Performance Status (PS): A Simple Predictor of Short-term Outcome of Cancer Patients with Solid Tumors Admitted to the Intensive Care Unit (ICU)

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Abstract. *Background: Admission of cancer patients with serious medical complications to the Intensive Care Unit (ICU) remains controversial. The aim of this study was to examine the 30-day all-cause mortality in cancer patients with solid tumors admitted to the ICU and to identify factors predicting 30-day mortality. Patients and Methods: A retrospective study was conducted in 69 consecutive cancer patients with solid tumors admitted to the ICU of a 400-bed general hospital in Greece, between October 2001 and October 2005. Demographics, ECOG performance status (PS) prior to hospitalization, stage of cancer, metastases, number of metastatic sites, prior chemotherapy, primary site of tumor, APACHE II score on ICU admission, development of ICU acquired infection, sepsis, multiple organ failure (MOF), need for mechanical ventilation (MV), length of ICU stay, hospital stay and 30-day mortality were examined. Results: The observed 30-day hospital mortality rate was 66.6% (n=46) with most deaths (n=32) occurring in the ICU. Univariate negative predictors of 30-day mortality were PS 3-4 (p=0.03), APACHE II score (p=0.001), MOF (p=0.001) and need for MV (p=0.001). Only PS 3-4 was an independent predictor in multivariate analysis (p=0.02). Conclusion: ECOG PS 3-4 prior to hospitalization was found to be a simple negative predictor of short-term outcome of cancer patients with solid tumors admitted to the ICU.*

The admission of cancer patients, with various medical complications, to the ICU remains controversial. The issue is the human and financial cost of intensive medical support for patients whose short-term survival is already poor. Many studies performed during the past three decades, discouraged the admission of such patients to the ICU (1-4).

Recent advances in the field of cancer therapeutics have improved cure rates, as well as expected survival times. Since haematologists and oncologists who treat patients with malignancies rarely manage ICU, there may be bias among ICU personnel, resulting in considerable disagreement on treatment requirements.

At the end of the 1990s, Groeger *et al.* (5) developed a mortality model for predicting the hospital outcome of ICU patients with various malignancies. This model is rather complex and consists of 16 variables. Its use is difficult in clinical practice. In their study, patients with haematological malignancies were included and all patients had been admitted to the ICU before 1998. Additional studies to better define the subpopulation of cancer patients who benefit from admission to the ICU are required.

We conducted a retrospective study in order to examine the outcome of cancer patients with solid tumors admitted to the ICU of our hospital. We also attempted to identify prognostic factors associated with short-term outcome.

Patients and Methods

This was a retrospective analysis of 69 consecutive cancer patients of our Oncology Department who were admitted to the ICU of the Henry Dunant Hospital, a 400-bed general hospital in Athens, Greece. No patients were excluded because of absence of records. All patients had solid tumors and were admitted to the ICU following medical complications between October 2001 and October 2005. Cancer patients admitted to the ICU for postsurgical monitoring and patients with haematological malignancies were excluded. There were no patients having received intensive chemotherapy followed by autologous stem cell transplantation. No patients were excluded *a priori* from ICU admission due to critical condition.

We examined gender, age, performance status (PS, according to ECOG) during the last month before hospitalization, primary site of cancer, stage of the disease, number of metastatic sites, previous chemotherapy for cancer, comorbidity, cause of ICU admission, APACHE II score on ICU admission, ICU-acquired infection,

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sepsis, multiple organ failure (MOF), need for mechanical ventilation (MV), ICU length of stay, hospital length of stay, outcome in the ICU, 30-day outcome.

Statistical analysis. The data were analyzed using appropriate software (SPSS, version 10). The differences were calculated using Fisher's Exact Test for dichotomous or categorical variables and the two-sample Wilcoxon test for continuous variables (6). A backward stepwise regression analysis was used to identify the set of independent variables that contributed significantly to the fit of the model (removing criterion, $p>0.10$). When a multilevel categorical variable was found to be significant, tests were conducted to determine whether some levels could be combined. Patient's ECOG PS (0-2 *vs.* 3-4), multiple organ failure developed in the ICU, and the need for mechanical ventilation were binary determinants; APACHE II score on ICU admission was interval-scaled determinant. The dependent variable was binary, with 1 denoting death and 0 denoting a live discharge from the hospital. The predictability of the final logistic regression model regarding patient mortality was assessed by comparing the expected and actual number of deaths; the fit of the model was assessed using the Hosmer-Lemeshow goodness-of-fit statistic (7). All reported *p*-values are two-sided.

Results

Patient and disease characteristics. From the 69 patients in our study, 43 were men and 26 women with a mean age of 61 years. Almost 40% had lung cancer, 13% colorectal, 8.6% ovarian, 7.2% breast and the rest a variety of solid tumors. During the last month before hospitalization and ICU admission, 45 patients had ECOG PS of 0-2 and 24 patients ECOG PS of 3-4. Almost 90% of our patients had stage IV cancer and almost 90% had received prior chemotherapy. None had received intensive chemotherapy followed by autologous stem cell transplantation. Patients and disease characteristics are presented in Table I.

Characteristics of ICU admission. All patients were admitted with medical complications of their solid tumor. None of them was admitted for scheduled postsurgery monitoring. The main reason for ICU admission was infection in 37.7% of patients, acute respiratory failure in 13% and bleeding/ hemoptysis in 10%. Mean APACHE II score at ICU admission was 18.1. ICU-acquired infection occurred in 24 patients (34.8%) and MOF in 26 patients (37.7%). MV was required in 44 patients (63.7%). Mean duration of MV was 5.8 days and mean ICU stay was 5.5 days. Patient characteristics at ICU admission are presented in Table I.

Outcome and prognostic factors. Vital status on day 30 was available for all patients. The all-cause 30-day mortality rate was 66.6% (n=46) with 72.7% (n=32) of the deaths occurring in the ICU. The results of univariate analysis are shown in Tables II and III.

The patient characteristics (age, gender) were not found to be of prognostic significance. Among the disease characteristics (primary site, metastasis, stage of disease, number of metastatic sites, previous chemotherapy, and ECOG PS) only PS was found to be of prognostic significance both in univariate and multivate analysis (Table IV). Among 24 cancer patients with ECOG PS of 3-4, before the onset of the medical complication resulting in the ICU admission, the 30-day mortality rate was 83.3% (n=20).

Among characteristics of ICU admission (APACHE II score, ICU-acquired infection, MOF, need for MV, duration of MV, length of ICU stay, hospital stay) high APACHE II score, MOF and need for MV were found to be negative predictors of short-term outcome in univariate analysis. The

Table I. *Patient and disease characteristics (n=69).*

	mean (±SD)	n	%
Age (years)	61.3 (13.3)		
Females		26	37.7
Comorbidity			
CAD		17	24.6
COPD		3	4.3
Renal failure		1	1.4
Metastases		57	82.6
No of metastatic sites	1.7 (1.1)		
Previous chemotherapy		61	88.4
Primary site			
Lung		27	39.1
Colon/rectum		9	13.0
Ovary		6	8.6
Breast		5	7.2
Pancreas		4	5.8
Prostate		4	5.8
Brain		3	4.3
Nasopharynx		3	4.3
Bladder		3	4.3
Kidney		2	2.9
Stomach		2	2.9
Esophagus		1	1.4
Disease stage			
I/II/III		7	10.1
IV		62	89.9
Performance status			
0-2		45	65.2
3-4		24	34.8
Reason for ICU admission			
Infection		26	37.7
Acute respiratory failure		9	13.0
Bleeding/hemoptysis		7	10.1
AMI/cardiogenic pulmonary edema		6	8.7
Acute abdomen		5	7.2
Multiple organ failure		4	5.8
Tamponade		4	5.8
Coma		3	4.3
Peritonitis		2	2.9
Other		3	4.3
APACHE II	18.1 (8.3)		
Need for mechanical ventilation		44	63.7

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; AMI, acute myocardial infraction.

Table II. *Differences in survival according to the univariate predictors of all-cause hospital mortality.*

	Non-survivors (n=46)		Survivors (n=23)		*p*
	n	(%)	n	(%)	
Age (years)	60.4	13.4	63.0	13.2	0.46
Female gender	20.0	43.5	6.0	26.1	0.19
Metastasis	38.0	82.6	19.0	82.6	1.00
Previous chemotherapy	40.0	86.9	21.0	91.3	0.71
Disease stage IV	42.0	91.3	20.0	86.9	0.67
Performance status III/IV	20.0	43.5	4.0	17.4	**0.03**
APACHE II	20.3	8.6	13.6	5.3	**0.001**
ICU-acquired infection	17.0	36.9	7.0	30.4	0.78
Multiple organ failure	24.0	52.2	2.0	8.7	**0.001**
Need for mech. ventilation	36.0	78.3	8.0	34.8	**0.001**
Duration of mech. ventilation (d)	5.6	6.7	5.4	5.0	0.78
Length of ICU stay (d)	6.0	7.0	5.1	5.4	0.86
Hospital stay (d)	18.6	22.5	19.1	19.3	0.93

Data are presented as mean ± SD or No. (%).

Table III. *Univariate analysis.*

Parameters	Odds ratio	95%	CI
Age >60 years	0.91	00.32-02.54	0.86
Female gender	2.17	00.72-06.53	0.19
Metastasis	1.00	00.26-03.74	1.00
Previous chemotherapy	0.63	00.11-03.42	0.71
Disease stage IV	1.57	00.32-07.71	0.67
Performance status III/IV	3.65	01.07-12.44	0.03
APACHE II>15	2.43	00.87-06.78	0.08
ICU-acquired infection	1.34	00.45-03.91	0.78
Multiple organ failure	11.45	02.40-54.59	0.001
Need for mech. ventilation	6.75	02.23-20.43	0.001

Table IV. *Multivariate analysis: independent predictors of all-cause hospital mortality; goodness-of-fit (Hossmer-Lemeshow) p>0.05 (χ^2).*

Performance status III/IV				
p=0.02	S.E.=0.77	R=0.17	Exp (B)=5.44	df=1

Positive predictive value=93.48%; negative predictive value=65.22%; overall=84.06%.

mean APACHE II score at ICU admission among non-survivors was 20.3 as opposed to 13.6 among survivors (p=0.001). Of 26 patients with MOF, 24 patients (92.3%) died within 30 days (p=0.001). Of the 44 patients requiring MV, 36 died within 30 days (p=0.001).

The above characteristics of ICU admission, namely APACHE II score, MOF and need for MV were not of prognostic significance in multivariate analysis.

Discussion

The admission of cancer patients to the ICU has always been controversial. Our study examined the morbidity and mortality rates in cancer patients with non-hematological malignancies admitted to the ICU. We examined the survival rate of these patients 30 days after ICU admission and tried to find prognostic factors for outcome in this group of patients.

A 30-day mortality rate of 66.6% was found, which is poor as compared with the outcome of patients without having underlying malignancies admitted to the ICU.

This result is in agreement with some previous studies (8) but differs significantly from others (9-12). When we compare mortality rates in different studies, we should take into account inclusion criteria. The majority of studies included patients with haematological malignancies, who are associated with higher mortality rates. Other studies included patients admitted for routine postsurgical monitoring and find lower mortality rates (9, 13, 14). We did not include patients with haematological malignancies nor patients admitted for post-surgical monitoring.

The 30-day mortality was not correlated with the primary site, metastases, number of metastatic sites, stage of the disease, previous chemotherapy for cancer. In other words, it was not correlated with tumor characteristics. Our study confirms that the necessity for MV is a significant prognostic factor predicting poor outcome. Sixty-four percent of our patients (n=44) were mechanically ventilated and the 30-day mortality rate of this cohort was 81.8% (n=36). This is in accordance with the results reported by Groeger *et al.* (11) on a large number of mechanically ventilated cancer patients, with a 76% hospital mortality rate. This is also in accordance with the results reported by Maschmeyer *et al.* (15) and Azoulay *et al.* (8) in recent publications but has also been shown consistently in older studies. This applies both to patients with haematological malignancies and solid tumors. A potential benefit of noninvasive ventilation, which reduces the need for tracheal intubation and improves survival, has been reported in a study by Conti *et al.* (16). This study included only patients with haematological malignancies and apparently needs confirmation with further studies, including patients with solid tumors.

Prognostic scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE II), the Simplified Acute Physiology Score (SAPS II), the Mortality Probability Models II and the Logistic Organ Dysfunction (LOD) have been valuated in large cohorts of ICU patients. APACHE II and SAPS-II have been specifically validated in cancer patients (17,18). In a recent study by Azoulay *et al.* (8), the LOD score was an independent predictive factor in multivariate analysis. In our study, the APACHE II score was found to be a significant prognostic factor of short-term outcome in univariate analysis.

In addition to APACHE II and MV, MOF was another factor in univariate analysis predicting poor outcome. In

most studies, it was not investigated but it was assumed that the requirement of MV and vasopressor support was a surrogate for MOF.

The most important finding of our study was the significance of ECOG PS before hospitalization. ECOG PS 3-4 was found to be a negative predictor, not only in univariate but also in multivariate analysis. It was the only parameter which was found to be of prognostic significance in multivariate analysis. ECOG PS is an attempt to quantify a patient's general well-being. It is used to determine whether a patient can receive chemotherapy, whether dose adjustment is necessary, whether a patient may be enrolled in a clinical trial. It is a simple but very useful tool in medical oncology. Unfortunately, medical oncologists rarely manage ICU and are not always involved in decision making about the admission of a cancer patient to the ICU. In most studies of cancer patients admitted to the ICU, ECOG PS before hospitalization was not examined. Instead, scoring systems as APACHE II, SAPS II, LOD at ICU admission have been considered, as mentioned above. ICU personnel are familiar with these scoring systems but these reflect the condition of the cancer patients after the onset of medical complications which led to the ICU admission.

Parameters which are commonly believed to have an adverse impact on prognosis so as to make aggressive medical support inappropriate, such as advanced age, metastatic disease and multiple metastatic sites, were not found of prognostic significance in our study. It is unreasonable to base important decisions on unproven "poor prognostic indicators".

We believe that despite our small sample size of 69 cancer patients, our retrospective study provides an aid in clinical decision-making.

As a result of cultural and social parameters in Greece and other Mediterranean countries, most patients do not make end-of-life decisions. Therefore the admission of cancer patients to the ICU is usually decided by the physicians (medical oncologists and the ICU personnel) and the patient's family. This approach is far from being ideal. We believe that our study can facilitate decision-making. Patients with ECOG PS 3-4 during the last month before hospitalization are evidently critically ill as a result of the underlying disease (cancer) and since the outcome is poor, should be discouraged from ICU admission.

Medical oncologists of cancer patient candidates for ICU admission should be involved in decision-making. ECOG PS 3-4 is a very good, simple negative predictor of short-term outcome for cancer patients with solid tumors admitted to the ICU and this finding should be validated in a prospective study.

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