

LETTER TO THE EDITOR



Prognostic factors for cancer patient admitted to a medical intensive care unit

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Introduction

New cancer treatments, in particular targeted therapy or immunotherapy, have increased outcomes in recent years [1,2]. As a result, there is an increasing demand for critical care and recent studies [3–5] have shown a growing number of cancer patients admitted to an intensive care unit (ICU) resulting in an improvement of their survival. Part of this improvement is a better selection of patients and earlier intervention [6,7]. However, in an ICU, care is invasive for immune-compromised, frail patients with one or several organ failures, with a risk of morbidity and/or can be deleterious. The question of admission to an ICU is based on two principles for cancer patients: to provide the best possible chance with better quality of life. Thiéry et al. [7] in a prospective study on 206 patients with cancer or hematological malignancies considered for ICU admission, showed that decisions are not yet optimal: 26% of patients diagnosed as being too sick to be admitted to an ICU were still alive at 30 days. Oncologists and intensive care specialists need significant prognostic factors to assist their decisions. Several large epidemiological studies [8–14] have explored prognostic factors for cancer patients admitted to an ICU. But these studies have grouped patients with solid tumors and hematological malignancies, the latter exhibiting a worse prognosis [4]. On the other hand, most studies have included postoperative patients who have a better prognosis [4,8,15]. In addition, most of them were conducted in specialized oncological ICUs, which may limit the extrapolation of their findings to general ICUs. Moreover, few studies were interested in the quality of life of cancer patients after the ICU stay [16,17]. To our knowledge, no study reported data on the resumption of anti-tumoral treatment. Yet, this data seems important to consider in the decision to transfer patients to intensive care.

The aim of this study was to identify prognostic factors of 30-day mortality for patients with solid cancer tumors (SCTs) admitted to a medical ICU, to compare patients who resumed an anti-tumoral treatment after intensive care and

those who did not, to describe notably the characteristics, the patient outcomes.

Material and methods

This study was an observational cohort study with retrospective data collection conducted in the two medical ICUs at the Bordeaux University Hospital. All consecutive patients (≥ 18 years old) with a histologically proven cancer admitted to the medical ICU, include high dependency unit patients, from 1 January 2010 to 31 December 2015 were included. Only the first admission was considered for patients with multiple ICU admissions. Patients with hematological malignancy (including lymphoma), complete remission for more than five years, presenting post-operative complications, and admitted to the ICU for endoscopic treatment, were excluded. Information was abstracted from the patient's medical chart. The study was conducted in accordance with the criteria of practical clinical research.

The primary objective was to identify prognostic factors for 30-day mortality from admission to ICU. Secondary objectives were to describe the population, the ICU stay, the ethical practices concerning shared decision making and limitation of life-sustaining treatment, the outcome of patients after ICU exit, to compare patients who resumed an anti-tumoral treatment after admission to the ICU and those who did not, and to describe the evolution of practices between 2010 and 2015.

Results

A total of 284 patients with solid cancers were hospitalized in the ICU during the study period and 49 patients (17%) were excluded (7 hematological malignancies, 16 endoscopy, 8 surgical admission, 12 missing data, 6 remission or no diagnosis of cancer). Finally, 235 patients were included in the present study.

The most frequent cancer types were lung (33%) and head and neck (23%). The majority of patients were in a metastatic setting (60%). Half of the patients were admitted to the ICU at night, the weekend or on a public holiday. The most common

reasons for ICU admission were sepsis (56%) and/or respiratory failure (52%) and 55% of patients presented one organ failure. During ICU stay, vasopressor support (noradrenaline and dobutamine) was required in 39%, adrenaline in 8%, non-invasive ventilation in 22%, high flow oxygen in 14%, mechanical ventilation in 26% and hemofiltration in 7% of patients, respectively. The mortality rate in ICU was 24%.

Patient, transfer and ICU stay characteristics are summarized in Table 1.

At 30 days, on the 235 patients admitted in ICU, 85 patients died; the mortality rate at 30 days was 36% including patients died in ICU. Characteristics associated with 30-day mortality in univariate analysis were: elevated number of organ failures, poor performance status, lung cancer, renal, cardiac and/or hepatic dysfunction (Supplementary Table S1). Six variables were retained for multivariate analysis: initial PS, transfer for septic shock, transfer at night, weekend or on a public holiday, lung cancer, number of organ failures, non-curative setting. In the final multivariate model, organ failure ≥ 3 (OR, 4.30; 95% CI, 1.77–4.30; $p = .005$) and non-curative setting (OR, 2.24; 95% CI, 1.09–4.61; $p = .028$) were significantly associated with higher 30-day mortality (Table 3).

After the ICU stay, on the 235 patients admitted in ICU, 118 patients (50%) returned home and 104 patients (44%) resumed an anti-cancer treatment. Ninety days after ICU admission, 118 patients (50% of patients admitted in ICU) were alive.

When comparing surviving patients according to resumption of anti-cancer treatment, participants who resumed an anti-cancer treatment had a good performance status (initial PS and PS at the end of the ICU stay ≤ 2), received chemotherapy before ICU, had one organ failure and low SAPS II score (Table 2).

Designation of a proxy was noted in 81% of cases and advance directives expressed only in 2%. For the decision to transfer to the ICU, the patient's referral oncologist was contacted in 57% of cases, opinions of family, nurses and patients were consulted in 40%, 28% and 7% of cases, respectively. Collective decisions were reported in the medical data in 21% of cases. Limitations of life-sustaining treatment were decided for 23% and 43% of patients during the admission and ICU stay, respectively. The therapeutic limitations concerned heart massage, use of adrenaline, hemofiltration and mechanical ventilation.

From 2010 to 2015, the numbers of oncology patients hospitalized in the ICU almost doubled from 27 to 47 and the ICU mortality rate decreased from 44% to 28%. Mechanical ventilation decreased from 41% to 28% and we noted an increased number of ethical decisions from 44% to 57%.

Discussion

Our cohort indicated that prognostic factors of 30-day mortality after admission in an ICU for patients with SCTs are the number of organ failures ≥ 3 and the non-curative setting.

The aim of our study was to define objective and rapidly assessable variables to help physicians in their decision to transfer or not to transfer oncology patients to an ICU.

Table 1. Description of patients, transfer and ICU stay characteristics, for patients with SCTs admitted to the general ICU – Bordeaux, France, 2010–2015 ($N = 235$).

Characteristics	$N = 235$ (%)
Age	61 (± 11.4)
Male	140 (59%)
Charlson comorbidity index	
≤ 2	28 (12%)
3–5	55 (23%)
≥ 5	152 (65%)
PS before ICU stay	
0–2	189 (84%)
3–4	35 (16%)
Types of cancer	
Lung	77 (33%)
Head and neck	54 (23%)
Colorectal	17 (7%)
Renal	16 (7%)
Gynecological	16 (7%)
Others	55 (23%)
Extension	
Local	27 (12%)
Locoregional	66 (28%)
Metastatic	142 (60%)
Number of metastatic sites	
0	95 (41%)
1	57 (24%)
≥ 2	82 (35%)
Cancer status	
Curative care	72 (31%)
Non-curative care	163 (69%)
Cancer treatment status	
Chemotherapy	111 (47%)
Radiochemotherapy	26 (11%)
No treatment	35 (15%)
Targeted therapy	22 (9%)
Immunotherapy	2 (1%)
Others	39 (17%)
Number of prior anti-tumoral therapies	
0	13 (6%)
1	118 (50%)
≥ 1	104 (45%)
Admission through the night, weekends or holidays	116 (49%)
Number of organ failures	
0–1 failure	130 (55%)
2 failure	66 (28%)
≥ 3 failure	39 (17%)
Causes of ICU admission	
Sepsis	131 (56%)
Respiratory	122 (52%)
Shock	80 (34%)
Neurological	60 (26%)
Renal	58 (25%)
Cardiological	27 (11%)
Hepatic	10 (4%)
SAPS II	44 (± 22)
Treatment during ICU stay	
Vasopressors	92 (39%)
Mechanical ventilation (MV)	61 (26%)
Non-mechanical ventilation (NMV)	51 (22%)
High flow oxygen therapy (HFOT)	
Adrenaline	33 (14%)
Hemofiltration	19 (8%)
Chemotherapy	16 (7%)
Others	6 (2.5%)
Length of ICU stay (days)	3 (1–5)
PS after ICU discharge ($n = 171$)	
0–2	116 (68%)
3–4	55 (32%)
Mortality in ICU	57 (24%)

ICU: intensive care unit; PS: performance status according to Eastern Cooperative Oncology Group; SAPS II: simplified acute physiology score II.

We chose parameters which could be assessed before ICU admission, and we thus excluded the SAPS II score which is a known prognostic factor [4,8–11,13,15,18]. The number of

Table 2. Comparison between patients who resumed an anti-tumoral treatment and those who did not.

Characteristics	Resumption of anti-tumoral treatment		<i>p</i>
	Yes, <i>n</i> = 104	No, <i>n</i> = 130	
PS before ICU stay			.01
0–2	93 (91%)	95 (79%)	
3–4	9 (9%)	26 (21%)	
Types of cancer			.18
Lung	28 (27%)	49 (37%)	
Head and neck	27 (26%)	27 (21%)	
Colorectal	10 (10%)	7 (5%)	
Renal	8 (8%)	8 (6%)	
Gynecological	5 (5%)	12 (9%)	
Others	28 (27%)	27 (21%)	
Extension			.12
Local	7 (7%)	20 (15%)	
Locoregional	30 (29%)	36 (28%)	
Metastatic	67 (64%)	74 (57%)	
Cancer status			.07
Curative care	29 (28%)	43 (34%)	
Non-curative care	75 (72%)	82 (66%)	
Cancer treatment status			.008
Chemotherapy	63 (61%)	48 (37%)	
Radiochemotherapy	13 (13%)	13 (10%)	
No treatment	7 (7%)	27 (21%)	
Targeted therapy	8 (8%)	14 (11%)	
Immunotherapy	1 (1%)	1 (1%)	
Others	12 (12%)	27 (21%)	
Number of prior anti-tumoral therapies			.52
0	3 (3%)	7 (5%)	
1	57 (55%)	64 (49%)	
≥4	44 (42%)	59 (45%)	
Number of organ failures			.02
0–1 failure	66 (63%)	63 (49%)	
2 failure	28 (27%)	38 (29%)	
≥8 failure	10 (10%)	29 (22%)	
Causes of ICU admission			
Sepsis	52 (50%)	79 (61%)	.09
Respiratory	49 (47%)	72 (55%)	.21
Shock	27 (26%)	53 (41%)	.02
Neurological	25 (24%)	35 (27%)	.62
Septic shock	23 (22%)	51 (40%)	.005
Renal	16 (15%)	42 (32%)	.003
Cardiological	8 (8%)	19 (15%)	.11
Hepatic	2 (2%)	8 (6%)	.19
Treatment during ICU stay			
Vasopressors	27 (26%)	65 (50%)	<.001
MV	17 (16%)	44 (34%)	.002
NMV	20 (19%)	31 (24%)	.40
HFOT	14 (13%)	19 (15%)	.80
Adrenaline	1 (1%)	18 (14%)	.003
Hemofiltration	4 (4%)	12 (9%)	.11
Chemotherapy	5 (5%)	1 (1%)	.05
PS after ICU discharge (<i>n</i> = 171)		<.001	
0–2	83 (81%)	32 (47%)	
3–4	19 (18%)	36 (53%)	
Aggravation of PS during ICU stay	0.43 (±0.8)	1.9 (±1.6)	<.001

PS: performance status according to Eastern Cooperative Oncology Group; MV: mechanical ventilation; NMV: non-mechanical ventilation.

organ failures, independently associated with 30-day mortality, seems an accurate variable and easily assessable by all physicians. Several studies reported similar results [4,7]. Taccone et al. [4] conducted a multicenter cohort in 198 general ICUs in Europe and reported mortality during ICU stay at 10%, 30% and 75% for cancer patients presenting 0, 2 organ failures and 3 or more organ failures, respectively. Interestingly, the number of organ failures was not a prognostic factor for non-cancer patients in this study. A non-curative setting, the other prognostic factor for 30-day

Table 3. Multivariate analysis of prognostic factors of 30-day mortality.

Characteristics	Odds ratio	95% confidence interval	
PS initial	1.690	0.768	3.718
Organ failure			
0–1 failure	Ref.		
2 failure	1.777	0.897	3.521
≥3 failure	4.298	1.77	10.437
Septic shock (yes vs. no)	1.389	0.721	2.678
Weekend/night/free day (yes vs. no)	1.642	0.809	3.334
Non-curative setting (yes vs. no)	2.240	1.091	4.598
Lung cancer	1.597	0.846	3.016

ICU: intensive care unit; PS: performance status according to Eastern Cooperative Oncology Group.

mortality in our study, has been more frequently debated in the literature [15]. Several studies did not report this factor as a prognostic factor [3,10–13], unlike others [3,9,19]. Mendoza et al. reported a metastatic setting as being a prognostic factor for mortality during hospitalization in a cohort of 147 patients with SCTs [20].

In study similar to ours, Azoulay et al. [11] analyzed prognostic factors of 30-day mortality after admission to an ICU. From 1990 to 1997, 120 patients with SCTs admitted to the medical ICU at a Paris university hospital were included. The 30-day mortality rate was 59% versus 36% for our cohort. Two prognostic factors of 30-day mortality were identified: mechanical ventilation and logistic organ dysfunction (LOD) score >6. The characteristics of the cancer or the co-morbidity of the patients were not prognostic factors of mortality. The non-curative setting as a prognostic factor in our study is probably related to the increase in solid cancer patients hospitalized in an ICU including patients in a metastatic setting. When we compared the characteristics of cancer patients admitted to an ICU in these two studies, done at an interval of 10 years, our study population comprised patients with more serious critical illness and more advanced oncological diseases. The median SAPS II score in the Azoulay study was lower (36 vs. 44), the number of metastatic patients was lower (42% vs. 60%) and patients in remission higher (16.6% vs. 9%) than our study. This phenomenon was confirmed by several studies [3–5,7,8] which described the increase in cancer patients admitted to an ICU, with more advanced cancers and more serious critical illness but with a similar decrease in mortality. This decrease in mortality is due to advances in resuscitation such as the development of noninvasive ventilation and earlier treatment for these patients [6,7,21–23]. We confirmed these data in our study, since between 2010 and 2015, the number of oncology patients hospitalized in the ICU almost doubled, mortality and the use of mechanical ventilation halved. These results are encouraging and show the interest of intensive care for patients with SCTs, even at an advanced stage.

To our knowledge, our study is the first to evaluate prognostic factors of resumption of anti-cancer treatment. The outcome depends on the reversibility of the acute episode and also on the treatment of the cancer after the ICU stays. Our results seem encouraging since almost half (44%) of

patients were able to resume specific treatment after hospitalization in the ICU. It seems that patients who resume anti-tumoral treatment have a less severe acute illness, a better performance status and a failure not related to their anti-tumoral treatment. Indeed, patients transferred to the ICU for septic shock and/or renal failure saw less resumption of their treatment. This can be due to side effects of chemotherapy such as septic shock on a chemo-induced aplasia, or nephrotoxicity of the anti-tumor treatment, thus compromising resumption of treatment.

The multidisciplinary decision, despite its importance, is not so easy to implement in usual practice, notably in the case of an emergency and when the transfer is often during the night, at the weekend or on a public holiday. Thus, being able to anticipate the decision to transfer cancer patients to an ICU or not is very important, but to inform or involve the patient in this decision is complex and difficult to achieve. The number of therapeutic limitations noted before and during the ICU stay increased between 2010 and 2015. One of the few studies interested in therapeutic limitations is that of Soares et al. [8] with a rate of therapeutic limitations (10%) lower than in our study. Finally, our study shows that the opinion of the patient is difficult to collect, since they are often unable to give it at the time of the acute episode, and advance directives are still not very common.

The most important limitation of our study was the retrospective nature and monocentric setting, limited to two medical ICU. In addition, we included patients with SCTs already admitted to the ICU. It would be interesting to include patients with SCTs when a decision to transfer to an ICU is to be made and to compare their outcomes (mortality, quality of life) whether subsequently admitted to the ICU or not.

Conclusion

Temporary ICU admission for patients with SCTs with one or two organ failures, even in a metastatic setting can be beneficial and may enable resumption of a specific treatment if the performance status is sufficient. This decision requires good cooperation between oncologists and intensive care specialists who are complementary in their knowledge.

Disclosure statement

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