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Infectious Disease

Defining Incidence and Risk Factors for Catheter-Associated Bloodstream Infections in an Outpatient Adult Hematopoietic Cell Transplantation Program

Marissa K. McDonald[1,*], Kathryn A. Culos[1], Katie S. Gatwood[1], Caleb Prow[1], Heidi Chen[2], Bipin N. Savani[3], Michael Byrne[3], Adetola A. Kassim[3], Brian G. Engelhardt[3], Madan Jagasia[3], Gowri Satyanarayana[4]

[1] *Department of Pharmaceutical Services, Vanderbilt University Medical Center, Nashville, Tennessee*
[2] *Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee*
[3] *Division of Hematology/Oncology, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee*
[4] *Division of Infectious Diseases, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee*

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A B S T R A C T

Allogeneic hematopoietic cell transplantation (HCT) patients are at an increased risk of developing central line–associated bloodstream infections (CLABSIs) due to prolonged periods of myelosuppression, immunosuppression, and indwelling catheter days. CLABSIs are among the most serious complications in HCT recipients and can lead to prolonged hospitalizations, intensive care unit admissions, lengthy antimicrobial therapies, and increased mortality. There is a lack of data regarding the incidence and risk factors associated with the development of CLABSIs in the HCT population undergoing outpatient transplantation. This was a single-center, retrospective analysis of adult patients who underwent allogeneic HCT between July 2012 and July 2016 in an outpatient transplant unit at a tertiary academic medical center. The primary outcome was the cumulative incidence of CLABSIs from the date of central line placement through the first 100 days post-transplantation. Secondary outcomes included risk factors for CLABSI, number of hospitalizations due to CLABSI, mortality rate at 6 months post-transplantation, and the cumulative incidence, speciation, and presence of multidrug resistance in identified microorganisms. Three hundred fifty-nine patients underwent allogeneic HCT at Vanderbilt University Medical Center and 352 were included for analysis. The cumulative incidence of CLABSIs was 9%, with the majority occurring within the first 30 days post HCT (67%). The use of a matched unrelated donor (MUD) and/or haploidentical donor (odds ratio, 3.993; 95% confidence interval [CI], 1.329 to 12.001; $P = .0136$) and use of an ablative conditioning regimen (odds ratio, 2.394; 95% CI, 1.052 to 5.446; $P = .0374$) were independently associated with development of a CLABSI on multivariate analysis. The most common organism implicated in CLABSI was *Staphylococcus epidermidis* (34%). Patients who developed a CLABSI had an almost 5 times higher risk of mortality at 6 months post-transplantation compared with patients who did not develop a CLABSI (hazard ratio, 4.932; 95% CI, 2.463 to 9.878; $P < .001$). There is a low incidence of CLABSIs in patients undergoing HCT in the outpatient setting. Patients who underwent HCT using a MUD or haploidentical donor and received ablative conditioning were at higher risk for developing CLABSIs. Overall mortality at 6 months post-transplantation was higher in patients who developed a CLABSI. Additional prospective studies are needed to confirm these observations.

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BACKGROUND

Allogeneic hematopoietic cell transplantation (HCT) is an established treatment for patients with various malignant and nonmalignant diseases. Due to prolonged periods of myelosuppression, immunosuppression, and indwelling catheter days, HCT patients are at high risk for developing central line–associated bloodstream infections (CLABSIs) [1-3]. CLABSIs are a serious complication in this patient population and can lead to prolonged hospitalizations, intensive care unit (ICU) admissions, lengthy antimicrobial therapies, and increased mortality [2]. Bloodstream infections in HCT patients have been reported to occur in 27% to 68% of recipients with an associated increased mortality rate of 12% to 25% [1,2,4-6]. Several risk factors for bloodstream infections after HCT have been described. These include age >18 years, underlying disease (ie,

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* Correspondence and reprint requests: Marissa K. McDonald, PharmD, Vanderbilt University Medical Center, 1211 Medical Center Drive, c/o Dept of Pharmacy Services B-131, Nashville, TN 37232. (M.K. McDonald).
E-mail address: marissa.mcdonald@vanderbilt.edu (M.K. McDonald).

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acute myeloid leukemia or myelodysplastic syndrome), late stage of underlying disease, high HCT comorbidity index, use of cord blood as a donor source, severe graft-versus-host disease (GVHD), mucositis, increased steroid use, presence of a central venous catheter (CVC), and neutropenia [5-7].

Although these studies provide valuable data with regard to incidence, risk, and outcomes associated with bloodstream infections, most of the available CLABSI data are based on research conducted in the inpatient setting. Advances in supportive care and other technologies have allowed for outpatient management of HCT patients, eliminating the need for routine inpatient admission from conditioning through neutrophil recovery. With close follow-up, patients transplanted in the outpatient setting display equivalent or superior outcomes to historical inpatient transplants [8]. This includes providing enhanced patient comfort and satisfaction, shorter hospital length of stay, reduced risk of nosocomial infections, and decreased health care costs and resource utilization [9,10]. At Vanderbilt University Medical Center (VUMC), more than 95% of HCTs are performed in the outpatient setting. VUMC operates an outpatient stem cell transplantation clinic where the majority of patients undergo the entire transplant process through daily ambulatory visits while residing in nearby housing. Brief admissions are scheduled for unrelated transplant thymoglobulin infusions and for haploidentical cell infusion/post-transplant cyclophosphamide. Patients may also be admitted for complications requiring closer monitoring such as febrile neutropenia or severe GVHD. Once stabilized, patients are discharged to resume outpatient clinical visits. The aim of this study was to describe the cumulative incidence and risk factors associated with CLABSI from the date of central line placement through the first 100 days post-transplantation at an outpatient HCT program.

METHODS

This was a single-center, retrospective analysis conducted at VUMC, a tertiary academic medical center located in Nashville, Tennessee. This study was approved by the Institutional Review Board and a waiver of informed consent was obtained.

Study Subjects

All patients who underwent allogeneic HCT between July 1, 2012, and July 31, 2016, were screened for inclusion. Patients were included if they were at least 18 years of age and underwent a first HCT with CVC placement at VUMC. Patients were excluded if they underwent a CVC placement outside of VUMC or if they underwent a second HCT.

Covariates and Definitions

Demographic data was collected using VUMC's HCT database and included age, gender, cancer diagnosis, conditioning regimen, use of total body irradiation (TBI), donor type, graft type, and survival at 6 months post-transplantation. Additional pretransplant variables recorded included an assessment of disease risk index (DRI), a validated tool for risk-stratifying HCT patients into 1 of 4 risk groups (low risk, intermediate risk, high risk, and very high risk) based on disease and remission status at time of transplant [11], history of prior CVC infections and/or malfunctions, history of prior port use, CVC type, and line placement data. Clinical data collected included all culture and sensitivity results, total line days (from line placement until removal, date of CLABSI or day 100 post-transplantation, whichever was earlier), GVHD data, including maximum grade and site, number of hospitalizations due to CLABSI, hospital and ICU length of stay (LOS), total number of procedures, and incidence of neutropenia at time of CLABSI. Neutropenia was defined as an absolute neutrophil count or total WBC <500 cells/mm^3 within 3 days before or after the identification of positive blood culture/s.

The primary outcome was the cumulative incidence of CLABSIs from the date of line placement through the first 100 days post-transplantation. Patients were censored after the first bloodstream infection. CLABSI was defined by the Centers for Disease Control and Prevention and the National Healthcare Safety Network criteria as a primary bloodstream infection in a patient with a CVC and the isolation of a recognized pathogen on at least 1 blood culture or in 2 or more blood cultures on separate occasions with associated fever (>38ºC), hypotension and/or chills if a common skin contaminant was isolated [12]. Data for diagnosis were confirmed through chart review and were adjudicated by an independent third-party clinician (a member of the institution's Infection Control and Prevention Department). Secondary outcomes included risk factors for CLABSIs, number of hospitalizations due to CLABSIs, mortality at 6 months post-transplantation, and the cumulative incidence, speciation, and multidrug resistance (MDR) data from microorganisms identified. MDR infections were defined as nonsusceptibility to at least 1 antimicrobial agent in 3 or more drug classes [13].

Statistical Analysis

All statistical analyses were completed using R version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria) [14]. Univariate analyses were conducted using the chi-square test for all categorical data and the Wilcoxon rank-sum test for all continuous data. A logistic regression model reporting odds ratio (OR), 95% confidence interval (CI), and corresponding *P* value was used to identify risk factors for CLABSI through multivariate analysis. The 4 risk factors evaluated included GVHD (based on grade), donor type, conditioning regimen intensity, and DRI. A Cox proportional hazards analysis reporting hazard ratio (HR), 95% CI, and corresponding *P* value was used to determine mortality risk at 6 months post-transplantation. For all analyses, a *P* value of $<.05$ was considered statistically significant.

RESULTS

Patient Characteristics

A total of 359 patients underwent allogeneic HCT at VUMC from July 2012 to July 2016. Seven patients met exclusion criteria, resulting in 352 patients included in the final analysis. The patient characteristics are presented in Table 1. The median age was 54 years, 60% were men, and the majority had an underlying hematologic malignancy with a DRI of intermediate or high risk. Approximately 41% of patients underwent transplantation using an ablative conditioning regimen and 22% of patients received TBI as part of their regimen. HCT donors included 59% matched unrelated donors (MUDs) and 36% matched related donors (MRDs), with the majority (84%) of stem cell sources being peripheral blood stem cells.

CLABSI Incidence and Microbiology

Thirty-three CLABSIs were diagnosed in 352 patients (9%). The median time to first CLABSI from date of line placement was approximately 20 days. The majority of CLABSIs (67%) occurred between day 0 and day +30 (Figure 1). Seventy percent of patients were neutropenic at time of CLABSI and had been neutropenic for a median of 6 days before CLABSI diagnosis.

Table 1
Patient Characteristics and Univariate Analysis of Predictors of CLABSI

	No CLABSI (n = 306)	CLABSI (n = 46)	*P* Value
Age, yr	51.0 ± 13.8 (55.1)	46.9 ± 15.4 (48.2)	.150
Male	192 (60)	18 (55)	.267
Cancer diagnosis			
ALL	33 (10)	2 (6)	.289
AML	114 (36)	15 (45)	
MDS	52 (16)	5 (15)	
NHL	48 (15)	2 (6)	
Acquired SAA	14 (4)	3 (9)	
Anem/Hemo*	9 (3)	1 (3)	
CLL	6 (2)	2 (6)	
CML	9 (3)	2 (6)	
HD	9 (3)	0 (0)	
MPS	12 (4)	0 (0)	
MM	2 (1)	1 (3)	
Other†	11 (3)	0 (0)	
Disease risk index			
Low risk	19 (6)	4 (12)	.282
Intermediate risk	161 (50)	13 (39)	
High risk	90 (28)	8 (24)	
Very high risk	26 (8)	3 (9)	
Unable to assess	23 (7)	5 (15)	
Mortality at 6 mo, yes‡	29 (9)	11 (33)	<.001
Regimen intensity			
Ablative	125 (39)	18 (56)	.061
Nonablative	194 (61)	14 (44)	
TBI, yes	62 (19)	14 (42)	.002
Donor type			
MRD	122 (38)	5 (15)	.009
MUD	186 (58)	23 (70)	.205
Haploidentical	11 (3)	5 (15)	.002
Graft type			
BM	31 (10)	4 (12)	.661
Cord blood	17 (5)	4 (12)	.117
PBSC	271 (85)	25 (76)	.169
GVHD, yes	157 (49)	7 (21)	.002
GVHD grade			
I	37 (23)	1 (14)	.576
II	92 (58)	4 (57)	
III	23 (15)	1 (14)	
IV	6 (4)	1 (14)	
GVHD location			
Skin	101 (32)	4 (12)	.020
Gastrointestinal	96 (30)	4 (12)	.029
Liver	5 (2)	3 (9)	.006
Prior port, yes	93 (29)	10 (30)	.890
Total number of lines	1.122 ± .442 (1)	1.061 ± .242 (1)	.540
Previous CVC infection, yes	15 (5)	4 (12)	.073
Previous CVC malfunction, yes	20 (6)	3 (9)	.532
Total procedures			
Outpatient procedures	3.129 ± 2.778 (2)	.242 ± .502 (0)	<.001
Inpatient procedures	1.216 ± 2.695 (0)	.818 ± 1.667 (0)	.240

Values are presented as mean ± SD (median) or n (%).
ALL indicates acute lymphoblastic leukemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; SAA, acquired severe aplastic anemia; CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia; NHL, non-Hodgkin lymphoma; HD, Hodgkin's disease; MPS, myeloproliferative syndrome; MM, multiple myeloma; BM, bone marrow; PBSC, peripheral blood stem cell.
* Anem/Hemo includes paroxysmal nocturnal hemoglobinuria and sickle cell disease.
† Other cancer diagnoses include acute biphenotypic or hybrid leukemia, blastic plasmacytoid dendritic cell neoplasm, MDS/MPS unclassifiable, solitary plasmacytoma, and therapy-related AML.
‡ Mortality at 6 mo post-transplantation.

A total of 35 isolates were retrieved from 33 subjects diagnosed with a CLABSI (Table 2). Two subjects had mixed infections with more than 1 implicated pathogen. Seventy-one percent of isolates were Gram-positive cocci, the most common being *S. epidermidis* (34% of total isolates). Gram-negative rods accounted for 30% of all isolates and fungi 6%. No clinically significant difference was seen regarding the spectrum of pathogens isolated by time interval during the HCT process, including the pre- and postengraftment periods. Of the bacterial microorganisms for which sensitivity data were available, approximately 31% were MDR. Our institution's HCT antimicrobial prophylaxis protocol at time of study is shown in Figure 2. All patients were receiving antimicrobials for prophylaxis or treatment on day of CLABSI. Approximately 61% of patients were receiving levofloxacin as bacterial prophylaxis, 18% were receiving cefuroxime, and 21% of patients had been broadened to empiric intravenous (IV) Gram-negative therapy for fever and neutropenia. Eighty-nine percent of patients receiving levofloxacin had a levofloxacin resistant isolate. Fifty percent of patients receiving cefuroxime had a cephalosporin

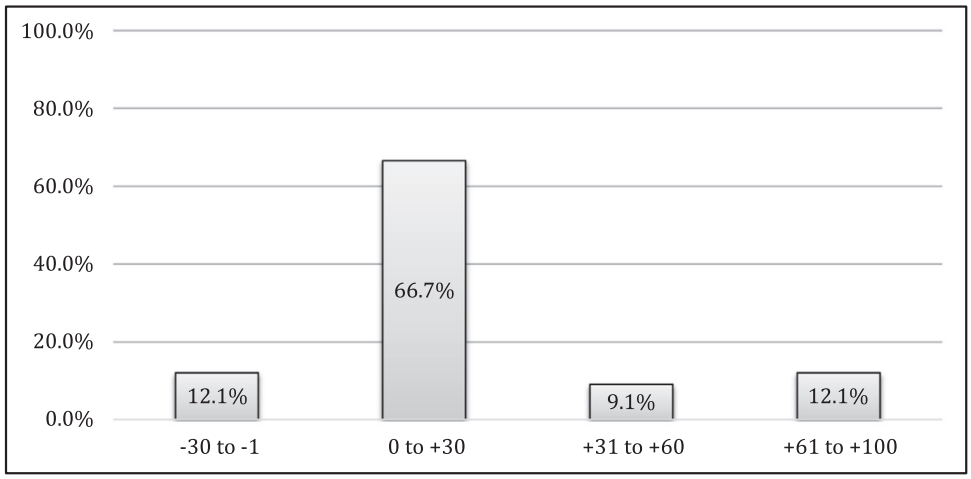

Figure 1. Number of subjects developing a CLABSI at intervals during the HCT process.

resistant isolate. Seventy-one percent of patients broadened to IV Gram-negative therapy for treatment had an isolate resistant to the specific Gram-negative therapy. Approximately 54% of patients were receiving micafungin for fungal prophylaxis, including the 2 patients who developed a fungal CLABSI, and the remaining were receiving fluconazole (24%), voriconazole (15%), or posaconazole (6%). For the 2 fungal isolates identified, *Candida krusei* was sensitive to voriconazole and resistant to fluconazole and amphotericin B, but echinocandin sensitivity was not performed. The *Candida glabrata* isolate was sensitive to both fluconazole and caspofungin.

Table 2
Microorganisms Causing CLABSI

Microorganism	Frequency (n = 35)	MDR (n = 11)
Gram-positive microorganisms		
Staphylococcus epidermidis	12 (34)	5 (45)
Enterococcus faecalis	3 (9)	0 (0)
Enterococcus faecium	3 (9)	2 (18)
Staphylococcus aureus (MSSA)	2 (6)	0 (0)
Corynebacterium jeikeium	1 (3)	0 (0)
Other Gram-positive cocci*	4 (11)	1 (9)
Gram-negative microorganisms		
Escherichia coli	3 (9)	2 (18)
Pseudomonas species†	2 (6)	0 (0)
Acinetobacter baumannii	1 (3)	0 (0)
Klebsiella oxytoca	1 (3)	1 (9)
Stenotrophomonas maltophilia	1 (3)	0 (0)
Fungal microorganisms		
Candida krusei	1 (3)	0 (0)
Candida glabrata	1 (3)	0 (0)

Values are presented as n (%).
MSSA indicates methicillin-sensitive *Staphylococcus aureus.*
* *Rothia mucilaginosa*, *Streptococcus intermedius*, *Streptococcus mitis*, and viridans group streptococcus.
† *P. aeruginosa* and *P. putida.*

Risk Factors for CLABSI

On univariate analysis (Table 1), there was a higher incidence of CLABSIs observed in patients who used TBI-containing regimens and haploidentical donors ($P = .002$ and $P = .002$). There was also a higher incidence of CLABSIs observed in younger patients, those who received ablative conditioning regimens, use of a MUD, use of cord blood as a stem cell source, and prior history of CVC infections; however, these were not found to be statistically significant. There was a lower incidence of CLABSIs observed in patients who developed GVHD ($P = .002$). Gender, cancer diagnosis, DRI, history of prior port use, prior history of CVC malfunctions, and number of procedures did not impact the risk of developing a CLABSI.

Results from the multivariate analysis are shown in Figure 3. The use of a MUD and/or haploidentical donor (OR, 3.993; 95% CI, 1.329 to 12.001; $P = .0136$) and administration of an ablative conditioning regimen (OR, 2.394; 95% CI, 1.052 to 5.446; $P = .0374$) were independently associated with an increased rate of CLABSI. Patients who developed GVHD grades II to IV were associated with a lower risk of developing a CLABSI (OR, .332; 95% CI, .126 to .873; $P = .0254$). The DRI before transplant did not show any significant association with CLABSI incidence (OR, .966; 95% CI, .417 to 2.235; $P = .9353$).

Patient Outcomes

On average, patients were admitted to the hospital at least once, with no significant difference in hospital LOS (9 days

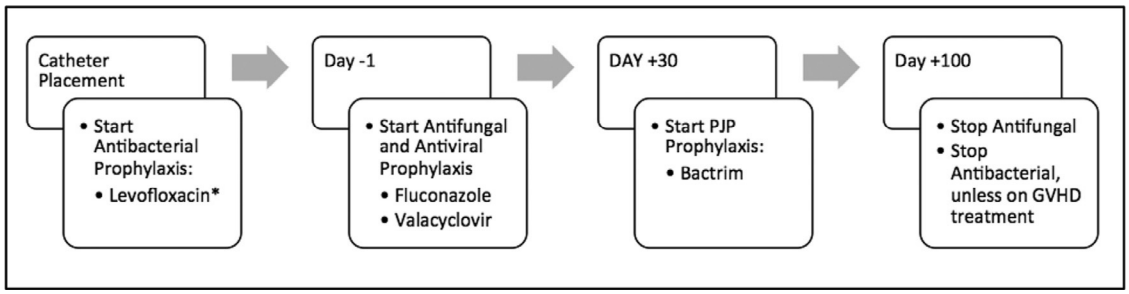

Figure 2. VUMC HCT antimicrobial prophylaxis protocol. *Cefuroxime was initiated in patients intolerant to levofloxacin and escalation to IV broad-spectrum beta-lactam was initiated for febrile neutropenia and continued through engraftment unless source identified.

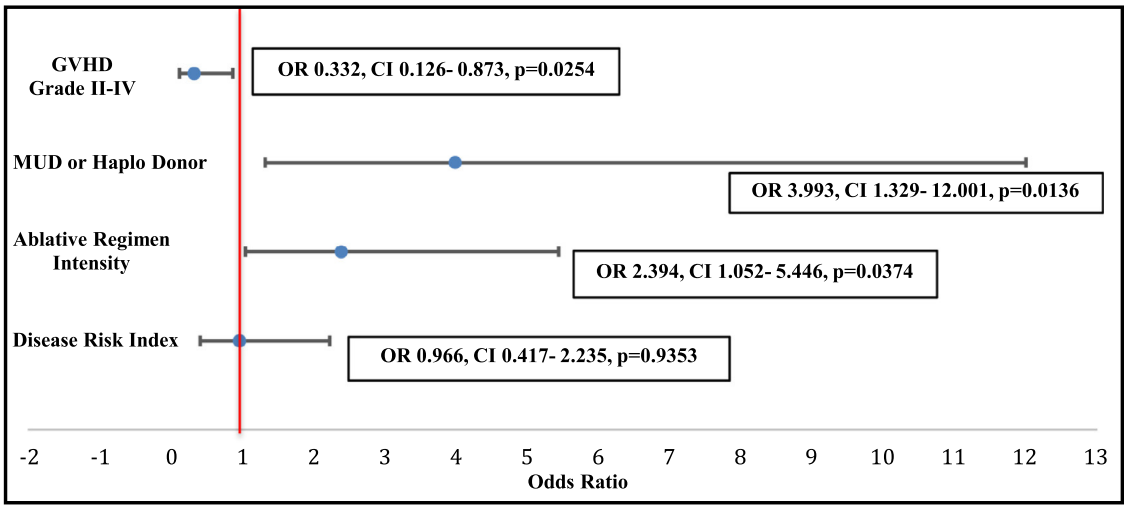

Figure 3. Multivariate analysis of predictors of CLABSI.

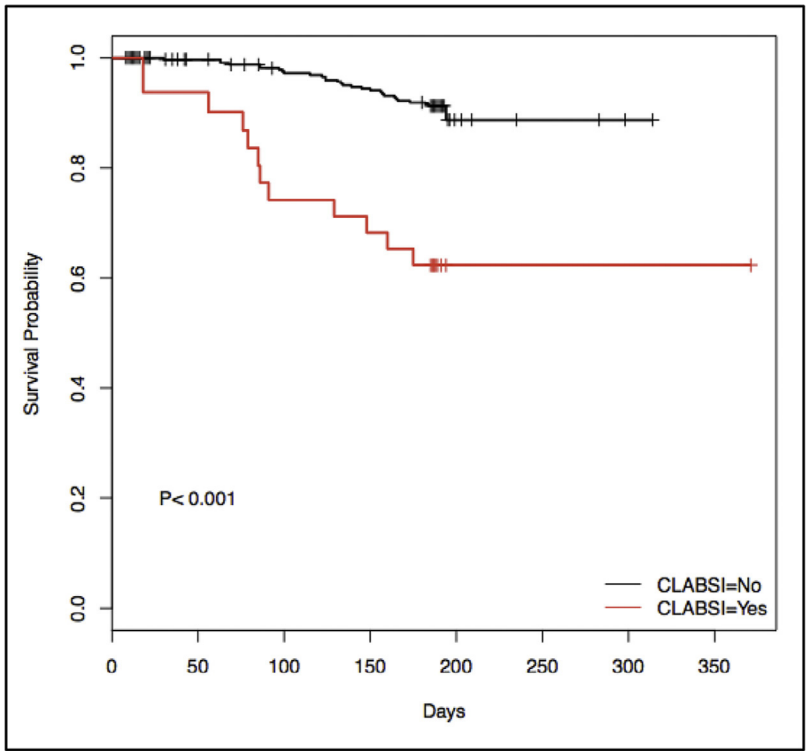

Figure 4. Kaplan-Meier survival analysis curve at 180 days post-transplantation.

versus 7 days; $P = .240$) or ICU LOS (8 days versus 1 day; $P = .130$) between the non-CLABSI and CLABSI groups respectively. Four patients (12%) who experienced a CLABSI did not require admission during the transplant process and were managed entirely in the outpatient setting. Ten patients (30%) who experienced a CLABSI were admitted specifically for CLABSI management.

In total, 40 of 352 (11%) patients died at 6 months post-transplantation, with increased mortality observed among patients who experienced a CLABSI (Figure 4). Patients who experienced a CLABSI had a nearly 5 times higher risk of mortality at 6 months post-transplantation when compared with patients who did not (HR 4.932; 95% CI, 2.463 to 9.878; $P < .001$).

DISCUSSION

Numerous studies have defined the incidence, risk factors, and outcomes associated with CLABSIs in patients undergoing HCT in the inpatient setting [2,5-7]. However, this study is the first analyzing CLABSIs in an outpatient HCT program. We report a 9% incidence of CLABSIs from the date of line placement to day +100, which is lower than the 27% to 68% incidence ranges reported by inpatient HCT studies [1,2,5,6]. This difference may be secondary to specific benefits that outpatient therapy offers, including shorter hospital LOS, reduced exposure to nosocomial pathogens and sick contacts, and less frequent CVC manipulation. In the outpatient setting, patients are required to have daily to weekly clinic visits through day

+100 for follow-up care. During these visits, catheters were only accessed as needed by trained nursing staff. This is in contrast to inpatient HCT recipients whose central lines may be accessed multiple times a day. Of note, more than 90% of patients received a triple lumen, long-term tunneled catheter in the right internal jugular before transplantation. This has been shown to increase patients' risk for bloodstream infections as compared with midline catheters or peripherally inserted central catheters, single or double lumens, and insertion into a subclavian vein [15]. However, because this has become a standard of care in HCT, we do not believe this has strongly impacted the number of CLABSIs seen in our program given the low reported incidence.

Consistent with previous studies, the most common Gram-positive bacteria isolated was *Staphylococcus epidermidis,* followed by *Enterococcus* species, and methicillin-sensitive *S. aureus* [1,5-7]. The most common Gram-negative bacteria isolated were *E. coli* and *Pseudomonas* species, also consistent with other reports [6,16]. Our current institutional sensitivity rate to levofloxacin for *E. faecalis* is 67%, *E. faecium* 18%, *S. epidermidis* 44%, *S. aureus* 62%, *Enterobacter cloacae* 91%, *E. coli* 73%, *Klebsiella pneumoniae* 94%, and *P. aeruginosa* 74%. We do not have institutional sensitivity rates for cefuroxime. Close to one-third of our microbiology isolates met the definition for MDR. Future studies at our institution will analyze CLABSI rates and the shift in MDR prevalence after changing our standard post-HCT prophylaxis from levofloxacin to penicillin VK on engraftment in August 2016.

The most common sources of most CLABSIs are the skin, oral mucosa, or the gastrointestinal tract [17]. Given the frequency of coagulase-negative staphylococci isolated, it is likely that the skin was a common source of infection in our patient population. This is most likely due to universal prophylaxis with levofloxacin, as there is increasing concern for fluoroquinolone resistance among coagulase-negative staphylococci pathogens [18], and reliance on patients to independently perform detailed line care at home. Our institution is investigating ways to better target common skin contaminants and other microorganisms seen in our outpatient HCT population by exploring antimicrobial and ethanol locks, as well as chlorhexidine baths [7]. Antimicrobial locks may provide additional antimicrobial prophylaxis to our current oral therapy, and can dwell in place while lines are not being accessed at home. Ethanol locks provide similar beneficial effect and can readily penetrate biofilm, has activity against both bacteria and fungi, and does not promote emergence of antimicrobial resistance. Chlorhexidine gluconate is an antiseptic agent that may decrease the microbial burden on patients' skin and prevent secondary environmental contamination. Results from previous studies suggest that daily bathing with chlorhexidine significantly reduces the development of bloodstream infections, particularly those caused by Gram-positive bacteria and fungi, and acquisition of MDR microorganisms [19]. Additional data regarding line care techniques in HCT patients needs further exploration before making recommendations regarding their use. A total of 8 of 33 patients (24%) who experienced a CLABSI met the definition for central line–associated mucosal barrier injury bloodstream infection (CLAMBI) [20]. Defining the impact of mucositis and the importance of good mouth hygiene on the prevention of CLAMBIs in the HCT population needs further investigation.

The results of our univariate and multivariate analyses are similar to prior studies, identifying younger age, receipt of ablative conditioning and TBI-based regimens, use of MUDs or haploidentical donors, and use of cord blood as a stem cell source to be potential risk factors for CLABSIs [2,5-7]. This is not surprising, as younger patients are more likely to receive ablative conditioning regimens and patients who receive cord blood as their stem cell source often experience delayed neutrophil engraftment, both leading to increased risk of prolonged and profound neutropenia. In our study, the majority of CLABSIs occurred between day 0 and day +30, during which time the majority (82%) of patients were neutropenic. Even though our study did not examine neutropenia as a risk factor for CLABSI, after further clinical review, it is possible that the pre- and periengraftment time period puts patients at a higher risk of developing a CLABSI. Since we found the majority of patients to be neutropenic at the time of CLABSI, and that the most common microorganism identified was *S. epidermidis* and other common skin contaminants, further investigation is warranted to determine if evaluation of neutropenic fevers led to incidental findings of infection. Published literature currently does not support the utility of surveillance blood cultures in HCT patients, as cultures infrequently yield significant results and have been associated with unnecessary medical interventions and added cost [21].

Patients who receive transplants from MUDs or haploidentical donors are at increased risk of developing GVHD, which increases the patient's risk of infection due to augmentation of immunosuppression as well as through disruption of the protective barriers in the gastrointestinal tract and the skin [22-24]. Interestingly, our study identified patients who experienced GVHD as having a lower likelihood of developing a CLABSI, which differs from previous studies [2,5,25]. This may be due to our study design, as we censored data collection at the time of first CLABSI. Seventy-nine percent of patients in our cohort developed a CLABSI from date of line placement through day +30, and data was not collected after the engraftment period when GVHD typically occurs. Additionally, patients who develop GVHD often required high-dose steroids, and received broad spectrum antimicrobial prophylaxis, which might have had an impact on the low incidence of CLABSIs. Further investigation is required to examine if different risk factors are associated with CLABSIs before engraftment compared with CLABSIs after engraftment.

We found that CLABSIs may have an association with increased mortality after HCT. Eleven percent of patients included in this analysis died by 6 months post-transplantation. When further examined, patients who experienced a CLABSI had a significant increase in mortality compared with patients who did not (33% versus 9%; $P < .001$), with an almost 5 times increased risk of death at 6 months post-transplantation. This is consistent with other findings reported in the literature [2,5-7]. With regards to cause of mortality, 1 death was identified as being directly related to bacteremia. However, despite an overall low incidence of infection-related mortality, the clear association between 6-month mortality and prior CLABSI was a striking finding of this study that warrants further investigation into the role CLABSI plays in transplant outcomes and survival. Of the patients who experienced a CLABSI, approximately 30% were hospitalized due to the infection and 9% were admitted to an ICU, increasing health care resource utilization and overall hospital costs.

Weaknesses of our study include the retrospective, single-center design, inpatient admission for management of outpatient complications (not exclusively an outpatient population), and censorship of data collection at the time of first CLABSI. Strengths of our study include being the first to evaluate CLABSIs in an outpatient HCT program, adjudication of all CLABSIs by an independent third party in the institution's infection

control department, and multivariate analysis of risk factors that may contribute to CLABSIs occurring before day +100.

In conclusion, our study demonstrates a low incidence of CLABSIs in patients undergoing outpatient HCT. Patients who receive outpatient HCT from a MUD or haploidentical donor and who undergo ablative conditioning regimens are at highest risk of developing CLABSIs, and are thereafter at an increased risk of 6-month mortality post-transplantation. Additional investigation is needed to assess if risk factors identified on retrospective analysis apply in prospective study design. In the future, having the ability to identify at-risk patients and modifying prophylactic antimicrobial regimens while implementing more rigorous infection prevention protocols, will be useful in further reducing the incidence of CLABSIs in the outpatient setting.

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