

An initiative to end-of-life decisions in cancer care

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Abstract

Care of cancer patients more than often becomes limited to providing only comfort measures at the advanced stage of their diseases. Patients or family should be given accurate, relevant and comprehensible information about the goals of the treatment options. These discussions should paint a realistic picture of the outcome to be expected with specific estimates of survival and anticipated quality of life; and patients appreciate these initiatives. Discussions need to be directed toward whether intensive care unit (ICU) admission should be considered or cardiopulmonary resuscitation (CPR) be initiated for an acute cardiopulmonary arrest. A model, comprised of 16 readily variables, can be used at the time of ICU admission to estimate the probability of mortality in critically ill cancer patients. Family members and physicians agree on end-of-life decisions approximately 70% of the time. In the rest, disagreement usually centres on the physician's view that life support is futile and patient's not so clear understanding of their true prognosis despite being told by their physicians. The resolution of this conflict involves clinical ethics committees and, in extreme cases, legal counsel deliberations. Based on in-depth literature search, the present review article aims at multidisciplinary initiative to approach end-of-life care in cancer patients with comprehensive decision-making.

KEY MESSAGES

- Set goals of care relative to cancer stage
- Relay accurate, relevant, comprehensible information about goals to patient or family
- Initiate discussions DNR orders
- No difference between withholding and withdrawing life sustaining therapy
- Comfort measures and attention to patient when goal changes to palliation
- Awareness of ethical, legal and economic considerations in end-of-life care

INTRODUCTION

The physician's role is "to cure sometimes, to relieve often and to comfort always"¹. In cancer patients, cure is always not possible. Seventy-eighty percent patients present in advance stage of their diseases where cure is not possible; giving symptom relief and providing comfort become the main goal of treatment plan. The goal of care must be relative to cancer stage. If the appropriate stage of the patient's illness can be recognized, treatment can be tailored

to the patient's needs by knowing the goals of treatment for that stage. In this framework, CPR or ICU transfer does not become a decision that needs to be made urgently but can be anticipated well in advance and becomes simply an aspect of care that can be considered in the light of the overall goals of treatment. At the onset of each stage and throughout the patient's care, goals of therapy need to be defined, refined, and carefully discussed. Thus, the question of whether to use a certain treatment modality, including CPR, is no longer a decision of whether to treat or not to treat. Rather the question becomes what is the most appropriate treatment that can be offered to this patient.

This review article is based on information gathered from searching Medline database. Furthermore, the reference lists of retrieved articles were screened. Data from abstracts, letters, and unpublished data were not considered. The aim of this review is to present a systematic approach towards initiating end-of-life decisions in cancer patients after a thorough and comprehensive search of literature.

GOALS OF CARE

Haines, Zalcberg, and Buchanan² have proposed a five-step staging system for patients with cancer that offers a framework for discussing goals of care relative to cancer

status.

Figure 1

Table 1: The Classification System for stages of cancer care

Stage	Goal
1	Diagnosis
2	Potential cure
3	Disease controllable but not curable
4	Failure of specific treatment aimed at cure or control; the pivotal point of management
5	Palliative management

In stage-one and -two, patients are newly diagnosed or receiving potentially curative therapy and should be considered candidates for aggressive therapy including ICU admission. Newly diagnosed patients should be told clearly of the immediate therapeutic options and anticipated future therapy to enable them to maintain some control and understand their role in the process. Patients should feel that, throughout their therapy, if the focus of care moves to a higher stage with less chance of meaningful or actual survival, explanations of care will be available and that, as commonly feared, they will not be abandoned.

In stage three, disease is controllable but not curable. In this stage a temporary remission may prolong life significantly. CPR is not to be offered for an acute cardiac event and that limits be discussed if a trial of mechanical ventilatory or hemodynamic support fails.

In stage four, specific treatment aimed at cure or control has failed. Stage four is often the most difficult stage to recognize and negotiate. Patients and families may need much emotional support at this time, and physicians may fear that any discussion about end-of-life care will remove all hope and create a sense of failure. With proper negotiation, this stage should not steal all hope but rather should replace hopes of cure with hopes of optimization of quality of life. Additionally, further treatment decisions should fall into place and patients may come to understand that CPR and aggressive ICU care are inappropriate. With patients at this stage of disease, poor negotiation or avoidance of the discussion of goals of care may lead to false hope and to inappropriate therapy.

In stage five, palliative management should be the goal. These patients should not undergo CPR, should not be admitted to an ICU, and all therapy should be directed

toward preparation for death.

INITIATING DECISIONS

Throughout the discussion of goals of care, in respecting a patient's autonomy, physicians must relay accurate, relevant, and comprehensible information to the patient.

Unfortunately, patients with cancer often are unable to participate in decisions regarding their health care because of medical or psychologic reasons. In these cases, families and physicians are forced to make medical and ethical decisions for a patient whose wishes may not be known ³.

Even though patients may want to take part in the decision, they may hesitate to express openly a preference for death ⁴. Physicians may hesitate to address the issue for the same reason or because of their different moral values ⁵. Further, physicians may not discern subtle signals from a hesitant patient simply because there is not enough time "to just talk" ⁶.

As caregivers evolve a relationship with their patients, discussions need to be directed toward whether CPR should be initiated for an acute cardiopulmonary arrest and whether extraordinary care including mechanical ventilation, blood products, antibiotics, pressors, artificial hydration and artificial nutrition should ever be undertaken. The use of CPR in various situations has been debated extensively since its initial description in 1960 by Kouwenhoven ⁷. The short-term success rate of CPR during the last 30 to 40 years has been 38.5% with a range of 13% to 59% survival at 24 hours ⁸. Long-term success, usually defined, as survival to discharge, has been more dismal, with a 14.6% survival rate and a range of 3% to 27% ⁹.

Many studies have attempted to look at pre-arrest variables that would help select patients likely to have a successful outcome. Most studies have identified cancer as an independent predictor of poor outcome. In patients with cancer-limited or metastatic-the initial response rate to CPR is similar to that of the general, non-cancer population. Survival to discharge, however, drops dramatically in patients with cancer, with a range of 0% to 5% ^{10,11}. Many physicians believe that offering CPR to patients with cancer, especially metastatic disease, only leads to transient prolongation of life with significant suffering imposed on patients and their families. Furthermore, CPR can be harmful if it interrupts a timely death ¹².

PATIENTS' PREFERENCES FOR THERAPY

Surveys have provided information on patients' preferences

for therapy in various scenarios. In general, patients prefer comfort measures to life prolongation when faced with terminal illness. Over 80% of patients say they would refuse nutrition, antibiotics, or mechanical ventilation if they were in a persistent vegetative state or were terminally ill ¹³. However, there is an important minority in all surveys who prefer aggressive therapy regardless of the scenario ¹⁴.

Ideally, physicians should be able to provide families and patients with estimates of survival and anticipated quality of life before ICU admission and be prepared to enter a palliative mode of care if the therapy fails. Groeger and colleagues ¹⁵ have developed a disease-specific multivariable logistic regression model to estimate the probability of hospital mortality in critically ill patients with cancer who are admitted to an ICU. The model, comprised of 16 unambiguous and readily available variables, can be used at the time of ICU admission and provides an accurate estimation of a patient with cancer's probability of hospital mortality once admitted to an ICU. Significant factors contributing to higher probabilities of hospital mortality are perturbations in physiology and increasing duration of hospitalization before ICU admission, recurrent or refractory malignancy, and worsening performance status before hospitalization.

Hospital mortality rates for patients with cancer in ICUs vary from 20% to 95% depending on the subpopulation being studied ^{15,16,17,18,19}. In contrast, hospital mortality rates for non-cancer ICU admissions range from 10% to 47% ²⁰. Also, when compared with other non-cancer subgroups admitted to the ICU, patients with malignancies tend to have a significantly worse long-term survival rate after discharge from the ICU ²¹.

PREDICTORS OF ICU MORTALITY IN CANCER PATIENTS

The lower mortality rates in patients with cancer reflect a better prognosis for patients admitted to the ICU for postoperative management: mortality rates for surgical patients range from 20% to 40%, compared with 40% to 95% for medical admissions ^{22,23,24}. In general, patients admitted after curative although extensive cancer surgeries seem to fare better than medical oncology patients admitted for problems such as acute respiratory failure, circulatory failure, and neurologic catastrophes ¹⁵. In addition, the incidence of extubation is higher in patients admitted for postoperative respiratory failure than in medical patients with cancer intubated for respiratory failure ²⁵.

Most studies include leukemia and lymphoma in the category of hematologic or systemic malignancy. Other soft tissue tumors such as adenocarcinomas, squamous cell carcinomas, and so forth, comprise the solid tumor group. Patients with hematologic cancers are often younger and potentially curable. These patients, however, often develop life-threatening complications that require intensive care, and their hospital mortality rate can be as high as 90% when they require mechanical ventilation. On the other hand, patients with solid tumors may be older but their cancers may be slow-growing. Therefore, they might have extended survival, and ICU support may be justified for these patients during a period of acute illness ²⁶.

Some studies have found that patients admitted to the ICU with a solid tumor have a lower mortality rate than those admitted for a hematologic malignancy ²⁷. Other authors have observed that although the mortality rate may be somewhat lower for non-ventilated solid tumor patients, once mechanical ventilation is initiated, the mortality rate of these patients approaches 63% to 91%, paralleling that of patients with systemic malignancies who are ventilated ²⁸. In addition, the six-month survival rate following ICU discharge is the same for both groups—approximately 21% ²⁶.

It is worth noting that certain subgroups of malignancies (i.e., breast cancer, colon cancer, testicular cancer, chronic lymphocytic leukemia, and multiple myeloma) have been described as having a more favorable prognosis, whereas other subsets (i.e., lung cancer and acute leukemia) have a more grim prognosis ^{25,29}.

Relapsed or recurrent cancer is negative predictor of ICU mortality ^{28,29}. Patient with an increasing number of metastatic sites and respiratory failure are less likely to survive hospitalization than patients with only one metastatic site ³⁰. Patients with progressive, relapsed, or recurrent disease would be subjected to more immunosuppressive and toxic cancer therapies that would increase the likelihood of acute illness than patients who have been cured of their underlying malignancy. Generally, when patients with incurable, progressive, or relapsed solid tumors or hematologic malignancies require mechanical ventilation, the prognosis is dismal, with hospital mortality rates approaching 70% to 90% ²⁸.

Even among patients admitted for medical emergencies, certain subgroups tend to fare better. For example, critically ill patients with cancer transferred to the ICU for metabolic problems (i.e. hypercalcemia, tumor lysis syndrome), cardiac

arrhythmias, or monitoring during drug administration have a mortality rate similar to that of non-ventilated patients without cancer. If respiratory failure develops, the prognosis is ominous. Other groups of patients that tend to do worse are those admitted with hepatic failure, with meningeal carcinomatosis, and after cardiac arrest ²⁴ .

Patients with intractable hypotension caused by sepsis that is not responding to fluid, antibiotics, and vasopressors also have a poor prognosis. In fact, persistent hypotension, presumably from septic shock, is often the final cause of death for the intubated patient with cancer ³¹ . As is the case with all critically ill individuals, the development of multiorgan system failure is also an important predictor of death. In patients with respiratory failure, the mortality rate increases as the number of systems affected increases

²⁵⁺²⁸⁺³²⁺³³ .

Frequently, as multiple systems begin to fail, a decision must be reached concerning renal replacement therapy. Acute renal failure in the critically ill patient with cancer can result from various causes, including complications from treatment (i.e., postsurgical or chemotherapy-associated renal failure), infiltration by neoplastic cells or their products (i.e., renal cell carcinoma or multiple myeloma), circulatory failure or sepsis, metabolic derangements, or as part of a multiorgan system failure process.

Many patients with cancer who develop acute renal failure in the critical care setting will require dialysis as part of their treatment. Cause of renal failure is a good predictor of mortality. In patients with metabolic derangements (such as acute tumor lysis syndrome, hypercalcemia, or hyperuricemia) or drug-related nephrotoxicity, survival rates are similar to those observed for the general population dialyzed for acute metabolic complications – 60% to 75%. This rate is in stark contrast to patients with cancer who develop acute renal failure in association with respiratory failure, sepsis, or multiorgan system failure; for these patients the mortality rate is 90% to 100% ³ .

CRITICAL CARE FOR PATIENTS WITH BONE MARROW TRANSPLANTATION

Bone marrow transplantation (BMT) has become an important treatment modality for certain malignant and nonmalignant hematologic disorders. Patients undergoing BMT can develop a wide array of life-threatening complications requiring ICU transfer. Post-transplantation patients admitted to the ICU after surgical procedures have a mortality rate of approximately 20% ¹⁶ . This rate is in stark

contrast to that of nonsurgical BMT patients who require mechanical ventilation. For these patients, the mortality is greater than 90% and approaches 100% in many centers ³⁴ . Bone marrow transplant patients admitted for medical complications but not requiring mechanical ventilation have a hospital mortality rate of 20% to 30% ³³ .

Numerous studies have attempted to establish reliable predictors to help identify which patients will require ICU transfer and mechanical ventilation. These patients have an extremely slim chance of surviving and require significant resources and support ¹⁵⁺²²⁺³³⁺³⁴ . Patients receiving autologous transplants have a less complicated post-transplantation course, but once mechanical ventilation is required the outcome is the same for autologous and allogeneic BMT patients ³ . Disease in relapse has been shown in some studies to be an independent predictor for ventilatory support ³⁴ . Mechanical ventilation in association with the presence of combined hepatic dysfunction (bilirubin >4mg/dL) and renal dysfunction (creatinine >2mg/dL) is strongly predictive of death, whereas other predictor characteristics are not ³ .

FINAL DECISIONS IN INTENSIVE CARE UNIT

Once a patient with cancer is admitted to the ICU, it is crucial that a multidisciplinary approach be taken. The intensivist and oncologist should define the proposed therapy clearly and its inherent risks and benefits to the patient. There must be consistent, ongoing support for the spiritual, cultural, and psychosocial needs of the patient and family members.

Withholding and withdrawing life-sustaining therapies are examples of the difficult and often complex decisions that must be made in the ICU. In the United States, there is a legal, ethical, and moral consensus that there are no differences between withholding and withdrawing life-sustaining therapy ³⁵ .

Often, the oncologist and the patient decide against aggressive life-support measures if there is no potential benefit. Comfort measures are provided on the hospital ward or in the patient's home and not in the ICU. If outcome is uncertain, however, and the patient has a chance for meaningful recovery, it is reasonable to admit that patient to the ICU and initiate life-sustaining treatment. The patient's response to the therapy must be evaluated constantly.

There are many different ways that intensive care can be shifted to palliative and comfort care ³⁵ . If patient has no

chance for survival, physician would recommend that all life-sustaining therapy be withdrawn and only comfort care be provided. In other cases, there may be only a small chance of survival, but the risks of further aggressive forms of therapy outweigh any potential benefit for the patient. In this case, the physician usually continues the present level of support but does not add other forms of therapy. Although it may be reasonable to provide life-sustaining measures, such as mechanical ventilation and vasopressor support, to critically ill patients, providing CPR in the event of cardiac arrest is not.

This approach requires that the physician understand clearly the various probabilities of survival. These probabilities must be communicated clearly to the patient or family so appropriate decisions can be made. It should be remembered that the patient, regardless of his or her chance for survival, can choose not to receive any or all forms of life-sustaining therapy at any time. The patient or surrogate also has the right to request withdrawal of support at any point in time, and the caregivers must respect this request.

WITHDRAWAL OF LIFE SUPPORT

Several issues regarding the actual withdrawal of life support should be discussed, particularly the withdrawal of artificial ventilatory support³⁵. Providing adequate sedation and pain control as support is withdrawn is of utmost importance. Many family members choose to be present when support is withdrawn; therefore, it is important to inform them that timing of death is unpredictable and cannot be controlled. The ICU practitioner should be attentive to the patient and the family throughout the procedure, providing relief of dyspnea to the patient as needed. Narcotics or sedatives should not be increased to hasten the time of death but should be administered as often as necessary to provide comfort to the dying patient.

Because the timing of death is often uncertain, the actual location of death may vary. Usually, however, after withdrawal of ventilatory and hemodynamic support, death usually occurs within a few hours in the ICU¹⁴. It is important that the needs of the family are met and privacy is respected. Monitors should be turned off, bed rails lowered, and family members who want to be with the patient at the time of death should be allowed to do so. Religious preferences should be respected.

ETHICAL PERSPECTIVES

The decision to initiate, continue, or withdraw intensive care

to the patient with cancer is often tremendously difficult. The bioethical principle of patient autonomy states that a competent individual has the right to decide for or against any medical treatment. A cornerstone of this principle, however, requires that the physician must provide the patient with a realistic understanding of the potential outcome of a therapy.

Numerous studies show that when outpatients were asked whether they would like to discuss life-sustaining therapy, nearly 70% said they would. Patients feel empowered by discussing these issues and wish their physicians would initiate conversation on this topic³⁶. Despite this enormous interest, very few individuals actually write advance directives. Fewer than half ever explicitly discuss their wishes with family members³⁷. Respondents cite lack of physician initiative as an important barrier to their giving advance directives^{13,36}.

An advance directive is a Living Will and/or a Durable Power of Attorney for Health Care (DPAHC)³⁸. The Living Will is a document in which the patient, in the event that he or she becomes terminally ill, directs the physician to withhold or withdraw life-sustaining treatment. The DPAHC allows patients to appoint an agent to make health care decisions in the event that they cannot speak for themselves. The agent is usually a family member or close friend who knows the patient's wishes. Physicians must understand the hierarchy of surrogate decision makers (i.e., spouse, adult children, parent, adult sibling, close friend)³⁵.

In theory, an advance directive should direct the physician to respect patient autonomy. In practice, the incidence of advance directives among patients with cancer is low. The diagnosis of malignancy can be emotionally overwhelming, and often patients are not prepared mentally to talk about end-of-life issues. Differences in belief systems, attitudes, and cultures among health care workers, patients, and families may add further to the difficulty in negotiating and offering end-of-life care³.

An important concern for those faced with interpreting advance directives is whether the stated choices are stable over time. Initial choices for less care, having an advance directive, and repeated discussions over time all make stable decisions more likely³⁹.

Unexpected complications from treatment often can occur, and there is little time for the physician to discuss the risks and benefits of life-sustaining therapy in the ICU. If the

patient is unable to speak for him or herself, and no surrogate is named, the physicians must try to glean the patient's wishes from available family members.

Family members and physicians disagree on end-of-life decisions approximately 30% of the time ⁴⁰. Studies have shown that many patients with cancer do not have a clear understanding of their true prognosis, despite being told by their physicians. These patients and surrogates tend to overestimate the probability of long-term survival ⁴¹.

Disagreement usually centers around the physician's view that life support is futile ³⁵. It is extremely difficult to define the concept of futility in a medical context. The term medical futility refers to a physician's determination that a therapy will be of no benefit to a patient and therefore should not be prescribed. But physicians use a variety of methods to make these determinations and may not arrive at the same conclusions.

Given the difficulties in defining futility, as well as the clinical, legal, and ethical complexities surrounding the problem, some ethicists have argued in favor of a procedural approach to resolving futility questions. According to this approach, conflicts over DNR orders and medical futility are resolved not through a policy that attempts to define futility in the abstract, but rather through a predefined and fair process that addresses specific cases ⁴².

When the physician and family disagree or family members disagree among themselves, a fair process includes extensive deliberation and consultation in an attempt to reach resolution including, a second physician opinion concurring with primary physician's determination of medical futility, transferring the care of the patient to a different physician or facility, presenting the case to the hospital's clinical ethics committee, or in extreme cases, obtaining legal counsel ^{43,44}.

The clinical ethics committees are not meant to be decision-making bodies; rather, they serve as impartial, unbiased groups that make recommendations to resolve the conflict at hand. In extreme cases, however, when all efforts at the institutional level have failed to resolve the conflict, the legal system must step in.

The courts often are influenced strongly by the medical facts of the case and the standard of care as set forth by the medical profession ³⁵. The courts particularly focus on whether the patient has the capacity to understand information regarding treatment risks and benefits. If the

patient understands this information, then the patient has the right to accept or refuse treatment. If the patient lacks that capacity (often determined by a psychiatrist), decision making for the patient must occur. If the patient's prognosis is not clear, the courts generally rule in favor of treating the patient to maintain life. If later it becomes apparent that continuing treatment is futile, courts have ruled to discontinue life support in certain cases ³⁵.

ECONOMIC PERSPECTIVES

Although formal studies focusing specifically on the cost of end-of-life care of critically ill oncology patients are lacking, critical care has become extremely expensive. As new modalities to treat cancer arise, there will be further focus on increased survival for the patient, and there undoubtedly will be continued need for treatment in the ICU. It is hoped that the medical profession, with advice from the community, will determine how resources should be allocated appropriately for ICU cancer care.

Physicians should always serve as patient advocates, and all patients must be cared for equally ³⁵. A patient's financial status should not influence the decision to initiate or withdraw life support in the ICU. When a surrogate is involved in the decision to withdraw life support, it is important to make sure there are no economic conflicts of interest. For patients who require long-term ventilatory support but do not require other aggressive forms of therapy, care can be provided in a specialized ward rather than ICU, provided the appropriately trained personnel are available.

GLOBAL SCENARIO

The United States has generated much of the world's medical, ethical, and legal literature on DNR orders. However, there is a limited published experience from colleagues abroad that is illuminating ⁴⁵. A critical care group from Belgium stated that the decision not to perform CPR or to discontinue therapy is ultimately made by the ICU staff ⁴⁶. An article published from a district hospital in England showed the consequences of not having a formal DNR policy. Orders in the chart were cryptic and haphazardly documented ⁴⁷. Physicians in Sweden, who also practice in the absence of a formal DNR policy, only document 18% of their DNR orders in the medical record with the majority written in coded language. 70% said they never or rarely discussed DNR decisions with family members and 90% never or rarely discussed the decision with the patient ⁴⁸.

CONCLUSION

Practitioners of critical care may be their own worst enemy when it comes to discussing end-of-life decisions with families. Over the years such a good job has been done promoting CPR, intensive care, and the technological marvels that accompany them, that therapies may have been actually oversold raising patients' expectations. Now is the time to invest in patient and physician education about the outcomes and costs of this care. Medical professionals and ethicists should set the standard for resolving the conflicts prevalent in critical care oncology. Statements issued by these groups have tremendous legal value when the courts are acting on a patient's behalf. The establishment of a strong institutional clinical ethics committee should be a priority, and clear protocols for decisions to initiate or withdraw life-sustaining care should be established and fully supported. It is imperative that health care providers be well educated in the laws that govern end-of-life decisions.

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