Recommendations for end-of-life care in the intensive care unit: A consensus statement by the American College of Critical Care Medicine

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Background: These recommendations have been developed to improve the care of intensive care unit (ICU) patients during the dying process. The recommendations build on those published in 2003 and highlight recent developments in the field from a U.S. perspective. They do not use an evidence grading system because most of the recommendations are based on ethical and legal principles that are not derived from empirically based evidence.

Principal Findings: Family-centered care, which emphasizes the importance of the social structure within which patients are embedded, has emerged as a comprehensive ideal for managing end-of-life care in the ICU. ICU clinicians should be competent in all aspects of this care, including the practical and ethical aspects of withdrawing different modalities of life-sustaining treatment and the use of sedatives, analgesics, and nonpharmacologic approaches to easing the suffering of the dying process. Several key ethical concepts play a foundational role in guiding end-of-life care, including the distinctions between withholding and withdrawing treatments, between actions of killing and allowing

to die, and between consequences that are intended vs. those that are merely foreseen (the doctrine of double effect). Improved communication with the family has been shown to improve patient care and family outcomes. Other knowledge unique to end-of-life care includes principles for notifying families of a patient's death and compassionate approaches to discussing options for organ donation. End-of-life care continues even after the death of the patient, and ICUs should consider developing comprehensive bereavement programs to support both families and the needs of the clinical staff. Finally, a comprehensive agenda for improving end-of-life care in the ICU has been developed to guide research, quality improvement efforts, and educational curricula.

Conclusions: End-of-life care is emerging as a comprehensive area of expertise in the ICU and demands the same high level of knowledge and competence as all other areas of ICU practice. (Crit Care Med 2008; 36:953–963)

KEY WORDS: ethics; intensive care unit; end-of-life; palliative care; decision making; quality improvement

The primary goals of intensive care medicine are to help patients survive acute threats to their lives while preserving and restoring the quality of those lives. These goals are frequently achieved, with approximately 75% to 90% of patients admitted to an intensive care unit (ICU) surviving to discharge (1). Even so, the ICU has become a common place to die; studies show that 22% of all deaths in the United States now occur in or after admission to an ICU (2).

Admission to the ICU is therefore often a therapeutic trial. Only when the trial fails do patients and families consider a change in goals, from restorative care to palliative care. This change, which has been called the transition from cure to comfort, is one of the most difficult and important aspects of medical and nursing practice in the ICU (3). Two truths ensure that this transition will remain difficult, despite our best efforts. "First is the widespread and deeply held desire not to be dead. Second is medicine's inability to predict the future, and to give patients a precise, reliable prognosis about when death will come. If death is the alternative, many patients who have only a small amount of hope will pay a high price to continue the struggle" (4).

The purpose of these recommendations is to improve the care of patients during this transition and through the dying process. These recommendations

build on those published in 2001 (5) and highlight recent developments in the field from a U.S. perspective. The recommendations do not quantitatively grade the level of evidence because most of the recommendations are based on ethical and legal principles that are not derived from empirically based evidence.

Patient and Family-Centered Care and Decision Making

Family-centered care, which sees patients as embedded within a social structure and web of relationships, is emerging as a comprehensive ideal for end-of-life care in the ICU (6, 7). This approach has important implications for decision making and communication.

Standards for Decision Making. In the United States and many other countries, limiting life support is ethically and legally justified under the principle of autonomy. U.S. law grants patients with decision-making capacity the right to refuse any and all therapies, including those that sustain life (1). This standard is problematic in the ICU, however, where as many as 95% of patients may not be able to make decisions for themselves because of either their illness or sedation (8).

When patients cannot make decisions for themselves, decisions are made on their behalf by surrogates, using either the "substituted judgment standard" (if the patient's values and preferences are known) or the "best interests standard" (if they are not). While these decisions are often reached by consensus with the patient and family, patients do have an opportunity to designate a specific individual as a healthcare proxy. When no individual has been specifically designated, many states define a legal hierarchy for choosing a designated surrogate (1). Table 1 provides some of the legal precedents for these principles in American law.

Legal guidelines regarding end-of-life decision making are less clear when patients without capacity lack an appropriate surrogate. Some states allow physicians to make decisions for such patients based on wishes expressed to the physicians when the patients had capacity. However, no state explicitly allows physicians to make decisions based on their view of the best interests of the patient (1). In general, we recommend against *ad hoc* decision making in these circumstances. One option is to ask the court to appoint a guardian for the patient. Another option is to develop a clear procedural guideline, including safeguards to protect the patient's interests (such as mandatory ethics committee review) (9).

In an effort to engage the patient directly in decision making, there may be times when sedatives and analgesics could be discontinued so that a patient may regain decisional capacity. Nevertheless, such attempts may not result in a return to lucidity because the patients' illness is too severe. Furthermore, the attempts may be inappropriate when the patients' wishes are known, death is imminent, or discontinuing drugs would cause significant pain and suffering. In these situations, surrogates should be entrusted to make decisions for the patient (10).

Patients and families must be given sufficient time to reach decisions at the end of life, and information should be delivered in ways that are sensitive to the patient's cultural, religious, and language needs. Physicians should take seriously their responsibility to make recommendations and guide families in ways that accord with their decision-making preferences. Merely providing treatment alternatives and asking patients and families to choose among them may make the patients and families feel solely responsible for the decision to forgo life-sustaining treatment, and this practice contrasts with the preferred practice of shared decision making (11). Some patients and families prefer to have physicians make these decisions (12). Asking patients and families how they prefer to make decisions is an important aspect of treating them with respect (13).

Resolving Conflict. End-of-life decisions are made readily and by consensus when communication among patients, their surrogates, and clinicians is satisfactory. Nevertheless, communication may not resolve all differences, especially when patients or families insist on interventions that clinicians consider inadvisable. In cases of conflict, the first step is for all parties to focus on obtaining clarity about the goals of care. Patients or their surrogates should determine what they hope to achieve—for example, restoring health, extending life, or relieving pain and suffering. For their part, physicians should provide information about the patient's prognosis and what goals can be accomplished by the use of specific interventions (14).

In the small number of cases where agreement is not possible, physicians are not obligated to offer therapies that they believe cannot achieve the goals of care, as mutually defined by the clinicians, patient, and surrogates (15, 16). When this occurs, the American Medical Association (17) and others have recommended a process-based approach to resolving conflicts over end-of-life issues. Central to this process is mediation by hospital ethics committees. Many hospitals have adopted policies based on this model, and at least one state has incorporated this approach into legislation (18).

Table 1. Important U.S. court cases addressing decision making at the end of life

Case	Importance
Schloendorff v. Society of New York Hospitals, 211 N.Y. 125, 105 N.E. 92 (1914)	Established that competent patients have a right to determine how their bodies can be used and that informed consent is required before therapeutic interventions can be performed.
In re Quinlan, 755 A2A 647 (H.J.), cert. Denied, 429 U.S. 922 (1976)	Declared that competent patients have a right to refuse interventions that, if they become incompetent, can be exercised by surrogates under the principle of substituted judgment.
Barber v. Superior Court, 147 Cal. App. 7d 1006 (Cal. App. 1983)	Clarified that surrogates can refuse any and all interventions on behalf of patients, based on a benefit-burden analysis.
In re Conroy, 486A 2d 1209 (N.J., 1985)	Established that, lacking surrogate knowledge of patient wishes, decisions can be made using a best interests standard if the burdens of interventions outweigh their benefits and if the pain of living is such that administering the interventions is inhumane.
Cruzan v. Director, Missouri Department of Health, 497 U.S. 261 (1990)	Accepted the right of competent patients to refuse interventions but allowed states to set the level of evidence required to determine the prior wishes of incompetent patients with which surrogate decisions are made.

Communication With Families. Caring for family members is an important part of caring for the critically ill patient. Family-centered care is based on the values, goals, and needs of the patient and family, including their understanding of the illness, prognosis, and treatment options and their expectations and preferences for treatment and decision making (6). Supporting families through the death of a loved one in the ICU frequently involves guiding them through "hoping for the best and planning for the worst" (14). Compassion requires honoring the family's hopes and simultaneously preparing them for the possibility of death (19). Framing discussions in these terms can help avoid and resolve conflicts as the patient's condition unfolds.

Communication between members of the ICU team and the family occurs in many settings, including the formal family conference as well as bedside communication. Communication skills are an important component of high-quality critical care, and there is increasing evidence regarding the importance of this skill for family outcomes (20–23). There is also increasing evidence supporting specific approaches that can improve communication and family experiences (22, 24, 25). Evidence shows that families are more satisfied with communication and have reduced psychological morbid-ity when clinicians spend more time during family conferences listening to families, value the family input, and support their emotions (22, 24, 26). Families also need ongoing and direct communication concerning the patient's prognosis (27, 28). A recent randomized trial showed that such strategies to improve communication with families can significantly reduce psychological morbidity in family members after the ICU stay (22). Other strategies for improving end-of-life communication are shown in Table 2.

In addition, some families may choose to be present during resuscitation and other invasive procedures (29). Research shows that these experiences may be highly valued by family members and need not interfere with the delivery of medical care. Allowing family members to be present for such procedures requires careful planning, including guidelines, the availability of support systems, and trained personnel (30).

Spirituality plays an important role in how some critically ill patients and clinicians cope with illness and death (31). Spirituality is not synonymous with religion. Each person's understanding of spirituality should be explored. Assessment of spiritual needs is not the exclusive domain of the chaplain but is part of the role of critical care clinicians, who should possess fundamental skills in spiritual assessment and referral (32).

Ethical Principles Relating to the Withdrawal of Life-Sustaining Treatment

Three ethical principles help to shape the current U.S. consensus around the withdrawal of life-sustaining treatment. While not all clinicians personally agree with each of them, these principles have broad-based support within the U.S. legal system and accepted clinical practice and thereby form the basis for the specific recommendations that follow (33). The three principles are as follows: 1) Withholding and withdrawing life support are equivalent; 2) there is an important distinction between killing and allowing to die; and 3) the doctrine of "double effect" provides an ethical rationale for providing relief of pain and other symptoms with sedatives even when this may have the foreseen (but not intended) consequence of hastening death (34–37).

Withholding vs. Withdrawing. Numerous surveys consistently show that clinicians are psychologically more comfortable withholding treatments than withdrawing them (38–40). The reasons for this are complex but relate to the fact that withholding is passive, whereas withdrawing is active and associated with a greater sense of moral responsibility. Despite this psychological preference, both philosophical and legal analyses have emphasized that clinicians should make no distinction between decisions to withhold or to withdraw (41). This is because whether any therapy is initiated or continued should be based solely on an assessment of its benefits vs. burdens and the preferences of the patient. Furthermore, in many cases the value of an intervention can only be determined after a trial of therapy. If clinicians are reluctant to withdraw therapies, they may be less inclined to give patients a trial of an indicated therapy and thereby may make premature decisions to withhold therapies that the patient would consider beneficial.

Killing vs. Allowing to Die. In the landmark case of Karen Ann Quinlan, physicians argued that withdrawal of mechanical ventilation from a patient was unethical, because it would kill the patient. Some philosophers have supported this view, arguing that since killing is defined as an act that is the proximate cause of a death, then withdrawal of life support is indeed an act of killing, but one that may be justified by the clinical

Table 2. Strategies for improving end-of-life communication in the intensive care unit (ICU)

1. Communication skills training for clinicians
2. ICU family conference early in ICU course (118)

   Evidence-based recommendations for conducting family conference:
     Find a private location (21).
     Increase proportion of time spent listening to family (26).
     Use "VALUE" mnemonic during family conferences (22).
       Value statements made by family members.
       Acknowledge emotions.
       Listen to family members.
       Understand who the patient is as a person.
       Elicit questions from family members.
     Identify commonly missed opportunities (25, 149).
       Listen and respond to family members.
       Acknowledge and address family emotions.
       Explore and focus on patient values and treatment preferences.
       Affirm nonabandonment of patient and family.
     Assure family that the patient will not suffer (24).
     Provide explicit support for decisions made by the family (24).

   Additional expert opinion recommendations for conducting family conference:
     Advance planning for the discussion among the clinical team
       Identify family and clinician participants who should be involved.
       Focus on the goals and values of the patient.
       Use an open, flexible process.
       Anticipate possible issues and outcomes of the discussion.
       Give families support and time.
3. Interdisciplinary team rounds
4. Availability of palliative care and/or ethics consultation (115, 116)
5. Development of a supportive ICU culture for ethical practice and communication (108)

circumstances and the consent of the patient or surrogate (33). The U.S. courts, however, have rejected this view. In Quinlan, for example, the court affirmed that patients or their surrogates have the right to refuse any unwanted medical treatment, even if life-sustaining. Therefore, the withdrawal of life-sustaining treatments is not legally considered a killing, and the actions of clinicians in this regard are described as "allowing the patient to die" from the underlying illness (42).

Intended vs. Merely Foreseen Consequences. Euthanasia is illegal in the United States, yet ICU clinicians have an obligation to make patients comfortable during the dying process, even when medications must be administered in doses that may shorten the patient's life. The philosophical doctrine of "double effect" is used to draw a moral distinction between giving medications with the intention to kill the patient vs. giving them with the intention to make the patient comfortable, but with the foreseen consequence of potentially hastening the patient's death.

This doctrine is controversial, since it relies on an assessment of the intentions of the clinician, which are subjective and can be mixed. Furthermore, in most situations individuals are morally responsible for all of the foreseen consequences of their actions, not just those that are intended (34, 36). Despite these philosophical difficulties, the principle is supported in the U.S. law and defines the line between euthanasia and acceptable palliative care. In the words of former U.S. Supreme Court Chief Justice Rehnquist, "It is widely recognized that the provision of pain medication is ethically and professionally acceptable even when the treatment may hasten the patient's death if the medication is intended to alleviate pain and severe discomfort, not to cause death" (43).

The intentions of the clinicians are therefore critically important in determining the legality of the large doses of medication that are sometimes administered in end-of-life care. Both in verbal communication and written documentation, clinicians must clearly express the intention to relieve the pain and suffering of the patient and the clinical signs that justify the administration of additional medications. Moreover, this intention is evidenced by practices that rely on an ongoing assessment of the patient's comfort, coupled with judicious titration of sedation and analgesia in accordance with clinical guidelines

Some have argued that the doctrine of double effect is not necessary, since studies suggest that the use of sedatives and analgesics at the end of life does not actually hasten death (44–46). The doctrine is still useful, however, for justifying those individual cases where the drugs clearly appear to hasten death but are necessary to control symptoms (47).

Practical Aspects of Withdrawing Life-Sustaining Treatments in the ICU

Practical advice around the withdrawal of life-sustaining treatments comes from a combination of theoretical considerations, empirical data, and clinical experience. Although the phrase "withdrawal of care" is often heard, it is important to distinguish between the withdrawal of life-sustaining interventions and the withdrawal of care. While the former is common, the latter should never occur. Language is important, particularly to patients and their families.

The Procedure of Withdrawing Life-Sustaining Treatment. A useful clinical framework for the withdrawal of life-sustaining treatment is to consider it as one of many critical care procedures. Clinicians should follow steps familiar to those from other procedures like tracheal intubation or central venous catheterization (48). Communication with the family and preparing them for the withdrawal process is an essential step. In particular, families should be prepared for the normal respiratory patterns that often precede death. Clinicians should avoid referring to these as "agonal respirations," since this term may erroneously imply to the family that these cause the patient to be in "agony." With appropriate palliative care, this breathing pattern is a natural part of dying and should not be associated with any discomfort.

As with other routine clinical procedures, an explicit plan of withdrawing life support helps ensure that nothing is overlooked, such as discontinuing routine treatments that provide no comfort to the patient (such as chest radiographs and blood draws). An explicit plan also prompts busy clinicians to make important contacts, such as with social workers, clergy, and organ donation coordinators (49).

Clinicians should be prepared to assist families in the dying process. The goal is to provide the patient and family a quiet, private space devoid of technology and alarms. This may be difficult in units where

curtains separate patient beds. When the dying process is prolonged or when demands for an ICU bed cannot be met in other ways, transfer to another area in the hospital may be unavoidable (50). The transition should occur smoothly with deference to the needs of the patient and family. Every effort should be taken to reassure family members that continuity of clinical care will be maintained.

Even though excellent palliative care can often be provided with no more than attentive and compassionate clinical assessment, there may be a tendency to continue cardiac, pulse oximetry, and even invasive hemodynamic monitoring in the ICU. Since such monitoring does not provide additional comfort to the patient and is not necessary to assess symptoms of distress, providers should critically review whether it should be continued. Family members, particularly those who have spent weeks tracking physiologic markers, may find themselves paying undue attention to the monitor instead of the patient. A specific conversation with the family about the rationale for stopping these forms of monitoring may relieve anxiety.

Considerations Around Specific Therapies. Once the transition from cure to comfort has been negotiated, all ICU therapies should be critically evaluated in terms of whether they make a net positive contribution to the comfort of the patient. This includes antibiotics, vasoactive drugs, renal dialysis, and ventricular assist devices. These treatments, including intravenous fluids and nutrition, do not provide comfort to dying patients and are not obligatory during the withdrawal of life support. Sometimes clinicians set limits on treatments that are not currently indicated (such as cardiopulmonary resuscitation) while continuing other forms of aggressive treatment. However, once the decision has been made to withhold a life-sustaining therapy (such as renal dialysis or vasopressors), clinicians should critically consider the rationale for continuing any other life-sustaining treatments (51, 52).

There are justifications for offering limited sets of life-sustaining treatments. The most compelling is when a patient has specifically refused one form of life-sustaining treatment on the basis of personal values, as for example when a patient refuses intubation while requesting other therapies. These wishes should be followed as long as they are consistent with good-quality care. However, preferences such as refusing endotracheal in-

tubation while insisting on other aspects of cardiopulmonary resuscitation are not consistent with good-quality care and should not be adopted as a plan of treatment.

Abrupt discontinuation of life-sustaining treatments, with the exception of mechanical ventilation, results in no discomfort. Therefore, there is no justification to wean treatments such as antibiotics, blood products, intravenous fluids, or cardiovascular support. Since rapid withdrawal of oxygen or ventilatory support may lead to dyspnea, there is a theoretical rationale for removing these supports gradually. Although a prolonged "terminal weaning" process has been advocated on the grounds that it removes a sense of responsibility from the family and clinicians, this process is not ethically required and may, by prolonging the dying process, actually contribute to patient distress (53). Therefore, the only justification for gradual reduction of ventilatory support is to allow time to control dyspnea through the titration of medications.

Considerable variation in practice attends to the decision of whether to extubate patients when withdrawing mechanical ventilation or whether to leave the endotracheal tube in place while the ventilator is weaned (54). Since survivors of critical illness frequently recall endotracheal tubes and suctioning as significant sources of discomfort, an argument can be made to remove artificial airways (55). Neither ethical principles nor current empirical evidence can support a dogmatic view on this question; clinicians should solicit input from team members and the family to make the decision in individual cases.

The use of noninvasive ventilation during end-of-life care should be evaluated by carefully considering the goals of care (56–58). There are two reasonable scenarios. A patient who has specifically refused intubation but desires other aspects of intensive care with the goal of prolonging survival may choose noninvasive ventilation. Alternatively, noninvasive ventilation may be used as a palliative technique to minimize dyspnea. When used for the latter indication, noninvasive ventilation should be stopped when it is no longer effective at relieving that symptom.

Pharmacologic Paralysis and End-of-Life Care. Neuromuscular blocking agents, such as pancuronium, vecuronium, and atracurium, can be involved in end-of-life care in two ways (5, 59). First,

clinicians may initiate use of these agents at the time of withdrawal of life support. This practice, whose primary purpose is to make the patient "look" comfortable during the dying process, is not acceptable. Since these agents have no sedative or analgesic effects, their use cannot be justified as being beneficial to the patient. Furthermore, their use makes it impossible to assess the patient's level of comfort, thereby thwarting an essential goal of end-of-life care. A second, more difficult situation occurs when a decision is made to withdraw life support from a patient who has been receiving paralytic agents for therapeutic reasons. The ideal solution in this circumstance is to allow the paralytic agent to wear off or to pharmacologically reverse its effects, allowing for better assessment of the patient. In some cases, however, the duration of action of these agents may be very prolonged, as when the patient has been receiving large doses of the drugs or when hepatic or renal failure has impaired their clearance. In these cases, the benefits of continuing with life support until neuromuscular function can be restored must be balanced against the burdens that this support imposes on the patient and family.

The question of how to manage patients receiving paralytic agents remains controversial. If prolonged paralysis is recognized as an iatrogenic complication of the patient's treatment, then insisting that this complication be resolved before acceding to the families request to withdraw life support could be seen as placing the concerns of the care team above those of the patient and family. These recommendations therefore take the following positions. First, paralytic agents should never be introduced at the time of withdrawal of life support. Second, when patients have been receiving paralytic agents for therapeutic reasons, neuromuscular function should ideally be restored before withdrawal of life support. Third, when restoring neurologic function would impose an unacceptable delay on the withdrawal of life support, withdrawal may proceed, with particular attention given to ensuring the comfort of the patient through the dying process, recognizing that signs of discomfort will be difficult to detect.

Symptom Management in End-of-Life Care

Declining or impaired cognition and decreased consciousness are common

among ICU patients (60). When patients cannot self-report their symptoms, clinicians may undertreat pain and suffering because of difficulty in identifying behavioral indicators of these symptoms (61).

Pain. More than 50% of seriously ill hospitalized patients report some level of pain (62). Pain in the ICU is often related to iatrogenic causes, procedures, and interventions. Moderately or severely uncomfortable procedures that are commonly performed in the ICU include suctioning, turning, catheter insertion, wound care, and the presence of endotracheal tubes (63, 64). Minimizing or eliminating iatrogenic sources of pain should be part of the pain relief plan.

When patients cannot self-report their degree of pain, standardized scoring systems based on physiologic variables and behavioral observations can provide an objective basis for pain management. The Behavioral Pain Scale was developed for use in the ICU with mechanically ventilated patients (65). The Behavioral Pain Scale has strong interrater reliability, moderate internal consistency, and discriminant validity (66, 67).

The Pain Assessment Behavior Scale is another simple, reliable, and valid instrument for assessing pain in adults when a self-report cannot be obtained. This instrument has strong internal consistency and interrater reliability, and the correlation between patient reports and Pain Assessment Behavior Scale suggests that this scale is a good measure of pain presence and intensity (68).

Dyspnea and Respiratory Distress. Dyspnea and respiratory distress are common symptoms among patients admitted to an ICU unit for oxygen and ventilatory support (69). Dyspnea is defined as the patient's subjective awareness of altered or uncomfortable respiratory functioning; respiratory distress is the observable corollary to dyspnea (70). Behavioral correlates of respiratory distress in mechanically ventilated patients include (in descending frequency) tachypnea and tachycardia, a fearful facial expression, accessory muscle use, paradoxic breathing (diaphragmatic), and nasal flaring (71).

The data to support specific treatment approaches for dyspnea during end-of-life care are sparse and incomplete. The best approach is to individualize the treatment based on the underlying source of the dyspnea, the patient's level of consciousness, and the patient's observed and perceived needs. Some approaches treat the symptom directly and thereby

prolong life. These include, for example, supplemental oxygen, corticosteroids, diuretics, and bronchodilators. Other approaches, like administration of opioids, also make the patient comfortable but may decrease consciousness. Clinicians should work with patients and families to determine the optimal approach, or combination of approaches, for each patient on an individual basis (70).

Delirium. Delirium is a disturbance of consciousness characterized by an acute onset and fluctuating course such that a patient's ability to receive, process, store, or recall information is impaired (72). When these symptoms are accompanied by increased motor activity, the condition is termed *agitated delirium*. Agitated delirium is relatively common in ICU patients as a consequence of their medical condition, substance intoxication or withdrawal, use of medication, or a combination of these factors (60, 73), and it prompts the use of sedatives and restraints to promote patient safety and avoid self-harm. Delirium, calm or agitated, is a common symptom among conscious ICU patients who are dying (74).

Distressing symptoms, such as pain or dyspnea, may contribute to agitated delirium, and analgesia and other treatments should be optimized before sedatives are employed (75). Removing restraints, promoting sleep, reducing noise and lights, and providing a soothing family member or staff presence are all strategies that may reduce the negative effects of delirium and minimize the need for sedation (76). Neuroleptic agents, such as haloperidol, are effective at reducing delirium-induced agitation. While sedation is the hallmark treatment for agitated delirium and is often necessary at the end of life (10), its use deprives the patient and family of possible meaningful interactions before death and should be used as a last resort.

Specific Medications. The goal of drug therapy as a component of end-of-life care is the alleviation or prevention of pain, dyspnea, and other distressing symptoms. The medications most commonly used in end-of-life care are summarized in Tables 3 and 4. As a general rule, any time an increase in an infusion dose is being considered due to reemergence of the signs or symptoms of suffering, intravenous bolus doses should be administered concurrently to achieve a rapid response. The routine use of a bolus-infusion approach should minimize the risk of unnecessary delays in response.

Opioids are the mainstay for the treatment of pain and dyspnea in dying patients and demonstrate additive sedative effects as a component of drug combinations for palliative sedation (77–81). The opioid analgesics recommended in recent multisociety practice guidelines are morphine, fentanyl, and hydromorphone (82). The effects of morphine on cardiac preload may also contribute to improvement of dyspnea in some patients by reducing pulmonary edema.

Morphine is recommended as the agent of choice for palliative care due to its efficacy, low cost, familiarity to the healthcare team, and potentially beneficial euphoric effects. Compared with other opioids, morphine is associated with a greater risk of histamine release causing urticaria at the injection site, pruritus, and flushing, which may be relieved by antihistaminic therapy (83). Fentanyl and hydromorphone are alternatives to morphine. Fentanyl has a very short duration of response and should be administered by continuous infusion in this setting. Although hydromorphone is considered to have less euphoric effect than morphine, available evidence does not suggest important differences in analgesic efficacy, adverse effects, or patient preference in the management of chronic and acute pain (84).

Benzodiazepines are the most frequently used and often preferred agents for sedation in the critical care unit, including sedation during end-of-life care (44, 77, 82, 85). They have no analgesic properties; their benefits in this setting derive from their sedative, hypnotic, anxiolytic, and amnestic effects. Lorazepam and midazolam are the most commonly used benzodiazepines. As with all centrally acting drugs, the time to onset of the benzodiazepines is primarily dependent on the lipid solubility of the drug. Midazolam is highly lipophilic and has the most rapid onset of effect following intravenous administration, with maximal response in approximately 5–10 mins. Lorazepam is the least lipid soluble of the parenteral benzodiazepines and requires up to 20–25 mins to achieve maximal response following intravenous administration (86, 87). There are no convincing data of important differences in clinical response or safety when each agent is used appropriately.

Propofol is an intravenous general an-

Table 3. Opioid analgesic agents (5, 79, 82)

	Equivalent Dose, IV[a]	Onset to Peak Effect, mins	Duration of Effect, hrs	Typical Adult Dose, IV	Typical Pediatric Dose, IV	Typical Infusion Rate
Morphine	10 mg	20–30	3–4	2–10 mg	0.1 mg/kg	0.05–0.5 mg·kg^{-1}·hr^{-1}
Fentanyl	100 µg	2–5	0.5–2	0.5–2 µg/kg	1–5 µg/kg	0.5–10 µg·kg^{-1}·hr^{-1}
Hydromorphone	1.5–2 mg	20–30	3–4	0.5–2 mg	—	—

IV, intravenous.

[a]Equivalent doses are approximations and are of limited value due to differences in onset and duration of effect.

Table 4. Sedative agents (5)

	Onset to Peak Effect, mins	Duration of Effect, hrs	Typical Initial Adult Dose, IV	Typical Initial Pediatric Dose, IV	Typical Initial Infusion Dose, Adult	Typical Initial Infusion Dose, Pediatric
Sedatives						
Lorazepam	20–25	2–4	1–3 mg	0.05 mg/kg	0.5–4 mg/hr	0.05–0.1 mg·kg^{-1}·hr^{-1}
Midazolam	5–10	1.5–2	0.02–0.1 mg/kg	0.1 mg/kg	1–5 mg/hr	0.05–0.1 mg·kg^{-1}·hr^{-1}
Propofol	1–2	0.1–0.4	1 mg/kg	1 mg/kg	10–50 µg·kg^{-1}·min^{-1}	10–50 µg·kg^{-1}·min^{-1}
Neuroleptics						
Haloperidol	25–30	2–4	0.5–20 mg	—	3–5 mg/hr	—

IV, intravenous.

esthetic widely used at sedative doses in critically ill patients. The primary advantages of propofol are its very rapid onset of effect combined with a rapid offset of effect, allowing relatively easy titration to the desired level of sedation (82, 88).

Other sedative agents, including the barbiturates and ketamine, have a limited role in this setting and can be considered for selected patients who may be refractory or intolerant to usual agents (47, 89).

Haloperidol is considered the drug of choice for treatment of delirium in critically ill patients (82, 90). Due to its long elimination half-life, haloperidol usually requires a loading regimen for initial control of symptoms. Haloperidol reaches maximal effect approximately 25–30 mins following an intravenous dose and can be repeated every 15–30 mins as needed (82). It has been suggested that the intravenous dose can be doubled every 30 mins until response is achieved (91); however, single adult doses >20 mg are rarely required or recommended. Haloperidol has no analgesic activity and does not have significant sedative effects as a single agent. It is typically combined with opioid analgesics and sedative agents to manage acute agitated behavior in critically ill patients.

Although many drugs can be used to treat pain and agitation at the end of life, the importance of the practitioner's familiarity with the drug cannot be overemphasized. In the last few hours of life, there may be only one chance to prevent pain, dyspnea, and delirium. As much expertise is necessary for the appropriate use of drug therapy at the end-of-life as for any other pharmacologic intervention in critical care.

Considerations at the Time of Death

Even when anticipated, the time surrounding the death of a patient can be stressful for both families and clinicians. Anticipation of the tasks that must be performed can help ensure that end-of-life care is delivered appropriately and compassionately.

Notification of Death. Pronouncing death is a solemn ritual and an important competency for end-of-life care (7). Senior physician leadership and the involvement of other professionals, such as the nurse, chaplain, or social worker, are important. The communication should avoid euphemisms and use plain language gently and empathically (*dead, dying, death,* and *die* are all words that are

rarely misunderstood) (92). Most families need reassurance that everything appropriate was done to help their family member. News of a patient's death should be given in person, whenever possible. When families must be contacted by telephone, special care should be taken in how the information is disclosed.

Determination of Brain Death. The frequency with which death is determined by neurologic criteria varies greatly depending on the patient population served by an ICU, but in one study of >6,000 patients who died in ICU, 6% were diagnosed as dead on the basis of neurologic criteria (93). Standard criteria for ascertaining the diagnosis of brain death in adults are available (94), although studies show considerable variability in how the diagnosis is made around the world (95). Similarly, criteria used for determining brain death in children are also variable, perhaps reflecting the fact that the guidelines for children have not been updated since 1987 (96). There is not general consensus on the advisability of having family members present at the time testing is performed (97).

Organ Donation. Organ and tissue donation is an integral part of end-of-life decisions and bereavement practices (98, 99). Routine questioning about advance directives and preferences at admission to the hospital may identify potential organ donors (100). Requests should focus on allowing families the opportunity to determine whether organ donation is consistent with either the patient's known wishes or what the patient would likely have wanted.

Donation by Cardiac Death (DCD) requires protocols for withdrawal of life-sustaining therapies under carefully controlled conditions (101). Some have concerns about the potential effect of DCD on the quality of end-of-life decision making and care in the ICU, but research and debate are needed to develop consensus regarding the best approach to achieve high-quality palliative care simultaneously with allowing patients and families the option of DCD.

Critical care professionals are responsible for the integrity of the organ donation process in collaboration with the organ procurement organization. Best practices require that the request is made in a private location and paced to give the family time to accept the death (98). United States regulations require that the person requesting organ donation be specifically trained to perform this task. Re-

lational aspects of how the information is shared with families have been shown to be more important than details of the specific content of the information. Training and clear role responsibilities for the interdisciplinary team can reduce the stress associated with requests for organ donation and increase donation rates.

Bereavement and Support. Bereavement and support services are essential to the delivery of high-quality palliative care, for both the family and the clinicians. Assisting families to cope with the impending death, complete important life tasks, and engage in meaningful rituals is a response to the family's anticipatory grief. The care of the body after death, making funeral plans, and deciding about autopsy are key bereavement tasks following a person's death. After a patient's death, families benefit from information about educational and spiritual resources, support groups, and contact information for mental health professionals with expertise in bereavement (6, 7, 19, 22, 98, 102).

Similarly, clinicians also have important bereavement needs. Although the needs of clinicians have not been routinely addressed, their unrecognized suffering and grief may undermine the effectiveness and quality of care (103, 104). An Institute of Medicine report stressed the importance of developing strategies to help professionals preserve their own integrity and well-being (105).

Needs of the Interdisciplinary Team. The clinical team needs to be interdisciplinary and committed to cooperation and clear communication. Significant discrepancies exist between critical care nurses and physicians about satisfaction with end-of-life decision-making processes, including ethical issues (106, 107). Physicians may be unaware of nurses' perspectives on conflict (108). More than half of the issues identified by critical care nurses as either obstructing or facilitating quality care for dying patients involve some aspect of communication (27).

End-of-life care requires support systems and resources for caregivers that address moral distress, burnout, and posttraumatic stress disorder (109–112). Systems of support may include regular debriefings after patient deaths, access to spiritual and psychosocial resources, and relief from responsibilities for some time after a patient dies (27, 104, 113). Within the ICU culture, norms for appropriate behavior, mutual support, communica-

tion, and resolution of ethical conflicts are essential.

Research, Quality Improvement, and Education

End-of-life care in the ICU, like many aspects of critical care, offers important opportunities for research, quality improvement, and education. There has been a growing literature on each of these topics in the past few years that can help guide researchers, clinicians, administrators, and educators.

Research. A recent interdisciplinary working group identified four areas of need for a research agenda to improve end-of-life care: defining the problems, identifying solutions, evaluating solutions, and overcoming barriers. In each of these areas, important unanswered questions were identified (114). Two important principles emerged: Interventions that are likely to improve the quality of care should be developed with preliminary data supporting their efficacy before being subjected to randomized trials, and outcome measures must be identified that can be used to demonstrate the improvements.

One lesson from prior research in this area is that large randomized trials of interventions should have supporting evidence from smaller studies demonstrating "proof of concept." A number of recent interventions have shown promising results, including standardized end-of-life family conferences with bereavement pamphlets and routine palliative care and ethics consultation (22, 115, 116). These studies suggest that end-of-life care can be improved but highlight the importance of preliminary data to establish feasibility and improvement in intermediate outcomes before launching large randomized trials to provide definitive proof of effectiveness.

The field needs to identify reliable, valid, feasible, and responsive outcome measures for end-of-life care. Outcome measures used to date include length of stay, intensity of care, families' psychological symptoms, and ratings of quality of care from ICU clinicians and family members. Each of these outcomes has important challenges. Several studies have used as the outcome measure ICU length of stay among patients who died (115–118). The rationale for this outcome measure is that if ICU days are decreased for those patients who ultimately die without an increase in overall

mortality rate, the intervention has reduced the "prolongation of dying." There are some important theoretical limitations to using ICU days as an outcome measure for such interventions. For example, an intervention that rushed families to make decisions might be associated with decreased family satisfaction with care and increased family depression, anxiety, or posttraumatic stress disorder (20, 21). Nonetheless, reducing ICU length of stay, particularly if it is associated with high levels of family satisfaction (115), seems like an appropriate surrogate marker for improved quality of care. Another potential assessment of quality of end-of-life care is family or clinician satisfaction with care. Patient satisfaction is not a practical outcome measure since the vast majority of patients are not able respond to questions at a time when end-of-life care is being provided in the ICU (119). Measures that have shown some evidence of reliability and validity after death in the ICU include the Quality of Dying and Death (49, 69, 120–122), the Family Satisfaction with ICU (123, 124), and the Critical Care Family Satisfaction Survey (125). Finally, there is evidence that improved communication about end-of-life care can significantly reduce psychological morbidity in family members after a death in the ICU (22).

Quality Improvement. Many publications exist on the issue of quality improvement in the critical care setting (126–134), and there is growing recognition that end-of-life care in the ICU is an important target for quality improvement efforts. Recently, a working group identified the domains of quality for end-of-life care, and these domains provide a framework for understanding the diverse issues and potential targets for quality improvement efforts focused on end-of-life care in the ICU (135). The domains were 1) patient- and family-centered decision making; 2) communication; 3) continuity of care; 4) emotional and practical support; 5) symptom management and comfort care; 6) spiritual support; and 7) emotional and organizational support for ICU clinicians.

There have been several recent publications of quality improvement efforts designed to improve end-of-life care in the ICU. A before-after quality improvement study of implementation of a standardized order form for withdrawal of life-sustaining therapies suggests efforts can improve care (49). There have also been recent efforts to define process mea-

sures for high-quality end-of-life care in the ICU (136, 137). Although these measures have not yet been validated, they have promise for improving the quality of care in all ICUs.

Education. Although education in this area is improving, studies document the deficiencies in education about end-of-life care for physicians and nurses (138–144). Considerable work has been done in education about end-of-life care that can be adapted to the ICU setting, including the development of training programs such as Education for Physicians on End-of-Life Care (145) and End-of-Life Nursing Education Consortium (146) and curricula developed for internal medicine residency training (147). The Initiative for Pediatric Palliative Care is a curriculum focused on the care of children (148). In addition, clinicians need opportunities to address their own emotions and reactions to working with dying patients and their families (144). Educational programs that offer clinicians the opportunity to talk about their experiences caring for dying critically ill patients and their families and the effect of providing this care on their own emotions and work attitudes can be valuable (113).

CONCLUSIONS

End-of-life care is emerging as a comprehensive area of expertise in the ICU and demands the same high level of knowledge and competence as all other areas of ICU practice. There has been an increased focus on research, education, and quality improvement to improve end-of-life care in the ICU setting. There is also increasing consensus within the field of critical care on some important principles, such as shared decision making and the importance of caring for patients' families. These revised guidelines incorporate these recent developments in an effort to further improve the care of patients dying in the ICU and their families.

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