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Characteristics and outcomes of cancer patients in European ICUs

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Abstract

Introduction: Increasing numbers of cancer patients are being admitted to the intensive care unit (ICU), either for cancer-related complications or for treatment-associated side effects,

yet there are relatively few data concerning the epidemiology and prognosis of cancer patients admitted to general ICUs. The aim of this study was to assess the characteristics of critically ill cancer patients, and to evaluate their prognosis.

Methods: This was a substudy from the Sepsis Occurrence in Acutely Ill Patients (SOAP) study, a cohort, multicenter, observational study which included data from all adult patients admitted to one of 198 participating ICUs from 24 European countries during the study period. Patients were followed up until death, hospital discharge, or for 60 days.

Results: Of the 3147 patients enrolled in the SOAP study, 473 (15%) had a malignancy: 404 (85%) with solid tumors and 69 (15%) with hematological cancer. Patients with solid cancers had the same severity of illness as the non-cancer population, but were older, more likely to be a surgical admission, and had a higher frequency of sepsis. Patients with hematological cancer were more severely ill and more commonly had sepsis, acute lung injury/acute respiratory distress syndrome, and renal failure than patients with other malignancies; these patients also had the highest hospital mortality rate (58%). The outcome of all cancer patients was comparable with that in the non-cancer population, with a 27% hospital mortality rate. However, in the subset of patients with more than 3 failing organs, more than 75% of patients with cancer died compared to about 50% of patients without cancer (p=0.01).

Conclusions: In this large European study, patients with cancer were more often admitted to the ICU for sepsis and respiratory complications than other ICU patients. Overall, the outcome of patients with solid cancer was similar to that of ICU patients without cancer; patients with hematological cancer had a worse outcome.

Introduction

Remarkable advances have been made in the early diagnosis and aggressive management of patients with malignancies, resulting in dramatic improvements in overall survival rates [1, 2]. As a result, increasing numbers of patients are admitted to the intensive care unit (ICU), either for cancer-related complications or for treatment-associated side effects [3]. Several studies have reported very high mortality rates for cancer patients after a long ICU stay, especially when they had leukopenia [4] or required mechanical ventilation [5], and aggressive management of life-threatening complications in these patients has been questioned [6]. In a prospective, longitudinal study performed in 26 ICUs, Azoulay et al. found that cancer patients were at a high risk of being denied ICU admission [7], in accordance with articles discouraging ICU admission or prolonged intensive care for cancer patients [6, 8]. However, other studies have highlighted reduced mortality rates in critically ill patients with cancer [9, 10], and the development of new procedures, such as non-invasive mechanical ventilation, may enable recommendations for ICU admission and appropriate utilization of ICU resources for cancer patients to be altered [11].

Several large epidemiologic studies have provided findings on prognostic factors for cancer patients admitted to the ICU [1, 12, 13], but these studies essentially concerned specialized oncological ICUs, so that extrapolation to general ICUs and hospitals can be difficult. There are several issues of particular interest: First, are mortality rates different for patients with and without cancer in a general ICU? In particular, as sequential assessment of organ failure is fundamental to predict outcome in the general ICU population [14], it would be interesting to know whether the relationship between the number of acute organ failures and mortality is different in patients with and without malignancy. Second, sepsis remains one of the major causes of admission for cancer patients in the ICU and is an important cause of hospital mortality and morbidity [15]. Moreover, treatment of cancer has

contributed to a growing number of immunocompromised patients with an increased incidence of nosocomial infections [16]; immunosuppression can result in a greater use of antibiotics, and more infections associated with multiresistant micro-organisms [17]. It is, therefore, also important to define whether cancer patients have more sepsis episodes and sepsis-related organ dysfunctions than non-cancer patients.

The Sepsis Occurrence in Acutely Ill Patients (SOAP) study [15] collected a large amount of data on all patients admitted to general (non-specialized) ICUs during a 2-week period. As there are relatively few data concerning the epidemiology and prognosis of cancer patients admitted to general ICUs or the epidemiology and patterns of sepsis syndromes in these patients [17, 18], the aim of this study was to assess the characteristics of critically ill cancer patients, and to evaluate their prognosis.

MATERIALS AND METHODS

Study Design

This study was a substudy of the prospective, multiple-center, observational SOAP study. The SOAP study [15] was designed to evaluate the epidemiology of sepsis and to identify various etiological, diagnostic, therapeutic and prognostic factors of ICU patients in European countries, and was endorsed by the European Society of Intensive Care Medicine. Since this observational study did not require any deviation from routine medical practice, institutional review board approval was either waived or expedited in participating institutions and informed consent was not required. As such, no supplementary review board documents were needed for the current sub-study. All patients >15 years old newly admitted to the ICU of a participating center (see the list of participating countries and centers in the Appendix) between May 1 and May 15, 2002, were included. Patients were followed up until death, hospital discharge, or for 60 days, whichever came first. Those who stayed in the

ICU for <24 hrs for routine postoperative observation were excluded. Patients who were readmitted and had been included on their first admission were not included for a second time.

Definitions

Full definitions are provided in an earlier publication [15]. Infection was defined as the presence of a pathogenic micro-organism in a sterile site (such as blood, abscess fluid, cerebrospinal fluid, or ascitis) and/or clinically suspected infection, plus the administration of antibiotics. Sepsis was defined according to standard criteria [19]. ICU-acquired sepsis was defined as sepsis occurring more than 48 hours after admission to the ICU. Patients were defined as having acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) if the arterial oxygen pressure to inspiratory oxygen fraction ratio (PaO_2/FiO_2) was less than 300 for ALI and less than 200 for ARDS and all of the following were present: bilateral infiltrates on the chest radiograph; no clinical evidence of heart failure; no chronic pulmonary disorders; mechanical ventilation. Organ failure was defined as a Sequential Organ Failure Assessment (SOFA) score >2 for the organ in question [20]. Patients were classified as surgical admissions if they had undergone surgery within 2 weeks preceding admission.

Cancer was identified as solid or hematological malignancy diagnosed before admission to the ICU. For solid tumors, the presence of metastases was also recorded. Patients with a prior history of cancer and with complete remission for over 5 years were not considered in the cancer group. Leukopenia was defined as a white blood cell count $<1000/mm^3$, and severe thrombocytopenia by a platelet count $<50000/mm^3$ [19].

Data Management

Data were collected prospectively using pre-printed case report forms following instructions available on a dedicated website. The steering committee was easily accessible to the

investigators and processed all queries during data collection. Data collection on admission included demographic data and comorbid diseases. Clinical and laboratory data for the Simplified Acute Physiology Score (SAPS) II [21] were reported as the worst value within 24 hrs after admission. Microbiological and clinical infectious data were reported daily as well as the antibiotics administered. A daily evaluation of organ function based on the SOFA score [14] was performed, with the most abnormal value for each of six organ systems (i.e., respiratory, renal, cardiovascular, hepatic, coagulation, and neurologic) being collected on admission and every 24 hrs thereafter. Data collection and quality control are described elsewhere [15].

Statistical Analysis

Data were analyzed using SPSS 13.0 for Windows (SPSS Inc., 2004). Descriptive statistics were computed for all study variables. A Kolmogorov-Smirnov test was used, and histograms and normal-quantile plots were examined to verify the normality of distribution of continuous variables. Discrete variables are expressed as counts (percentage) and continuous variables as means ± standard deviation (SD) or median (25th – 75th percentiles). For demographics and clinical characteristics of the study groups, differences between groups were assessed using a chi-square, Fisher's exact test, Student's t-test or Mann-Whitney U test, as appropriate.

Multivariate logistic regression analysis with hospital mortality as the dependent variable was conducted in patients with solid and hematological cancer. Only variables associated with a higher risk of hospital mortality ($p<0.25$) on a univariate basis were introduced in the multivariate model. Colinearity between variables was excluded prior to modeling. A Hosmer-Lemeshow goodness-of-fit test was performed and Nagelkerke pseudo r^2, classification tables, and odds ratios (OR) with 95% confidence interval (CI) were

computed. Variables considered in the analysis were, therefore, demographic variables, co-morbidities, SAPS II score on admission, organ failure as assessed by the SOFA score on admission, presence of metastases, type of admission (medical or surgical), reason for admission, sepsis, source of infection, type of micro-organism (*Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, *Escherichia coli*, *Candida* spp) following results of descriptive data on infection incidence, mechanical ventilation, renal replacement therapy (hemofiltration or hemodialysis), administration of inotropes and/or vasopressor agents, presence of leukopenia, thrombocytopenia, ALI or ARDS. Kaplan-Meier survival curves were plotted and compared using a signed logrank test. All statistics were two-tailed and a $p<0.05$ was considered significant.

RESULTS

Demography

From 3147 patients enrolled during the study period, 473 (15%) had a malignancy. Of these, 69 (15%) had hematological cancer and 404 (85%) had solid tumors, of whom 100 had evidence of metastases. The patients with solid tumors were older than the patients without cancer and were more commonly male (Table 1). Surgical admissions accounted for nearly 70% of the patients with solid cancer compared to 41% of those without cancer, and 20% of those with hematological cancer (Table 1). Gastrointestinal (GI), thoracic, and renal/urological surgery were more common, and cardiovascular and neurosurgery less common, in patients with solid tumors than in those without cancer. Cancer patients were more commonly admitted for respiratory reasons, but less commonly for acute neurological diseases and trauma. SAPS II and SOFA scores were comparable in patients with solid tumors and those without cancer, but both scores were significantly higher in patients with hematological cancer than in those without cancer. The median lengths of stay in the ICU

were quite similar in the three groups, but cancer patients had longer hospital stays than those without cancer. Co-morbidities were different among the groups, with a lower prevalence of cardiac insufficiency in patients with solid tumors, and more patients with acquired immunodeficiency syndrome (AIDS) in patients with hematological cancer. Corticosteroids and chemotherapy were more commonly used in patients with cancer than in those without.

Frequency, Distribution and Patterns of Sepsis

Of 1177 (37% of the total population) patients with identified infection, 217 (18%) had cancer (Table 1). More patients with hematological cancer had severe sepsis and septic shock than patients without cancer, already on admission. There was no difference in the rate of ICU-acquired infections among the three groups. The most common site of infection in all three groups, both at admission and during the ICU stay, was the lung (Table 2). Abdominal infections occurred more frequently in patients with solid cancer compared with patients without cancer. Patients with hematological cancer had more episodes of bacteremia than patients without cancer. The most common microorganisms are presented in Table 2. *Escherichia coli* was more frequently isolated in cancer patients than in patients without cancer. There was no significant difference in the microorganisms recovered from blood cultures (data not shown).

Organ dysfunction

Renal (37% vs 29%, p=0.01) and neurological (26% vs 20%, p=0.02) dysfunction were less common in patients with solid tumors than in those without cancer, and these differences were already present at admission. Patients with hematological cancer more commonly had respiratory (55% vs 40%, p=0.01), circulatory (50% vs 32%, p=0.001), and especially

coagulation (45% vs 8%, p<0.001) dysfunction during the ICU stay than patients without cancer. As expected, leukopenia was more common in patients with solid tumors and in patients with hematological cancer (Table 3). Patients with hematological cancer had lower PaO_2/FiO_2 ratios and a higher incidence of ALI/ARDS than patients without cancer. There were no differences in the number of failing organs per day [median 2.0 (IQR 1.0-3.0)] for the three groups, however the mean number of organ failures was higher in patients with hematological cancer than in patients without cancer (p=0.02). Figure 1 shows the number of organs failing and the corresponding mortality. Hospital mortality increased with the number of organs failing, especially in cancer patients when more than 3 organs failed (121/241 [50%] non-cancer patients vs. 29/37 [78%] patients with cancer, p=0.01).

Monitoring and therapy

Arterial catheters were more commonly used in patients with hematological cancer, but pulmonary artery catheters were less commonly used in patients with solid tumors (Table 3), and this difference was not explained by the type of surgery (cardiac surgery in particular) or the frequency of heart failure in a multivariable analysis.

Mechanical ventilation was used in more than 60% of patients with similar median duration. Patients with hematological cancer were more often treated with hemofiltration, vasopressors, and inotropes.

Outcome

ICU (20% vs 18%) and hospital (27% vs 23%) mortality rates were similar in patients with solid tumors and those without cancer, but medical patients had a higher hospital mortality rate than surgical patients (41% vs. 21%, p<0.001). However in multivariable analysis, surgical status was not an independent predictor of mortality in solid cancer patients.

Patients with hematological cancer had higher ICU (42% vs. 18%) and hospital (58% vs 23%) mortality rates than non-cancer patients (both $p<0.001$) (Figure 2). The same pattern was present when only the patients with sepsis were analyzed in the three groups (Figure 3).

In a multivariable analysis, in the patients with solid tumors, SAPS II score, sepsis, ALI/ARDS, and mechanical ventilation were associated with increased hospital mortality (Table 4). In patients with hematological cancer, SAPS II score and ALI/ARDS were associated with increased hospital mortality (Table 5).

DISCUSSION

This study showed that 15% of patients admitted to European ICUs have cancer (mostly solid tumors). Previous studies described only oncological patients in specialized ICUs [4-6], or were based on retrospective analyses of patients admitted to a single center without comparison with a non-cancer population [1, 10, 22]. Analysis of a large American database of more than 7 million adult hospital admissions showed that only 9% of admissions were associated with a diagnosis of cancer [23]; however no specific data were presented on ICU admissions. Overall in our study, the outcome of patients with solid cancer was comparable with that of the general ICU population, with a 27% hospital mortality rate. However, in patients with more than 3 organs failing, more than 75% of patients with cancer died compared to 50% of patients without cancer.

We report our results separately for patients with solid and hematological malignancies as these populations are quite different [10]. Patients with hematological cancers were more severely ill and more commonly had sepsis than patients without cancer, resulting in the highest ICU and hospital mortality rates. The poor prognosis of patients with hematological malignancies who require ICU admission has been well documented, with global hospital mortality rates of 45-55% [22, 24], increasing to 72% when mechanical

ventilation is required [25]. However, recent reports have stressed that aggressive treatment of critical illness events, as well as starting chemotherapy in the ICU for a life-threatening malignancy-related complication, can be lifesaving even when infection or organ failure is present [26].

In contrast, patients with solid tumors had similar severity scores and general profiles to the non-cancer population; they were somewhat older and more commonly had sepsis, factors associated with a worse outcome, but they were more commonly surgical admissions, a factor generally associated with a better outcome than medical admissions [27].

The ICU mortality rate for cancer patients in our study is lower than that previously reported [28]; however a direct comparison is difficult because of the lack of data on the origin of cancer in our study and the possibility that less “aggressive” malignancies could have been included. More recent papers have reported ICU mortality rates of 40-69% [22, 24, 29, 30]; a lower mortality rate of just 10% was reported in one study but half of the patients were admitted for uncomplicated monitoring [31].

The intensity of treatment was the same in cancer patients as in the general population, as shown by the similar use of mechanical ventilation, vasoactive agents, and hemofiltration. Patients with solid tumors were less likely to be monitored with a pulmonary artery catheter, and this was not explained by the differences in heart surgery or by the higher frequency of cardiac failure.

Sepsis is one of the major causes of ICU admission for cancer patients and is an important cause of hospital mortality and morbidity. Cancer has been reported in about 17% of medical admissions associated with sepsis [18, 32], with a higher incidence in patients with hematological cancer, probably because of associated leukopenia [33]. Indeed, infection was the main cause of admission for these patients (52%) in our study with a predominance of respiratory infections, as reported previously [17, 34, 35]. Apart from a higher incidence

of *E. coli* and abdominal infections in patients with solid tumors than in non-cancer patients, which could not be explained by the larger number of surgical admissions in solid tumor patients nor by the incidence of surgical wound infections, we found a similar spectrum of microorganisms in patients with and those without cancer, even for infections due to *Candida* species, which are usually more common in leukopenic cancer patients [36]. ICU-acquired infection rates were also comparable. These observations suggest that these patients can be treated with the same antibiotic protocols as other ICU patients if there is no febrile neutropenia.

A multivariable analysis identified a higher severity score and the presence of ALI/ARDS as independent prognostic factors for hospital mortality in patients with hematological cancers, and a higher SAPS II score, mechanical ventilation, presence of sepsis, and presence of ALI/ARDS in solid cancer patients. APACHE II [37] and SAPS II [38] scores have been specifically validated in certain groups of critically ill cancer patients. The SOFA score also has good prognostic value in critical hemato-oncologic disease, suggesting that outcome for ICU cancer patients is determined primarily by the organ dysfunctions induced by complications rather than by the stage of the underlying malignancy [12, 39, 40]. Our study confirms that survival is dependent on the number of organ failures and that respiratory insufficiency, especially when mechanical ventilation is required [13, 41-43], is associated with the highest risk of death.

A limitation of our study, which was not focused specifically on cancer patients, is that we had no specific information about the characteristics of the cancer, including type, stage, histological findings, anticancer treatments, or performance status. The defined groups of ‘solid’ and ‘hematological’ cancers encompass different diseases with different biological behaviors and severities, thus we could not correlate mortality to these characteristics. However, in the ICU setting, the physiological changes induced by the acute illness may

represent the major determinant for the outcome of patients more than cancer-related characteristics [4]. In addition, the group of cancer patients with more than 3 organ failing was small and conclusions on the influence of organ dysfunction on mortality should be made with caution. Finally, decisions to limit therapy, and particularly “do not resuscitate” (DNR) orders, were not recorded.

Conclusions

The interesting aspect of our study was the inclusion of consecutive admissions of cancer and non-cancer patients during the same, albeit limited, time period. This study can be seen as an audit of clinical practice in Europe concerning the admission of patients with cancer to the ICU, the intensity of treatment, and the types of complications. Thus, our results have ethical implications. Malignancies are becoming increasingly common, especially as the population ages, and cancer patients will likely represent an increasing proportion of ICU populations. As the mortality rate in patients with cancer in our study was similar to that reported in recent studies and cancer patients underwent complete resuscitation and monitoring, our observations suggest that patients with a poor functional status or refractory malignancy are not being admitted to the ICU; treatment of critical complications resulted in acceptable rates of ICU mortality, without evidence of futile therapy. Similar to previous observations [3, 13, 38], our study emphasizes that ICU admission should not be denied only on the basis of a patient having a neoplastic disease.

Key Messages

- Fifteen percent of patients admitted to European ICUs have cancer
- ICU and hospital mortality rates were similar in patients with solid tumors and those without cancer
- Our study emphasizes that ICU admission should not be denied only on the basis of a patient having a neoplastic disease

Abbreviations

AIDS: Acquired immunodeficiency syndrome

ALI: Acute lung injury

ARDS: Acute respiratory distress syndrome

CI: Confidence interval

DNR: Do-not-resuscitate

FiO_2: Inspired fraction of oxygen

ICU: Intensive care unit

OR: Odds ratios

PaO_2: Arterial partial pressure of oxygen

SAPS: Simplified acute physiology score

SD: Standard deviation

SOAP: Sepsis in Acutely ill Patients

SOFA: Sequential organ failure assessment

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

JLV conceived the initial SOAP study. AA, CS, RM, YS, and JLV participated in the design and coordination of the SOAP study. YS performed the statistical analyses. FT and JLV drafted the present manuscript. All authors read and approved the final manuscript.

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Table 1. Demographic characteristics of patients.

	No Cancer	Solid tumors	Hematological cancers
	(n=2674)	**(n=404)**	**(n=69)**
Age, years	59.6 ± 17.9	66.4 ± 12.1[$]	62.1 ± 15.9
Male[a]	1619 (61.2%)	265 (66.6%)*	36 (52.9%)
Type of admission			
Medical	1581 (59.1%)	123 (30.4%)[$]	55 (79.7%)*
Surgical	1093 (40.9%)	281 (69.6%)[$]	14 (20.3%)*
Neurosurgery	131 (11.9%)	20 (7.1%)*	1 (7.1%)
Digestive surgery	284 (26.0%)	174 (61.9%)[$]	7 (50%)
Thoracic surgery	28 (2.5%)	24 (8.5%)[$]	2 (14.2%)
Cardiovascular surgery	453 (41.4%)	13 (4.6%)[$]	3 (21.4%)
Renal/urological surgery	25 (2.3%)	22 (7.8%)[$]	0
Other surgery	136 (12.4%)	23 (8.2%)*	1 (7.1%)
Admission source			
Hospital floor	639 (26.4%)	118 (33.1%)*	36 (61.0%)[$]
ER/ambulance	849 (35.1%)	56 (15.7%)[$]	8 (13.6%)[$]
Recovery room	623 (25.7%)	152 (42.7%)[$]	9 (15.3%)
Other hospital	309 (12.8%)	30 (8.4%)*	6 (10.2%)
Reason for admission			
Surveillance	192 (7.6%)	54 (14.8%)[$]	1 (1.4%)
Digestive/liver	236 (9.3%)	88 (24.1%)[$]	9 (13.0%)
Respiratory	432 (17.0%)	96 (26.3%)[$]	32 (46.4%)[$]
Cardiovascular	874 (34.5%)	56 (15.3%)[$]	19 (27.5%)
Hematological	24 (0.9%)	3 (0.8%)	0
Neurological	446 (17.6%)	36 (9.9%)[$]	3 (4.3%)*
Renal	81 (3.2%)	19 (5.2%)	4 (5.8%)
Metabolic	60 (2.4%)	10 (2.7%)	1 (1.4%)
Trauma	179 (7.1%)	2 (0.5%)[$]	0*
Comorbidities and therapies on admission			
COPD	292 (10.9%)	42 (10.4%)	6 (8.7%)
Diabetes	200 (7.5%)	24 (5.9%)	2 (2.9%)
Liver cirrhosis	103 (3.9%)	18 (4.5%)	0
AIDS	12 (0.4%)	3 (0.7%)	3 (4.3%)*
Heart failure	276 (10.3%)	22 (5.4%)*	9 (13%)
Corticosteroids	123 (4.6%)	28 (6.9%)*	14 (20.3%)[$]
Chemotherapy	8 (0.3%)	10 (2.5%)[$]	7 (10.1%)[$]
SAPS II	36.0 ± 16.8	36.8 ± 17.6	53.5 ± 18.5[$]
Incidence of sepsis			
Sepsis	960 (35.9%)	168 (41.5%)[$]	49 (71%)[$]
Severe sepsis	780 (29.1%)	110 (27.2%)	40 (57.9%)[$]
Septic shock	380 (14.3%)	57 (14.1%)	23 (33.3%)[$]
Sepsis on admission	634 (23.7%)	107 (26.5%)	36 (52.2%)[$]
ICU-acquired sepsis	228 (8.5%)	43 (10.6%)	8 (11.6%)
Severe sepsis on admission	462 (17.3%)	64 (15.8%)	26 (37.7%)[$]
Septic shock on admission	197 (7.4%)	31 (7.7%)	15 (21.7%)[$]
Admission SOFA	5.2 ± 3.8	4.6 ± 3.6	7.0 ± 4.6*
ICU stay, days	3.0 [1.7-7.0]	3.0 [1.8-6.4]	3.8 [1.7-8.6]
Hospital stay, days	14.0 [7.0-31.0]	20.0 [12.0-33.0]*	22.5 [10.0-38.0]*

ER: emergency room; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; ICU: intensive care unit; COPD: chronic obstructive pulmonary disease; AIDS: acquired

immunodeficiency syndrome; * $p<0.05$ versus no-cancer group; \$ $p<0.001$ versus no-cancer group; [a] 35 missing values

Table 2. Characteristics of infected patients according to the type of malignancy.

	No cancer (n=960)	Solid tumors (n=168)	Hematological cancer (n=49)
Criteria for infection			
Clinically suspected	750 (78.1%)	136 (81%)	38 (77.6%)
Microbiologically confirmed	666 (69.4%)	114 (67.9%)	34 (69.5%)
Clinical signs and micro-organism	383 (39.9%)	71 (42.5%)	14 (28.6%)
Source of infection			
Respiratory	648 (67.5%)	108 (64.3%)	38 (77.6%)
Abdominal	200 (20.8%)	56 (33.3%)$^{\$}$	7 (14.3%)
Blood stream	196 (20.4%)	26 (15.5%)	16 (32.7)*
Skin	132 (13.8%)	23 (13.7%)	3 (6.1%)
Urinary	133 (13.9%)	22 (13.1%)	4 (8.2%)
Catheter	87 (9.1%)	18 (10.7%)	6 (12.2%)
Cerebrospinal fluid	15 (1.6%)	0 (0.0%)	0 (0.0%)
Unknown	53 (5.5%)	7 (4.1%)	3 (6.1%)
Gram-positive bacteria			
Streptococcus group D	97 (10.1%)	21 (12.5%)	5 (10.2%)
Streptococcus pneumoniae	42 (4.3%)	3 (1.7%)	1 (2.0%)
MRSA	131 (13.6%)	28 (16.6%)	5 (10.2%)
Other cocci	20 (2.1%)	3 (1.8%)	0
Gram-negative bacteria			
Pseudomonas	132 (13.7%)	21 (12.5%)	10 (20.4%)
Escherichia coli	114 (11.8%)	34 (20.2%)$^{\$}$	10 (20.4%)*
Enterobacter	53 (5.5%)	13 (7.7%)	1 (2.0%)
Klebsiella	60 (6.2%)	11 (6.5%)	0
Proteus	39 (4.0%)	9 (5.3%)	1 (2.0%)
Acinetobacter	37 (3.8%)	3 (1.7%)	2 (4.0%)
Haemophilus	33 (2.4%)	3 (1.8%)	1 (2.0%)
Fungi			
Candida albicans	125 (13%)	28 (16.7%)	3 (6.1%)
Candida non-albicans	37 (3.9%)	9 (5.4%)	3 (6.1%)
Other fungi	13 (1.3%)	3 (1.7%)	1 (2.0%)

MRSA: methicillin-resistant *Staphylococcus aureus;* *$p<0.05$ versus no-cancer group; $\$p<0.001$ versus no-cancer group.

Table 3. Respiratory and hematological dysfunction, ICU monitoring and treatment.

	No Cancer (n=2674)	Solid tumors (n=404)	Hematological cancer (n=69)
Mechanical ventilation	1724 (64.5%)	253 (62.6%)	48 (69.6%)
ALI/ARDS	325 (12.2%)	47 (11.6%)	21 (30.4%)$
PaO_2/FiO_2	202.8 [133.4-295.0]	224.0 [144.0-324.3]	140.0 [94.0-206.2]$
MV, days/patient	3.0 [1.0-7.0]	2.0 [1.0-6.0]	4.0 [2.0-6.0]
Leukopenia	43 (1.6%)	14 (3.5%)*	17 (24.6%)$
Thrombocytopenia	373 (13.9%)	52 (12.9%)	35 (50.7%)$
Pulmonary artery catheter	430 (16.1%)	37 (9.2%)$	14 (20.3%)
Central venous catheter	1896 (70.9%)	317 (78.5%)	59 (85.5%)
Arterial catheter	1882 (70.4%)	304 (75.2%)	54 (78.3%)$
Vasopressors	1089 (40.7%)	163 (40.3%)	41 (59.4%)*
Inotropes	505 (18.9%)	61 (15.1%)	20 (29.0%)*
Hemofiltration	184 (6.9%)	16 (4.0%)	11 (15.9%)*
Hemodialysis	121 (4.5%)	16 (4.0%)	4 (5.8%)

MV: mechanical ventilation; ALI: acute lung injury; ARDS: acute respiratory distress syndrome; PaO_2: arterial partial pressure of oxygen; FiO_2: inspired fraction of oxygen; *: $p < 0.05$ versus no-cancer group; $: $p<0.001$ versus no-cancer group

Table 4. Prognostic factors for hospital mortality by multivariate forward stepwise logistic regression analysis in patients with solid cancer (n=404)

	OR	**(95% CI)**	*p value*
SAPS II*	1.07	(1.05-1.08)	<0.001
Sepsis	2.1	(1.2-3.7)	0.01
ALI/ARDS	2.5	(1.2-5.3)	0.014
Mechanical ventilation	2.4	(1.2-4.7)	0.015

OR: odds ratio; CI: confidence interval; SAPS: Simplified Acute Physiology Score; ALI: acute lung injury; ARDS: acute respiratory distress syndrome; *on admission. Hosmer and Lemeshow goodness-of-fit test $\chi 2$ = 10.15 (p=0.26). This model has a 79.5% correct classification (50.9% for non-survivors and 90.3% for survivors).

Table 5. Prognostic factors for hospital mortality by multivariate forward stepwise logistic regression analysis in patients with hematological cancer (n=69)

	OR	**(95% CI)**	*p value*
SAPS II*	1.07	(1.0.-1.2)	0.002
ALI/ARDS	5.3	(1.4-20.4)	0.015

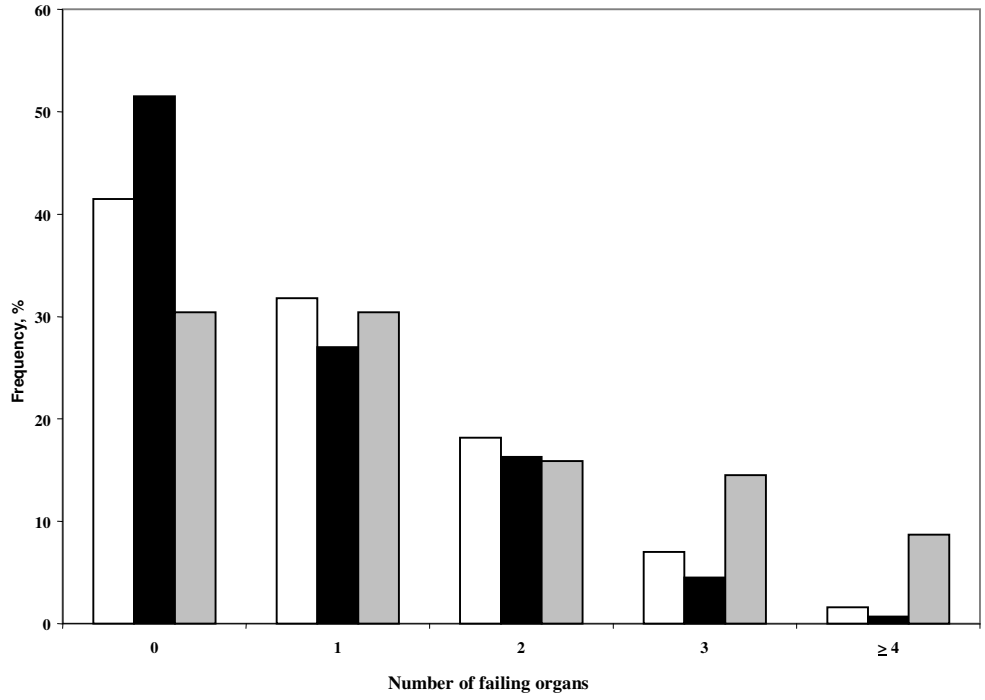
OR: odds ratio; CI: confidence interval; SAPS: Simplified Acute Physiology Score; ALI: acute lung injury; ARDS: acute respiratory distress syndrome; *on admission. Hosmer and Lemshow goodness-of-fit test $\chi 2$ = 15.53 (p=0.1). This model has a 75.4% correct classification (80.0% for non-survivors and 69.0% for survivors).

Figure legends

Figure 1. Maximum number of organ dysfunctions during the ICU stay (upper panel) and hospital mortality according to the number of organ dysfunctions (lower panel) in the three groups of patients. White bars: no cancer; gray bars: hematological cancer; black bars: solid tumors.

Figure 2. Kaplan Meier 60-day survival curves of the three groups of patients. Log Rank score = 20.78, p-value < 0.01.

Figure 3. Hospital mortality in the three groups of patients overall and in patients with sepsis. White bars: no cancer; gray bars: hematological cancer; black bars: solid tumors. *p<0.001 versus no-cancer group.


60
50
40
30
20
10
0
Frequency, %
0
1
2
3
≥ 4
Number of failing organs

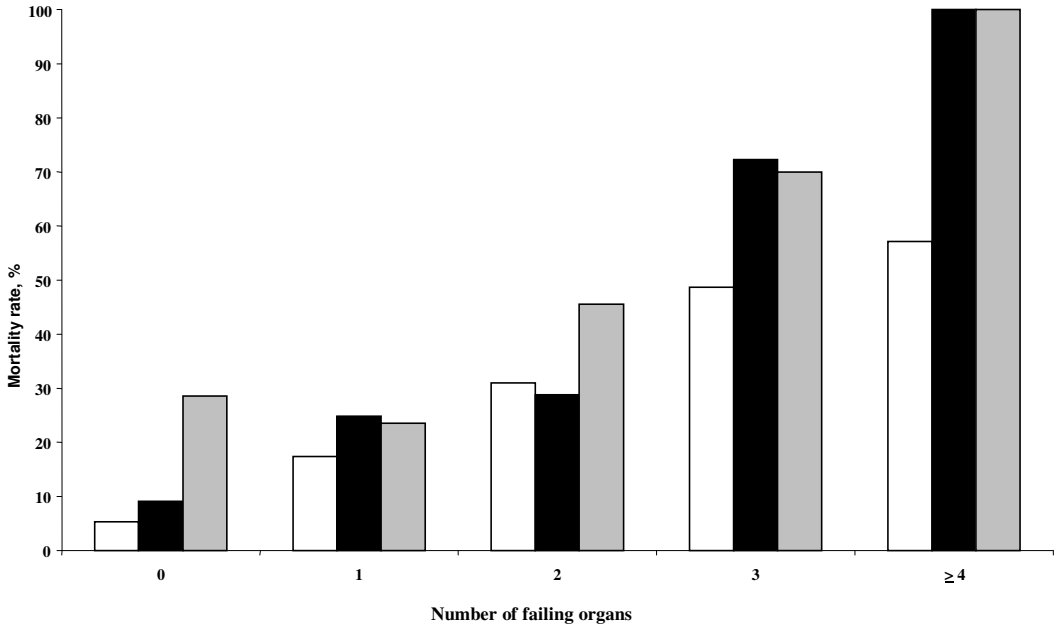

100
90
80
70
60
50
40
30
20
10
0
Mortality rate, %
0
1
2
3
≥ 4
Number of failing organs

Figure 1

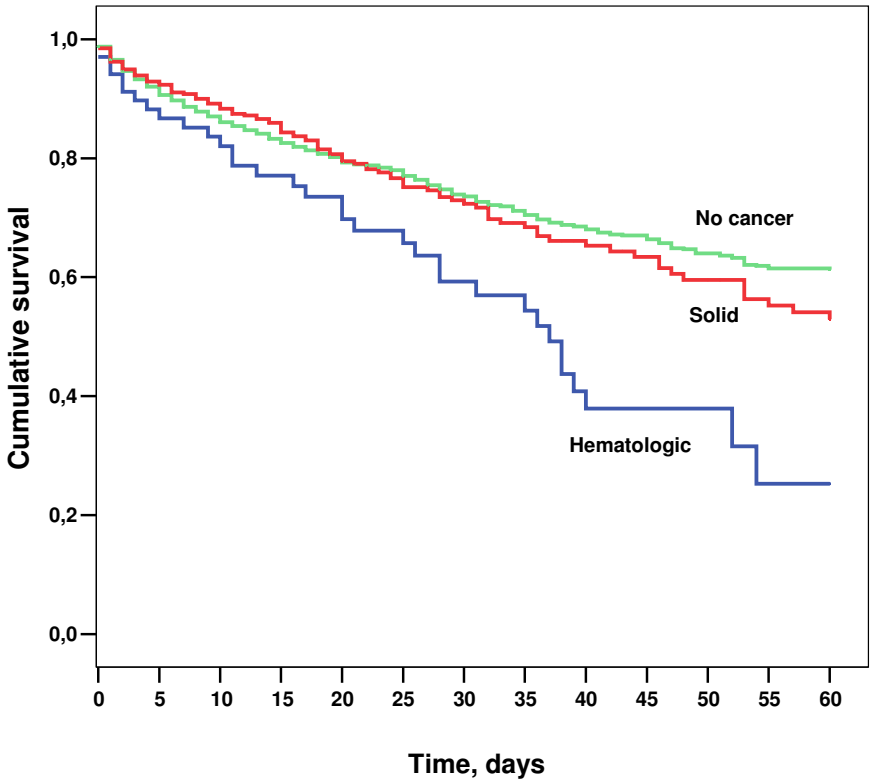

Cumulative survival
1,0
0,8
0,6
0,4
0,2
0,0
0
5
10
15
20
25
30
35
40
45
50
55
60
Time, days
No cancer
Solid
Hematologic

Figure 2

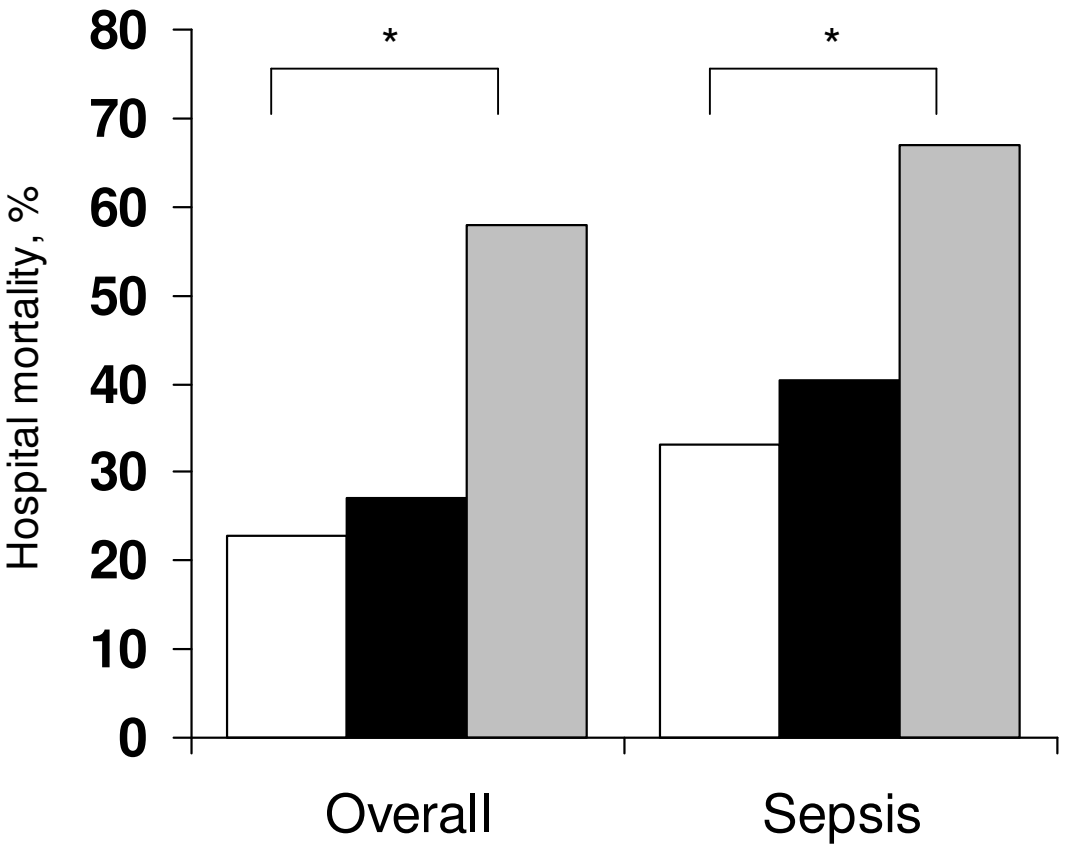


Figure 3