Infection (2014) 42:875–881
DOI 10.1007/s15010-014-0651-z

CLINICAL AND EPIDEMIOLOGICAL STUDY

Intensive care unit-acquired blood stream infections: a 5-year retrospective analysis of a single tertiary care hospital in Korea

S. J. Lim · J. Y. Choi · S. J. Lee · Y. J. Cho · Y. Y. Jeong · H. C. Kim · J. D. Lee · Y. S. Hwang

Received: 10 December 2013 / Accepted: 18 June 2014 / Published online: 17 July 2014

Abstract
Purpose Bloodstream infections (BSIs) are serious complications with high mortality and morbidity in patients with critical illness. This study was conducted to analyze the clinical and microbiological characteristics as well as outcomes in patients with intensive care unit (ICU)-acquired BSIs.
Methods Data from 1,545 patients admitted to the ICU were retrospectively collected from January 2005 to December 2010. ICU-acquired BSI was defined as a positive blood culture for a clinically significant bacterial or fungal pathogen obtained >72 h after admission to the ICU. Data on clinical and demographic characteristics, comorbid illness, causes of infections, causative pathogens, and clinical outcomes were analyzed.
Results Among the 1,545 ICU patients analyzed, 129 ICU-acquired BSIs occurred in 124 patients. Catheter-related BSIs (CR-BSIs) and ventilator-associated pneumonia (VAP) were the most common causes (29.4 and 20.9 %, respectively). The most common isolates were *Staphylococcus aureus* in 35 (25.7 %) and *Candida* species in 32 (24.8 %) cases. Ninety-eight patients died (overall hospital mortality rate, 75.9 %). ICU-acquired BSI-related mortality occurred in 23 (63.8 %) and 7 (19.4 %) of the VAP and CR-BSIs cases, respectively. The most commonly isolated microorganisms from these fatalities were *S. aureus* (12, 25.7 %) and *Acinetobacter* species (12, 25.7 %). In 99 ICU-acquired BSI cases, patients did not receive adequate empirical antimicrobial treatment at the onset of BSIs, whereas the patients in 30 cases did.
Conclusion ICU-acquired BSIs may be associated with high mortality in patients with critical illness. Meticulous infection control and adequate treatment may reduce ICU-acquired BSI-related mortality.

Keywords ICU · Blood stream infection · Acquired · Cause

S. J. Lim · J. Y. Choi · S. J. Lee · Y. J. Cho · Y. Y. Jeong · H. C. Kim (✉) · J. D. Lee · Y. S. Hwang
Department of Internal Medicine, College of Medicine, Gyeongsang National University, Jinju, Korea
e-mail: hochkim@gnu.ac.kr

S. J. Lee · Y. J. Cho · Y. Y. Jeong · H. C. Kim · J. D. Lee · Y. S. Hwang
Gyeongsang Institute of Health Sciences, Gyeongsang National University, Jinju, Korea

Introduction

Critically ill patients are particularly vulnerable to nosocomial infections [1]. The risk of acquiring a nosocomial infection is 2–7 times greater in the intensive care unit (ICU) [2–4], which accounts for approximately half of all hospital acquired infections [5, 6]. The most prevalent nosocomial infections in the ICU are catheter-related blood stream infections (CR-BSIs), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infections (CA-UTI). These infections are strongly linked to increases in morbidity, mortality, and health care expenses [7–10]. The severity of underlying disease, frequency of invasive diagnostic and therapeutic procedures that breach normal host defenses, contaminated life support equipment, and the prevalence of drug-resistant microorganisms are critical factors in the high rate of infections.

A multicenter surveillance study in Korea investigating nosocomial infections reported that the overall rate of nosocomial infection is 3.7 per 100 patients discharged; and urinary tract infection, pneumonias, and surgical site

infection were the most common infections in order of frequency. BSIs were the fourth most common nosocomial infection [11]. Because ICU-acquired BSIs are associated with higher in-hospital mortality [12, 13], vigorous infection control, early detection, and treatment are necessary to prevent ICU-acquired BSIs and their attributable mortality. In Korean ICUs, the number of nosocomial infections has increased annually [14]; however, information regarding BSIs specifically acquired in ICUs is lacking [15–17].

The objective of this study was to investigate the incidence of ICU-acquired BSIs, to identify the causes of these infections (i.e., the site or source of infection and the isolated causative microorganisms, irrespective of the primary reason for ICU admission), and to determine the overall hospital mortality rate and factors associated with death as well as the impact of adequate antimicrobial treatment on mortality in patients with ICU-acquired BSIs at a regional tertiary hospital in Korea.

Materials and methods

Study population

Data regarding blood culture results were collected from electronic medical records of patients admitted to the ICU in Gyeongsang University Hospital, Jinju, Korea (15 medical ICU and 900 total beds) between January 2005 and December 2010.

We only retrieved data of blood culture-positive patients and retrospectively assessed whether the positive blood culture was adequate for ICU-acquired BSIs. An ICU-acquired BSI was defined as a positive blood culture result for a clinically significant bacterial or fungal pathogen obtained >72 h after admission to the ICU. We analyzed the demographic, physiologic, and laboratory data; Acute Physiology and Chronic Health Evaluation II (APACHE II) physiology score; the site or source of infection; and the isolated microorganisms and outcomes in patients with confirmed ICU-acquired BSIs.

Patients were assessed differently according to whether they had been admitted to the ICU more than two times or whether >1 microorganism was isolated from their blood cultures during a single ICU admission due to a cause other than infection with the isolated organism. For oral care in the ICU, we used daily rinsing with chlorhexidine in the morning. This study was approved by the institutional review board of Gyeongsang University Hospital.

Definitions

The cause of ICU-acquired infection was classified using the Centers for Disease Control and Prevention (CDC) definitions [18, 19]. VAP-related BSIs were defined as a positive blood culture, for which microbiological isolates from the tracheal aspirate and blood cultures were likely to represent the same infection, in the presence of clinical evidence of pneumonia (e.g., fever >38.2 °C, purulent airway secretion, leukocytosis >12,000/mm^3, and new or progressive infiltrate on the chest radiograph). CR-BSIs were defined as cases of positive tip culture from an intravascular device that had been removed 2 days prior to, or after, the positive blood culture result and for which the microbiological isolates from the tip and blood cultures were likely to represent the same species or compatible mixed growth. UTI-associated BSIs were similarly defined as isolation of the same pathogen from the urine and blood cultures in the presence of clinical evidence of UTI. Surgical wound- or soft tissue infection-associated BSIs were diagnosed if cultures were obtained from the respective sites in association with a BSI. Intra-abdominal infection-associated BSIs were defined as isolation of the same pathogen from the blood and purulent material from the intra-abdominal space, obtained using an aseptic procedure, in the presence of clinical evidence of intra-abdominal infection.

ICU-acquired BSI-related death was defined as death caused by deterioration of patients' clinical conditions due to ICU-acquired BSIs when other causes of death were excluded after a review of medical records.

Data analysis

Categorical data are presented as numbers and percentages, and continuous data, as the mean ± standard deviation. Each variable was analyzed using a Pearson's Chi-square test or Mann–Whitney U test. Survival differences were estimated using the Pearson's Chi-square test and Kaplan–Meier curves, using the log-rank test. We also evaluated the factors associated with death in these patients using multivariate logistic regression analysis. Differences were considered statistically significant if $p < 0.05$. All analyses were performed with SPSS version 18.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics of patients

Among 1,545 patients (male:female 1,015:530; mean age 65.3 ± 13.8 years) admitted to the ICU during the study period, 129 ICU-acquired BSI episodes were identified in 124 patients (male:female 73:51; mean age 65 ± 12.7 years). The estimated risk for ICU-acquired BSIs was 5.3

per 1,000 patient days. Five patients developed two episodes of ICU-acquired BSIs due to different causes. Ninety-one (73.3 %) patients had an underlying disease. For 129 episodes of BSIs, the mean number of positive blood cultures in these patients was 1.6 ± 1.2 (range 1–9). The mean duration of ICU stay was 40.6 ± 44.5 days, and the median time interval between ICU admission and the time of diagnosis of ICU-acquired BSI was 23 ± 20.9 days. The APACHE II score, body temperature, white blood cell count, and C-reactive protein levels were 22.2 ± 5.99, 37.1 ± 0.82 °C, 13,169.2 ± 8,672.5 mm^3, and 113.3 ± 73.19 mg/L, respectively, at the time of diagnosis of ICU-acquired BSIs (Table 1).

The source of infection and microorganisms isolated from patients with intensive care unit-acquired blood stream infections

The source of infection was identified in 87 of 129 episodes of ICU-acquired BSIs. CR-BSIs were identified in 38 (29.4 %) patients; VAP in 27 (20.9 %); UTI in 7 (5.4 %); wound infection or surgical- or sore-related BSI in 10 (7.7 %); intra-abdominal infection in 3 (2.3 %); and other infections in 2 (1.5 %) patients. The source of infection was not identified in 42 (32.5 %) patients. More than 1 microorganism was isolated in 6 out of 124 patients, with a total of 136 microorganisms being isolated from the study population. Among these, the most commonly isolated organisms were *Staphylococcus aureus* ($n = 35$; 25.7 %), *Candida* species ($n = 32$; 24.8 %), *Enterococcus* species ($n = 18$; 13.9 %), and *Acinetobacter* species ($n = 17$; 13.1 %) (Table 2). In the 38 patients with CR-BSIs, the most commonly isolated microorganisms were *Candida* species ($n = 18$; 47.3 %) and *S. aureus* ($n = 12$; 31.5 %). In the 27 patients with VAP-related BSIs, the most commonly isolated microorganisms were *Acinetobacter* species ($n = 12$; 44.4 %), *S. aureus* ($n = 7$; 25.9 %), and *Klebsiella pneumoniae* ($n = 3$; 11.1 %) (Table 3).

Table 1 Baseline patient characteristics

Characteristic	Number (%) or mean ± SD
M:F	73:51
Mean age (years)	65 ± 12.7
Underlying disease (%)	
Malignancy	25 (20)
Hematologic disease	6 (4.8)
Diabetes	49 (39)
Liver cirrhosis	11 (8)
COPD	19 (15)
Renal failure	8 (6.4)
Alcoholism	
APACHE II score	13 (10.4)
At admission	22.5 ± 6.53
At the time of diagnosis of ICU-acquired BSI	22.2 ± 5.99
ICU stay (days)	41 ± 44.5
Time interval between ICU admission and at the time of diagnosis of ICU-acquired BSI (days)	23 ± 20.9
Body temperature, at the time of diagnosis of ICU-acquired BSI (°)	37.1 ± 0.82
CRP, at the time diagnosis of ICU-acquired BSI (mg/L)	113.3 ± 73.19
Use of vasopressor, at the time of diagnosis of ICU-acquired BSI (%)	96/129 (74.4)

Data are presented as mean with standard deviation or number (%) unless otherwise indicated

COPD chronic obstructive pulmonary disease, *APACHE* acute physiology and chronic health evaluation, *ICU* intensive care unit, *BSI* blood stream infection, *WBC* white blood cell, *CRP* C-reactive protein

Outcomes of intensive care unit-acquired blood stream infections

Among the 129 cases of ICU-acquired BSIs, 98 patients died (overall hospital mortality rate, 75.9 %), and 36 of these 98 deaths (36.7 %) were due to ICU-acquired BSIs. Eighty patients died in our hospital (general ward or ICU), and 18 patients were discharged to other hospitals because of irreversible organ failure, and these patients were classified as dead patients. Eight patients were discharged to other hospitals with improvement, and these patients were classified as patients who survived. Thirty-four patients were transferred to the general ward and were discharged to their homes with improvement. The duration of survival in the ICU was significantly shorter in patients who died because of ICU-acquired BSIs than in patients with ICU-acquired BSIs who died due to other causes (27.2 ± 29.4 and 68.7 ± 80.9 days, respectively; $p = 0.003$; Fig. 1). The hospital mortality rate in patients with CR-BSIs or VAPs was not significantly different from that in patients with any other causes of infection (68.4 and 79.1 % for CR-BSIs and other infections, respectively; 85.1 and 73.5 % for VAPs and other infections, respectively; $p > 0.05$). Additionally, the rate of overall hospital mortality in all patients with BSIs due to fungal infections was not different from the rate of mortality due to nonfungal infections (74.2 and 75.5 %; $p > 0.05$). Among patients with ICU-acquired BSI-related death, VAPs ($n = 23$; 63.8 %) and CR-BSIs ($n = 7$; 19.4 %) were the most common infections. Additionally, the most commonly isolated microorganisms were *S. aureus* ($n = 12$; 33.3 %) and *Acinetobacter* species ($n = 12$; 33.3 %) in these patients (Tables 4).

Table 2 The source of infection and isolated microorganisms of intensive care unit-acquired blood stream infections

Source of infection	Number (%) ($n = 129$)
Catheter-related BSI	38 (29.4)
VAP	27 (20.9)
Wound infection, sore or surgical	10 (7.7)
Urinary tract infection	7 (5.4)
Intra-abdominal infection	3 (2.3)
Others	2 (1.5)
Not identified	42 (32.5)
Microorganism	**Number (%) ($n = 136$)[a]**
Staphylococcus aureus	35 (25.7)
Candida species	32 (24.8)
Enterococcus faecium	18 (13.9)
Acinetobacter species	17 (13.1)
Coagulase (−) Staphylococcus	7 (5.1)
Escherichia coli	5 (3.6)
Klebsiella pneumoniae	4 (2.9)
Staphylococcus epidermidis	3 (2.2)
Staphylococcus haemolyticus	3 (2.2)
Stenotrophomonas maltophilia	2 (1.4)
Pseudomonas aeruginosa	2 (1.4)
Corynebacterium species	2 (1.4)
Serratia marcescens	1 (0.7)
Enterobacter cloacae	1 (0.7)
Citrobacter freundii	1 (0.7)
Bacillus species	1 (0.7)
Enterococcus faecalis	1 (0.7)
Burkholderia cepacia	1 (0.7)

Data are presented as number (%) unless otherwise indicated

BSI blood stream infection, *VAP* ventilator-associated pneumonia

[a] More than 1 microorganism was isolated from 6 patients; the total number of isolated microorganisms was 136 in the study population

Table 3 Isolated microorganisms of intensive care unit-acquired catheter-related BSI and VAP

Source of infection	Microorganism	Number (%) ($n = 39$)
Catheter-related BSI	*Candida* species	18 (46.1)
	Staphylococcus aureus	12 (30.7)
	Acinetobacter baumannii[a]	2 (5.1)
	Coagulase (–) Staphylococcus[a]	2 (5.1)
	Staphylococcus epidermidis	2 (5.1)
	Enterococcus faecium	1 (2.5)
	Escherichia coli	1 (2.5)
	Enterococcus faecalis	1 (2.5)
		Number (%) ($n = 28$)
VAP	*Acinetobacter baumannii*	12 (44.4)
	Staphylococcus aureus[b]	7 (25.9)
	Klebsiella pneumoniae	3 (11.1)
	Enterococcus faecium	2 (7.4)
	Escherichia coli[b]	2 (7.4)
	Stenotrophomonas maltophilia	1 (3.7)
	Pseudomonas aeruginosa	1 (3.7)

Data are presented as number (%) unless otherwise indicated

BSI blood stream infection, *VAP* ventilator-associated pneumonia

[a] 2 different microorganisms were isolated from 1 patient; the total number of patients was 38

[b] 2 different microorganisms were isolated from 1 patient; the total number of patients was 27

Among 129 cases of ICU-acquired BSIs, 30 cases (23.2 %) received adequate antimicrobial treatment, which was defined as the use of antimicrobials to which the isolated microorganism was sensitive, as determined by the drug sensitivity test. However, adequate antimicrobial treatment was not administered in 99 (76.8 %) cases. The overall mortality rate of patients who received adequate antimicrobial treatment was 70 %, compared to 76.6 % for patients who did not receive adequate antimicrobial treatment. These rates indicate that there was no significant difference between the mortality rates regardless of the adequacy of antimicrobial treatment. In the 99 ICU-acquired BSI cases in which patients did not receive adequate antimicrobial treatment, the most common causes were CR-BSI (29 cases), VAP (22 cases), wound infection (8 cases), and UTI (5 cases). The most commonly isolated pathogens in these cases were *S. aureus* ($n = 30$), *Candida* species ($n = 26$), and *Acinetobacter* species ($n = 3$) (Table 5). For patients who had received adequate antimicrobial treatment, the most common causes were CR-BSI (9 cases), VAP (5 cases), wound infection (2 cases), and UTI (2 cases).

In the multivariate analysis to assess the factors associated with mortality in these patients, only APACHE II scores were significantly associated with death (Table 6).

Discussion

This study aimed at evaluating the characteristics and outcomes of ICU-acquired BSIs in a medical ICU at a tertiary care hospital. The results indicated that CR-BSIs and VAPs were the most common causes of ICU-acquired BSIs and that they may contribute to death among critically ill patients admitted to the ICU.

During the study period, the incidence of ICU-acquired BSIs was 8.1 %, which was higher than that observed in other studies. According to a study from China that

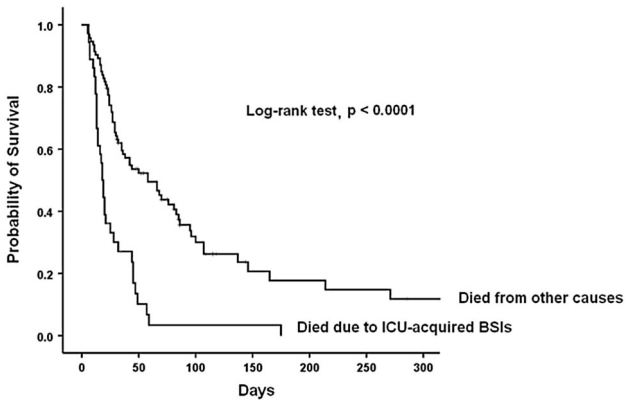

Fig. 1 Kaplan–Meier survival curve in patients with ICU-acquired BSIs during ICU stay. The duration of survival was significantly different for patients who died due to ICU-acquired BSIs and for patients who died from other causes

Table 4 Source of infection and isolated microorganisms in patients with intensive care unit-acquired blood stream infection-related mortality

	Number (%) ($n = 36$)
Source of infection	
VAP	23 (63.8)
Catheter-related BSI	7 (19.4)
Wound infection, sore or surgical	2 (5.5)
Urinary tract infection	2 (5.5)
Intra-abdominal infection	1 (2.7)
Not identified	1 (2.7)
Microorganism	
Staphylococcus aureus	12 (33.3)
Acinetobacter species	12 (33.3)
Candida species	4 (11.1)
Escherichia coli	4 (11.1)
Enterococcus faecium	2 (5.5)
Klebsiella pneumoniae	2 (5.5)
Stenotrophomonas maltophilia	1 (2.7)

Data are presented as number (%) unless otherwise indicated

VAP ventilator-associated pneumonia, *BSI* blood stream infection

Table 5 Source of infection and isolated microorganisms in patients with inadequate antimicrobial treatment before the onset of intensive care unit-acquired blood infection

	Number (%) ($n = 99$)
Source of infection	
Catheter-related BSI	29 (19.4)
VAP	22 (63.8)
Wound infection, sore or surgical	8 (5.5)
Urinary tract infection	5 (5.5)
Microorganism	
Staphylococcus aureus	30 (33.3)
Acinetobacter species	3 (33.3)
Candida species	26 (11.1)

Data are presented as number (%) unless otherwise indicated

VAP ventilator-associated pneumonia, *BSI* blood stream infection

Table 6 Multivariate logistic regression analysis for the factors associated mortality in patients with intensive care unit-acquired blood infections

	Odds ratio (95 % CI)	p value
Age	0.987 (0.952–1.024)	0.495
Sex	1.071 (0.408–2.811)	0.89
Presence of underlying disease	0.601 (0.212–1.705)	0.339
Source of infections	1.032 (0.700–1.521)	0.873
CR-BSI vs. non-CR-BSI	1.320 (0.140–12.420)	0.808
VAP vs. non-VAP	0.452 (0.069–2.947)	0.406
Isolated microorganism		
Fungus vs. non-fungus	0.588 (0.188–1.838)	0.361
MRSA vs. non-MRSA	0.607 (0.199–1.848)	0.379
APACHE II score at the time of BSIs	1.137 (1.039–1.244)	0.005
Adequate antimicrobial treatment	1.547 (0.518–4.619)	0.434

CR-BSI catheter-related blood stream infection, *VAP* ventilator-associated pneumonia, *APACHE* acute physiology and chronic health evaluation, *MRSA* methicillin-resistant *Staphylococcus aureus*

included 1980 patients and was published in 2009, the incidence of ICU-acquired BSIs was 5.9 % [20]. Additionally, in a study of 6,339 an ICU admission at 2 university-affiliated hospitals in Australia, the incidence of ICU-acquired BSIs was 5.2 % [13]. In a French study of 3,247 ICU admissions, 232 patients (6.8 %) acquired nosocomial BSIs [8]. The relatively higher incidence of ICU-acquired BSIs may be related with the longer ICU stays, over 40 days in mean, in our study population.

In our study, CR-BSIs were the most common ICU-acquired BSIs followed by VAPs (29.4 and 20.9 %), respectively. In another Korean study, respiratory infection was the most common cause of BSIs (38.2 %; 95/249 cases), whereas CR-BSIs were the cause in only 1.6 % (4/294) of cases [21]. An Australian study found that 34 cases (20.4 %) were caused by CR infections [13] and that about 30 % of ICU-acquired BSIs in the French study were associated with intravascular catheters [8]. The relatively higher proportion of CR-BSIs in our study than that in other studies might be explained by the lack of guidelines for intravascular catheterization in our hospital during the study period; further, this may have contributed to the relatively high incidence of CR-BSIs in this study.

The overall mortality was >70 % in this study population. Crude mortality rates of 25–66 % for 10 years of study have been reported in patients with ICU-acquired BSIs [13]. In our study, VAP was one of the most common types of infection, with a high mortality rate of >80 %. In addition, the APACHE II score at the time of ICU admission and diagnosis of ICU-acquired BSIs was approximately 22 in these patients, suggesting the presence of severe underlying diseases and infections that undoubtedly contributed to the high mortality rate in these cases.

The most commonly isolated microorganisms in this study were *S. aureus* and *Candida* species. These two microorganisms were the causative pathogens in 80 % of cases and may be associated with higher incidences of CR-BSIs in this study. The microorganisms isolated in cases of ICU-acquired BSIs may differ from study to study depending on the cause of BSIs. In a study of ICU-acquired BSIs in Canada, the most common isolates were *S. aureus*, coagulase-negative staphylococci, and *Enterococcus faecalis* [22].

Among the 98 patients who died in the ICU or hospital during the study period, 36 patients died due to ICU-acquired BSIs, which accounted for 37.7 % of the overall mortality rate in the study population. This strongly suggests that meticulous infection control in ICUs may reduce ICU-related mortality in critically ill patients.

The mortality rates in BSI patients differed according to the source of infection and the causative microorganism. In our study, VAPs had the highest mortality rate (85 %; 23 of 27 cases) and accounted for 63 % of ICU-acquired BSI-related mortality. In contrast, only 7 of 38 patients with CR-BSIs died (mortality rate of 18.4 %). The most common microorganisms isolated from ICU-acquired BSI-related mortality cases were *S. aureus* and *Acinetobacter* species. These microorganisms were also the major pathogens responsible for ICU-acquired VAPs in this study. A German study assessing nosocomial *S. aureus* infections in ICUs revealed that BSIs and pneumonia due to *S. aureus* may be associated with high mortality [23]. In a Chinese study, the overall mortality due to nosocomial *S. aureus* BSIs was 28 %. *S. aureus* was associated with a high proportion of inappropriate empirical antibiotics treatment [24]. *Acinetobacter* species were the most common causative organisms in VAP-associated with BSIs, and they were the major causative microorganisms responsible for BSI-related mortality in this study. Moreover, most *Acinetobacter* species isolated in the ICU were resistant to imipenem, and they may be associated with high ICU mortality, especially in cases of bacteremia [25].

The rate of inadequate empirical antimicrobial treatment was relatively high and most cases of inadequate antimicrobial treatment were associated with fungal or methicillin-resistant *S. aureus* (MRSA) infections. In our hospital practice, usual empirical antimicrobial treatment was not covered with fungal or MRSA infection even in patients with severe infection. This explains the high rate of inadequate antimicrobial treatment in this study.

Although inadequate antimicrobial treatment was significantly associated with mortality in patients with nosocomial infections in previous studies, the adequacy of antimicrobial treatment did not affect mortality in our study. In previous studies on the influence of inadequate antimicrobial treatment for nosocomial infections, including BSIs, in ICU patients, inadequate antimicrobial treatment significantly increased the mortality rates among critically ill patients [26, 27]. However, another study showed a significant difference in the mortality rate [28]. In particular, one study found that BSIs due to *S. aureus or Pseudomonas aeruginosa* were associated with an increase in hospital mortality rates even though adequate antimicrobial therapy was provided [29].

Our study has some limitations. This study was performed using a retrospective methodology; therefore, we could not determine if the duration of hospital stay was lengthened as a secondary outcome of ICU-acquired BSIs or if BSIs were caused because of the extended hospital stay. Additionally, because the study population included patients from a single facility, our findings may not be directly generalizable to different microbiological environments worldwide. Another limitation of this study is that it focused on mortality as the only outcome; other signs and symptoms of disease severity were not evaluated. Finally, due to the retrospective nature of this study, we could only assess confirmed cases of ICU-acquired BSIs; therefore, the number of ICU-acquired BSI cases may have been underestimated.

ICU-acquired BSIs may be caused by infectious agents from endogenous or exogenous sources. The most common mode of transmission is direct contact. Therefore, the best practices for preventing healthcare-associated infections include hand hygiene, standard precautions, isolation precautions, and prudent antimicrobial use [30], which may decrease ICU-acquired infections including BSIs as well as mortality among ICU patients. In addition, aseptic procedures and antimicrobial management in the ICU may reduce ICU-acquired infections and the emergence of antimicrobial-resistant strains, which will help reduce mortality rates due to ICU-acquired infections.

In conclusion, this study showed that ICU-acquired BSIs were associated with mortality among critically ill patients admitted to the ICU, which strongly indicates that appropriate infection control systems may reduce the incidence of ICU-acquired BSIs and the related mortality among ICU patients.

Conflict of interest The authors declare that they have no conflict of interests.

References

1. Barsanti MC, Woeltje KF. Infection prevention in the intensive care unit. Infect Dis Clin North Am. 2009;23:703–25.
2. Donowitz LG, Wenzel RP, Hoyt JW. High risk of hospital-acquired infection in the ICU patient. Crit Care Med. 1982;10:355–7.
3. Weinstein RA. Epidemiology and control of nosocomial infections in adult intensive care units. Am J Med. 1991;91:179S–84S.
4. Wenzel RP, Thompson RL, Landry SM, Russell BS, Miller PJ, Ponce de Leon S, et al. Hospital-acquired infections in intensive care unit patients: an overview with emphasis on epidemics. Infect Control. 1983;4:371–5.
5. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis. 2004;39:309–17.
6. Arya SC, Agarwal N. Nosocomial infections in adult intensive-care units. Lancet. 2003;362:493–4.
7. Valles J, Leon C, Alvarez-Lerma F. Nosocomial bacteremia in critically ill patients: a multicenter study evaluating epidemiology and prognosis. Spanish Collaborative Group for Infections in Intensive Care Units of Sociedad Espanola de Medicina Intensiva y Unidades Coronarias (SEMIUC). Clin Infect Dis. 1997;24:387–95.
8. Garrouste-Orgeas M, Timsit JF, Tafflet M, Misset B, Zahar JR, Soufir L, et al. Excess risk of death from intensive care unit-acquired nosocomial bloodstream infections: a reappraisal. Clin Infect Dis. 2006;42:1118–26.
9. Renaud B, Brun-Buisson C. Outcomes of primary and catheter-related bacteremia. A cohort and case-control study in critically ill patients. Am J Respir Crit Care Med. 2001;163:1584–90.
10. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009;302:2323–9.
11. Kim JM, Park ES, Jeong JS, Kim KM, Oh HS, Yoon SW, et al. Multicenter surveillance study for nosocomial infections in major hospitals in Korea. Nosocomial Infection Surveillance Committee of the Korean Society for Nosocomial Infection Control. Am J Infect Control. 2000;28:454–8.
12. Digiovine B, Chenoweth C, Watts C, Higgins M. The attributable mortality and costs of primary nosocomial bloodstream infections in the intensive care unit. Am J Respir Crit Care Med. 1999;160:976–81.
13. Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al. Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. Crit Care. 2011;15:R100.
14. Kwak YG, Cho YK, Kim JY, Lee SO, Kim HY, Kim YK, et al. Korean Nosocomial Infections Surveillance System, Intensive Care Unit Module Report: data Summary from July 2008 through June 2009 and Analysis of 3-Year Results. Korean J Nosocomial Infect Control. 2010;15:14–25.
15. Pai H. Nosocomial infections in intensive care unit: epidemiology and control strategy. Hanyang Med Rev. 2011;31:153–8.
16. Park ES, Jin HY, Jeong SY, Kweon OM, Yoo SY, Park SY, et al. Healthcare-associated infection surveillance in small and medium sized hospitals. Korean J Nosocomial Infect Control. 2011;16:54–62.
17. Jeon MH, Park WB, Kim SR, Chun HK, Han SH, Bang JH, et al. Korean Nosocomial Infections Surveillance System, Intensive Care Unit Module Report: data Summary from July 2010 through June 2011. Korean J Nosocomial Infect Control. 2012;17:28–39.
18. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control. 1988;16:128–40.
19. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36:309–32.
20. Ding JG, Sun QF, Li KC, Zheng MH, Miao XH, Ni W, et al. Retrospective analysis of nosocomial infections in the intensive care unit of a tertiary hospital in China during 2003 and 2007. BMC Infect Dis. 2009;9:115.
21. Hong SK, Hong SB, Lim CM, Koh Y. The characteristics and prognostic factors of severe sepsis in patients who were admitted to a medical intensive care unit of a tertiary hospital. Korean J Crit Care Med. 2009;24:28–32.
22. Laupland KB, Kirkpatrick AW, Church DL, Ross T, Gregson DB. Intensive-care-unit-acquired bloodstream infections in a regional critically ill population. J Hosp Infect. 2004;58:137–45.
23. Gastmeier P, Sohr D, Geffers C, Behnke M, Daschner F, Ruden H. Mortality risk factors with nosocomial *Staphylococcus aureus* infections in intensive care units: results from the German Nosocomial Infection Surveillance System (KISS). Infection. 2005;33:50–5.
24. Chen R, Yan ZQ, Feng D, Luo YP, Wang LL, Shen DX. Nosocomial bloodstream infection in patients caused by *Staphylococcus aureus*: drug susceptibility, outcome, and risk factors for hospital mortality. Chin Med J (Engl). 2012;125:226–9.
25. Marra AR, Camargo LF, Pignatari AC, Sukiennik T, Behar PR, Medeiros EA, et al. Nosocomial bloodstream infections in Brazilian hospitals: analysis of 2,563 cases from a prospective nationwide surveillance study. J Clin Microbiol. 2011;49:1866–71.
26. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. Chest. 1999;115:462–74.
27. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. Chest. 2000;118:146–55.
28. Zaragoza R, Artero A, Camarena JJ, Sancho S, Gonzalez R, Nogueira JM. The influence of inadequate empirical antimicrobial treatment on patients with bloodstream infections in an intensive care unit. Clin Microbiol Infect. 2003;9:412–8.
29. Osmon S, Ward S. Fraser VJ, Kollef MH: hospital mortality for patients with bacteremia due to *Staphylococcus aureus* or *Pseudomonas aeruginosa*. Chest. 2004;125:607–16.
30. Sreeramoju P. Preventing healthcare-associated infections: beyond best practice. Am J Med Sci. 2013;345:239–44.