Admission Criteria and Prognostication in Patients with Cancer Admitted to the Intensive Care Unit

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Critical care of patients with cancer has progressed despite many challenges in recent decades. In the early 1980s, a cancer diagnosis was considered a contraindication for admission to an intensive care unit (ICU). The advent of successful antineoplastic therapies, improved supportive care, and consumer demand initially validated the benefits of critical care for these patients. A desire to pursue more aggressive therapies in search of enhanced patient outcomes also led to practice changes within the critical care environment in the 1990s. This article provides an overview of these historical perspectives and the current state of the science regarding admission to ICUs, care of patients who have cancer in the ICU, and prognostication for critical illness among patients with cancer.

HISTORICAL PERSPECTIVES OF CANCER AND CRITICAL CARE

ICUs developed in the 1960s and flourished in the 1970s with the implementation of resuscitation standards for acute life-threatening dysrhythmias and perfection of trauma management skills associated with the Vietnam War. Initial critical care was provided for cardiac, surgical, and trauma patients although many patients with chronic medical disorders such as chronic obstructive pulmonary disease and chronic renal failure required the technologies available only in an ICU setting. The first antineoplastic therapies to provide potential for long-term disease-free survival were surgical interventions aimed at removing tumors at an early stage. Late in the 1970s...
medical antineoplastic therapy first realized its major successes with Hodgkin disease and testicular cancer, both of which occur frequently in young adults. Childhood leukemia treatment exceeded these success rates, mandating a revision in ICU admission policies for children. Experience with oncologic therapies such as blood and bone marrow transplantation that produced extreme myelosuppression and organ dysfunction led some academic medical centers to dedicate intensive care beds to provide specialized care to these patients.3

Despite advances in antineoplastic therapy and supportive care treatments that provided a growing number of patients who have cancer with an opportunity to become “cancer survivors,” the lack of accessibility to intensive care resources persisted. Intensive care clinicians perceived that responses to cancer therapy were poor, and the ability of patients to survive physical insults such as critical illness were deemed appropriate reasons to limit care.2–4 As oncologic success stories became commonplace, consumers demanded equal treatment, and prognostic variables became better defined, as did acceptance of critical care for these patients.5 A suggestion to assist clinicians in reversing their biases is described in an article by LeCuyer and colleagues6 and mirrored by an editorial7 stating that a change of view is needed of patients who have cancer to “see them as people living with a chronic illness that may have minimal impact on their day-to-day lives.” The literature suggests that studies published within the last decade report improved outcomes for patients with cancer as opposed to those before 1999,2,5,8 with some investigators defining intensive care admission after 1996 as an independent predictor for a more positive outcome.7,9 These improvements in outcomes have been attributed to improved patient triage, enhanced management of oncologic emergencies, perfection of critical care interventions for common acute ICU conditions such as severe sepsis and acute respiratory distress syndrome, and advances in hematology/oncology.5,8

Patients with cancer are often admitted to ICUs and several variables are used to determine best practices in their management. Professional society guidelines for intensive care admission, discharge, and triage are available and can be used as a guide for evaluation of patients.10 Based on a comprehensive review of the literature describing critical care of patients with cancer, this article further defines reasons for appropriate admission to the ICU that are unique to oncologic patients. Clinicians should evaluate and interpret suggested admission criteria based on their institutional capacity, particularly the sophistication of general care available, and patient acuity that requires ICU admission for high levels of nursing care rather than the need for specific intensivist skills. Some patients with cancer have high acuity and the need for increased frequency of assessment and physical interventions may necessitate critical care admission, but not because of clear critical illness.

Approximately 62% of patients with cancer are considered “survivors,” as shown by an expected survival beyond 5 years.5,11 This information paired with the data that show 1 in 10 patients with cancer will require expertise provided by intensive care clinicians demonstrates that selective critical care is reasonable and morally necessary.12–14

**ICU ADMISSION AND RESTRICTION POLICIES AND PATIENTS WITH CANCER**

More than 28% of all health care expenditures occur in the last 6 months of life, and appropriate allocation of scarce critical care beds is an essential component of managing limited resources and controlling health care costs.14 One method to ensure objective decision-making when triaging patients for ICU admission is to use
predetermined admission or restriction criteria developed for adult and pediatric patients by the Society of Critical Care Medicine. These guidelines offer options of admission criteria using 1 of 3 models: a prioritization model (eg, highest priority with greatest potential benefit), a diagnosis model (eg, specific medical diagnoses or clinical conditions), or an objective parameters model (eg, specific clinical symptoms such as third-degree heart block or hemoglobin less than 7 mg/dL). The priority model of this document specifically states “priority 4 are those patients who are generally not appropriate for ICU admission. For example: metastatic cancer unresponsive to chemotherapy and/or radiation therapy (unless the patient is on a specific treatment protocol).” The context of this example may continue to encourage decision-making based on prediction of outcome, a concept that continues to elude definition. If using the prioritization model for creation of admission criteria, the principle of justice would dictate that ICUs use a valid and reliable mortality prediction model for determination of admission. One study defines metastatic cancer as 1 of only 2 variables statistically significant for refusal for ICU admission despite the presence of general guidelines that did not define specific diagnoses.

The operationalization of these recommendations or a similar institution-based document has been inconsistent among ICU clinicians. Published studies assessing the application of recommendations demonstrate that ICU clinicians do not necessarily use these guidelines in daily practice. As many as 75% of clinicians do not adhere to their own admission guidelines and 79% do not have restriction guidelines. Within the framework of these recommendations, several investigators have attempted to define objective criteria for triaging patients with cancer for ICU admission. Groeger and Aurora define broad categories of admission criteria: (1) postoperative care, (2) management of medical emergencies related to cancer or its treatment, and (3) monitoring during intensive oncologic treatments. They further state that 3 principles guiding decisions will lead to the best use of critical care resources. First, the clinician should determine whether the status of the critical care complication and the disease suggest a high likelihood of meaningful survival as defined by the patient and physician. Second, is the patient’s autonomy or prior expressed wishes being respected? Lastly, the principle of distributive justice should be employed when there are limited ICU resources. These principles were mirrored in a study of Israeli intensive care physicians. The Australian Classification System outlines stages of cancer based on the goals of care and recommends that ICU care should be delivered only if the goals of care are clearly beneficial to quality and quantity of life. These classifications are (1) newly diagnosed, (2) cure is possible, (3) probable control of disease, (4) treatment failure indicates probable supportive care objective, and (5) palliative symptom control. When using this system, critical care is always provided to class 1 and 2 patients, is evaluated on a case-by-case basis for class 3 and 4 patients, and is considered contraindicated for class 5 patients.

COMMON CAUSES OF CRITICAL ILLNESS

Critical illness in patients with cancer can vary as widely as the different tumor types themselves. The critical care literature examining outcomes and reasons for critical illness in patients who have cancer concurs that the best outcomes are realized when careful patient selection for ICU care is employed. Consensus dictates that the best candidates for use of critical care resources among patients with cancer are patients at presentation for their initial cancer diagnosis, when there are clearly promising treatment options for their cancer and critical illness, or when crises occur in patients who do not have active malignancy. Critical illness, however, arises in
many patients in whom clear indications are not present, and each patient should be considered in the context of current malignant disease, status of comorbid health conditions, and ability to survive the critical illness and the time it takes to return to pre-illness level of functioning. Understanding specific situations that may precipitate critical illness is valuable for planning best care. When there are insufficient data to predict prognosis of a patient confidently, it is reasonable to initiate critical care intervention with reassessment of the patient’s status after 3 to 7 days. This range of time may be necessary to obtain key diagnostic data, or to assess initial responses to interventions. Patients with cancer who prove to have irreversible complications or who do not quickly improve with perceived definitive therapy are less likely to survive the critical illness. No improvement in the patient’s critical illness during this “therapeutic trial of critical care interventions” may result in cessation of mechanical support, a decision not to escalate care, or a definitive discussion with a health care proxy regarding additional interventions deemed unhelpful for achieving the goal of comfort. Unique critical care applications in patients with cancer include postoperative care, special considerations of solid tumors and hematologic malignancies, and situations in which the crisis is unrelated to the tumor or its therapy.

When considering all patients with cancer who require ICU care, the most common reasons for ICU admission are: (1) respiratory failure, (2) postanesthetic recovery, (3) infection and sepsis, (4) bleeding, and (5) oncologic emergencies. Respiratory failure is the most common reason for ICU admission for all groups of patients with cancer, but the implications vary depending on the reason for respiratory compromise. Studies suggest that postoperative support and a positive response to noninvasive ventilation are patient characteristics that indicate a better prognosis. Some subpopulations have specific common critical illnesses that must always be considered in planning for ICU use and necessary nurse training or resource allocation. For instance, although acute intracranial events such as increased intracranial pressure, hemorrhage, or status epilepticus are uncommon with many cancers, their management must be within the scope of the local ICU if the oncologists are treating patients with brain tumors. Patients with hematologic malignancies also require advanced blood component support, pheresis capabilities, and continuous renal replacement therapy (CRRT) to manage the complications common to their disease. Unique causes of critical illness and potentially valid reasons for admission to an ICU are now described according to the neoplastic diagnosis or treatment modality.

Postoperative Care

One of the most common uses of critical care is for postoperative patients with complex or large tumor resection. Although many patients who have cancer require surgery, those most likely to require postoperative critical care support include brain tumors, esophageogastric cancer, head and neck cancer, hepatic cancer or metastases to the liver, lung cancer, ovarian cancer, pancreatic cancer, and urologic malignancies. Surgical critical care units provide immediate stabilization and recovery after prolonged surgical procedures, monitor for multisystem complications such as bleeding, dysrhythmias, fluid and electrolyte imbalance, glycemic events, hypotension, or ischemic organ failure. Use of critical care in these patients has assisted surgeons to develop more advanced and aggressive procedures that have positively influenced survival. ICU survival in this patient population exceeds 80%, and long-term survival is common. Surgical interventions for supportive care such as semipermanent central line insertions, or palliative interventions such as stent placement are also important for care of patients with cancer who occasionally require
intensive care resources. At the forefront for all decisions concerning surgical intervention and ICU care is the concern of immediate survival benefit. The next variable to contribute to decision-making is the status of the underlying cancer and likelihood that the surgical procedure will provide enhanced quality and quantity of life.

**Patients with Solid Tumor Malignancies**

Patients with solid tumor malignancies also require critical care support when they present initially or with recurrent bulky disease that erodes vessels and tissues, or compresses body organs, causing hemorrhage or organ failure. These patients frequently undergo surgical resection, debulking, or reconstructive surgical procedures. Patients with solid tumors are also more likely to receive palliative surgical interventions such as stenting, embolization, catheter or shunt placement, or diverting procedures. The unique critical care needs of these patients vary based on the location, initial size, stage of disease, and growth rate of the tumor, but principles of care are consistent. In all patients, possible and probable complications can be anticipated and advanced planning about the extent of supportive interventions to be offered should be discussed with patients and their health care decision-makers.

When known, the tumor growth rate may be 1 of the most significant variables to predict critical illness. Tumors with rapid proliferation rates are quick to metastasize and create life-threatening complications but are also the most immediately responsive to antineoplastic therapy. For example, patients presenting with advanced stage small cell lung cancer are at risk for immediate severe, life-threatening complications such as airway obstruction, superior vena cava obstruction, pericardial effusions, or pleural effusions, but may have rapid and dramatic dissipation of symptoms soon after chemotherapy.

Tumor location, size, and stage of disease are the next considerations. Initially, complications should be anticipated related to the location of the primary tumor and what will occur when it shrinks with therapy or when it continues to grow before therapy has adequate time to work or despite treatment. When planned transfer to the ICU has been determined appropriate, predicting likely complications based on the primary tumor location and penetration of nearby organs could facilitate early involvement of intensivists as consultants. Their consultation and awareness of the patient’s clinical disease and goals of care can enhance a rapid and more successful transfer of service if needed. For example, a tumor of the esophagus that has extension into the tracheal wall could shrink with therapy, but leave a tracheoesophageal fistula that would require immediate surgery. Another example is a patient with head and neck cancer that is impinging on the carotid artery and could have tumor erosion into the carotid or nearby vessels with massive bleeding. In both cases, the specific emergency and its approximate timing may be predictable, with definable early signs or symptoms, and proactive discussions could help determine the critical care course of care.

The next consideration for patients with solid tumors involves the actual or potential high-risk sites of metastases and crises that may arise. Because the risk of brain metastases is high in patients with small cell lung cancer, clinicians should be constantly vigilant for mental status changes or signs and symptoms of possible seizure activity. Recognition of the metastatic pattern of each tumor type is helpful in planning critical care interventions.

The disease trajectory in patients with solid tumors may vary, enabling many patients with metastatic but slow-growing disease to live long and productive lives despite having metastatic cancer. High functional performance before critical illness has been shown to influence outcomes positively. Functional activity or performance status scoring such as the Karnofsky Performance Scale Index, Functional
Assessment of Cancer Therapy (FACT), or Memorial Symptom Assessment Scale (MSAS) can be useful for identifying patients who will either fare well or do poorly with critical care interventions. As with other malignancies, the need for mechanical ventilation among patients with solid tumors remains an important poor prognostic predictor for mortality.

Patients with Hematologic Malignancies

Patients with hematologic malignancies present with different critical care issues from those with solid tumor malignancies. First, the nature of these malignancies is diffuse at diagnosis, producing general body responses to widespread malignancy such as capillary permeability syndrome, clotting, and catabolism that consequently trigger complications such as respiratory distress, hypotension, disseminated intravascular coagulation, renal insufficiency, and hepatic dysfunction. All treatments for these malignancies include the whole body and total marrow destruction, which leads to severe complications of myelosuppression such as bleeding and sepsis. In addition, these tumors are more likely to have rapid proliferation rates that result in excessive cell turnover before and during therapy. The consequences may include critical illnesses such as leukostasis, tumor lysis syndrome, or disseminated intravascular coagulation. These patients frequently present with multisystem dysfunction and respiratory failure, often the result of serious infection. Because many patients experience prolonged marrow suppression, and receive frequent and prolonged antibiotic treatment, it is common for them to have infections with resistant organisms, opportunistic and unusual microbial disease, and refractory infectious complications. Recovery from critical illness in these patients most often directly correlates with their establishment of disease remission and white blood cell recovery. Several studies validate that implementation of mechanical ventilation also predicts for poorer outcome. Progress has been made in the last decade and recent literature reports patients with hematologic malignancies surviving an ICU episode requiring mechanical ventilation on average of 22% to 42% of the time compared with less than 20% survival in the 1980s and 1990s. Proposed reasons for this finding reflect the same advances in cancer care that have enhanced outcomes in other patient populations. The length of time a patient’s white blood cells are depressed may lead to a more prolonged ICU course while awaiting evidence of bone marrow recovery and resolution of complications.

Patients Undergoing Hematopoietic Stem Cell Transplantation

Critical care admission has also been provided based on use of specific therapies. For many years the trajectory of hematopoietic stem cell transplantation (HSCT) required severely myelosuppressive, high-dose chemotherapy, or radiation followed by infusion of a foreign antigenic material (another person’s bone marrow or concentrated hematopoietic stem cells). The aim of this intensive therapy is total irradication of cancer. The serious complication rate for these patients who were receiving a potentially curative treatment exceeded 20% to 40%, requiring frequent admission to the ICU. The rationale for delivering this high level of support has been the hope for cure in these individuals. It was believed that allogeneic transplant patients experienced more frequent and higher severity of critical illness, but this assumption has not proven true in many studies. Common reasons for ICU admission for patients with hematopoietic stem cell therapies have included respiratory distress, severe bleeding, sepsis, rejection disorders such as graft-versus-host disease (GVHD), and chemotherapy toxicities such as hepatic
venoocclusive disease or renal failure. The need for mechanical ventilation and presence of GVHD have been markers for greater severity of illness and have been consistently predictive for poorer outcomes in transplant patients. One study also affirmed that patients requiring mechanical ventilation with concomitant hepatic and renal dysfunction had the highest mortality. Alveolar hemorrhage as the source of respiratory failure also holds a potential for poorer outcome. One British study spanning 10 years of a large number of patients reported vasopressor use as predictive for lower survival, although this has not proven statistically significant in other studies. For those patients who do immediately survive mechanical ventilation, 6-month survival is considerably better than in many other patients who have cancer, varying from 27% to 88%.

In the past 2 decades, hematopoietic stem cell treatments have evolved into a more predictable and less toxic therapy, and now many of these same patients experience less myelosuppression, and receive better antirejection therapies, closer genetically matched cellular therapies, and advanced supportive measures. These patients have realized a dramatic decrease in need for critical care support from a high of 44% in the 1980s to 8% to 20% today. In a meta-analysis of pediatric HSCT patients, the investigators caution that straightforward interpretation of these advances in outcomes may be premature because of study limitations such as transplant criteria, biases of single center data, reduction in use of invasive mechanical ventilation, or selection bias for critical care intervention that may have changed. Several investigators have reported that ICU survival for HSCT patients has also improved from approximately 20% to 37.8% to 48.3%, attributable to improved cell-processing techniques, enhanced antirejection regimens, and better supportive care. Long-term survival (6–12 months) of these patients was once as low as 3%, but now averages 21.6% to 32.5%.

Other Reasons for Critical Care Support for Patients with Cancer

Other cancer-therapy driven critical care needs have been documented with administration of specific toxic chemotherapy, biotherapy, or radiotherapy treatments. Most antineoplastic therapies are associated with a risk of hypersensitivity. Moderate to severe hypersensitivity reactions have been identified in approximately 2% to 43% of patients receiving therapy. This variability is in part caused by adjustment of treatment regimens, and institution of antianaphylaxis premedications once serious reactions have been identified. Intensive vital signs, cardiac monitoring, or life-support after hypersensitivity reactions may be required by some patients. Administration of high-dose interleukin 2 to patients with renal cell cancer or melanoma has required critical care support in many patients, but is still administered because of toxicity reversibility and potential for cure in a small number of patients.

The final indications for use of critical care in patients with cancer are those general medical-surgical problems that arise during the course of antineoplastic therapy. Even when patients present for antineoplastic treatment with a good performance status, there is a high incidence of complications related to underlying medical disorders, such as hyperglycemia with diabetes, or respiratory distress in patients with chronic obstructive pulmonary disease. Cancer therapies may also exacerbate underlying conditions such as coronary artery disease or ulcerative colitis. In many cases, these complications are viewed as reversible given the stable status of the disease at the time the patient began treatment. For conditions in which a clear medical treatment is available that will stabilize the medical complication, aggressive support is usually offered. It may become apparent through the process of aggressive care that these
same medical disorders make it impossible for the patient to receive optimal antineoplastic therapy.

**GENERAL PREDICTORS FOR OUTCOME**

The research literature that defines outcomes for critical care of patients who have cancer spans close to 3 decades. Some studies stratified patients with cancer as a subgroup, and others studied only patients with cancer. The most consistent finding and predictor of outcome was the status of the malignancy. In newly diagnosed patients in whom there was an effective therapy option, the patients fared better than when the malignancy was persistent despite receiving treatment. Clinicians continue to debate the merit of offering aggressive antineoplastic therapy while the patient is critically ill, although studies support the administration of therapy, showing that it can be safely and successfully performed and provide immediate relief of certain tumor-related critical care crises.\(^{22,51-53}\) Most patients in these studies, however, had rapidly proliferative hematologic malignancies, making it difficult to generalize these findings to patients with solid tumor malignancies.\(^{51}\) The authors’ experience shows that patients with solid tumor masses causing the critical illness tolerate antineoplastic therapy and their critical illness resolves when and if their tumor shrinks. Those patients who have the best prognosis are those whose malignancy is in remission or quiescent at the time of the critical illness.\(^{3,51}\) There is considerable variability in findings when comparing early literature (before 1996) and studies published after that time. ICU mortality for patients with cancer before 1996 ranged from 44% to 98%,\(^ {26,54-63}\) but today it ranges from 23% to 57%.\(^ {9,25,28}\) Six-month survival has also improved from 2%–14% to 33%–66%.\(^ {25,64}\) A summary of the literature since 1979 has yielded a consistent number of prognostic indicators for short- and long-term survival from critical illness; these are summarized in **Box 1**. The literature spans a long period, and more recent oncologic advances have influenced outcomes in certain patient populations. For example, advances in cell processing and antirejection treatments have altered the critical illness profile for many HSCT patients. The advent of small molecule tyrosine kinase inhibitors has also improved long-term disease-free status for many chronic leukemia patients who would have previously converted to high-risk acute leukemia. Interventional radiologic procedures have enhanced nonsurgical management of obstructive processes in solid tumors, reducing the need for aggressive surgery and ICU care. The advent of effective noninvasive ventilation techniques has also reduced the need for mechanical ventilation and is suggested to be

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**Box 1**

**Prognostic predictors for improved survival of critical illness by patients with cancer**

- Postoperative support and monitoring is the only indication for critical care
- Quiescent cancer or malignancy in remission
- Good performance status at onset of critical illness
- Critical illness for less than 7 days
- Immune suppression lasting for less than 7 to 10 days
- Absence of fungal infection
- Absence of comorbidities
- Reason for ICU care found to be correctable or amenable to treatment

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independently associated with improved survival even after adjustment for matching variables. \(^9,65\)

Early studies of critical care outcomes in patients with cancer describe lower survival rates in patients requiring vasopressors, mechanical ventilation, with prolonged neutropenia, or with septic shock. \(^4,41,58,62,66\) Older age was evaluated as a potential poor prognostic variable in most studies, but did not prove significant, reinforcing that age alone should not be used in planning care for critically ill patients with cancer. \(^67\) These variables do not show the same significance in more recent studies. Survival from mechanical ventilation has improved from 20% in the 1980s \(^4,26,63\) to approximately 32% in studies since 1999. \(^8,9,64\) The cause of the respiratory failure requiring mechanical ventilation is perhaps the most significant contribution to the variability of outcomes for these patients. \(^3,30\) Mechanical ventilation postoperatively has the greatest success rate for extubation, discharge from the hospital, and general outcomes. Patients in whom there is an unclear cause for respiratory failure are least likely to survive mechanical ventilation and ICU stay. \(^24\) Specific predictors for low survival after mechanical ventilation include unknown cause, alveolar hemorrhage, multiorgan failure, refractory malignant disease, and prior performance status. \(^29,38,42,47,58,60\) Prolonged mechanical ventilation in the absence of multiorgan failure is not associated with higher mortality.

Neutropenia is no longer predictive of mortality, although prolonged neutropenia still confers an increased risk for severe and refractory infections. \(^28,53\) More recent studies of critical illness in patients with cancer report outcomes similar to those of other chronic medical patients. \(^64,66\) According to 1 investigator, \(^68\) approximately 15% of patients with cancer require a protracted ICU stay exceeding 21 days, yet their survival to discharge is not so grim as expected (about 18% are alive at discharge). The implication is that length of ICU care may not necessarily be prognostic for poor outcomes, and additional variables must be considered in determining futility for this patient population. \(^68\)

Renal failure in all ICU patients implies a risk of mortality between 40% and 90%, but stable statistics despite advances in renal replacement therapies suggest that the population of patients may be older and surviving other complications to develop renal impairment later. \(^3\) Recent studies since the use of CRRT became common are sparse but suggest improved outcomes in select patients who are not experiencing multiorgan failure. \(^69–71\) Early use of dialysis may predict better outcomes also. \(^71,72\) The presence of active malignancy continues to be an independent predictor of higher mortality in patients with renal failure and cancer. \(^3\) Anecdotal experience and case reports with CRRT suggests reduced mechanical ventilation, decreased use of vasopressors, and improved short-term outcomes in patients experiencing tumor lysis syndrome or hepatorenal failure, in whom survival may be 60% to 75%. \(^3,69,73,74\) The cause of renal impairment is an important variable in determining the overall prognosis associated with mortality in critically ill patients with cancer, with metabolic derangements having more promising outcomes than patients with primary renal disease and multiorgan failure. \(^3,69\)

Several studies have specifically addressed the short- and long-term benefit of cardiopulmonary resuscitation (CPR) in patients with cancer. In most studies of CPR in general care the diagnosis of cancer is described as an independent predictor of poor outcome. \(^3,62,66,70,72\) In most studies, immediate 24-hour survival from resuscitation matches statistics of other critically ill patients at about 38%, but the survival to discharge is lower than the 14% reported for other medical patients. \(^3,68,72\) More recent studies of CPR in patients with cancer demonstrates improved survival to discharge, but a longer rehabilitation and lower 6-month survival rate than with other patient
populations. Pediatric resuscitation yields a lower survival rate for all patients, and those with cancer rarely survived to be discharged from the hospital. An additional variable that contributes to poorer outcomes in these patients is a lower performance status before the resuscitation. In 1 report, patients who were critically ill, then had a cardiac arrest, had a poorer outcome than those patients who experienced a sudden and unexpected arrest. Patients with sudden cardiac arrest had dysrhythmias, sudden metabolic alterations, and cardiac complications; whereas those who suffered cardiopulmonary arrest after becoming critically ill were more likely to suffer from chronic and progressive organ failure. Health care providers should develop a relationship with patients with cancer that enables them to clarify patients’ wishes before an acute event, and continually to evaluate and communicate changing goals of care that may influence the patients’ decisions regarding resuscitation.

BARRIERS TO PREDICTING OUTCOME IN PATIENTS WHO HAVE CANCER

Before analysis of severity of illness or prognostic scoring systems and their application in critical illness among patients who have cancer, it is essential to consider the potential variables that may interfere with their accuracy. First, all scoring systems are used with patients after they present with critical illness and are hence flawed for use in any capacity as a preadmission screening tool. Potential confounding variables of the prognostication systems when applied to patients with cancer include short-term treatment-related organ compromise associated with cancer treatment, potential influence of chronic immune suppression, unpredictable tumor responses to treatment, the impact of reversible oncologic emergencies on initial acuity measures, and the lack of sensitivity of these same measures in patients whose malignancy is initially understaged. Organ compromise is common after initiation of many anticancer therapies, but the effects are usually time limited. Individual responses to organ toxicity are difficult to predict, as they may be altered by the patient’s underlying cancer, previous organ insults, degree of immune compromise, and previous general health. Patients’ responses to interventions for sepsis and coagulopathy are influenced by long-term persistent exposures to antigens and development of antimicrobial resistance, factors not easily incorporated into acuity scoring systems. Even in patients newly diagnosed with cancer, who are perceived to have the greatest successful outcome in critical illness, there are ill-defined factors that make 1 person’s tumor shrink considerably, whereas in the same time frame, another person’s tumor quadruples in size and effect. In these patients, the presence of high acuity scores is less reflective of their prognostic outcome of critical care than of the tumor response to treatment. The converse is true with oncologic emergencies such as tumor lysis syndrome or disseminated intravascular coagulation, which may be a positive reflection of tumor destruction even although acuity is increased in the short term. Many tumor effects and treatment plans are short term, with only a small poorly identifiable window of time to treat the cancer successfully. Thus, tumor- and treatment-related variables influencing acuity scoring may not be truly reflective of mortality, but instead a mirror of the combined effects of tumor growth, destruction, or treatment adverse effects. In some cases, the initial staging incorrectly identifies all existing tumors, influencing individual responses and leading to initially low acuity scores with a resurgence of symptoms as advanced or metastatic disease becomes symptomatic. More often, cancer has a rapid progression of symptoms with unclear variables influencing any 1 individual’s chance of fully responding to treatment without lasting adverse effects on organ function.
Several specific studies regarding outcomes of sepsis in patients with cancer have been performed. The prevalence of research interest in this patient population has been attributed to the frequency of this adverse effect of cancer or its treatment, and the necessity for admission to the ICU. It is estimated that 2% to 10% of patients experience an episode of sepsis or septic shock during cancer therapy.66,67 Because there are unpredictable variables such as organism-specific virulence, the host’s level of immunosuppression, and antibiotic resistance, studies have shown that there are few easily identifiable predictors of outcomes.76 Although this is also true of the general ICU patient, the variables that seem to influence outcome are more often cancer specific rather than infection related in critical illness caused by sepsis.65,77

PROGNOSTIC SCORING SYSTEMS AND APPLICATION TO CRITICALLY ILL PATIENTS WHO HAVE CANCER

Prognostic scoring systems for predicting general ICU patients’ outcomes and oncology-specific patients’ outcomes have been studied extensively, but primarily using a retrospective design, and not yet showing the patient specificity that would be required to use them for individual patient advisement.71 Despite extensive effort to create the ideal objective tool for critical care outcome prediction, studies continue to show that expert clinicians are better able to use available scoring system data combined with their own knowledge to better predict specific patient outcomes.19,25,75 Despite this, there remains diversity in predicted cause of critical illness and mortality and postmortem findings.77 The misdiagnosis of cardiac conditions and opportunistic infections suggests that perhaps improved diagnostic techniques and more accurate diagnosis may yield altered outcomes in these patients. Initial prognostication scoring systems in ICUs implemented in the 1980s include the Acute Physiology and Chronic Health Evaluation (APACHE-I, II, III), and its shortened version called the Simplified Acute Physiology Score (SAPS-II).43,71,78,79

The APACHE-III summarizes patient data to produce a severity-of-illness score that is usually performed at admission to the ICU, and 24 to 48 hours later. The degree of organ failure is entered into an equation to predict mortality. In medical-surgical patients and patients with cancer, this has been identified as inadequate to predict individual patient outcomes, but instead is more useful for planning staffing, describing case mix index, or for ICU performance benchmarking. Attempts have been made to modify the APACHE to account for oncologic variables such as reversible hematologic, gastrointestinal, or hepatic failure caused by therapy toxicities. This instrument is called the Intensive Care Mortality Model (ICMM) and provides cancerspecific factors to best identify the unique prognostic risks.3,71 This model was further developed and tested at 72 hours after admission to the ICU with better discrimination for survivors versus nonsurvivors.80,81 The ICMM scale used information yielded from the APACHE studies as a baseline, and built on an earlier study of this model,82 and defines 72 hours as a more sensitive predictive time for assessment of patients with cancer who are critically ill.66,78,80 SAPS-II uses similar data to the APACHE scoring system, but with fewer data points. The Therapeutic Index Scoring System (TISS-28 or TISS-76) measure severity of illness based on technologies required to provide care. Studies of APACHE scoring in oncology patients overpredicted critical illness, whereas TISS often underpredicted degree of critical illness because of lower use of invasive monitoring and aggressive diagnostic interventions in some patients with cancer.3 In a systematic review of prognostic models studied in critically ill patients with cancer, use of these models clarified that general prognostic models were adequate for identification of the very sick and very well patients, but tended to
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<th>Scoring System</th>
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<td>APACHE I</td>
<td>Scoring of medical diagnoses, comorbidities, and diagnostic test findings to predict ICU mortality. Performed on day of admission and 48 hours after admission, so not discriminating for patients who are not the “sickest” at the time of admission.</td>
<td>Johnson, Gordon, Fitzgerald, 198659</td>
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| SAPS III  | Refinement of terms and normal values for enhanced prediction of mortality.  | Pene, Aubron, Azoulay, et al, 2006<sup>19</sup>  
|           |                                                                             | Santolaya, Alvarez, Aviles, et al, 2008<sup>93</sup>  
|           |                                                                             | Soares & Salluh, 2006<sup>46</sup>  |
| ICMM      | MPM II was used as a basis to identify common ICU prognostic criteria and    | Berghmans, Paesmans, Sculier, 2004<sup>101</sup>  
|           | enhancement with oncology specific variables for improved mortality prediction| Groeger, Lemeshaw, Price, et al, 1998<sup>82</sup>  
|           |                                                                             | Santolaya, Alvarez, Aviles, et al, 2008<sup>93</sup>  
|           |                                                                             | Soares, Fontes, Dantas, et al, 2004<sup>43</sup>  |
| MPM I     | Diagnostic predictions made based on reason for ICU admission, and abnormal  | Groeger, Lemeshaw, Price, et al, 1998<sup>82</sup>  
|           | diagnostic test results, but without inclusion of primary diagnosis.         | Soares, Fontes, Dantas, et al, 2004<sup>43</sup>  |
| MPM II    | Attempts to refine sensitivity to identify thresholds of frequency in the case| Groeger, Lemeshaw, Price, et al, 1998<sup>82</sup>  
|           | mix of specific diagnoses beyond which the model is not predictive.          | Santolaya, Alvarez, Aviles, et al, 2008<sup>93</sup>  
|           |                                                                             | Soares, Fontes, Dantas, et al, 2004<sup>43</sup>  |
| MPM III   | Application of model in broader case mix of recent critically ill patients to| Higgins, Kramer, Nathanson, et al, 2009<sup>87</sup>  
|           | validate predictive value; this model was consistent in most groups, but    | Nathanson, Higgins, Kramer, et al, 2009<sup>88</sup>  
|           | performed less consistently in the medical critical illness group, which    |                                                                             |
|           | comprised approximately 50% of the group.                                   |                                                                             |
| SOFA      | Organ failure assessment throughout the ICU hospitalization among septic    | Ho, 2007<sup>95</sup>  
|           | patients, but name changed from “sepsis-related” to “sequential” once       | Minne, Abu-Hanna, de Jonge, 2008<sup>77</sup>  
|           | determined it could be applied in other critically ill patients; a single    | Owczuk, Wujtewicz, Sawicka, et al, 2004<sup>96</sup>  
|           | score assigned for each of 6 organ systems based on physiologic (eg,           | Peres, Melot, Lopes Ferreira, et al, 2002<sup>84</sup>  
|           | hypotension) and resource needs (eg, need for vasopressors for blood         | Santolaya, Alvarez, Aviles, et al, 2008<sup>93</sup>  
|           | pressure support)                                                          | Silfvast, Pettia, Ihalainen, et al, 2003<sup>34</sup>  
|           |                                                                             | Timsit, Fosse, Troche, et al, 2002<sup>35</sup>  |
| LOD       | A system of physiologic and biologic variables collected at the time and     | Metnitz, Lang, Valentin, et al, 2001<sup>176</sup>  
|           | intermittently throughout ICU hospitalization with regression analysis of    | Pene, Aubron, Azoulay, et al, 2006<sup>19</sup>  
|           | organ dysfunction parameters.                                               | Santolaya, Alvarez, Aviles, et al, 2008<sup>93</sup>  
|           |                                                                             | Timsit, Fosse, Troche, et al, 2001<sup>171</sup>  |
| MODS      | Organ failure scoring system with a unique definition of cardiovascular     | Peres, Melot, Lopes Ferreira, et al, 2002<sup>84</sup>  
|           | failure compared with SOFA; failure is calculated based on a mathematical    | Santolaya, Alvarez, Aviles, et al, 2008<sup>93</sup>  
|           | formula combining physiologic variables and resource intensity.              |                                                                             |
underestimate the risk of mortality for patients with cancer. The oncology-specific ICMM model developed by Groeger and colleagues showed better discrimination for oncology-specific prognostic variables and assisted in identification of high-risk patient groups, but the SAPS-II performed best overall across all studies. Use of a modified ICMM at 72 hours after ICU admission provided enhanced discrimination since many patients with cancer do not exhibit their highest acuity at the time of admission like other ICU patients. The Mortality Prediction Model (MPM) II showed sensitivity for mortality prediction when ICU patients were homogeneous in nature, but recent revisions and development of the MPM-III has been tested and validated on a wider range of patients. On retrospective data from 2004 and 2005, the severity adjustment model MPM-III calibrates and discriminates across a broad population. The application of the MPM-III scoring system in patients with cancer has not been tested. One published risk profile scoring system with a small patient series incorporated cancer- and treatment-related factors, comorbid health conditions, and general health and performance status to create a low, moderate, or high risk for critical illness category. This clinical tool was not further developed or statistically validated.

Because of poor performance of these instruments in patients with sepsis, more recent researchers have attempted to incorporate the prognostic implications of organ failure into predictive models such as the Logistic Organ Failure (LOD), Sequential Organ Failure (SOFA) Score and Multiple Organ Dysfunction Score (MODS). These scores have been compared with earlier models in an attempt to improve discrimination for predicting specific patients’ outcomes. Calculation of organ dysfunction by these models has been successful in categorizing extremes in illness, but remains nonspecific in predicting patient outcomes. However, they provide meaningful data for clinicians to use in conjunction with their expert judgment to counsel patients and families regarding the severity of their illness and possible outcomes. Several studies have used these scales on a daily basis rather than on the first day of critical illness, so that trends can be identified. This practice is especially important in patients with cancer, who are unlikely to experience their highest level of acuity on admission to the ICU like trauma or surgical ICU patients. Even these more sophisticated scoring systems are flawed, and only the SOFA has the desirable sensitivity to predict outcome in patients with shock, sepsis, and hematologic malignancy. A summary of all the prognostic scoring systems used for assessment of ICU severity of illness in patients with cancer is provided in Table 1.

SUMMARY AND RECOMMENDATIONS

There used to be a difference between patients with and without cancer using ICU resources and specific patient outcomes. In the ICU environment, patients with cancer constitute similar frequency of ICU admissions to other medical illnesses, which reflects a distribution of care similar to that seen with inpatient admissions and suggests that opinion biases regarding the appropriate use of critical care in patients with cancer has dissipated. Improved understanding of the interventions performed in select patients that will yield best outcomes has led to equalization of prognosis between patients with cancer and other medical ICU patients. The ICU is frequently used to support patients with cancer after surgery, those presenting with oncologic emergencies, acute treatment-related complications, immune compromise and serious infection, and when medical-surgical disorders become exacerbated. The most predictive influencers of outcome, such as status of the malignancy, degree of
organ failure, and perceived reversibility of the crisis, should be considered when determining the appropriateness of critical care use. Newly diagnosed patients in whom effective therapy has yet to be given or take effect and those with quiescent or disease remission remain the best candidates to receive critical care for any unexpected crisis. No clear scoring system has yet been developed that can prospectively predict survival or response to critical care interventions for patients with cancer. Without statistical guidance, the gold standard for decision-making regarding implementation of critical care for patients with cancer remains collaborative and proactive multidisciplinary planning, including oncology specialists, intensive care clinicians, and patients or their health care proxies.

REFERENCES

15. Guidelines for developing admission and discharge policies for the pediatric intensive care unit. Pediatric Section Task Force on Admission and Discharge Criteria, Society of Critical Care Medicine in conjunction with the American


