MAJOR ARTICLE

Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study

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Background. Nosocomial bloodstream infections (BSIs) are important causes of morbidity and mortality in the United States.

Methods. Data from a nationwide, concurrent surveillance study (Surveillance and Control of Pathogens of Epidemiological Importance [SCOPE]) were used to examine the secular trends in the epidemiology and microbiology of nosocomial BSIs.

Results. Our study detected 24,179 cases of nosocomial BSI in 49 US hospitals over a 7-year period from March 1995 through September 2002 (60 cases per 10,000 hospital admissions). Eighty-seven percent of BSIs were monomicrobial. Gram-positive organisms caused 65% of these BSIs, gram-negative organisms caused 25%, and fungi caused 9.5%. The crude mortality rate was 27%. The most-common organisms causing BSIs were coagulase-negative staphylococci (CoNS) (31% of isolates), *Staphylococcus aureus* (20%), enterococci (9%), and *Candida* species (9%). The mean interval between admission and infection was 13 days for infection with *Escherichia coli,* 16 days for *S. aureus*, 22 days for *Candida* species and *Klebsiella* species, 23 days for enterococci, and 26 days for *Acinetobacter* species. CoNS, *Pseudomonas* species, *Enterobacter* species, *Serratia* species, and *Acinetobacter* species were more likely to cause infections in patients in intensive care units ($P < .001$). In neutropenic patients, infections with *Candida* species, enterococci, and viridans group streptococci were significantly more common. The proportion of *S. aureus* isolates with methicillin resistance increased from 22% in 1995 to 57% in 2001 ($P < .001$, trend analysis). Vancomycin resistance was seen in 2% of *Enterococcus faecalis* isolates and in 60% of *Enterococcus faecium* isolates.

Conclusion. In this study, one of the largest multicenter studies performed to date, we found that the proportion of nosocomial BSIs due to antibiotic-resistant organisms is increasing in US hospitals.

Bloodstream infections (BSIs) are major causes of morbidity and mortality. On the basis of data from death certificates, these infections are the 10th leading cause of death in the United States [1], and the age-adjusted death rate has risen by 78% over the past 2 decades [2]. The true incidence of nosocomial BSIs is unknown, but it is estimated that ~250,000 cases occur annually in the United States [3].

Recent studies reported the incidence of BSIs to be between 1% in intensive care unit (ICU) patients [4] and 36% in bone-marrow transplant recipients [5]. The crude rate mortality ranged from 12% in total hospital populations to 80% in ICU patients [6–10]. In recent series of ICU patients, crude mortality rates ranged from 35%–53% [4, 11]. The rate of mortality directly attributable to BSIs in these populations has been estimated to be 16%–40% [7, 11]. Among ICU patients with BSI, the length of stay was prolonged by 7.5–25 days and the total hospitalization time by 4.5–32 days [4, 7, 11]. Inappropriate empirical antimicrobial therapy is an important predictor of death in these patients [7, 12, 13].

Throughout the 1960s and 1970s, gram-negative organisms were most frequently isolated from patients with nosocomial BSIs. Since then, infections due to

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gram-positive organisms have become increasingly frequent [2, 14, 15]. In addition, antibiotic resistance rates have been rising during the past 2 decades for all predominant organisms, including *Staphylococcus aureus* [14, 16, 17], coagulase-negative staphylococci [18, 19], enterococci [20], and gram-negative pathogens [15, 21, 22]. In the face of emerging multiresistant organisms, antimicrobial prophylaxis and treatment have become increasingly difficult, and timely and accurate epidemiological information is needed for guiding appropriate empirical therapy. Analyses of *Candida* BSIs have shown trends to selection of non-*albicans* species, some of which are difficult to treat with first-generation azoles [23]. This study was conducted to assess the epidemiological features of nosocomial BSIs in the United States, the species distribution, and the antimicrobial susceptibilities of causative pathogens.

MATERIALS AND METHODS

The Surveillance and Control of Pathogens of Epidemiologic Importance (SCOPE) Project is based at Virginia Commonwealth University in Richmond, Virginia, and includes 49 hospitals of various sizes (range, 60–1200 beds) that are geographically dispersed throughout the United States (figure 1) [14, 24]. The data generated by the SCOPE Project have shown a high correlation with data from the National Nosocomial Infection Surveillance (NNIS) program of the Centers for Disease Control and Prevention (CDC; Altanta, GA) [24].

Study design. Clinical data were prospectively collected by local infection control practitioners using a standardized case-report form and forwarded to the coordinating center along with each microbiological isolate. The study began in 1995 and continues to the present. Patients admitted from 1 March 1995 through 30 September 2002 to 1 of the 49 hospitals participating in the SCOPE project were eligible if they met the criteria for a nosocomial BSI. A nosocomial BSI was diagnosed if 1 or more culture of blood drawn at least 48 h after admission yielded a pathogenic organism. If the bloodstream isolate was a potential skin contaminant (e.g., diphtheroids, *Propionibacterium* species, *Bacillus* species, coagulase-negative staphylococci, or micrococci), the presence of an intravascular catheter and the initiation of targeted antimicrobial therapy were required for the diagnosis, as well as at least 1 of the following findings: temperature of >38.0°C or <36.0°C, chills, and/or systolic blood pressure of <90 mm Hg. BSI episodes that represented relapses were excluded. However, second episodes that occurred during separate admissions were included as separate cases. We studied the data from all eligible episodes of BSI.

Figure 1. Approximate locations of the hospitals in the Surveillance and Control of Pathogens of Epidemiological Importance [SCOPE] Program.

The data that were routinely collected included the patient's age, sex, location at the onset of BSI (ICU vs. non-ICU ward), clinical service at the onset of BSI, and predisposing clinical conditions, as well as the species distribution and antimicrobial susceptibility of causative pathogens and the outcome during hospitalization (i.e., crude mortality). Predisposing clinical conditions that were routinely recorded included neutropenia (defined as an absolute neutrophil count of <1000 cells/μL), receipt of peritoneal dialysis or hemodialysis, and/or presence of intravascular catheters (i.e., central lines, arterial catheters, or peripheral intravenous catheters). Sources of secondary BSI were identified by cultures of samples obtained from distant sites that yielded the same pathogen with an identical resistance pattern.

Incidence. To calculate incidence rates, we collected admission data from the participating hospitals. The 7 hospitals that participated for <12 months in the study were excluded, leaving 42 hospitals for this analysis. Incidence rates were calculated as number of BSIs per 10,000 hospital admissions.

Microbiological methods. Blood cultures were processed at the participating hospitals. The identification of blood isolates and susceptibility testing were done with the routine methods in use at the affiliated laboratories. All affiliated laboratories were College of American Pathologists–certified, and all microbiological methods used were consistent with current NCCLS recommendations. Data from all hospitals were used for analysis, and denominators for individual antimicrobial agents may vary because not all hospitals test and report all drugs. Several subprojects have evaluated samples of organisms from this study and have included validation measures, such as reidentification of species and retesting of antimicrobial susceptibilities in the Special Microbiology Laboratory at the University of Iowa College of Medicine; the Department of Epidemiology at the Virginia Commonwealth University Medical Center; and the Institute for Medical Microbiology, Immunology and Hygiene at the University of Cologne, Germany [25–29].

Statistical analysis. The results were expressed as the mean ± SD or as a proportion of the total number of patients or isolates. For continuous variables, mean values were com-

Table 1. Incidence rates and distribution of pathogens most commonly isolated from monomicrobial nosocomial bloodstream infections (BSIs) and associated crude mortality rates for all patients, patients in intensive care units (ICU), and patients in non-ICU wards.

Pathogen	BSIs per 10,000 admissions	Percentage of BSIs (rank)			Crude mortality, %		
		Total (n = 20,978)	ICU (n = 10,515)	Non-ICU ward (n = 10,442)	Total	ICU	Non-ICU ward
CoNS	15.8	31.3 (1)	35.9 (1)[a]	26.6 (1)	20.7	25.7	13.8
Staphylococcus aureus[b]	10.3	20.2 (2)	16.8 (2)[a]	23.7 (2)	25.4	34.4	18.9
Enterococcus species[c]	4.8	9.4 (3)	9.8 (4)	9.0 (3)	33.9	43.0	24.0
Candida species[c]	4.6	9.0 (4)	10.1 (3)	7.9 (4)	39.2	47.1	29.0
E scherichia coli	2.8	5.6 (5)	3.7 (8)[a]	7.6 (5)	22.4	33.9	16.9
Klebsiella species	2.4	4.8 (6)	4.0 (7)[a]	5.5 (6)	27.6	37.4	20.3
Pseudomonas aeruginosa	2.1	4.3 (7)	4.7 (5)	3.8 (7)	38.7	47.9	27.6
Enterobacter species	1.9	3.9 (8)	4.7 (6)[a]	3.1 (8)	26.7	32.5	18.0
Serratia species[b]	0.9	1.7 (9)	2.1 (9)[a]	1.3 (10)	27.4	33.9	17.1
Acinetobacter baumannii	0.6	1.3 (10)	1.6 (10)[a]	0.9 (11)	34.0	43.4	16.3

NOTE. *Bacteroides* species (n = 150; 1.4% of isolates) ranked ninth in non-ICU wards. CoNS, coagulase-negative staphylococci.

[a] $P < .05$ for patients in ICUs vs. patients in non-ICU wards.

[b] Significantly more frequent in patients without neutropenia.

[c] Significantly more frequent in patients with neutropenia.

pared using 2 sample t tests for independent samples. Differences in proportions were compared using a χ^2 test or Fisher's exact test, as appropriate. Mean values are reported with SDs. All tests of significance are 2-tailed; α was set at .05. The Mann-Whitney U test was performed to test the equality of continuous variables. All statistical analyses were done using SPSS software (SPSS).

RESULTS

Study population and patient characteristics. During the 7.5-year study period, a total of 24,179 infections with 27,847 organisms were reported by participating hospitals. Of these, 3432 clinically significant episodes of BSI (15%) were identified in pediatric patients (≤16 years of age). Patients had a mean age of 51 ± 26.5 years (range, 0–102 years). Forty-four percent of patients were female.

Approximately 51% (50.5%) of hospital-acquired BSIs occurred in the ICU. The clinical services most commonly diagnosing and reporting BSIs were internal medicine (38%), general surgery (20%), and pediatrics (13.5%).

The most frequent underlying conditions (recorded as diagnoses at admission) were malignancy, in 4237 patients (17.5%); cardiac conditions, in 3626 patients (15%); and gastrointestinal conditions, in 3269 patients (13.5%). However, underlying conditions were not specified for 4356 patients (14%).

Among the potential factors predisposing patients to BSI, intravascular devices were the most frequent. Central venous catheters were in place in 17,484 patients (72%), peripheral intravenous catheters were in place in 8426 patients (35%), and arterial catheters were in place in 3821 patients (16%). Urinary catheters were in place in 11,101 patients (46%). A total of 5791 patients (24%) were receiving total parenteral nutrition, and 1896 patients (8%) needed dialysis at the onset of BSI. Most of these patients underwent hemodialysis (1769 patients vs. 127 who underwent peritoneal dialysis). Ventilator support was necessary for 7844 patients (32%). Overall, 6618 patients died during hospitalization, accounting for a crude mortality rate of 27%.

The system-wide incidence of BSI was 60 cases per 10,000 hospital admissions. When stratified by pathogen, system-wide incidence rates of BSI due to the most commonly isolated pathogens varied between 1 and 16 cases per 10,000 admissions, which were the incidence rates for BSI due to *Acinetobacter baumannii* and CoNS, respectively (table 1). The median hospital incidence of BSI was 43 cases per 10,000 hospital admissions (range, 6–252). Incidences did not vary significantly over time (mean ± SD, 54 ± 40 cases per 10,000 admissions in 1996 vs. 52 ± 38 in 2001), and no trend could be observed.

Microbiological features. Thirteen percent of all episodes of BSI (n = 3201) were polymicrobial. Of 20,978 monomicrobial episodes, a total of 13,665 episodes (65%) were caused by gram-positive organisms and 5278 (25%) by gram-negative organisms. Fungi, mainly *Candida* species, were isolated in a total of 2002 episodes (9.5%). Anaerobic bacteria accounted for 1.3% of BSIs. These proportions did not change significantly during the study period. The rank order of the major pathogens (table 1) shows that CoNS accounted for nearly one-third of all nosocomial BSIs (31%), followed in rank by *S. aureus* (20%), enterococci (9%), and *Candida* species (9%). *E. coli* (6% of episodes) and *Klebsiella* species (5%), were the most common gram-negative organisms.

Table 2. Distribution of nosocomial bloodstream infections (BSIs) and most frequently isolated pathogens causing BSIs, by clinical service.

Clinical service, class of BSI, pathogen[a]	No. (%) of BSIs
Internal medicine	
All BSIs	9088 (37.6)[b]
Monomicrobial BSIs	
CoNS	2131 (27.1)
S. aureus	2121 (27.0)
Enterococci	775 (9.9)
General surgery	
All BSIs	4788 (19.8)[b]
Monomicrobial BSIs	
CoNS	1197 (29.7)
S. aureus	745 (18.5)
Candida species	427 (10.6)
Pediatric	
All BSIs	3275 (13.5)[b]
Monomicrobial BSIs	
CoNS	1381 (46.8)
Candida species	311 (10.5)
S. aureus	295 (10.0)
Adult hematology/oncology	
All BSIs	2655 (11.0)[b]
Monomicrobial BSIs	
CoNS	688 (30.1)
S. aureus	339 (14.8)
Enterococci	235 (10.3)
Cardiothoracic surgery	
All BSIs	2044 (8.5)[b]
Monomicrobial BSIs	
CoNS	564 (30.9)
S. aureus	361 (19.8)
Enterococci	177 (9.7)
Neurosurgery	
All BSIs	869 (3.6)[b]
Monomicrobial BSIs	
CoNS	254 (33.9)
S. aureus	165 (22.0)
Enterococci	57 (7.6)
Orthopedics	
All BSIs	353 (1.5)[b]
Monomicrobial BSIs	
S. aureus	81 (25.4)
CoNS	78 (24.5)
E. coli	32 (10.0)
Pediatric hematology/oncology	
All BSIs	243 (1.0)[b]
Monomicrobial BSIs	
CoNS	98 (44.7)
S. aureus	17 (7.8)
Klebsiella species	16 (7.3)
Urology	
All BSIs	238 (1.0)[b]
Monomicrobial BSIs	
CoNS	66 (31.3)
Candida species	31 (14.7)
S. aureus	31 (14.7)
Obstetrics	
All BSIs	209 (0.9)[b]
Monomicrobial BSIs	
E. coli	63 (33.5)
S. aureus	22 (11.7)
Enterococci	22 (11.7)

NOTE. CoNS, coagulase-negative staphylococci; *E. coli, Escherichia coli; S. aureus, Staphylococcus aureus.*

[a] The 3 pathogens most commonly isolated in each service.

[b] Percentage of the total of 24,179 BSIs at all study hospitals.

CoNS, *Enterobacter* species, *Serratia* species, *A. baumannii,* and *Candida* species were more likely to be isolated from patients in ICUs ($P < .001$), whereas *S. aureus, Klebsiella* species and *E. coli* were more common in patients in wards ($P < .001$). No significant differences were seen for enterococci or *Pseudomonas aeruginosa* (table 1).

When stratified by clinical service, the following patterns emerged: CoNS were the most frequently isolated pathogens for all services, except orthopedics and obstetrics, where *S. aureus* and *E. coli* , respectively, were more frequently isolated. *S. aureus* , enterococci, and *Candida* species usually followed in various rank orders (table 2).

When different age groups were compared, the proportion of CoNS decreased from 49% in patients <1 year to 27% in patients >65 years, whereas the proportion of *S. aureus* in the same patient populations increased from 9.5% to 24%, respectively. For gram-negative pathogens and *Candida* species, the proportions remained stable.

When patients were stratified into those with neutropenia and those without neutropenia, 2 differences emerged. BSI due to *S. aureus* was more common among nonneutropenic patients (21%, compared with 9% among neutropenic patients), whereas BSI due to viridans group streptococci was more common among patients with neutropenia (2%, compared with 0.5% among nonneutropenic patients). Other organisms accounted for about the same proportion (absolute difference, <2%) of BSIs in each group.

In patients with monomicrobial BSIs, the crude mortality (table 1) ranged from 21% and 22% (for CoNS and *E. coli,* respectively) to 39% (for *P. aeruginosa* and *Candida* species).

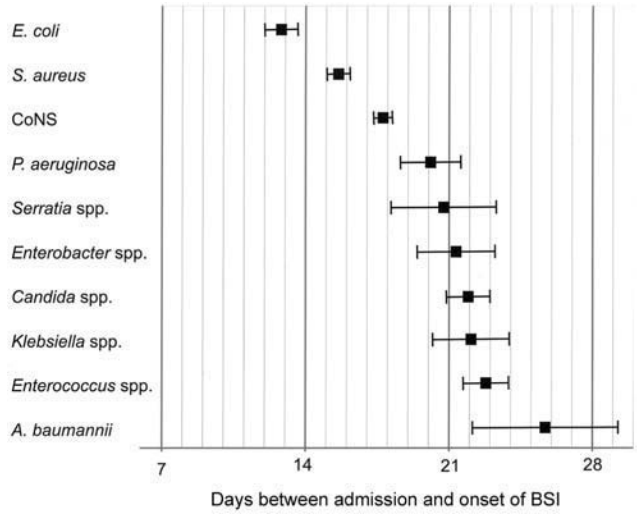

Figure 2. Time interval between hospital admission and onset of infection for the most frequently isolated pathogens in a series of 24,179 cases of nosocomial bloodstream infection (BSI). *A. baumannii, Acinetobacter baumannii;* CoNS, coagulase-negative staphylococci; *E. coli, Escherichia coli; P. aeruginosa, Pseudomonas aeruginosa; S. aureus, Staphylococcus aureus.*

In ICU patients, the crude mortality ranged from 26% and 34% (for CoNS and *E. coli,* respectively) to 48% and 47% (for *P. aeruginosa* and *Candida* species, respectively). In patients with polymicrobial BSIs, the crude mortality was 32%.

The mean time from hospital admission to onset of BSI due to the major pathogens (figure 2) ranged from 12 days (for *E. coli*) to 26 days (for *A. baumannii*). Time to infection decreased with increasing age, from 26 days, in patients <1 year of age, to 16 days, in patients >65 years of age. No significant seasonal or geographical patterns could be observed for any of the organisms when different time periods and US geographical regions (northwest, northeast, southwest, and southeast) were compared.

Primary BSI, in which no source could be determined, was seen in 12,893 patients (53%). Secondary BSI originated from intravenous catheters in 5749 patients (24%), from the urinary tract in 1580 patients (6.5%), and from the lower respiratory tract in 1539 patients (6%). However, culture samples from distant sites were infrequently collected; therefore, some points of origin might not have been detected.

Of the 1890 *Candida* isolates causing nosocomial BSI, *C. albicans* was the most common, accounting for 54% of cases of *Candida* BSI, followed in rank order by *C. glabrata* (19%), *C. parapsilosis* (11%), and *C. tropicalis* (11%) (figure 3). Crude mortality was lowest for *C. albicans* infection (37%) and highest for *C. krusei* infection (59%) (figure 3). There was an increase in the proportion of *Candida* species isolated from blood cultures from 8% in 1995 to 12% in 2002 ($P < .001$, trend analysis). Also, the proportions of *C. albicans* and *C. parapsilosis* among these isolates increased between 1995 and 2002, but the proportions of *C. tropicalis* and *C. glabrata* decreased.

Antimicrobial susceptibility. Methicillin resistance was detected in 1699 *S. aureus* isolates (41% of tested isolates) and in 4946 CoNS isolates (75%). The proportion of *S. aureus* isolates with methicillin resistance was significantly higher among ICU patients than among ward patients (44% vs. 40%; $P = .004$), and there was also a trend toward a higher proportion of *S. aureus* isolates resistant to methicillin among patients without neutropenia than among patients with neutropenia (42% vs. 32%; $P = .054$, figure 4). The proportion of *S. aureus* isolates resistant to methicillin increased from 22% in 1995 to 57% in 2001 ($P < .001$, trend analysis; figure 5).

Among enterococcal isolates, vancomycin resistance was found in 60% of *E. faecium* isolates and in 2% of *E. faecalis*

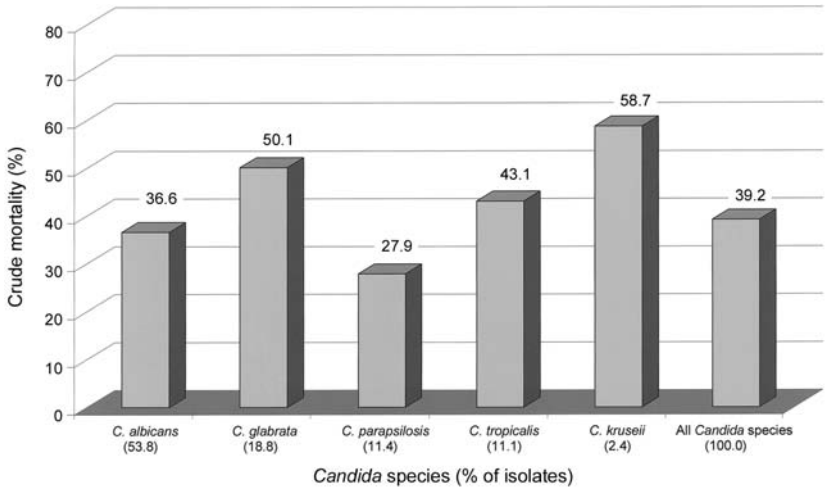

Figure 3. Distribution of *Candida* species in 1890 cases of *Candida* bloodstream infection and associated crude mortality

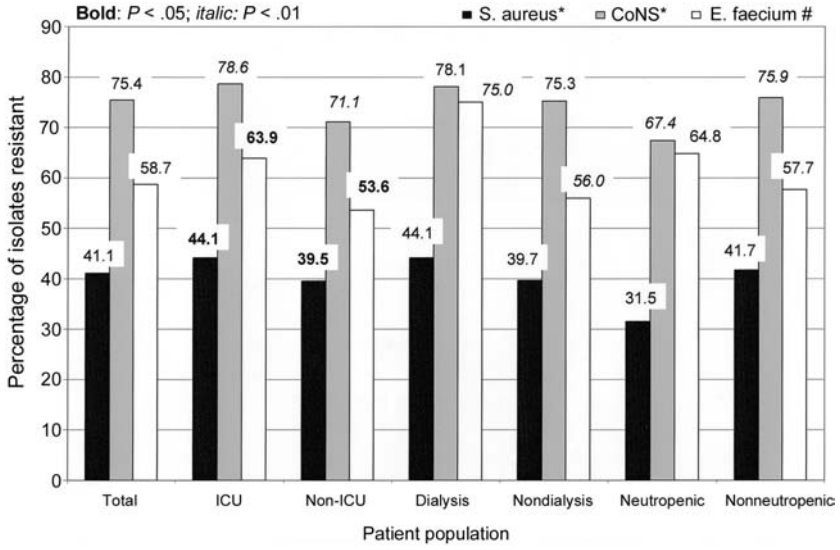

Figure 4. Antimicrobial resistance among gram-positive isolates ($n = 13,665$) recovered from selected patient populations with bloodstream infection. * Percentage resistant to methicillin. # Percentage resistant to vancomycin. ICU, intensive care unit. CoNS, coagulase-negative staphylococci; *E. faecium, Enterococcus faecium; S. aureus, Staphylococcus aureus.*

isolates (figure 5). Among viridans group streptococci, decreased susceptibility to penicillin (MICs of ⩾0.25 mg/L) and to erythromycin was detected in 39 (35%) of 112 isolates and 44 (42%) of 104 of isolates, respectively.

Antimicrobial resistance levels for the most common gram-negative organisms causing nosocomial BSIs are shown in table 3. A relatively high proportion of *E. coli* isolates displayed resistance to ampicillin, piperacillin, and ampicillin-sulbactam (44%, 41%, and 39%, respectively). Resistance to trimethoprim-sulfamethoxazole was seen in 19% of isolates. Third-generation cephalosporins, aminoglycosides, and ciprofloxacin displayed activity against most isolates, as did imipenem and aztreonam (⩽5% of isolates were resistant). For *Klebsiella* isolates, third-generation cephalosporins, aminoglycosides, fluoroquinolones, aztreonam, and imipenem were active against >80% of isolates tested. For *Enterobacter* isolates, imipenem

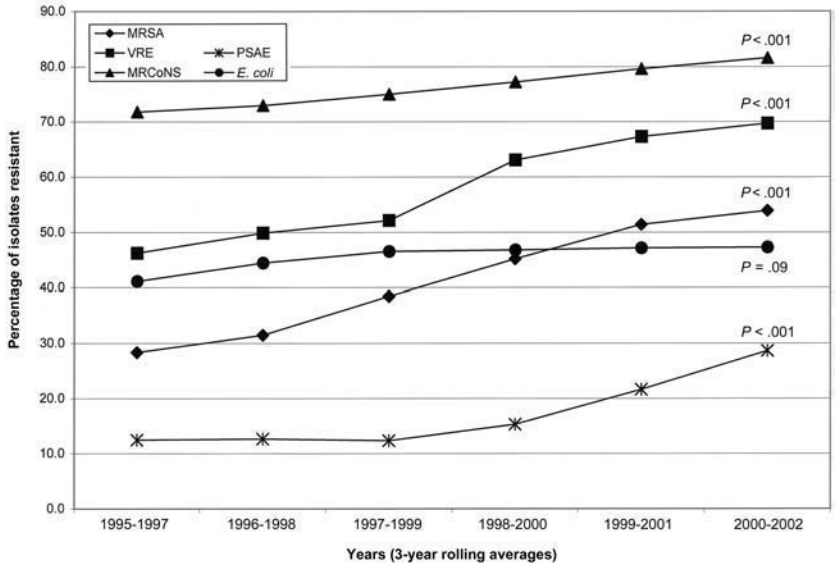

Figure 5. Rates of antimicrobial resistance rates over time (3-year rolling average) among gram-positive isolates (methicillin-resistant *Staphylococcus aureus* [MRSA], methicillin-resistant coagulase-negative staphylococci (MRCoNS), vancomycin-resistant *Enterococcus faecium* [VRE], ampicillin-resistant *Escherichia coli [E. coli],* and ceftazidime-resistant *Pseudomonas aeruginosa* [PSAE]) recovered in a series of 24,179 cases of nosocomial bloodstream infection.

Table 3. Rates of antimicrobial resistance among gram-negative organisms most frequently isolated from patients with nosocomial bloodstream infection.

	Escherichia coli		*Enterobacter* species		*Klebsiella* species		*Pseudomonas aeruginosa*		*Serratia* species	
Antimicrobial drug	No. of isolates	Percentage resistant	No. of isolates	Percentage resistant	No. of isolates	Percentage resistant	No. of isolates	Percentage resistant	No. of isolates	Percentage resistant
Ampicillin	1126	43.8	ND	…	894	98.4	ND	…	ND	…
Amp-Sulb	711	40.8	ND	…	667	39.6	ND	…	ND	…
Piperacillin	630	38.7	467	33.8	562	33.6	554	11.2	190	16.3
Tic-Clv	416	20.0	264	38.6	393	27.2	315	16.8	101	16.8
Cefazolin	1041	12.4	ND	…	911	23.7	ND	…	ND	…
Cefotaxime	499	1.8	366	33.9	486	11.7	ND	…	173	7.5
Ceftazidime	793	1.9	658	38.9	777	12.9	825	15.5	287	7.7
Cefuroxime	451	6.9	270	60.7	414	20.8	ND	…	ND	…
Imipenem	682	0.4	643	0.6	636	0.8	700	14.3	195	2.6
Aztreonam	435	2.5	295	35.3	337	14.6	451	26.2	111	6.3
Ciprofloxacin	754	4.6	468	8.1	646	9.0	732	20.2	198	8.6
Gentamicin	1048	3.9	688	8.6	876	14.0	791	19.5	294	4.4
Tobramycin	600	3.7	469	12.8	579	17.4	643	10.4	201	14.9
TMP-SMX	1113	19.3	755	12.7	924	14.6	ND	…	335	4.2

NOTE. Amp-Sulb, ampicillin-sulbactam; ND, not done; Tic-Clv, ticarcillin-clavulanate; TMP-SMX, trimethoprim-sulfamethoxazole.

displayed the greatest activity (1% were resistant). Of the *P. aeruginosa* isolates, 11%, 14%, and 16% were resistant to piperacillin, imipenem, and ceftazidime, respectively. Resistance to ciprofloxacin was seen in 20% of tested isolates. Of note, the proportion of *P. aeruginosa* isolates resistant to ceftazidime increased from 12% in 1995 to 29% in 2001 ($P < .001$, trend analysis; figure 5).

DISCUSSION

In the face of increasing antimicrobial resistance, surveillance programs have become important in defining the species distribution and resistance patterns of pathogens causing BSIs, and thus are providing the basis for appropriate empirical therapy. Data from Ibrahim et al. [30] showed that mortality rates doubled, from 30% to 60%, when inappropriate empirical antibiotic therapy was given to ICU patients with BSIs.

There are several differences between this surveillance project and other networks that monitor a variety of infections and/or countries [14–16, 31]. The SCOPE project focuses entirely on nosocomial BSIs in the United States and constitutes the largest nongovernmental surveillance project in this area. It is a clinically oriented surveillance project, collecting data on defined infections, not on culture results alone. Moreover, the surveillance encompasses the entire hospitalized population at the sentinel hospitals, rather than just those patients in ICUs.

As in other series, the dominance of gram-positive pathogens has been documented in this study. However, our design might have led to an overestimation of BSIs due to CoNS, because even though strictly defined clinical signs were required for inclusion in the study, patients with only 1 blood culture yielding CoNS were eligible. Recent studies have shown that the proportion of contaminants is lower if 2 or more positive blood culture results (of samples drawn within a few hours of each other) were required for inclusion [9, 32, 33]. However, this should be minimized somewhat by the strict clinical definitions used by SCOPE to ascertain the clinical relevance of the positive blood culture. In addition, SCOPE data have shown a high correlation to the NNIS data [24].

The proportion of BSIs due to *Candida* species in our study differs significantly from previously reported data. A recent NNIS study [23] showed significant decreases in BSIs due to *Candida* species and *C. albicans* but reported a significant increase in BSIs due to *C. glabrata* in ICUs from 1989 through 1999. In contrast, we found a significant increase in the proportion of *Candida* species among isolates from blood cultures, from 8% in 1995 to 12% in 2002. Furthermore, the proportions of *C. albicans* and *C. parapsilosis* among these isolates increased from 1995 through 2002, whereas the proportions of *C. tropicalis* and *C. glabrata* decreased.

The rate of resistance to methicillin that we identified among *S. aureus* infections was higher than that identified in northern Europe [34] but comparable to rates of resistance reported in other series from the United States [15, 35]. The rate of resistance to vancomycin in *E. faecium* infections was comparable to those in recent studies from the United States [15, 35] but higher than those observed in recent European studies [34, 36].

In our series, the prevalence of resistance to vancomycin among *E. faecium* isolates was significantly higher among those

recovered from neutropenic patients. Several recent studies found neutropenia to be independently associated with vancomycin-resistant enterococcal (VRE) infection when comparing patients with vancomycin-resistant and patients with vancomycin-susceptible enterococcal BSIs [37, 38]. In contrast, Lucas and co-authors [39], in comparing vancomycin-susceptible and vancomycin-resistant enterococcal BSIs , did not find neutropenia to be a risk factor for BSIs due to VRE.

Increasing resistance to penicillin, other β-lactam antibiotics, and macrolides has been documented in viridans group streptococci isolated from neutropenic patients with cancer [40, 41]. In our study, 34% and 42% of viridans group streptococci displayed decreased susceptibility to penicillin and macrolides, respectively. These rates are in accordance with recent data from Germany [40] but are lower than rates in southern Europe [41].

CoNS and *Candida* species were more likely to be isolated from patients in ICUs, thus influencing empirical antibiotic therapy, whereas *S. aureus* and *E. coli* were more commonly isolated from patients in non-ICU wards. Viridans group streptococci were more frequently seen in patients with neutropenia, whereas *S. aureus* was more commonly seen in nonneutropenic patients. In addition, we found enterococci, *Candida* species, and *Serratia* species more frequently in patients without neutropenia.

The finding of a higher proportion of resistance to tobramycin, compared with gentamicin, for several of the gram-negative organisms should not be taken to imply that gentamicin has better activity against these organisms. Rather, this finding is due to the variation in the antibiotics tested at the local laboratories. Thus, the true aminoglycoside susceptibility lies somewhere between the 2 values.

In conclusion, our data demonstrate one-half of all nosocomial BSIs occur in the critical-care setting, although a minority of patients receive care there. The high rates of antibiotic resistance, as well as local patterns of species distribution and drug susceptibilities in certain patient populations, should guide empirical therapy of nosocomial BSIs.

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