULTS

Data were collected on 81 children who underwent a first CVC repair procedure (see Table, SDC 1). Forty-seven (58%) children had a diagnosis of cancer; 24 (51%) of whom had hematologic malignancies, and the remainder had solid tumors. Fewer than 20% of our subjects had short bowel syndrome. In total, 56 (69%) of subjects were immunocompromised, including 19 children who underwent hematopoietic stem cell transplantation during the study period for either malignant or non-malignant disorders.

Sixty-six subjects had a tunneled CVC, 54 had double lumen catheters and 62 had their CVC located in the upper chest or neck. The method of repair was not recorded in 10 patients, but of those that were clearly documented, approximately half of the repairs were performed using glue. In the pre-repair period, antibiotics were given for a median of 6 (IQR 0–19) days. In the post repair period, the median number of catheter days was 30 (IQR 29–30), with a median of 2 (IQR 0–12) days receiving antibiotics.

We found a mean pre-repair bacteremia rate of 9.9 per 1000 catheter days, taking all catheter days into account, and a similar mean rate of 9.0 episodes of bacteremia per 1000 catheter days after excluding days on antibiotics (Table 1). The pre-repair mean rates of CLABSI were 6.2 per 1000 total catheter days, and 7.7 per 1000 catheter days when antibiotics were not used. The incidence rate ratios (IRR), which represents the within-patient change in risk of bacteremia or CLABSI between the pre- and post-repair periods, were significantly elevated, both for bacteremia and CLABSI. For example, the risk of CLABSI showed a greater than two-fold increase (IRR 2.15, 95% CI 1.02 – 4.53, p = 0.045) when all catheter days were included, and a four-fold increase when days on antibiotics were excluded (IRR 4.07, 95% CI 1.43 – 11.57, p = 0.008; Table 1). Twelve patients received antibiotics during the entire 30 days post-repair and thus could not be included in the analysis of risk while off antibiotics.

The rate of bacteremia did not appear to decrease with time in the 30 days following CVC repair. Overall bacteremia rates occurring during the 1st, 2nd, and 3rd, ten-day periods after repair were 19.1, 12.2, and 27.5 per 1000 catheter days without antibiotics, respectively.

During the pre-repair period, receipt of parenteral nutrition was associated with CLABSI (Table 2). Other characteristics, including type of CVC, were not associated with frequency of bacteremia or CLABSI. In the subgroup analyses, we found no significant modification of the relationship between repair and CLABSI in the post- versus pre-repair periods, adjusted for days off antibiotics, by any of the demographic or clinical features examined (Table 3).

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The distribution of organisms isolated from our patient population included coagulase negative *staphylococci* (36%), viridans group streptococci (9.8%), *Escherichia coli* (9.8%), *Enterococcus faecalis* (8.2%) and *Staphylococcus aureus* (8.2%). Overall, 8% of isolates were drug-resistant organisms (methicillin-resistant *S. aureus* and vancomycin-resistant *Enterococcus*), and 10 out of the 53 cultures were polymicrobial. A total of 8 patients had at least 1 episode of bacteremia both in the month before and the month after repair of the CVC. Of those 8, two had the same organism isolated during both periods. In one case the organism was *S. aureus*, and there was an interval of 56 days between the two episodes. In the other case, the organisms were coagulase negative staphylococci, and there was an interval of 31 days between the positive blood cultures.

Very few serious sequelae occurred during the study period. Eight patients spent time in the ICU in the post-repair period, but the indications for transfer were not related to CVC complications or CLABSI. No patients died during the study period. Twenty-one (25.6%) patients had their CVC removed within the 30 days following repair, due to malfunction (48%), infection (33%), or because the CVC was no longer required for therapy (19%).

DISCUSSION

To our knowledge, this is the first study to examine the relationship between CVC repair and risk of bacteremia or CLABSI. We found a markedly increased risk of developing both bacteremia and CLABSI in the 30 days following repair of a broken CVC. This relationship was even more striking after restricting the time at risk to days without antibiotics and, therefore, days at greatest risk of CLABSI.

One prior study assessed repair kit outcomes in adults, in terms of subsequent functionality and longevity of the catheter itself, but did not assess the risk of infection.[17] Logically, compromised integrity of the sterile lumen of a CVC could facilitate entry of bacteria into the bloodstream, but data to support this hypothesis have been lacking. This study demonstrates that repair of a broken CVC in pediatric patients is associated with a 2–4 fold higher risk of CLABSI during the 30 days following repair. Quantification of this risk may help to inform individual patient care decisions, but also highlights opportunities to optimize hospital policies regarding management of CVC breakage.

The risks and cost of surgical replacement of a broken CVC may still outweigh the risks of CLABSI due to repair in some patients. However, alternative measures might help to mitigate this increased risk post-repair. Our data are consistent with a higher risk of bacteremia or CLABSI during days off antibiotics, which support a possible role for antimicrobial prophylaxis after catheter repair. Some attractive potential strategies include antibiotic or ethanol locks following CVC repair to reduce CLABSI.[13,14,15] For example, vancomycin locks, which are the best studied antibiotic lock,[16,17] could theoretically impact the outcome of nearly 60% of the CLABSI observed in our study (those due to organisms susceptible to vancomycin). In addition, formal risk-stratification criteria could be developed to determine the relative risks of CVC repair (with or without the use of adjunctive antimicrobial strategies) versus replacement.

Young age and underlying medical condition (malignancies) have been shown to be closely associated with increased rates of CLABSI in certain populations.[2] In our study, we found that parenteral nutrition was associated with risk of CLABSI in the pre-repair period. However, we did not find that age, underlying diagnosis, immunocompromised state, parenteral nutrition, catheter type, or repair type modified the effect of catheter break and repair on the risk of CLABSI. Our study was not designed to specifically evaluate this issue, however, and power to detect such differences was limited. Additional prospective studies

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would be valuable to determine which patient groups are at highest risk of CLABSI following catheter repair, and might benefit most from an alternative approach.

This study is limited by its retrospective design. We restricted our study period to 30 days before and after a CVC repair to focus on CLABSI that would be more likely temporally related to the repair procedure. Therefore, our study was not designed to detect longer-term outcomes or adverse sequelae in the several months following a catheter breakage and repair. Our data suggest that CVC repair may be associated with an increased risk of infection for a period at least as long as 30 days. The available data precluded evaluation of potentially important predictors of CLABSI, such as the exact time interval between breakage and repair. It is also possible that some patients may have received care outside of our institution that we were unable to capture through chart and database review, such as diagnosis of CLABSI or antibiotic treatment, which could affect the study outcomes. This is unlikely to have occurred frequently, however, given that most children with long term CVCs receive all their chronic disease care at this tertiary referral center. Furthermore, such missing information would likely have occurred with equal frequency during the pre- and post-repair periods. Despite these limitations, this study addresses an important and timely issue in pediatric medicine that has not been reported previously and the design of the study offers important benefits. The case crossover design allows each patient to serve as his/her own control, limiting the effect of confounding by underlying conditions. In addition, although our study population represents a single center, our hospital's catchment area includes a large geographic segment of the United States, and focuses on medically complex, chronically ill children, who are the most likely out of the pediatric population to be affected by CVC breakage and CLABSI. Given that the mean baseline CLABSI rate pre-repair in our study population was similar to rates reported around the country in pediatric hospitals, these findings may be generalizable to other settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Comparison of bacteremia and CLABSI incidence during the periods before and after catheter repair

Definitions of bloodstream infection and catheter days at risk	Infections per 1,000 catheter days				
	Pre-repair Mean(SD)	Post-repair Mean(SD)	IRR[a]	95% C.I.	P value
Bacteremia:					
All catheter days included	9.88 (17.83)	24.49 (59.44)	1.87	1.05–3.33	0.03
Days on antibiotics excluded	8.99 (24.52)	33.79 (96.16)	4.13	1.69–10.06	0.002
CLABSI:					
All catheter days included	6.17 (15.01)	14.85 (45.39)	2.15	1.02–4.53	0.045
Days on antibiotics excluded	7.74 (23.74)	21.10 (75.08)	4.07	1.43–11.57	0.008

[a] Average within-patient incidence rate ratio estimated from conditional Poisson regression for matched data

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Table 2

Relationship between clinical characteristics and occurrence of bacteremia and CLABSI during the pre-repair period

Characteristic[a]	**Any Bacteremia**		**P value**	**Any CLABSI**		**P value**
N (%)	**Yes**	**No**		**Yes**	**No**	
	N=21	**N=60**		**N=13**	**N=68**	
Age ≤3 years	12 (57.14)	25 (41.67)	**0.22**	7 (53.85)	30 (44.12)	**0.52**
Primary diagnosis:			**0.34**			**0.66**
Cancer	15 (71.43)	32 (53.33)		9 (69.23)	38 (55.88)	
Short bowel syndrome	3 (14.29)	12 (20.00)		2 (15.38)	13 (19.12)	
Other	3(14.29)	16 (26.67)		2(15.38)	17 (25.00)	
Immunocompromised	17 (80.95)	39 (65)	**0.17**	10 (76.92)	46 (67.65)	**0.51**
Catheter type:			**0.95**			**0.77**
PICC	2 (9.52)	6 (10)		1 (7.69)	7 (10.29)	
Tunneled	19 (90.48)	54 (90)		12 (92.31)	61 (89.71)	
Parenteral nutrition	12 (57.14)	22 (36.67)	**0.10**	9 (69.23)	25 (36.76)	**0.03**

PICC = peripherally inserted central catheter

[a]Characteristics not mutually exclusive.

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Table 3

Effect of patient subgroups on incidence rate ratio of CLABSI in the post- vs. pre-repair period, adjusted for days off antibiotics

Characteristic	IRR[a]	95% CI	P value[b]
Age:			
≤3 years	3.73	0.88 – 15.72	0.31
>3 years	4.49	0.98 – 20.63	
Primary diagnosis:			
Cancer	3.95	1.16 – 13.51	0.65
Short bowel syndrome	11.82	0.77 – 181.88	
Immunocompromised:			
Yes	4.05	1.20 – 13.67	0.91
No	4.15	0.55 – 31.61	
Parenteral nutrition:			
Yes	3.93	0.97 – 15.83	0.89
No	4.27	0.88 – 20.60	
Catheter Type:			
PICC[c]	0	NA	0.28
Tunneled	4.25	1.46 – 12.37	
Repair Type:			
Glued	5.24	1.14 – 24.09	0.81
Glue-less	3.42	0.65 – 17.91	

IRR = Incidence rate ratio, PICC = peripherally inserted central catheter

[a] Within-patient incidence rate ratio based on conditional Poisson regression for matched data for subgroups

[b] Based on Wilcoxon rank sum test of comparison of median incidence rate differences between two groups

[c] There were no infections in the post-repair period for PICC, therefore confidence intervals could not be generated.