Prognosis of Cancer Patients in the ICU: Much Work Remains

To the Editor:

As intensivists who are especially concerned for patients with cancer in the ICU, we have read with great interest the study by Rosa et al[1] published in the May issue of the Journal. We would like to congratulate the authors for conducting this study in a tertiary referral hospital where many patients with cancer are referred and receive care daily.

The data on the results of ICU care in subjects with cancer are mostly the result of studies conducted in cancer centers or cooperative groups that are especially involved in the care of such patients, like the study group we are participating in (Groupe de Recherche en Réanimation Respiratoire en Onco-Hématologie, http://www.grrroh.com/, *Accessed May 22, 2017*). They are representative of selected teams and thus may only demonstrate a volume effect as previously described (eg, in some patients with cancer suffering from acute respiratory failure, septic shock, or other comorbidities).[2-4] However, Soares et al[5] retrospectively reviewed 9,946 subjects with cancer (solid: 8,956 [90%]; hematological: 990 [10%]) admitted to 70 ICUs (51 [72.9%] located in general hospitals and 19 [27.1%] in cancer centers) during 2013 (medical admission: 5,017 [50.4%]; urgent surgery admissions: 483 [4.9%]; elective surgery admissions: 4,446 [44.7%]). Most importantly, the authors found that ICU admissions in cancer centers were not associated with lower ICU mortality, hospital mortality, or better resource utilization when compared with ICU admissions in general hospitals. This is an argument, among others, against the establishment of specialized ICUs, at least for oncology patients, such as those admitted for management after elective surgery. This remains to be determined for hematological patients, for whom there may be a potential benefit.[6]

We believe that other elements need to be clarified and commented upon. The first concerns the epidemiology of patients suffering from cancer hospitalized in ICUs. The study by Taccone et al[7] is dated (subjects included in the SOAP study, which collected a large amount of data on all subjects admitted to general [non-specialized] ICUs during a 2-week period [between May 1 and 15, 2002]). To the best of our knowledge, there are no data for hematological patients, except for those in the study by Taccone et al.[7] Epidemiology of cancer patients is most clear for those suffering from solid tumors, especially in the study of Puxty et al[8] performed in Scotland. A total of 118,541 subjects met the inclusion criteria in this study conducted between 2000 and 2009. Overall, 6,116 subjects (5.2% [95% CI 5.0–5.3%]) developed a critical illness and were admitted to the ICU within 2 y. This percentage is less than that found in a previous study in the same subjects by Bos et al[9] (140,154 subjects with unplanned ICU admission between January 2007 and January 2011; solid cancers: 10.9% of all ICU subjects).

We believe that future studies must not include subjects with hematological and solid cancers together and that the term cancer patient should be abandoned. The worst in-ICU prognosis of solid cancer, except those admitted in the ICU after planned surgery, patients was demonstrated several years ago and in a large study[10] of approximately 36,860 subjects with cancer. The research was conducted between 2006 and 2011 in 4 hospitals in the Netherlands linked to the Dutch National Intensive Care Evaluation registry, among whom 2,374 (6.4%) were admitted to the ICU.[7,11] In this study, the long-term prognosis (evaluated after 30, 365, and 730 d of ICU admission) was better for hematological subjects. The largest study on subjects with solid cancer retrospectively analyzed the unplanned admissions of 12,290 subjects in 80 ICUs in the Netherlands over a 4-y period.[9] Approximately 59.3% of all admissions were surgical (albeit unplanned), and these had a mortality rate (9.0% vs 8.9% in the ICU and 17.4% vs 14.6% in the hospital) like that of subjects with no diagnosis of cancer. In patients with solid tumors, efforts must be made to differentiate the prognosis of those admitted to the ICU after planned surgery and others (emergency surgery, medical conditions, or securing an act for diagnostic or therapeutic purposes). The distinction between the in-ICU and in-hospital prognosis between these subgroups of subjects with solid cancer was made several years ago by Soares et al.[12]

Management in the ICU may be very different, especially for the decision of withholding or withdrawing active therapies after an ICU trial. Recent data suggest that these decisions may be sure after 1–3 d in oncological patients, but only after 7 d in hematological ones.[13] Also, Rosa et al[1] do not report in their study one of the strongest determinants, which is Eastern Cooperative Oncology Group performance status, as recently confirmed, for survival in the ICU and after discharge.[14,15]

Table 1. Studies Reporting Rate of Anti-Tumoral Therapies After ICU Discharge

Reference	Cancer	*N*	Years	In-ICU Survival (%)	In-Hospital Survival (%)	6-Month Survival (%)	Anti-Tumoral Therapy After ICU (%)	Modification of Initial Anti-Tumoral Therapy After ICU
Roques etal (2009)[16]	BPC	105	1997–2006	57	45.7	27.6	62.5	NR
Andrejak etal (2011)[17]	BPC	76	1996–2006	52.6	48.7	13.2	10.8	NR
Bonomi etal (2012)[18]	BPC	1,134	1992–2005	NR	66.8	27.1	18.9	NR
Kim etal (2014)[19]	BPC	95	2009–2011	NR	22.1	NR (1-y survival 10%)	52.4	NR
Soares etal (2014)[4]	BPC	449	2011	72	61.2	45.2	50.2	34.3
Razazi etal (2015)[20]	BPC	125	1995–2010	83	68.8	47.5 (1-y survival: 30%)	69.8	NR
Camus etal (2015)[21]	Colorectal	89	2003–2012	NR	20.4	NR	69	31
Auclin etal (2017)[22]	Mixed solid tumors	262	2009–2014	66.4	56.1	NR (90-d survival: 48.1%)	52.7	NR

BPC = bronchopulmonary cancers
NR = not reported

We fully agree with the authors that the field of research on patients with cancer admitted to ICU is still wide. Among the questions unanswered, 2 of the major elements likely to be evaluated are the possibility of reintegrating an optimal anti-neoplastic project after a stay in the ICU and the quality of life. The first element has been reported to date only in 8 studies with incomplete data, often coming from very small subtypes of subjects with cancer (Table 1). Only 2 imperfect studies report quality of life of subjects with cancers after ICU discharge.[14,23] The decrease in quality of life may not be related to the fact that these patients have cancer but may simply relate to the ICU stay, as suggested in a large multi-center, prospective cohort study.[24] It must finally be remembered that all of these data are valid only in developed or developing countries, where ICU beds are numerous and where the medical care of such patients is possible, mainly because the care is probably more expensive than that of other ICU patients (transfusions, antibiotics, antifungals, hematopoietic growth factors, etc.).[25]

We believe, as do Rosa et al,[1] that critical care is essential in the supportive care of patients with cancer, sometimes even in those requiring palliative care.[26,27] As concluded by Bos et al,[11] we believe that despite the fact that 1 of 16 cancer patients was admitted to an ICU, ICU support for this group should not be considered futile. However, other studies seem necessary to better define their prognosis in the short, medium, and long term, with careful being taken to include only patients who are comparable (ie, oncology vs hematological ones, admission after planned surgery vs others) before definitive conclusions can be made.

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Prognosis of Cancer Patients in the ICU: Much Work Remains—Reply

In reply:

We read with great interest the excellent comments of Vincent et al regarding the mortality of adult critically ill subjects with cancer. The prognosis of patients with malignancies admitted to the ICU has improved considerably in the last 4 decades due to the evolution of critical care and supportive oncology.[1] This trend is observed not only in patients with solid cancers, but also in patients with hematological malignancies. The 80% ICU mortality rate found in studies of the 1980s and 1990s[2-5] has decreased to values around 30–40% today.[6,7] Consequently, the current ICU mortality rates of cancer patients are comparable with those of patients without cancer admitted to general ICUs.[8] The mere use of the diagnosis of cancer as a reason to refuse ICU treatment is no longer acceptable, and new approaches should be developed with the aim to match the potential benefit of critical care with the needs and perspectives of cancer patients and their families.

Unfortunately, in our study[9] we did not compare the mortality rates of patients with solid neoplasms with those with hematological neoplasms, and this remains as an evidence gap due to the scarce literature about this issue. Some studies have shown that subjects with hematological malignancies have higher ICU mortality rates when compared with subjects with solid cancers.[8] However, conflicting data exist about this finding. For example, Azoulay et al,[10] in a prospective multi-center cohort of 1,011 critically ill subjects with hematological malignancies, showed a hospital survival rate of 60%, a statistic similar to those found in a mixed population of ICU patients.[11] The study of van Vliet et al[12] showed that the ICU mortality rate of subjects with solid neoplasms was comparable with the rate for those with hematological tumors. Moreover, some evidence suggests that the accumulation of organic dysfunction during ICU stay is a better predictor of mortality than the type of malignancy per se. The publication of Soares et al[6] on 700,000 critically ill subjects with cancer showed that mortality was predicted by severity of organ failures and performance status and not by cancer-related characteristics, such as the type of malignancy and neutropenia.

For these reasons, we agree with Vincent et al that more studies are necessary to evaluate the course of different cancer subtypes during critical illness. Cancer is a heterogeneous group of diseases, and the prognostic model of ICU mortality for cancer patients would be improved by refinements related to the interaction between the critical illness and specific characteristics of each cancer subtype. Confounding factors, such as type of ICU admission (medical, emergency surgery, or elective surgery), time between ICU indication and ICU admission, performance status before ICU admission, degree of organ dysfunction during ICU stay, optimal cancer therapy, and rates of withdrawal and withholding support therapy during ICU stay, must be controlled to obtain improved estimates of specific cancer subtype effects on the course of critical illness. In addition, long-term outcomes, such as the incidence of post-intensive care syndrome among patients (ie, depression, anxiety, post-traumatic stress disorder, cognitive impairment, physical impairment) and their families (ie, depression, anxiety, post-traumatic stress disorder), should be evaluated for a more complete analysis of the impact of critical care on this specific population of patients. Surviving the critical illness is just the first step; we must evolve to improve long-term of quality of life cancer patients admitted to the ICU and their families.

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