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Bloodstream infections in patients with hematological malignancies at the adult hematology ward of Yamagata University Hospital

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ABSTRACT

Objectives: This study was initiated to determine the local profile of bloodstream infections (BSIs) in patients with hematological malignancies. Particular attention was given to the characteristics of BSIs associated with death.

Patients and Methods: 255 patients hospitalized in the adult hematology ward of Yamagata University Hospital for chemotherapy from January 2003 to December 2007 were studied retrospectively, and BSIs were identified. To examine the characteristics of BSIs associated with death, BSIs with onset within 21 days prior to patients' death were defined as critical BSIs and compared to non-critical BSIs.

Results: A total of 119 BSIs were identified in 67 of 255 patients. Of 119 BSIs, 29 (24.3%) could be classified as critical BSIs. On logistic regression analysis, profound neutropenia (ANC=0 cells/μL) (OR=19.9; 95% CI=3.6 to 109.4; $P<0.01$) was the independent factor most associated with BSI onset. And Performance status 4 of the Eastern Cooperative Oncology Group criteria (bedridden status) (OR=20.1; 95% CI=4.4 to 91.0; $P<0.01$) was the independent factor most associated with critical BSI episodes. On univariate analysis, pneumonia and gastrointestinal disturbance were associated with critical BSI episodes. The pathogens were markedly different between critical and non-critical BSIs. The most common pathogens in critical BSIs were *Enterococcus* species (11 of 29; 37.9%), whereas *Staphylococcus* species were most common in non-critical BSIs (42 of 90; 46.7%).

Conclusion: We determined the local profile of BSIs, and these data are useful for risk-based, empirical choosing of antimicrobial therapy in our ward. BSIs associated with death occur in patients with severe underlying conditions, so that non-antimicrobial supportive therapy needs to be implemented to improve BSI patients' survival.

Key words : bloodstream infection, hematological malignancy, neutropenia

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INTRODUCTION

In spite of the development of antimicrobial therapy, bloodstream infection (BSI) is a major cause of death in patients with hematological malignancies[1, 2]. In the 1960s, the relationship between neutropenia and infection was first recognized, and the mortality rate in neutropenic patients with leukemia and Gram-negative infections was 91%[3]. The introduction of empirical antimicrobial therapy altered the management of febrile neutropenia[4]. Since then, the outcomes of febrile neutropenia have improved with the choice of more effective, less toxic, broad-spectrum antibiotics. In the adult hematology ward of Yamagata University Hospital, empirical antimicrobial therapy choices have been made according to the guidelines published by the Infectious Diseases Society of America (IDSA)[5].

The use of antimicrobial prophylaxis in neutropenic patients remains controversial. The problems of prophylaxis are the lack of survival benefits and the risk of inducing antimicrobial resistance[6]. However, the benefits of antimicrobial prophylaxis have been emphasized by two major double-blind, placebo-controlled trials with levofloxacin, which showed very significant reductions in all infection-related events[7, 8]. In our ward, antimicrobial prophylaxis has been given to patients with dose-intensity chemotherapy, such as remission-induction therapy for acute leukemia, salvage therapy for malignant lymphoma, and conditioning regimens for hematopoietic stem cell transplantation (HSCT), and moderately myelosuppressive chemotherapy, such as the CHOP regimen for lymphoma. However, in the face of emerging multidrug-resistant organisms and the dynamic epidemiology of pathogens, empirical and prophylactic antimicrobial therapies have become increasingly difficult for the patients with hematological malignancies, who are highly compromised patients. Hence, the aim of this study was to determine the local profile of BSIs; in order to improve the outcome of BSI patients, particular attention was given to the characteristics of BSIs associated with death.

MATERIALS AND METHODS

Setting: This study was conducted in the adult hematology ward of Yamagata University Hospital. Approximately 120 patients with hematological malignancies are admitted to this ward annually; half of them are newly diagnosed. The ward has 20 to 30 beds with 3 clean rooms.

Study design and patients: All hospitalized patients with hematological malignancies between January 1, 2003, and December 31, 2007 were included in this study. The medical records and computerized microbiology laboratory records were searched to identify BSIs in these patients. Patients with a history of BSIs were selected as BSI patients. A BSI with its onset within 21 days before the patient's death was classified as a critical BSI and considered to be associated with the patient's death, regardless of the underlying disease status[9].

Definitions: The following terms were defined prior to data analysis. A BSI was defined as bacteremia and fungemia documented by detection of at least one specimen in a blood culture from a patient with a systemic inflammatory response syndrome (e.g., fever, tachycardia, tachypnea, or leukocytosis); when

the isolate was a potential skin contaminant (such as coagulase-negative staphylococci [CoNS], a *Bacillus*, or *Corynebacterium* species), to confirm the BSI, the two following criteria had to be met: (A) the presence of an intravascular catheter; and (B) the initiation of anti-microbial therapy[1), 9), 10)]. Sequential blood cultures yielding the same pathogen were considered to be one episode of BSI. One blood culture yielding two significant pathogens was considered to be two episodes caused by each pathogen. The onset of a BSI was defined as the day of the first positive blood culture. Gastrointestinal (GI) disturbance was defined as the clinical symptoms of diarrhea and paralytic ileus.

Microbiology: Bloodstream isolates were identified at the species level with the VITEK system (from BIOMERIEUX) according to the manufacturer's instructions. The MICs were determined with frozen plates in accordance with the Clinical Laboratory Standards Institute (CLSI) guidelines[11)]. MRSA was defined as *Staphylococcus aureus* that was resistant to oxacillin (MIC >4 μg/mL).

Statistical analysis: Continuous variables were compared using the Mann-Whitney U test (non-normally distributed variables). Categorical variables were evaluated using the chi-square or the two-tailed Fisher's Exact Test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association that emerged. Values are expressed as the means ± standard deviation (continuous variables) or as percentages of the group from which they were derived (categorical variables). A P value of <0.05 was considered statistically significant. Multivariate analysis was used to identify independent risk factors for BSI patients and to analyze the specific features of critical BSIs. For this analysis, logistic regression was used, and variables were incorporated. All statistical analyses were performed using the PASW software, version 17.0 for Windows.

RESULTS

During the 5-year study period (2003 to 2007), 255 hospitalized patients were enrolled. They were newly diagnosed with hematological malignancies at the adult hematology ward. Their complete medical records were available for analysis.

Predisposing factors for BSI onset

A total of 119 BSIs were identified in 67 of 255 patients (incidence: 26.2%). The predisposing factors for the BSI patients are presented in Table 1. On univariate analysis, diagnosis of acute leukemia (47.8% BSI patients vs. 9.6% non-BSI patients), a history of allogeneic hematopoietic stem cell transplantation (35.8% vs. 8.0%, respectively), a history of a central venous catheter (80.6% vs. 38.3%, respectively), a complication of GI disturbance (37.3% vs. 15.4%, respectively), duration of neutropenia (67.2% vs. 17.5%, respectively), and profound neutropenia (73.1% vs. 14.9%, respectively) were significantly more frequent in BSI patients than in non-BSI patients. On logistic regression analysis, performance status 4 (P=0.014), GI disturbance (P=0.005), profound neutropenia (ANC=0 cells/μL) (P=0.001) was the independent factors associated with BSI patients. The patients with profound neutropenia were treated with dose-intensity chemotherapy, such as remission-induction therapy for acute leukemia, salvage therapy for malignant lymphoma, and conditioning regi-

Table 1. Predisposing factors for BSI onset in 255 patients with hematological malignancies

Factors	No. (%) of BSI patients n = 67	No. (%) of Non-BSI patients n = 188	P-value (Univariate)	P-value (Multivariate)
Mean ± SD age (y)	56 ± 18	62 ± 16	0.28	0.60
Male sex	37 (55.2)	102 (54.3)	0.89	0.63
Diagnosis				
Acute leukemia	32 (47.8)	18 (9.6)	<0.01	0.10
Malignant lymphoma	22 (32.8)	105 (55.8)	0.01	0.25
Multiple myeloma	8 (11.9)	41 (21.8)	0.11	0.53
Others	5 (7.5)	24 (12.8)	----	----
History of therapy				
Chemotherapy and others	38 (56.7)	167 (88.8)	----	----
Autologous HSCT*	5 (7.5)	6 (3.2)	0.26	0.99
Allogeneic HSCT	24 (35.8)	15 (8.0)	<0.01	0.86
Performance status 4**	20 (29.8)	43 (22.9)	0.25	0.01
History of CV* catheter	54 (80.6)	72 (38.3)	<0.01	0.36
Complications				
Pneumonia	11 (16.4)	25 (13.3)	0.55	0.27
GI* disturbance	25 (37.3)	29 (15.4)	<0.01	<0.01
Duration of neutropenia***				
ANC* <500 cells/μl for ≥ 7 days	45 (67.2)	33 (17.5)	<0.01	0.31
Degree of neutropenia***				
0 < ANC < 1000 cells/μl	14 (20.9)	103 (54.8)	<0.01	0.47
ANC = 0 cells/μl (profound)	49 (73.1)	28 (14.9)	<0.01	<0.01
Mortality	42 (62.7)	63 (33.5)	----	----

*HSCT indicates hematopoietic stem cell transplantation; GI, gastrointestinal; CV, central venous; ANC, absolute neutrophil count.
**Performance status 4 of the Eastern Cooperative Oncology Group criteria (ECOG) indicates bedridden status.
***Duration and degree of neutropenia were evaluated before BSI onset in BSI patients. In non-BSI patients, the most prolonged duration and the minimum ANC during admission were evaluated.

mens for HSCT.

Mortality

The BSI patients had a higher mortality (42 of 67; 62.7%) than the non-BSI patients (63 of 188; 33.5%). Of 67 BSI patients, 25 (37.7%) had a history of critical BSIs. The BSI patients without a history of critical BSIs also had a higher mortality (17 of 42; 40.5%) than the non-BSI patients. This rate may be explained by fungal and viral infections that are related to mortality in neutropenic patients, but are difficult to detect as BSIs. In fact, 15 of 42 BSI patients (35.7%) who died were suspected of having fungal infections with positive β-D-glucan values, and 3 of 42 BSI patients (7.1%) had aspergillus pneumonia. Death caused by underlying disease was difficult to be distinguished from other causes, because many complications, such as infections, drug toxicity, chemotherapy-induced organ damage, and disease progression, were present when the

Table 2. Predisposing factors for death caused by first BSI in 67 BSI patients

Factor	No. (%) of BSI patients		*P*-value (Univariate)
	Non-survivors (n = 13)	Survivors (n = 54)	
Mean ± SD age (y)	69 ± 9	52 ± 19	<0.01
Male sex	6 (46.2)	31 (57.4)	0.54
Diagnosis of acute leukemia	5 (38.5)	27 (50.0)	0.54
No remission of the underlying disease	11 (84.6)	41 (75.9)	0.71
Allogeneic HSCT	2 (15.3)	22 (40.7)	0.11
Performance status 4	12 (92.3)	8 (14.8)	<0.01
Presence of CV catheter	10 (76.9)	42 (77.8)	1.00
Presence of pneumonia	5 (38.5)	6 (11.1)	0.03
Presence of GI disturbance	10 (76.9)	15 (27.8)	<0.01
ANC < 500 cells/μl for ≥ 7 days	7 (53.8)	23 (42.6)	0.54
Profound neutropenia (ANC = 0 cells/μl)	7 (53.8)	42 (77.8)	0.09

patients with hematological malignancies died.

Predisposing factors for death caused by first BSI.

Of 67 BSI patients, 13 (19.4%) died within 21 days after the first BSI onset. In these patients, the main cause of death was considered to be the first BSI. Predisposing factors for death caused by the first BSI are presented in Table 2. Advanced age (69±9 y, non-survivors vs. 52±19 y, survivors), performance status 4 (92.3% vs. 14.8%, respectively), presence of pneumonia (38.5% vs. 11.1%, respectively), and presence of GI disturbance (76.9% vs. 27.8%, respectively) were significantly more common in the non-survivors than in the survivors. On the other hand, the factors that were statistically significant predisposing factors for BSI onset (Table 1), such as diagnosis of acute leukemia, allogeneic HSCT, duration of neutropenia, and profound neutropenia, were not significantly different between non-survivors and survivors.

Species Distribution of Pathogens

The species distribution of pathogens isolated in critical and non-critical BSIs was markedly different (Table 3). The common pathogens in critical BSIs were *Enterococcus* species (11 of 29; 37.9%), MRSA (5 of 29; 17.2%), and Pseudomonas species (5 of 29; 17.2%). CoNS were not isolated in critical BSIs, although they were most common in non-critical BSIs (32 of 90; 35.6%). Similarly, *Corynebacterium* species, *Streptococcus* species, and *Bacillus* species were rare in critical BSIs but common in non-critical BSIs. With respect to fungal BSI, only 3 (3.3%) fungal BSIs caused by *Candida parapsilosis* were observed, and all of them were non-critical BSIs.

The frequencies of pneumonia and GI disturbance with BSIs were: 14.3% and 64.3% in MRSA BSIs; 18.7% and 75.0% in *Enterococcus* BSIs; and 33.3% and 33.3%. in *Pseudomonas* BSIs.

Characteristics of Critical BSIs

One of the clinical problems in patients with hematological malignancies was recurrence of BSI episodes during the course of cyclic chemotherapy and salvage therapy for relapse of disease. Therefore, the number of BSI

Table 3. Species distribution of pathogens isolated in critical and non-critical BSIs

Pathogen	No. (%) of BSIs		
	Critical $n = 29$	Non-critical $n = 90$	Total $n = 119$
Gram-positive organisms, all	20 (69.0)	69 (76.7)	89 (74.8)
Staphylococcus species			
CoNS*	0	32 (35.6)	32 (26.9)
MSSA**	2 (6.9)	1 (1.1)	3 (2.5)
MRSA***	5 (17.2)	9 (10.0)	14 (11.7)
Enterococcus species			
Enterococcus faecalis	9 (31.0)	3 (3.3)	12 (10.1)
Enterococcus faecium	1 (3.4)	2 (2.2)	3 (2.5)
Enterococcus gallinarum	1 (3.4)	0	1 (0.8)
Corynebacterium species	1 (3.4)	8 (8.9)	9 (7.5)
Streptococcus species	0	8 (8.9)	8 (6.7)
Bacillus species	1 (3.4)	6 (6.7)	7 (5.9)
Gram-negative organisms, all	9 (31.0)	18 (20.0)	27 (22.7)
Pseudomonas species	5 (17.2)	4 (4.4)	9 (7.5)
Other Gram-negative species			
Escherichia coli	0	5 (5.6)	5 (4.2)
Enterobacter cloacae	1 (3.4)	3 (3.3)	4 (3.3)
Stenotrophomonas maltophilia	2 (6.9)	1 (1.1)	3 (2.5)
Klebsiella pneumoniae	1 (3.4)	2 (2.2)	3 (2.5)
Aeromonas hydrophila	0	2 (2.2)	2 (1.7)
Acinetobacter anitratus	0	1 (1.1)	1 (0.8)
Fungi *Candida parapsilosis*	0	3 (3.3)	3 (2.5)

*CoNS indicates coagulase-negative staphylococci;**MSSA, methicillin-sensitive staphylococcus aureus; ***MRSA, methicillin-resistant staphylococcus aureus.

episodes in each patient varied from 1 to 7 episodes (41 patients with 1 episode, 10 patients with 2 episodes, 10 patients with 3 episodes, 4 patients with 4 episodes, 1 patient with 5 episodes, 1 patient with 7 episodes). To examine the characteristics of critical and non-critical BSI episodes, the factors were classified into three categories: patient-related factors, treatment-related factors, and pathogen-related factors (Table 4). For patient-related factors, performance status 4 (82.8% of critical BSI episodes vs. 12.2% of non-critical BSI episodes), presence of pneumonia (27.6% vs. 6.7%, respectively), and presence of GI disturbance (69.0% vs. 31.1%, respectively) were significantly different between critical and non-critical BSI episodes. For treatment-related factors, fluoroquinolone prophylaxis, prior exposure to antimicrobial therapy, and empirical therapy did not differ significantly between critical and non-critical BSI episodes. For pathogen-related factors, *Enterococcus* species as the pathogen was significantly more common (37.9% vs. 5.6%, respectively) in critical BSIs than in non-critical BSI episodes. On logistic regression analysis, performance status 4 (OR=20.1; 95% CI=4.4 to 91.0; $P<0.001$) was the independent factor most associated with critical BSI episodes.

Table 4. Characteristics of critical and non-critical BSI episodes

Characteristic at BSI onset	No. (%) of BSIs		*P*-value (Univariate)	*P*-value (Multivariate)
	Critical $n = 29$	Non-critical $n = 90$		
Patient-related factors				
No remission of the underlying disease	24 (82.8)	68 (75.6)	0.58	0.96
Performance status 4	24 (82.8)	11 (12.2)	<0.01	<0.01
ANC <500 cells/μl for $\geq$ 7 days	13 (44.8)	39 (43.3)	0.88	0.79
Presence of CV catheter	25 (86.2)	73 (81.1)	0.72	0.35
Presence of pneumonia	8 (27.6)	6 (6.7)	<0.01	0.20
Presence of GI disturbance	20 (69.0)	28 (31.1)	<0.01	0.17
Treatment-related factors				
Fluoroquinolone prophylaxis	23 (79.3)	71 (78.9)	0.96	0.12
Prior exposure to antimicrobial therapy				
Cephalosporins	18 (62.1)	43 (47.8)	0.18	0.35
Carbapenems	10 (34.5)	21 (23.3)	0.34	0.40
None	5 (17.2)	40 (44.4)	----	----
Empirical therapy				
Cephalosporins	8 (27.6)	33 (36.7)	0.50	0.26
Carbapenems	7 (24.1)	15 (16.7)	0.53	0.66
Aminoglycoside plus other antimicrobial agents	10 (34.5)	30 (33.3)	1.00	0.21
Pathogen-related factors				
MRSA	5 (17.2)	9 (10.0)	0.47	0.19
Enterococcus species	11 (37.9)	5 (5.6)	<0.01	0.09
Pseudomonas species	5 (17.2)	4 (4.4)	0.06	0.23

Susceptibility Patterns of BSI Pathogens

The susceptibility patterns of major BSI pathogens are presented in Table 5, but only antibiotics tested in all strains of each pathogen are shown. Previous studies[19] showed the close association between the use of antibiotics and the emergence of antibiotic resistance. Resistance to cefozopran, which we often used empirically, was seen in 57% of MRSAs, 94% of *Enterococcus* species, 33% of *Corynebacterium* species, and 28% of *Bacillus* species. Resistance to levofloxacin, which we often used prophylactically, was observed in 69% of CoNSs, 93% of MRSAs, 88% of *Enterococcus* species, 44% of *Corynebacterium* species, 25% of *Streptococcus* species, 43% of *Bacillus* species, and 33% of *Pseudomonas* species. Most pathogens tested were sensitive to vancomycin, but two strains of *Streptococcus* species isolated from 2 patients were resistant. One of these patients had acute myelogenous leukemia (AML) and had prior exposure to vancomycin in our ward. Another patient with myelodysplastic syndrome (MDS) had four admissions to another hospital, and the medical records were not available for determining whether vancomycin had been used.

DISCUSSION

Strategies to minimize ineffective antimicrobial therapy for BSI have been identified by practice guidelines[5), 20)]. In addition, clinicians

Table 5. Susceptibility patterns of BSI pathogens

Pathogen (no. of strains)	Percentage (%) of resistance to tested antibiotics				
	AMP	CZOP	IPM	LVFX	VCM
CoNS (32)	---	0	16	69	0
MRSA (14)	---	57	64	93	0
Enterococcus species (16)	19	94	---	88	0
Corynebacterium species (9)	44	33	---	44	0
Streptococcus species (8)	0	0	---	25	25
Bacillus species (7)	14	28	---	43	0
Pseudomonas species (9)	---	11	33	33	---

AMP indicates ampicillin (resistant, ≥16); CZOP, cefozopran (resistant, ≥32); IPM, imipenem (resistant, ≥16); LVFX, levofloxacin (resistant, ≥8; ≥4 in staphylococcal BSIs); VCM, vancomycin (resistant, ≥16).

can improve the therapy for BSI by using empirical antimicrobial therapy based on individual patient characteristics and the prevailing pathogens and their antimicrobial susceptibility profiles in their hospitals. In this study, among patients with hematological malignancies, the predisposing factors for BSI onsets, predisposing factors for death caused by BSI, species distribution of pathogens with susceptibility patterns, and characteristics of critical BSI episodes were identified.

Patients with hematological malignancies are at high-risk for BSI due to chemotherapy-induced neutropenia. The attack rate of BSI in neutropenic patients is high (11%-38%)[12)-15)]. In our study, 76.0% (194 of 255) of patients had histories of neutropenia, and BSI occurred in 32.5% (63 of 194) of these patients; this rate was consistent with previous reports.

Neutropenia is the strongest risk factor for infection[21)], and bacteremia usually develops when ANC falls to <100 cells/μL[22), 23)]. Furthermore, we have often observed that BSI improves rapidly after the appearance of neutrophils in peripheral blood at the end of myelosuppression, albeit at ANC <100 cells/μL. Therefore, we distinguished profound neutropenia with ANC=0 cells/μL from neutropenia with 0<ANC<1000 cells/μL for the analysis. In 30.1% (77 of 255) of patients, the minimum ANC decreased to the level of ANC=0 cells/μL before BSI onset in BSI patients and during admission in non-BSI patients. On multivariate analysis, a history of profound neutropenia was strongly associated with BSI. In contrast, neutropenia with 0<ANC<1000 cells/μL was significantly less common in BSI patients than in non-BSI patients. These results suggest that the risk of BSI onset markedly increased with the absence of neutrophils in the peripheral blood.

BSIs are recognized to have high mortality rates. However, mortality studies vary in both measures and populations[16)]. Wisplinghoff et al. reported that the overall mortality rate in BSI patients with hematological malignancies and solid neoplasms was 32%[1)]. In the present study, the mortality rate (62.7%) of the BSI patients was two-fold higher than the previously reported rate, presumably because

of other factors that affect mortality, such as fungal infection, chemotherapy toxicity, and underlying disease progression. On the other hand, 19.4% (13 of 67) of BSI patients died within 21 days after the first BSI onset.

In the analysis of predisposing factors for death caused by first BSI, performance status 4, presence of pneumonia, and presence of GI disturbance were significantly more common in non-survivors than in survivors. Thus, performance status 4 and GI disturbance were associated with not only BSI onset but also death caused by BSI. However, profound neutropenia was not significantly different between non-survivors and survivors, even though which is the major predictor for BSI onset. These results might reflect the pathophysiological difference between BSI onset and recovery from BSI. Poor performance status, GI disturbance and profound neutropenia permit the pathogens to invade into the body and proliferate, resulting in onset of BSIs. Furthermore, it is thought that the patients with poor performance status and severe complications were difficult to keep their general conditions until the recovery of bone marrow functions.

To make further investigations of characteristics of BSIs associated with death, we distinguished critical BSI episodes from non-critical BSI episodes and compared the characteristics of each BSI episodes. For patient-related factors, performance status 4, presence of pneumonia, and presence of GI disturbance were significantly different between critical and non-critical BSI episodes. This result was consistent with the result of the analysis of predictors for death caused by BSI, and moreover, performance status 4 was the independent factor most associated with critical BSI episodes on multivariate analysis. On the other hand, the percentage of no remission of the underlying disease was not significantly different between critical and non-critical BSI episodes. For this reason, we could not take into account the achievement of remission when we determined the underlying disease status at BSI onset. In fact, most patients with non-critical BSIs achieved remission of underlying disease despite showing no remission at BSI onset.

With respect to treatment-related factors, 82.8% of critical BSI episodes occurred in patients with prior exposure to antimicrobial therapy in our ward. In addition, *Enterococcus* species, MRSA, and *Pseudomonas* species (common pathogens in critical BSIs) were partially resistant to cefozopran, which we often used empirically, and levofloxacin, which we used for prophylaxis. These findings suggest that multidrug-resistant organisms produced by exposure to broad-spectrum antibiotics selectively remained and may have led to critical BSIs.

For pathogen-related factors, *Enterococcus* species were the most common pathogens in critical BSIs, and 75.0% (12 of 16) of BSI caused by *Enterococcus* species followed GI disturbances. These findings suggest that *Enterococcus* species translocate to the bloodstream following chemotherapy-induced GI disturbances and cause critical BSIs. This hypothesis is generally consistent with previous reports. Caballero et al. reported that the mortality rate of patients with cases of enterococcal bacteremia was high, although it has often been related to a patient's underlying conditions rather than to the infection itself[17]. To prevent enterococcal BSIs, the barrier function of the bowel mucosa should be

maintained. In general, the depletion of nutrients in the bowel lumen is accompanied by degenerative changes in the bowel mucosa[18]. Thus, appropriate nutritional support may prevent enterococcal BSIs and improve patients' outcomes.

All 16 *Enterococcus* strains tested were vancomycin-sensitive. Four patients with enterococal BSI were given vancomycin after BSI onset, but all of these patients died without recovery of marrow function due to progression of underlying disease. Widespread empirical use of vancomycin for suspected enterococcal BSI in patients with severe underlying conditions is undesirable, since overuse might facilitate the emergence of vancomycin-resistant *Enterococcus* strains. Assessment of the predictive factors identified in this study might help to avoid the overuse of antibiotics.

Our study had two limitations that must be acknowledged. First, our analysis was retrospective, and it was performed at a single center; thus, the results are not necessarily applicable to other settings. Second, our results were based on the findings of only a few cases; therefore, it is unclear whether studies with a large number of cases would lead to the same conclusions.

In conclusion, the local profiles of BSIs identified are useful for choosing risk-based empirical antimicrobial therapy in our ward. Furthermore, BSIs associated with death occur in patients with severe underlying conditions, so that non-antimicrobial supportive therapy needs to be implemented to improve BSI patients' survival. The results of this study invite investigations of effective non-antimicrobial supportive therapy.

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