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Ambulatory Pediatric Oncology CLABSIs: Epidemiology and Risk Factors

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Abstract

Background—To compare the burden of central line-associated bloodstream infections (CLABSIs) in ambulatory versus inpatient pediatric oncology patients, and identify the epidemiology of and risk factors associated with ambulatory CLABSIs.

Procedure—We prospectively identified infections and retrospectively identified central line days and characteristics associated with CLABSIs from January 2009 to October 2010. A nested case-control design was used to identify characteristics associated with ambulatory CLABSIs.

Results—We identified 319 patients with central lines. There were 55 ambulatory CLABSIs during 84,705 ambulatory central line days (0.65 CLABSIs per 1,000 central line days (95% CI 0.49, 0.85)), and 19 inpatient CLABSIs during 8,682 inpatient central line days (2.2 CLABSIs per 1,000 central lines days (95% CI 1.3, 3.4)). In patients with ambulatory CLABSIs, 13% were admitted to an intensive care unit and 44% had their central lines removed due to the CLABSI. A secondary analysis with a sub-cohort, suggested children with tunneled, externalized catheters had a greater risk of ambulatory CLABSI than those with totally implantable devices (IRR 20.6, $P < 0.001$). Other characteristics independently associated with ambulatory CLABSIs included bone marrow transplantation within 100 days (OR 16, 95% CI 1.1, 264), previous bacteremia in any central line (OR 10, 95% CI 2.5, 43) and less than 1 month from central line insertion (OR 4.2, 95% CI 1.0, 17).

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Conclusions—In pediatric oncology patients, three times more CLABSIs occur in the ambulatory than inpatient setting. Ambulatory CLABSIs carry appreciable morbidity and have identifiable, associated factors that should be addressed in future ambulatory CLABSI prevention efforts. *Pediatr Blood Cancer* 2013;60:1882–1889.

Keywords

central line-associated blood stream infection; central venous catheter/access device; epidemiology; oncology; outpatient management; pediatric; quality improvement

INTRODUCTION

Children with cancer require frequent infusions of intensive chemotherapy regimens, parenteral nutrition, and blood products. Central lines are integral to pediatric cancer care, as they facilitate the safe delivery of these treatments and contribute to increased survival rates [1,2]. The benefits of central lines must be balanced against the risk they pose for developing central line-associated bloodstream infections (CLABSIs) [3–7]. While work has been done to decrease these harmful infections in hospitalized oncology patients [8–11], less attention has been paid to the ambulatory setting [10,12], despite most oncology patients being discharged with central lines [12–18].

CLABSIs in ambulatory pediatric oncology patients cause significant morbidity. Eight percent of all ambulatory pediatric oncology implantable ports are removed due to CLABSIs [19], 9.5% of ambulatory pediatric oncology patients with a CLABSI are admitted to an intensive care unit within 24 hours of hospital admission, 62% are hospitalized for seven or more days, and 1% die during their hospitalization [20]. Additionally, CLABSIs cost up to \$45,000 per infection [21,22]. One study found twice the number of ambulatory compared to inpatient pediatric oncology CLABSIs (41 vs. 17, respectively), suggesting a higher ambulatory burden of CLABSI [16]. This burden has not been explicitly investigated, and risk factors for CLABSIs in ambulatory pediatric oncology patients have not been clearly identified, as available studies involve mixed ambulatory and inpatient pediatric oncology subjects [15,16], bone marrow transplant patients only [23], or non-consensus CLABSI definitions [20].

This study compares the burden of ambulatory versus inpatient pediatric oncology CLABSIs, and identifies the epidemiology of and risk factors associated with ambulatory pediatric oncology CLABSIs. We hypothesized that the absolute number of ambulatory CLABSIs is greater than inpatient CLABSIs, ambulatory CLABSIs carry appreciable morbidity and that modifiable risk factors can be identified. It is imperative that we understand ambulatory CLABSI epidemiology to reduce the morbidity associated with these infections, examine how we allocate resources to reduce CLABSIs between ambulatory and inpatient populations, and inform future CLABSI prevention efforts in ambulatory pediatric oncology populations.

METHODS

Setting and population

We prospectively collected data on infections and retrospectively collected central line days and patient and catheter characteristics on pediatric oncology patients in a tertiary, university-affiliated hospital. The pediatric oncology division annually sees approximately 200 patients with new oncologic diagnoses, performs 35 stem cell transplants and conducts 7,000 clinic visits.

All pediatric patients 21 years old or less with a central line managed in our pediatric oncology clinic between January 1, 2009 and October 1, 2010 were included. We identified potential patients with central lines through institutional billing data for an oncology clinic visit and then screened their electronic and written charts for the presence of a central line. Identified patients with a central line were included from the first day they had a central line within the study window. To avoid reviewing charts of patients with low potential for having a central line, we only pursued full chart reviews on patients seen three or more times in our clinic during the study window. Patients seen fewer than three times over 21 months were typically in remission or seen in consultation only, and were excluded based on the assumption that they were without a central line (N = 448). This was confirmed by full chart reviews on a 10% random sample of these patients (N = 50). Only one of these patients had a central line, and it was removed during the first 2 months of the study.

Our institution implemented a central line maintenance care bundle aimed at reducing inpatient CLABSI in November of 2009, although this intervention had minimal impact between November 2009 and October 2010 [9].

Definitions and Data Sources

We utilized the National Healthcare Safety Network (NHSN) definition of CLABSI [16,20,24,25] to identify ambulatory CLABSI, with the timeframe altered to indicate the ambulatory setting. The primary outcome, ambulatory CLABSI, met the following criteria: (1) the first positive culture was drawn greater than 48 hours after discharge from an inpatient stay or less than 48 hours after admission, to be consistent with the current NHSN definition of inpatient CLABSI which can occur up to 48 hours after discharge [25], (2a) any blood culture positive for a pathogenic organisms or (2b) more than one blood culture positive for common skin contaminant organisms, and (3) which are not associated with another infectious source [25]. The risk of missing CLABSI because antibiotic treatment was started after the first positive culture is low as non-neutropenic febrile patients with central lines often do not receive empiric antibiotics in our institution and neutropenic, febrile patients with double lumen catheters receive cultures from both lumens prior to antibiotics. Our institution has stable patients complete antibiotic courses at home. CLABSI rates were defined as CLABSI per 1,000 central line days. Each patient with a central line contributed only one central line-day per day, even if the patient had more than one central line [25]. Patients contributed line days from the first day of our study window, if the line was already in place, or from the date of line placement. Line days accrued until line

removal, discharge to another institution's care or the last day of study window, and whether or not lines were accessed.

In January of 2009, we began prospectively tracking all positive blood cultures in pediatric oncology patients. Blood cultures were drawn at the discretion of care providers and our institution did not employ a routine blood culture surveillance protocol. Potential cases were identified by passive and active surveillance: nurses reported all laboratory-confirmed, positive blood cultures drawn within or outside our institution to an Infection Preventionist (IP), fellows followed all outside hospital blood cultures and IPs independently searched laboratory blood culture databases for pediatric oncology patients. Our pediatric oncology division hospitalizes all patients with positive blood cultures, and all patients are admitted to our hospital, even if they are initially stabilized at an outside emergency department. All positive ambulatory blood cultures were retrospectively adjudicated as CLABSI by the same IP (M.P.), utilizing both chart and laboratory data.

For all patients with a central line, demographic information including age, gender, diagnosis, disease relapse status (clinician noted "relapse" anywhere in chart), date of relapse, central line type (tunneled, externalized catheters (TEs), totally implantable devices (TIDs), peripherally inserted central catheters (PICC) and other), and insertion and removal dates were collected. For patients with a positive blood culture, we collected additional patient, infectious and outcome characteristics: insurance type, bone marrow transplant history, current steroid use, current immunosuppressant use, current antibiotic use (including prophylaxis), high-intensity chemotherapy regimen (acute leukemia induction, consolidation, and intensification phases, bone marrow transplant regimen within the past 6 months, and chemotherapy regimens that cause grade four neutropenia in greater than 50% of patients [26]), mucositis (clinician noted "mucositis" anywhere in chart), graft-versus-host disease, neutropenia (absolute neutrophil count less than 500), red blood cell or platelet transfusion within the last week, skin breakdown at central line site or skin breakdown at another site (nursing documentation of skin breakdown on a standardized assessment form), organism, polymicrobial infection, associated symptoms, other infectious sources, prior ambulatory or inpatient bacteremias, length of stay, intensive care unit admission within 72 hours of admission, reason for central line removal and death. All characteristics were postulated based on previous research [3], had biologically plausible explanations for causality of a CLABSI and were specified before data collection with the exception of high-intensity chemotherapy regimen. This variable was added to better account for host susceptibility to infection. Collection of inpatient CLABSI data was previously described [9].

Nested Case–Control Study

To identify time-varying characteristics associated with ambulatory CLABSI, we conducted a nested case–control study. Cases were defined as incident ambulatory CLABSI (i.e., a patient's first CLABSI within the study window) to assure independence and reduce bias from unmeasured patient level factors. Controls did not have an ambulatory CLABSI and were matched on presence of a central line at a clinic visit within one month of the case's CLABSI. This matching scheme, based on previous pediatric oncology literature [3],

may account for unmeasured changes in central line care practices over the study window. Two controls were selected for each case because three controls would have prevented complete matching.

Statistical Analyses

The absolute number of CLABSI in the ambulatory versus inpatient settings (burden of disease) was compared using descriptive statistics. CLABSI rates with 95% confidence intervals (CI) were calculated assuming a Poisson distribution. Ambulatory versus inpatient CLABSI patient demographics, infectious organisms and outcomes were compared with Fisher's exact tests and Wilcoxon rank sum tests. For the nested case-control study, unadjusted conditional logistic regression was used to estimate the association of patient characteristics and CLABSI. Given the number of events ($N = 43$), we performed an adjusted conditional logistic regression model using only characteristics significantly associated with CLABSI in the bivariable analysis ($P < 0.05$) [3]. To ensure line type was not collinear with significant characteristics from the bivariable analysis, we assessed the variance inflation factor (VIF) after simple regression; case/control status was the outcome, and line type and each of the significant bivariable characteristics were independent variables.

Secondary analyses included Poisson regressions to compare CLABSI rates for ambulatory patients versus inpatients adjusting for line type, and to compare ambulatory patients with TEs versus TIDs [23]. Both comparisons used data from November 2009 to October 2010, after our inpatient unit began collecting line days by central line type. Statistical analyses were completed in Stata 11 (Stata Corp, College Station, TX). This study was approved by the Johns Hopkins University School of Medicine Institutional Review Board.

RESULTS

There were 972 unique patients 21 years old or less seen in the oncology clinic between January 1, 2009 and October 1, 2010. Five hundred twenty-four of these patients (54%) were seen three or more times during the study window and underwent a full chart review. Three hundred nineteen of these patients (61%) had 418 central lines (243 TIDs, 121 TEs, 54 PICC/other lines), contributing 93,387 central line days (73,393 in TIDs, 18,218 in TEs, 1,776 in PICC/other lines) at any point during the study window.

Inpatient Versus Ambulatory CLABSI

There were 84,705 ambulatory central line days and 55 ambulatory CLABSI for an ambulatory CLABSI incidence rate of 0.65 CLABSI per 1,000 central line days (95% CI 0.49, 0.85). There were 8,682 inpatient central line days and 19 inpatient CLABSI for an inpatient CLABSI incidence rate of 2.2 CLABSI per 1,000 central lines days (95% CI 1.3, 3.4). The absolute number of CLABSI in the ambulatory setting (burden of disease) was 2.9 times higher than the inpatient setting and the CLABSI incidence was 70% less (incidence rate ratio (IRR) 0.30, 95% CI 0.17, 0.53).

A large difference in central line days composition was noted in the ambulatory as compared to inpatient arenas (18% ambulatory TE central line days vs. 51% inpatient TE central line

days). Given prior research suggesting TE lines increase CLABSI risk [9], we compared ambulatory and inpatient CLABSI rates adjusting for central line type, and the adjusted incidence rate ratio was no longer significant (IRR 1.6; 95% CI 0.81, 3.1) (Table I).

Epidemiology of Ambulatory CLABSIs

Forty-three patients had 55 ambulatory CLABSIs. Eight patients experienced two CLABSIs and two patients experienced three CLABSIs. Forty-one patients (75%) were male and 29 (53%) had a hematologic malignancy. Seventeen patients (31%) were neutropenic at CLABSI diagnosis and 11 patients (19%) were within 100 days of a bone marrow transplant. A large majority of infections occurred in TE central lines (82%). One-third of infections were polymicrobial and 56% were gram negative. Seven patients (13%) were admitted to the intensive care unit within 72 hours of admission, 24 (44%) had their lines removed due to the infection and 1 patient (1.8%) died during their CLABSI hospitalization. Statistically significant differences between ambulatory and inpatient CLABSIs included male gender (75% vs. 42% respectively), neutropenia (31% vs. 74%), mucositis (1.8% vs. 32%), active graft versus host disease (7.2% vs. 32%), TEDs (82% vs. 68%) and median length of stay after CLABSI (6 days vs. 18 days) (Table II).

Nested Case–Control Analysis

We identified 43 incident ambulatory CLABSIs and matched them with 86 controls. Bivariable analyses yielded the following significant associations with ambulatory CLABSIs in the nested case–control cohort: acute myeloid leukemia (AML) diagnosis compared to all other diagnoses (odds ratio (OR) 7; 95% CI 1.4, 33), less than 1 month from central line insertion (OR 2.68; 95% CI 1.01, 7.1), high-intensity chemotherapy regimen (OR 4.46; 95% CI 2.0, 10), bone marrow transplant within 100 days (OR 14.5; 1.8, 117), red blood cell or platelet transfusion within 1 week (OR 3.1; 95% CI 1.3, 7.5), previous bacteremia in any central line (OR 6.3; 95% CI 2.3, 17) and neutropenia (OR 5.47; 95% CI 1.8, 17) (Table III).

Thirty-four patients with an ambulatory CLABSI had TE lines (79%), compared to only seven controls (8%). Central line type, although limited by sample size, had the highest association with case/control status in the bivariable analyses, preventing the applicability of a conditional logistic regression model. For this reason, a secondary analysis was performed to examine the CLABSI-central line type association. The ambulatory CLABSI rate for patients with TE catheters was 2.88 CLABSIs per 1,000 central line days and the rate for TIDs was 0.14 (IRR 20.6, 95% CI 7.6, 69) (Table I). All VIF's were less than 1.3, suggesting little to no collinearity between central line type and characteristics significantly associated with CLABSIs in the bivariable analysis.

An adjusted conditional logistic regression model, excluding central line type but using the other characteristics significantly associated with CLABSIs in the bivariable analysis found bone marrow transplant within 100 days (OR 16, 95% CI 1.1, 264), previous bacteremia in any central line (OR 10, 95% CI 2.5, 43) and less than 1 month from central line insertion (OR 4.2, 95% CI 1.0, 17) were independently associated with ambulatory CLABSI (Table IV).

DISCUSSION

This study identified almost three times more ambulatory than inpatient CLABSI in a pediatric oncology cohort. CLABSI rates were comparable between ambulatory and inpatients after adjusting for central line type. CLABSI caused appreciable morbidity, with 13% of patients being admitted to an intensive care unit within 72 hours and 44% of central lines being removed due to the CLABSI. In an unadjusted analysis, TE lines were associated with ambulatory CLABSI, and ambulatory TE lines had significantly higher CLABSI rates when compared to TIDs (IRR 20.6). High-risk periods for ambulatory CLABSI include within 100 days of bone marrow transplant, less than one month from central line insertion and patients with previous bacteremia in any central line. These characteristics could be targeted in future prevention efforts.

This study draws attention to the almost three times higher burden of CLABSI disease in ambulatory pediatric oncology patients when compared to hospitalized children. While research on interventions to reduce pediatric CLABSI has proceeded [9,10,27,28], focus on ambulatory CLABSI prevention remains minimal [10] despite more oncology children contracting CLABSI outside the hospital [10,16]. This result is potentially similar for non-oncologic disease processes such as cystic fibrosis and short gut syndrome, and further research should explore the burden of CLABSI in ambulatory patients with other pediatric and adult diagnoses. It may be logical to expect a larger CLABSI burden in ambulatory patients because there were ten times more patient-days at risk in the ambulatory setting (84,705 vs. 8,682) and inpatients potentially experience increased vascular accesses [29]. Regardless, ambulatory CLABSI cause appreciable morbidity, comparable to inpatient CLABSI [9]. It is imperative that ambulatory CLABSI prevention research be undertaken to reduce these harmful infections at a level comparable to inpatient efforts because almost three times more children are contracting ambulatory CLABSI.

Most demographic and clinical characteristics were comparable between inpatient and ambulatory CLABSI patients [9], suggesting prevention strategies used in hospitalized settings [9,10] may reduce ambulatory CLABSI. Significantly increased rates of neutropenia, active graft versus host disease, mucositis and length of stay in inpatient CLABSI may be due to selection bias; inpatient chemotherapy or illness severity that led to an inpatient admission may predispose inpatients to these conditions. The rate of polymicrobial ambulatory CLABSI in this study (33%) was higher than previously reported inpatient rates [3], but comparable to ambulatory rates [20]. This could suggest an ambulatory trend towards more polymicrobial infections, which would be worrisome as patients with polymicrobial CLABSI have longer lengths of stays [20]. Ambulatory CLABSI are different from inpatient due to the involvement in central line care of non-medically trained caregivers and homecare nurses. Research should continue to explore differences between inpatient and ambulatory CLABSI, and whether inpatient CLABSI reduction interventions can be applied in the ambulatory setting where non-medically trained caregivers provide line care.

In an analysis excluding central line type, bone marrow transplant within 100 days, previous bacteremia in any central line and less than one month from central line insertion were

independently associated with ambulatory CLABSI. It is possible that patients within 100 days of a bone marrow transplant and less than one month from line insertion are at increased risk for ambulatory CLABSI because of the large number of line accesses for intravenous medications, blood products and blood draws during these periods. These may also be markers for severity of illness and decreased immune responses. Also, during the first month following insertion of a new central line, families may still be learning line maintenance practices, as ambulatory pediatric oncology patient families in our institution flush lines and change dressings at home, and are taught how to keep lines dry when bathing with adjuncts to provide an impermeable line cover. Previous bacteremia, the third independent risk factor, may be a marker for a disease process that requires frequent line accesses or a pattern of substandard line care. Previous studies of hospitalized pediatric oncology patients also suggested less than one month from line insertion is an independent risk factor for CLABSI [3]. As best practice bundles have reduced CLABSI in pediatric inpatients [8–10,27,28,30,31], healthcare providers should devote extra care and attention towards minimizing accesses and optimizing line care during times when patients are at increased CLABSI risk [23]. Antibiotic or ethanol catheter locks [4,32–34], or antibiotic coated catheters [35] also could be considered to reduce ambulatory CLABSI morbidity.

This and other studies [3,9,12,23,36] suggest TE lines are associated with an increased risk for CLABSI when compared to TIDs. In this study, line type was associated with CLABSI status in the bivariable analyses and in secondary analyses, patients with TE lines had higher ambulatory CLABSI rates than patients with TIDs. This association may be caused by the increased frequency of accesses in TE lines, leaving those children at higher risk for CLABSI. This idea is supported by previous research suggesting maintenance practices are critical to preventing CLABSI in children [8,27] and that increased accesses increase the risk for CLABSI by eightfold [29]. The TE-CLABSI association may be confounded by indication bias, as children with TEs are often at the beginning of vigorous chemotherapeutic regimens and have depressed immune systems. Research is needed to explore whether increased accesses cause an increased CLABSI risk, after adjusting for disease severity, treatment course and other potential confounders beyond the scope of this study. This research would clarify whether line type causes increased CLABSI risk or is a marker for increased accesses. Until this research is undertaken, clinicians should have low thresholds for removing and replacing infected TE lines and future research should pursue scientifically based protocols for line removal. Additionally, families and providers accessing TE lines should be trained extensively in recommended aseptic line care technique [37].

This study has several limitations. First, the retrospective nature of our adjudication and central line ascertainment processes introduce the possibility of misclassification bias. We minimized this risk by having a single, trained IP adjudicate all CLABSI. Some bacteremia events may not have been captured, although that is unlikely given our catchment area. Additionally, potential misclassification bias exists because data on relapse, mucositis, antibiotic use and other similar items were gleaned from clinician documentation, which may have been inaccurate. Second, our sample size precluded inclusion of specific diagnoses in the multivariable model to assess other factors possibly associated with ambulatory CLABSI. Third, patient illness severity was approximated with measures such

as relapse and recent bone marrow transplant, but these do not account for other signs and symptoms of severe oncologic disease. This study was conducted at a tertiary care center and results may not be generalizable to centers without large bone marrow transplant services. We were only able to compare inpatient and ambulatory CLABSI rates by central line type from November 2009 to October 2010 and it is unclear if they would have been different using the entire study window. Finally, an effort to reduce inpatient pediatric oncology patient CLABSIs was begun in November 2009 [9]. While there was no appreciable decrease in hospitalized patient CLABSI rates during the first year of this intervention [9], it is unclear how the increased focus on inpatient CLABSIs affected ambulatory data. The mean ambulatory CLABSI rate per 1,000 central line days was 0.67 before November 2009 and 0.63 after November 2009, suggesting little initial impact of the inpatient intervention on ambulatory CLABSI rates.

In conclusion, ambulatory pediatric oncology patient CLABSIs occur at almost three times the rate as hospitalized pediatric oncology patient CLABSIs. These infections carry appreciable morbidity and have identifiable, associated factors that should be addressed in future CLABSI prevention efforts. Research should be undertaken to understand if the burden of CLABSIs is higher in ambulatory adults and children with non-oncologic disease processes and to understand best practices to prevent these harmful infections.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE I
Ambulatory and Inpatient Central Line-Associated Blood Stream Infection (CLABSI) Rates

	CLABSI	Total central line days	CLABSI rate per 1,000 central line days	Incidence rate ratio (95% CI)	P-value
Overall CLABSI rates					
Ambulatory CLABSI	55	84,705	0.65	0.30 (0.17, 0.53)	<0.001
Inpatient CLABSI	19	8,682	2.2		
CLABSI rates by central line type					
Ambulatory CLABSI					
Totally implantable devices (TID)	5	35,651	0.14	1.6 (0.81, 3.1)	0.18
Tunneled, externalized catheters (TE)	23	7,973	2.88		
Peripherally inserted central catheters/other	0	707	0		
Inpatient CLABSI					
Totally implantable devices (TID)	1	1,761	0.57		
Tunneled, externalized catheters (TE)	10	2,607	3.8		
Peripherally inserted central catheters/other	2	742	2.7		

Data in the CLABSI rates by central line type are only from November 2009 to October 2010 because collection of central line days by central line type (denominator of rate) only began on the inpatient unit in November 2009. The 1.6 incidence rate ratio and 0.18 P-value compare inpatient versus ambulatory CLABSI rates adjusting for central line type. The incidence rate ratio comparing the ambulatory CLABSI rate in patients with TE catheters to the ambulatory CLABSI rate in patients with TID catheters was 20.6 (95% CI 7.6, 69). For the Inpatient CLABSI, one infection was in a Cook catheter and one in a Peripherally Inserted Central Catheter.

TABLE II

Epidemiology and Comparison of All Ambulatory and Inpatient Central Line-Associated Blood Stream Infections (CLABSI) January 2009 to October 2010

	Ambulatory CLABSI (N = 55) (%)	Inpatient CLABSI (N = 19) (%)	P-value
Demographics			
Unique patients	43	18	
Median age at infection in years	9.4 (IQR 2, 16)	14 (IQR 7, 19)	0.07
Male gender	41 (75)	8 (42)	0.02
Race			
Caucasian	33 (60)	9 (47)	0.12
African American	18 (33)	6 (32)	
American Asian/Pacific Islander	2 (3.6)	—	
Other	2 (3.6)	4 (21)	
Ethnicity: not Hispanic	54 (98)	17 (89)	0.16
Clinical characteristics			
Malignancy type			0.10
Hematologic	29 (53)	11 (58)	
Solid	24 (44)	5 (26)	
Non-oncologic BMT	2 (3.6)	3 (16)	
Neutropenic (ANC < 500)	17 (31)	14 (74)	0.002
Mucositis	1 (1.8)	6 (32)	<0.001
Active graft versus host disease	4 (7.2)	6 (32)	0.015
Bone marrow transplant within 100 days of infection	11 (19)	8 (42)	0.07
Central line type			0.04
Totally implantable devices	10 (18)	3 (16)	
Tunneled, externalized catheters	45 (82)	13 (68)	
Peripherally inserted central catheters	—	2 (11)	
Other	—	1 (5.3)	
Microbiology			
Polymicrobial	18 (33)	2 (11)	0.08
Total organisms	78	21	
Gram positive organisms	32 (41)	10 (48)	0.58
Staphylococcus, Coagulase-negative	17 (22)	3 (14)	
Enterococcus	7 (8.9)	4 (19)	
<i>Enterococcus faecalis</i>	7 (8.9)	3 (14)	
<i>Enterococcus gallinarum</i>	—	1 (4.8)	
<i>Streptococcus viridans</i>	3 (3.8)	1 (4.8)	
<i>Staphylococcus aureus</i>	2 (2.6)	—	
Gram negative organisms	44 (56)	10 (48)	0.58
Enterobacter	10 (13)	1 (4.8)	
<i>Enterobacter cloacae</i>	8 (10)	1 (4.8)	
<i>Enterobacter asburiae</i>	1 (1.3)	—	

	Ambulatory CLABSI (N = 55) (%)	Inpatient CLABSI (N = 19) (%)	P-value
<i>Enterobacter</i> sp.	1 (1.3)	—	
<i>Klebsiella</i>	7 (9)	3 (14)	
<i>Klebsiella pneumoniae</i>	4 (5.1)	3 (14)	
<i>Klebsiella oxytoca</i>	2 (2.6)	—	
<i>Klebsiella</i> sp.	1 (1.3)	—	
<i>Pseudomonas</i>	5 (6.4)	1 (4.8)	
<i>Pseudomonas aeruginosa</i>	3 (3.8)	1 (4.8)	
<i>Pseudomonas oryzae</i>	1 (1.3)	—	
<i>Pseudomonas fluorescens</i>	1 (1.3)	—	
<i>Escherichia coli</i>	8 (10)	3 (14)	
<i>Acinetobacter</i>	5 (6.4)	1 (4.7)	
<i>Acinetobacter baumannii/calcoaceticus</i>	3 (3.8)	—	
<i>Acinetobacter</i> sp.	2 (2.6)	1 (4.8)	
<i>Stenotrophomonas maltophilia</i>	3 (3.8)	—	
<i>Pantoea agglomerans</i>	2 (2.6)	—	
Fungal	2 (2.6)	1 (4.8)	0.58
All Candida	2 (2.6)	1 (4.8)	
<i>Candida albicans</i>	2 (2.6)	—	
<i>Candida glabrata</i>	—	1 (4.8)	
Outcomes			
Admitted to pediatric intensive care unit within 72 hours	7 (13)	2 (11)	1.0
Died during hospitalization	1 (1.8)	2 (11)	0.18
Median length of stay after CLABSI (days)	6 (IQR 4, 10)	18 (IQR 11, 32)	<0.001
Central line removed because of infection	24 (44)	6 (32)	0.42

Single organisms in ambulatory CLABSI group not mentioned: *Achromobacter*, *Bacillus circulans*, *Citrobacter freundii*, *Gordonia species*, *Micrococcus luteus*, *Moraxella osloensis*, and *Ochrobactrum anthropi*. Single organisms in inpatient CLABSI group not mentioned: *Citrobacter* sp., *Clostridium tertium*, and *Corynebacterium jeikeium*. The *P*-value of 0.58 next to the gram positive, gram negative, and fungal infection headings compares total gram positive, gram negative and fungal organisms for ambulatory versus inpatient CLABSIs. IQR, interquartile range. Bold font represents statistically significant associations ($P < 0.05$).

TABLE III

Characteristics Associated With Patients' First Ambulatory Central Line-Associated Blood Stream Infection (CLABSI) in Bivariable Analyses

Characteristics	CLABSI (N = 43) (%)	Controls (N = 86) (%)	Odds ratio (95% CI)	P-value (bivariable)
Demographics				
Mean age at infection or clinic visit in years	10.4 (sd 6.8)	10.4 (sd 6.2)	1 (0.94, 1.1)	0.99
Gender (% male)	30 (70)	50 (58)	0.61 (0.28, 1.3)	0.21
Insurance type				
Commercial/blue cross	11 (26)	21 (24)	Ref	Ref
HMO	14 (33)	31 (36)	0.82 (0.31, 2.1)	0.69
Medicaid	15 (35)	31 (36)	0.92 (0.34, 2.5)	0.86
Other	3 (7.5)	3 (3.5)	1.9 (0.35, 10)	0.46
Clinical characteristics				
Malignancy type				
Hematologic	23 (53.5)	50 (58.1)	Ref	Ref
Solid	18 (41.9)	35 (40.7)	1.1 (0.50, 2.2)	0.90
Non-oncologic BMT	2 (4.7)	1 (1.2)	4.0 (0.36, 44)	0.26
Acute myeloid leukemia diagnosis	7 (16)	2 (2.3)	7 (1.4, 33)	0.015
Relapse before infection or clinic visit	10 (23)	10 (12)	2.19 (0.85, 5.7)	0.10
Mucositis	0	2 (2.3)	—	—
Active graft versus host disease	1 (2.3)	3 (3.5)	0.67 (0.07, 6.4)	0.73
Central line type				
Totally implantable devices (TID)	9 (21)	79 (92)	See below	See below
Tunneled, externalized catheters (TE)	34 (79)	7 (8)		
Less than 1 month from central line insertion	10 (23)	8 (9.3)	2.68 (1.01, 7.1)	0.048
Current steroid use	8 (19)	18 (21)	0.88 (0.36, 2.1)	0.77
Current immunosuppressant use	5 (12)	2 (2.3)	8.6 (0.98, 75)	0.052
Current antibiotic use	36 (84)	63 (73)	2.2 (0.75, 6.3)	0.15
High-intensity chemotherapy regimen	33 (77)	32 (37)	4.46 (2.0, 10)	<0.001
Bone marrow transplant within 100 days of infection or clinic visit	8 (19)	2 (2.3)	14.5 (1.8, 117)	0.012
Red blood cell or platelet	13 (30)	9 (11)	3.1 (1.3, 7.5)	0.013
Transfusion within 1 week of infection or clinic visit				
Neutropenic (ANC < 500)	13 (30)	7 (8.1)	5.47 (1.8, 17)	0.003
Skin breakdown at central line site	2 (4.7)	2 (2.3)	2.0 (0.28, 14)	0.49
Other skin breakdown	5 (12)	8 (9.3)	1.3 (0.40, 4.1)	0.68
Previous bacteremia in this central line	10 (23)	9 (11)	2.3 (0.92, 6.0)	0.075
Previous bacteremia in any central line	20 (47)	11 (13)	6.3 (2.3, 17)	<0.001

Only incident CLABSIs within the study window were used for this analysis. For the central line type variable, the large association between TE lines and the CLABSI group and TID lines and the control group prevented the use of a conditional logistic regression model as central line type was as predictive of CLABSI as knowing the case/control status. Bold font represents statistically significant associations ($P < 0.05$).

TABLE IV

Characteristics Associated With Ambulatory Central Line-Associated Blood Stream Infection (CLABSI) in Multivariable Analyses

Clinical Characteristics	Odds ratio (95% CI)	P-value (multivariable)
Acute myeloid leukemia diagnosis	2.7 (0.34, 21)	0.35
Less than 1 month from central line insertion	4.2 (1.0, 17)	0.048
High-intensity chemotherapy regimen	2.2 (0.73, 6.7)	0.16
Bone marrow transplant within 100 days of infection or clinic visit	16 (1.1, 264)	0.046
Red blood cell or platelet transfusion within 1 week of infection or clinic visit	1.4 (0.33, 6.3)	0.63
Neutropenic (ANC < 500)	2.1 (0.39, 11)	0.39
Previous bacteremia in any central line	10 (2.5, 43)	0.001

Only incident CLABSIs within the study window were used (N = 43). Central line type was not included in this model because central line type was as predictive of CLABSI as knowing the case/control status. Only the variables listed were included in the multivariable model because they were all significantly associated with CLABSIs in bivariable analyses ($P < 0.05$). The high-intensity chemotherapy regimen definition overlaps with the definition of bone marrow transplant within 100 days of infection or clinic visit as all participants in the bone marrow transplant within 100 days group are necessarily in the high-intensity chemotherapy regimen group (eight CLABSI cases and two controls). When these patients were excluded from the high-intensity chemotherapy regimen group for the multivariable model, there were no changes in the statistical associations noted above (Supplemental Table). Bold font represents statistically significant associations ($P < 0.05$).