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Clinical Research

Defining Incidence, Risk Factors, and Impact on Survival of Central Line-Associated Blood Stream Infections Following Hematopoietic Cell Transplantation in Acute Myeloid Leukemia and Myelodysplastic Syndrome

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A B S T R A C T

Central line-associated blood stream infections (CLABSI) commonly complicate the care of patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) after allogeneic stem cell transplantation (HCT). We developed a modified CLABSI (MCLABSI) definition that attempts to exclude pathogens usually acquired because of disruption of mucosal barriers during the vulnerable neutropenic period following HCT that are generally included under the original definition (OCLABSI). We conducted a retrospective study of all AML and MDS patients undergoing HCT between August 2009 and December 2011 at the Cleveland Clinic (N = 73), identifying both OCLABSI and MCLABSI incidence. The median age at transplantation was 52 years (range, 16 to 70); 34 had a high (≥3) HCT comorbidity index (HCT-CI); 34 received bone marrow (BM), 24 received peripheral stem cells (PSC), and 15 received umbilical cord blood cells (UCB). Among these 73 patients, 23 (31.5%) developed OCLABSI, of whom 16 (69.6%) died, and 8 (11%) developed MCLABSI, of whom 7 (87.5%) died. OCLABSI was diagnosed a median of 9 days from HCT: 5 days (range, 2 to 12) for UCB and 78 days (range, 7 to 211) for BM/PSC ($P < .001$). MCLABSI occurred a median of 12 days from HCT, with similar earlier UCB and later BM/PSC diagnosis ($P = .030$). Risk factors for OCLABSI in univariate analysis included CBC ($P < .001$), human leukocyte antigen (HLA)-mismatch ($P = .005$), low $CD34^+$ count ($P = .007$), low total nucleated cell dose ($P = .016$), and non-Caucasian race ($P = .017$). Risk factors for OCLABSI in multivariable analysis were UCB ($P < .001$) and high HCT-CI ($P = .002$). There was a significant increase in mortality for both OCLABSI (hazard ratio, 7.14; CI, 3.31 to 15.37; $P < .001$) and MCLABSI (hazard ratio, 6.44; CI, 2.28 to 18.18; $P < .001$). CLABSI is common and associated with high mortality in AML and MDS patients undergoing HCT, especially in UCB recipients and those with high HCT-CI. We propose the MCLABSI definition to replace the OCLABSI definition, given its greater precision for identifying preventable infection in HCT patients.

BACKGROUND

Hospital-acquired infections occur in 5% of hospitalized patients. Hospital-acquired bloodstream infections afflict 250,000 patients annually [1]. Central line-associated blood stream infections (CLABSI) are a subset of blood stream infections that are particularly dangerous, with a mortality rate of 12% to 25% [1,2]. There were 19,000 CLABSI in intensive care unit (ICU) patients and 23,000 CLABSI in patients hospitalized in non-ICU settings in 2009 [1]. This equates to a median incidence of 1.14 CLABSI (varying from 0.2 to 4.2 infections across institutions) per 1,000 catheter days in non-ICU patients [1,3]. Recent quality initiatives have decreased the number of CLABSI in ICU settings from 43,000 in 2001 to 18,000 in 2009, a reduction of 58% [1]. Other interventions in the ICU have been associated with a reduction of CLABSI by as much as 66% to 68% [4,5]. Non-ICU patients, who account for over one-half of documented CLABSI, are not as well studied [1]. This population includes patients with hematologic malignancies undergoing allogeneic stem cell transplantation (HCT), who have inherently compromised immune function at baseline because of their malignancy, which is further incapacitated secondary to treatment, including both the transplantation preparative regimen and immunosuppression to prevent graft-versus-host disease (GVHD). Central venous catheter (CVC) placement and other intravascular procedures predispose to CLABSI; however, blood stream infections can also arise from disruption of mucosal barriers by mucositis and GVHD of the gastrointestinal tract and skin.

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The National Healthcare Safety Network (NHSN) defines CLABSI as a primary blood stream infection in a patient with a CVC at the time of diagnosis or during the previous 48-hour time period before blood stream infection diagnosis [6]. Clinicians differ in their identification of infections as being a CLABSI [7]. Furthermore, this original definition of CLABSI (OCLABSI) includes pathogens that arise from sources unrelated to the presence of a central line, such as enteric gram-negative *bacilli* and *streptococcus viridans*, as they likely entered the bloodstream across compromised mucosal barriers. We have therefore developed a modified CLABSI definition (MCLABSI), which excludes these hospital-associated blood stream infections [8]. MCLABSI includes all of the pathogens under the NHSN definition of CLABSI except *Viridans* group *streptococci* species in patients with mucositis, and *Enterococcus, Enterobacteriaceae*, or *Candida* species in patients with neutropenia or GVHD of the gut.

We estimated the incidence of OCLABSI and MCLABSI, identified risk factors for OCLABSI, and assessed the impact of OCLABSI and MCLABSI on survival in acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patients undergoing HCT.

METHODS

Patients and Assessment

All consecutive AML and MDS patients who underwent HCT from August 2009 to December 2011 in the Cleveland Clinic Unified Transplant Database were included in this study. Patients were treated on HCT protocols that were reviewed and approved by the Cleveland Clinic's Institutional Review Board with signed informed consent obtained from all patients. Patient and transplantation characteristics and outcomes were obtained from the Unified Transplant Database.

The occurrence of OCLABSI and MCLABSI were identified and catalogued in the Infection Prevention Database for this population. Diagnosis of CLABSI under both definitions required identification of a recognized pathogen on at least 1 blood culture (or in 2 or more blood cultures drawn on separate occasions if a common skin contaminant was isolated) as per NHSN guidelines [9]. Incidence of CLABSI was identified using the criteria as defined above by members of the infection control team, who also recorded the specific causative pathogen(s) and the time of diagnosis following HCT.

Statistical Analysis

OCLABSI and MCLABSI were estimated using the Kaplan-Meier method. Cox proportional hazards analysis was used to identify risk factors for OCLABSI and all-cause mortality; risk factor analysis for MCLABSI could not be performed because of a limited number of events. Multivariable risk factors were identified using stepwise Cox analysis with a variable entry criterion of $P \leq .10$ and a variable retention criterion of $P \leq .05$. Cox results are presented as the hazard ratio (HR), 95% CI, and corresponding P value. Further assessment of OCLABSI risk factors included bootstrap analysis. One thousand bootstrap samples of size 73 were selected with replacement from the data. Cox analysis was done on each of the 1,000 samples, and results were summarized as the percentage of times each variable occurred in the bootstrap analyses. Variables that occurred in >50% of the bootstrap models were considered significant. Two models were calculated for mortality: one that included OCLABSI and one that included MCLABSI.

Non-CLABSI variables used in all risk factor analysis included gender, race, age, prior transplantation, diagnosis, number of prior chemotherapy regimens, prior radiation therapy, comorbidity index (HCT-CI), donor relationship, human leukocyte antigen (HLA) match, recipient or donor cytomegalovirus (CMV) serostatus, months from diagnosis to transplantation, transplantation type, cell source, $CD34^+$ dose, and total nucleated cell (TNC) dose. Neutrophil engraftment (absolute neutrophil count or ANC) $\geq 500/mL^3$ was also analyzed as a risk factor for OCLABSI. In all risk factor analyses, posttransplantation variables were analyzed as time-varying covariates.

Incidence of OCLABSI and MCLABSI were compared between cord blood cells (CBC) and bone marrow (BM) and/or peripheral stem cells (PSC) using the log-rank test. Days to OCLABSI, MCLABSI, and neutrophil engraftment were compared using the Wilcoxon rank-sum test. Analyses were done using SAS software (SAS Institute, Inc., Cary, NC). All statistical tests were two-sided, and $P \leq .05$ was used to indicate statistical significance.

Table 1
Patient Demographics, Past Therapies, Stem Cell Characteristics, and Outcome of Transplantation

Variable	No. of Subjects
Gender	
Male	48 (65.8)
Female	25 (34.2)
Race	
White	68 (93.2)
Black	3 (4.1)
Asian, American Indian	2 (2.8)
Age in years at transplantation, median (range)	52 (16-70)
Prior transplantation	
Myeloablative	3 (4.1)
Autologous	2 (2.7)
Mini-allogeneic	1 (1.4)
None	67 (91.8)
Diagnosis	
AML	44 (60.3)
MDS	29 (39.7)
No. of prior chemotherapy regimens	
0	9 (12.3)
1	26 (35.6)
2	17 (23.3)
3	14 (19.2)
4	6 (8.2)
6	1 (1.4)
Prior radiation therapy	
Yes	3 (4.1)
No	70 (95.9)
Comorbidity score (HCT-CI)	
Low (0)	11 (15.1)
Intermediate (1-2)	28 (38.4)
High (3+)	34 (46.6)
Months from diagnosis to transplantation, median (range)	6.2 (2.2-141.0)
Donor relationship	
Unrelated	49 (67.1)
Sibling	24 (32.9)
HLA	
Match	65 (89.0)
Mismatch	8 (11.0)
Transplantation type and cell source	
MA − BM	34 (46.6)
MA − PSC	8 (11.0)
MA − CBC	12 (16.4)
RIC − PSC	7 (9.6)
RIC − CBC	3 (4.1)
Mini-allogeneic − PSC	9 (12.3)
Preparative regimen	
Bu/Cy	42 (57.5)
Cy/Flu/TBI	12 (16.4)
Flu/TBI	9 (12.3)
Bu/Flu	7 (9.6)
Flu/Cy/TBI/ATG	3 (4.1)
$CD34^+$ dose $\times 10^6$/kg, median (range)	2.42 (0.01-10.01)
TNC dose $\times 10^8$/kg, median (range)	2.35 (0.19-16.33)
GVHD prophylaxis regimen	
CSA/MMF	36 (49.3)
FK/MMF	11 (15.1)
FK/MTX	26 (35.6)
Worst mucositis during admission, WHO grade (n = 61)	
0	9 (14.8)
1	21 (34.4)
2	14 (23.0)
3	15 (24.6)
4	2 (3.3)
Days until PMN $\geq$ 500/μL (n = 66), median (range)	15 (6-77)
Days until platelets $\geq$ 20,000 (n = 62), median (range)	20 (11-170)
Hospital stay, days (n = 64), median (range)	29 (10-111)
Months of follow-up among living patients (n = 39), median (range)	15.0 (4.2-30.7)

(*continued on next page*)

Table 1
(*continued*)

Variable	No. of Subjects
Posttransplantation events	
100-d mortality	11 (15.1)
Relapse	19 (26.0)
Death	34 (46.6)
Cause of death (n = 34)	
Relapse	14 (41.2)
Infection	9 (26.5)
Nonpulmonary organ failure	5 (14.7)
Acute GVHD	3 (8.8)
Chronic GVHD	2 (5.9)
Pulmonary	1 (2.9)

AML indicates acute myeloid leukemia; MDS, myelodysplastic syndrome; HCT-CI, hematopoietic cell transplantation comorbidity index; HLA, human leukocyte antigen; MA, myeloablative; RIC, reduced-intensity conditioning; BM, bone marrow; PSC, peripheral stem cells; CBC, cord blood cells; Bu, busulfan; Cy, cyclophosphamide; Flu, fludarabine; TBI, total body irradiation; ATG, anti-thymocyte globulin; TNC, total nucleated cell; CSA, cyclosporine; MMF, mycophenolate mofetil; MTX, methotrexate; PMN, polymorphonuclear cells; GVHD, graft-versus-host disease.
Data are presented as n (%) unless otherwise noted.

RESULTS

Patient Characteristics

A total of 149 patients, of whom 73 had AML or MDS, underwent allogeneic hematopoietic cell blood or BM transplantation from August 2009 to December 2011. The baseline patient characteristics for these patients identified with AML or MDS are summarized in Table 1. Among this population, median age at HCT was 52 years (range, 16 to 70), they had received a median of 2 prior chemotherapy regimens, 6 had undergone previous transplantations, and 3 had previous radiation therapy. The HCT-CI was low to intermediate (<3) in 39 patients (53%) and high (≥3) in 34 patients (47%). HCT donors included 24 sibling and 49 unrelated individuals; 54 HCT were myeloablative, and 19 were reduced-intensity conditioning; and stem cell sources were 34 BM, 24 PSC, and 15 UCB. There was a median of 6.2 months (range, 2.2 to 141) between AML/MDS diagnosis and HCT. The median $CD34^+$ dose was 2.42×10^6/kg (range, 0.01 to 10.01) and TNC dose of 2.35×10^8/kg (range, 0.19 to 16.33). Median length of hospital stay was 29 days (n = 64; range, 10 to 111), with 15 days until polymorphonuclear cells (PMN) > 500 (n = 66; range, 6 to 77), and 20 days until platelets > 20,000 (n = 62; range, 11 to 170).

CLABSI Incidence and Causative Pathogens

Table 2 shows the prevalence and diagnosis of OCLABSI and MCLABSI in the study population. Among the 73 patients with AML or MDS, 23 (32%) developed CLABSI under the standard NHSN definition, and 8 (11%) had MCLABSI (Figure 1). Median onset was 9 days (range, 2 to 211) for OCLABSI and 12 days (range, 5 to 176) for MCLABSI. Onset varied depending on stem cell source: UCB recipients developed OCLABSI at a median of 5 days (range, 2 to 12), whereas the BM and/or PSC recipients developed OCLABSI at a median of 78 days (range, 7 to 211; $P < .001$). MCLABSI was diagnosed less frequently (4 UCB and 4 BM and/or PSC); however, with a similar discrepancy of 7 days (range, 5 to 12) and 77 days (range, 13 to 176) for UCB and BM and/or PSC, respectively ($P = .030$). Time until PMN recovery was noted to be 28 days (n = 13; range, 19 to 77) for UCB and 14 days (n = 53; range, 6 to 24; $P < .001$) for BM/PSC.

Etiologies of OCLABSI included 11 enteric gram-negative *bacilli*, 7 *Streptococcus viridans* group, 6 *enterococcus* (3 vancomycin resistant), 5 *Staphylococcus epidermidis* (3 methicillin resistant), 2 fungal species, 2 gram-positive *bacilli*, 1 *Pseudomonas*, 1 other *Streptococcus* species, and 1 *Stenotrophomonas*. Pathogens isolated in MCLABSI included 5 *Staphylococcal epidermidis* (3 methicillin resistant), 2 *Streptococcus viridans* group, 2 gram-positive *bacilli*, 1 vancomycin resistant, and 1 P*seudomonas*. Four patients had polymicrobial CLABSI including 2 MCLABSI, and 5 (all of whom died) had more than one separately documented CLABSI, 4 of which were MCLABSI. Table 3 shows the timing and pathogen responsible in the 23 patients diagnosed with OCLABSI and the 9 MCLABSI diagnosed in 8 patients.

Risk Factors for OCLABSI and Mortality

Univariable risk factor analysis for OCLABSI (Table 4) revealed an association with cord blood transplantation ($P < .001$), HLA-mismatch ($P = .005$), low $CD34^+$ count ($P = .007$), low TNC dose ($P = .016$), and non-Caucasian race ($P = .017$). Risk factors for OCLABSI in multivariable analysis were UCB (HR, 14.19; CI, 5.41 to 37.18; $P < .001$) and high HCT-CI (HR, 4.68; CI, 1.81 to 12.13; $P = .002$). Bootstrap analysis confirmed the significance of UCB and high HCT-CI in multivariable analysis, which appeared in 91.3% and 72.0% of 1,000 bootstrap samples, respectively. Based on stem cell source and HCT-CI, the risk of OCLABSI occurrence was stratified into 4 distinct groups as shown in Figure 2.

In univariable analysis, mortality was strongly associated with OCLABSI (HR, 3.72; CI 1.88 to 7.36; $P < .001$) and MCLABSI (HR 2.96; CI, 1.27 to 6.89; $P = .012$). Other univariable risk factors for mortality included MDS diagnosis (HR 3.08; CI, 1.53 to 6.19; $P = .002$), age at transplantation (HR, 1.65 per 10-year increase; CI, 1.18 to 2.30; $P = .003$). Multivariable analysis confirmed the strong association of OCLABSI (HR, 7.14; CI 3.31to 15.37; $P < .001$) and MCLABSI (HR, 6.44; CI, 2.28 to 18.18; $P < .001$) with mortality, adjusting for MDS diagnosis (HR, 5.21; $P < .001$ in the model containing OCLABSI; HR, 4.71, $P < .001$ in the MCLABSI model) and age (HR, 1.81 per 10-year increase; $P = .004$ OCLABSI model; HR, 1.60; $P = .009$ MCLABSI model).

DISCUSSION

AML and MDS patients undergoing HCT are at high risk of therapy-related morbidity and mortality. One of the greatest

Table 2
Prevalence and Onset of OCLABSI/MCLABSI and Days Until Neutrophil Engraftment by Stem Cell Source

Variable	Overall (n = 73)	CBC (n = 15)	BM/PSC (n = 58)	*P* Value (CBC vs BM/PSC)
No. of OCLABSI (%)	23 (31.5)	11 (73.3)	12 (20.7)	<.001
Days after transplantation, median (range)	9 (2-211)	5 (2-12)	78 (7-211)	<.001
No. of MCLABSI (%)	8 (11.0)	4 (26.7)	4 (6.9)	.006
Days after transplantation, median (range)	12 (5-176)	7 (5-12)	77 (13-176)	.030
Days until PMN ≥500/μL, median (range)	15 (6-77)	28 (19-77)	14 (6-24)	<.001

OCLABSI indicates original definition central line-associated blood stream infection; MCLABSI, modified definition central line-associated blood stream infection; CBC, cord blood cells; BM, bone marrow; PSC, peripheral stem cells; PMN, polymorphonuclear cells.

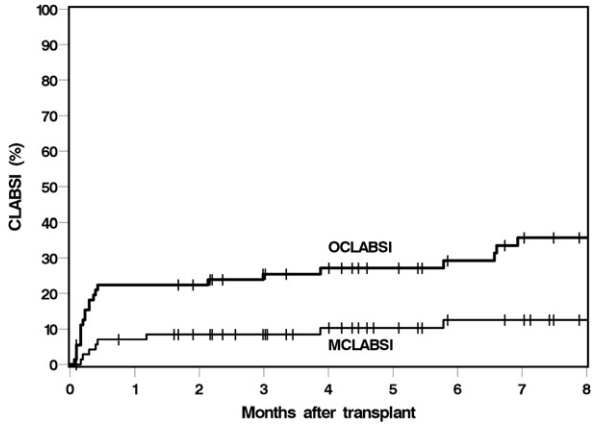

Figure 1. Original and modified definition CLABSI after HCT (n = 73). Of 73 AML/MDS patients, 23 (32%) developed CLABSI under the standard NHSN definition, and 8 (11%) were diagnosed with MCLABSI. Median onset of OCLABSI was 9 days (range, 2 to 211) versus 12 days (range, 5 to 176) for MCLABSI.

contributors to poor outcome is infection, and CLABSI is potentially avoidable. We rigorously identified AML and MDS HCT patients who developed blood stream infections, and found that both the original NHSN-defined CLABSI and our modified CLABSI are strongly associated with mortality.

Table 3
Diagnosis of OCLABSI/MCLABSI, Causative Organism, and Mortality Outcome

HCT Type	Day	Causative Organism(s)	FU Day	FU Status	Cause of Death
MA	2	*K. pneumoniae*	49	Dead	Infection
MA	3	*K. pneumoniae*	105	Dead	Relapse
RIC	3	VRE	23	Dead	Enterocolitis
MA	3	*E. coli*	605	Alive	
MA	5	*GPB, *S. haemolytica*, *S. viridans*, VRE	742	Alive	
MA	5	*S. viridans*	382	Alive	
MA	5	*S. viridans*	409	Alive	
MA	5	*Enterobacter spp.*	93	Dead	Acute GVHD
MA	6	**S. viridans*	58	Dead	Acute GVHD
	50	**Clostridium spp.*			
MA	7	*K. pneumoniae*	226	Dead	Relapse
	114	*K. pneumoniae, E. cloacae*			
	135	*E. cloacae*			
MA	7	*E. coli*	217	Dead	Relapse
MA	9	**P. aeruginosa*	68	Dead	Multiorgan failure
	59	*Enterobacter spp.*			
MA	9	*K. oxytoca*	264	Dead	Relapse
	36	*MRSE			
MA	11	*R. mucilaginosa, S. mitis*	165	Alive	
RIC	12	**S. viridans*	631	Dead	Infection
MA	13	*MRSE	135	Dead	Relapse
MA	65	*C. tropicalis*	78	Dead	Infection
Mini	91	VRE	143	Dead	Relapse
MA	118	*MRSE, *S. viridans*	376	Dead	Relapse
	140	*Enterobacter spp.*			
MA	176	**S. epidermidis*	186	Dead	Relapse
Mini	200	*E. coli, S. viridans*	532	Alive	
MA	201	*E. cloacae*	456	Alive	
MA	211	*S. maltophilia*, VRE	274	Dead	Acute MI

OCLABSI indicates original-definition central-line associated bloodstream infection; MCLABSI, modified-definition central-line associated bloodstream infection; HCT, hematopoietic cell transplantation; FU, follow-up; MA, myeloablative; RIC, reduced-intensity conditioning; VRE, vancomycin-resistant *enterococcus*; GPB, gram-positive *bacilli*; MRSE, methicillin-resistant *streptococcus epidermidis*; GVHD, graft-versus-host disease; MI, myocardial infarction.

* Incidences of MCLABSI.

Table 4
Univariable Risk Factors for OCLABSI in AML/MDS

Variable	HR	95% CI	*P* Value*	Boot-Strap†
Cell source				91.3%
BM/PSC	1.28	0.38-4.24	.69	
CBC/PSC	10.26	3.21-32.82	<.001	
CBC/PSC + BM	8.79	3.77-20.51	<.001	
Comorbidity score (HCT-CI)				72.0%
Intermediate/low	1.45	0.29-7.21	.65	
High/low	3.65	0.83-16.10	.09	
High/intermediate + low	2.52	0.59-10.81	.21	
Race				36.3%
Non-Caucasian/Caucasian	3.78	1.27-11.24	.017	
Neutrophil engraftment				35.8%
Yes/No	0.30	0.06-1.54	.15	
Prior transplantation				28.3%
Yes/No	2.65	0.78-8.97	.12	
HLA				25.8%
Mismatch/match	4.34	1.57-12.03	.005	
Recipient or donor CMV status				18.6%
Positive/negative	2.35	0.70-7.92	.17	
Months from diagnosis to transplantation				18.3%
Per 12-mo increase	1.01	0.81-1.25	.95	
TNC dose, $\times 10^8$/kg				17.0%
Per 1 $\times 10^8$/kg increase	0.78	0.64-0.96	.016	
Transplantation type				11.4%
RIC/mini	1.26	0.18-9.00	.82	
MA/mini	1.92	0.45-8.26	.38	
Prior radiation therapy				7.2%
Yes/no	1.08	0.15-8.07	.94	
Gender				6.7%
Male/female	1.32	0.54-3.22	.54	
Number of prior chemotherapy regimens				6.2%
Per 1 regimen increase	1.34	0.97-1.84	.07	
Diagnosis				6.1%
AML/MDS	2.46	0.91-6.66	.08	
Donor relationship				5.6%
Unrelated/sibling	1.70	0.67-4.32	.27	
$CD34^+$ dose, $\times 10^6$/kg				5.5%
Per 1 $\times 10^6$/kg increase	0.72	0.56-0.91	.007	
Age at transplantation				4.6%
Per 10-year increase	1.05	0.75-1.47	.76	

OCLABSI indicates original-definition central-line associated blood stream infection; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; HR, hazard ratio; HCT-CI, hematopoietic cell transplantation comorbidity index; BM, bone marrow; PSC, peripheral stem cells; CBC, cord blood cells; HLA, human leukocyte antigen; TNC, total nucleated cells; RIC, reduced-intensity conditioning; MA, myeloablative conditioning.

* ≤.05 considered significant.

† Percentage in 1,000 bootstrap analyses, >50% considered significant.

The bacterial flora included in the MCLABSI definition more accurately reflect blood stream infections acquired secondary to CVC from known skin contaminants, eliminating oropharyngeal and gastrointestinal flora likely obtained by translocation of these species across compromised mucocutaneous surfaces, which are included in the OCLABSI definition. Given its greater precision, we believe the MCLABSI rate is the endpoint that should be measured when analyzing the success of CLABSI prevention programs. We documented that prevalence of MCLABSI was markedly less than OCLABSI, as similarly seen in the study by DiGiorgio et al. that originally redefined CLABSI [8]. Finally, the NHSN has modified their blood stream infections protocol to account for mucosal surface injury [9].

Certain transplantation subpopulations are particularly prone to CLABSI. Multivariable analysis revealed that high HCT-CI and umbilical CBC source are associated with more frequent CLABSI. HCT-CI is used during pretransplantation evaluation to predict HCT outcome. The efficacy of this

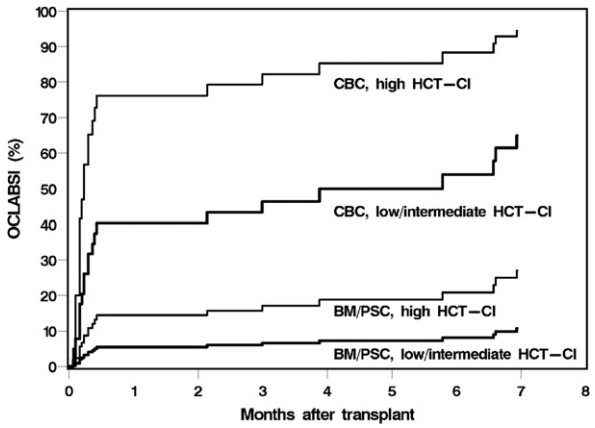

Figure 2. OCLABSI based on stem cell source and hematopoietic cord transplantation comorbidity index (HCT-CI). Four distinct risk groups for OCLABSI were found based on stem cell source (cord blood cells versus bone marrow/peripheral stem cells) and HCT-CI (high versus intermediate/low).

index was recently evaluated prospectively, revealing correlation with 2-year nonrelapse mortality and overall survival, especially when the HCT-CI was 0-2. In AML and MDS, the HCT-CI was found to be the best predictor of nonrelapse mortality [10]. In our study, high HCT-CI ($\geq$3) was associated with an HR of 3.65 (CI, 0.83 to 16.10; $P = .09$) for OCLABSI and an HR of 2.62 (CI, 0.87 to 7.87; $P = .09$) for mortality when compared to a low HCT-CI (0), stressing the importance of careful assessment of comorbidities before transplantation.

Numerous studies have found overall survival, relapse, relapse-free survival, and transplantation-related mortality using UCB comparable to those for PSC [11-13]. However, one clear disadvantage in all these studies is delayed time to PMN recovery compared to singly mismatched PSC, although infection rates were comparable between the 2 stem cell sources. Our study confirmed delayed PMN recovery (28 days for UCB versus 14 days for PSC) and also revealed increased CLABSI rates in UCB recipients. Furthermore, OCLABSI occurred earlier in patients undergoing UCB, with a median onset of CLABSI at 5 days in UCB and 78 days in BM and/or PB. Another study demonstrated similar delayed PMN recovery time (29 days for UCB versus 14 days for PSC) and increased early (<50 days) infections in UCB recipients [14]. Therefore, extra vigilance is necessary in those receiving CBC, given their increased susceptibility to CLABSI during prolonged neutropenia.

Further pressure is added to CLABSI prevention programs given the role of CLABSI as an institutional and individual quality measure. CLABSI and its treatment increase the economic burden on both the individual patient and our health care system, costing $11,971 to $54,000 per case [5]. Hospitals have the obligation of reporting incidence of CLABSI to the NHSN, as its occurrence affects compensation by the Centers for Medicare & Medicaid Services. Furthermore, CLABSI rates are public knowledge as they are available on the CMS website. These financial incentives have led to close internal surveillance of the occurrence of CLABSI and the efficacy of various preventative measures [15].

CONCLUSION

CLABSI is unfortunately common and often fatal in patients with AML and MDS undergoing HCT, especially in CBC recipients with a higher HCT-CI. Improvements in the current system of infection prevention depend on precise definition of CLABSI to aid diagnosis, confirm eradication, and develop effective surveillance programs. We argue that the MCLABSI definition more precisely identifies the CVC as the source of infection. Efforts to identify patients at highest risk of CLABSI, careful adherence to preventative infectious control measures, and design of methods to enhance immune reconstitution following transplantation could improve outcome in a substantial portion of patients.

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