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Critically ill cancer patient in intensive care unit: Issues that arise

Eirini Kostakou, MD [1], Nikoletta Rovina, MD [1], Magdalini Kyriakopoulou, MD [1], Nikolaos G. Koulouris, MD [1], Antonia Koutsoukou, MD [1,*]

ICU, 1st Department of Respiratory Medicine, University of Athens Medical School, "Sotiria" Hospital, 152 Mesogion Ave, GR-11527, Athens, Greece

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ABSTRACT

Advances in the management of malignancies and organ failures have led to substantial increases in survival as well as in the number of cancer patients requiring intensive care unit (ICU) admission. Although effectiveness of ICU in this group remains controversial, the heterogeneity of its population in terms of the nature and curability of their disease and the severity of critical illness and underlying conditions may explain the plethora of issues arising when considering cancer patients for ICU admission, especially from the view of limited resources and ICU beds.

The most frequent reasons leading a cancer patient to ICU are postoperative, respiratory failure, infection, and sepsis. Although reasons of admission, nature and number of organ failures, type of malignancy, and therapies that have preceded ICU admission may affect outcome, reliable scoring systems or survival predictors are missing. Literature suggests that organ dysfunction should be managed at its onset, whereas aggressive ICU management should be reappraised after a few days of full support.

A multidisciplinary treating team of physicians should aid in changing the goals from restorative to palliative care when there appears to be no possible benefit from any treatment. End-of life-decisions and code status should be made by consensus, based on patients' autonomy and dignity. Further interventional multicenter studies are required to assess post-ICU burden, long-term medical outcomes, and quality of life in this cohort of patients.

1. Introduction

Over the past decades, progress on the early detection and management (whether radical or supportive) of cancer patients has led to a significant increase in survival rates [1]. As a result, the number of patients admitted to the intensive care unit (ICU), either for cancer-related complications or for treatment-associated side effects is steadily increasing [2-6].

Throughout the 1980s and early 1990s, the unfavourable outcomes of critically ill cancer patients requiring life support prompted some clinicians to favor either denial of ICU admission or early treatment limitation decisions for these patients [7-10]. More specifically, reports on patients with hematologic malignancies were very disappointing, regarding both in-hospital as well as long-term survival rates [11]. As a result, in 1999, the American College of Critical Care Medicine issued guidelines for ICU admission, discharge and triage, placing cancer patients, especially those with metastatic cancer, in a category unlikely to benefit from ICU care [12].

However, recent data suggest that an increased number of patients with solid and hematologic malignancies may actually benefit from intensive care support with improved outcomes [13-16]. This improvement may be attributed to improved patient triage, advances in the management of oncological emergencies, better understanding and treatment of critical illness as well as to advances in hematology/oncology [17].

Nowadays, it is known that a great proportion of ICU beds are being held by cancer patients. Taccone et al [4], in a subgroup analysis emerging from a 15-day surveillance study Sepsis Occurence in Acutely ill Patients (SOAP) conducted in 2008 in 198 European ICUs, found that cancer patients, mostly patients with solid tumors and hematologic malignancies, accounted for up to 15% of all ICU admissions. Patients with solid cancer had the same severity of illness as the noncancer population, whereas the outcome of all solid cancer patients was comparable with that of noncancer subjects. Patients with hematologic malignancies were more severely ill and had the highest hospital mortality [4]. The high prevalence of cancer patients treated in ICUs was confirmed by another recent multicenter study in 22 Brazilian ICUs. Soares et al [5] found that almost 20% of all ICU admissions were patients with cancer. Therefore, although the former belief that cancer patients as a whole should not be admitted to the ICU due to increased mortality does not stand, these patients do not constitute a homogeneous group and, thus, different criteria apply in each case. Consequently, issues arise as to which criteria should apply to admit a cancer patient to the ICU, to continue treatment, or to make a transition from cure to comfort, whereas taking into account the unavailability of ICU beds and the significantly reduced financial budgets for hospital units. The need to devise an appropriate ICU admission policy based on the potential of patient recovery is

* Corresponding author. Tel.: +30 210 7763718.
E-mail address: Koutsoukou@yahoo.gr (A. Koutsoukou).
[1] Tel.: +30 210 7763718; fax: +30 210 7781250.

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imperative. This way, patients without a reasonable prospect of recovery would not be admitted to the ICU. Medically non-effective policy is thus avoided, and consequently, patients and relatives do not undergo any unnecessary suffering. On the contrary, critically ill patients with a reasonable prospect of recovery would not be deprived of ICU admission.

2. Methods

The information in this review is based on results of a Medline, Bethesda, Maryland, USA and OVID (New York, NY) search for studies during the last 2 decades. The keywords used were related to cancer (cancer, tumor, malignancy, chemotherapy, and bone marrow transplantation), intensive care (ICU, intensive care, mechanical ventilation, sepsis, and shock), and ethics (palliative care, futility, and end-of-life care). We read relevant articles in full, searched their reference lists, and chose the most relevant based on findings and clinical significance. Bibliographies of identified articles, guidelines, and conference proceedings of professional societies were reviewed for additional references.

2.1. Cancer patients in the ICU

There are many reasons leading a cancer patient to the ICU but the most frequent do not differ from those of the general population. Patients with malignancies require ICU admission for postoperative recovery, respiratory failure requiring intubation and mechanical ventilation, infection and sepsis, bleeding, and oncological emergencies, the first 3 being the most frequent [18-21]. In the study of Soares et al [5], the most frequent cause of ICU admission was postoperative care (57%). Sepsis and respiratory failure followed, accounting for 15% and 10%, respectively. Scheduled or emergency surgical resection of solid tumors is the most common reason for postoperative care in this group of patients [5,22]. Postoperative management in the ICU offers immediate stabilization as well as complication treatment, thus giving the opportunity for more radical and aggressive surgical therapies.

Acute respiratory failure in critically ill cancer patients is usually the consequence of pneumonia, acute respiratory distress syndrome (ARDS), diffuse alveolar hemorrhage, pulmonary embolism, aspiration, and/or the disease itself with or without airway obstruction. A better understanding of the mechanisms behind the ARDS entity accompanied by the use of protective ventilation strategies has contributed to the increased survival rate observed in the last few years in patients with cancer and respiratory failure [23].

Cancer patients have a 3- to 5-fold greater risk of severe sepsis in comparison with noncancer patients, thus needing ICU admission more often [24]. Angus et al [2] showed that more than 15% of severe sepsis patients have been diagnosed with some kind of malignancy and that these patients have a 30% higher mortality risk, compared with other severe sepsis patients. Severe sepsis incidence and mortality vary widely among tumor types. Patients with neutropenia or with hematologic malignancies appear to be particularly vulnerable to this situation [24,25]. Regarding the site of infection, as shown by the study of Taccone et al [4], the respiratory tract is the most frequent site for all types of cancer, with blood stream infections also being frequent, especially for patients with hematologic malignancies. Early recognition and aggressive treatment of severe sepsis, as recommended by the Surviving Sepsis Campaign [26], are associated with improved survival [25].

Oncological emergencies include situations induced by the disease itself or by chemotherapy or radiation therapy. Chemotherapy-induced complications are myelosuppression and its consequences, cardiotoxicity, and pulmonary complications. Acute tumor lysis syndrome, leukostasis, superior vena cava syndrome, and hemophagocytic syndrome are among the oncological emergencies, which can take place any time during the evolution of the disease and may lead to ICU admission [27].

2.2. Appropriate triage policy: reliable predictors for outcome

In 2005, Thiery et al [19] conducted a prospective, 1-year hospital-wide study of all cancer and hematology patients, for whom admission to the ICU was requested, regardless of whether admission was granted or not. They found that 20% of patients who were not admitted because they were considered “too well” died before hospital discharge, and 25% of the patients who were not admitted because they were considered “too sick” survived [19]. These findings undoubtedly imply inaccurate clinical judgment by the intensivists; thus a need for reliable predictors of outcome and criteria for an appropriate triage policy arises.

Outcome may be related to reasons of admission. Overall hospital mortality of cancer patients treated in the ICU is 30%, ranging, however, between 58% in patients admitted because of medical complications and 11% or even less in scheduled surgical patients [5,6,8,9,22,28-33]. Bos et al [22] analyzed 28 973 patients admitted to the ICU after elective surgery and found an ICU mortality of 1.4%. The nature and number of organ failures as predictors of mortality have been confirmed by different researchers [9,16,21,25,34-36]. Darmon et al [21] studied 100 patients with newly diagnosed cancer requiring immediate ICU admission and cancer chemotherapy and found that patient survival was strongly dependent on the number of organ failures with a 30-day mortality approaching 90% if 6 or more organs were failing.

There are studies showing that the type of malignancy may have an impact on the outcome. A 58% ICU mortality was recorded in patients with hematologic malignancies, as compared with 27% in patients with solid tumors [4]. This discrepancy may be due to the fact that hematologic patients develop more complications and need more life-sustaining procedures. Indeed, hematologic patients appeared more often with sepsis, bacteremia, and septic shock and with the need for hemodialysis, vasopressors, and inotropes. Moreover, this group more frequently developed ARDS, circulatory dysfunction, coagulopathy, and leucopenia [4]. It should be noted, however, that, in recent prospective studies, much lower mortality has been reported in this cohort of patients [15,16]. Special concern has been given to the role of neutropenia in ICU outcome. Although neutropenia has been shown to be an independent risk factor for increased mortality in ICU patients with hematologic malignancy [20,35], this finding was not confirmed in a recent matched case-control study [37] nor when the entire population of critically ill cancer patients was studied [5]. Furthermore, it should be noted that recent chemotherapy treatment, which is expected to impair immune responses to infection, was not found to have a prognostic impact on patients with severe sepsis or septic shock [38].

Regarding the therapies that have preceded ICU admission, hematopoietic stem cell transplantation (HCT) was of adverse prognostic significance in many studies. However, the last few years, the prognosis of autologous and allogeneic HCT has changed [14,32,39-42]. In autologous HCT recipients, as in other critically ill cancer patients, the short-term risk of death was dependent only upon the number and type of organ dysfunctions [42], whereas in recipients of allogeneic HCT, mortality remained extremely high [41].

Several studies have been made in an effort to elucidate the best prognostic score for the outcome of cancer patients in the ICU and thus to facilitate ICU admission policies for these patients. Soares et al [43] studied the most commonly used severity-of-illness scores: Acute Physiology and Chronic Health Evaluation II, Simplified Acute Physiology Score II, and the Mortality Probability Model II. Unlike the prognostication they offer for the general population, none of the evaluated severity scores was found to be accurate in predicting outcome for critically ill cancer patients. General scores significantly underestimated mortality as compared with the observed mortality, whereas the Cancer Mortality Model, a model combining both general and cancer-specific elements, tended to overestimate mortality.