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Comparison of Characteristics of Bacterial Bloodstream Infection between Adult Patients with Allogeneic and Autologous Hematopoietic Stem Cell Transplantation

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A B S T R A C T

Although autologous and allogeneic hematopoietic stem cell transplantation (HSCT) are fundamentally different procedures, a tailored approach to bacterial bloodstream infection (BSI) according to the type of HSCT has not yet been suggested. We evaluated the characteristics of BSI after HSCT, with a focus on comparison of BSIs between recipients of autologous HSCT (auto-HSCT) and allogeneic HSCT (allo-HSCT). Among 134 patients (59 received allo-HSCT and 75 received auto-HSCT) who underwent HSCT, BSIs were reported earlier in patients who underwent auto-HSCT, compared with those who underwent allo-HSCT (mean 12.1 ± 3.4 days versus 32.8 ± 27.1 days, $P = .006$). Among patients receiving allo-HSCT, postneutrophil-engraftment bacterial BSI showed an association with grade ≥ 2 acute graft-versus-host disease (GVHD). In patients who underwent auto-HSCT, results of multivariate analysis showed that not receiving prophylactic antibiotics ($P = .004$) and having elevated serum C-reactive protein ($P = .034$) were risk factors of BSI. Elevated CRP ($P = .01$) and acute GVHD $\geq$ grade 2 ($P = .002$) were independent risk factors in patients who underwent allo-HSCT. Those differences originated mainly from the impact of acute GVHD-related postengraftment BSIs of patients who underwent allo-HSCT. To establish the best defense strategy against BSI, the distinctive natures of bacterial BSI after HSCT between auto-HSCT and allo-HSCT should be considered.

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INTRODUCTION

Bacterial bloodstream infection (BSI) is a common and sometimes fatal event in patients who undergo hematopoietic stem cell transplantation (HSCT). Although advances in HSCT, such as the use of prophylactic antibiotics, reduced-intensity conditioning (RIC), and improved supportive care, have contributed to a substantial reduction of morbidity and mortality, the incidence of bacterial BSI has been reported to range from 20% to 43%, even after the year 2000 [1-4].

There are a wide variety of reports concerning types, risk factors, and mortality rates of BSI in HSCT recipients. Allogeneic HSCT (allo-HSCT), compared with autologous HSCT (auto-HSCT) [4], status of underlying disease [4], and age >18 years [5] are frequently reported risk factors for bacterial BSI among patients undergoing HSCT. In previous studies, among recipients of allo-HSCT, HSCT from a matched unrelated donor (MUD) compared with HSCT from matched sibling donor (MSD) [1,6], human leukocyte antigen (HLA) matching [4,7], combined acute graft-versus-host disease (GVHD) [5-7], and pretransplantation elevation of inflammatory markers, such as serum C-reactive protein (CRP) and ferritin [8], have also been proposed as factors causing BSI.

Although auto-HSCT and allo-HSCT are fundamentally different procedures, current guidelines [9-12] propose uniform recommendations regarding bacterial infection, including BSI, regardless of the type of HSCT. In a survey of pharmacists from 31 transplantation centers (30 from the United States and 1 from Mexico) taken during the 2003 Tandem BMT meeting in Keystone, Colorado, all centers reported using a similar approach to bacterial prophylaxis for auto-HSCT and allo-HSCT [13]. Few studies comparing the nature of BSI according to the type of HSCT have been reported.

In the current study, we evaluated pretransplantation risk factors for BSI after HSCT, with a particular focus on comparing BSIs between recipients of allo-HSCT and auto-HSCT, to provide useful information for developing a tailored strategy to overcoming BSI according to the type of HSCT.

MATERIALS AND METHODS
Patient Population
We analyzed a retrospective cohort of patients who underwent either allo-HSCT or auto-HSCT at a single institution, Gachon University Gil Medical Center, between November 2002 and June 2012. Patients were included if they were age ≥18 years and had a complete set of clinical, laboratory, and microbiologic data with well-preserved electronic medical records. Patients who received a second HSCT were excluded from the current study. This study was reviewed and approved by the Institutional Review Board of Gachon University Gil Medical Center (approval number: GAIRB 2974-2012).

HSCT Procedures and Supportive Care for Prevention of Bacterial BSI
In most patients (121 of 134, 90.3%), a 7-French nontunneled subclavian central venous catheter was inserted just before the start of conditioning, and the other 13 patients underwent implantation of a 12-French–sized tunneled Hickman catheter for HSCT. Transplantation procedures were performed in single rooms containing a HEPA-filtered laminar flow hood. To avoid exposing recipients to bacterial pathogens, health care workers in contact with recipients were required to follow appropriate hand hygiene practices. Although gowns or other protective clothing were not compulsory, visitors from outside the patients' room were discouraged. A low-bacteria diet was provided to the patients during the period of absolute neutrophil count (ANC) <500/μL. In principle, antimicrobial prophylaxis was decided according to the decision of attending physicians. However, the prophylactic use of antibiotics was established as a general institutional policy during the mid-2000s: until January 2006, only 1 of 22 patients received prophylactic antibiotics, whereas 103 of 122 patients (84.4%) who underwent HSCT thereafter received antibacterial prophylaxis. Since 2009, every patient has received antibiotic prophylaxis. Patients receiving prophylactic antibacterial antibiotics used ciprofloxacin 500 milligrams per os twice daily from the start of conditioning until neutrophil engraftment. Standard GVHD prophylaxis included either cyclosporine or tacrolimus in combination with methotrexate.

Definitions and Report of Bacterial Bloodstream Infection
Blood cultures were obtained in response to fever or other suspicion of systemic infection. The definition of BSI is as follows: (1) isolation of bacteria not normally known to colonize the skin from at least 1 blood culture, or (2) for bacteria that typically colonize the skin, such as coagulase-negative Staphylococcus or viridians group of Streptococcus, the presence of either 2 consecutive positive blood cultures, 2 positive blood cultures within 3 days, or ≥1 positive peripheral blood culture plus ≥1 positive blood culture from

the central venous catheter site is required. A gram-negative isolate that demonstrated resistance to at least 2 antibiotics used in empirical therapy (third- and fourth-generation cephalosporins, carbapenems, or piperacillin-tazobactam) was defined as multi-drug resistant (MDR). Day 0 was defined as the last date of stem cell infusion. Date of neutrophil engraftment was defined as the first of at least 3 consecutive days of an ANC >500/μL. In the current study, reports of bacterial BSIs from day 0 to day +100 were analyzed. Grading of acute GVHD was performed according to established criteria [14].

Statistical Analysis
Potential risk factors of BSI were dichotomized and their relationships to BSI were analyzed. Analyzed risk factors included type of HSCT (allogeneic versus autologous), age (>40 versus ≤40 years, because the modified European Group for Blood and Marrow Transplantation risk score [15] classified age >40 years as a risk factor for inferior survival of patients undergoing HSCT and we thought that BSI is one of the major components of overall poor treatment outcome of HSCT), gender, disease (acute myeloid leukemia versus others), amount of infused CD34$^+$ stem cell (≥5.0 versus <5.0 × 10^6/kg, because 5.0 × 10^6/kg is usually regarded as the optimal amount of peripheral blood stem cell collection [16]), HCT comorbidity index score [17] (score 0 versus ≥1, considering the number of analyzed patients in each group), and preceding use of antibiotics from conditioning for prophylactic intent. The impact of blood levels of C-reactive protein (≥.5 mg/dL versus < .5 mg/dL) and albumin (≥3.5 mg/dL versus <3.5 mg/dL) was evaluated according to the cut-off value of the institution. Ferritin values within 10 days from the first day of conditioning were also included in the analysis (≥1000 ng/mL versus <1000 ng/mL according to the results of a previous study [18]). Among patients who underwent allo-HSCT, modified European Group for Blood and Marrow Transplantation score (0 to 2 versus ≥1, considering the number of analyzed patients in each group), concomitant acute GVHD (grades 0 and 1 versus ≥grade 2 [7]), type of donor, and intensity of conditioning were also evaluated. To determine the association between incidence of BSI and potential clinical and laboratory risk factors, the Fisher exact test or the chi-square test were used as appropriate, and multiple binary logistic regression tests were performed as univariate and multivariate analysis. Independent variables with $P < .1$ were included for multivariable analyses. All values were 2-sided and statistical significance was accepted at the level of $P < .05$.

RESULTS
Patient Characteristics
Out of 170 patients, 134 patients (78.8%) satisfied the inclusion criteria (59 patients underwent allo-HSCT and 75 patients underwent auto-HSCT). Most patients who underwent allo-HSCT (53 of 59 patients) and auto-HSCT (74 of 75 patients) acquired hematopoietic stem cells by peripheral blood mobilization. Forty-four bacterial isolates from 36 patients (26.9%, 22 patients with allo-HSCT and 14 patients for auto-HSCT) were reported. BSI occurred more frequently in patients who underwent allo-HSCT ($P = .019$ by chi-square test), compared with those who underwent auto-HSCT. Detailed characteristics of the analyzed patients are shown in Table 1.

BSIs of Allo-HSCT and Auto-HSCT
BSIs of auto-HSCT were reported earlier (mean [SD], 12.1 [3.4] days), compared with those of allo-HSCT (mean [SD], 32.8 [27.1] days), with statistical significance ($P = .006$ by Mann-Whitney test). Contrary to patients who underwent auto-HSCT who experienced no episodes of postneutrophil-engraftment bacterial BSI, 8 of 22 patients (36.4%) who underwent allo-HSCT experienced postneutrophil-engraftment bacterial BSI, and 7 of the 8 patients had concomitant grade ≥2 acute GVHD.

MDR gram-negative bacterial BSI was more common in patients who underwent allo-HSCT, compared with those who underwent auto-HSCT. BSIs after allo-HSCT were more fatal: 7 of 21 patients who underwent allo-HSCT (33.3%) died of BSI, whereas only 1 of 14 patients who underwent auto-HSCT died of BSI. Mortality due to catheter-related BSI was higher among patients who underwent allo-HSCT, compared with those who underwent auto-HSCT (Table 2).

Table 1
Patient Characteristics

Potential Risk Factor	Overall (N = 134)	Allo-HSCT (n = 59)	Auto-HSCT (n = 75)
Age, yr			
Median (range)	45 (18-68)	35	51 (22-68)
≤40	49 (36.5%)	35 (59.3%)	14 (18.7%)
>40	85	24	61
Gender			
Male	77 (57.5%)	29 (49.2%)	48 (64.0%)
Female	57	30	27
Disease			
Acute myeloid leukemia	41 (30.6%)	31 (52.5%)	10 (13.3%)
Others	93 (69.4%)	28 (47.5%)	65 (86.7%)
Acute lymphoblastic leukemia	5	5	0
Biphynotypic acute leukemia	6	6	0
Myelodysplastic syndrome	3	3	0
Severe aplastic anemia	5	5	0
Chronic myelogenous leukemia	6	6	0
Lymphoma	30	1	29
Multiple myeloma	38	2	36
Time of transplantation			
≤180 d	85 (63.4%)	30 (50.8%)	55 (73.3%)
>180 d	49	29	20
CD34$^+$ cell			
Median (range)	4.17 (1.0-20.0)	3.80 (1.0-17.0)	5.48 (1.2-20.0)
≥5.0 × 10^6/kg	44 (32.8%)	17 (28.8%)	27 (36.0%)
<5.0 × 10^6/kg	81 (60.4%)	41 (69.5%)	40 (53.3%)
No record	9	1	8
HCT-CI			
Score 0	92 (68.7%)	48 (81.4%)	44 (58.7%)
Score ≥1	42	11	31
Prophylactic antibiotics			
Yes	104 (77.6%)	43 (72.9%)	61 (81.3%)
No	30	16	14
Elevated C-reactive protein			
Yes	65 (48.5%)	35 (59.3%)	30 (40.0%)
No	69	24	45
Serum albumin			
≥3.5 mg/dL	99 (73.9%)	39 (66.1%)	60 (80.0%)
<3.5 mg/dL	35	20	15
Serum ferritin			
≥1000 ng/mL	41 (30.6%)	29 (49.2%)	12 (16.0%)
<1000 ng/mL	75 (56.0%)	26 (44.1%)	49 (65.3%)
Not checked	18	4	14
mEBMT score after allograft			
Score 0 to 2	-	31 (52.5%)	-
Score ≥3	-	28	-
Acute GVHD			
Grade 0 to 1	-	39 (66.1%)	-
Grade ≥2	-	13 (22.0%)	-
Not evaluable (early death)		7	
Source of allograft			
Matched sibling	-	33 (55.9%)	-
Others	-	26 (44.1%)	-
Matched unrelated		24	
1-locus mismatched unrelated		1	
Umbilical cord blood		1	
Conditioning of allograft			
Myeloablative	-	52 (88.1%)	-
Nonmyeloablative	-	7	-
Status before allograft			
In CR	-	52 (88.1%)	-
Not in CR	-	7	-

Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; auto-HSCT, autologous hematopoietic stem cell transplantation; d, days; HCT-CI, hematopoietic cell transplantation-comorbidity index; mEBMT, modified European Group for Blood and Marrow Transplantation; CR, complete remission.

Evaluation of Risk Factors of BSI

Type of central venous catheter did not have an influence on the incidence of catheter-related BSI: 2 of 13 patients (15.3%) with a Hickman catheter and 9 of 121 patients (7.4%) with a nontunneled central venous catheter experienced catheter related BSI ($P = .214$). Elevated CRP ($P < .001$) and no prophylactic antibiotics ($P < .021$) showed independent associations with higher incidence of BSI in the entire patient population.

In multivariate analysis, among 59 patients who underwent allo-HSCT, elevated CRP ($P = .01$) and acute GVHD ≥ grade 2 ($P = .002$) showed associations with BSI. For 75 patients who underwent auto-HSCT, elevated CRP ($P = .034$) and no prophylactic antibiotic use ($P = .004$) were found to be independent risk factors of BSI. In multivariate analysis of the entire patient population, CRP elevation and no antibiotic prophylaxis maintained significant risk (Table 3).

Table 2
Etiologic Agents of Bacterial Bloodstream Infection

	Allo-HSCT 28 Bacterial Isolates from 22 Patients	Auto-HSCT 16 Bacterial Isolates from 14 Patients

Gram positive	Overall reported BSIs: 10 isolates
	    Methicillin-resistant (MR) CNS: 5
	    Methicillin-susceptible (MS) SA: 1
	    MRSA: 1
	    Vancomycin-susceptible *Enterococcus*: 1
	    Vancomycin-resistant *Enterococcus*: 2
	Defined as catheter-related BSI: 7 isolates
	Fatal BSI: 4 isolates
	    1 patient died of MCRNS
	    1 patient died of VRE
	    1 patient died of MRSA
	    1 patient died with VRE (died of disease Progression)
		Overall reported BSIs: 5 isolates
		    MRCNS: 2
		    MSSA: 1
		    MRSA: 1
		    α-hemolytic *Streptococcus*: 1
		Defined as catheter-related BSI: 4 isolates
		Fatal BSI: none

Gram negative	Overall reported BSIs: 18 isolates
	    Klebsiella pneumoniae: 3
	    Escherichia coli: 5
	    Acinetobacter baumanii: 3
	    Enterobacter cloacae: 2
	    Sternotrophomonas maltophilia: 2
	    Pseudomonas aerusinosa: 1
	    Undefined gram (-) rods: 2
	Defined as MDR gram (-) rods: 8 isolates
	Fatal BSI: 3 isolates
	    2 patients died of MDR *A. baumanii*
	    1 patient died with MDR undefined g(-) rod (died of massive intestinal bleeding)
		Overall reported BSIs: 11 isolates
		    K. pneumoniae: 6
		    E. coli: 3
		    Citrobacter braakii: 1
		    Agrobacterium radiobacter: 1
		
		Defined as MDR-gram (-) rods: 1 isolate
		Fatal BSI: 1 isolate
		    1 patient died of *K. pneumoniae*

Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; auto-HSCT, autologous hematopoietic stem cell transplantation; BSI, bloodstream infection; CNS, coagulase-negative *staphylococci*; SA, *Staphylococcus aureus*; MDR, multi-drug resistant.

DISCUSSION

In the current study, different characteristics of bacterial BSI were observed between patients who underwent allo-HSCT and those who underwent auto-HSCT, although patients in both groups received identical supportive care to prevent bacterial infection during the HSCT procedure.

A beneficial role of prophylactic antibiotics in patients with auto-HSCT was demonstrated in our study as well as in a previous meta-analysis [19]. Because the majority of BSI events occurred during the preneutrophil-engraftment period, with relatively less incidence of BSI by MDR pathogen, it can be assumed that early introduction of broad-spectrum antibiotics as a prophylaxis for bacterial BSI could lead to reduced incidence of bacterial BSI in patients receiving auto-HSCT: it appears to be an one-shot game decided by a single round. However, to provide confirmation, further prospective studies are needed.

Among patients who underwent allo-HSCT, the incidence of bacterial BSI showed a significant increase according to the occurrence of ≥grade 2 acute GVHD: among 13 patients with ≥grade 2 acute GVHD, 11 patients had a bacterial BSI and 10 of them experienced BSI after

Table 3
Univariate and Multivariate Analysis for Risk Factors of Bacterial Bloodstream Infection

Potential Risk Factor	Overall (N = 134)			Allo-HSCT (n = 59)			Auto-HSCT (n = 75)		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Univariate analysis									
Allogeneic transplantation	2.59	1.18-5.68	.017						
Age >40 yr	.64	.29-1.38	.253	1.37	.47-3.99	.565	.49	.13-1.88	.298
Male gender	.66	.31-1.43	.291	.59	.20-1.71	.330	1.02	.30-3.41	.980
Acute myeloid leukemia	2.34	1.05-5.19	.037	1.14	.40-3.28	.812	3.67	.87-15.37	.076
CD34$^+$ cell <5.0 × 10^6/kg	2.36	.93-6.01	.072	1.06	.33-3.44	.926	8.67	1.04-72.32	.046
HCT-CI score ≥1	.95	.42-2.18	.905	2.40	.64-9.07	.197	.75	.22-2.50	.637
Without antibiotics	5.85	2.43-14.06	<.001	1.45	.45-4.68	.532	35.63	7.64-166.21	<.001
Elevated CRP	7.14	2.84-17.94	<.001	5.30	1.50-18.70	.010	8.11	2.03-32.44	.003
Serum albumin <3.5 mg/dL	2.33	1.02-5.33	.044	3.11	1.01-9.57	.048	1.11	.27-4.63	.882
Serum ferritin >1000 ng/mL	2.02	.84-4.87	.116	1.92	.61-5.98	.263	.55	.61-4.91	.589
Modified EBMT score ≥3		Not analyzed		1.18	.41-3.39	.763		Not analyzed	
Acute GVHD grade ≥2		Not analyzed		15.95	3.00-84.67	.001		Not analyzed	
Not matched sibling donor		Not analyzed		.91	.32-2.64	.869		Not analyzed	
Myeloablative conditioning		Not analyzed		1.56	.28-8.84	.614		Not analyzed	
Transplantation without CR		Not analyzed		.69	.16-2.99	.624		Not analyzed	
Multiple myeloma		Not analyzed			Not analyzed		1.86	.56-6.19	.312
Multivariate analysis									
Without antibiotics	3.32	1.20-9.21	.021	-			19.77	2.57-152.29	.004
Elevated CRP	7.38	2.51-21.67	<.001	8.97	1.70-47.42	.010	12.74	1.22-133.48	.034
Acute GVHD grade ≥2	-			20.96	2.98-147.35	.002	-		

OR indicates odds ratio; CI, confidence interval; CRP, C-reactive protein; HCT-CI, hematopoietic cell transplantation-comorbidity index; EBMT, European Group for Blood and Marrow Transplantation; GVHD, graft-versus-host disease; CR, complete remission.

initiating corticosteroids with or without immunosuppressant for treatment of acute GVHD during the postneutrophil-engraftment period. In addition, 8 of the 10 patients, patients had a report indicating growth of resistant bacteria; MDR-gram negative rods (n = 4), vancomycin-resistant *Enterococcus* (n = 2), and methicillin-resistant coagulase-negative *staphylococci* (n = 2). Strong association of acute GVHD with an increase of bacterial BSI has been reported in several previous studies [5-7]. Poutsiaka et al. [7] reported an association of BSI and acute GVHD after HSCT. In their study, no relationship was observed between the occurrence of BSI and acute GVHD grade 1, and only acute GVHD grades ≥2 showed an association with incidence of BSI. They reported that median time to development of acute GVHD grades ≥2 (49 of 211 patients, 23.2%) was 24 days (interquartile range, 16 to 36 days). Regarding these results, we can assume that development of moderate to severe acute GVHD and subsequent administration of systemic corticosteroids with or without immunosuppressant may contribute to higher and later occurrence of bacterial BSI in patients receiving allo-HSCT, compared with those receiving auto-HSCT. Although we did not evaluate the direct correlation between use of systemic steroids and incidence of BSI, it can be easily postulated because all 13 patients with acute GVHD ≥grade 2 received systemic steroids with a dose of ≥1 mg/kg of prednisolone or equivalent, whereas only 2 of 46 patients with no or grade 1 acute GVHD received systemic corticosteroids. Because none of the 13 patients received prophylactic antibiotics in response to acute GVHD ≥grade 2 and its resultant systemic corticosteroid use, the effect of prophylactic antibiotics for prevention of bacterial infection during systemic treatment of moderate to severe acute GVHD could not be evaluated.

Antibiotic prophylaxis failed to result in a decrease of bacterial BSI in patients who underwent allo-HSCT. Recent studies have also reported a limited role of the current antibiotic prophylaxis in the setting of allo-HSCT: a Canadian prospective study was conducted for comparison of 2 consecutive cohorts (empiric antibacterial strategy [n = 127] versus prophylactic strategy [n = 111]) of patients receiving outpatient-based HSCT [20]. Prophylactic use of antibiotics contributed to a reduction of bacterial BSI in patients who underwent auto-HSCT (P = .001), but not in those who underwent allo-HSCT (P = .19). In a retrospective study of 246 patients who underwent allo-HSCT, a new quinolone-based prophylactic antibiotic regimen showed no superiority to the old regimen (trimethoprime sulfamethoxazole, vancomycin, and nystatin, all per os) in terms of the occurrence of BSI and 6-month mortality [21]. However, with still insufficient evidence, it is dangerous to conclude that administration of prophylactic antibiotics is unnecessary in allo-HSCT recipients. Rather, it is more reasonable to explain that the beneficial effect of prophylactic antibiotics was counterbalanced by BSIs of later onset and more resistant pathogens caused by post-allo-HSCT conditions, such as prolonged use of immunosuppressant because of acute GVHD, etc.

Greater frequency of MDR bacterial isolates among patients with allo-HSCT can be explained by the baseline patient characteristics. Most patients who underwent allo-HSCT had acute leukemia, myelodysplastic syndrome, or aplastic anemia, and they experienced more prolonged periods of neutropenia in general, compared with patients with lymphoma or multiple myeloma; therefore, they received more repeated and heavy treatment with broad-spectrum antibiotics. A significant increase in cases of

MDR bacterial infection has been reported in patients with allo-HSCT [2-3,22], and they are one of the critical factors causing mortality [3,22]; therefore, antibiotic resistance is a major concern of allo-HSCT. Oliveira et al. [3] prospectively collected data from 13 Brazilian HSCT centers to characterize the epidemiology of BSI and to identify factors associated with infection due to MDR gram-negative isolates. They reported an association with treatment with third-generation cephalosporin and being a patient at one of the hospitals with infection due to MDR gram-negative isolates. Results of a retrospective cohort study conducted by the Mayo Clinic revealed that prophylactic levofloxacin with penicillin (or doxycycline for penicillin-allergic patients) may contribute to the emergence of resistant gram-negative infections in allo-HSCT recipients over time [23]. Considering these previous studies and the result of the current study showing that the majority of BSIs combined with acute GVHD ≥grade 2 were caused by resistant pathogens, routine prophylactic antibiotic use in response to acute GVHD ≥grade 2 may not be an effective strategy. Rather, close observation of patients with repetitive and thorough history taking and physical examination, regular checks of chest X-ray and blood inflammatory markers, and consultation with infectious disease specialists could be a better approach. Empiric antibiotics should be chosen by infectious disease specialists considering not only the patient's previous history of antibiotic use, but also the particularity of the institution.

Although serum CRP is a nonspecific inflammatory marker, elevated CRP (≥.5 mg/dL) before transplantation remained an independent risk factor in multivariate analysis. This result is in line with findings of a previous study reported by Kanda et al. [8], although a higher level of serum ferritin is not. Because .5 mg/dL was the upper limit of the normal range of CRP in our institution, we used a different cut-off value of serum CRP (.5 mg/dL) compared with that reported in the study by Kanda et al. (.3 mg/dL). Whether .3 mg/dL or .5 mg/dL was used as a cut off, elevation of baseline CRP was proven to be an independent risk factor of bacterial BSI by at least 2 retrospective studies. Considering the results, a stronger recommendation of prophylactic antibiotic use for patients with elevated CRP could be cautiously considered, at least in the case of auto-HSCT.

Posttransplantation CRP elevation is also known to be related to transplantation-related complications in patients receiving allo-HSCT [24-25]. To determine if serum CRP before HSCT is a predictive factor of bacterial BSI, a prospective study in patients with HSCT is warranted.

Contrary to a previous study conducted in the 1990s that reported HSCT with a MUD donor, compared with HSCT with an MSD donor, was as a risk factor for bacterial BSI [6], in the current study, the source of the allograft had no impact on the risk of bacterial BSI. However, improvement of acute GVHD prophylaxis might reduce the incidence of acute GVHD and resultant bacterial infection. Because of a small sample size and the retrospective nature of the current study, we cannot make a conclusive statement that MUD is comparable to MSD in terms of bacterial BSI. We believe that this should be validated in future studies. As most patients who underwent allo-HSCT had either MSD (n = 33) or MUD (n = 24) as a source of allograft, we could not evaluate the risk of BSIs in patients with alternative sources of allografts, such as those from HLA-mismatched donors, haplo-identical donors, and umbilical cord blood transplantation. This should also be evaluated in the future analysis.

Limitations of the current study include a relatively small number of patients and retrospective analysis. However, the results of our study demonstrate differences between bacterial BSIs after auto-HSCT and allo-HSCT clearly enough to provide useful information for developing a future strategy to overcoming BSI according to the type of HSCT.

In conclusion, except for elevation of pretransplantation serum CRP, allo-HSCT and auto-HSCT have different risk factors, and BSI after auto-HSCT occurred earlier and showed better clinical outcomes compared with BSI after allo-HSCT. To establish the best defense strategy against BSI, the distinctive natures of bacterial BSI after allo-HSCT and auto-HSCT should be considered.

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