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Risk Factors and Prognosis of Nosocomial Bloodstream Infections Caused by Extended-Spectrum-β-Lactamase-Producing *Escherichia coli*▽

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Extended-spectrum-β-lactamase (ESBL)-producing *Escherichia coli* (ESBLEC) is an increasing cause of community and nosocomial infections worldwide. However, there is scarce clinical information about nosocomial bloodstream infections (BSIs) caused by these pathogens. We performed a study to investigate the risk factors for and prognosis of nosocomial BSIs due to ESBLEC in 13 Spanish hospitals. Risk factors were assessed by using a case-control-control study; 96 cases (2 to 16% of all nosocomial BSIs due to *E. coli* in the participating centers) were included; the most frequent ESBL was CTX-M-14 (48% of the isolates). We found CTX-M-15 in 10% of the isolates, which means that this enzyme is emerging as a cause of invasive infections in Spain. By repetitive extragenic palindromic sequence-PCR, most isolates were found to be clonally unrelated. By multivariate analysis, the risk factors for nosocomial BSIs due to ESBLEC were found to be organ transplant (odds ratio [OR] = 4.8; 95% confidence interval [CI] = 1.4 to 15.7), the previous use of oxyimino-β-lactams (OR = 6.0; 95% CI = 3.0 to 11.8), and unknown BSI source (protective; OR = 0.4; 95% CI = 0.2 to 0.9), and duration of hospital stay (OR = 1.02; 95% CI = 1.00 to 1.03). The variables independently associated with mortality were a Pitt score of >1 (OR = 3.9; 95% CI = 1.2 to 12.9), a high-risk source (OR = 5.5; 95% CI = 1.4 to 21.9), and resistance to more than three antibiotics, apart from penicillins and cephalosporins (OR = 6.5; 95% CI = 1.4 to 30.0). Inappropriate empirical therapy was not associated with mortality. We conclude that ESBLEC is an important cause of nosocomial BSIs. The previous use of oxyimino-β-lactams was the only modifiable risk factor found. Resistance to drugs other than penicillins and cephalosporins was associated with increased mortality.

Gram-negative organisms are an important cause of nosocomial bloodstream infections (BSIs) (33), particularly when the source of the BSI is the urinary, respiratory, or gastrointestinal tract. Recently, the reemergence of Gram-negative organisms as a cause of primary BSIs has also been reported (1). In the United States, *Escherichia coli* is the fifth most common cause of nosocomial BSIs and is the first most common cause among Gram-negative organisms, and BSIs caused by *E. coli* are reported to be associated with a crude mortality rate of 22% (34); in Spain, it is the second most common cause of nosocomial BSIs (23).

In recent years, extended-spectrum ß-lactamases (ESBLs), particularly those of the CTX-M family, have spread worldwide among *E. coli* strains inside and outside hospitals (20, 26); consequently, the prevalence of BSIs caused by ESBL-producing *E. coli* has significantly increased (24, 28). ESBLs confer resistance to penicillins and cephalosporins and are frequently associated with resistance to fluoroquinolones, aminoglycosides, and trimethoprim-sulfamethoxazole (18); thus, ESBL-producing microorganisms are frequently truly multidrug resistant. Both antibiotic resistance and inappropriate empirical therapy are independently associated with increased rates of mortality among individuals with *E. coli* bacteremia (16, 19).

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ESBL production has been shown to be associated with delayed appropriate therapy and an increased risk of death (30). Thus, identification of the risk factors for BSIs due to ESBL-producing *E. coli* might help to identify patients who should receive empirical coverage against these organisms and may also be useful for control purposes.

The epidemiology of ESBL-producing *E. coli* within the hospital environment shows some differences from that of other multidrug-resistant organisms (29) but also from that of other ESBL-producing organisms, such as *Klebsiella pneumoniae*. The latter frequently affects patients admitted to high-risk areas (such as the intensive care unit [ICU] and the neonatal ICU), are predominantly clonally spread, and until recently, typically produced ESBLs from the TEM and SHV families (18), whereas nosocomial ESBL-producing *E. coli* more frequently affects patients admitted to conventional hospital units, are frequently clonally unrelated, and usually produce enzymes from the CTX-M family (25). While many studies have investigated the risk factors for nosocomial BSIs caused by ESBL-producing *K. pneumoniae* or mixed infections caused by members of the family *Enterobacteriaceae* (26), there are scarce data concerning ESBL-producing *E. coli*. The objective of the study described here was to investigate the risk factors, molecular epidemiology, and prognosis of nosocomial BSIs due to ESBL-producing *E. coli*.

MATERIALS AND METHODS

Setting and design. Thirteen tertiary-care Spanish hospitals took part in the study described here, which was conducted between October 2004 and January 2006. The risk factors for nosocomial BSIs due to ESBL-producing *E. coli* were studied by using a case-control-control design (25). A case patient was defined as any adult (>14 years old) with a nosocomial BSI due to ESBL-producing *E. coli*. Cases were recruited prospectively through the daily review of blood culture results at the participating centers. For the study of risk factors, two base populations were considered. The first was made up of patients with nosocomial sepsis ("sepsis population"), who were identified as all admitted patients from whom blood for culture was taken because of suspected nosocomial sepsis (the blood cultures could be negative or positive for any organism except ESBL-producing *E. coli*). The second constituted patients with nosocomial BSIs due to non-ESBL-producing *E. coli* (the "*E. coli* BSI population"). Two controls per case were chosen from both populations. Controls were matched to cases for hospital, ward type (medical, surgical, or intensive care), and time period (1 month after the case). Control patients were randomly selected from among the eligible patients by a computerized method by using the blood culture register numbers in the microbiology laboratory of each participating hospital. The prognosis of BSI due to ESBL-producing *E. coli* was studied in the case patients by prospectively following the patients until discharge or in-hospital death.

We followed the recommendations of the STROBE statement for reporting the results of observational studies (32). The study was approved by the local ethics committees of the participating centers.

Definitions. A case of sepsis or BSI was defined as nosocomial when an infection presented in patients who had been hospitalized for 48 h or more. The following variables were recorded: demographics, comorbidities, the severity of the underlying conditions according to the Charlson index (4), the surgical procedures performed and the antimicrobial agents received during the present admission, whether mechanical ventilation or a urinary or vascular catheter was present, the endoscopic procedures performed in the previous 2 days, whether an organ transplant had been performed during the previous year, the source of the bacteremia (according to both clinical and microbiological criteria), whether severe sepsis or septic shock was present at the time of presentation (2), and the antimicrobial treatment and mortality at days 14 and 30. Empirical treatment was considered appropriate when an antimicrobial regimen that included an active antimicrobial (that is, one to which the organism causing the bacteremia was susceptible *in vitro*) at the recommended doses was initiated in the first 24 h after the blood sample for culture was drawn.

Microbiological studies. ESBL-producing isolates were sent to a reference laboratory (Hospital Universitario Virgen Macarena, Seville, Spain), where identification to the species level was confirmed by use of the API 20E system (bioMérieux) and ESBL production was determined by broth microdilution, according to the CLSI guidelines (8). Susceptibility to the antimicrobials listed in Table 1 was evaluated by microdilution (8). A resistance score was calculated as the number of antibiotic families (carbapenems, fluoroquinolones, β-lactam–β-lactam inhibitor combinations, trimethoprim-sulfamethoxazole, aminoglycosides, and tigecycline), apart from penicillins and cephalosporins, to which the isolate showed resistance, including those cases in which resistance to only one antibiotic in the family occurred. ESBLs were characterized by isoelectric focusing (Phastsystem; Pharmacia), PCR of the *bla* genes (14), and sequencing. Strain relationships were studied by repetitive extragenic palindromic sequence (REP)-PCR (31); isolates with similar REP-PCR patterns were also studied by using pulsed-field gel electrophoresis (PFGE) with XbaI endonuclease, according to a standardized XbaI PFGE Pulsenet protocol (http://www.pulsenet-europe.org/); dendrograms were inferred from the Dice similarity coefficient by use of a tolerance of 1%. CTX-M-15-producing isolates were further studied in order to identify O25b:H4 and sequence type 131 (ST131) clones; the phylogenetic group was determined by multiplex PCR (5); O25b typing was performed by a previously described PCR with primers rfbO25b.r and rfblbis.f (6); and analysis for allele 3 of *pabB*, which corresponds to ST131, was also performed by PCR with specific primers (7). The genetic relatedness of the CTX-M-15-producing isolates was studied by PFGE, as specified above.

Statistical analysis. For the investigation of risk factors, crude odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by conditional logistic regression. Multivariate analysis was also performed by conditional logistic regression. The variables introduced into the multivariate analysis included those with a crude P value of <0.1, those that were biologically sound, and those found in previous studies of ESBL-producing *Enterobacteriaceae*. Models including and excluding the variable "hospital" were performed; however, since no significant differences were shown, the models without that variable are reported here. Interactions between paired variables were also analyzed. Variables were selected by use of a stepwise backward process; previous hospital stay was kept in the final model in order to provide an OR adjusted for the time at risk. Variables associated with mortality were studied by calculating crude relative risks (RRs) and 95% CIs; multivariate analysis was performed by logistic regression. Data were analyzed by using the STATA (version 9.2) software package (StataCorp, College Station, TX).

RESULTS

Ninety-six case patients with nosocomial BSIs due to ESBL-producing *E. coli* were included. The median percentage of nosocomial BSIs due to *E. coli* caused by ESBL-producing isolates in participating hospitals was 8% (range, 2 to 16%). The median incidence density was 0.20 cases per 10,000 patient-days (range, 0.11 to 1.70).

Overall, 78 isolates (81%) produced a CTX-M ESBL and 18 (19%) produced an SHV ESBL. The specific types of ESBLs were CTX-M-14, 46 isolates (48% of the isolates) from 12 hospitals; CTX-M-9, 13 (14%) from 8 hospitals; CTX-M-15, 10 (10%) from 5 hospitals; CTX-M-32, 9 (9%) from 6 hospitals; CTX-M-1, 2 (2%) from 1 hospital; SHV-12, 17 (18%) from 8 hospitals; and SHV-2a, 1 (1%) (2 isolates produced 2 CTX-M enzymes). As regards the clonal relationship, only two isolates producing CTX-M-14 and obtained from the same hospital were clonally related by REP-PCR and PFGE. Seven of 10 CTX-M-15-producing isolates belonged to the B2 phylogroup and were positive for the O25b O type and the allele-specific *pabB* polymorphism by PCR assays. These seven isolates comprised six distinct PFGE types (<60% similarity). Susceptibility testing results are shown in Table 1. The resistance scores were 0 for 11 isolates (11%), 1 for 30 (31%), 2 for 25 (26%), 3 for 14 (15%), and 4 for 16 (17%).

The features of the case patients are shown in Table 2. Fifty

TABLE 1. Susceptibilities to different antimicrobial agents of 96 extended-spectrum-β-lactamase-producing *Escherichia coli* isolated from blood cultures

Antimicrobial agent	No. (%) susceptible isolates
Cefotaxime	2 (2)[a]
Ceftazidime	58 (60)[a]
Cefepime	32 (32)[a]
Amoxicillin-clavulanate	59 (62)
Piperacillin-tazobactam	86 (89)
Ticarcillin-clavulanate	18 (19)
Imipenem	96 (100)
Meropenem	96 (100)
Ertapenem	96 (100)
Ciprofloxacin	28 (29)
Amikacin	96 (100)
Gentamicin	71 (74)
Tobramycin	81 (84)
Tigecycline	95 (99)
Trimethoprim-sulfamethoxazole	41 (43)
Fosfomycin	93 (97)

[a] Data were obtained by using the breakpoints for the *Enterobacteriaceae* (all ESBL-producing isolates should be interpreted as resistant, according to CLSI guidelines).

patients (52%) were admitted to medical services, 32 (33%) to surgical services, and 14 (15%) to an intensive care unit. The control group for the sepsis population was made up of 190 patients (for 2 case patients, 1 control could not be found), and that for the *E. coli* BSI population was made up of 186 patients (for 6 case patients, 1 control could not be found). In Tables 2 to 4, control patients for the nosocomial sepsis population are referred to as control group A, and control patients with nosocomial bloodstream infections due to non-ESBL-producing *E. coli* are referred to as control group B. The results of the univariate analysis of risk factors for BSIs due to ESBL-producing *E. coli* are shown in Tables 2 and 3. With regard to the sepsis population, the following variables were introduced into the multivariate analysis: age, gender, previous hospital stay,

TABLE 3. Source of nosocomial bloodstream infections caused by ESBL-producing *Escherichia coli* compared with that in control patients with nosocomial bloodstream infection due to non-ESBL-producing *E. coli*

Source	No. (%) of patients		OR (95% CI)	*P*
	Cases (n = 96)	Control group B (n = 186)		
Urinary tract infection	34 (35)	63 (34)	1.0 (0.6–1.8)	0.7
Intra-abdominal infection[a]	24 (25)	45 (24)	1.0 (0.7–1.9)	0.8
Respiratory tract infection[b]	6 (6)	7 (4)	1.7 (0.4–1.8)	0.3
Vascular catheter infection	8 (8)	7 (4)	1.6 (0.9–2.6)	0.1
Other	5 (5)	9 (5)	1.0 (0.3–3.6)	0.8
Unknown	19 (20)	55 (30)	0.6 (0.3–1.1)	0.07

[a] Biliary tract infection in 12 case patients and 28 control patients.
[b] Pneumonia in four case patients and five control patients.

TABLE 2. Univariate analysis of risk factors for nosocomial bloodstream infection due to ESBL-producing *Escherichia coli* compared with those for control patients from the nosocomial sepsis population and control patients with nosocomial bloodstream infection due to non-ESBL-producing *E. coli*

Factor	No. (%) of cases (n = 96)	Analysis with control group A (n = 190)			Analysis with control group B (n = 186)		
		No. (%) of patients	OR (95% CI)	*P*	No. (%) of patients	OR (95% CI)	*P*
Age > 65 years	45 (47)	97 (51)	0.8 (0.5–1.3)	0.5	115 (62)	0.5 (0.3–0.8)	0.01
Female gender	42 (44)	73 (38)	1.2 (0.7–2.0)	0.3	76 (41)	1.1 (0.6–1.8)	0.6
Charlson index > 2	40 (42)	64 (34)	1.4 (0.8–2.3)	0.1	71 (38)	1.1 (0.7–1.9)	0.5
Organ transplant	9 (9)	9 (5)	2.0 (0.7–5.4)	0.1	5 (3)	3.7 (1.2–11.5)	0.02
Diabetes mellitus	28 (29)	38 (20)	1.6 (0.9–5.4)	0.08	43 (23)	1.3 (0.7–2.3)	0.2
Chronic pulmonary disease	16 (17)	27 (14)	1.2 (0.6–2.3)	0.5	23 (12)	1.4 (0.7–2.8)	0.3
Heart failure	13 (14)	24 (13)	1.0 (0.5–2.2)	0.8	24 (23)	1.0 (0.5–2.1)	0.8
Neoplasia	31 (32)	61 (32)	1.0 (0.5–1.7)	0.9	77 (41)	0.6 (0.4–1.1)	0.1
Liver cirrhosis	8 (8)	11 (6)	1.4 (0.5–3.8)	0.4	11 (6)	1.4 (0.5–3.7)	0.4
Chronic renal insufficiency	18 (19)	28 (15)	1.3 (0.6–2.5)	0.3	23 (12)	1.6 (0.8–3.2)	0.1
Immunosuppressive drug treatment	20 (21)	34 (18)	1.2 (0.6–2.2)	0.5	33 17()	1.2 (0.6–2.2)	0.5
Obstructive urinary disease	16 (17)	18 (10)	1.9 (0.9–3.9)	0.07	24 (13)	1.3 (0.6–2.6)	0.3
Biliary disease	10 (10)	14 (7)	1.4 (0.9–3.9)	0.3	15 (13)	0.7 (0.3–1.6)	0.4
Neutropenia	6 (6)	9 (5)	1.3 (0.4–3.4)	0.5	15 (8)	0.7 (0.2–2.0)	0.5
Hemodialysis	4 (4)	5 (3)	1.3 (0.6–2.8)	0.4	1 (1)	8.0 (0.8–191.7)	0.04
Central venous catheter	45 (47)	88 (46)	1.0 (0.6–1.6)	0.9	77 (40)	1.3 (0.8–2.1)	0.2
Foley catheter	43 (45)	65 (34)	1.5 (0.9–2.5)	0.08	70 (38)	1.3 (0.8–2.2)	0.2
Mechanical ventilation	8 (8)	22 (12)	0.6 (0.2–1.6)	0.3	18 (10)	0.8 (0.3–2.0)	0.7
Surgery	32 (33)	62 (33)	1.0 (0.6–4.7)	0.9	48 (26)	1.4 (0.8–2.4)	0.1
Endoscopic procedure	9 (9)	10 (5)	1.8 (0.7–4.7)	0.1	13 (7)	1.3 (0.5–3.3)	0.4
Urological procedure	7 (7)	5 (3)	2.9 (0.8–9.4)	0.06	10 (5)	1.3 (0.5–3.7)	0.5
Previous antimicrobial use	69 (72)	92 (48)	2.7 (1.6–4.6)	<0.001	96 (52)	2.3 (1.4–4.0)	0.001
Aminopenicillin use	13 (14)	31 (16)	0.8 (0.3–1.6)	0.5	37 (20)	0.6 (0.3–1.2)	0.1
Oxyimino-β-lactam use	35 (37)	28 (15)	3.3 (1.8–5.9)	<0.001	17 (9)	5.7 (2.9–10.9)	<0.001
Carbapenem use	8 (8)	16 (8)	0.9 (0.4–2.3)	0.9	8 (4)	2.0 (0.7–5.5)	0.1
Fluoroquinolone use	24 (25)	28 (15)	1.9 (1.0–3.5)	0.03	27 (15)	1.9 (1.0–3.6)	0.03
Previous hospital stay[a]	24 (31)	18 (18)		0.05	15 (13)		0.001

[a] Data in this row have units of mean number of days (standard deviation).

TABLE 4. Multivariate analysis of risk factors for nosocomial bloodstream infection due to ESBL-producing *Escherichia coli*

Control group and risk factor	β coefficient	OR (95% CI)	*P*
Control group A			
Diabetes mellitus	0.5	1.6 (0.9–2.9)	0.09
Previous oxyimino-β-lactam use	1.16	3.1 (1.7–5.7)	<0.001
Hospital stay (per day)	0.007	1.00 (0.99–1.01)	0.1
Control group B			
Transplant	1.57	4.8 (1.4–15.7)	0.009
Previous oxyimino-β-lactam use	1.79	6.0 (3.0–11.8)	<0.001
Unknown source	−0.71	0.4 (0.2–0.9)	0.03
Hospital stay (per day)	0.02	1.02 (1.00–1.03)	0.01

Charlson index, diabetes mellitus, obstructive disease of the urinary tract, the presence of a urinary catheter, the performance of any other invasive procedure involving the urinary tract, and previous antimicrobial use. With regard to the nosocomial BSIs due to the *E. coli* population, the following variables were introduced into the multivariate analysis: age, gender, previous hospital stay, Charlson index, organ transplantation, the use of hemodialysis, the previous use of antimicrobials, and an unknown source. The following variables were independently associated with bacteremia due to ESBL-producing *E. coli* in the sepsis population: diabetes mellitus and the previous use of oxyimino-β-lactams. For the *E. coli* BSI population, the independent risk factors were previous hospital stay, organ transplantation, the previous use of oxyimino-β-lactams, and an unknown source of BSI (protective) (Table 4). By considering the risk factors found with regard to the *E. coli* BSI population (and using >20 days of a previous hospital stay as the cutoff point), only 8 cases (8%) had no risk factors, 36 (38%) had one, 37 (38%) had two, and 15 (16%) had more than two.

Among the patients with nosocomial BSIs due to ESBL-producing *E. coli*, 27 (28%) presented with severe sepsis or septic shock; 43 (45%) received inappropriate antimicrobial therapy. The crude mortality rates were 25% (24 patients) at day 14 and 30% (29 patients) at day 30. Inappropriate empirical therapy was not associated with a significantly increased risk of mortality by 14 days or 30 days. The results of the multivariate analysis of the variables associated with mortality at 14 and 30 days are shown in Table 5. We found no significant differences in epidemiology, clinical features, or prognosis by type of ESBL produced (data not shown).

DISCUSSION

Our study shows that ESBL-producing *E. coli* caused a significant proportion of all nosocomial BSIs due to *E. coli* in the participating hospitals, although there were significant differences in incidence. Whether this heterogeneity of incidence relates to differences in antimicrobial consumption or to the epidemiology of ESBL-producing *E. coli* in the area concerned remains to be investigated. The features of ESBL-producing *E. coli* isolated from patients with nosocomial BSIs resemble those for ESBL-producing *E. coli* isolated from patients with community-onset infections and colonization in Spain (21, 22, 27). In a study from Israel, patients colonized with ESBL-producing enterobacteria were at an increased risk of developing BSIs during their hospital stays (3). We hypothesize that many patients were probably colonized at admission and developed the infection in hospital. In fact, the molecular typing results obtained by REP-PCR and PFGE argue strongly against the frequent cross-transmission of ESBL-producing *E. coli* isolates causing BSIs in the participating hospitals. Other typing techniques, such as multilocus sequence typing, may find that isolates with different PFGE types belong to the same sequence typing group; however, although this technique is very useful for the long-term delineation of clonal evolution, it is not so for short-term epidemiological analysis (9). Whether plasmid transmission is a relevant means of spread of ESBLs among *E. coli* isolates in the hospital setting, as was demonstrated with ESBL-producing *K. pneumoniae*, is a question that not yet been thoroughly studied.

CTX-M-14 has been the predominant ESBL in community isolates in Spain, being obtained from urinary tract infections and fecal samples (21, 22). However, CTX-M-15, which is associated with the global spread of clonal group ST131 (15) and the predominant ESBL in many countries worldwide, has recently emerged in Spain and has been found to spread in the community, nursing homes, and hospitals in Madrid (17). In our study, 10% of cases produced CTX-M-15, and most of them belonged to the ST131 clonal group; these cases were detected in five hospitals from Madrid, Barcelona, and Mallorca, suggesting local differences in the spread of these isolates.

The best control group for use in the investigation of risk factors depends on the specific research question (12). We used two control groups: one to investigate the risk factors for ESBL-producing *E. coli* in patients with nosocomial sepsis and one to investigate nosocomial BSIs due to *E. coli*. The risk factors found in a comparison with controls from the nosocomial sepsis population might be nonspecifically associated with BSIs due to *E. coli*; this could be the case for diabetes mellitus. The fact that previous oxyimino-β-lactam use was associated with ESBL-producing *E. coli* in comparisons with both the nosocomial sepsis and the *E. coli* nosocomial BSI populations indicates that this is a true risk factor, although the OR found with the second population is probably overestimated (12). Finally, although only 9% of the case patients had undergone an organ transplant, we found that organ transplantation was independently associated with ESBL-producing *E. coli* in patients with nosocomial BSIs due to *E. coli*. Studies described in recent reports found that ESBL-producing *E. coli* frequently causes infections in transplant patients (10, 11, 13). We hypothesize that an organ transplant may act as a surrogate marker for other variables which may increase the probability of colonization and invasive infection due to ESBL-producing *E. coli*.

From a clinical point of view, one important aspect is the fact that about half of the patients with BSIs due to ESBL-producing *E. coli* received inappropriate empirical therapy, although mortality was associated with the severity of the clinical situation, the BSI source, and infections with highly resistant isolates rather than inappropriate therapy. Since inappropriate therapy was an independent predictor of mortality in

TABLE 5. Univariate and multivariate analyses of risk factors for 14-day and 30-day mortality among patients with bloodstream infections due to extended-spectrum β-lactamase-producing *Escherichia coli*

Time of mortality measure and risk factor	No. of patients who died/total no. of patients (%)	RR (95% CI)	*P* for RR	Adjusted OR (95% CI)	*P* for adjusted OR
14-day mortality					
Gender					
Male	13/54 (24)	1.0 (0.5–2.1)	0.8		
Female	11/42 (26)				
Age (yr)					
>65	12/45 (27)	1.1 (0.5–2.2)	0.7		
14–65	12/51 (24)				
Charlson index					
>2	15/40 (38)	2.3 (1.1–4.7)	0.01		
0-2	9/56 (16)				
Pitt score					
>1	17/37 (46)	3.8 (1.7–8.4)	<0.001	3.9 (1.2–12.9)	0.02
0–1	7/59 (12)				
High-risk source[a]					
Yes	19/48 (40)	3.8 (1.5–9.3)	0.001	5.5 (1.4–21.9)	0.01
No	5/48 (10)				
Severe sepsis or shock					
Yes	15/27 (56)	4.2 (2.1–8.5)	<0.001	4.6 (1.4–15.2)	0.01
No	9/69 (13)				
Resistance score					
>3	8/16 (50)	2.5 (1.2–4.8)	0.02	6.5 (1.4–30.0)	0.01
0–3	16/80 (20)				
Empirical treatment					
Inappropriate	11/43 (26)	1.0 (0.5–2.0)	0.9		
Appropriate	11/53 (25)				
30-day mortality					
Gender					
Male	16/54 (30)	1.0 (0.05–1.9)	0.8		
Female	13/42 (26)				
Age (yr)					
>65	14/45 (31)	1.0 (0.5–1.9)	0.8		
14-65	15/51 (29)				
Charlson index					
>2	18/40 (45)	2.3 (1.2–4.3)	0.008	2.7 (0.8–9.0)	0.09
0-2	11/56 (20)				
Pitt score					
>1	21/37 (57)	4.3 (2.0–9.0)	<0.001	5.5 (1.9–21.3)	0.002
0–1	8/59 (14)				
High-risk source[a]					
Yes	23/48 (48)	3.8 (1.7–9.0)	<0.001	5.8 (1.5–21.7)	0.008
No	6/48 (13)				
Severe sepsis or shock					
Yes	17/27 (63)	3.7 (2.0–6.6)	<0.001	3.5 (1.1–11.6)	0.03
No	12/69 (17)				
Resistance score					
>3	8/16 (50)	1.9 (1.0–3.5)	0.07	4.9 (1.0–23.0)	0.04
0–3	21/80 (26)				
Empirical treatment					
Inappropriate	13/43 (30)	1.0 (0.5–1.8)	0.9		
Appropriate	16/53 (30)				

[a] High-risk source: intra-abdominal infection, respiratory tract infection, and unknown source.

two recent large cohorts of patients with BSIs due to *E. coli*, our study may have been underpowered to detect such an association.

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