




Original Article

Risk factors for central line-associated bloodstream infection in the pediatric intensive care setting despite standard prevention measures

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Abstract

Objective: Identify risk factors for central line-associated bloodstream infections (CLABSI) in pediatric intensive care settings in an era with high focus on prevention measures.

Design: Matched, case–control study.

Setting: Quaternary children's hospital.

Patients: Cases had a CLABSI during an intensive care unit (ICU) stay between January 1, 2015 and December 31, 2020. Controls were matched 4:1 by ICU and admission date and did not develop a CLABSI.

Methods: Multivariable, mixed-effects logistic regression.

Results: 129 cases were matched to 516 controls. Central venous catheter (CVC) maintenance bundle compliance was >70%. Independent CLABSI risk factors included administration of continuous non-opioid sedative (adjusted odds ratio (aOR) 2.96, 95% CI [1.16, 7.52], $P = 0.023$), number of days with one or more CVC in place (aOR 1.42 per 10 days [1.16, 1.74], $P = 0.001$), and the combination of a chronic CVC with administration of parenteral nutrition (aOR 4.82 [1.38, 16.9], $P = 0.014$). Variables independently associated with lower odds of CLABSI included CVC location in an upper extremity (aOR 0.16 [0.05, 0.55], $P = 0.004$); non-tunneled CVC (aOR 0.17 [0.04, 0.63], $P = 0.008$); presence of an endotracheal tube (aOR 0.21 [0.08, 0.6], $P = 0.004$), Foley catheter (aOR 0.3 [0.13, 0.68], $P = 0.004$); transport to radiology (aOR 0.31 [0.1, 0.94], $P = 0.039$); continuous neuromuscular blockade (aOR 0.29 [0.1, 0.86], $P = 0.025$); and administration of histamine H2 blocking medications (aOR 0.17 [0.06, 0.48], $P = 0.001$).

Conclusions: Pediatric intensive care patients with chronic CVCs receiving parenteral nutrition, those on non-opioid sedative infusions, and those with more central line days are at increased risk for CLABSI despite current prevention measures.

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Introduction

Healthcare-associated infections (HAI) occur in 10%–20% of critically ill children,^{1,2} with central line-associated bloodstream infection (CLABSI) being one of the most prevalent.^{1,3} CLABSI are defined by the National Healthcare Safety Network (NHSN) of the U.S. Centers for Disease Control and Prevention.⁴ Since the early 2000s, evidence-based insertion and maintenance bundles for

central venous catheters (CVCs) have substantially decreased CLABSI in children in intensive care units (ICUs).^{5–9}

While the evolution of prevention bundles has improved CVC care, there are many additional factors that affect CLABSI risk. Previous work has demonstrated that CLABSI risk factors in the pediatric intensive care setting include high number of line accesses, prolonged dwell time, receipt of parenteral nutrition, ICU as location for line placement, presence of concurrent CVCs, active intra-abdominal pathology, immunosuppression, more patients per ICU nurse, unscheduled medication administrations, non-Caucasian race, and primary language other than English.^{10–21} Despite current prevention efforts and attention to known risk factors, CLABSI continue to be a significant source of morbidity and mortality and a cost burden on the healthcare system.^{3,22–27} Additionally, the characteristics of patients admitted to pediatric

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ICUs have changed since initial development of CVC insertion and maintenance bundles, suggesting there may be unrecognized risk factors for CLABSI.²⁸ Previous work illustrates a targeted CVC maintenance bundle has the greatest impact on CLABSI rates in children^{9,29}; thus, it is imperative to identify risk factors for patients who develop CLABSI despite receiving standard prevention approaches to consider whether bundles can be modified further. Our primary aim was to identify contemporary risk factors for the development of CLABSI in pediatric intensive care settings in the context of high focus on standard preventive measures.

Methods

Study design and population

We conducted a single center, retrospective, case–control study at Boston Children’s Hospital (BCH), a 410 bed, free-standing children’s hospital with 107 ICU beds at the time of the study. The BCH Institutional Review Board determined this study qualified as exempt from the requirements of 45 CFR 46. STROBE guidelines were followed (Appendix 1).

Case patients were identified via BCH Infection Prevention and Control as having met the NHSN definition for a CLABSI.⁴ NHSN guidelines for reporting of single common commensal organisms and of mucosal barrier injury laboratory-confirmed bloodstream infections were followed, excluding these patients as cases.⁴ Case patients were admitted to the Neonatal ICU (700 admissions/year), Medical/Surgical ICU (2100 admissions/year), Cardiac ICU (1300 admissions/year, includes nearly all term newborns with congenital heart disease), or the Medical ICU (850 admissions/year) from January 1, 2015 through December 31, 2020. ICU nurses are assigned to work in a specific ICU, but there is a small group that staffs all four ICUs. CVC types included umbilical venous catheters (UVCs), port-a-caths (ports), tunneled CVCs, non-tunneled CVCs, and peripherally inserted central catheters (PICCs)⁴. Exclusion criteria were age less than two months or greater than 21 years, corrected gestational age less than 37 weeks, and a second CLABSI involving the same CVC. Each case was matched to four controls defined as patients with an ICU stay of at least two days, with a CVC in place for at least two days, and who did not develop a CLABSI. Cases and controls were matched on ICU and date of admission (+/– one calendar month from case admission date).

The BCH CVC insertion bundle for CLABSI prevention includes a checklist for insertion, proper hand hygiene, use of a prepackaged CVC kit, use of maximal sterile barriers, and appropriate antisepsis with chlorhexidine-alcohol. The BCH CVC maintenance bundle for CLABSI prevention includes daily discussion of CVC need, appropriate disinfection of needleless connectors and catheter hubs prior to CVC access, replacement of needleless connectors and tubing at intervals no longer than every 96 hours, CVC dressing changes every 7 days unless indicated sooner, and daily chlorhexidine gluconate treatment (wipes) for patients aged 2 months and older. Since November 2017, bundle compliance at BCH has been monitored via Kamishibai card (K-card) audits, allowing for auditing of all elements of the bundle.³⁰ Since this time, compliance with all elements of the bundle has been >70% across all four ICUs, with lower compliance for daily discussion of CVC need and completion of daily chlorhexidine gluconate treatments (wipes). K-card audits were completed weekly for a minimum of 15–20 audits in each ICU per month so not all cases and controls received a K-card audit and some may have received more than one. There were no changes to the CVC bundles when K-card auditing was implemented.

A list of potential risk factors was developed by literature review and expert consensus (Appendix 2). The final variables were retrospectively extracted from the electronic medical record (Appendix 3). The period of interest for case patients spanned the three calendar days before and the calendar day of the positive blood culture that defined the CLABSI. For control patients, the period of interest spanned the ICU admission date or CVC placement date (whichever happened later) to the CVC removal date or ICU discharge date (whichever happened sooner). Data validation was completed through independent, random review of raw data for 20% of participants (KM and KR). Variables with >5% discrepancy rate were manually checked for all participants (Appendix 4).

Statistical analysis

Continuous data were summarized using medians and inter-quartile ranges. Categorical data were presented as counts and percentages. Crude and adjusted odds ratios for CLABSI with 95% confidence intervals and *P* values were calculated using univariate and multivariable mixed-effects logistic regression to account for clustering within matched sets of cases and controls. For the assessment of blood product administration as a risk factor in both univariate and multivariable analyses, we excluded patients who received extracorporeal membrane oxygenation support because they routinely receive large volumes of blood products. A two-tailed *P* value of <0.05 was considered statistically significant. Variables with a *P* < 0.05 in univariate analysis were included in the multivariable model. Sensitivity analysis was also performed excluding a subset of matched sets (*n* = 14) that had a gap of one or more calendar days during their ICU stay without a CVC in place. Statistical analysis was performed using Stata (version 16.1, StataCorp LLC, College Station, Texas). The overall sample size provided 80% power for detecting clinically meaningful associations between predictor variables and CLABSI outcomes (odds ratio = 1.3) using univariate and multivariable logistic regression analysis, assuming a two-tailed 5% alpha. Power calculations were performed using GPower (version 3.1.9, University of Dusseldorf, Germany).

Results

There were 129 unique CLABSI cases among 122 different patients, which were matched to 516 controls (Figure 1). Table 1 displays the study population demographics and key outcomes. Case patients were significantly younger than control patients (median 8.9 months vs. 28.4 months, *P* < 0.001) and had a significantly longer ICU stay (median 16 days vs. 8.9 days, *P* = 0.003). A lower proportion of patients with CLABSI survived to ICU discharge (79.1% vs. 91.1%, *P* < 0.001). Case patients had higher median PIM3 scores with associated risk of mortality of 3.3% vs. <1%, but these were available on only a subset of patients admitted to the MSICU and MICU. Table 2 displays the microbiology of CLABSI pathogens. Figure 2 illustrates the annual CLABSI rate by ICU.

Table 3 summarizes the univariate analysis, which revealed seven factors associated with increased odds of CLABSI and 20 factors associated with decreased odds of CLABSI. The seven factors associated with increased odds of CLABSI included CVC location in the subclavian vein (OR 1.89, 95% CI [1.15, 3.13], *P* = 0.013), a tunneled CVC (OR 3.52 [2.1, 5.88], *P* < 0.001), duration of CVC dwell (OR 1.16 per 10-day increase [1.08, 1.25], *P* < 0.001), history of stem cell transplant (OR 3.27 [1.35, 7.9],

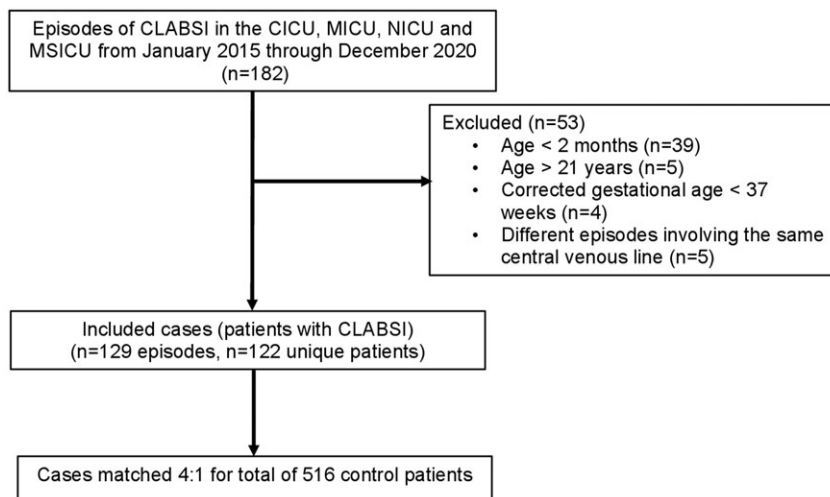
Table 1. Patient characteristics and key outcomes

Characteristic	Case Patients (n=129)	Control Patients (n=516)	P value
Age at admission, months, median (IQR)	8.9 (3.9, 42.4)	28.4 (6.1, 114.2)	<0.001
Weight percentile at admission, median (IQR)	12.0 (0.4, 34.6)	8.9 (0.4, 41.7)	0.648
Male sex, n (%)	64 (49.6%)	271 (52.5%)	0.561
Unit of Admission, n (%)			0.999
Neonatal ICU	16 (12.4%)	64 (12.4%)	
Medical ICU	21 (16.3%)	84 (16.3%)	
Medical – Surgical ICU	42 (32.6%)	168 (32.6%)	
Cardiac ICU	50 (38.8%)	200 (38.8%)	
Survival to discharge, n (%)	102 (79.1%)	470 (91.1%)	<0.001
ICU length of stay ^a , median (IQR)	16 (7, 34)	8.9 (4.9, 19.9)	0.003
Medical/Surgical, n (%)			0.59
Medical	58 (45%)	244 (47.5%)	
Surgical	71 (55%)	270 (52.5%)	
Type of Admission, n (%)			0.06
Elective	63 (48.8%)	296 (57.4%)	
Emergent	66 (51.2%)	220 (42.6%)	
PIM3 Score on Admission, median (IQR) ^b	−3.4 (−4.6, −2.8)	−4.6 (−6, −3.4)	<0.001

Abbreviations: CLABSI, central line-associated bloodstream infection; ICU, intensive care unit; IQR, interquartile range; PIM, pediatric index of mortality.

^aLength of Stay Definitions: Case = date of CLABSI to ICU discharge, Controls = ICU admission to ICU Discharge.

^bAvailable for 57 cases and 239 controls admitted to the MISCU and MICU.

**Figure 1.** Assembly of study population.

$P = 0.009$), presence of GI tract insufficiency (OR 1.86 [1.2, 2.88], $P = 0.006$), the combination of a chronic CVC (CVC in place for >21 days) and receipt of parenteral nutrition (OR 2.11 [1.39, 3.2], $P < 0.001$), and receipt of parenteral nutrition (OR 1.48 [1.01, 2.18], $P = 0.049$).

As shown in Table 4, the three variables independently associated with increased odds of CLABSI in multivariable analysis included administration of continuous non-opioid sedative (adjusted odds ratio (aOR) 2.96, 95% CI [1.16, 7.52], $P = 0.023$), number of days with one or more CVC in place (aOR 1.42 per 10 days [1.16, 1.74], $P = 0.001$), and the combination of a chronic

CVC and administration of parenteral nutrition (aOR 4.82 [1.38, 16.9], $P = 0.014$). Variables independently associated with lower odds of CLABSI in multivariate analysis included CVC location in an upper extremity or non-tunneled CVC; presence of an endotracheal tube or Foley catheter; transport to radiology; continuous neuromuscular blockade; and administration of histamine H2 blocking medications.

A post hoc sensitivity analysis excluding matched sets ($n=14$) that had a gap of one or more calendar days during their ICU stay without a CVC in place showed similar results to those reported above (Appendix 5).

Table 2. Microbiology of central line-associated bloodstream infections among case patients

Organism	Number of Cases (n=129)
Gram-positive	
<i>Staphylococcus aureus</i> ^a	19 (14.7%)
<i>Enterococcus faecalis</i>	15 (11.6%)
Coagulase-negative staphylococci	5 (3.9%)
<i>Enterococcus faecium</i>	3 (2.3%)
<i>Streptococcus agalactiae</i>	1 (0.8%)
<i>Micrococcus</i> species	1 (0.8%)
Gram-negative	
<i>Enterobacter</i> species	12 (9.3%)
<i>Klebsiella pneumoniae</i>	8 (6.2%)
<i>Serratia marcescens</i>	6 (4.7%)
<i>Stenotrophomonas maltophilia</i>	5 (3.9%)
<i>Klebsiella oxytoca</i>	3 (2.3%)
<i>Pseudomonas aeruginosa</i>	2 (1.6%)
<i>Acinetobacter</i> species	2 (1.6%)
<i>Kalamiella piersonii</i>	1 (0.8%)
<i>Escherichia coli</i>	1 (0.8%)
<i>Brevundimonas</i> species	1 (0.8%)
Yeast	
<i>Candida</i> species	10 (7.8%)
Polymicrobial	
	34 (26.4%)

^a3 (15.8%) of *S. aureus* CLABSIs, were MRSA.

Discussion

In this retrospective, case–control study of ICU CLABSI at a large, quaternary children’s hospital over a six-year period, we identified that higher number of days with a CVC in place, receiving a continuous non-opioid sedative infusion, and having a chronic CVC while also receiving parenteral nutrition were independently associated with increased odds of CLABSI.

Many of our results align with work done at our institution over a decade ago, with similar findings despite modifications of our CVC insertion and maintenance bundles in accordance with updated guidelines and standards.^{8,12,17,31} The repeat identification of several risk factors in this new study that are similar to prior predictors highlights that despite routine modification of prevention bundles, there are patient characteristics associated with increased risk for CLABSI that offer potential opportunities for further prevention efforts. Additionally, the Solutions for Patient Safety Network recently showed that attaining >95% reliability to the CVC maintenance bundle was associated with lower CLABSI rates.⁹ It is possible that our results could be different if we were able to achieve this level of reliability. BCH, like most peer institutions, is continuously working to improve bundle reliability with the hopes of decreasing CLABSI rates. Even so, we (and many other hospitals) have observed decreased CLABSI rates over the last decade, including among ICU patients, but we continue to strive to reduce rates as low as possible. Our work highlights the need to continue to improve compliance with current bundles, but also to consider additional approaches that might further reduce CLABSI rates in critically ill children.

Parenteral nutrition is a known risk factor for CLABSI.^{10,12–14} Previous work has also suggested that intraabdominal pathology and gastrointestinal dysfunction are associated with increased CLABSI risk.^{10,12,15,32,33} Many of these patients also receive parenteral nutrition for varying periods of time. To assess whether

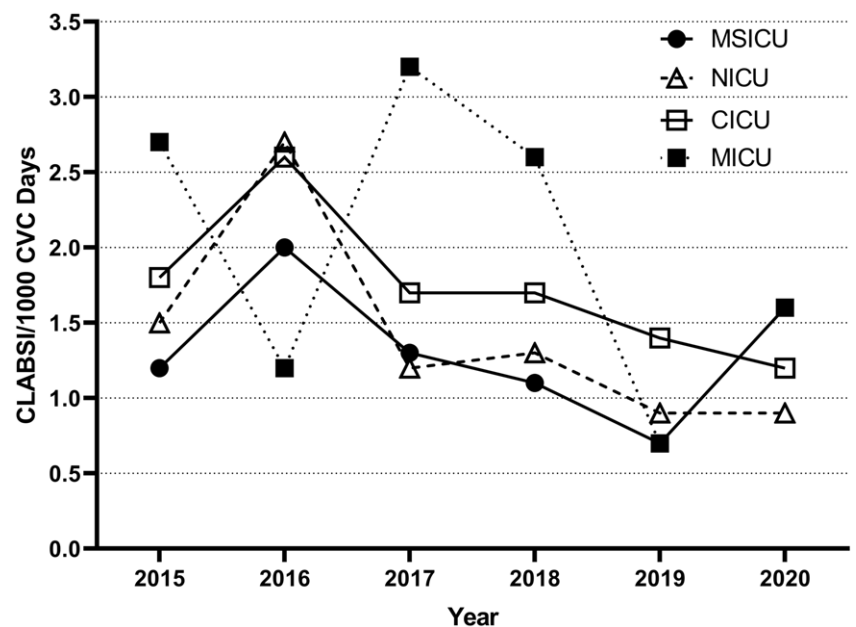


Figure 2. Annual CLABSI rate (per 1000 CVC days) for each intensive care unit. *Note:* The rates for both the MSICU and MICU were 0.7 in 2019 and 1.6 in 2020, so the data points overlap. Abbreviations: CLABSI, central line-associated bloodstream infection; CVC, central venous catheter; MSICU, medical/surgical intensive care unit; NICU, neonatal intensive care unit; CICU, cardiac intensive care unit; MICU, medical intensive care unit.

Table 3. Univariate analysis of risk factors for the development of central line-associated bloodstream infections in the pediatric intensive care setting

Predictor	Case Patients (n=129)	Control Patients (n=516)	Crude Odds Ratio (95% CI)	P value
CVC characteristics				
Anatomic location of placement				
Internal jugular vein	32 (24.8%)	231 (44.8%)	0.34 (0.21, 0.54)	<0.001
Subclavian vein	29 (22.5%)	71 (13.8%)	1.89 (1.15, 3.13)	0.013
Upper extremity vein	62 (48.1%)	298 (57.8%)	0.64 (0.43, 0.97)	0.035
Lower extremity vein	29 (22.5%)	92 (17.8%)	1.34 (0.83, 2.15)	0.227
Type of CVC				
Port	6 (4.7%)	12 (2.3%)	2 (0.75, 5.33)	0.166
PICC	76 (58.9%)	318 (61.6%)	0.88 (0.58, 1.33)	0.545
Tunneled	36 (27.9%)	57 (11.1%)	3.52 (2.1, 5.88)	<0.001
Non-tunneled	33 (25.6%)	280 (54.3%)	0.21 (0.13, 0.34)	<0.001
Number of CVC lumens ^a				
Single	36 (22.8%)	129 (17.1%)	Reference	
Double	107 (67.7%)	525 (69.7%)	1.37 (0.9, 2.09)	0.171
Triple	15 (9.5%)	99 (13.1%)	1.84 (0.96, 3.52)	0.083
Concurrent CVCs present				
Number of days with one or more CVC(s) in place	15 (7, 33)	7 (4, 16)	1.16 per 10-day increase (1.08, 1.25)	<0.001
Concurrent invasive medical devices				
Chest tube	24 (18.6%)	214 (41.5%)	0.29 (0.17, 0.48)	<0.001
Endotracheal tube	54 (41.9%)	407 (78.9%)	0.16 (0.1, 0.26)	<0.001
Foley catheter	40 (31%)	359 (69.6%)	0.18 (0.12, 0.29)	<0.001
Gastro-jejunostomy tube	30 (23.3%)	126 (24.4%)	0.94 (0.6, 1.48)	0.783
Gastrostomy tube	41 (31.8%)	175 (33.9%)	0.91 (0.6, 1.37)	0.653
Nasoduodenal or nasal jejunal tube	33 (25.6%)	216 (41.9%)	0.48 (0.31, 0.74)	0.001
Nasogastric tube	47 (36.4%)	344 (66.7%)	0.27 (0.17, 0.41)	<0.001
Ostomy	14 (10.9%)	55 (10.7%)	1.02 (0.54, 1.93)	0.939
Two or more invasive gastric devices	12 (9.3%)	44 (8.5%)	1.09 (0.57, 2.14)	0.782
Immunocompromising conditions				
History of solid organ transplant	7 (5.4%)	50 (9.7%)	0.52 (0.23, 1.19)	0.122
History of stem cell transplant	11 (8.5%)	17 (3.3%)	3.27 (1.35, 7.9)	0.009
Neutropenia (ANC <500 cells/ μ L)	4 (3.1%)	29 (5.6%)	0.53 (0.18, 1.55)	0.25
Oncologic condition	12 (9.3%)	41 (8%)	1.22 (0.59, 2.51)	0.594
Intra-hospital transport				
Cardiac catheterization or EP Lab	5 (3.9%)	59 (11.4%)	0.3 (0.12, 0.78)	0.013
Interventional radiology	1 (0.8%)	67 (13%)	0.05 (0.01, 0.39)	0.004
Operating room	16 (12.4%)	147 (28.5%)	0.34 (0.19, 0.6)	<0.001
Radiology	14 (10.9%)	153 (10.9%)	0.28 (0.16, 0.51)	<0.001
Administration of alteplase	18 (14%)	105 (20.4%)	0.63 (0.37, 1.09)	0.102
Administration of blood products ^b				
Cryoprecipitate	1 (0.9%)	29 (6%)	0.14 (0.02, 1.01)	0.051
Fresh frozen plasma	6 (5.2%)	59 (12.2%)	0.38 (0.16, 0.91)	0.029
Packed red blood cells	32 (27.6%)	215 (44.5%)	0.45 (0.28, 0.72)	0.001
Platelets	17 (14.7%)	88 (18.2%)	0.76 (0.43, 1.34)	0.342

(Continued)

Table 3. (Continued)

Predictor	Case Patients (n=129)	Control Patients (n=516)	Crude Odds Ratio (95% CI)	P value
Weight <5%tile	69 (53.9%)	222 (46.7%)	1.4 (0.9, 2.1)	0.105
Weight >85%tile	7 (5.5%)	38 (8%)	0.65 (0.28, 1.54)	0.327
Presence of GI tract dysfunction				
Ileus	102 (79.1%)	416 (80.6%)	0.91 (0.56, 1.48)	0.696
Ischemia	44 (34.1%)	183 (35.5%)	0.94 (0.63, 1.42)	0.775
Insufficiency	44 (34.1%)	117 (22.7%)	1.86 (1.2, 2.88)	0.006
Continuous neuromuscular blockade infusion	23 (17.8%)	191 (37%)	0.37 (0.22, 0.6)	<0.001
Continuous opioid sedative infusion	72 (55.8%)	341 (66.1%)	0.64 (0.43, 0.95)	0.028
Continuous nonopioid sedative infusion	83 (64.3%)	387 (75%)	0.59 (0.38, 0.9)	0.014
Stress ulcer prophylaxis				
PPI	84 (65.1%)	315 (61.1%)	1.19 (0.79, 1.8)	0.395
H2 blockers	70 (54.3%)	392 (76%)	0.33 (0.21, 0.51)	<0.001
Combination of PPI + H2 blocker	41 (31.8%)	221 (42.8%)	0.64 (0.43, 0.95)	0.026
Source of nutrition				
Chronic CVC + parenteral nutrition	49 (38%)	117 (22.7%)	2.11 (1.39, 3.2)	<0.001
Chronic parenteral nutrition	38 (29.5%)	67/237 (28.3%)	1.27 (0.74, 2.17)	0.384
Combination of enteral + parenteral	43 (33.3%)	174 (33.7%)	0.98 (0.65, 1.49)	0.941
Enteral nutrition	99 (76.7%)	432 (83.7%)	0.63 (0.39, 1.02)	0.06
Parenteral nutrition	72 (55.8%)	238 (46.1%)	1.48 (1.01, 2.18)	0.049

Abbreviations: CLABSI, central line associated bloodstream infection, CVC, central venous catheter, ANC, absolute neutrophil count, EP, electrophysiology, GI, gastrointestinal, PPI, proton pump inhibitor, H2, histamine H2 receptor, chronic CVC, CVC in place for >21 days.

Note: For categorical variables (except for "Number of CVC Lumens"), the reference group for the estimated odds ratio is all other participants who are not in that category.

^aIncluded 158 CVCs for cases and 743 CVCs for controls.

^bExcludes patients who received extracorporeal membrane support during ICU admission.

certain subgroups of patients receiving parental nutrition were at greater risk for CLABSI, composite variables were developed. We found that the composite risk factor of chronic CVC (CVC in place for >21 days) and administration of parenteral nutrition was associated with increased risk of CLABSI. Additionally, we assessed other markers of gastrointestinal tract function including the presence of an ostomy, the presence of single and multiple invasive gastric devices, or the presence of gut ischemia, ileus, or insufficiency, but these variables were not significantly associated with CLABSI in this study. Our results indicate that despite current CLABSI prevention bundles, patients receiving parenteral nutrition remain at high risk for CLABSI, and those who also have a chronic CVC in place are at even greater risk. Additionally, 46% of the patients who qualified for our chronic CVC and parenteral nutrition composite variable also qualified for having GI insufficiency suggesting that this specific population is at greater risk. Large, multicenter studies are needed to assess parenteral nutrition parameters such as osmolarity and anticoagulants as well as glucose, amino acid, and lipid content and their potential association with CLABSI risk. Such further work to characterize differences among patients receiving parenteral nutrition who develop CLABSI compared with those who do not can help clinicians identify children at highest risk and guide new strategies to reduce their risk. While this work is being done, interventions at the bedside to mitigate the increased risk of CLABSI in patients receiving parenteral nutrition could include use of peripheral

access points for intermittent medications and collection of blood draws at the time the CVC is being accessed to administer a new bag of parenteral nutrition.

Surprisingly, we found that patients with a CVC and a concurrent endotracheal tube or Foley catheter, as well as those receiving continuous neuromuscular blockade or stress ulcer prophylaxis with histamine blockers had a decreased odds of CLABSI. We speculate that a possible explanation is that intubated patients, especially those receiving continuous neuromuscular blockade, are more likely to have a nurse with fewer patient assignments (1 nurse to 1 patient or 1 nurse to 2 patients across the ICUs at BCH), facilitating higher reliability with all elements of the CVC maintenance bundle.^{31,34,35} The role of stress ulcer prophylaxis in critically ill pediatric patients remains largely unknown but it is more commonly used in the sickest patients who also usually have a lower nurse to patient ratio which might facilitate higher CVC maintenance bundle reliability.^{36,37} Additionally, patients receiving continuous neuromuscular blockade may be less likely to self-contaminate their CVC or tamper with the dressing. Finally, some bloodstream infections in patients with endotracheal tubes or Foley catheters may meet criteria to be considered secondary to pneumonia or urinary tract infection, respectively, leading to them not being categorized as CLABSI.⁴

Over the last two decades, much CLABSI research has assessed line characteristics and their relationship to CLABSI. It is well established that temporary, non-tunneled CVCs are associated

Table 4. Multivariable analysis of risk factors for the development of central line-associated bloodstream infections in the pediatric intensive care setting

Covariate	Adjusted Odds Ratio (95% CI)	P value
Anatomic location of placement		
Upper extremity vein	0.16 (0.05, 0.55)	0.004
Type of CVC		
Non-tunneled	0.17 (0.04, 0.63)	0.008
Number of days with one or more CVC(s) in place	1.42 per 10 days (1.16, 1.74)	0.001
Concurrent invasive medical devices		
Endotracheal tube	0.21 (0.08, 0.6)	0.004
Foley catheter	0.3 (0.13, 0.68)	0.004
Intra-hospital transport <72 hours prior to CLABSI		
Radiology	0.31 (0.1, 0.94)	0.039
Presence of GI tract dysfunction		
Insufficiency	Omitted due to collinearity	
Continuous neuromuscular blockade infusion at time of CLABSI	0.29 (0.1, 0.86)	0.025
Continuous opioid sedative infusion at time of CLABSI	Omitted due to collinearity	
Continuous nonopioid sedative infusion at time of CLABSI	2.96 (1.16, 7.52)	0.023
Stress ulcer prophylaxis		
H2 blockers	0.17 (0.06, 0.48)	0.001
Source of nutrition		
Chronic CVC + parenteral nutrition	4.82 (1.38, 16.9)	0.014

Abbreviations: CLABSI, central line associated bloodstream infection, CVC, central venous catheter, EP, electrophysiology, GI, gastrointestinal, PPI, proton pump inhibitor, H2, histamine H2 receptor.

with greater CLABSI risk.^{10,12,38} Interestingly, in our multivariable analysis, the presence of a non-tunneled CVC was associated with a significantly decreased odds of CLABSI. It is standard in all ICUs at our institution for an emergent, non-tunneled CVC to be transitioned to a PICC as soon as possible (as suggested by a prior multicenter QI study), resulting in shorter duration of non-tunneled CVC dwells which could explain this finding.³⁸ Additionally, a substantial proportion of our non-tunneled CVCs are placed in the operating room as opposed to at the bedside in the ICU. Finally, we found that the use of an upper extremity vein, most commonly for PICC placement, is associated with a significantly decreased odds of CLABSI.

We also found that patients transported out of the ICU to radiology had a decreased odds of CLABSI and those receiving continuous non-opioid sedative infusions had an increased odds of CLABSI. The first finding may reflect the fact that patients need to have some degree of clinical stability to leave the ICU, and therefore, they may be less ill and at lower risk of bloodstream infection. It is also common practice in our institution that when these patients are being cared for in non-ICU locations by other providers, such as anesthesia, their CVCs are not routinely accessed for intermittent medications, thereby decreasing risk of introduction of bacteria into the bloodstream. Our finding that patients receiving continuous non-opioid sedative infusions (primarily dexmedetomidine and/or midazolam) have increased odds of CLABSI warrants further study. It could be explained by our institutional practice of weaning continuous sedative infusions rather than transitioning to equivalent enteral medications (which

can lead to prolonged infusions). Other possibilities include immune suppression by these agents, including the recently described inhibition of bacterial phagocytosis of Gram-negative bacilli in vitro by dexmedetomidine.^{39,40}

In our multivariable analyses, there was no significant association between the administration of packed red blood cells or other blood products and CLABSI development; this potential association was only evaluated for patients who did not experience extracorporeal membrane oxygenation support during their ICU admission. Multiple prior studies have demonstrated a relationship between the administration of blood products and the development of CLABSI.^{10,12,17} This unexpected finding might be explained by recent changes in practice, including preferentially administering blood products through peripheral access points, different leukocyte depletion methods, and more frequent changing of needleless connectors.³¹

As with all case-control studies, our study has limitations. One limitation is generalizability, as our patient population may not be representative of other pediatric ICUs. It is also possible that there is unmeasured confounding related to the absence of certain variables influencing CLABSI risk (such as ICU capacity or proportion of nurses in traveler roles). The use of automated data introduces the possibility of incorrect and/or missing data. We attempted to mitigate this limitation through our random, manual data validation. Our data also depended on the completeness and accuracy of the original documentation. We were unable to assess several known risk factors (such as race, primary language, and number of line accesses) in this study due to substantial missing

data. There are practice differences among our four ICUs, resulting in some variables (such as illness severity scores) being available for only certain patients. Our population included a few subgroups of interest (patients who have had a history of a stem cell transplant, patients who have had multiple CLABSI with different lines) with relatively small numbers, such that no meaningful conclusions about risk factors within these patient groups could be reached. Additionally, we chose not to match controls on age to evaluate it as a risk factor, to avoid similarity between cases and controls on other risk factors which could have made identification of significant risk factors more challenging, and to improve generalizability of our findings to critically ill children of all ages (given that >75% of cases were younger than 5 years).

In summary, our work demonstrates that pediatric ICU patients with a greater number of CVC days, those receiving parenteral nutrition in the presence of a chronic CVC, and those receiving continuous non-opioid sedative infusions are at increased risk for CLABSI in the context of high but imperfect adherence to current prevention measures. Improving reliability of practice for core CVC bundle elements and developing novel strategies to further reduce CLABSI risk in the current era should be prioritized. Further research should focus on characterizing the differences in patients receiving parenteral nutrition who develop CLABSI compared with those who do not.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/ice.2024.131>

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