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Clearance of Tunneled Central Venous Catheter Associated Blood Stream Infections in Children

Maziar M. Nourian, B.S., **Angelina L. Schwartz, B.S.**, **Austin Stevens, R.N.**, **Eric R. Scaife, M.D.**, and **Brian T. Bucher, M.D.**

Division of Pediatric Surgery, Department of Surgery, University of Utah School of Medicine, Salt Lake City, UT

Abstract

Background—The optimal time to reinsert central venous catheters (tCVC) after a documented central line associated blood stream infection (CLABSI) is unclear. The goal of this study is to identify risk factors for children who develop persistent bacteremia after tCVC removal due to CLABSI.

Methods—We performed a retrospective case-control study from a tertiary children's hospital. Children who underwent removal of a tCVC due to CLABSI were included in our analysis. Our primary outcome was persistent bacteremia after tCVC removal defined by a persistently positive blood culture. Salient patient demographic and clinical factors were extracted from the medical record.

Results—A total of 140 patients met inclusion criteria and 27 (19%) had a persistent CLABSI after removal of the tCVC. There were no significant differences between the patients who cleared their bacteremia and those who develop persistent bacteremia. The median (IQR) time to positive blood culture after tCVC removal was 2.7 days (1.7– 4.0).

Conclusions—We did not identify any patient risk factors distinguishing between a child who will clear a CLABSI versus develop a persistent CLABSI after tCVC removal. Blood stream infection clearance was rapid after tCVC removal, supporting a brief line holiday prior to tCVC reinsertion.

Keywords

Central Venous Catheter; CLABSI; bacteremia; children

1. Introduction

Tunneled central venous catheters are commonly used in infants and children for long term intravenous access such as chemotherapy or total parental nutrition (TPN) in the outpatient

Correspondence should be sent to Maziar M. Nourian BS, Division of Pediatric Surgery, Department of Surgery, Primary Children's Hospital, 100 N. Mario Capecchi Drive Salt Lake City, UT 84113 (maziar.nourian@hsc.utah.edu, Telephone- (801) 662-2950).

setting. [1, 2] However, the infectious complications associated with tCVCs, such as central line associated blood stream infections (CLABSI), are a burden to both the patient in terms of increased morbidity and to the health care system with increased readmission and heath care utilization. [3] In 2013, it was estimated that CLABSI rates were 0.78 per 1,000 in-hospital days. [4] Treatment options for CLASBI typically includes antibiotic therapy as first line therapy. Removal of the tCVC is reserved for failure of medical therapy, clinical deterioration or persisting or relapsing bacteremia. [5]

For infants and in children, in particular, removal of the tCVC requires hospital admission until a second tCVC or temporary central venous catheter (such as a Peripherally Inserted Central Catheter) can be placed. [6] This additional hospitalization leads to an inconvenience for families and an economic burden to the health care system. Evidence based guidelines on the insertion and management of central venous catheters and the diagnosis and management of CLABSI have been previously published. [7, 8] Unfortunately, the majority of these guidelines were developed with data from adult populations and data on pediatric CVC infections is scarce. In addition, these guidelines primarily address the management of CLABSI in term of a catheter removal and very few studies have identified when it is safe to reinsert a tCVC after a CLABSI or recommend mirroring adult populations.[8] The guidelines also indicate organism specific aggressive antibiotic treatment of infected lines in order to prevent removal of long term catheters but unfortunately most the data is in adult populations. [2]

Therefore, there is significant practice variability between centers on the timing of reinsertion of a tCVC after a documented CLABSI. [3] Furthermore, there is little evidence to guide clinicians regarding how long a “line holiday” should be observed before replacing a long-term catheter in fear of immediate colonization. In the previous studies in adults, a single study suggested a line holiday of 1–3 days after catheter removal with appropriate antimicrobial therapy and no persistent bacteremia. [9] Other recommendations suggest delaying reinsertion after appropriate antibiotic therapy and repeat negative blood cultures with a line holiday of 5–10 days. [10] The goal of this study is to identify patient specific risk factors for persistent bacteremia after tCVC removal for a CLASBI in children. We hypothesize patient and microbiologic risk factors influence the development of persistent bacteremia in children and can be used to guide clinicians on tCVC reinsertion in high risk populations.

2. Methods

2.1 Study Design

We performed a retrospective cohort analysis to identify children who have had a documented CLABSI due to tCVC and subsequently underwent tCVC removal. After obtaining institutional review board (IRB #00087998) approval, we review the medical records of an academic children’s hospital between January 1st, 2000 to April 1st, 2015. Inclusion criteria for the study where patients who: (1) had a documented CLABSI based on IDSA guidelines, (2) had an indwelling tCVC with or without subcutaneous port at the time of BSI, and (3) subsequently underwent tCVC removal due to failure of medical

management.[8] Exclusion criteria included patients whose tCVC infection cleared with antibiotic therapy alone and did not undergo tCVC removal.

2.2 Data Collected

We abstracted patient demographic data including: race, gender, age at the time of tCVC removal, weight, height, and BMI. Medical history collected included: use of antibiotics prior to tCVC removal, TPN, chemotherapy within 30 days, steroid use within 30 days, immunosuppression within 30 days, gastrointestinal failure (defined as any child who had necrotizing enterocolitis, Hirshprung's disease, or any history of intestinal resection), oxygen usage, dialysis, history of malignancy, and history of congenital heart disease. tCVC information collected included duration, number of lumens, location, indication for placement, accessing at the time of placement, number of previous placements. Factors such as ethanol and antimicrobial locks were inconsistently documented in the electronic medical record and therefore not collected. Daily microbiology data (including organisms and antimicrobial resistance) was collected five days prior to and after tCVC removal.

2.3 Outcomes

Our primary outcome was persistent positive (PP) blood cultures defined as blood cultures obtain after tCVC removal that resulted in growth of a causative organism within five days. Patients who had cleared bacteremia (CL) were defined as those who had blood cultures obtained after tCVC removal that did not result in growth of organisms after five days in culture. The current practice at this institution is to draw blood cultures daily from the line and peripherally until no growth is detected on culture. Time to positivity defined as time between line removal and first positive blood culture in the 27 PP patients. Secondary outcomes included: length of admission, length of pre-removal antibiotic use (defined as the difference between the start of antibiotics and the date of tCVC removal), time until reinsertion (defined as the time difference between removal of the old tCVC and insertion of a new tCVC.

2.4 Statistical Analysis

Data were entered into REDCAP data bases and then exported to be analyzed using JMP Pro (Version 12, Cary, NC). Descriptive statistics were used to describe the distribution of the dependent and independent variables. All children, regardless of medical history, that cleared bacteremia (CL) after tCVC removal were grouped together and compared to children who had a persistently positive (PP) bacteremia after tCVC removal. Univariate analysis was performed using Fischer or Pearson's Chi-square tests for categorical variables and Wilcoxon Rank-Sum Test for continuous variables. Statistical significance was defined as $p<0.05$.

3. Results

3.1 Patient Risk Factors

Of the 140 patients that met inclusion criteria, 113 of the patients had a CLABSI that cleared after removal of the tCVC whereas 27 patients had a persistently positive CLABSI after tCVC removal (PP). Table 1 describes the patient demographics and relevant risk factors of

the study participants. There were no significant differences in age, gender or BMI between the CL and PP groups. There were also no significant differences in history of cardiac disease, GI failure, and malignancy between the CL and PP groups. The use of home TPN, chemotherapy, steroids, dialysis was similar between the two groups. Of note, none of the PP patients had sites of infection such as cardiac vegetations as shown on ECHO cardiogram (data not shown). Multiple lumens, as defined as more than one lumen, was not statistically significant between CL and PP groups (34% vs 15%, p=0.06). There were no differences in number of previous tCVCs, or the venous location of tCVC placement between the CL and PP patients. Of patients who had tCVC associated CLABSI, 93% of the CL group was started on antibiotics compared to 88% of the persistent group (p=0.43). The average tCVC duration was 139 days for the cleared group and 160 days for the persistent group (p=0.64). The majority (84%) of patients presented with a tCVC associated CLABSI from the outpatient setting.

3.2 Microbiology Analysis

The distributions of causative organisms are shown in Table 2. There are no statistical significant differences in causative organisms between CL and PP in cases of Gram positive, Gram negative, polymicrobial, and fungal infections. A single MRSA CLABSI was found in the PP group a clinically questionable finding. A detailed analysis comparing common and uncommon organisms was conducted between CL and PP groups but yielded no clinically significant results which is featured in Table 2.

3.3 Outcomes

Of all the tCVCs in our analysis, 78% (n=108) had a new tCVC re-inserted with 88 from the CL group and 20 of the PP group. Of the lines that were reinserted, none of the CL group became re-infected however 25% of the re-inserted PP lines became re-infected. One patient required a second removal and the remaining four patients were treated with antibiotics alone. The median (IQR) time to positive blood culture result after tCVC removal in PP was 2.7 days (1.7– 4.0 days). The median (IQR) time to reinsertion after removal was 2.9 (1.9–4.9) days.

4. Discussion

This study examined the patient and microbiologic factors associated with persistent bacteremia after a tCVC associated CLABSI. The study yielded three main findings. First, there were no statistically significant demographic or patient factors predicting the development of a persistently positive CLABSI. Second, the median time to positivity of blood cultures after tCVC removal was 2.7 days (1.7–4.0). Lastly, our results indicate an observed line holiday of close to 3 days.

The literature on CLABSIs in children seems to indicate that tCVC’s represent a challenging group in terms of infections especially for children receiving TPN or IV infusions though the tCVC. [11] These findings were further supported by Fallon and colleagues in which they showed tCVC used for TPN attributed to a higher early complication rate attributable to infection. [1] Other researchers have focused on risk factors such as catheter dwell time as a

risk for tunneled catheter associated blood stream infections and demonstrated higher incidence of infection in catheters placed longer than 7 weeks. [6] Our data demonstrates no significant differences in demographics, antibiotic use, tCVC dwell time, and indication between the two groups. This would indicate it is difficult to predict based on patient factors whether a child will develop persistent bacteremia.

Of the organisms isolated from of these recurrent infections in children with cancer, CONS seemed to be predominate isolated species. [12] When dividing cancer patients, there seems to be a difference of organisms responsible for CLABSI from the outpatient to inpatient setting with more gram negative bacteria in the outpatients utilizing long term catheters such as a tunneled catheter. [13] Our study demonstrates that there were no significant differences between types of bacteria or fungus in the two groups. We did however find that Pseudomonas species were more likely to appear in the CL group however this may lack clinical significance as *Pseudomonas* infected lines are typically removed after infection [8]. These findings add to the body of literature on the microbiological results of CLABSIs may help guide practices of antibiotic therapy and when to remove or re-place a CVC.

In studies in pediatric hematology/oncology patients, CLABSIs increased health care costs by $70,000 and increase the hospital length of stay by 3 weeks. [14] Our findings also show that overall hospital length of stay was unrelated to tCVC reinsertion and similar between the two groups indicating. In the patients who develop persistent bacteremia the median time to detection was 2.7 days. Overall all tCVCs had a median replacement time of 2.9 days. Surgeon preference generally dictates the time of line holiday however most surgeons at our institution wait least 48 hours based off anecdotal evidence.

Despite an accepted consensus on line holidays with estimates 1–10 days, our results support the current practices of an average line holiday of 3 days prior to tCVC reinsertion [9, 10]. Our results further support a line holiday of 3 days as it would cover all the CL (113) patients and half of the PP (14) patients. With this recommendation 91% (127/140) would fall within this recommended line holiday and waiting longer to reinsert would be up to clinical discretions of underlying co-morbidities of original line placement.

This study had several limitations. This study was retrospective and bias can be draw from changes in practice management. Due to the small sample size individual risk factors such as past medical history (ex- cancer or GI failure) were grouped between cleared bacteremia and persistent positive. In addition, this small sample size may be underpowered to detect small, yet clinically relevant risk factors. Another limitation is the inconsistent documentation of ethanol and antimicrobial locks which in previous studies has demonstrated effectiveness in preventing infections and may have overestimated the incidence of our PP group which could have biased our sample. Future studies should address the difference between cleared and persistent positive groups focused on individual risk factors. Additionally, recommendations based off findings could lead to re-insertion of tCVC before microbiology lab results would have returned which may be unexpectedly slow in fungal line infections. There is potential bias in the study as the data was extracted from only one academic pediatric hospital. Despite these limitations, there is currently no evidence as to when can pediatric surgeons safely replace a previously infected line and our paper seeks to address

this rare but important issue which is why we believe future studies should focus on combining data from a multicenter approach and create better guidelines.

5. Conclusion

We did not identify any patient or microbiologic risk factors distinguishing between a child who will clear a CLABSI versus develop a persistent CLABSI after tCVC removal. Of the tCVC that showed to be PP, the time to positivity was a median of 2.7 days IQR (1.7–4.0). Finally, our study supports current practices of line holidays lasting 3 days after removal of tCVC. This research helps add to the body of literature regarding tCVC and CLABSI in children and future research should focus on clinical practices that validate risk factors identify children who are candidates for early replacement of tCVC.

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TABLE 1

Patient demographics and risk factors. Cleared Bacteremia (CL) Persistent PositiveBacteremia (PP)

Factors		CL (n=113)	PP (n=27)	P value
Demographics				
Age (years)		4.7	5.2	0.9
Race (n, %)				0.1
	White	72 (64%)	22 (82%)	
	Asian	5 (4%)	0 (0%)	
	Black	2 (2%)	2 (7%)	
	Hispanic	18 (16%)	1 (4%)	
	Other	17 (15%)	2 (7%)	
Gender (Male) (n, %)		59 (52%)	16 (59%)	0.53
BMI (kg/m^2)		16.5	15.9	0.28
Risk Factors (n, %)				
Home TPN		49 (43%)	15 (56%)	0.28
Chemo last 30 days		38 (34%)	9 (33%)	1
Steroid last 30 days		5 (4%)	3 (11%)	0.18
GI Failure		35 (31%)	12 (44%)	0.26
Renal Dialysis		2 (2%)	0 (0%)	1
Malignancy		57 (50%)	11 (41%)	0.52
Congenital Heart Disease		35 (31%)	8 (30%)	1
Line Information				
Line Type				
	Port	92 (81%)	20 (74%)	0.43
	Broviac	21 (19%)	6 (22%)	0.79
Multiple Lumens		38 (34%)	4 (15%)	0.06
Location of Line				0.51
	Internal Jugular	23 (20%)	7 (26%)	
	Subclavian	73 (65%)	16 (59%)	
	Other	17 (15%)	4 (15%)	
Line Indication				
	TPN	32 (28%)	11 (41%)	0.25
	Chemotherapy	51 (45%)	10 (37%)	0.52
	Frequent Blood Draws	17 (15%)	4 (15%)	1
	Medications	33 (29%)	8 (30%)	1
# of Previous CVC		1.4	1.3	0.39
Antibiotics before removal		105 (93%)	24 (88%)	0.43
Antibiotic Length of usage (Days)		9.5	11.4	0.72
Duration Line (Days)		139	161	0.64

Factors	CL (n=113)	PP (n=27)	P value
New Line inserted	88 (79%)	20 (77%)	0.80

TABLE 2

Microbiology of Central Line Associated Blood Stream Infection. Cleared Bacteremia (CL) Persistent Positive Bacteremia (PP) Coagulase Negative Staphylococcus species (CONS)

Organism/Type	Cleared (n=113)	Persistent (n=27)	P value
Gram Positive	69	19	0.51
CONS	35	9	0.82
S. epidermidis	30	8	0.48
E. faecalis	7	5	0.06
MSSA	3	2	0.25
MRSA	0	1	0.04
Gram Negative	56	10	0.29
Pseudomonas spp.	16	0	0.04
Klebseilla spp	10	3	0.71
Enterobacter	6	2	0.65
Citrobacter	0	1	0.04
Fungal	7	4	0.22
Mycobacterium	3	1	0.58
Polymicrobial	15	3	1.0