

# Managing Dying: Medical Care and Decision Making at the Very End-of-Life

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## Introduction

Advances in technology and pharmacology have extended the average life-span and improved patient outcomes across medical disciplines. As a result, end-of-life can be difficult to accept. Patients may remain hopeful they can overcome illness and continue living even in the setting of incurable conditions and multi-organ failure. As medical developments have resulted in more life sustaining treatments, decisions of what to do or not do have become more complex. Thus, patients, families, and providers may struggle to understand choices and decisions in managing very end-of-life care.

As the practice of medicine has become more sub-specialized and fragmented, fewer and fewer physicians are involved in very end-of-life care. Inpatient hospital care is increasingly relegated to hospitalists, intensivists, and certain subspecialists. Even in the hospital, end-of-life issues may be addressed by hospice and palliative care specialists. Thus, many physicians and house staff have less exposure to issues related to end-of-life care.

The aim of this manuscript is to define common issues and options specific to the very end-of-life as well as categorize the very end-of-life by organ system failure. This paper is not meant to be a comprehensive discussion of symptom management nor an ethical debate involving very end-of-life care, but rather to pragmatically clarify basic distinctions and choices related to the manner and management of dying.

## Options for Intervention or Withdrawal of Life-Prolonging Therapies at End-of-Life

When considering medical interventions at the very end-of-life, it is important to delineate options including: do not resuscitate orders, "active" euthanasia, "passive" euthanasia, physician-assisted suicide, withdrawal of life support, narcotic drips, terminal sedation, withdrawal of hydration/nutrition, and termination of other life sustaining treatments (eg. dialysis and cardiac devices) Table 1.

Term	Definition
DNR/DNI	Cardiopulmonary resuscitation and intubation
Active Euthanasia	A physician or a third-party intentionally ending the life of a patient at the voluntary and competent request of that individual [1-3]
Passive Euthanasia	The decision to not intervene when a medical intervention might well be life-saving
Assisted Suicide (Physician-assisted death)	The provision of medications to a patient to self-administer and end his or her life [1-2]
Morphine Drip	An opioid infusion commonly used at the end of life to relieve pain and/or respiratory distress
Terminal Sedation	Sedation used at the end of life to relieve intractable pain and suffering
Withdrawal of Life Support	The active cessation of an intervention currently provided to a critically ill patient [17-18]
Withholding of Life Support	The active decision to not initiate or escalate a life-sustaining intervention [18]

**"Active" euthanasia** is defined as a physician or a third-party intentionally ending the life of a patient suffering from an incurable disease, at the voluntary and competent request of that individual [1-3]. The word euthanasia is from the Greek 'eu' (good)'thanatos' (death); while many would argue in favor of allowing it as ethical, merciful and appropriate, it is illegal in the United States. Euthanasia is legal in the Netherlands and a handful of other countries throughout the world.

**"Passive" euthanasia** is a term that implies not intervening when a medical intervention may be life-saving (eg. not implanting a pacemaker in a patient with sick sinus syndrome or not giving antibiotics to a patient with urosepsis) [4]. If a patient has a terminal condition with an inevitable outcome, the manner by which he or she approaches the end-of-life is vitally important [6, 7].

**Physician-assisted suicide** (or what some prefer to call medical aid in dying or physician-assisted death) involves the provision of medications to a patient to self-administer with intent to end their own life [1, 2]. Symptom alleviation in a terminal condition may hasten death, which some contend is only a degree away from causing death [8]. Sometimes symptoms are so distressing that patients request assisted death for total relief [2, 5-6]. While criteria for physician-assisted suicide vary by state, the patient must be a terminally ill adult with decisional capacity. Clinical criteria for physician-aid in dying are available [11]. The notion of assisted death is a multifaceted and controversial, involving a confluence of medical, ethical, legal, personal, cultural, and religious factors [2]. In the United States, physician-assisted suicide is legal in California, Colorado, DC, Hawaii, Maine (September 2019), Oregon, Vermont, New Jersey (August 2019), and Washington (Vacco vs. Quill 521 U.S. 793, 1997).

**Narcotic infusions** with intravenous morphine or other opioids are common at the end-of-life to relieve intractable pain or respiratory distress [8]. Despite the effect of hastening death, use of high-dose narcotics is widely accepted if the overriding goal is relief of pain and suffering. Such use is appropriate, legal, ethical, distinct from euthanasia and accepted under the doctrine of double effect. Furthermore, the use of sedation to relieve intolerable suffering among terminally ill patients is considered acceptable medical practice [12].

**Terminal sedation** is distinct from both active euthanasia and narcotic infusions. While there has been some debate about its definition, terminal sedation involves the titration of sedatives and analgesics to achieve pain and symptom control which may result in permanent unconsciousness [8]. Palliative sedation is a type of sedation implemented to diminish awareness and relieve intractable suffering at the end-of-life [13]. While it has been postulated that the difference between palliative and terminal sedation lies in the intention, the intervention, and the outcome, others doubt a distinction all together [14].

Historically, **cardiopulmonary resuscitation (CPR)** was developed for patients with coronary disease with arrhythmias, not as a “rite of passage” for all patients dying with terminal diseases. In these patients, cardiopulmonary resuscitation is generally considered futile. However, many hospital policies and some state laws require discussion with patients and families to opt out of CPR. Some authors have proposed alternatives (such that the default option is to not perform CPR in patients with terminal diseases), but this has not been widely accepted [15]. It is essential to consider factors beyond the stage of disease, such as performance status and treatment options when making decisions regarding CPR [16]. It is the responsibility of the provider to identify and present appropriate treatment options to all patients and their families, especially in the setting of imminent death. Providers must sensitively balance those options with realistic goals of care.

**Withdrawal of a life-sustaining treatment** involves the active cessation of an intervention currently provided to a critically ill patient [17, 18]. Refusal of treatment, withdrawal

of ventilatory support, and/or the refusal of artificial nutrition and hydration may cause or hasten death [8]. The controversial distinction between withdrawal of treatment and withholding treatment is commonly encountered in very end-of-life care. Withholding a life-sustaining treatment involves the active decision to not initiate or escalate a life-sustaining intervention [18]. Withdrawal of treatment involves a reversal of a previous intervention meant to sustain life. In either case, the patient’s death results from his or her underlying disease [18]. “Whether a physician withdraws or withholds a futile therapy has the same ethical implications if the intent (relief of suffering, avoidance of unwarranted intrusions/procedures, and so on) and the end (dignified death) are the same” [19].

Although there is no established definition of futile treatment, it is often defined as care that will not significantly improve nor reverse an underlying condition contributing to a patient’s ultimate death [20]. Some clinicians describe medical futility as a clinical action that serves no useful purpose in attaining a specified goal for a patient [21].

### Categorizing Types of Death by Dominant Organ System Failure

When caring for a patient as they approach the end-of-life, it is advantageous to anticipate the manner of death to prepare for optimal symptom management. In many cases, death results predominantly as a failure of one organ system. Understanding the disease status and patient course may help providers to anticipate and manage very end of life care. Symptomatic progression and management is often similar despite the differing pathologies that result in organ failure (eg. respiratory failure from metastatic disease, COPD, pulmonary fibrosis, etc. or liver failure from cirrhosis or metastatic disease). Deaths from metabolic causes

System Issues	Signs and Symptoms
Respiratory Failure	Dyspnea, hypoxia, accessory muscle use, tachypnea
Hepatic Failure	Jaundice, abdominal distension, peripheral edema, bleeding, encephalopathy
Cardiac Failure	Pulmonary and peripheral edema, cardiac arrhythmias
Renal Failure	Oliguria or anuria, encephalopathy, cardiac arrhythmias, pulmonary edema, electrolyte derangements, acidosis
Neurologic Failure	Seizures, muscle spasticity, apnea, lack of brain stem reflexes
Gastrointestinal Failure	Bowel obstruction, nausea, vomiting, inability to tolerate orals
Bone Marrow Failure	Pancytopenia, bleeding, fatigue, shortness of breath, tachycardia
Intensive Care Unit Death	Terminal extubation, discontinuation of vasopressors, withdrawal of treatment

(eg. liver failure, renal failure, hypercalcemia) may be easier than deaths from respiratory failure, diffuse bone metastases, central nervous system disease, and bowel obstruction. Table 2

Some common scenarios are described below; with the understanding there may be overlap.

### **The Respiratory Death**

Dyspnea is an uncomfortable awareness of breathing, breathlessness, or distressing shortness of breath. It is often associated with extensive secretions, cough, chest pain, fatigue, and air hunger [8, 22]. Dyspnea can be particularly stressful for both patients and their families. The pathophysiology of end-of-life dyspnea involves disturbances in the bronchi, pulmonary congestion, decreased hemoglobin carrying capacity, and ventilation variability as a consequence of neuromuscular disease [22, 23]. Treating the underlying cause of dyspnea is critical to relieving this complex symptom. Oxygen, mechanical ventilation, anxiolytics, and opioids are four strategies with proven efficacy to ease dyspnea at the end-of-life [24]. There are variations of oxygen concentrations and flow rates. High-concentration and high-flow oxygen refers to heated and humidified oxygen with a flow rate up to 60 liters per minute and a maximum of 90% oxygen [25]. Deaths from respiratory failure are often the most difficult to manage at home and many of these patients are better served as inpatients at a hospital or hospice facility.

### **The Cardiac Death**

Remodeling of the myocardium in the form of an end-stage cardiomyopathy may result in fatal arrhythmias, dyspnea, and both pulmonary and peripheral edema. Patients with critical illness and cardiac failure may require hemodynamic support in the form of vasopressors to support organ perfusion. In these cases, initiating or continuing vasopressors may prolong the dying process rather than changing its outcome [27]. In addition to initiation and withdrawal of vasopressors, deactivating pacemakers and defibrillators are common cardiovascular-related concerns at the end-of-life. Improvements in healthcare and technology have allowed many cardiac conduction support devices to outlive the patients [28]. A patient's decision to deactivate their pacemaker or defibrillator is a reflection of autonomy and should be respected and honored by the clinician. Contrary to popular thought, there are no established ethical or legal distinctions between deactivating pacemakers versus internal cardiac defibrillators [28]. Many patients and cardiologists feel more comfortable turning off a defibrillator, but less so with deactivating a pacemaker particularly if the patient is pacer dependent.

### **The Neurologic Death**

#### **Brain Death**

The term and definition of 'brain death' was offered by Henry Beecher and refers to the irreversible loss of all brain function [1968]. The idea of brain death by neurologic criteria and its concordance or discordance with death of a human being is a point of contention [30]. The American Academy of Neurology defines

clinical brain death as apnea and the lack of brain stem reflexes in the absence of complicating medical conditions, intoxication, or poisoning [31]. The continuation of artificial life-sustaining treatments in patients who are brain dead may have detrimental consequences for patients and families [32]; how long do these treatments continue, when, and how, are they withdrawn? In the United States, all 50 states acknowledge neurological criteria for determining death as a matter of law. However, there is state to state variation in the interpretation of the law [33].

#### **Corticosteroids in Neurologic Death**

Most patients with primary or metastatic brain tumors at end-of-life will be on dexamethasone to reduce intracranial edema and alleviate symptoms. It is preferred over other corticosteroids due to its low index of water and sodium retention as well as its long biologic half-life which potentiates its anti-inflammatory properties [34, 35]. Dexamethasone decreases vasogenic edema surrounding brain tumors making it preferred compared with other corticosteroids. These anti-edema effects are due to reduced permeability of tumor capillaries [36-38] as well as the disruption of the inflammatory pathway through the inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) [35, 39-40]. One option to be offered to patients and families at very end-of-life is the abrupt withdrawal of corticosteroids which may hasten death due to brain swelling as well as precipitate an adrenal crisis [34, 41].

#### **Management of Seizures**

Structural brain damage, electrolyte disturbances, and medications may contribute to seizure development. Examples of structural brain damage include: anoxic brain injury, hemorrhage, primary tumors, metastases, abscesses, and radiation necrosis [42]. The sole presence of a brain tumor or brain metastasis does not alone justify prophylaxis with antiepileptics. However, if a patient with a brain tumor or brain metastasis develops a seizure in the absence of a reversible cause that is an indication for initiation of long-term anticonvulsants [42]. Medications to treat seizures include benzodiazepines (lorazepam, midazolam), barbiturates (phenobarbital), and antiepileptics (phenytoin, levetiracetam, carbamazepine). When patients are no longer able to take these medications orally, some may be given via rectal suppositories; these include carbamazepine, benzodiazepines, paraldehyde, barbiturates, and valproic acid [43].

#### **Neurodegenerative Disorders**

Patients with advanced neurodegenerative conditions such as amyotrophic lateral sclerosis (ALS) often experience spasticity, fatigue, pain, sialorrhea, and respiratory failure at the end-of-life. Weakness of diaphragmatic, intercostal, and oropharyngeal muscles contribute to ineffective cough, retained secretions, and pneumonia [44]. Unfortunately, patients with progressive neurodegenerative disorders demonstrate a pseudobulbar affect and develop depression at the end-of-life [45]. Aggressive symptom management in the terminal period of ALS is critically important [46]. Muscle relaxants, opioids and adjuvant pain medication, and anti-secretagogues are some therapies that can

be effective in ALS. Patients and families often struggle with the difficult decision to initiate or withdraw ventilatory support and enteral feedings as respiratory and swallowing function decline.

### **The Renal Failure Death**

Renal dysfunction in critically-ill patients with significant comorbidities is often progressive and irreversible. The decision to initiate hemodialysis lies in whether a patient's renal dysfunction is likely to be temporary or permanent and whether the prognosis of their other underlying diseases warrants renal replacement therapy. Patients receiving maintenance hemodialysis have higher mortality rates than the general population [47]. Just as patient heterogeneity and medical comorbidities affect the initiation of dialysis, they also influence decisions relating to the withdrawal of patients on maintenance dialysis. Death will generally ensue about eight days after stopping dialysis in patients with end stage renal disease. [48]. Some patients on maintenance hemodialysis with other terminal diseases will opt to stop dialysis, whereas others opt to continue.

Given the reflex tendency in medicine to fix what we can fix, patients with end-stage cancer and obstructive uropathy often undergo interventions to relieve obstruction whereas death from renal failure might have been the more merciful way to go. Careful consideration should be taken prior to placing stents or percutaneous nephrostomies in people with terminal diseases.

### **The Liver Failure Death**

Whether due to advanced cirrhosis, hepatitis, or metastatic disease, death with liver failure is one in which the patient will drift away often gradually with worsening hepatic encephalopathy. Along with increasing jaundice, there is often increasing abdominal distention from ascites and peripheral edema. Early encephalopathy can be associated with some agitation before sedation and eventually coma set in. There is a tendency to treat hepatic encephalopathy with lactulose or rifaximin which may only prolong suffering and delay death, thus requiring a discussion with patients and families about goals of care at end-of-life. Treating the symptoms related to encephalopathy using opioid, antipsychotics or benzodiazepines may be preferential.

### **The Intensive Care Unit Death**

The challenging transition from delivering care with a curative intent to delivering high-quality end-of-life care is commonly encountered in the intensive care unit (ICU) [50]. Withdrawal of mechanical ventilation is the most common form of life-support withdrawal in the ICU [50]. "There is an ethical responsibility to anticipate and treat iatrogenic symptoms such as pain, dyspnea-associated respiratory distress, anxiety, delirium, post-extubation stridor, and excessive bronchopulmonary secretions" [51]. The use of opioids, benzodiazepines, antipsychotics, and anticholinergics may help mitigate these symptoms.

Despite the expectation that death may be imminent once a decision is made to stop artificial ventilation or vasopressor support, families should be informed prior to terminal extubation that their loved ones may survive for hours to days. Patients with

terminal illness are often transferred to the ICU without having engaged in goals of care discussions. Once in the ICU, most of these patients are no longer able to participate in discussions about their prognosis, goals of care, and desires—obliging their families to act as surrogates. In other cases, such as with trauma or a sudden CNS event, there often isn't time for patients or families to have prepared for decisions about goals of care or withdrawal of life support. Decisions in the ICU may include whether to wake up a sedated patient to say good-bye or whether to keep a patient alive on life support until family or friends from out of town can come to the bedside.

### **The Bowel Obstruction Death**

Bowel obstruction is common in patients with gastrointestinal and gynecologic malignancies as a result of peritoneal carcinomatosis. While some of these patients may have their obstruction relieved by resection, bypass, diversion or stenting, many patients with poor performance status, advanced disease, and ascites are not candidates for surgery or cannot successfully have their obstruction relieved. Placing a reverse percutaneous endoscopic gastrostomy tube may help relieve nausea and vomiting, but is often not completely effective. A variety of pharmacologic treatments (steroids, metoclopramide, antiemetics, and octreotide receptor analogues) have been utilized with variable documentation of success [52]. These patients require a frank discussion about the role of intravenous hydration and nutrition once they become unable to eat and drink.

### **Artificial Nutrition and Hydration**

Patients rely upon artificial nutrition and hydration (ANH) to not only preserve life, but also to meet dietary and nutritional needs. There is no evidence that ANH prolongs life among patients who are dying [12]. Despite this lack of evidence, many clinicians and families view ANH as life-prolonging treatment [13]. ANH in terminally ill patients may be futile or even harmful [14]; some risks include aspiration, pneumonia, diarrhea, and gastrointestinal distress [53]. Some factors that contribute to familial encouragement and continuation of ANH include the need for active interventions to promote longevity and failure to accept the terminality of the underlying condition [54]. "We seem to have forgotten the difference between people who die because they stop taking in food and water, and people who stop taking in food and water because of the natural dying process" [54]. Education of patients, families, and caregivers surrounding the dying process is critical. Loss of appetite at the end-of-life is normal and does not contribute significantly to suffering [55].

### **The Bone Marrow Failure Death**

Patients with end-stage marrow disorders such as leukemia, myelodysplasia, and multiple myeloma suffer complications of pancytopenia with anemia, infections, and bleeding. Anemia in patients with end-stage disease is multifactorial; it is often influenced by chronic inflammation, erythropoietin deficiency, bone marrow infiltration, bleeding, hematinic depletion, and medication effects [56]. Transfusions are often utilized to alleviate symptoms of breathlessness, bothersome bleeding, and profound

fatigue [57] and typically provide symptomatic relief of a few-weeks duration [56]. Blood transfusions may be interpreted as both palliative and life-sustaining [19]. Platelet transfusions can be given to treat or prevent bleeding, although a minority of patients may ultimately become refractory due to alloimmunization. Perhaps one of the most efficacious characteristics of red blood cell transfusion is the rapidity by which it provides symptom relief and improvement of patient well-being. However, the need for and desire to continue transfusion support, even though it has been viewed as palliative, has been a barrier for enrolling patients with hematologic malignancies on hospice due to reimbursement issues. Patients and their physicians may be unwilling to forgo transfusions for symptom relief, even if no other disease remitting therapy is being provided. A few hospice agencies do support blood transfusions for symptom relief and efforts are underway to re-visit funding to allow for more hospice patients continuing transfusion support [58].

## Conclusion

As clinicians, we do not determine whether someone will die—we all die—but our interventions may help to determine when and how they die. Palliative Care has flourished in response to the incorporation of symptom and suffering alleviation in medicine. While there continues to be advances in palliative and hospice medicine, there are limits to the symptom relief that palliative care can provide.

Treatment goals and life goals are multifactorial and vary among patients. While some patients highly value quality of life, others adamantly wish for the greatest number of days on this earth. Discussions regarding goals of care and education about the dying process and choices that can be made are important to have early in disease process in anticipation of the expected or unexpected decline. While the decision to initiate a life-sustaining treatment is a difficult one, it can be even more challenging for patients and their families to terminate such life-sustaining therapies. The Hippocratic Oath incites physicians to alleviate pain, suffering, and fear. This Oath reinforces that our responsibility as physicians to alleviate suffering and pain at the end-of-life is equally as fundamental as our responsibility to preserve life.

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