ORIGINAL RESEARCH

Sepsis-Associated Outcomes in Critically Ill Patients with Malignancies

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Abstract

Rationale: Sepsis is a major cause of mortality among critically ill patients with cancer. Information about clinical outcomes and factors associated with increased risk of death in these patients is necessary to help physicians recognize those patients who are most likely to benefit from ICU therapy and identify possible targets for intervention.

Objectives: In this study, we evaluated cancer patients with sepsis chosen from a multicenter prospective study to characterize their clinical characteristics and to identify independent risk factors associated with hospital mortality.

Methods: Subgroup analysis of a multicenter prospective cohort study conducted in 28 Brazilian intensive care units (ICUs) to evaluate adult cancer patients with severe sepsis and septic shock. We used logistic regression to identify variables associated with hospital mortality.

Measurements and Main Results: Of the 717 patients admitted to the participating ICUs, 268 (37%) had severe sepsis (n = 142, 53%) or septic shock (n = 126, 47%). These patients comprised the population of the present study. The mean score on the third version of the Simplified Acute Physiology Score was 62.9 ± 17.7 points, and the median Sequential Organ Failure Assessment score was 9 (7–12) points. The most frequent sites of infection were the lungs (48%), intraabdominal region (25%), bloodstream as primary infection (19%), and urinary tract (17%). Half of the patients had microbiologically proven infections, and Gram-negative bacteria were the most common pathogens causing sepsis (31%). ICU and hospital mortality rates were 42% and 56%, respectively. In multivariable analysis, the number of acute organ dysfunctions (odds ratio [OR], 1.48; 95% confidence interval [CI], 1.16–1.87), hematological malignancies (OR, 2.57; 95% CI, 1.05–6.27), performance status 2–4 (OR, 2.53; 95% CI, 1.44–4.43), and polymicrobial infections (OR, 3.74; 95% CI, 1.52–9.21) were associated with hospital mortality.

Conclusions: Sepsis is a common cause of critical illness in patients with cancer and remains associated with high mortality. Variables related to underlying malignancy, sepsis severity, and characteristics of infection are associated with a grim prognosis.

Keywords: cancer; infection; intensive care; malignancy; sepsis

Although major advances in the care of patients with cancer over the past few decades have resulted in improved survival, there are still complications during the course of disease that are associated with significant morbidity and mortality. With the improvement of cancer care, patients live longer, and immunosuppression caused by the underlying disease and owing to aggressive and prolonged treatments increase their susceptibility to severe infections (1).

In the context of patients with cancer admitted to intensive care units (ICUs), sepsis is a major concern because one in every six patients with sepsis admitted to an ICU has cancer, and sepsis is the leading reason for ICU admission in patients with cancer (1–4). The incidence of sepsis in patients with cancer is approximately 10-fold greater than in the noncancer population (2). In comparison to general patients with sepsis, patients with cancer also experience prolonged lengths of stay and higher morbidity and mortality (5).

Most of the studies in critically ill cancer patients with sepsis done to date were single-center retrospective studies performed in cancer centers, which reduces the generalizability of their findings. In addition, most studies were done in developed countries, and there is a lack of information on the outcomes of these patients in developing countries with elevated sepsis mortality and where there is a shortage of ICU beds and unequal resource allocation, such as Brazil (6, 7). Therefore, information about clinical outcomes and factors associated with increased risk of death in these patients is necessary to help physicians recognize those patients who are most likely to benefit from ICU therapy and identify possible targets for intervention (8). Although some indicators of poor prognosis have already been recognized, there is a need for better risk stratification assessment. Such information is essential for planning the provision of ICU services, especially in emerging countries such as Brazil.

In this study, we evaluated cancer patients with sepsis chosen from a multicenter prospective study to describe their clinical characteristics and to identify independent risk factors present on the first day of admission that were associated with hospital mortality.

Methods

Design, Setting, and Eligibility Criteria

This study was a subgroup analysis of a multicenter prospective cohort study conducted in 28 Brazilian ICUs between August 1 and September 30, 2007 (4). The full list of participating sites and investigators is given in the Appendix. The study was observational and did not require any deviation from routine medical practice. The Cancer Institute Ethics Committee approved the study (013/07). Local institutional review boards at each participating institution, as well as the Brazilian National Ethics Commission, approved the trial. Informed consent was not required in any of the participating centers.

We evaluated all adult patients (≥18 yr) with a definite diagnosis of cancer and sepsis at ICU admission or during their ICU stay. Patients in complete cancer remission for more than 5 years and readmissions to the ICU were not considered.

Infection was defined as the presence of a pathogenic microorganism in a sterile site (such as blood, cerebrospinal fluid, or ascites) or clinically suspected infection that needed administration of antibiotics (9, 10). *Sepsis* was defined according to the consensus definitions (11). *Severe sepsis* was defined as sepsis associated with organ dysfunction, and septic shock was characterized by persistent arterial hypotension unexplained by other causes (a systolic arterial pressure <90 mm Hg, a mean arterial pressure <60 mm Hg, or a reduction in systolic blood pressure >40 mm Hg from baseline, despite adequate volume replenishment, in the absence of other cause of hypotension).

Data Collection and Processing

For data collection, we used preprinted case report forms on the first day in the ICU. For patients who developed sepsis during their ICU stay, data analyzed (other than those related to the sepsis episode) in this study were those obtained during the first day of the ICU stay.

We collected the following information in every studied patient: demographics; clinical and laboratory data, including concomitant diseases; reason for ICU admission; type of admission (medical or surgical); Sequential Organ Failure Assessment (SOFA) score (12); score on the third version of the Simplified Acute Physiology Score (SAPS 3) (13); and the Adult Comorbidity Evaluation 27 (ACE-27) score (14). Organ failure was defined as a SOFA score of at least 2 points for the organ in question (15). The need for dialysis, vasopressors, and ventilatory support (invasive and noninvasive mechanical ventilation) was also assessed.

Cancer- and treatment-related variables were recorded, and this included performance status (PS) based on the Eastern Cooperative Oncology Group scale (16) and type of cancer (solid or hematological malignancy). For solid tumors, the presence of metastases was also recorded. Cancer status was classified in remission (without evidence of recurrence), active (diagnosed within the last 3 mo), and relapse (recurrent disease). *Neutropenia* was defined as a neutrophil count less than 500/mm^3. Microbiological and clinical infection data were also reported. *Standardized mortality rate* (SMR), defined as the quotient of observed to predicted mortality by SAPS 3 admission score, was also estimated using the customized equation for Caribbean and South American countries (13). Vital status at hospital discharge was the main outcome of interest.

Statistical Analysis

Data were analyzed using IBM SPSS 20.0 for Windows software (IBM, Armonk, NY). Descriptive statistics were computed for all study variables. Discrete variables were expressed as counts (percentage), and continuous variables were reported as mean ± standard deviation or median (25–75% interquartile range [IQR]) as appropriate.

For demographics and clinical characteristics of the study groups, differences between groups were assessed using the χ^2 test, Fisher's exact test, Student's *t* test, or the Mann-Whitney U test, as appropriate. Univariate and multivariable logistic regression were used to identify factors associated with hospital mortality (17). Linearity between each continuous variable and the dependent variable was demonstrated using locally weighted scatterplot smoothing (17). Variables yielding *P* values less than 0.2 by univariate analysis, and those considered

clinically relevant were entered in the multivariable analysis to estimate the independent association of each covariate with the dependent variable.

The results of multivariable analysis were summarized as odds ratios (ORs) and respective 95% confidence intervals (CIs). Possible interactions were tested. The area under the receiver operating characteristic curve was used to assess model discrimination. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test (17). With this test, *P* values greater than 0.05 indicate a good fit for the model. All statistics were two-tailed, and *P* < 0.05 was considered significant.

Results

Characteristics of the Study Population

Of the 717 patients admitted to the 28 participating ICUs during the study period, 268 (37%) patients had sepsis and constituted the present study population. Table 1 depicts the patients' main characteristics. Patients were admitted to the ICU at a median of 3 (IQR, 0–13) days after hospital admission, and the median durations of ICU and hospital stays were 7 (IQR, 4–16) and 22 (IQR, 13–38) days, respectively. The mean SAPS 3 score was 63 ± 18 points. Using the customized equation for evaluating SAPS 3 scores among Central and South American patients, we estimated the probability of death in 52.9% (95% CI, 49.6–56.2%), and the SMR was 1.05 (95% CI, 0.90–1.23).

Ventilatory support was required by 203 patients (76%) during their ICU stay. Vasopressors and renal replacement therapy were used in 155 (59%) and 49 (18%) patients, respectively. The most common

Table 1. Patients' characteristics and univariate analysis of predictors of hospital mortality

Variables	All Patients (n = 268)	Survivors (n = 119, 44%)	Nonsurvivors (n = 149, 56%)	Odds Ratio (95% CI)	P Value
Age, yr	63.1 ± 15.0	64.0 ± 16.1	62.5 ± 14.1	0.99 (0.97–1.00)	0.401
Male sex	126 (47%)	57 (48%)	69 (46%)	1.07 (0.66–1.73)	0.892
Hospital stay before ICU admission, days	3 (0–13)	2 (0–8)	4 (0–15)	1.11 (0.95–1.30)	0.187
Medical admission	169 (63%)	61 (51%)	108 (72%)	2.51 (1.51–4.16)	0.001
ACE-27 comorbidity score					
None or mild	128 (48%)	60 (50%)	68 (46%)	Ref.	0.512
Moderate to severe	140 (52%)	59 (50%)	81 (54%)	1.21 (0.75–1.96)	
SAPS 3 score, points	62.9 ± 17.7	55.8 ± 16.5	68.6 ± 16.6	1.05 (1.03–1.06)	<0.001
SOFA score on first day in ICU, points	9 (7–12)	8 (7–11)	11 (8–13)	1.21 (1.12–1.31)	<0.001
Acute organ failures, *n*	4 (3–4)	3 (3–4)	4 (3–5)	1.52 (1.22–1.88)	<0.001
Cancer-related characteristics					
Type of cancer					
Locoregional solid tumor	154 (57%)	81 (68%)	73 (49%)	Ref.	0.006
Metastatic solid tumor	79 (30%)	28 (24%)	51 (34%)	2.02 (1.16–3.54)	
Hematological malignancy	35 (13%)	10 (8%)	25 (17%)	2.77 (1.25–6.17)	
Cancer status					
Controlled and/or in remission	29 (11%)	16 (13%)	13 (9%)	Ref.	0.301
Active newly diagnosed	145 (54%)	66 (55%)	79 (53%)	1.47 (0.66–3.28)	
Active recurrence and/or progression	94 (35%)	37 (31%)	57 (38%)	1.90 (0.82–4.40)	
Performance status					
0–1	115 (43%)	67 (56%)	48 (32%)	Ref.	<0.001
2–4	153 (57%)	52 (44%)	101 (68%)	2.71 (1.65–4.47)	
Neutropenia	31 (12%)	10 (8%)	21 (14%)	1.79 (0.81–3.96)	0.209
Bone marrow transplantation	8 (3%)	1 (1%)	7 (5%)	5.82 (0.71–47.95)	0.080
Chemotherapy and/or radiotherapy	145 (54%)	64 (54%)	81 (54%)	1.02 (0.63–1.66)	0.999
Cancer-related complications	134 (50%)	48 (40%)	86 (58%)	2.02 (1.24–3.30)	0.007
Organ support					
Dialysis	49 (18%)	8 (7%)	41 (28%)	5.32 (2.38–11.87)	<0.001
Vasopressors	155 (59%)	43 (36%)	112 (75%)	5.35 (3.15–9.06)	<0.001
Ventilatory support					
No	65 (24%)	51 (43%)	14 (9%)	Ref.	<0.001
NIV	24 (9%)	12 (8%)	12 (10%)	3.64 (1.35–9.85)	
NIV with subsequent intubation for MV	43 (16%)	17 (14%)	26 (17%)	5.57 (2.38–13.04)	
MV	136 (51%)	39 (33%)	97 (65%)	9.06 (4.51–18.22)	
Outcome data					
ICU LOS, days	7 (4 – 16)	6 (3–11)	9 (5–21)	—	0.001
Hospital LOS, days	22 (13 – 38)	20 (15–35)	24 (11–40)	—	0.482
End-of-life decisions	47 (17%)	—	—		—
ICU mortality	114 (42%)	—	—		—
Hospital mortality	149 (56%)	—	—		—

Definition of abbreviations: ACE-27 = Adult Comorbidity Evaluation 27; CI = confidence interval; ICU = intensive care unit; LOS = length of stay; MV = mechanical ventilation; NIV = noninvasive ventilation; Ref. = reference category; SAPS 3 = third version of the Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment.
The results are expressed as mean ± standard deviation, median (25–75% interquartile range), and n (%).

reasons for ICU admission were severe sepsis or septic shock (39%), followed by complications in the postoperative period (23%) and acute respiratory failure (17%).

Cancer-related Characteristics

There were 239 patients (89%) with active cancer, and 233 patients (87%) had solid tumors (Table 1). Only 35 (13%) of the patients had hematologic cancers, which comprised mostly non-Hodgkin lymphomas (4% of the entire study population), acute leukemias (4%), and multiple myeloma (3%). The most frequent primary sites of solid tumors were

gastrointestinal (25%), urogenital (15%), lung (9%), liver and biliary tract (8%), head and neck (7%), brain (7%), and breast (6%).

Infection-related Characteristics

In Table 2, we report the main infection-related characteristics. Nosocomial infections were more frequent than community-acquired infections in our patients. Pneumonia was the most frequent site of infection (48%), followed by intraabdominal, primary bloodstream, and urinary tract infections (25%, 19%, and 17%, respectively). Microbiological documentation of sepsis was obtained for

50% of the patients. Gram-negative bacteria were more often isolated in microbiologically documented infections (31%) than Gram-positive bacteria (13%) were, and 36 patients (13%) had polymicrobial infections.

Outcome Analysis

The ICU and in-hospital mortality rates were 42% and 56%, respectively. End-of-life decisions (to withdraw or withhold life-sustaining therapies) were made in 17% of the patients. In the univariate analysis, predictors of in-hospital mortality were type of admission, hospital length of stay before

Table 2. Infection-related characteristics and univariate analysis of predictors of hospital mortality*

Variables	All Patients (n = 268)	Survivors (n = 119, 44%)	Nonsurvivors (n = 149, 56%)	Odds Ratio (95% CI)	P Value
Proof of infection					
Clinically suspected	133 (50%)	69 (58%)	64 (43%)	Ref.	0.021
Microbiologically proven, one pathogen	99 (37%)	40 (34%)	59 (40%)	1.59 (0.94–2.69)	
Microbiologically proven, polymicrobial	36 (13%)	10 (8%)	26 (17%)	2.80 (1.25–6.27)	
Severity					
Severe sepsis	142 (53%)	78 (66%)	64 (43%)	Ref.	<0.001
Septic shock	126 (47%)	41 (34%)	85 (57%)	2.53 (1.54–4.16)	
Acquisition					
Community	87 (32%)	40 (34%)	47 (32%)	Ref.	0.208
Nosocomial, at ICU admission	107 (40%)	41 (34%)	66 (44%)	1.37 (0.77–2.43)	
Nosocomial, after ICU admission	74 (28%)	38 (32%)	36 (24%)	0.81 (0.43–1.50)	
Pathogens*					
Gram-positive bacteria	34 (13%)	13 (11%)	21 (14%)	—	—
Coagulase-negative *Staphylococcus*	13 (5%)	5 (4%)	8 (5%)	—	—
Staphylococcus aureus, MSSA	11 (4%)	5 (4%)	6 (4%)	—	—
Staphylococcus aureus, MRSA	11 (4%)	3 (3%)	8 (5%)	—	—
Pneumococci	4 (1%)	1 (1%)	3 (2%)	—	—
Gram-negative bacteria	83 (31%)	33 (28%)	50 (34%)	—	—
Escherichia coli	27 (10%)	13 (11%)	14 (9%)	—	—
Pseudomonas spp.	29 (11%)	8 (7%)	21 (14%)	—	—
Klebsiella spp.	27 (10%)	12 (10%)	15 (10%)	—	—
Acinetobacter spp.	7 (3%)	3 (3%)	4 (3%)	—	—
Serratia spp.	1 (1%)	0	1 (1%)	—	—
Stenotrophomonas maltophilia	3 (1%)	2 (2%)	1 (1%)	—	—
Fungi					
Candida spp.	12 (4%)	4 (3%)	8 (5%)	—	—
Aspergillus spp.	1 (1%)	1 (1%)	0	—	—
Other infectious agents	39 (15%)	10 (8%)	29 (19%)	—	—
Virus	2 (1%)	0	2 (1%)	—	—
Site of infection					
Lung	130 (48%)	60 (50%)	70 (47%)	0.87 (0.54–1.41)	0.662
Intraabdominal	67 (25%)	24 (20%)	43 (29%)	1.61 (0.91–2.84)	0.136
Urinary tract	45 (17%)	20 (17%)	25 (17%)	0.99 (0.52–1.90)	0.999
Primary bloodstream infection	51 (19%)	20 (17%)	31 (21%)	1.30 (0.70–2.42)	0.502
Skin and/or soft tissue	26 (10%)	6 (5%)	10 (7%)	1.36 (0.48–3.84)	0.754
Surgical site infection	18 (7%)	9 (8%)	9 (6%)	0.79 (0.30–2.05)	0.803
Central nervous system	3 (1%)	2 (2%)	1 (1%)	0.40 (0.04–4.41)	0.844
Sinusitis	1 (1%)	0	1 (1%)	—	—
Other or unknown	17 (6%)	7 (6%)	10 (7%)	1.15 (0.43–3.12)	0.980
More than one site of infection	71 (26%)	28 (24%)	43 (29%)	1.32 (0.76–2.29)	0.399

Definition of abbreviations: CI = confidence interval; ICU = intensive care unit; MSSA = methicillin-sensitive *S. aureus*; MRSA = methicillin-resistant *S. aureus*; Ref. = reference category.
The results expressed as n (%).
*One hundred thirty-five patients had microbiologically proven infections; patients could have more than one pathogen.

| Variables	Coefficients	Odds Ratio (95% CI)	P-value
Medical admission			
No		1.00	
Yes	0.534	1.71 (0.95–3.07)	0.075
Organ dysfunctions (n)	0.389	1.48 (1.16–1.87)	0.001
Type of cancer			
Locoregional solid tumor		1.00	
Metastatic solid tumor	0.555	1.74 (0.93–3.27)	0.084
Hematological malignancies	0.943	2.57 (1.05–6.27)	0.038
Performance status			
0–1		1.00	
2–4	0.927	2.53 (1.44–4.43)	0.001
Proof of infection			
Clinically suspected		1.00	
Microbiologically proven, one pathogen	0.329	1.39 (0.78–2.48)	0.268
Microbiologically proven, polymicrobial	1.320	3.74 (1.52–9.21)	0.004
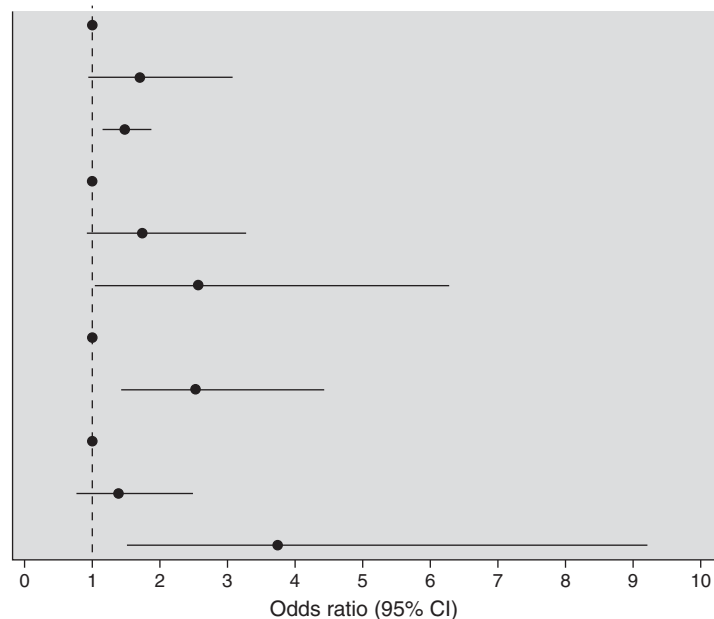
Figure 1. Multivariable analysis and adjusted odds ratios for hospital mortality of critically ill cancer patients with sepsis. Odds ratios greater than 1.0 indicate an increased risk of death. Constant, −2.566; area under the receiving operating characteristic curve, 0.74 (95% CI, 0.68–0.79); Hosmer-Lemeshow goodness-of-fit $\chi^2 = 7.182$; $P = 0.517$. CI = confidence interval.

ICU admission, individual organ failures, SOFA score at Day 1, SAPS 3 score, type of cancer, cancer status, PS, cancer-related complications, and need for organ support (Table 1). Additionally, nosocomial infections as well as polymicrobial infections and septic shock were associated with in-hospital mortality (Table 2). In the logistic regression analysis, the number of organ dysfunctions, hematological malignancy, poor PS, and presence of polymicrobial infections were independent predictors of in-hospital mortality (Figure 1).

Table 3 shows the combination of the factors associated with mortality in multivariable analysis. The concomitance of solid metastatic disease or hematological malignancy with poor PS and/or more than two organ failures was associated with reduced chance of survival. Patients with sepsis and good PS and fewer organ failures had an increased likelihood of survival.

Discussion

In the present study, we demonstrated that sepsis was a frequent complication of critically ill patients with cancer, and it was associated with substantial ICU and hospital mortality (42% and 56%, respectively). The mortality rates in our patients are comparable to those reported in previous studies (1, 18) and are in accordance with predicted mortality based on the SAPS 3 score. Moreover, our patients were admitted to the ICU with a median of four organ failures, illustrating substantial disease severity. As expected, mortality rates were higher for patients with septic shock and for those with hospital-acquired infection than for those with community-acquired sepsis. In addition, patients with poor PS and polymicrobial infections had increased risk of hospital death. It is also noteworthy that mortality risk in our patients was related more to the intensity of sepsis *per se* than to characteristics of underlying malignancy, because the presence of organ dysfunctions was associated with increased mortality and the presence of

Table 3. Intensive care unit and hospital mortality rates for subgroups of patients with cancer and sepsis

Clinical Characteristics	ICU Mortality	Hospital Mortality
All patients, n = 268	42% (36–48%)	56% (50–62%)
Patients with good PS, n = 115	30% (23–39%)	42% (33–51%)
Patients with poor PS, n = 153	52% (44–59%)	66% (58–72%)
Locoregional solid tumor + good PS, n = 79	27% (18–37%)	36% (26–46%)
Locoregional solid tumor + OF ⩽2, n = 126	39% (31–48%)	50% (41–58%)
Metastatic cancer + poor PS + OF >2, n = 47	60% (45–72%)	70% (54–80%)
Hematological patients + OF ⩽2, n = 8	13% (2–47%)	50% (21–79%)
Hematological patients + OF >2, n = 27	67% (48–81%)	78% (59–89%)

Definition of abbreviations: ICU = intensive care unit; OF = organ failure; PS = performance status.
Data are reported as percentage (95% confidence interval).

neutropenia and disease progression was not.

Rational patient selection for ICU admission in critically ill cancer patients may improve the use of ICU resources by admission of patients who have favorable prospects for survival. In this regard, the results of the present study are in accordance with the literature demonstrating that characteristics previously considered important for survival, such as neutropenia and disease progression, are no longer reliable for assessing the potential benefits of ICU admission (1, 19, 20).

Important variables identified in our study that are determinants of hospital mortality are the patient's level of functioning as assessed by PS and the number of organ dysfunctions at admission, as well as the presence of hematological malignancy. Evaluations for these risk factors are easily done before or early during ICU admission and may help to identify patients who will benefit most from ICU admission.

Previous studies correlated the delay between physiological derangement and intervention before ICU admission with increased mortality (21). Early aggressive management of organ dysfunctions could prevent progression to multiorgan failure and death (18). Early recognition and treatment of patients with sepsis requires close collaboration between hematologists and intensivists and can ultimately improve the outcomes of this specific subset of patients. In addition, our results can assist physicians in triage processes for ICU admission and decisions related to patients' care.

In this study, the presence of hematological disease was an independent risk factor for mortality in multivariable analysis. Previous studies demonstrated that this patient population is at risk for increased mortality during severe sepsis (18), although recent trials demonstrated improved outcomes in critically ill patients with hematological malignancies (22–24).

As such, decisions to admit these patients to the ICU must be made regarding previous PS (another independent risk factor identified in the present study) and availability of potentially life-prolonging treatments (25).

We identified polymicrobial infections as an independent risk factor for mortality. Previous studies indicated that these infections have more than doubled in frequency since the early 1970s and currently account for 14–31% of documented bacterial infections in cancer patients, a picture similar to the one described in our study (26, 27). Polymicrobial sepsis comprises predominantly tissue-based infections and is associated with greater morbidity and mortality than is monomicrobial infection (28, 29). We also demonstrated the importance of considering these infections in ICU patients with cancer, based on the fact that clinical suspicion of polymicrobial sepsis may lead to early changes in empirical antimicrobial therapy. These infections commonly need treatment with a broad antimicrobial regimen and are frequently related to inadequate choice of antibiotics (30).

Because hospitalized patients with cancer are at increased risk for severe infections, especially by multidrug-resistant organisms, choosing the initial empirical antibiotic therapy in these patients is often a clinical challenge. In this regard, surveillance data from the geographical area, the institution, and the ward may be helpful (31). Our results highlight the importance of continuous microbiological surveillance studies and preventive measures such as removal of unnecessary invasive devices in ICUs that support critically ill cancer patients with the objective of monitoring and preventing infections caused by antibiotic-resistant pathogens.

Some strengths of our study are worth mentioning. This is a prospective multicenter study that comprised mostly ICUs not specializing in cancer. As such, the chance of bias is reduced compared with single-center retrospective studies, and the external validity of our results is higher, especially for general ICUs that admit cancer patients.

Our study also has limitations. Despite the fact that the presence of hematological disease was an independent risk factor for mortality, few (13%) of our patients had hematological malignancies, so these results must be interpreted with caution. Few patients had opportunistic infections, including those caused by invasive fungi and viruses, and we could not assess the burden of these specific agents in relation to patient outcomes. We could not assess data on specific prescribed antimicrobial agents and control of sepsis source; therefore, data regarding the adequacy of antimicrobial regimens were not collected. Moreover, we also did not assess the use of adjunctive therapies for sepsis and processes of care. We did not evaluate patients after their first day in the ICU, so we were not able to assess other risk factors in relation to outcome occurring after this date, nor could we gather information regarding the response to ICU treatment. Our definition of *sepsis*, as used in previous studies (1, 24), included patients with microbiological evidence of microbiological comprobation, as well as those without such evidence, which may lead to several biases. Another limitation concerns the comparison of cancer patients with a huge heterogeneity in case mix and distinct drug toxicities associated with cancer-specific treatments.

To conclude, sepsis is a common cause of critical illness in patients with cancer and remains associated with high mortality. The degree of sepsis severity as measured by number of failing organs, poor prior functional status, hematological as compared with solid malignancy, and polymicrobial infection were associated with worse prognosis in patients with sepsis and cancer. ■

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Appendix

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