Characteristics and outcomes of patients with cancer requiring admission to intensive care units: A prospective multicenter study*

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Objective: To evaluate the characteristics and outcomes of patients with cancer admitted to several intensive care units. Knowledge on patients with cancer requiring intensive care is mostly restricted to single-center studies.

Design: Prospective, multicenter, cohort study.

Setting: Intensive care units from 28 hospitals in Brazil.

Patients: A total of 717 consecutive patients included over a 2-mo period.

Interventions: None.

Measurements and Main Results: There were 667 (93%) patients with solid tumors and 50 (7%) patients had hematologic malignancies. The main reasons for intensive care unit admission were postoperative care (57%), sepsis (15%), and respiratory failure (10%). Overall hospital mortality rate was 30% and was higher in patients admitted because of medical complications (58%) than in emergency (37%) and scheduled (11%) surgical patients (p < .001). Adjusting for covariates other than the type of

admission, the number of hospital days before intensive care unit admission (odds ratio [OR], 1.18; 95% confidence interval [CI], 1.01–1.37), higher Sequential Organ Failure Assessment scores (OR, 1.25; 95% CI, 1.17–1.34), poor performance status (OR, 3.40; 95% CI, 2.19–5.26), the need for mechanical ventilation (OR, 2.42; 95% CI, 1.51–3.87), and active underlying malignancy in recurrence or progression (OR, 2.42; 95% CI, 1.51–3.87) were associated with increased hospital mortality in multivariate analysis.

Conclusions: This large multicenter study reports encouraging survival rates for patients with cancer requiring intensive care. In these patients, mortality was mostly dependent on the severity of organ failures, performance status, and need for mechanical ventilation rather than cancer-related characteristics, such as the type of malignancy or the presence of neutropenia. (Crit Care Med 2010; 38:9–15)

KEY WORDS: cancer; intensive care unit; mortality; multicenter study; outcome

ntensive care units (ICUs) have become essential for the care of patients with cancer. In recent large multicenter studies, these patients accounted for up to 15% of all ICU admissions (1–3). Patients with cancer require ICU admission for postopera-

tive care after major surgical resections, severe cancer- or chemo-radiation-related complications, and concurrent severe acute illnesses. However, admitting patients with cancer to the ICU may be a matter of substantial controversy. Although advances in oncology and sup-

portive care seem to be associated with improvements in patients' survival rates, many intensivists are still reluctant to transfer these patients to the ICU. In contrast, the inappropriate institution of full code, thus prolonging the life of patients with dismal chances of recovery, may re-

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text,

and links to the digital files are provided in the HTML and PDF versions of this article on the journal's Web site (www.ccmjournal.org).

This study was supported, in part, by Instituto Nacional de Câncer.

Dr. Soares and Dr. Bozza are supported, in part, by individual research grants from CNPq. The remaining authors have not disclosed any potential conflicts of interest.

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DOI: 10.1097/CCM.0b013e3181c0349e

sult in medical futility and, consequently, suffering and dissatisfaction for patients, relatives, and the ICU team.

A better understanding of the factors that potentially influence patients' outcomes can help healthcare professionals make appropriate management decisions. During the last decade, medical literature has a multitude of studies demonstrating improved survival rates for critically ill patients with cancer and expanding the knowledge on their outcomes and prognostic factors in different scenarios (4-12). Nonetheless, most of them were single-centered studies conducted in specialized hemato-oncologic ICUs, which may limit the extrapolation of their findings to general ICUs. To our knowledge, only two studies on this subject carried out in multiple institutions were reported in the literature. The first one was published by Groeger and coworkers more than one decade ago (13). Very recently, Taccone et al studied the subgroup of patients with malignancies from the Sepsis Occurrence in Acutely Ill Patients (SOAP) study, conducted in 2002 (3). Therefore, we conducted a multicenter study with the aim of evaluating the characteristics and outcomes of patients with cancer requiring intensive care.

PATIENTS AND METHODS

Design and Setting

This was a multicenter, prospective, cohort study conducted in 28 Brazilian ICUs over a 2-mo period. The study was coordinated by the Instituto Nacional de Câncer, Rio de Janeiro, Brazil, on behalf of the Brazilian Research in Intensive Care Network (BRICNet). A total of 138 investigators from 94 different Brazilian ICUs registered in the BRICNet database were invited to participate in the study. Forty-five centers responded to the invitation and 28 agreed to participate in the study. The complete list of investigators and centers appears in the Appendix. The present study was strictly observational and every clinical decision was at the discretion of the attending physician. The Brazilian National Ethics Committee approved the study and the need for informed consent was waived. In addition, the study protocol was reviewed by the ethics committees or Institutional Review Boards at each participating site.

Selection of Participants, Data Collection, and Definitions

All patients aged ≥18 yrs old with a definite diagnosis of cancer requiring ICU ad-

mission between August 1, 2007 and September 30, 2007 were evaluated. Patients in complete remission for >5 years, those with an ICU stay of <24 hrs, and readmissions were not considered. Transfers from other nonparticipating ICUs (n = 7) were not considered as readmissions.

Data were collected, using a specific and standardized case report form sent by regular mail from the coordinating center to all participating ICUs. Each local investigator received a copy of the research project including a glossary with all definitions and procedures for data collection, and completed a form on ICU characteristics. Local investigators were responsible for training local staff for data collection, supervising data collection, controlling data completeness and quality, and they were instructed to contact the coordinating center in case there were questions or problems during the data collection phase. All study documents were made available online at the website www.bricnet.org.

Demographic, clinical, and laboratory data were collected during the first day of ICU including hospital location before ICU admission, main diagnosis for ICU admission, weight loss of >10% of usual body weight within the previous 3 mos, comorbidities, performance status (PS) (Eastern Cooperative Oncology Group scale) (14), and cancer- and treatment-related data. The second and third versions of the Simplified Acute Physiology Score (SAPS II and SAPS 3) were estimated, using data from the ICU admission (±1 hr) and from the first 24 hrs of ICU stay, respectively (1, 15). The Sequential Organ Failure Assessment (SOFA) score was also calculated on the first day of ICU (16). Patients were classified based on the reason for ICU admission in medical, scheduled surgical, and emergency surgical. Comorbidities were evaluated, using the Adult Comorbidity Evaluation-27, which grades a wide range of comorbid diseases and conditions according to the severity of organ decompensation and prognostic impact (17). An overall comorbidity score (none, mild, moderate, or severe) is assigned based on the highest ranked single ailment. Patients with hematologic malignancies were categorized as low- or high-grade (10). Neutropenia was defined as a neutrophil count <500/mm³. During ICU stay, the need for mechanical ventilation (MV) for >24 hrs, vasopressors, and dialysis were also recorded. Infection was defined as the presence of a pathogenic microorganism in a sterile milieu (such as blood or cerebrospinal fluid) and/or clinically suspected infection that justified the administration of antibiotics (18). Sepsis was diagnosed according to the current definitions (19). Vital status at hospital discharge was the outcome.

Data Entry and Processing

The ICU characterization forms were sent by e-mail to the coordinating center. All patients' forms were sent by regular mail. Data entry was centralized and performed by a single investigator (P.B.O.), using a Microsoft Access database (Microsoft Corporation, Redmond, WA). Data consistency was assessed by another single author (M.S.) through a rechecking procedure of a 10% random sample of patients. Data were screened in detail by three investigators (M.S., J.I.F.S., P.B.O.) for missing information, implausible and outlying values, logical errors, and insufficient details. In case of nonconformity, local investigators were contacted to provide the requested information.

Statistical Analysis

Standard descriptive statistics were used to describe the study population. Continuous variables were reported as mean ± standard deviation or median (25%-75% interguartile range [IQR]). Univariate and multivariate logistic regression were used to identify factors associated with hospital mortality (20). Linearity between each continuous variable and the dependent variable was demonstrated, using locally weighted scatterplot smoothing (20). In case of nonlinearity, the variable was stratified according to the inflection points and clinical significance. For categorical variables with multiple levels, the reference level was attributed to the one with the lowest probability of the dependent variable. Variables yielding p < .2 by univariate analysis and those considered clinically relevant were entered in the multivariate analysis to estimate the independent association of each covariate with the dependent variable. SAPS II and three scores were not entered in the multivariate analyses because they encompass other covariates, such as age, variables used to define organ failures, severe comorbidities, and underlying malignancies (1, 15). Results were summarized as odds ratios and respective 95% Confidence Intervals. Possible interactions were tested. The area under the receiver operating characteristic curve was used to assess the models' discrimination; an area under the receiver operating characteristic curve of 1.0 denotes perfect, whereas a value close to 0.50 indicates no apparent accuracy (21). The Hosmer-Lemeshow goodness-of-fit test was used to evaluate agreement between the observed and expected results across all strata of probabilities of the outcome of interest (calibration) (20). With this test, p > .05 indicates a good fit for the model. Two-tailed p < .05 was considered statistically significant.

Table 1. Characteristics of participating centers (n = 28)

Variables	n (%), Median (IQR)
Hospital characteristics	
Type of hospital	
University/affiliated	11 (39%)
Private	17 (61%)
Hospital beds	210 (120-360)
< 200	12 (43%)
200-499	10 (36%)
>500	6 (21%)
Hospital facilities	
Intermediate/step-down	8 (29%)
unit	
Oncology service/	20 (71%)
department	
Radiation therapy unit	15 (54%)
Chemotherapy	22 (79%)
Bone marrow transplant	12 (43%)
ICU characteristics	
Type of ICU	
General	23 (82%)
Oncologic	5 (18%)
Closed ICU	17 (61%)
ICU beds	20 (12-30)
<10	6 (21%)
11–20	11 (39%)
>20	11 (39%)
11–20	11 (39%)

ICU, intensive care unit; IQR, 25%–75% interquartile range.

RESULTS

Characteristics of Participating Hospitals and ICUs

A total of 28 ICUs from 28 hospitals participated in the study. Five (18%) hospitals were reference centers specifically dedicated to the care of patients with cancer. There were oncology departments in 20 (71%) institutions. The main characteristics of the participating hospitals and ICUs are depicted in Table 1. The median contribution from each center was 15 patients (25%–75% IQR = 7–32; full range = 3–156).

Characteristics of the Study Population

During the study period, of 5385 ICU admissions to the participating ICUs, 1157 (21.5%) were patients with cancer. Of these patients, 753 (65.1%) were considered eligible for the study; 404 (34.9%) had ICU length of stay <24 hrs and were not considered for the study. Excluding readmissions and patients with missing data (cancer-related and outcome data), a total of 717 patients constituted the study population (Fig. 1).

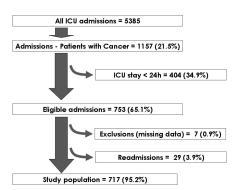


Figure 1. Study flow chart. *ICU*, intensive care unit.

There were 667 (93%) patients with solid tumors and 50 patients (7%) had hematologic malignancies. The patients' main characteristics are depicted in Table 2. The primary sites of solid tumors were lower gastrointestinal (n = 122; 17%), urogenital (n = 82; 11%), upper gastrointestinal (n = 82; 11%), lung (n = 58; 8%), brain (n = 57; 8%), head and neck (n = 56; 8%), pancreas/liver/billiary tract (n = 51; 7%), breast (n = 50; 7%), gynecologic (n = 34; 5%), and others (n = 74;10%). The main hematologic malignancies were non-Hodgkin's lymphomas (n = 18; 3%), acute leukemias (n = 13;2%), multiple myeloma (n = 11; 2%), and others (n = 8; 1%). Previous anticancer treatments included surgery for tumor resections (n = 484; 68%), chemotherapy (n = 290; 40%), and radiation therapy (n = 158; 22%). Eleven patients (2%) underwent bone marrow transplant (autologous = 9; allogenic = 2). Anticancer treatments were employed alone or in combination, according to the hemato/ oncologist responsible for each patient. Cancer- and treatment-related acute complications at the time of ICU admission were frequent and included: neutropenia (n = 52; 7%); intracranial mass effect (n = 49; 7%); airway obstruction (n = 37; 5%); chemotherapy-induced complications (n = 34; 5%); radiation therapy induced complications (n = 13; 2%); deep vein thrombosis (n = 32; 5%); spinal cord compression (n = 12; 2%); hypercalcemia (n = 11; 2%); and tumor lysis syndrome (n = 6; 1%).

Comorbidities were indentified in 512 patients (71%) and the most frequent were: arterial hypertension (n = 332; 46%); diabetes mellitus (n = 113; 16%); chronic pulmonary disease (n = 84; 12%); and coronary artery disease (n = 56; 8%).

Sources, Types, and Reasons for ICU Admission

The main sources of admission were the operating/recovery rooms (n = 442; 62%), ward/floor (n = 165; 23%), emergency department (n = 87; 12%), and step-down units or other ICUs (n = 23; 3%). Almost half of the studied population was comprised of patients who had undergone a scheduled surgical procedure (n = 381; 53%); 257 patients (36%) were admitted to the ICU because of medical complications and 79 patients (11%) were admitted post emergency surgical procedures. The main reasons for ICU admission were postoperative care (n = 408; 57%), sepsis (n = 107; 15%), respiratory failure excluding sepsis (n = 74; 10%), neurologic complications (n = 35; 5%), cardiovascular complications (n = 19; 3%), renal/metabolic complications (n = 17; 2%), and others (n = 57; 8%). As expected, scheduled surgical patients had lower severity of illness and SOFA scores, required less life-sustaining therapies, and presented more frequently with locoregional solid tumors, better PS, and less severe comorbidities. Comparisons of the main patients' characteristics according to the type of admission are reported in Table 2.

Outcome Analysis

During the ICU stay, vasopressors were used in 222 (31%), MV in 304 (42%), and dialysis in 60 (8%) patients. Twenty patients (3%) received urgent anticancer treatments in the ICU (chemotherapy, n = 18; radiation therapy, n = 2). ICU-acquired infections occurred in 131 patients (18%).

The ICU and hospital mortality rates were 21% and 30%, respectively, and were higher in patients admitted because of medical complications, followed by emergency surgical and scheduled surgical patients. The length of stay in ICU (4 days [25%–75% IQR = 3–16] vs. 3 days [QR = 2–5], p = <.001) and in hospital (19 days [IQR = 8–37] vs. 11 days [IQR = 7–21[, p = <.001) was higher in nonsurvivors than in survivors. Main outcome data are depicted in Table 2.

End-of-life (EOL) decisions (to with-hold or withdraw life-sustaining therapies) were made in 72 patients (10%) after a median of 4 days (2–15) in the ICU. Of these patients, 48 (67%) died in the ICU, 21 (30%) were discharged from the ICU, and three patients were discharged

Table 2. Patients' characteristics and outcomes according to the type of admission^a

Variables	All Patients $(n = 717)$	Scheduled Surgery $(n = 381, 53\%)$	Emergency Surgery (n = 79, 11%)	Medical (n = 257, 36%)	p^b
Age, yrs	61.2 ± 15.4	61.7 ± 14.4	61.8 ± 16.1	60.7 ± 16.7	.815
Male gender	351 (49%)	186 (49)	36 (46%)	129 (50%)	.770
Hospital stay before ICU	1 (0-6)	1 (1–3)	3 (1–8)	2 (0–9)	.041
admission, days	1 (0-0)	1 (1-5)	3 (1-0)	2 (0-3)	.041
SAPS II score, points	32.1 ± 7.2	22.2 ± 11.2	38.9 ± 15.4	44.5 ± 16.1	<.001
SAPS 3 score, points	48.7 ± 19.0	35.9 ± 10.6	53.7 ± 13.8	66.3 ± 15.2	<.001
SOFA on the 1 st day of ICU,	7 (5–10)	6 (5–8)	8 (6–11)	9 (7–12)	<.001
Type of cancer					
Locoregional solid tumor	473 (66%)	301 (79%)	60 (76%)	112 (44%)	<.001
Metastatic solid tumor	194 (27%)	78 (20.5%)	15 (29%)	101 (39%)	~.001
Low-grade hematologic	20 (3%)	0	2 (2.5%)	18 (7%)	
malignancy	20 (070)	v	2 (2.070)	10 (170)	
High-grade hematologic	30 (4%)	2 (0.5%)	2 (2.5%)	26 (10%)	
malignancy	30 (470)	2 (0.370)	2 (2.370)	20 (1070)	
Cancer status					
Controlled/remission	63 (9%)	21 (6%)	9 (11%)	33 (13%)	<.001
Active-newly diagnosed	426 (59%)	267 (70%)	50 (63%)	109 (42%)	<.001
Active-newly diagnosed Active-recurrence/progression	228 (32%)	93 (24%)	20 (25%)	115 (45%)	
Performance status	220 (3270)	93 (2470)	20 (2370)	113 (43%)	
0–1	448 (62%)	308 (81%)	45 (57%)	95 (37%)	<.001
2–4	269 (38%)	73 (19%)	34 (43%)	162 (63%)	<.001
Neutropenia	52 (7%)	73 (19%) 7 (2%)	4 (5%)	41 (16%)	<.001
Recent weight loss	94 (13%)	28 (7%)	14 (18%)	52 (20%)	<.001
Any comorbidity	512 (71%)	264 (69%)	60 (76%)	188 (73%)	.365
Comorbidity score (ACE-27)	312 (1170)	204 (0970)	00 (7070)	100 (7370)	.505
None-mild	392 (55%)	233 (61%)	41 (52%)	118 (46%)	.001
Moderate-severe	325 (45%)	148 (39%)	38 (48%)	139 (54%)	.001
Mechanical ventilation on ICU	190 (27%)	51 (13%)	34 (43%)	105 (41%)	<.001
admission	130 (21/0)	31 (1370)	34 (4370)	103 (4170)	<.001
Dialysis on ICU admission	25 (4%)	4 (1%)	4 (5%)	17 (7%)	<.001
Vasopressors on ICU admission	138 (19%)	41 (11%)	19 (24%)	78 (30%)	<.001
Infection on ICU admission	194 (27%)	` /	` /	` /	<.001
Outcome data	194 (21%)	16 (4%)	35 (44%)	143 (56%)	<.001
ICU LOS (days)	3 (2-7)	2 (2-4)	5 (2–11)	5 (3–11)	<.001
Hospital LOS (days)	3 (2–7) 13 (7–26)	2 (2–4) 8 (6–10)	20 (9–33)	18 (8–34)	<.001
End-of-life decisions	72 (10%)	7 (2%)	20 (9–33) 7 (9%)	58 (24%)	<.001
ICU mortality	151 (21%)	` /		` /	<.001
Hospital mortality	' '	21 (6%)	18 (23%)	112 (44%)	<.001
поѕрнаі тогіанцу	218 (30%)	41 (11%)	29 (37%)	148 (58%)	<.001

ICU, intensive care unit; LOS, length of stay; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment; ACE-27, Adult Comorbidity Evaluation.

"Results expressed as mean \pm standard deviation, median (25%–75% interquartile range), n (%); ^breported p values refer to comparisons among the different types of ICU admission.

alive from the hospital. EOL decisions were made more frequently in medical patients.

As expected, the SAPS II (46.9 \pm $17.4 \text{ vs. } 25.6 \pm 12.4, p < .001), \text{ SAPS } 3$ $(64.9 \pm 17.8 \text{ vs. } 41.7 \pm 14.9, p < .001),$ and SOFA (10 [8–13] vs. 6 [5–8], p <.001) scores were higher in nonsurvivors than survivors. The results of univariate analysis of predictive factors for hospital mortality in all studied patients are reported in the supplemental data and Tables 1 and 2 (Supplementary Digital Content 1, http://links.lww.com/CCM/A68; Supplementary Digital Content 2, http://links.lww.com/CCM/A67; Supplementary Digital Content 3, http://links.lww.com/CCM/A69). Hospital stay before ICU admission, SOFA score, PS, cancer status, the category of the underlying malignancy, bone marrow transplant, neutropenia, a moderate or severe comorbidity score, recent weight loss, infection at the time of ICU admission, and the need for MV, dialysis, or vasopressors were entered in the multivariate analysis. The final model for characteristics independently associated with increased hospital mortality is depicted in Table 3. Adjusting for other covariates, age, dialysis, vasopressors, the underlying malignancy and neutropenia were not associated with mortality.

In a second analysis, scheduled surgical patients were excluded. The results of the univariate analysis are given in Table 2. Admission because of medical complications, recent weight loss, higher SOFA scores, poor PS, an active malignancy, and the need for MV were the independent outcome predictors in this subgroup of patients (Table 4).

DISCUSSION

In this study, the characteristics and outcomes of a large cohort of unselected patients with cancer requiring intensive care were evaluated and these patients corresponded to one fifth of all ICU admissions. To the best of our knowledge, this is the first multicenter study specifically designed with this aim since the seminal study of Groeger et al published in 1998 (13). In that study, 1483 patients admitted to the ICUs of four referral cancer centers in the United States served as the developmental population for the

Table 3. Multivariate analysis of predictors of hospital mortality in all patients admitted to the ICUs (n = 717)

Variables	Coefficients	Odds Ratio (95% CI)	p
Type of admission			
Scheduled surgical		1.00	
Emergency surgical	0.900	2.46 (1.28-4.73)	.007
Medical	1.733	5.66 (3.43–9.33)	<.001
Hospital stay before ICU admission [Ln (days $+$ 0.5)]	0.165	1.18 (1.01–1.37)	.033
SOFA on the 1 st day of ICU (points)	0.224	1.25 (1.17–1.34)	<.001
Performance status		, ,	
0-1		1.00	
2–4	1.223	3.40 (2.19-5.26)	<.001
Cancer status		,	
Controlled/remission		1.00	
Active-newly diagnosed	1.010	2.75 (1.19-6.32)	.018
Active-recurrence/progression	0.803	2.23 (0.96–5.20)	.063
Mechanical ventilation	0.883	2.42 (1.51–3.87)	<.001
Constant	-5.518	, ,	

ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; CI, confidence interval. Area under receiver operating characteristic curve = 0.88 (95% CI, 0.86–0.91); Hosmer-Lemeshow goodness-of-fit ($\chi^2=4.305; p=.829$).

Table 4. Multivariate analysis of predictors of hospital mortality in medical and emergency surgical patients (n = 336)

Variables	Coefficients	Odds Ratio (95% CI)	p
Type of admission			
Emergency surgical		1.00	
Medical	0.825	2.28 (1.21-4.32)	.011
Recent weight loss >10%	0.829	2.29 (1.15-4.55)	.018
SOFA on the 1st day of ICU (points)	0.196	1.22 (1.12–1.33)	<.001
Performance status			
0-1		1.00	
2–4	1.277	3.59 (2.08-6.18)	<.001
Cancer status			
Controlled/remission		1.00	
Active-newly diagnosed	1.166	3.21 (1.33-7.76)	.010
Active-recurrence/progression	0.901	2.46 (1.01–601)	.048
Mechanical ventilation	0.976	2.66 (1.50-4.71)	.001
Constant	-4.544		

ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; CI, confidence interval. Area under receiver operating characteristic curve = 0.81 (95% CI, 0.77–0.86); Hosmer-Lemeshow goodness-of-fit ($\chi^2=8.707; p=0.368$).

critical care medicine score. They observed a hospital mortality rate of 42%. Over the last decade, advances in oncology and intensive care coupled with an improved selection of patients likely to benefit from ICU management have translated into better survival rates. Nonetheless, most of the studies demonstrating improvement in patients' outcomes were conducted in single centers and specialized hemato-oncologic ICUs. Very recently, Taccone et al evaluated 473 patients with solid tumors and hematologic malignancies (15% of the patients) included in the SOAP study over a 2-wk period (3). They found a global hospital mortality rate of 29% and the main outcome predictors were higher SAPS II scores and the need for MV. However, as that study was not specifically designed to evaluate patients with cancer, the lack of information on cancer-related characteristics other than the group of malignancies (solid or hematologic) imposes limitations to the interpretation of its results. A new multicenter study in this population is of critical importance.

We found a relatively low global hospital mortality rate of 30%, but half of the patients were admitted for postoperative care after scheduled surgeries with an expectedly lower mortality rate (11%). Although the outcomes may vary depending on case-mix, hospital mortality rates (53%) described in medical and emergency surgical patients are similar to

those reported in more recent singlecenter studies on critically ill patients with cancer (range = 44%-63%) (4, 5, 10, 11, 22–28). Adjusting for other covariates including the type of admission, mortality was more dependent on the severity of organ failures at the time of ICU admission, poor PS, need of MV, and active disease. Although these outcome predictors have been reported in previous studies (3, 4, 7, 11, 13, 24, 25, 27, 28), the present study confirms that the type of malignancy per se and the presence of neutropenia do not mainly influence a patient's short-term mortality. However, the relatively low number of patients with bone marrow transplant imposed limitations to evaluate appropriately their contribution to the patients' outcomes.

The present study has many positive features including a large sample size and a multicenter and prospective design. By evaluating a contemporary cohort of patients from institutions with different characteristics, it provides a description of the current ICU admission practices and outcomes for these patients. Nevertheless, the present study has also potential limitations. Although almost thirty ICUs have participated, the study was carried out in a single country and some caution is needed with the extrapolation of our results because possible selection biases concerning different standards of care cannot be excluded. On the other hand, as patients from nonspecialized ICUs were also evaluated, the findings of the present study may be more representative of the practice in general hospitals and therefore more suitable to generalization. Furthermore, the present study does not represent an audit of Brazilian ICUs regarding the care provided to patients with cancer. In general, the frequencies of EOL decisions were relatively lower than those reported in the literature (6, 9, 10), but half of the patients were admitted after a scheduled surgical procedure. If only medical and scheduled surgical patients are considered, the frequency of EOL decisions is similar to other reports (6, 9, 10, 22, 25). However, as there is not yet a legal regulation on EOL care in Brazil (29), and only EOL decisions shared by the ICU team, oncologists, and patient's relatives (which is generally the rule in Brazil in ICUs) were considered, possible underestimation cannot be completely ruled out.

In conclusion, one in five ICU admissions in the participating centers was in patients with malignancies. This large

multicenter study reports encouraging survival rates for patients with cancer requiring intensive care. Mortality was mostly dependent on the severity of organ failures, PS, and need for MV rather than cancer-related characteristics, such as the type of malignancies or the presence of neutropenia. Our results suggest that selected patients with cancer can benefit from ICU admission.

ACKNOWLEDGMENTS

We thank the Instituto Nacional de Câncer, especially the Department of Clinical Research, and CNPq for all their support.

REFERENCES

- Moreno RP, Metnitz PG, Almeida E, et al: SAPS 3—From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive* Care Med 2005; 31:1345–1355
- Zimmerman JE, Kramer AA, McNair DS, et al: Acute Physiology and Chronic Health Evaluation (APACHE) IV: Hospital mortality assessment for today's critically ill patients. Crit Care Med 2006; 34:1297–310
- Taccone FS, Artigas AA, Sprung CL, et al: Characteristics and outcomes of cancer patients in European ICUs. Crit Care 2009; 13:R15
- Kress JP, Christenson J, Pohlman AS, et al: Outcomes of critically ill cancer patients in a university hospital setting. Am J Respir Crit Care Med 1999; 160:1957–1961
- Staudinger T, Stoiser B, Mullner M, et al: Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. Crit Care Med 2000; 28:1322–1328
- Azoulay E, Alberti C, Bornstain C, et al: Improved survival in cancer patients requiring mechanical ventilatory support: Impact of noninvasive mechanical ventilatory support. Crit Care Med 2001; 29:519–525
- Soares M, Salluh JI, Spector N, et al: Characteristics and outcomes of cancer patients requiring mechanical ventilatory support for >24 hrs. Crit Care Med 2005; 33:520–526
- Darmon M, Thiery G, Ciroldi M, et al: Intensive care in patients with newly diagnosed malignancies and a need for cancer chemotherapy. Crit Care Med 2005; 33:2488–2493
- Vandijck DM, Benoit DD, Depuydt PO, et al: Impact of recent intravenous chemotherapy on outcome in severe sepsis and septic shock patients with hematological malignancies. Intensive Care Med 2008; 34:847–855
- Benoit DD, Vandewoude KH, Decruyenaere JM, et al: Outcome and early prognostic indicators in patients with a hematologic malignancy admitted to the intensive care unit

- for a life-threatening complication. *Crit Care Med* 2003; 31:104–112
- 11. Pène F, Percheron S, Lemiale V, et al: Temporal changes in management and outcome of septic shock in patients with malignancies in the intensive care unit. *Crit Care Med* 2008; 36:690–696
- Soares M, Salluh JI, Carvalho MS, et al: Prognosis of critically ill patients with cancer and acute renal dysfunction. *J Clin Oncol* 2006; 24:4003–4010
- Groeger JS, Lemeshow S, Price K, et al: Multicenter outcome study of cancer patients admitted to the intensive care unit: A probability of mortality model. *J Clin Oncol* 1998; 16:761–770
- 14. Zubrod CG, Schneiderman M, Frei E III, et al: Appraisal of methods for the study of chemotherapy of cancer in man: Comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. *J Chron Dis* 1960; 11:7–33
- Le Gall J-R, Lemeshow S, Saulnier F: A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993; 270:2957–2963
- 16. Vincent JL, Moreno R, Takala J, et al: The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/ failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive* Care Med 1996; 22:707–710
- Piccirillo JF: Adult Comorbidity Evaluation-27. Comorbidity data collection form. 2001. Available at http://oto.wustl.edu/clinepi/downloads.html. Accessed November 15, 2008
- Vincent JL, Sakr Y, Sprung CL, et al: Sepsis in European intensive care units: Results of the SOAP study. Crit Care Med 2006; 34: 344–353
- Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003; 31:1250–1256
- Hosmer DW, Lemeshow S: Applied Logistic Regression. Second Edition. New York, Wiley-Interscience, 2000
- Hanley JA, McNeil BJ: The meaning and use of the area under receiver operating characteristic (ROC) curve. *Radiology* 1982; 143: 29–36
- Vieira JM Jr, Castro I, Curvello-Neto A, et al: Effect of acute kidney injury on weaning from mechanical ventilation in critically ill patients. Crit Care Med 2007; 35:184–191
- Schellongowski P, Benesch M, Lang T, et al: Comparison of three severity scores for critically ill cancer patients. *Intensive Care Med* 2004; 30:430–436
- 24. Azoulay E, Moreau D, Alberti C, et al: Predictors of short-term mortality in critically ill patients with solid malignancies. *Intensive Care Med* 2000; 26:1817–1823
- Soares M, Carvalho MS, Salluh JIF, et al: Effect of age on survival of critically ill pa-

- tients with cancer. Crit Care Med 2006; 34: 715-721
- Thiery G, Azoulay E, Darmon M, et al: Outcome of cancer patients considered for intensive care unit admission: A hospital-wide prospective study. *J Clin Oncol* 2005; 23: 4406–4413
- 27. Maschmeyer G, Bertschat FL, Moesta KT, et al: Outcome analysis of 189 consecutive cancer patients referred to the intensive care unit as emergencies during a 2-year period. *Eur J Cancer* 2003; 39:783–792
- 28. Soares M, Salluh JI, Ferreira CG, et al: Impact of two different comorbidity measures on the 6-month mortality of critically ill cancer patients. *Intensive Care Med* 2005; 31: 408–415
- Soares M, Terzi RG, Piva JP: End-of-life care in Brazil. *Intensive Care Med* 2007; 33: 1014–1017

APPENDIX

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