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Bloodstream Infections Caused by *Enterococcus* spp: A 10-year Retrospective Analysis at a Tertiary Hospital in China*

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Summary: In order to discover the risk factors for 30-day mortality in bloodstream infections (BSI) caused by *Enterococcus* spp. strains, we explored the clinical and therapeutic profile of patients with *Enterococcus* spp. BSI and the characteristics of this condition. A total of 64 patients with BSI caused by *Enterococcus* spp. who were treated in our hospital between 2006 and 2015 were included in the study. The clinical features of patients, microbiology, and 30-day mortality were collected from the electronic medical records database and analyzed. The results showed that there were 38 patients infected by *Enterococcus faecalis* (*E. faecalis*), 24 by *Enterococcus faecium* (*E. faecium*), 1 by *Enterococcus casseliflavus* (*E. casseliflavus*), and 1 by *Enterococcus gallinarum* (*E. gallinarum*). A Charlson comorbidity score ≥5, corticosteroid treatment, placement of catheters or other prosthetic devices and history of antibiotic use were found more frequently in *E. faecium* BSI patients than in *E. faecalis* patients (P=0.017, P=0.027, P=0.008 and P=0.027, respectively). Furthermore, the univariate and multivariate analysis showed that corticosteroid treatment (OR=17.385, P=0.008), hospital acquisition (OR=16.328, P=0.038), and vascular catheter infection (OR=14.788, P=0.025) were all independently associated with 30-day mortality. Our results indicate that *E. faecalis* and *E. faecium* are two different pathogens with unique microbiologic characteristics, which cause different clinical features in BSI, and the empiric antimicrobial treatments are paramount for patients with enterococcal BSI.

Key words: *Enterococcus faecalis*; *Enterococcus faecium*; bloodstream infections; mortality; risk factors

Enterococci are normal bacterial inhabitants in the human and animal intestine[1–3]. There are more than 50 enterococci species, but only a few cause clinical infections in humans. *Enterococcus faecalis* (*E. faecalis*) and *Enterococcus faecium* (*E. faecium*) were found to account for more than 90% of clinical enterococcal isolates[4]. In the last two decades, enterococci have emerged as one of the major pathogens that cause nosocomial infections including the urinary tract, respiratory tract, intraperitoneal, and bloodstream infections (BSI)[5, 6]. Immunocompromised patients, critically ill patients, and patients with prosthetic devices placed, such as catheters, are at the highest risk for acquiring an enterococci infection[7].

BSI has been attracting attention because it is a major cause of morbidity and mortality throughout the world[8, 9]. BSI can be caused by a wide variety of microorganisms, including, but not limited to, *Escherichia coli*, *Klebsiella* spp., *Staphylococcus aureus*, and *Enterococcus* spp.. Previous studies have shown that *Enterococcus* spp. are an important pathogen causing BSI[10]. Butler *et al* reported that BSI caused by *E. faecalis* and *E. faecium* were independently associated with hospital costs and length of stay[11]. In severe cases, enterococci BSI also can cause death. Billington *et al* found that the overall fatality rate of BSI caused by *E. faecalis* and *E. faecium* was 22.8%, and the incidence of BSI caused by *E. faecalis* was higher than that caused by *E. faecium*[12]. Besides the species of *Enterococcus*, the Charlson severity index, pulmonary infection, and nosocomial infection were also risk factors for motality of patients with *Enterococcus* spp. BSI. Additional research identified catheter retention as an independent predictor of mortality caused by *Enterococcus* spp. BSI[13]. Thus, many risk factors seem to be responsible for the death in patients with *Enterococcus* spp. BSI, which requires further investigation.

The characteristics of *Enterococcus* spp. BSI in China are underexplored. There were only few studies focusing on bacteremia caused by *Enterococcus* spp. and the conclusions are inconsistent[14–16]. Therefore, we aimed to investigate the clinical and therapeutic profile of patients with *Enterococcus* spp. BSI and the characteristics of this condition in a teaching hospital in China. We also aimed to identify the risk factors of mortality at 30 days for *E. faecalis* and *E. faecium* BSI.

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1 MATERIALS AND METHODS

1.1 Study Design and Data Collection

This research was a monocentric retrospective observational cohort study. All patients with BSI caused by *Enterococcus* spp. were recruited from our university hospital (accommodating 1200 acute- and long-term beds) in China between January 1, 2006 and December 31, 2015. The clinical data of each case were collected from the electronic medical records. Based on these data, the Charlson comorbidity score was calculated for each patient[17]. The Simplified Acute Physiology Score II (SAPSII) and Mortality in Emergency Department Sepsis (MEDS), which were derived from both laboratory parameters and clinical evaluation, were calculated for patients confirmed to have BSI 24 h after their intensive care unit (ICU) admission[18, 19].

1.2 Bacteriologic Detection

Bacterial strains isolated from patients were identified using a VITEK 2 system (Biomérieux, Marcy l'Etoile, France). Antibiotic susceptibility was tested using the VITEK2 system or the disk diffusion method. Minimal inhibitory concentration (MIC) breakpoints were based on the guidelines of standard Clinical and Laboratory Standards Institute (CLSI) for 2014.

1.3 Definitions

BSI were defined as at least one positive blood culture for one of the *Enterococcus* spp. studied. Identification of the original source of the BSI was determined using bacteriologic sampling at the presumed source and medical reports of clinical examination[20]. A second physician was consulted for the controversial cases.

The comorbidity of each case was reviewed carefully. Heart diseases primarily included primary hypertension, coronary heart disease, and heart valve disease. The causes of chronic liver diseases included hepatitis virus, drugs, and alcohol, among others. Patients were recorded to have corticosteroid treatment if they had more than 1-week intravenous, systemic application of corticosteroid.

We sought to identify the site where the infection was acquired for each case. If this could not be accurately confirmed and BSI occurred > 48 h after hospitalization admission, the infection was considered hospital acquired[20]. The BSI were determined to be health care associated if the BSI began < 48 h after hospital admission and if one or more of the criteria defined by Friedman *et al* were met (intravenous chemotherapy or hemodialysis during the last 30 days, home intravenous therapy or wound care during the last 30 days, hospitalization for at least 2 days during the last 90 days, residence in a long-term care facility)[20, 21]. The BSI of all other cases were considered community acquired.

The clinical status of each patient was evaluated according to medical reports. For patients with missing information, the following definitions were used: severe sepsis, blood lactate > 4 mmol/L; organ dysfunction and hypotension, <90/40 mmHg before fluid resuscitation; septic shock, persistent hypotension despite fluid resuscitation requiring vasopressive drugs[20].

The positive history of antibiotic use was defined as following: within one month before the BSI episodes; the patient receiving at least one antimicrobial agent for more than 5 days.

1.4 Ethical Statement

In the study, all procedures involving human participants were in accordance with the ethical standards of the Shenzhen University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study informed consent is not required.

1.5 Statistical Analysis

The patient characteristics and BSI were shown as number (percentage) and compared using the chi-square test or Fisher's exact test. Risk factors for 30-day mortality were analyzed with a univariate logistic regression model. Variables associated with $P<0.05$ were selected for the multivariate logistic regression model. The logistic regression model was constructed by a backward selection approach based on the Wald statistic. The interaction in the multivariate logistic regression model was analyzed according to the Wald statistic. P values < 0.05 were regarded as statistically significant. All data were analyzed using the statistical software SPSS (version 14.0, USA).

2 RESULTS

2.1 Patient Inclusion and Characteristics

There were 71 *Enterococcus* spp. BSI episodes corresponding to 64 patients in our hospital over the 10-year period. Seven BSI cases were recurrent episodes in patients already included in the study. The non-repetitious *Enterococcus* spp. BSI cases were as follows: 38 patients with *E. faecalis* BSI, 24 patients with *E. faecium* BSI, 1 patient with *E. casseliflavus* BSI, and 1 patient with *E. gallinarum* BSI. As the BSI caused by *E. casseliflavus* and *E. gallinarum* were seldom found in clinical practice, we further analyzed the clinical characteristics of BSI caused by *E. faecalis* and *E. faecium*, which are shown in table 1. We found that *E. faecalis* BSI accounted for 61.3% (38/62) and *E. faecium* BSI accounted for 38.7% (24/62) of the *Enterococcus* spp. BSI in this study. Median patient age was 54 years (interquartile range [IQR], 40–73 years), and the percentage of patients with a Charlson comorbidity score ≥ 5 was 43.5% (27/62). Less than half of the patients (43.5%, n=27) were hospitalized in the ICU at the onset of or following BSI. Of these patients, 37.1% (10/27) had a SAPS II score ≥ 40, and 29.6% (8/27) had a MEDS score ≥ 13.

Different characteristics in patients with *E. faecalis* or *E. faecium* BSI were analyzed. The results are shown in table 1. *E. faecium* BSI patients had a Charlson comorbidity score ≥ 5 more frequently than *E. faecalis* BSI patients (62.5% *vs*. 31.6%, P=0.017). More *E. faecium* BSI patients experienced corticosteroid treatment and catheter or other prosthetic device placement than *E. faecalis* BSI patients (33.3% *vs*. 10.5%, P=0.027; 83.3% *vs*. 50.0%, P=0.008, respectively).

2.2 Characteristics of BSI Caused by *E. faecalis* and *E. faecium*

The characteristics of BSI patients caused by *E. faecalis* or *E. faecium* are shown in table 2. There was no difference in the acquisition of BSI and 30-day mortality rate between *E. faecalis* and *E. faecium* groups. However, vascular catheter infection rate was higher in *E. faecium* BSI patients than in *E. faecalis* BSI patients (25.0% *vs*. 5.3%, P=0.047). Antimicrobial resistance against ampicillin, ciprofloxacin, and high-level gentamicin was

higher in the *E. faecium* BSI group than in the *E. faecalis* BSI group (79.2% *vs*. 2.6%, *P*<0.001; 75.0% *vs*. 42.1%, *P*=0.011; 54.2% *vs*. 18.4%, *P*=0.003, respectively). And the history of antibiotic use was more frequently seen in the *E. faecium* BSI group than in the *E. faecalis* BSI group (54.2% *vs*. 26.3%, *P*=0.027).

Table 1 Baseline characteristics of patients with *E. faecalis* and *E. faecium* BSI

Variables[a]	All patients (*n*=62)	*E. faecalis* (*n*=38)	*E. faecium* (*n*=24)	*P* value
Age (years), median (IQR)	54 (40–73)	52 (36–73)	56 (45–75)	NS
Male	39 (62.9)	25 (65.8)	14 (58.3)	NS
Comorbidity				
Solid tumor	8 (12.9)	4 (10.5)	4 (16.7)	NS
Hematologic tumor	2 (3.2)	1 (2.6)	1 (4.2)	NS
Diabetes	12 (19.4)	8 (21.1)	4 (16.7)	NS
COPD	3 (4.8)	2 (5.3)	1 (4.2)	NS
Peptic ulcer disease	3 (4.8)	2 (5.3)	1 (4.2)	NS
Heart disease	24 (38.7)	15 (39.5)	9 (37.5)	NS
Stroke	14 (22.6)	9 (23.7)	5 (20.8)	NS
Chronic renal failure	8 (12.9)	3 (7.9)	5 (20.8)	NS
Liver disease	4 (6.5)	2 (5.3)	2 (8.3)	NS
Charlson comorbidity score				
≤ 2	27 (43.5)	20 (52.6)	7 (29.2)	NS
3–4	8 (12.9)	6 (15.8)	2 (8.3)	NS
≥5	27 (43.5)	12 (31.6)	15 (62.5)	0.017
SAPSII score (*n*=27)				
≤ 20	5 (18.5)	4 (25.0)	1 (9.1)	NS
20–40	12 (44.4)	7 (43.8)	5 (45.5)	NS
≥40	10 (37.1)	5 (31.2)	5 (45.5)	NS
MEDS score (*n*=27)				
≤ 4	6 (22.2)	5 (31.3)	1 (9.1)	NS
5–12	13 (48.2)	8 (50.0)	5 (45.5)	NS
≥13	8 (29.6)	3 (18.7)	5 (45.5)	NS
Immunosuppression				
Immunosuppressive treatment	3 (4.8)	3 (7.9)	0 (0.0)	NS
Corticosteroid treatment	12 (19.4)	4 (10.5)	8 (33.3)	0.027
Chemotherapy	2 (3.2)	1 (2.6)	1 (4.2)	NS
Catheter or other prosthetic device	39 (62.9)	19 (50.0)	20 (83.3)	0.008

[a]Values are *n* (%) or as otherwise indicated. NS: non-significant; COPD: chronic obstructive pulmonary disease. SAPSII: Simplified Acute Physiology Score II; MEDS: Mortality in Emergency Department Sepsis

Table 2 Characteristics of BSI caused by *E. faecalis* and *E. faecium*

Variables[a]	All patients (*n*=62)	*E. faecalis* (*n*=38)	*E. faecium* (*n*=24)	*P* value
Acquisition				NS
Community acquired	10 (16.1)	7 (18.4)	3 (12.5)	
Health care associated	14 (22.6)	11 (28.9)	3 (12.5)	
Hospital acquired	38 (61.3)	20 (52.6)	18 (75.0)	
ICU	32 (51.6)	19 (50.0)	13 (54.2)	
Medical unit	14 (22.6)	10 (26.3)	4 (16.7)	
Surgical unit	9 (14.5)	5 (13.2)	4 (16.7)	
Other	7 (11.3)	4 (10.5)	3 (12.5)	
BSI source				
Vascular catheter infection	8 (12.9)	2 (5.3)	6 (25.0)	0.047
Respiratory tract infection	15 (24.2)	11 (28.9)	4 (16.7)	NS
Intra-abdominal infection	11 (17.7)	6 (15.8)	5 (20.8)	NS
Urinary tract infection	22 (35.5)	15 (39.5)	7 (29.2)	NS
Unknown source or primary bacteremia	6 (9.7)	4 (6.5)	2 (8.3)	NS
≥2 bacteria	8 (12.9)	5 (13.2)	3 (12.5)	NS
Severe sepsis or septic shock	13 (21.0)	7 (18.4)	6 (25.0)	NS
Antimicrobial resistance				
Ampicillin	20 (32.3)	1 (2.6)	19 (79.2)	<0.001
Ciprofloxacin	34 (54.8)	16 (42.1)	18 (75.0)	0.011
Vancomycin	0 (0.0)	0 (0.0)	0 (0.0)	
High-level gentamicin	20 (32.3)	7 (18.4)	13 (54.2)	0.003
History of antibiotic use	23 (37.1)	10 (26.3)	13 (54.2)	0.027
30-day mortality	13 (21.0)	6 (15.8)	7 (29.2)	NS

[a]Values are expressed as *n* (%) or as otherwise indicated. NS: non-significant; BSI: bloodstream infections; ICU: intensive care unit; high-level gentamicin: MIC >500 μg/mL

2.3 Univariate Analysis of Risk Factors for 30-day Mortality Associated with BSI

The 30-day mortality rate of this study was 21.0% (13/62). The risk factors for 30-day mortality associated with *Enterococcus* spp. BSI were analyzed by univariate analysis. It was found that age (≥ 65), male, comorbidity, and tumors were not risk factors for 30-day mortality (table 3). The Charlson comorbidity score ≥ 5 and MEDS score ≥ 13 were also not identified to be risk factors for 30-day mortality in this study. However, the SAPSII score ≥ 40, which reflects illness severity and high mortality, was associated with 30-day mortality (*P*=0.039). Two additional variables, corticosteroid treatment and in-dwelling catheter or other prosthetic device also indicated risk for 30-day mortality associated with *Enterococcus* spp. BSI (*P*=0.002 and *P*=0.001, respectively).

Table 3 Univariate analysis of risk factors (clinical characteristics of patients) for 30-day mortality associated with BSI caused by *Enterococcus* spp.

Variables[a]	Patients at 30th day			*P* value
	All patients (*n*=62)	Alive (*n*=49)	Dead (*n*=13)	
Age (years) ≥65	25 (40.3)	18 (36.7)	7 (53.8)	0.264
Male	39 (62.9)	31 (63.3)	8 (61.5)	0.909
Comorbidity				
Solid tumor	8 (12.9)	6 (12.2)	2 (15.4)	0.670
Hematologic tumor	2 (3.2)	1 (2.0)	1 (7.7)	0.378
Diabetes	12 (19.4)	9 (18.4)	3 (23.1)	0.703
COPD	3 (4.8)	3 (6.1)	0 (0.0)	1.000
Peptic ulcer disease	3 (4.8)	2 (4.1)	1 (7.7)	0.513
Heart disease	24 (38.7)	17 (34.7)	7 (53.8)	0.208
Stroke	14 (22.6)	10 (20.4)	4 (30.8)	0.466
Chronic renal failure	8 (12.9)	5 (10.2)	3 (23.1)	0.347
Chronic liver disease	4 (6.5)	4 (8.2)	0 (0.0)	0.571
Charlson comorbidity score ≥5	27 (43.5)	20 (40.8)	7 (53.8)	0.400
SAPSII score ≥40	10 (37.1)	4 (22.2)	6 (66.7)	*0.039*
MEDS score ≥13	8 (29.6)	3 (16.7)	5 (55.6)	0.072
Immunosuppression				
Immunosuppressive treatment	3 (4.8)	2 (4.1)	1 (7.7)	0.513
Corticosteroid treatment	12 (19.4)	5 (10.2)	7 (53.8)	0.002
Chemotherapy	2 (3.2)	1 (2.0)	1 (7.7)	0.378
Catheter or other prosthetic device	39 (62.9)	26 (53.1)	13 (100.0)	0.001

[a]Values are expressed as *n* (%) or as otherwise indicated. COPD: chronic obstructive pulmonary disease. SAPSII: Simplified Acute Physiology Score II; MEDS: Mortality in Emergency Department Sepsis

Table 4 Univariate analysis of risk factors for 30-day mortality associated with BSI caused by *Enterococcus* spp.

Variables[a]	Patients at 30th day			*P* value
	All patients (*n*=62)	Alive (*n*=49)	Dead (*n*=13)	
Acquisition				
Hospital acquired	38 (61.3)	26 (53.1)	12 (92.3)	0.01
ICU	32 (51.6)	23 (46.9)	9 (69.2)	0.153
Medical unit	14 (22.6)	10 (20.4)	4 (30.8)	0.466
Surgical unit	9 (14.5)	9 (18.4)	0 (0.0)	0.184
Other	7 (11.3)	7 (14.3)	0 (0.0)	0.328
BSI source				
Vascular catheter infection	8 (12.9)	3 (6.1)	5 (38.4)	0.008
Respiratory tract infection	15 (24.2)	11 (22.4)	4 (30.8)	0.193
Intra-abdominal infection	11 (17.7)	11 (22.4)	0 (0.0)	0.1
Urinary tract infection	22 (35.5)	18 (36.7)	4 (30.8)	0.196
Unknown source or primary bacteremia	6 (9.7)	6 (12.2)	0 (0.0)	0.571
Enterococcal species				
E. faecalis	38 (61.3)	32 (65.3)	6 (46.2)	0.208
E. faecium	24 (38.7)	17 (34.7)	7 (53.8)	0.208
≥2 BSI	8 (12.9)	5 (10.2)	3 (23.1)	0.347
Severe sepsis or septic shock	13 (21.0)	6 (12.2)	7 (53.8)	0.003
Antimicrobial resistance				
Ampicillin	20 (32.3)	13 (26.5)	7 (53.8)	0.094
Ciprofloxacin	34 (54.8)	22 (44.9)	12 (92.3)	0.002
Vancomycin	0 (0.0)	0 (0.0)	0 (0.0)	
High-level gentamicin	20 (32.3)	12 (24.5)	8 (61.5)	0.019
History of antibiotic use	23 (37.1)	14 (28.6)	9 (69.2)	0.01

[a]Values are expressed as *n* (%) or as otherwise indicated. NS: non-significant; BSI: bloodstream infections; ICU: intensive care unit; high-level gentamicin: MIC >500 μg/mL

As shown in table 4, we identified hospital acquisition, vascular catheter infection, and severe sepsis or septic shock were risk factors for 30-day mortality associated with *Enterococcus* spp. BSI (*P*=0.01, *P*=0.008, and *P*=0.03, respectively). In terms of antimicrobial resistance, we found ciprofloxacin and high-level gentamicin resistance as risk factors for 30-day mortality associated with *Enterococcus* spp. BSI (*P*=0.002 and *P*=0.019, respectively). And the history of antibiotic use was also revealed to be a risk factor for 30-day mortality associated with *Enterococcus* spp. BSI (*P*=0.01).

2.4 Multivariate Analysis of Risk Factors Associated with 30-day Mortality in Patients with *Enterococcus* spp. BSI

In order to determine the independent contribution of each factor to the 30-day mortality associated with *Enterococcus* spp. BSI, multiple logistic regression analysis was performed. Variables associated with *P*<0.05 in the univariate analysis of risk factors were selected for the multivariate logistic regression analysis. Because only ICU patients (*n*= 27) were evaluated by the SAPS II, the SAPSII score≥40 was not chosen as a variable for multivariate analysis of all patients. As all the patients were subjected to the evaluation of severe sepsis and septic shock, which can greatly affect the SAPS II scores, the two variables were chosen for the multivariate analysis. Thus, corticosteroid treatment, hospital acquisition, vascular catheter infection, severe sepsis or septic shock, ciprofloxacin, high-level gentamicin resistance and history of antibiotic use were used as independent variables and 30-day mortality was used as a dependent variable in the multivariate model. It was found that corticosteroid treatment (OR: 17.385, 95% CI: 2.079–145.366; *P*=0.008), hospital acquisition (OR, 16.328, 95% CI, 1.168–228.209; *P*=0.038), vascular catheter infection (OR: 14.788, 95% CI: 1.405–155.625; *P*=0.025), and ciprofloxacin resistance (OR: 12.734, 95% CI: 1.040–155.955; *P*=0.047) were independently associated with 30-day mortality (table 5).

Table 5 Multivariate analysis of risk factors associated with 30-day mortality in patients with *Enterococcus* spp. BSI

Factors	OR (95% CI)	*P* value
Corticosteroid treatment	17.385 (2.079–145.366)	0.008
Hospital acquired	16.328 (1.168–228.209)	0.038
Vascular catheter infection	14.788 (1.405–155.625)	0.025
Ciprofloxacin resistance	12.734 (1.040–155.955)	0.047

3 DISCUSSION

This study explored the characteristics of *Enterococcus* spp. BSI in a Chinese teaching hospital. Most patients who contracted BSI in this study were elderly male, which is consistent with some studies indicating that BSI are more likely to occur in the older male patients[22–24]. In our cohort, 43.5% of patients had a Charlson score ≥5, indicating that patients included in this study had severe clinical conditions. Also multiple comorbidities were found, such as heart disease (38.7%), stroke (22.6%), diabetes (19.4%), and chronic renal failure (12.9%), which was similar to those reported in other studies on *Enterococcus* spp[12, 14]. Patients with malignancy (16.1%) were less in this study than in other studies[12, 25]. Of the patients in the present study, 51.6% were hospitalized in the ICU. This high prevalence of ICU patients is comparable to that found by Ceci *et al*[18] but higher than those reported in other studies[26–28]. It was suggested that patients in the ICU are at higher risk for acquiring *Enterococcus* spp. BSI than other patients.

Herein we also revealed different features of *E. faecalis* and *E. faecium* BSI (tables 1 and 2). For example, the percentage of *E. faecium* BSI patients who had the Charlson comorbidity score ≥5, corticosteroid treatment, vascular catheter infection and history of antibiotic use was higher than that of E. *faecalis* BSI patients. Conde-Estévez and colleagues found that patients with surgical ward admission, >5 days of previous cephalosporin treatment, >5 days of carbapenem treatment, previous penicillin administration, SAPS score >30 at admission, and hepatobiliary disease were more often associated with *E. faecium* BSI than with *E. faecalis* BSI[27]. In our study cephalosporin and quinolone treatment was more frequently seen in *E. faecium* BSI than in *E. faecalis* BSI. The discrepancy may be due to the different clinical status of patients. For example, patients in the Conde-Estévez study were primarily surgical patients and those with severe critical disease, while the majority of the patients in the present study had chronic diseases.

All the *Enterococcus* spp. isolates from the present study were susceptible to vancomycin, and no vancomycin resistant *Enterococcus* (VRE) was found. VRE infection has been on rise and is an urgent clinical problem that needs to be solved in many countries[29]; however, in China currently the VRE infection rate is relatively lower than that in western countries. Our study, along with the recent report by Zhao *et al* identifying that VRE *E. faecium* only accounted for 1.9% of all *E. faecium* strains[30], confirmed the lower rate of VRE infection in China. However, higher levels of antimicrobial resistance against ampicillin, ciprofloxacin, and high-level gentamicin were demonstrated in *E. faecium* BSI than in *E. faecalis* BSI, which is in accordance with previous studies[12]. And we also found more *E. faecium* BSI patients had the history of antibiotic use than E. *faecalis* BSI patients did, which may explain why *E. faecium* BSI patients were resistant to more antimicrobial agents.

In the current study, the 30-day mortality rate of *Enterococcus* spp. BSI was found to be 21%, which is in line with a previous research[25]. Risk factors associated with 30-day mortality detected by univariate and multivariate analysis consisted of corticosteroid treatment, hospital acquired infection, vascular catheter infection, and ciprofloxacin resistance. Previous studies associated corticosteroid use with increased mortality in BSI caused by *S. aureus*, coagulase-negative staphylococci (CoNS), *E. coli,* and *Pseudomonas aeruginosa*[31, 32]. We also identified that corticosteroid therapy could increase the mortality in *Enterococcus* spp. BSI. Thus, corticosteroid therapy should be used cautiously for BSI patients, especially for those with severe critical disease.

Reigadas *et al* found that enterococcal catheter-related BSI caused as high as 33% mortality in an 8-year period retrospective study[33]. Similarly, we found that vascular catheter infection caused 38.4% mortality and was a risk factor for 30-day mortality in *Enterococcus* spp. BSI by multivariate analysis. It was suggested that catheters should be cautiously used and if possible, they should be avoided or removed timely. Furthermore, our results confirmed previous findings that hospital acquired infection and ciprofloxacin resistance were additional risk factors for *Enterococcus* spp. BSI[12].

Nevertheless, there were several limitations in the present study. First, it was a retrospective study, and as a result, the patient characteristics, comorbidities, and some other information were obtained based on review of patient records rather than an interview or clinical examination at the time of infection, which may lead to a bias. In addition, although this study reviewed *Enterococcus* spp. BSIs over a 10-year period in a teaching hospital, the study was monocentric and the number of patients in the present study was relatively small. Multi-centric studies with a large sample size are still needed to further demonstrate the results found in this study.

In conclusion, our study provides a comprehensive understanding of BSI caused by *E. faecalis* and *E. faecium* strains occurring in a Chinese teaching hospital. The key findings are that patients with *E. faecium* BSI are more often associated with comorbidity diseases, corticosteroid treatment, in-dwelling catheter or other prosthetic device and history of antibiotic use than *E. faecalis* BSI patients. Additionally, the 30-day mortality rate of this study is 21.0%. Corticosteroid treatment, hospital acquired infection, vascular catheter infection, and ciprofloxacin resistance are risk factors for 30-day mortality in *Enterococcus* spp. BSI. These findings indicate that infections by *E. faecalis* and *E. faecium* are different and suggest enterococcal BSI patients should be empirically given antimicrobial treatments.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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