

E. Velasco · M. Soares · R. Byington · C. A. S. Martins ·  
M. Schirmer · L. M. C. Dias · V. M. S. Gonçalves

## Prospective evaluation of the epidemiology, microbiology, and outcome of bloodstream infections in adult surgical cancer patients

Published online: 28 July 2004  
© Springer-Verlag 2004

**Abstract** The aim of this study was to describe the epidemiology and microbiology of bloodstream infections (BSIs) among adult surgical cancer patients and to determine independent factors that influence in-hospital mortality. The study enrolled 112 consecutive episodes of BSIs in adult surgical cancer patients during a 26-month period. The median age of the patients was 64.5 years, and crude in-hospital mortality was 19.6%. The median time from surgery to the index blood culture was 11 days and from index blood culture to death was 4.5 days. Seventy-five percent of the patients had an advanced tumor disease, 36.6% were under intensive care, and 68.7% had a central venous catheter in place at the time the bloodstream infection was diagnosed. Associated infected sites were present in 57.1% of the episodes. There were 328 noninfectious co-morbid conditions. Poor performance status, weight loss, hypoalbuminemia, and ventilatory support accounted for 67.4% of them. There was a predominance of aerobic gram-negative bacilli (62%), followed by gram-positive cocci (26.6%) and fungi (9.3%). The observed mortality rates associated with

these organism groups were similar (23.6% vs 15% vs 28.6%, respectively;  $P=0.44$ ). The most frequent organisms were *Enterobacter* spp., coagulase-negative staphylococci, *Klebsiella* spp., *Acinetobacter* spp., and fungi. Nonfermentative strains predominated in patients with catheters. Thirty-five (30.2%) pathogens were considered resistant. There was no significant difference in the mortality rate between patients with resistant and those with nonresistant organisms (20% vs 26%, respectively;  $P=0.49$ ). Logistic regression analysis showed  $\geq 4$  co-morbid conditions, advanced tumor, thoracic surgery, catheter retention, and pulmonary infiltrates as independent predictors of mortality. Medical and infection control measures addressing certain variables amenable to intervention might reduce the negative impact of postoperative infectious morbidity and mortality of BSIs in adult surgical cancer patients.

E. Velasco (✉)  
Rua General Glicério 486/1002,  
22245-120 Rio de Janeiro, Brazil  
e-mail: evelasco@inca.gov.br  
Tel.: +55-21-25066138

M. Soares  
Hospital do Câncer, Instituto Nacional de Câncer, Centro de  
Tratamento Intensivo,  
Praça Cruz Vermelha 23,  
20230-130 Rio de Janeiro, Brazil

R. Byington  
Hospital do Câncer, Instituto Nacional de Câncer,  
Praça Cruz Vermelha 23,  
20230-130 Rio de Janeiro, Brazil

C. A. S. Martins · M. Schirmer · L. M. C. Dias ·  
V. M. S. Gonçalves  
Hospital do Câncer, Instituto Nacional de Câncer, Comissão de  
Controle de Infecção Hospitalar,  
Praça Cruz Vermelha 23,  
20230-130 Rio de Janeiro, Brazil

### Introduction

Oncology patients undergoing major and complex operations have a high degree of morbidity and mortality, mainly because of postoperative infectious complications [1]. Despite all modern healthcare resources for preventing and controlling these complications, hospital-acquired bloodstream infections (BSIs) remain one of the major life-threatening infectious conditions in these patients. The majority of studies on surgical patients with nosocomial infections analyze the epidemiology and risk factors for surgical-site infection [2] as well as the relationship between the type of organisms isolated from wound cultures and postoperative bacteremia [3, 4].

To our knowledge, prospective studies to examine prognostic factors associated with BSIs in patients with malignancies submitted to elective surgeries have not been undertaken. Nosocomial surveillance studies for BSIs have shown a high prevalence of these infections among patients submitted to aggressive surgical intervention with the purpose of diagnosing, staging, or treating the underlying disease [5, 6].

Therefore, we performed a 26-month prospective cohort study at a tertiary cancer center with two objectives. The first one was to describe the epidemiology and microbiology of BSIs among adult surgical patients. Our second goal was to determine independent factors influencing in-hospital mortality in order to identify a subgroup of surgical patients at higher risk of death.

## Patients and methods

The Hospital do Câncer, Instituto Nacional de Câncer, in Rio de Janeiro, Brazil, is a 206-bed tertiary oncology care center that provides specialized hematology/oncology care and is equipped with a 10-bed medical/surgical intensive care unit. Annually, about 7,860 patients are admitted for the diagnosis and treatment of malignancies, and about 5,700 (73%) of them undergo surgical procedures.

We prospectively evaluated, between June 2000 and July 2002, all consecutive adult ( $\geq 18$  years) inpatients with solid tumors submitted to an elective surgery who presented positive blood cultures (BCs) within 30 days of surgery. All patients who entered the operating room were considered to have had surgery.

Blood samples for culture were collected by nursing staff, and the standard protocol required at least two samples for culture before or at the moment of antibiotic initiation. If a central venous catheter (CVC) was in place, at least two samples were obtained simultaneously from the catheter hub and from a peripheral site. Each isolate from a positive BC was assessed to determine whether it represented, on the basis of clinical or microbiological data, true bacteremia or contamination. If potential skin contaminants (e.g., coagulase-negative staphylococci (CNS), corynebacteria other than *Corynebacterium jeikeium*, diphtheroids, *Propionibacterium* spp., *Bacillus* spp., or micrococci) were isolated, at least two separate positive BCs had to be obtained from different sites in order for the episode to be considered a true infection. In addition, the treating physician had to consider the infection to be clinically significant, warranting the commencement of antimicrobial therapy.

A BSI episode was defined as a period beginning with the first positive BC (index BC) and ending when the patient became afebrile and was without clinical and laboratory signs of infection, or upon death if the patient died during the infectious episode. All positive BCs occurring during the same clinical infectious illness were considered representative of the same BSI episode, even if multiple sources were evident. Crude in-hospital mortality, used as the measure of outcome, was defined as the number of patients who died with BSI divided by the total number of patients with the infection.

BSIs were defined according to the criteria of the Centers for Disease Control (CDC) [7]. Primary BSI referred to bacteremia or fungemia for which there was no documented focal source, including infections that resulted from intravascular catheter infection. Associated BSI episodes were those that occurred concomitantly or immediately prior to a clinically or laboratory-proven site of infection. Catheter-related BSI was defined as the appearance of fever, chills/rigors, or hypotension within 1 h after catheter flushing or manipulation and a return to normal condition within 24 h of catheter removal without antimicrobial treatment; the appearance of fever, chills/rigors, or hypotension concomitant with a catheter exit site or subcutaneous tunnel infection; or recovery of the same microorganism from blood and catheter tip (roll-plate semiquantitative culture with  $\geq 15$  cfu) without an apparent active focus.

The following variables were analyzed: demographics of the patients, underlying conditions, clinical stage of cancer, performance status (Karnofsky score) [8], BSI classification (monomicrobial or polymicrobial) according to the number of species of organisms isolated during the entire episode, type of BSI (transitory or persistent) when organisms were isolated only within the first 48 h or when BCs remained positive for more than 48 h, presence and type of CVC, infectious and noninfectious co-morbid conditions

(evaluated within the 7 days after the index BC), hyperglycemia (serum glucose level  $>200$  mg/dl or therapy with an oral hypoglycemic agent or insulin), hypoalbuminemia (serum albumin  $\leq 2.8$  mg), recent 30-day weight loss  $\geq 10\%$ , and neurologic dysfunction (a new or old focal deficit). Hypotension was defined as a sustained ( $\geq 1$  h) decrease in the systolic blood pressure of at least 40 mmHg from baseline or a resultant systolic blood pressure of  $<90$  mmHg after adequate fluid replacement and in the absence of any antihypertensive drug. Patients with major vascular or locally invasive tumors or those with metastasis were considered to have advanced disease.

The following organisms were considered antimicrobial-resistant bacteria: ceftazidime-resistant gram-negative bacilli, penicillin-resistant enterococci and streptococci, and oxacillin-resistant *Staphylococcus aureus*. Initial empiric therapy, prior to any change in regimen made as a result of culture yield, was correlated with the in vitro susceptibility of the BC isolate(s). Therapy was deemed inadequate when the organisms isolated were resistant in vitro to all the antibiotics administered or when the antimicrobial agents administered were not directed toward a specific class of microorganisms isolated, such as fungi. The antibiotics had to be administered for at least 48 h in order to be evaluated for their effect on outcome.

Blood specimens were inoculated into Bactec Peds Plus vials and Bactec Plus anaerobic/aerobic vials (Becton–Dickinson Microbiology Systems, Sparks, MD, USA). All cultures were processed in a Bactec 9240 continuous-monitoring system (Becton–Dickinson) and incubated until microbial growth was detected or for 5 days. Isolates from positive bottles were identified by standard methods, using the automated Vitek System (bioMérieux, Lyon, France) [9, 10]. The Kirby–Bauer diffusion test and the E test were performed in accordance with the guidelines for each organism tested. All negative bottles remained incubated for 30 days. Both antibiotic-resistant and intermediately susceptible organisms were considered to be resistant when resistance percentages were calculated. BCs positive for yeast were further processed in the mycological laboratory. Yeasts were identified on the basis of morphology and biochemical characteristics (API 20C; bioMérieux, Marcy l’Etoile, France). Non-yeast fungi were identified on the basis of morphology.

Continuous variables were analyzed by using the Student’s *t* test for normally distributed variables and the Mann-Whitney rank-sum test for non-normally distributed variables. Categorical variables were compared by the chi-square test (with Yates’ correction where applicable) or Fisher’s exact test, as appropriate. All statistical tests were two-sided, and *P* values of  $\leq 0.05$  were considered statistically significant. Variables with a *P* value of  $<0.10$  in univariate analyses and those known to be biologically important were included in a stepwise multivariate logistic regression analysis. Calculations were performed using SPSS software, version 11 for Windows (SPSS, Chicago, IL, USA).

## Results

The study enrolled 112 episodes of BSI occurring in 112 patients. The median number of days that elapsed from surgery to the index BC was 11 days (range, 0–43 days) and from the index BC to death was 4.5 days (range, 0–36 days). Forty-one (36.6%) patients were under intensive care at the time of or within the 10 days preceding the BSI. The overall in-hospital mortality was 19.6% ( $n=22$  deaths).

The origin of BSI could not be determined in 5.4% of the episodes. The BSI was considered to be associated with other sites in 57.1% of the cases and related to the CVC in 37.5%. BSI associated with other sites had the highest crude mortality rate (25%), followed by BSI of

unknown origin (16.7%) and CVC-related BSI (11.9%) ( $P=0.25$ ). A total of 159 concomitantly infected sites were clinically or laboratory documented. The most frequent diagnoses were surgical-site infection (32.1%), pneumonia (30.2%), and urinary tract infection (13.8%).

Tables 1, 2 show the main characteristics of the patients and the association of these characteristics with a fatal outcome. Patients who had advanced tumor disease, pulmonary infiltrates, and thoracic surgery were more likely to die. There was a statistical trend toward a higher proportion of deaths associated with polymicrobial infections in comparison with monomicrobial infections ( $P=0.06$ ).

Most CVCs were inserted for short-term purposes (73/77; 94.8%). We did not observe a significant difference in outcome between patients with and patients without a CVC (18.2% vs 22.9%, respectively;  $P=0.75$ ). The median length of time from the index BC to CVC removal was 1 day (range, 0–13 days) and did not differ between survivors (median, 1 day; range, 0–13 days) and nonsurvivors (median, 2 days; range, 0–6 days) ( $P=0.80$ ). The majority of catheters (73%) were removed within the first 72 h after the index BC result was obtained. There was a tendency toward a higher rate of CVC retention in nonsurvivors ( $P=0.07$ ). The risk of death decreased 82% with catheter withdrawal in comparison with catheter retention.

There were three deaths among patients submitted to thoracic surgery. In two cases, diagnostic surgical procedures were performed in hypoxemic patients with

very poor functional status: one had a large mediastinum mass and superior vena cava obstruction and the other had diffuse interstitial infiltrates. The third patient was submitted to a pneumectomy with large chest wall resection.

A total of 328 noninfectious co-morbid conditions were observed during the entire study period (mean,  $2.9\pm 1.7$ ). Nonsurvivors had a higher number of co-morbid conditions than survivors (mean,  $4.0\pm 1.5$  vs  $2.7\pm 1.6$ ;  $P<0.01$ ; respectively). We noticed a trend towards a higher mortality rate among patients with  $\geq 3$  co-morbidities in comparison with those with 0–2 co-morbidities (26.2% vs 10.6%, respectively; OR, 2.98; 95%CI, 0.91–10.27;  $P=0.07$ ). However, patients with  $\geq 4$  co-morbidities (39 patients; 34.8%) were at a significant risk of death (OR, 4.55; 95%CI, 1.53–13.83;  $P<0.01$ ). Poor performance status, weight loss, hypoalbuminemia, and need of ventilatory support were associated with death in the univariate analysis (Table 3). The median duration of mechanical ventilatory support after the index BC was similar in both groups (survivors, 12 days; range, 1–44 days, vs nonsurvivors, 9 days; range, 1–37 days;  $P=0.55$ ).

A total of 150 pathogens were recovered from blood in the first 48 h of infection. The most frequent isolates were *Enterobacter* spp., CNS, *Klebsiella* spp., *Acinetobacter* spp., and fungi (Table 4). Overall, there was a predominance of aerobic gram-negative bacilli (62%), followed by gram-positive cocci (26.6%) and fungi (9.3%) ( $P<0.001$ ). The observed mortality rates associated with these organism groups were similar (23.6% vs 15% vs 28.6%,

**Table 1** Demographics and main characteristics associated with death in 112 adult surgical cancer patients with BSIs

Characteristic	All patients (n=112)	Survivors (n=90)	Nonsurvivors (n=22)	OR (95%CI)	P value
Mean age in years ( $\pm$ SD)	60.5 $\pm$ 15.7	60.1 $\pm$ 15.3	62.5 $\pm$ 17.4	–	0.34
Sex					
Female [no. (%)]	46 (41.1)	38 (42.2)	08 (36.4)	1	
Male [no. (%)]	66 (58.9)	52 (57.8)	14 (63.3)	0.78 (0.26–2.27)	0.79
Extent of tumor					
Limited disease [no. (%)]	28 (25.0)	27 (30.0)	1 (4.5)	1	
Advanced disease [no. (%)]	84 (75.0)	63 (70.0)	21 (95.5)	9.0 (1.16–191.74)	0.03
Surgical procedures [no. (%)]					
Upper abdominal <sup>a</sup> [no. (%)]	35 (31.3)	27 (30.0)	8 (36.4)	1.33 (0.50–3.55)	0.75
Colon/rectum [no. (%)]	32 (28.6)	26 (28.9)	6 (27.3)	0.92 (0.33–2.62)	1.0
Head and neck [no. (%)]	6 (5.4)	6 (6.7)	0	NA	0.60
Nervous system [no. (%)]	19 (17.0)	17 (18.9)	2 (9.1)	0.43 (0.09–2.02)	0.35
Thoracic [no. (%)]	5 (4.5)	2 (2.2)	3 (13.6)	6.95 (1.08–44.48)	0.05
Genitourinary tract [no. (%)]	9 (8.0)	8 (8.9)	1 (4.5)	0.49 (0.06–4.12)	0.69
Bone/skin-soft tissue [no. (%)]	6 (5.4)	4 (4.4)	2 (9.1)	2.15 (0.37–12.57)	0.34
Presence of CVC					
Yes [no. (%)]	77 (68.7)	63 (70.0%)	14 (63.6%)	1	
No [no. (%)]	35 (31.3)	27 (30.0%)	8 (36.4%)	0.75 (0.28–2.00)	0.75
CVC removal <sup>b</sup>					
Yes [no. (%)]	71 (92.2)	60 (95.2%)	11 (78.6%)	1	
No [no. (%)]	06 (7.8)	03 (4.8)	03 (21.4)	0.18 (0.03–1.03)	0.07

CVC, central venous catheter

<sup>a</sup>Esophagus, gastrointestinal tract, hepatobiliary tract, pancreas, spleen

<sup>b</sup>Calculated from patients in whom a CVC was present: 63 survivors and 14 nonsurvivors

**Table 2** Additional characteristics associated with death in 112 adult surgical cancer patients with BSIs

Characteristic	No. (%) of patients			OR (95%CI)	P value
	All patients (n=112)	Survivors (n=90)	Nonsurvivors (n=22)		
Concomitant infected sites	97 (86.6%)	77 (85.6%)	20 (90.9%)	1.69 (0.35–8.10)	0.73
Pulmonary infiltrate <sup>a</sup>	48 (42.9%)	34 (37.8%)	14 (63.6%)	2.88 (1.09–7.58)	0.05
Surgical site infection	51 (45.5%)	38 (42.2%)	13 (59.1%)	1.98 (0.77–5.10)	0.24
BSI classification					
Monomicrobial	68 (60.7)	59 (65.6)	09 (40.9)	1	
Polymicrobial	44 (39.3)	31 (34.4)	13 (59.1)	2.75 (0.95–8.03)	0.06
Type of BSI					
Persistent	20 (17.9)	18 (20.0)	02 (9.1)	1	
Transitory	92 (82.1)	72 (80.0)	20 (90.9%)	2.50 (0.49–17.26)	0.35
Primary infection					
Yes	48 (42.9)	42 (46.7)	06 (27.3)	1	
No	64 (57.1)	48 (53.3)	16 (72.7)	0.43 (0.13–1.32)	0.16
Inadequate therapy	45 (48.4)	34 (47.2)	11 (52.4)	1.23 (0.41–3.66)	0.87

BSI, bloodstream infection

<sup>a</sup>Radiological lung infiltrates at time of or after index blood culture

respectively;  $P=0.44$ ). The distribution of organism groups was also similar in monomicrobial ( $n=68$ ) and polymicrobial infections ( $n=82$ ): gram-negative rods (61.7% vs 62.2%, respectively), gram-positive cocci (29.4% vs 26.8%), and fungi (7.3% vs 10.9%). We noticed a higher proportion of fungal isolates in persistent infections than in transitory episodes (21.4% vs 6.5%, respectively;  $P=0.03$ ).

Gram-negative rods, gram-positive cocci, and fungi were equally distributed between episodes with and without CVC (rods: 58.6% vs 69.5%,  $P=0.20$ ; cocci: 30.7% vs 21.7%,  $P=0.25$ ; and fungi: 10.6% vs 6.5%,  $P=0.63$ ). Fermentative bacilli were more commonly isolated from patients without catheters (58.7% vs 33.6%, respectively;  $P<0.01$ ). However, nonfermentative isolates were more predominant in patients with CVCs (25% vs 10.8%, respectively;  $P=0.05$ ). There was no association between polymicrobial BSIs and the presence or the absence of a catheter (41.6% vs 34.3%, respectively;  $P=0.60$ ).

A total of 116 (77.3%) microorganisms were available for comparison of susceptibility tests. Thirty-five (30.2%) pathogens were considered resistant. We did not observe a

statistically significant difference in the mortality rate between episodes with resistant and episodes with nonresistant organisms (20% vs 26%, respectively;  $P=0.49$ ). Among the 93 episodes of gram-negative bacteremia, there was not a statistically significant difference in mortality between episodes due to antibiotic-resistant versus susceptible organisms (20.7% vs 25%, respectively;  $P=0.65$ ).

When the variables studied were entered into the multiple logistic regression analysis, five factors were found to independently influence the in-hospital mortality (Table 5): presence of  $\geq 4$  co-morbid conditions, advanced tumor disease, thoracic surgery, CVC retention, and presence of pulmonary infiltrates.

## Discussion

The present prospective cohort study is unique in evaluating the epidemiology and microbiology of nosocomial BSIs in surgical cancer patients and the association of possible variables with death. Most of the published

**Table 3** Distribution of 328 noninfectious co-morbid conditions associated with death in 112 adult surgical cancer patients with BSIs

Main co-morbid condition	No. (%) of patients			95%CI	P value
	All patients (n=112)	Survivors (n=90)	Nonsurvivors (n=22)		
Weight loss	47 (42.0)	35 (38.9)	12 (54.2)	1.89 (0.74–4.83)	0.27
Hypoalbuminemia	42 (37.5)	32 (35.6)	10 (45.5)	1.51 (0.59–3.88)	0.54
Karnofsky score $\leq 60$	94 (83.9)	72 (80.0)	22 (100)	NA	0.02
Hypotension	26 (23.2)	17 (18.9)	9 (40.9)	2.97 (1.09–8.08)	0.05
Ventilatory support	38 (33.9)	25 (27.8)	13 (59.1)	3.76 (1.43–9.88)	0.01
Renal insufficiency	21 (18.8)	13 (14.4)	08 (36.4)	3.38 (1.19–9.66)	0.04
Hyperglycemia	20 (17.9)	17 (18.9)	03 (13.6)	0.68 (0.18–2.56)	0.80
Neurologic dysfunction	21 (18.8)	16 (17.8)	05 (22.7)	1.36 (0.44–4.23)	0.56

NA, not applicable

**Table 4** Distribution of the most common pathogens recovered from the blood of adult surgical cancer patients within the first 48 h of the BSI episode

Microorganism	No. (%) of isolates
<i>Enterobacter</i> spp.	23 (15.3)
Coagulase-negative staphylococci <sup>a</sup>	19 (12.6)
<i>Klebsiella</i> spp.	14 (9.3)
<i>Acinetobacter</i> spp.	14 (9.3)
Fungi <sup>b</sup>	14 (9.3)
<i>Pseudomonas aeruginosa</i>	12 (8.0)
<i>Staphylococcus aureus</i>	11 (7.3)
Enterococci	09 (6.0)
<i>Escherichia coli</i>	07 (4.6)
<i>Serratia</i> spp.	06 (4.0)
Streptococci	06 (4.0)
<i>Citrobacter</i> spp.	05 (3.3)
<i>Proteus</i> spp.	04 (2.6)
Other	06 (4.0)

<sup>a</sup>Of these, 11 were *Staphylococcus epidermidis*.

<sup>b</sup>Of these, 9 were *Candida* spp. (4 *Candida albicans*, 4 *Candida tropicalis*, 1 *Candida glabrata*), 2 *Rhodotorula rubra*, 1 *Rhodotorula glutinis*, 1 *Hansenula anomala*, and 1 *Penicillium* spp.

**Table 5** Multivariate analysis of putative risk factors for mortality in 112 adult surgical cancer patients with BSIs

Variable	Odds ratio (95%CI)
Co-morbid conditions ( $n \geq 4$ )	4.71 (1.42–15.64)
Advanced tumor	34.34 (2.56–459.97)
Thoracic surgery	17.24 (2.03–146.10)
CVC retention	8.85 (1.04–75.25)
Pulmonary infiltrates	3.36 (0.98–11.47)

data originated from patients hospitalized in intensive care units following complex surgical procedures [11, 12].

The limitations of our study derive from the lack of evaluation of patients' clinical status at admission and the lack of adjustment for the course of clinical illness after the surgical procedure. Nevertheless, considering that all operations were elective and that patients' overall conditions were stable with few or no co-morbid conditions at admission, we may speculate that the burden of postoperative clinical status is a direct consequence of complex surgeries for advanced malignant diseases.

Risk factors that independently affect the outcome in multivariate analysis include advanced tumor, thoracic surgery, presence of  $\geq 4$  co-morbid conditions, CVC retention, and pulmonary infiltrates. The wide confidence interval found to the OR of some variables may be due to low statistical power or, in some cases, it may be a reflection of associated co-morbid conditions.

The influence of CVC removal on the outcome of BSIs has been evaluated mainly in nonsurgical cancer patients [13–15]. These studies demonstrated an association of catheter removal with a better prognosis. Catheter withdrawal was not considered appropriate in patients with unstable hemodynamic and hematologic conditions or in

those with a higher probability of death. As stated, catheter retention could be merely a marker of the underlying illness.

Our prognostic final model shows that CVC removal had a significant protective effect on patient outcome. Since the majority of vascular lines were in place for short-term duration, the tendency was to withdraw them immediately for any suspicion of catheter-related infection. This was evidenced by the finding that 73.2% of removals occurred within the first 72 h of a positive BC, and also by the 1-day median time from index BC to CVC removal. Like other authors [16], we found a lower, although not statistically significant (27.3% vs 72.7%;  $P=0.16$ ), proportion of deaths in primary BSIs in comparison with BSIs associated with other infected sites.

The severity of illness, the functional status, and the number of co-morbid conditions in hospitalized patients are increasingly being recognized as important predictors of patient outcome [17]. Moreover, patients with advanced cancers submitted to extensive radical resections have a significantly longer operating time and hospital stay with greater transfusion requirements than those with more limited resections [18]. In our study, the impact of postoperative complications can be inferred from the short time interval between the index BC and death, the seriousness of co-morbid diseases, and the poor performance status. Invasive procedures and the prevalence of resistant organisms also might have contributed to the unfavorable outcome.

In this study, gram-negative bacilli represented 62% of the isolates. This finding highlights the importance of these organisms as the main etiologic agents of BSI in our surgical population. The observed high prevalence of *Acinetobacter* spp., *Enterobacter* spp., and *Pseudomonas* spp. strains is similar to findings of other studies [19–21] in which the authors emphasized the importance of endogenous origin and hospital cross-acquisition in these infections. Martino et al. [22] have also shown a high frequency of catheter-related nonfermentative bacteremia in cancer patients, which was attributed to contaminated fluids, instruments, and material used for patient care. Our study demonstrates that 66% of the cases of gram-negative bacteremia occurred in patients with a CVC in place, with a significant predominance of nonfermentative isolates.

*Candida* spp. have become one of the most common etiologic isolates in BSIs among critically ill surgical patients [23]. Our data demonstrate fungi as the third leading type of organism, together with *Klebsiella* spp. and *Acinetobacter* spp., while *Candida* spp. infections accounted for 64% of bloodstream fungal infections. A temporal trend study in US hospitals [24] has shown a 124% rise in fungal infection rates in general surgical services. This trend was attributed to the strong association of *Candida* infections with the severity of underlying illness, antibiotic exposure, and degree of *Candida* colonization [13, 24, 25]. Other investigators [26] have pointed out the importance of intestinal fungal translocation, total parenteral nutrition, prolonged central vein catheterization, and the cross-transmission route in the

pathogenesis of postoperative fungal infections. The high proportion of fungal isolates during persistent BSIs may be related to variables commonly associated with or able to perpetuate fungemia, such as poor performance status, colonization of patients by yeast, presence of central lines, parenteral nutrition, and antibiotic pressure.

The impact of nosocomial candidemia on outcome is well documented in several studies and is associated with high morbidity and with an increase of hospitalization and total costs [26–28]. In our study, fungi were the fifth most common pathogen recovered from BCs, accounting for 9.3% of the isolates. Several authors have demonstrated that candidemia occurred in compromised patients treated with broad-spectrum antibiotics, many of whom were hospitalized in intensive care units, with organ dysfunction, and who underwent invasive procedures [28, 29]. The attributed mortality is high and depends on the study design and the population under investigation. Although not reaching a statistically comparative significant rate, the observed 28.6% rate of in-hospital mortality due to fungi in the present study represents the highest rate among all groups of organisms. Nevertheless, it is lower than the 36% in-hospital mortality observed at 28 days in the study of Blot et al. [29].

We found no significant difference in the mortality rate between causative microorganisms or between resistant and nonresistant organisms. In vitro resistance of gram-negative bacilli to ceftazidime has been considered indicative of extended-spectrum  $\beta$ -lactamase production or the hyperproduction of Bush group 1 (Amp C)  $\beta$ -lactamases. Although some investigators [30, 31] have shown a strong association between antibiotic-resistant infections and high morbidity and mortality rates, neither we nor other authors [32] were able to demonstrate any adverse effect of resistant isolates on outcome. The administration of inadequate antimicrobial treatment to critically ill patients with BSI has been shown to be associated with poor outcome [33]. In our study, empirical inappropriate therapy was not significantly associated with death. Differences in patient populations, causative organisms, and infection sites may explain these findings. Besides, in our institution, infectious disease specialists have provided prompt consultation, ensuring optimal management of infections and antimicrobial therapy.

In summary, this study provides further insight into the epidemiology and outcome of BSIs in this subgroup of surgical patients at high risk of serious postoperative complications. Direct surveillance activities with rigid adherence to antibiotic and infection control measures in order to minimize colonization pressure and bacterial cross-transmission between patients may effectively interfere with factors associated with an infection-related unfavorable outcome. Moreover, improving preoperative clinical status and tumor staging evaluation can potentially decrease the morbidity and mortality of these major and complex operations.

## References

- Velasco E, Thuler LCS, Martins CAS, Dias LMC, Gonçalves VMSC (1996) Risk factors for infections after abdominal surgery for malignant disease. *Am J Infect Control* 24:1–6
- Haley RW, Culver DH, Morgan WN, White JW, Emori TG, Hooton TM (1985) Identifying patients at high risk of surgical wound infections. *Am J Epidemiol* 121:206–215
- Petti CA, Sanders LL, Trivette SL, Briggs J, Sexton DJ (2002) Postoperative bacteremia secondary to surgical site infection. *Clin Infect Dis* 34:305–308
- Gottlieb GS, Fowler VG, Kong LK, McClelland RS, Gopal AK, Marr KA, Li J, Sexton DJ, Glower D, Corey GR (2000) *Staphylococcus aureus* bacteremia in the surgical patient: a prospective analysis of 73 postoperative patients who developed *Staphylococcus aureus* bacteremia at a tertiary facility. *J Am Coll Surg* 190:50–57
- Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, Wolff M, Spencer RC, Hemmer M (1995) The prevalence of nosocomial infection in intensive care units in Europe (EPIC). *J Am Med Assoc* 274:639–644
- Rello J, Ricart M, Mirelis B, Quintana E, Gurgui M, Net A, Prats G (1994) Nosocomial bacteremia in a medical-surgical intensive care unit: epidemiologic characteristics and factors influencing mortality in 111 episodes. *Intensive Care Med* 20:94–98
- Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM (1988) CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 16:128–140
- Karnofsky DA, Burchenot JH (1949) The clinical evaluation of chemotherapeutic agents in cancer. In: MacLead CM (ed) *Evaluation of chemotherapeutic agents*. Columbia University, New York, pp 191–205
- Miller JM, O'Hara CM (1995) Substrate utilization systems for the identification of bacteria and yeast. In: Murray PR, Baron EJ, Pfaller MA, Tenoer FC, Tenover FC, Tenover FC (eds) *Manual of clinical microbiology*. American Society for Microbiology, Washington, pp 103–109
- National Committee for Clinical Laboratory Standards (2000) *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically*. Approved standard M7-A5. NCCLS, Wayne
- Blumberg HM, Jarvis WR, Soucie JM, Edwards JE, Patterson JE, Pfaller MA, Rangel-Frausto MS, Rinaldi MG, Saiman L, Wiblin RT, Wenzel RP, The National Epidemiology of Mycoses Survey (NEMIS) Study Group (2001) Risk factors for candidal BSIs in surgical intensive care unit patients: the NEMIS prospective multicenter study. *Clin Infect Dis* 33:177–186
- Pittet D, Tarara D, Wenzel RP (1994) Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributed mortality. *J Am Med Assoc* 271:1598–1601
- Nguyen MH, Peacock JE Jr, Tanner DC, Morris AJ, Nguyen ML, Snyderman DR, Wagener MM, Yu VL (1995) Therapeutic approaches in patients with candidemia: evaluation of a multicenter, prospective, observational study. *Arch Intern Med* 155:2429–2435
- Nucci M, Silveira MI, Spector N, Silveira F, Velasco E, Akiti T, Barreiros G, Derossi A, Colombo AL, Pulcheri W (1998) Risk factors for death among cancer patients with fungemia. *Clin Infect Dis* 27:107–111
- Velasco E, Byington R, Martins CAS, Schirmer M, Dias LMC, Gonçalves VMSC (2003) Prospective evaluation of the epidemiology, microbiology, and outcome of bloodstream infections in hematologic patients in a single cancer center. *Eur J Clin Microbiol Infect Dis* 22:137–143
- Renaud B, Brun-Buisson C (2001) Outcomes of primary and catheter-related bacteremia: a cohort and case-control study in critically ill patients. *Am J Respir Crit Care Med* 163:1584–1590

17. Pompei P, Charlson ME, Ales K, MacKenzie CR, Norton M (1991) Relating patient characteristics at the time of admission to outcomes of hospitalization. *J Clin Epidemiol* 44:1063–1069
18. Cuschieri A, Weeden S, Fielding J, Bancewicz J, Craven J, Joypaul V, Sydes M, Fayers P (1999) Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical Co-operative Group. *Br J Cancer* 79:1522–1530
19. D'Agata EMC, Thayer V, Schaffner W (2000) An outbreak of *Acinetobacter baumannii*: the importance of cross-transmission. *Infect Control Hosp Epidemiol* 21:588–591
20. Cantón R, Oliver A, Coque TM, Varela MC, Pérez-Días JC, Baquero F (2002) Epidemiology of extended-spectrum  $\beta$ -lactamase-producing *Enterobacter* isolates in a Spanish hospital during a 12-year period. *J Clin Microbiol* 40:1237–1243
21. Thuong M, Arvaniti K, Ruimy R, de la Salmoniere P, Scanvic-Hameg A, Lucet JC, Regnier B (2003) Epidemiology of *Pseudomonas aeruginosa* and risk factors for carriage acquisition in an intensive care unit. *J Hosp Infect* 53:274–282
22. Martino R, Gomez L, Pericas R, Salazar R, Sola C, Sierra J, Garau J (2000) Bacteremia caused by non-glucose-fermenting gram-negative bacilli and *Aeromonas* species in patients with haematological malignancies and solid tumours. *Eur J Clin Microbiol Infect Dis* 19:320–323
23. Vincent JL, Anaissie E, Bruining H, Demajo W, el-Ebiary M, Haber J, Hiramatsu Y, Nitenberg G, Nystrom PO, Pittet D, Rogers T, Sandven P, Sganga G, Schaller MD, Solomkin J (1998) Epidemiology, diagnosis and treatment of systemic candidal infection in surgical patients under intensive care. *Intensive Care Med* 24:206–216
24. Beck-Sagué CM, Jarvis WR, The National Nosocomial Infections Surveillance System (1993) Secular trends in the epidemiology of nosocomial fungal infections in the United States, 1980–1990. *J Infect Dis* 167:1247–1251
25. Pittet D, Monod M, Suter PM, Frenk E, Auckenthaler R (1994) *Candida* colonization and subsequent infections in critically ill surgical patients. *Ann Surg* 220:751–758
26. Wey SB, Mori M, Pfaller MA, Woollen RF, Wenzel RP (1989) Risk factors for hospital-acquired candidemia. *Arch Intern Med* 149:2349–2353
27. Gudlaugsson O, Gillespie S, Lee K, Vande Berg J, Hu J, Messer S, Herwaldt L, Pfaller M, Diekema D (2003) Attributable mortality of nosocomial candidemia, revisited. *Clin Infect Dis* 37:1172–1177
28. Pappas PG, Rex JH, Lee J, Hamill RJ, Larsen RA, Powderly W, Kauffman CA, Hyslop N, Mangino JE, Chapman S, Horowitz HW, Edwards JE, Dismukes WE, The NIAID Mycoses Study Group (2003) A prospective observational study of candidemia: epidemiology, therapy, and influences on mortality in hospitalized adult and pediatric patients. *Clin Infect Dis* 37:634–643
29. Blot SI, Vandewoude KH, Hoste EA, Colardyn FA (2002) Effects of nosocomial candidemia on outcomes of critically ill patients. *Am J Med* 113:480–485
30. Lortholary O, Fagon JY, Hoi AB, Slama MA, Pierre J, Giral P, Rosenzweig R, Gutmann L, Safar M, Acar J (1995) Nosocomial acquisition of multiresistant *Acinetobacter baumannii*: risk factors and prognosis. *Clin Infect Dis* 20:790–796
31. Acar JF (1997) Consequences of bacterial resistance to antibiotics in medical practice. *Clin Infect Dis* 24(Suppl 1): S17–S18
32. Blot S, Vandewoude K, De Bacquer D, Colardyn F (2002) Nosocomial bacteremia caused by antibiotic-resistant gram-negative bacteria in critically ill patients: clinical outcome and length of hospitalization. *Clin Infect Dis* 34:1600–1606
33. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH (2000) The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest* 118:146–155