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Last Days of Life (PDQ®)–Health Professional Version

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Overview

Despite progress in developing treatments that have improved life expectancies for patients with advanced-stage cancer, the American Cancer Society estimates that 595,690 people will die from cancer in 2016.[1] People with cancer die under various circumstances. A report of the Dartmouth Atlas Project analyzed Medicare data from 2003 to 2007 for cancer patients older than 65 years who died within 1 year of diagnosis.[2] Across the United States, 29% of patients died in a hospital, with 61.3% hospitalized at least once in the last month of life. In addition, 24% of patients were admitted to an intensive care unit at least once. Approximately 6% of patients nationwide received chemotherapy in the last month of life. Conversely, about 55% of patients who died used hospice service; however, the average length of stay was only 8.7 days, and 8.3% of patients were enrolled in the last 3 days of life. Significant regional variations in the descriptors of end-of-life (EOL) care remain unexplained.

Patient and family preferences may contribute to the observed patterns of care at the EOL. Patient recall of EOL discussions, spiritual care, or early palliative care, however, are associated with less-aggressive EOL treatment and/or increased utilization of hospice.[3-7] In addition, death in a hospital has been associated with poorer quality of life and increased risk of psychiatric illness among bereaved caregivers.[8] (Refer to the PDQ summary on Planning the Transition to End-of-Life Care in Advanced Cancer for more information.) Thus, it is important to help patients and their families articulate their goals of care and preferences near the EOL.

This summary provides clinicians with information about anticipating the EOL; the common symptoms patients experience as life ends, including in the final hours to days; and treatment or care considerations. The decisions commonly made by patients, families, and clinicians are also highlighted, with suggested approaches. The goal of this summary is to provide essential information for high-quality EOL care.

In this summary, unless otherwise stated, evidence and practice issues as they relate to adults are discussed. The evidence and application to practice related to children may differ significantly from information related to adults. When specific information about the care of children is available, it is summarized under its own heading.

References

1. American Cancer Society: Cancer Facts and Figures 2016. Atlanta, Ga: American Cancer Society, 2016. Available online. Last accessed June 15, 2018.
2. Goodman DC, Fisher ES, Chang CH, et al.: Quality of End-of-Life Cancer Care for Medicare Beneficiaries: Regional and Hospital-Specific Analyses. Lebanon, NH: Dartmouth Institute for Health Policy & Clinical

Practice, 2010. Available online. Last accessed January 5, 2018.

3. Wright AA, Zhang B, Ray A, et al.: Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. JAMA 300 (14): 1665-73, 2008. [PUBMED Abstract]
4. Mack JW, Cronin A, Keating NL, et al.: Associations between end-of-life discussion characteristics and care received near death: a prospective cohort study. J Clin Oncol 30 (35): 4387-95, 2012. [PUBMED Abstract]
5. Balboni TA, Paulk ME, Balboni MJ, et al.: Provision of spiritual care to patients with advanced cancer: associations with medical care and quality of life near death. J Clin Oncol 28 (3): 445-52, 2010. [PUBMED Abstract]
6. Temel JS, Greer JA, Muzikansky A, et al.: Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 363 (8): 733-42, 2010. [PUBMED Abstract]
7. Hui D, Kim SH, Roquemore J, et al.: Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. Cancer 120 (11): 1743-9, 2014. [PUBMED Abstract]
8. Wright AA, Keating NL, Balboni TA, et al.: Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. J Clin Oncol 28 (29): 4457-64, 2010. [PUBMED Abstract]

Anticipating the End of Life

The Final Days to Weeks of Life

Providing excellent care toward the end of life (EOL) requires an ability to anticipate when to focus mainly on palliation of symptoms and quality of life instead of disease treatment.[1] Certain symptoms such as anorexia or delirium indicate that the patient is approaching the last weeks or months of life.[2]

Another strategy is to follow a patient’s functional status over time and use changes to determine when to focus more on palliation and less on disease treatment. For example, one group of investigators [3] retrospectively analyzed nearly 71,000 Palliative Performance Scale (PPS) scores obtained from a cohort of 11,374 adult outpatients with cancer who were assessed by physicians or nurses at the time of clinic visits. The PPS is an 11-point scale describing a patient’s level of ambulation, level of activity, evidence of disease, ability to perform self-care, nutritional intake, and level of consciousness.

The investigators assigned patients to one of four states:

- Stable (PPS score, 70–100).
- Transitional (PPS score, 40–60).
- EOL (PPS score, 10–30).
- Dead.

Of the 4,806 patients who died during the study period, 49% were recorded as being in the transitional state, and 46% were recorded as being in the stable state. For a patient who was in the transitional state, the probability of dying within a month was 24.1%, which was less than that for a patient in the EOL state (73.5%). The results suggest that serial measurement of the PPS may aid patients and clinicians in identifying the approach of the EOL.

Impending Death

Impending death, or actively dying, refers to the process in which patients who are expected to die within 3 days exhibit a constellation of symptoms.[4] In the final days of life, patients often experience progressive decline in their neurocognitive, cardiovascular, respiratory, gastrointestinal, genitourinary, and muscular function, which is characteristic of the dying process. A number of highly specific clinical signs can be used to help clinicians establish the diagnosis of impending death (i.e., death within days).[5,6]

Impending death is a diagnostic issue rather than a prognostic phenomenon because it is an irreversible physiologic process. The ability to diagnose impending death with confidence is of utmost importance to clinicians because it could affect their communication with patients and families, and inform complex health care decisions such as hospital discharge, discontinuation of prescription medications, artificial nutrition, use of life support measures, and enrollment on clinical care pathways.[7,8] Because clinicians often overestimate survival,[9,10] they often hesitate to diagnose impending death without adequate supporting evidence.

One study examined five signs in cancer patients, beginning when they were recognized as actively dying. Investigators reported that the median time to death from the onset of death rattle was 23 hours; from the onset of respiration with mandibular movement, 2.5 hours; from the onset of cyanosis in extremities, 1 hour; and from the onset of pulselessness on the radial artery, 2.6 hours.[11]

The Investigating the Process of Dying study systematically examined physical signs in 357 consecutive cancer patients.[6] Among the ten target physical signs, there were three early signs and seven late signs. The early signs had high frequency, occurred more than 1 week before death, and had moderate predictive value that a patient would die in 3 days. Early signs included the following:

- Decreased level of consciousness (Richmond Agitation Sedation Scale score of –2 or lower).
- Decreased performance status (Palliative Performance Scale score ≤20%).
- Dysphagia of liquids.

The late signs occurred mostly in the last 3 days of life, had lower frequency, and were highly specific for impending death in 3 days. Late signs included the following:[6]

- Pulselessness on the radial artery.
- Respiration with mandibular movement.
- Decreased urine output.
- Cheyne-Stokes breathing.
- Death rattle.
- Apnea periods.

- Peripheral cyanosis.

In particular, the high positive likelihood ratios (LRs) of pulselessness on the radial artery (positive LR, 15.6), respiration with mandibular movement (positive LR, 10), decreased urine output (≤200 cc/d) (positive LR, 15.2), Cheyne-Stokes breathing (positive LR, 12.4), and death rattle (positive LR, 9) suggest that these physical signs can be useful for the diagnosis of impending death.[6] Because of low sensitivity, the absence of these signs cannot rule out impending death. A prospective observational study that examined vital signs in the last 7 days of life reported that blood pressure and oxygen saturation decreased as death approached. However, a large proportion of patients had normal vital signs, even in the last 12 hours of life. Moderate changes in vital signs from baseline could not definitively rule in or rule out impending death in 3 days. Therefore, predicting death is difficult, even with careful and repeated observations.[12]

Several other late signs that have been found to be useful for the diagnosis of impending death include the following:[13]

- Nonreactive pupils (positive LR, 16.7; 95% confidence interval [CI], 14.9–18.6).
- Decreased response to verbal stimuli (positive LR, 8.3; 95% CI, 7.7–9).
- Decreased response to visual stimuli (positive LR, 6.7; 95% CI, 6.3–7.1).
- Inability to close eyelids (positive LR, 13.6; 95% CI, 11.7–15.5).
- Drooping of the nasolabial fold (positive LR, 8.3; 95% CI, 7.7–8.9).
- Hyperextension of the neck (positive LR, 7.3; 95% CI, 6.7–8).
- Grunting of vocal cords (positive LR, 11.8; 95% CI, 10.3–13.4).
- Upper gastrointestinal bleeding (positive LR, 10.3; 95% CI, 9.5–11.1).

In conclusion, bedside physical signs may be useful in helping clinicians diagnose impending death with greater confidence, which can, in turn, assist in clinical decision making and communication with families.

Care During the Final Hours of Life

The recognition of impending death is also an opportunity to encourage family members to notify individuals close to the patient who may want an opportunity to “say good-bye.” In the final hours of life, care should be directed toward the patient and the patient’s loved ones. In addition to continuing a careful and thoughtful approach to any symptoms a patient is experiencing (refer to the Symptoms During the Final Months, Weeks, and Days of Life section of this summary), preparing family and friends for a patient’s death is critical. Preparations include the following:

- Acknowledging the symptoms that are likely to occur.
- Articulating a plan to respond to the symptoms.
- Eliciting fears or concerns of family members.
- Assuring that respectfully allowing life to end is appropriate at this point in the patient’s life.

Encouraging family members who desire to “do something” to participate in the care of the patient (e.g., moistening the mouth) may be helpful. In the final days to hours of life, patients often have limited, transitory moments of lucidity. Family members should be prepared for this and educated that this is a natural aspect of the dying process and not necessarily a result of medications being administered for symptoms or a sign that the patient is doing better than predicted. Despite their limited ability to interact, patients may be aware of the presence of others; thus, loved ones can be encouraged to speak to the patient as if he or she can hear them.

Educating family members about certain signs is critical. In the final hours of life, patients often experience a decreased desire to eat or drink, as evidenced by clenched teeth or turning from offered food and fluids. This behavior may be difficult for family members to accept because of the meaning of food in our society and the inference that the patient is “starving.” Family members should be advised that forcing food or fluids can lead to aspiration. Reframing will include teaching the family to provide ice chips or a moistened oral applicator to keep a patient’s mouth and lips moist. Finally, the death rattle is particularly distressing to family members. (Refer to the Death Rattle section in the Symptoms During the Final Months, Weeks, and Days of Life section of this summary for more information.) It is important to assure family members that death rattle is a natural phenomenon and to pay careful attention to repositioning the patient and explain why tracheal suctioning is not warranted.[14]

For patients who die in the hospital, clinicians need to be prepared to inquire about the family’s desire for an autopsy, offering reassurance that the body will be treated with respect and that open-casket services are still possible, if desired.

Health care professionals, preferably in consultation with a chaplain or religious leader designated by the patient and/or family, need to explore with families any fears associated with the time of death and any cultural or religious rituals that may be important to them. Such rituals might include placement of the body (e.g., the head of the bed facing Mecca for an Islamic patient) or having only same-sex caregivers or family members wash the body (as practiced in many orthodox religions). When death occurs, expressions of grief by those at the bedside vary greatly, dictated in part by culture and in part by their preparation for the death. Chaplains are to be consulted as early as possible if the family accepts this assistance. Health care providers can offer to assist families in contacting loved ones and making other arrangements, including contacting a funeral home. (Refer to the PDQ summary on Spirituality in Cancer Care for more information.)

References

1. Lorenz K, Lynn J, Dy S, et al.: Cancer care quality measures: symptoms and end-of-life care. Evid Rep Technol Assess (Full Rep) (137): 1-77, 2006. [PUBMED Abstract]
2. Maltoni M, Caraceni A, Brunelli C, et al.: Prognostic factors in advanced cancer patients: evidence-based clinical recommendations--a study by the Steering Committee of the European Association for Palliative Care. J Clin Oncol 23 (25): 6240-8, 2005. [PUBMED Abstract]
3. Sutradhar R, Seow H, Earle C, et al.: Modeling the longitudinal transitions of performance status in cancer outpatients: time to discuss palliative care. J Pain Symptom Manage 45 (4): 726-34, 2013. [PUBMED Abstract]
4. Hui D, Nooruddin Z, Didwaniya N, et al.: Concepts and definitions for "actively dying," "end of life,"

"terminally ill," "terminal care," and "transition of care": a systematic review. J Pain Symptom Manage 47 (1): 77-89, 2014. [PUBMED Abstract]

5. Domeisen Benedetti F, Ostgathe C, Clark J, et al.: International palliative care experts' view on phenomena indicating the last hours and days of life. Support Care Cancer 21 (6): 1509-17, 2013. [PUBMED Abstract]
6. Hui D, dos Santos R, Chisholm G, et al.: Clinical signs of impending death in cancer patients. Oncologist 19 (6): 681-7, 2014. [PUBMED Abstract]
7. Ellershaw J, Ward C: Care of the dying patient: the last hours or days of life. BMJ 326 (7379): 30-4, 2003. [PUBMED Abstract]
8. Hui D, Con A, Christie G, et al.: Goals of care and end-of-life decision making for hospitalized patients at a canadian tertiary care cancer center. J Pain Symptom Manage 38 (6): 871-81, 2009. [PUBMED Abstract]
9. Lamont EB, Christakis NA: Prognostic disclosure to patients with cancer near the end of life. Ann Intern Med 134 (12): 1096-105, 2001. [PUBMED Abstract]
10. Hui D, Kilgore K, Nguyen L, et al.: The accuracy of probabilistic versus temporal clinician prediction of survival for patients with advanced cancer: a preliminary report. Oncologist 16 (11): 1642-8, 2011. [PUBMED Abstract]
11. Morita T, Ichiki T, Tsunoda J, et al.: A prospective study on the dying process in terminally ill cancer patients. Am J Hosp Palliat Care 15 (4): 217-22, 1998 Jul-Aug. [PUBMED Abstract]
12. Bruera S, Chisholm G, Dos Santos R, et al.: Variations in vital signs in the last days of life in patients with advanced cancer. J Pain Symptom Manage 48 (4): 510-7, 2014. [PUBMED Abstract]
13. Hui D, Dos Santos R, Chisholm G, et al.: Bedside clinical signs associated with impending death in patients with advanced cancer: preliminary findings of a prospective, longitudinal cohort study. Cancer 121 (6): 960-7, 2015. [PUBMED Abstract]
14. Shimizu Y, Miyashita M, Morita T, et al.: Care strategy for death rattle in terminally ill cancer patients and their family members: recommendations from a cross-sectional nationwide survey of bereaved family members' perceptions. J Pain Symptom Manage 48 (1): 2-12, 2014. [PUBMED Abstract]

Symptoms During the Final Months, Weeks, and Days of Life

Overview

The available evidence provides some general description of frequency of symptoms in the final months to weeks of the end of life (EOL). However, when the results of published studies of symptoms experienced by patients with advanced cancer are being interpreted or compared, the following methodological issues need to be considered:[1]

- Variation in the instrument used to assess symptoms and/or severity of symptoms.
- Variation in the timing of symptom assessment and whether the assessments were repeated over time.
- Population studied in terms of specific cancers, or a less specified population of people with cancer.
- Whether patients were recruited in the outpatient or inpatient setting.

- Whether specialized palliative care services were available.

Results of one of the larger and more comprehensive studies of symptoms in ambulatory patients with advanced cancer have been reported.[2] Ambulatory patients with advanced cancer were included in the study if they had completed at least one Edmonton Symptom Assessment System (ESAS) in the 6 months before death. The ESAS is a patient-completed measure of the severity of nine symptoms (anxiety, lack of appetite, depression, drowsiness, nausea, pain, shortness of breath, tiredness, and well-being). Analysis of the changes in the mean symptom intensity of 10,752 patients (and involving 56,759 assessments) over time revealed two patterns:[2]

- The mean scores for pain, nausea, anxiety, and depression remained relatively stable over the 6 months before death.
- Shortness of breath, drowsiness, well-being, lack of appetite, and tiredness increased in severity over time, particularly in the month before death.

In terms of symptoms closer to the EOL, a prospective study documented the symptom profile in the last week of life among 203 cancer patients who died in acute palliative care units.[3][Level of evidence: II] The proportion of patients able to communicate decreased from 80% to 39% over the last 7 days of life. ESAS anorexia, drowsiness, fatigue, poor well-being, and dyspnea increased in intensity closer to death. In contrast, ESAS depression decreased over time. Dysphagia of solids and liquids and urinary incontinence were also present in an increasing proportion of patients in the last few days of life. Less common but equally troubling symptoms that may occur in the final hours include death rattle and hemorrhage.

The following sections summarize some of the common symptoms and potential approaches to ameliorating those symptoms, based on available evidence. A final note of caution is warranted. Symptoms often cluster, and the presence of a symptom should prompt consideration of other symptoms to avoid inadvertently worsening other symptoms in the cluster. For example, a systematic review of observational studies concluded that there were four common clusters of symptoms (anxiety-depression, nausea-vomiting, nausea-appetite loss, and fatigue-dyspnea-drowsiness-pain).[4]

Delirium

Terminal delirium occurs before death in 50% to 90% of patients.[5] Most patients have hypoactive delirium, with a decreased level of consciousness. Agitation, hallucinations, and restlessness may occur in a small proportion of patients with hyperactive and/or mixed delirium. Delirium is associated with shorter survival and complicates symptom assessment, communication, and decision making. Furthermore, it can be extremely distressing to caregivers and health professionals.[6-8] Risk factors associated with terminal delirium include hypoxic encephalopathy, metabolic factors, and lack of reversible factors such as psychoactive medications and dehydration.[9] Safety measures include protecting patients from accidents or self-injury while they are restless or agitated. The use of restraints should be minimized. Reorientation strategies are of little use during the final hours of life. Education and support for families witnessing a loved one’s delirium are warranted.

There are no randomized controlled trials on the management of delirium in patients with terminal delirium.

[10] (Refer to the PDQ summary on Delirium for a complete review.) Care of the patient with delirium can include stopping unnecessary medications, reversing metabolic abnormalities (if consistent with the goals of care), treating the symptoms of delirium, and providing a safe environment. Agents known to cause delirium include corticosteroids, chemotherapeutic agents, biological response modifiers, opioids, antidepressants, benzodiazepines, and anticholinergic agents. In a small, open-label, prospective trial of 20 cancer patients who developed delirium while being treated with morphine, rotation to fentanyl reduced delirium and improved pain control in 18 patients.[11][Level of evidence: II]

Onset of effect and nonoral modes of delivery are considered when an agent is being selected to treat delirium at the EOL. Agents that can be used to manage delirium include haloperidol, 1 mg to 4 mg orally, intravenously, or subcutaneously.[12] The dose is usually repeated every 4 to 6 hours but in severe cases can be administered every hour. Chlorpromazine can be used, but intravenous administration can lead to severe hypotension; therefore, it should be used cautiously.[13] Other agents that may be effective include olanzapine, 2.5 mg to 20 mg orally at night (available in an orally disintegrating tablet for patients who cannot swallow);[14][Level of evidence: II] quetiapine;[15] and risperidone (0.5–2 mg).[16] While no randomized clinical trial demonstrates superiority of any agent over haloperidol, small (underpowered) studies suggest that olanzapine may be comparable to haloperidol. Finally, although benzodiazepines (such as lorazepam) or atypical antipsychotics typically exacerbate delirium, they may be useful in delirium related to alcohol withdrawal and for hyperactive delirium that is not controlled by antipsychotics and other supportive measures. In intractable cases of delirium, palliative sedation may be warranted.

In dying patients, a poorly understood phenomenon that appears to be distinct from delirium is the experience of auditory and/or visual hallucinations that include loved ones who have already died (also known as EOL experience). Although patients may sometimes find these hallucinations comforting, fear of being labeled confused may prevent patients from sharing their experiences with health care professionals.[17] Family members at the bedside may find these hallucinations disconcerting and will require support and reassurance. Consultation with the patient’s or family’s religious or spiritual advisor or the hospital chaplain is often beneficial.

Fatigue

Fatigue is one of the most common symptoms at the EOL and often increases in prevalence and intensity as patients approach the final days of life.[18] Fatigue at the EOL is multidimensional, and its underlying pathophysiology is poorly understood.[19] It may be associated with drowsiness, weakness, and sleep disturbance. Scores on the Palliative Performance Scale also decrease rapidly during the last 7 days of life.[20] No clinical trials have been conducted in patients with only days of life expectancy. Methylphenidate may be useful in selected patients with weeks of life expectancy.[21] (Refer to the PDQ summary on Fatigue for more information.)

Dyspnea

Dyspnea, described as shortness of breath or air hunger, is one of the most distressing symptoms for patients and often increases as patients approach the last weeks and days of life.[2,22] The prevalence of dyspnea in adults diagnosed with cancer varies from 21% to 90%, correlated with lung cancer and advanced disease.[23][Level of evidence: II] Dyspnea may predict shortened survival.

The etiology of dyspnea is usually advanced malignant disease, although other risk factors include ascites, chronic obstructive pulmonary disease, deconditioning, and pneumonia. Dyspnea occurs when more respiratory effort is necessary to overcome obstruction or restrictive disease (e.g., tumor or pleural effusions), when more respiratory muscles are required to maintain adequate breathing (e.g., neuromuscular weakness or cachexia), or when there is an increase in ventilatory need (e.g., hypercapnia or metabolic acidosis).[24] Aggressive interventions such as thoracentesis to treat potentially reversible causes may or may not be appropriate; patients' prognosis, goals of care, and logistics are first to be taken into account.

In the last days of life, many patients may be confused, making assessment of dyspnea more challenging. Objective measures such as respiratory rate, oxygen saturation, and use of accessory muscles have limited association with patients' subjective sensation of dyspnea.[23] Caregivers may be able to provide a surrogate response.[25] The Respiratory Distress Observation Scale was developed for patients who could not self-report; however, correlation with patient's expression of dyspnea was weak to moderate.[26]

The principles and practices for palliation of dyspnea in patients with days of survival are similar to those for patients with longer life expectancies. Opioids, given orally, intravenously, or subcutaneously, are considered to be the first-line option.[27] Patients with evidence of bronchoconstriction may be given bronchodilators.

Corticosteroids may be considered for patients without clear contraindications. Patients with hypoxemia would benefit from supplemental oxygen use. Patients with severe dyspnea and hypoxemic/hypercapnic respiratory failure may require bilevel positive airway pressure and/or high-flow oxygen, which represent noninvasive alternatives to intubation and mechanical ventilation.[28,29] Antibiotics may provide relief from infectious sources of dyspnea; however, the use of these agents should be consistent with a patient's goals of care. If a patient experiences bronchospasm in conjunction with dyspnea, glucocorticoids or bronchodilators can provide relief. Bronchodilators are used with caution because they can increase anxiety, leading to a worsened sense of dyspnea.

In rare situations, dyspnea may be refractory to all of the treatments described above. In such cases, palliative sedation may be indicated, using benzodiazepines, barbiturates, or neuroleptics. Indeed, refractory dyspnea is the second most common indication for palliative sedation, after agitated delirium.[30] (Refer to the Palliative Sedation section of this summary for more information.)

Pain

The prevalence of pain is between 30% and 75% in the last days of life.[18,31] The assessment of pain may be complicated by delirium. Many patients fear uncontrolled pain during the final days of life, but experience suggests that most patients can obtain pain relief and that very high doses of opioids are rarely indicated.[32] Indeed, the average intensity of pain often decreases as patients approach the final days.[2]

Some patients, family members, and health care professionals express concern that opioid use may hasten death. Several studies refute the fear of hastened death associated with opioid use. In several surveys of high-dose opioid use in hospice and palliative care settings, no relationship between opioid dose and survival was found.[32-35]

The principles of pain management remain similar to those for patients earlier in the disease trajectory, with opioids being the standard option. (Refer to the PDQ summary on Cancer Pain for a more complete review of parenteral administration of opioids and opioid rotation.) Because consciousness may diminish during this time and swallowing becomes difficult, practitioners need to anticipate alternatives to the oral route. In one study, as patients approached death, the use of intermittent subcutaneous injections and intravenous or subcutaneous infusions increased.[36] Both intravenous and subcutaneous routes are effective in delivering opioids and other agents in the inpatient or home setting. For patients who do not have a preexisting access port or catheter, intermittent or continuous subcutaneous administration provides a painless and effective route of delivery.[37]

Cough

Cough is a relatively common symptom in patients with advanced cancer near the EOL. In one small study, 33% of patients with advanced cancer who were enrolled in hospice and who completed the Memorial Symptom Assessment Scale reported cough as a troubling symptom.[38] This compares to a prevalence of lack of energy (68%), pain (63%), and dyspnea (60%). The treatment of troublesome coughing in patients in the final weeks to days of life is largely empiric, although diagnostic imaging or evaluation may occasionally be of value. In another study of patients with advanced cancer admitted to acute palliative care units, the prevalence of cough ranged from 10% to 30% in the last week of life.[3] (Refer to the PDQ summary on Cardiopulmonary Syndromes for more information about common causes of cough for which evaluation and targeted intervention may be indicated.) However, simple investigations such as reviewing medications or eliciting a history of symptoms compatible with gastroesophageal reflux disease are warranted because some drugs (e.g., angiotensin-converting enzyme inhibitors) cause cough, or a prescription for antacids may provide relief. In addition, patients may have comorbid conditions that contribute to coughing.

The cough reflex protects the lungs from noxious materials and clears excess secretions. The reflex is initiated by stimulation of peripheral cough receptors, which are transmitted to the brainstem by the vagus nerve. Activation of the central “cough center” mechanism causes a deep inspiration, followed by expiration against a closed glottis; then the glottis opens, allowing expulsion of the air.[39] The empiric approach to cough may be organized as follows:

- **Expectorants** increase bronchial fluids and reduce the viscosity of secretions, which improves the likelihood of successfully clearing the material. Guaifenesin is commonly available in over-the-counter cold or cough remedies. A reasonable dose is 200 to 400 mg every 4 to 6 hours.
- **Antimuscarinics** decrease oral secretions, which may initiate a cough reflex if the patient cannot swallow adequately (refer to the Death Rattle section of this summary for more information).
- **Centrally acting antitussives** suppress the putative cough center in the brain stem. All opioids have antitussive properties. Dextromethorphan is available in over-the-counter cough suppressants. Codeine is commonly prescribed initially; if it is not effective, then patients receive a more potent opioid such as morphine. However, evidence suggests that morphine [40] or hydrocodone [41] is preferable.

As discussed in the Dyspnea section of this summary, the use of bronchodilators, corticosteroids, or inhaled steroids is limited to specific indications, given the potential risks and the lack of evidence of benefit outside of specific indications.

Constipation

The prevalence of constipation ranges from 30% to 50% in the last days of life.[3,31] The use of laxatives for patients who are imminently dying may provide limited benefit. Such patients often have dysphagia and very poor oral intake. Treatment of constipation in patients with only days of expected survival is guided by symptoms. If indicated, laxatives may be given rectally (e.g., bisacodyl or enemas).

Dysphagia

Functional dysphagia and structural dysphagia occur in a large proportion of cancer patients in the last days of life. Specifically, patients often experience difficulty swallowing both liquids and solids, which is often associated with anorexia and cachexia. In one study of cancer patients, the oral route of opioid administration was continued in 62% of patients at 4 weeks before death, in 43% at 1 week before death, and in 20% at 24 hours before death.[36] The clinical implication is that essential medications may need to be administered through other routes, such as intravenous, subcutaneous, rectal, and transdermal. Nonessential medications are discontinued.

Supplemental nutrition is of no known benefit and may increase the risk of aspiration and infections. Instead of tube-feeding or ordering nothing by mouth, providing a small amount of food for enjoyment may be reasonable if a patient expresses a desire to eat.

Death Rattle

Death rattle, also referred to as excessive secretions, occurs when saliva and other fluids accumulate in the oropharynx and upper airways in a patient who is too weak to clear the throat. Rattle does not appear to be distressing for the patient; however, family members may perceive death rattle as indicating the presence of untreated dyspnea. Thus, the family will benefit from learning about the nature of this symptom and that death rattle is not associated with dyspnea.

Rattle is an indicator of impending death, with an incidence of approximately 50% to 60% in the last days of life and a median onset of 16 to 57 hours before death.[20,42,43] Two types of rattle have been identified:[44,45]

- Real death rattle, or type 1, which is probably caused by salivary secretions.
- Pseudo death rattle, or type 2, which is probably caused by deeper bronchial secretions due to infection, tumor, fluid retention, or aspiration.

In one retrospective chart review, rattle was relieved in more than 90% of patients with salivary secretions, while patients with secretions of pulmonary origin were much less likely to respond to treatment.[45]

The results of clinical trials examining various pharmacologic agents for the treatment of death rattle have so far been negative.[46] A small, double-blind, randomized, controlled trial that compared scopolamine to normal saline found no statistical significance.[47] Another randomized study revealed no difference between atropine and placebo.[48] Results of other randomized controlled studies that examined octreotide,[49] glycopyrrolate,[50] and hyoscine butylbromide [51] versus scopolamine were also negative.

Despite the lack of clear evidence, pharmacologic therapies are used frequently in clinical practice.[52,53] Among the options described above, glycopyrrolate may be preferred because it is less likely to penetrate the central nervous system, and fewer adverse effects are reported with glycopyrrolate than with other antimuscarinic agents, which could worsen delirium. Glycopyrrolate is available parenterally and in oral tablet form. Doses typically range from 1 mg to 2 mg orally or 0.1 mg to 0.2 mg intravenously or subcutaneously every 4 hours, or by continuous intravenous infusion at a rate of 0.4 mg to 1.2 mg per day. Repositioning may be helpful. Suctioning of excessive secretions may be considered for some patients.

Myoclonus

Health care professionals need to monitor patients for opioid-induced neurotoxicity, which could cause myoclonus, hallucinations, and confusion and may mimic terminal delirium. When opioid-induced neurotoxicity is suspected, opioid rotation may be considered.[11] Nonsteroidal anti-inflammatory drugs are often contraindicated in these patients because of the risk of bleeding and renal failure.

Myoclonus is defined as sudden and involuntary movements caused by focal or generalized muscle contractions. The duration of contractions is brief and may be described as shocklike. There are many potential causes of myoclonus, most of which probably stem from the metabolic derangements anticipated as life ends. Medications are an important etiology, especially because many medications may be discontinued. Opioids are probably the most common medication-related cause of myoclonus. The reported prevalence of opioid-induced myoclonus ranges greatly, from 2.7% to 87%.[54]

When opioids are implicated in the development of myoclonus, rotation to a different opioid is the primary treatment. In patients with rapidly impending death, the health care provider may choose to treat the myoclonus rather than make changes in opioids during the final hours. Benzodiazepines, including clonazepam, diazepam, and midazolam, have been recommended.[54-56] The anticonvulsant gabapentin has been reported to be effective in relieving opioid-induced myoclonus,[57] although other reports implicate gabapentin as a cause of myoclonus.[58,59][Level of evidence: III] In one small randomized study, hydration was found to reduce myoclonus.[60][Level of evidence: I]

Fever

There are no reliable data on the frequency of fever. A prospective study of 232 adults with terminal cancer admitted to a hospice and palliative care unit in Taiwan indicated that fever was uncommon and of moderate severity (mean score, 0.37 on a scale of 1–3).[61] There was no increase in fever in the 2 days immediately preceding death. In addition to considering diagnostic evaluation and therapeutic intervention, the clinician needs to carefully assess whether the patient is distressed or negatively affected by the fever.

There are no data showing that fever materially affects the quality of the experience of the dying person. While infection may cause a fever, other etiologies such as medications or the underlying cancer are to be strongly considered. While the main objective in the decision to use antimicrobials is to treat clinically suspected infections in patients who are receiving palliative or hospice care,[62-64][Level of evidence: II] subsequent information suggests that the risks of using empiric antibiotics do not appear justified by the possible benefits for people near death.[65]

Catastrophic Hemorrhage

Hemorrhage is an uncommon (6%–14%) yet extremely distressing event, especially when it is sudden and catastrophic.[66] Patients with bone marrow failure or liver failure are susceptible to bleeding caused by lack of adequate platelets or coagulation factors; patients with advanced cancer, especially head and neck cancers, experience bleeding caused by fungating wounds or damage to vascular structures from tumor growth, surgery, or radiation. Patients may also experience gastrointestinal bleeding from ulcers, progressive tumor growth, or chemotherapy-induced mucositis.

The management of catastrophic bleeding may include identification of patients who are at risk for catastrophic bleeding and careful communication about risk and potential management strategies. However, two qualitative interview studies of clinicians whose patients experienced catastrophic bleeding at the EOL suggest that it is often impossible to anticipate bleeding and that a proactive approach may cause patients and families undue distress.[67,68] Furthermore, the lack of evidence that catastrophic bleeding can be prevented with medical interventions such as transfusions needs to be taken into account in discussions with patients about the risks of bleeding.

Another strategy is to prepare to administer anxiolytics or sedatives to patients who experience catastrophic bleeding, between the start of the bleeding and death. However, there is little evidence supporting the effectiveness of this approach;[66,68] the experience of clinicians is often that patients become unconscious before the drugs can be administered, and the focus on medications may distract from providing patients and families with reassurance that suffering is unlikely. Nevertheless, the availability of benzodiazepines for rapid sedation of patients who experience catastrophic bleeding may provide some reassurance for family caregivers.

After the death of a patient from a catastrophic hemorrhage, team members are encouraged to verbalize their emotions regarding the experience, and their questions need to be answered.

References

1. Moens K, Higginson IJ, Harding R, et al.: Are there differences in the prevalence of palliative care-related problems in people living with advanced cancer and eight non-cancer conditions? A systematic review. J Pain Symptom Manage 48 (4): 660-77, 2014. [PUBMED Abstract]
2. Seow H, Barbera L, Sutradhar R, et al.: Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. J Clin Oncol 29 (9): 1151-8, 2011. [PUBMED Abstract]
3. Hui D, dos Santos R, Chisholm GB, et al.: Symptom Expression in the Last Seven Days of Life Among Cancer Patients Admitted to Acute Palliative Care Units. J Pain Symptom Manage 50 (4): 488-94, 2015. [PUBMED Abstract]
4. Dong ST, Butow PN, Costa DS, et al.: Symptom clusters in patients with advanced cancer: a systematic review of observational studies. J Pain Symptom Manage 48 (3): 411-50, 2014. [PUBMED Abstract]
5. Solano JP, Gomes B, Higginson IJ: A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 31 (1): 58-69, 2006. [PUBMED Abstract]

6. Morita T, Tsunoda J, Inoue S, et al.: Communication Capacity Scale and Agitation Distress Scale to measure the severity of delirium in terminally ill cancer patients: a validation study. Palliat Med 15 (3): 197-206, 2001. [PUBMED Abstract]
7. Breitbart W, Gibson C, Tremblay A: The delirium experience: delirium recall and delirium-related distress in hospitalized patients with cancer, their spouses/caregivers, and their nurses. Psychosomatics 43 (3): 183-94, 2002 May-Jun. [PUBMED Abstract]
8. Bruera E, Bush SH, Willey J, et al.: Impact of delirium and recall on the level of distress in patients with advanced cancer and their family caregivers. Cancer 115 (9): 2004-12, 2009. [PUBMED Abstract]
9. Lawlor PG, Gagnon B, Mancini IL, et al.: Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. Arch Intern Med 160 (6): 786-94, 2000. [PUBMED Abstract]
10. Candy B, Jackson KC, Jones L, et al.: Drug therapy for delirium in terminally ill adult patients. Cochrane Database Syst Rev 11: CD004770, 2012. [PUBMED Abstract]
11. Morita T, Takigawa C, Onishi H, et al.: Opioid rotation from morphine to fentanyl in delirious cancer patients: an open-label trial. J Pain Symptom Manage 30 (1): 96-103, 2005. [PUBMED Abstract]
12. Centeno C, Sanz A, Bruera E: Delirium in advanced cancer patients. Palliat Med 18 (3): 184-94, 2004. [PUBMED Abstract]
13. Cowan JD, Palmer TW: Practical guide to palliative sedation. Curr Oncol Rep 4 (3): 242-9, 2002. [PUBMED Abstract]
14. Breitbart W, Tremblay A, Gibson C: An open trial of olanzapine for the treatment of delirium in hospitalized cancer patients. Psychosomatics 43 (3): 175-82, 2002 May-Jun. [PUBMED Abstract]
15. Skrobik YK, Bergeron N, Dumont M, et al.: Olanzapine vs haloperidol: treating delirium in a critical care setting. Intensive Care Med 30 (3): 444-9, 2004. [PUBMED Abstract]
16. Han CS, Kim YK: A double-blind trial of risperidone and haloperidol for the treatment of delirium. Psychosomatics 45 (4): 297-301, 2004 Jul-Aug. [PUBMED Abstract]
17. Callanan M, Kelley P: Final Gifts: Understanding the Special Awareness, Needs, and Communications of the Dying. New York, NY: Poseidon Press, 1992.
18. Toscani F, Di Giulio P, Brunelli C, et al.: How people die in hospital general wards: a descriptive study. J Pain Symptom Manage 30 (1): 33-40, 2005. [PUBMED Abstract]
19. Yennurajalingam S, Bruera E: Palliative management of fatigue at the close of life: "it feels like my body is just worn out". JAMA 297 (3): 295-304, 2007. [PUBMED Abstract]
20. Hui D, dos Santos R, Chisholm G, et al.: Clinical signs of impending death in cancer patients. Oncologist 19 (6): 681-7, 2014. [PUBMED Abstract]
21. Minton O, Richardson A, Sharpe M, et al.: Drug therapy for the management of cancer-related fatigue. Cochrane Database Syst Rev 7: CD006704, 2010. [PUBMED Abstract]
22. Tishelman C, Petersson LM, Degner LF, et al.: Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death. J Clin Oncol 25 (34): 5381-9, 2007. [PUBMED Abstract]
23. Bruera E, Schmitz B, Pither J, et al.: The frequency and correlates of dyspnea in patients with advanced

cancer. J Pain Symptom Manage 19 (5): 357-62, 2000. [PUBMED Abstract]

24. Ripamonti C: Management of dyspnea in advanced cancer patients. Support Care Cancer 7 (4): 233-43, 1999. [PUBMED Abstract]
25. Hui D, Morgado M, Vidal M, et al.: Dyspnea in hospitalized advanced cancer patients: subjective and physiologic correlates. J Palliat Med 16 (3): 274-80, 2013. [PUBMED Abstract]
26. Campbell ML: Psychometric testing of a respiratory distress observation scale. J Palliat Med 11 (1): 44-50, 2008 Jan-Feb. [PUBMED Abstract]
27. Ben-Aharon I, Gafter-Gvili A, Paul M, et al.: Interventions for alleviating cancer-related dyspnea: a systematic review. J Clin Oncol 26 (14): 2396-404, 2008. [PUBMED Abstract]
28. Hui D, Morgado M, Chisholm G, et al.: High-flow oxygen and bilevel positive airway pressure for persistent dyspnea in patients with advanced cancer: a phase II randomized trial. J Pain Symptom Manage 46 (4): 463-73, 2013. [PUBMED Abstract]
29. Nava S, Ferrer M, Esquinas A, et al.: Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. Lancet Oncol 14 (3): 219-27, 2013. [PUBMED Abstract]
30. Maltoni M, Scarpi E, Rosati M, et al.: Palliative sedation in end-of-life care and survival: a systematic review. J Clin Oncol 30 (12): 1378-83, 2012. [PUBMED Abstract]
31. Conill C, Verger E, Henríquez I, et al.: Symptom prevalence in the last week of life. J Pain Symptom Manage 14 (6): 328-31, 1997. [PUBMED Abstract]
32. Thorns A, Sykes N: Opioid use in last week of life and implications for end-of-life decision-making. Lancet 356 (9227): 398-9, 2000. [PUBMED Abstract]
33. Bercovitch M, Waller A, Adunsky A: High dose morphine use in the hospice setting. A database survey of patient characteristics and effect on life expectancy. Cancer 86 (5): 871-7, 1999. [PUBMED Abstract]
34. Sykes N, Thorns A: The use of opioids and sedatives at the end of life. Lancet Oncol 4 (5): 312-8, 2003. [PUBMED Abstract]
35. Bercovitch M, Adunsky A: Patterns of high-dose morphine use in a home-care hospice service: should we be afraid of it? Cancer 101 (6): 1473-7, 2004. [PUBMED Abstract]
36. Coyle N, Adelhardt J, Foley KM, et al.: Character of terminal illness in the advanced cancer patient: pain and other symptoms during the last four weeks of life. J Pain Symptom Manage 5 (2): 83-93, 1990. [PUBMED Abstract]
37. Anderson SL, Shreve ST: Continuous subcutaneous infusion of opiates at end-of-life. Ann Pharmacother 38 (6): 1015-23, 2004. [PUBMED Abstract]
38. Schonwetter RS, Roscoe LA, Nwosu M, et al.: Quality of life and symptom control in hospice patients with cancer receiving chemotherapy. J Palliat Med 9 (3): 638-45, 2006. [PUBMED Abstract]
39. Homsi J, Walsh D, Nelson KA: Important drugs for cough in advanced cancer. Support Care Cancer 9 (8): 565-74, 2001. [PUBMED Abstract]
40. Wee B, Browning J, Adams A, et al.: Management of chronic cough in patients receiving palliative care: review of evidence and recommendations by a task group of the Association for Palliative Medicine of Great Britain and Ireland. Palliat Med 26 (6): 780-7, 2012. [PUBMED Abstract]

41. Homsi J, Walsh D, Nelson KA, et al.: A phase II study of hydrocodone for cough in advanced cancer. Am J Hosp Palliat Care 19 (1): 49-56, 2002 Jan-Feb. [PUBMED Abstract]
42. Morita T, Ichiki T, Tsunoda J, et al.: A prospective study on the dying process in terminally ill cancer patients. Am J Hosp Palliat Care 15 (4): 217-22, 1998 Jul-Aug. [PUBMED Abstract]
43. Kåss RM, Ellershaw J: Respiratory tract secretions in the dying patient: a retrospective study. J Pain Symptom Manage 26 (4): 897-902, 2003. [PUBMED Abstract]
44. Bennett MI: Death rattle: an audit of hyoscine (scopolamine) use and review of management. J Pain Symptom Manage 12 (4): 229-33, 1996. [PUBMED Abstract]
45. Wildiers H, Menten J: Death rattle: prevalence, prevention and treatment. J Pain Symptom Manage 23 (4): 310-7, 2002. [PUBMED Abstract]
46. Lokker ME, van Zuylen L, van der Rijt CC, et al.: Prevalence, impact, and treatment of death rattle: a systematic review. J Pain Symptom Manage 47 (1): 105-22, 2014. [PUBMED Abstract]
47. Likar R, Molnar M, Rupacher E, et al.: A clinical study examining the efficacy of scopolamin-hydrobromide in patients with death rattle (a randomized, double-blind, placebo-controlled study). Z Palliativmed 3 (1): 15-9, 2002.
48. Heisler M, Hamilton G, Abbott A, et al.: Randomized double-blind trial of sublingual atropine vs. placebo for the management of death rattle. J Pain Symptom Manage 45 (1): 14-22, 2013. [PUBMED Abstract]
49. Clark K, Currow DC, Agar M, et al.: A pilot phase II randomized, cross-over, double-blinded, controlled efficacy study of octreotide versus hyoscine hydrobromide for control of noisy breathing at the end-of-life. J Pain Palliat Care Pharmacother 22 (2): 131-8, 2008. [PUBMED Abstract]
50. Likar R, Rupacher E, Kager H, et al.: [Efficacy of glycopyrronium bromide and scopolamine hydrobromide in patients with death rattle: a randomized controlled study]. Wien Klin Wochenschr 120 (21-22): 679-83, 2008. [PUBMED Abstract]
51. Wildiers H, Dhaenekint C, Demeulenaere P, et al.: Atropine, hyoscine butylbromide, or scopolamine are equally effective for the treatment of death rattle in terminal care. J Pain Symptom Manage 38 (1): 124-33, 2009. [PUBMED Abstract]
52. Wee B, Hillier R: Interventions for noisy breathing in patients near to death. Cochrane Database Syst Rev (1): CD005177, 2008. [PUBMED Abstract]
53. Bennett M, Lucas V, Brennan M, et al.: Using anti-muscarinic drugs in the management of death rattle: evidence-based guidelines for palliative care. Palliat Med 16 (5): 369-74, 2002. [PUBMED Abstract]
54. Mercadante S: Pathophysiology and treatment of opioid-related myoclonus in cancer patients. Pain 74 (1): 5-9, 1998. [PUBMED Abstract]
55. Eisele JH Jr, Grigsby EJ, Dea G: Clonazepam treatment of myoclonic contractions associated with high-dose opioids: case report. Pain 49 (2): 231-2, 1992. [PUBMED Abstract]
56. Cherny N, Ripamonti C, Pereira J, et al.: Strategies to manage the adverse effects of oral morphine: an evidence-based report. J Clin Oncol 19 (9): 2542-54, 2001. [PUBMED Abstract]
57. Mercadante S, Villari P, Fulfaro F: Gabapentin for opiod-related myoclonus in cancer patients. Support Care Cancer 9 (3): 205-6, 2001. [PUBMED Abstract]

58. Scullin P, Sheahan P, Sheila K: Myoclonic jerks associated with gabapentin. Palliat Med 17 (8): 717-8, 2003. [PUBMED Abstract]
59. Zhang C, Glenn DG, Bell WL, et al.: Gabapentin-induced myoclonus in end-stage renal disease. Epilepsia 46 (1): 156-8, 2005. [PUBMED Abstract]
60. Bruera E, Sala R, Rico MA, et al.: Effects of parenteral hydration in terminally ill cancer patients: a preliminary study. J Clin Oncol 23 (10): 2366-71, 2005. [PUBMED Abstract]
61. Chiu TY, Hu WY, Chen CY: Prevalence and severity of symptoms in terminal cancer patients: a study in Taiwan. Support Care Cancer 8 (4): 311-3, 2000. [PUBMED Abstract]
62. White PH, Kuhlenschmidt HL, Vancura BG, et al.: Antimicrobial use in patients with advanced cancer receiving hospice care. J Pain Symptom Manage 25 (5): 438-43, 2003. [PUBMED Abstract]
63. Clayton J, Fardell B, Hutton-Potts J, et al.: Parenteral antibiotics in a palliative care unit: prospective analysis of current practice. Palliat Med 17 (1): 44-8, 2003. [PUBMED Abstract]
64. Reinbolt RE, Shenk AM, White PH, et al.: Symptomatic treatment of infections in patients with advanced cancer receiving hospice care. J Pain Symptom Manage 30 (2): 175-82, 2005. [PUBMED Abstract]
65. Nakagawa S, Toya Y, Okamoto Y, et al.: Can anti-infective drugs improve the infection-related symptoms of patients with cancer during the terminal stages of their lives? J Palliat Med 13 (5): 535-40, 2010. [PUBMED Abstract]
66. Harris DG, Noble SI: Management of terminal hemorrhage in patients with advanced cancer: a systematic literature review. J Pain Symptom Manage 38 (6): 913-27, 2009. [PUBMED Abstract]
67. McGrath P, Leahy M: Catastrophic bleeds during end-of-life care in haematology: controversies from Australian research. Support Care Cancer 17 (5): 527-37, 2009. [PUBMED Abstract]
68. Harris DG, Finlay IG, Flowers S, et al.: The use of crisis medication in the management of terminal haemorrhage due to incurable cancer: a qualitative study. Palliat Med 25 (7): 691-700, 2011. [PUBMED Abstract]

Care Decisions in the Final Weeks, Days, and Hours of Life

The Decision to Discontinue Chemotherapy

A significant proportion (approximately 30%) of patients with advanced cancer continue to receive chemotherapy toward the end of life (EOL), including a small number (2%–5%) who receive their last dose of chemotherapy within 14 days of death.[1-3] Chemotherapy administered until the EOL is associated with significant adverse effects, resulting in prolonged hospitalization or increased likelihood of dying in an intensive care unit.[4,5] Thus, the lack of definite or meaningful improvement in survival leads many clinicians to advise patients to discontinue chemotherapy on the basis of an increasingly unfavorable ratio of benefit to risk.

Ultimately, the decision to initiate, continue, or forgo chemotherapy is made collaboratively and is consistent with the expected risks and benefits of treatment within the context of the patient's goals of care. However, the following reasons independent of the risks and benefits may lead a patient to prefer chemotherapy and are potentially worth exploring:

- Patients with cancer express a willingness to endure more complications of treatment for less benefit than do people without cancer.[6]
- Patients report that receiving chemotherapy facilitates living in the present, perhaps by shifting their attention away from their approaching death. However, patients want their health care providers to inquire about them personally and ask how they are doing.[7]
- Patients and physicians may mutually avoid discussions of options other than chemotherapy because it feels contradictory to the focus on providing treatment.[8]

The Decision to Enroll in Hospice

Patients with advanced cancer who receive hospice care appear to experience better psychological adjustment, fewer burdensome symptoms, increased satisfaction, improved communication, and better deaths without hastening death.[9-12] The rate of hospice enrollment for people with cancer has increased in recent years; however, this increase is tempered by a reduction in the average length of hospice stay. Because of the association of longer hospice stays with caregivers' perceptions of improved quality of care and increased satisfaction with care, the latter finding is especially concerning.[13,14]

Multiple patient demographic factors (e.g., younger age, married status, female gender, white race, greater affluence, and geographic region) are associated with increased hospice enrollment. In one study, however, physician characteristics were more important than patient characteristics in determining hospice enrollment.[15] This may reflect the observation that patients concede more control to oncologists over time, especially if treatment decisions involve noncurative chemotherapy for metastatic cancer.[16]

There are many potential barriers to timely hospice enrollment. Barriers are summarized in the following paragraphs on the basis of whether they arise predominantly from the perspective of the patient, caregiver, physician, or hospice, including eligibility criteria for enrollment. The purpose of this section is to provide the oncology clinician with insights into the decision to enroll in hospice, and to encourage a full discussion of hospice as an important EOL option for patients with advanced cancer. The related study [17] provides potential strategies to address some of the patient-level barriers.

Patient-level barriers: Patients often express a sense that it would be premature to enroll in hospice, that enrolling in hospice means giving up, or that enrolling in hospice would disrupt their relationship with their oncologist.[17] The difficulty in recognizing when to enroll in hospice may explain the observations that the trend in increasing hospice utilization has not led to a reduction in intensive treatment, including admission to intensive care units at the EOL.[18,19]

Patients may agree to enroll in hospice in the final days of life only after aggressive medical treatments have clearly failed. Given the likely benefit of longer times in hospice care, patient-level predictors of short hospice stays may be particularly relevant. One group of investigators conducted a retrospective cohort study of 64,264 adults with cancer admitted to hospice.[20] Sixteen percent stayed 3 days or fewer, with a range of 11.4% to 24.5% among the 12 participating hospices. The following factors (and odds ratios [ORs]) were independently associated with short hospice stays in multivariable analysis:

- Male sex (OR, 1.22).
- Married status (OR, 1.23).
- Age 65 years or older (OR, 0.90).
- Nonwhite ethnicity (OR, 0.89).
- Hematologic malignancy (OR, 1.52).
- Nursing home residence (OR,1.52).
- Medicaid insurance (OR, 0.83).

Caregiver-level barriers: In a survey of 53 caregivers of patients who died of lung cancer while in hospice, only 35% of caregivers felt that patients should have received hospice care sooner. The highest rates of agreement with potential reasons for deferring hospice enrollment were for the following three survey items:[21]

- Continued anticancer treatments (63%).
- A decline in health that was too rapid to allow earlier use of hospice (55%).
- Unfamiliarity with hospice services before enrollment (42%).

Only 22% of caregivers agreed that the family member delayed enrollment because enrolling in hospice meant giving up hope.

Physician-level barriers: In a survey of 273 physicians, 65% agreed that a barrier to hospice enrollment was the patient preference for simultaneous anticancer treatment and hospice care. Almost half of physicians believed (incorrectly) that patients must have do-not-resuscitate and do-not-intubate orders in place to qualify for hospice.[21] The lack of timely discussions with oncologists or other physicians about hospice care and its benefits remains a potentially remediable barrier to the timing of referral to hospice.[22-24]

Hospice-level barriers: The Medicare hospice benefit requires that physicians certify patients' life expectancies shorter than 6 months and that patients forgo curative treatments. Patients who are enrolled in hospice receive all care related to their terminal illnesses through hospice, although most hospice reimbursement comes through a fixed per diem. Thus, hospices may have additional enrollment criteria.

One group of investigators conducted a national survey of 591 hospices that revealed 78% of hospices had at least one policy that could restrict enrollment.[25] Sixty-one percent of patients could not be receiving chemotherapy, 55% could not be receiving total parenteral nutrition, and 40% could not be receiving transfusions. Only 8% restricted enrollment of patients receiving tube feedings. The percentage of hospices without restrictive enrollment practices varied by geographic region, from a low of 14% in the East/West South Central region to a high of 33% in the South Atlantic region.

A further challenge related to hospice enrollment is that the willingness to forgo chemotherapy does not identify patients who have a high perceived need for hospice care. Investigators conducted conjoint interviews of 300 patients with cancer and 171 family caregivers to determine the perceived need for five core hospice services (visiting nurse, chaplain, counselor, home health aide, and respite care).[26] Patients willing to forgo chemotherapy did not have different levels of perceived needs. In a multivariable model, the following patient factors predicted a greater perceived need for hospice services:

- African American ethnicity.
- Less social support.
- Worse functional status.
- More psychological symptoms.

The following family factors predicted a greater perceived need for hospice services:

- Worse caregiver self-reported health.
- Caregiver working outside the home.
- Worse patient functional status.

Choosing the Desired Place of Death

Many patients with advanced-stage cancer express a desire to die at home,[27] but many will die in a hospital or other facility. Patients who die at home, however, appear to have a better quality of life than do patients who die in a hospital or intensive care unit, and their bereaved caregivers experience less difficulty adjusting.[12] Dying at home is also associated with better symptom control and preparedness for death and with caregivers' perceptions of a higher-quality death.[28]

Enrollment in hospice increases the likelihood of dying at home, but careful attention needs to be paid to caregiver support and symptom control. One group of investigators analyzed a cohort of 5,837 hospice patients with terminal cancer for whom the patient's preference for dying at home was determined.[29] Of the 5,837 patients, 4,336 (79%) preferred to die at home. Patients who preferred to die at home were more likely to do so (56% vs. 37%; OR, 2.21). In multivariable analysis, the following factors (with percentages and ORs) were correlated with a greater likelihood of dying at home:

- At least one hospice visit per day in the first 4 days (61% vs. 54%; OR, 1.23).
- Married status (63% vs. 54%; OR, 1.35).
- Advance directive available (65% vs. 50%; OR, 2.11).

Conversely, patients were less likely to die at home (OR, <1) if there was:

- Moderate or severe pain (43% vs. 69%; OR, 0.56).
- Higher functional status as measured by the Palliative Performance Scale (OR, 0.53).

However, not all patients prefer to die at home, e.g., patients who are unmarried, nonwhite, and older.[29] Thus, the oncology clinician strives to facilitate a discussion about preferred place of death and a plan to overcome potential barriers to dying at the patient's preferred site.

References

1. Earle CC, Neville BA, Landrum MB, et al.: Trends in the aggressiveness of cancer care near the end of life. J Clin Oncol 22 (2): 315-21, 2004. [PUBMED Abstract]
2. Setoguchi S, Earle CC, Glynn R, et al.: Comparison of prospective and retrospective indicators of the quality of end-of-life cancer care. J Clin Oncol 26 (35): 5671-8, 2008. [PUBMED Abstract]
3. Ho TH, Barbera L, Saskin R, et al.: Trends in the aggressiveness of end-of-life cancer care in the universal health care system of Ontario, Canada. J Clin Oncol 29 (12): 1587-91, 2011. [PUBMED Abstract]
4. Wright AA, Zhang B, Ray A, et al.: Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. JAMA 300 (14): 1665-73, 2008. [PUBMED Abstract]
5. Wright AA, Zhang B, Keating NL, et al.: Associations between palliative chemotherapy and adult cancer patients' end of life care and place of death: prospective cohort study. BMJ 348: g1219, 2014. [PUBMED Abstract]
6. Donovan KA, Greene PG, Shuster JL, et al.: Treatment preferences in recurrent ovarian cancer. Gynecol Oncol 86 (2): 200-11, 2002. [PUBMED Abstract]
7. Buiting HM, Terpstra W, Dalhuisen F, et al.: The facilitating role of chemotherapy in the palliative phase of cancer: qualitative interviews with advanced cancer patients. PLoS One 8 (11): e77959, 2013. [PUBMED Abstract]
8. Buiting HM, Rurup ML, Wijsbek H, et al.: Understanding provision of chemotherapy to patients with end stage cancer: qualitative interview study. BMJ 342: d1933, 2011. [PUBMED Abstract]
9. Addington-Hall JM, O'Callaghan AC: A comparison of the quality of care provided to cancer patients in the UK in the last three months of life in in-patient hospices compared with hospitals, from the perspective of bereaved relatives: results from a survey using the VOICES questionnaire. Palliat Med 23 (3): 190-7, 2009. [PUBMED Abstract]
10. Wallston KA, Burger C, Smith RA, et al.: Comparing the quality of death for hospice and non-hospice cancer patients. Med Care 26 (2): 177-82, 1988. [PUBMED Abstract]
11. Connor SR, Pyenson B, Fitch K, et al.: Comparing hospice and nonhospice patient survival among patients who die within a three-year window. J Pain Symptom Manage 33 (3): 238-46, 2007. [PUBMED Abstract]
12. Wright AA, Keating NL, Balboni TA, et al.: Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. J Clin Oncol 28 (29): 4457-64, 2010. [PUBMED Abstract]
13. Teno JM, Shu JE, Casarett D, et al.: Timing of referral to hospice and quality of care: length of stay and bereaved family members' perceptions of the timing of hospice referral. J Pain Symptom Manage 34 (2): 120-5, 2007. [PUBMED Abstract]
14. Finlay E, Shreve S, Casarett D: Nationwide veterans affairs quality measure for cancer: the family assessment of treatment at end of life. J Clin Oncol 26 (23): 3838-44, 2008. [PUBMED Abstract]
15. Keating NL, Herrinton LJ, Zaslavsky AM, et al.: Variations in hospice use among cancer patients. J Natl

Cancer Inst 98 (15): 1053-9, 2006. [PUBMED Abstract]

16. Keating NL, Beth Landrum M, Arora NK, et al.: Cancer patients' roles in treatment decisions: do characteristics of the decision influence roles? J Clin Oncol 28 (28): 4364-70, 2010. [PUBMED Abstract]
17. Vig EK, Starks H, Taylor JS, et al.: Why don't patients enroll in hospice? Can we do anything about it? J Gen Intern Med 25 (10): 1009-19, 2010. [PUBMED Abstract]
18. Bergman J, Saigal CS, Lorenz KA, et al.: Hospice use and high-intensity care in men dying of prostate cancer. Arch Intern Med 171 (3): 204-10, 2011. [PUBMED Abstract]
19. Wright AA, Hatfield LA, Earle CC, et al.: End-of-life care for older patients with ovarian cancer is intensive despite high rates of hospice use. J Clin Oncol 32 (31): 3534-9, 2014. [PUBMED Abstract]
20. O'Connor NR, Hu R, Harris PS, et al.: Hospice admissions for cancer in the final days of life: independent predictors and implications for quality measures. J Clin Oncol 32 (28): 3184-9, 2014. [PUBMED Abstract]
21. Ford DW, Nietert PJ, Zapka J, et al.: Barriers to hospice enrollment among lung cancer patients: a survey of family members and physicians. Palliat Support Care 6 (4): 357-62, 2008. [PUBMED Abstract]
22. Mack JW, Cronin A, Keating NL, et al.: Associations between end-of-life discussion characteristics and care received near death: a prospective cohort study. J Clin Oncol 30 (35): 4387-95, 2012. [PUBMED Abstract]
23. Keating NL, Landrum MB, Rogers SO Jr, et al.: Physician factors associated with discussions about end-of-life care. Cancer 116 (4): 998-1006, 2010. [PUBMED Abstract]
24. Huskamp HA, Keating NL, Malin JL, et al.: Discussions with physicians about hospice among patients with metastatic lung cancer. Arch Intern Med 169 (10): 954-62, 2009. [PUBMED Abstract]
25. Aldridge Carlson MD, Barry CL, Cherlin EJ, et al.: Hospices' enrollment policies may contribute to underuse of hospice care in the United States. Health Aff (Millwood) 31 (12): 2690-8, 2012. [PUBMED Abstract]
26. Casarett DJ, Fishman JM, Lu HL, et al.: The terrible choice: re-evaluating hospice eligibility criteria for cancer. J Clin Oncol 27 (6): 953-9, 2009. [PUBMED Abstract]
27. Steinhauser KE, Christakis NA, Clipp EC, et al.: Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA 284 (19): 2476-82, 2000. [PUBMED Abstract]
28. Hales S, Chiu A, Husain A, et al.: The quality of dying and death in cancer and its relationship to palliative care and place of death. J Pain Symptom Manage 48 (5): 839-51, 2014. [PUBMED Abstract]
29. Jeurkar N, Farrington S, Craig TR, et al.: Which hospice patients with cancer are able to die in the setting of their choice? Results of a retrospective cohort study. J Clin Oncol 30 (22): 2783-7, 2012. [PUBMED Abstract]

Forgoing Potentially Life-Sustaining Treatments

A necessary goal of high-quality end-of-life (EOL) care is the alleviation of distressing symptoms that can lead to suffering. An important strategy to achieve that goal is to avoid or reduce medical interventions of limited effectiveness and high burden to the patients. There is, however, a great deal of confusion, anxiety, and miscommunication around the question of whether to utilize potentially life-sustaining treatments (LSTs) such as mechanical ventilation, total parenteral nutrition, and dialysis in the final weeks or days of life. To ensure that the best interests of the patient—as communicated by the patient, family, or surrogate decision maker—determine the decisions about LSTs, discussions can be organized around the following questions:

- What are the patient's goals of care?
- How do the potential benefits of LST contribute to achieving the goals of care, and how likely is the desired outcome?
- How do the potential harms of LST detract from the patient's goals of care, and does the likelihood of achieving the desired outcome or the value the patient assigns to the outcome justify the risk of harm?
- What considerations—other than the potential benefits and harms of LST—are relevant to the patient or surrogate decision maker?
- What other resources—e.g., chaplain or clinical ethicist—would help the patient or family with decisions about LST?

Ethical Perspectives

Medicine is a moral enterprise. The decisions clinicians make are often highly subjective and value laden but seem less so because, equally often, there is a shared sense of benefit, harm, and what is most highly valued. Occasionally, disagreements arise or a provider is uncertain about what is ethically permissible. For example, an oncologist may favor the discontinuation or avoidance of LST, given the lack of evidence of benefit or the possibility of harm—including increasing the suffering of the dying person by prolonging the dying process—or based on concerns that LST interferes with the patient accepting that life is ending and finding peace in the final days. A provider also may be uncertain about whether withdrawing treatment is equivalent to causing the patient's death. Conversely, the patient may continue to request LST on the basis of personal beliefs and a preference for potential prolonged life, independent of the oncologist's clinical risk-benefit analysis.

Individual values inform the moral landscape of the practice of medicine. The potential conflicts described above are opportunities to refine clinicians' understanding of their beliefs and values and to communicate their moral reasoning to each other as a sign of integrity and respect.[1] As clinicians struggle to communicate their reasons for recommendations or actions, the following three questions may serve as a framework:[2]

- Who makes the decision?
- By what criteria do they make the decision?
- How are conflicts among decision makers resolved?

In the event of conflict, an ethics consult may be necessary to identify the sources of disagreement and potential solutions, although frameworks have been proposed to guide the clinician.[3] The following paragraphs summarize information relevant to the first two questions.

Respect for patient autonomy is an essential element of the relationship between oncology clinician and patient. Respect for autonomy encourages clinicians to elicit patients' values, goals of care, and preferences and then seek to provide treatment or care recommendations consistent with patient preferences.[4] Autonomy is primarily a negative right to be free from the interference of others or, in health care, to refuse a recommended treatment or intervention.[5] On the basis of potential harm to others or deliberate harm to themselves, there are limits to what patients can expect in terms of their requests. More controversial limits are imposed when oncology clinicians feel they are asked to violate their ethical integrity or when the medical effectiveness of a treatment does not justify the burden.[2]

Perceived conflicts about the issue of patient autonomy may be avoided by recalling that promoting patient autonomy is not only about treatments administered but also about discussions with the patient.[4] It is acceptable for oncology clinicians to share the basis for their recommendations, including concerns such as clinician-perceived futility.[6,7]

The following criteria to consider forgoing a potential LST are not absolute and remain a topic of discussion and debate; however, they offer a frame of reference for deliberation:

- The possibility of forgoing a potential LST is worth considering when either the clinician perceives that the medical effectiveness of an intervention is not justified by the medical risks or the patient perceives that the benefit (a more subjective appraisal) is not consistent with the burden.
- The goal of forgoing a potential LST is to relieve suffering as experienced by the patient and not to cause the death of the patient.[8] Measures that deliberately seek to end the life of the patient are more problematic.
- There is probably no difference between withholding or withdrawing a potential LST because the goal in both cases is to relieve or avoid further suffering.[9]
- The burden and suffering associated with medical interventions from the patient’s perspective are the most important criteria for forgoing a potential LST. Distinctions between simple interventions (e.g., intravenous hydration) and more complicated interventions (e.g., mechanical ventilation) do not determine supporting the patient’s decision to forgo a treatment.[10]

Religious and Spiritual Beliefs

Awareness of the importance of religious beliefs and spiritual concerns within medical care has increased substantially over the last decade. (Refer to the PDQ summary on Spirituality in Cancer Care for a review.) National consensus guidelines were published in 2009 and recommended the following:[11]

- That all patients receive a screening assessment for religious and spiritual concerns, followed by a more complete spiritual history.
- That all patients receive a formal assessment by a certified chaplain.
- That such information is placed in patient records, with follow-up at all appropriate times, including hospitalization at the EOL.

An interprofessional approach is recommended: medical personnel, including physicians, nurses, and other professionals such as social workers and psychologists, are trained to address these issues and link with chaplains, as available, to evaluate and engage patients. A survey of nurses and physicians revealed that most nurses (74%) and physicians (60%) desire to provide spiritual care, which was defined as "care that supports a patient's spiritual health."[12] The more commonly cited barriers associated with the estimated amount of spiritual care provided to patients included inadequate training and the belief that providing spiritual care is not part of the medical professional's role. Most nurses (79%) desired training in spiritual care; fewer physicians (51%) did.

Evidence strongly supports that most cancer patients desire dialogue about these issues with their physicians, other staff as appropriate, and hospital chaplains, if indicated.[13] About half of patients acknowledge that they are not receiving such support from a religious community, either because they are not involved in one or because they do not perceive their community as supportive.[14] Regardless of such support, patients may report substantial spiritual distress at the EOL, ranging from as few as 10% or 15% of patients to as many as 60%.[15] (Refer to the PDQ summary on Spirituality in Cancer Care for more discussion about spiritual distress.) Distress may range from anger at God to a feeling of unworthiness, to lack of meaning. Such distress, if not addressed, may complicate EOL decisions and increase depression.

Finally, it has been shown that addressing religious and spiritual concerns earlier in the terminal-care process substantially decreases the likelihood that patients will request aggressive EOL measures.[16] In contrast, patients who have received strong support from their own religious communities alone are less likely to enter hospice and more likely to seek aggressive EOL care.[15] It has also been shown that providing more comprehensive palliative care increases spiritual well-being as the EOL approaches.[17]

Artificial Hydration

The potential indications for artificial hydration in the final weeks or days of life may be broadly defined by the underlying goal of either temporarily reversing or halting clinical deterioration or improving the comfort of the dying patient.[18] Although artificial hydration may be provided through enteral routes (e.g., nasogastric tubes or percutaneous gastrostomy tubes), the more common route is parenteral, either intravenously by catheter or subcutaneously through a needle (hypodermoclysis).

Although uncontrolled experience suggested several advantages to artificial hydration in patients with advanced cancer, a well-designed, randomized trial of 129 patients enrolled in home hospice demonstrated no benefit in parenteral hydration (1 L of normal saline infused subcutaneously over 4 hours) compared with placebo (100 mL of normal saline infused subcutaneously over 4 hours).[19] There were no differences in survival, symptoms, quality of life, or delirium.

A prospective evaluation of the outcomes of 161 patients with advanced-stage abdominal cancers who received parenteral hydration in accordance with Japanese national guidelines near the EOL suggests there is little harm or benefit in hydration.[20] The median survival of the cohort was 20 days (range, 1–84 days); the mean volume of parenteral hydration was 912 ± 495 mL/day. There were no significant trends in global quality of life, discomfort, or physical symptoms for ill or good; signs of fluid retention were common but not exacerbated. However, patients expressed a high level of satisfaction with hydration and felt it was beneficial. The guidelines specify that patients with signs of volume overload should receive less than 1 L of hydration per day. When the investigators stratified patients into two groups—those who received at least 1 L of parenteral hydration per day and those who received less than 1 L/day—the prevalence of bronchial secretions was higher and hyperactive delirium was lower in the patients who received less than 1 L.[20]

Any discussion about the risks or benefits of artificial hydration must include a consideration of patient and family perspectives.[21] Requests for artificial hydration or the desire for discussions about the role of artificial hydration seem to be driven by quality-of-life considerations as much as considerations for life prolongation.[22] Families may be helped with this decision when clinicians explain that use of artificial hydration in patients with cancer at the EOL has not been shown to help patients live longer or improve quality of life. Additionally, families can be educated about good mouth care and provision of sips of water to alleviate thirst.[23] The oncology clinician needs to approach these conversations with an open mind, recognizing that the harm caused by artificial hydration may be minimal relative to the perceived benefit, which includes reducing fatigue and increasing alertness.[24]

Artificial Nutrition

The following discussion excludes patients for whom artificial nutrition may facilitate further anticancer treatment or for whom bowel obstruction is the main manifestation of their advanced cancer and for whom enteral or total parenteral nutrition may be of value.[25] Furthermore, artificial nutrition as a supplement may benefit the patient with advanced cancer who has a good performance status, a supportive home environment, and an anticipated survival longer than 3 months.[26,27]

The decisions about whether to provide artificial nutrition to the dying patient are similar to the decisions regarding artificial hydration. The American Academy of Hospice and Palliative Medicine (AAHPM) recommends that individual clinical situations be assessed using clinical judgment and skill to determine when artificial nutrition is appropriate. Recognizing that the primary intention of nutrition is to benefit the patient, AAHPM concludes that withholding artificial nutrition near the EOL may be appropriate medical care if the risks outweigh the possible benefit to the patient.[28]

Food should be offered to patients consistent with their desires and ability to swallow. The benefit of providing artificial nutrition in the final days to weeks of life, however, is less clear. One study has concluded that artificial nutrition—specifically, parenteral nutrition—neither influenced the outcome nor improved the quality of life in terminally ill patients.[29]

Providing artificial nutrition to patients at the EOL is a medical intervention and requires establishing enteral or parenteral access. Considerations of financial cost, burden to patient and family of additional hospitalizations and medical procedures, and all potential complications must be weighed against any potential benefit derived from artificial nutrition support.

In discussions with patients, the oncology clinician needs to recognize that the patient perception of benefit is worth exploring; as a compromise or acknowledgment of respect for the patient's perspective, a time-limited trial may be warranted.[30]

Anti-infectives

The administration of anti-infectives, primarily antibiotics, in the last days of life is common, with antibiotic use reported in patients in the last week of life at rates ranging from 27% to 78%.[31-33] Because of wide heterogeneity in the measurement of antibiotic use, assessment of symptom response, and lack of comparisons between those receiving antimicrobials with those not receiving them, the benefit of antimicrobials is currently hard to define.[31] The infections most likely to respond are urinary tract, skin, or eye infections; those less likely to be managed by antimicrobials, such as pneumonia, may be better managed with symptomatic measures.[34-36] One additional setting in which antimicrobial use may be warranted is that of contagious public health risks such as tuberculosis.[34] There is also concern that the continued use of antimicrobials in the last week of life leads to increased risk of developing drug-resistant organisms.[37]

In general, most practitioners agree with the overall focus on patient comfort in the last days of life rather than providing curative therapies with unknown or marginal benefit, despite their ability to provide the therapy.[31,34,36-38]

Transfusions

Anemia is common in patients with advanced cancer; thrombocytopenia is less common and typically occurs in patients with progressive hematological malignancies. The decision to transfuse either packed red cells or platelets is based on a careful consideration of the overall goals of care, the imminence of death, and the likely benefit and risks of transfusions. The decision to use blood products is further complicated by the potential scarcity of the resource and the typical need for the patient to receive transfusions in a specialized unit rather than at home.

There are no randomized or controlled prospective trials of the indications, safety, or efficacy of transfused products. It should be recognized, however, that many patients will have received transfusions during active disease treatment or periods of supportive care. Such patients may have notions of the importance of transfusions related to how they feel and their life expectancies.

Several considerations may be relevant to the decision to transfuse red blood cells:

- The response in terms of improvement in fatigue and breathlessness is modest and transitory.[39]
- A significant proportion of patients die within 14 days of transfusion, which raises the possibility that transfusions may be harmful or that transfusions were inappropriately given to dying patients.[39]
- Decisions to transfuse red cells should be based on symptoms and not a trigger value.[40]
- Transfusion of rare blood types or human leukocyte antigen–compatible platelet products is more difficult to justify.[41]

Cardiopulmonary Resuscitation

Broadly defined, resuscitation includes all interventions that provide cardiovascular, respiratory, and metabolic support necessary to maintain and sustain the life of a dying patient. It is important for patients, families, and proxies to understand that choices may be made to specify which supportive measures, if any, are given preceding death and at the time of death. People often believe that there is plenty of time to discuss resuscitation and the surrounding issues; however, many dying patients do not make choices in advance or have not communicated their decisions to their families, proxies, and the health care team. If these issues are unresolved at the time of EOL events, undesired support and resuscitation may result. Studies suggest that this aggressive care is associated with worse patient quality of life and worse adjustment to bereavement for loved ones.[42,43]

Narrowly defined, a do-not-resuscitate (DNR) order instructs health care providers that, in the event of cardiopulmonary arrest, cardiopulmonary resuscitation (CPR, including chest compressions and/or ventilations) should not be performed and that natural death be allowed to proceed. DNR orders must be made before cardiac arrest and may be recommended by physicians when CPR is considered medically futile or would be ineffective in returning a patient to life. A DNR order may also be made at the instruction of the patient (or family or proxy) when CPR is not consistent with the goals of care.

It is advisable for a patient who has clear thoughts about these issues to initiate conversations with the health care team (or appointed health care agents in the outpatient setting) and to have forms completed as early as possible (i.e., before hospital admission), before the capacity to make such decisions is lost. Although patients with end-stage disease and their families are often uncomfortable bringing up the issues surrounding DNR orders, physicians and nurses can tactfully and respectfully address these issues appropriately and in a timely fashion. Lack of standardization in many institutions may contribute to ineffective and unclear discussions around DNR orders.[44]

References

1. Kaldjian LC: Communicating moral reasoning in medicine as an expression of respect for patients and integrity among professionals. Commun Med 10 (2): 177-83, 2013. [PUBMED Abstract]
2. Pellegrino ED: Decisions to withdraw life-sustaining treatment: a moral algorithm. JAMA 283 (8): 1065-7, 2000. [PUBMED Abstract]
3. Goold SD, Williams B, Arnold RM: Conflicts regarding decisions to limit treatment: a differential diagnosis. JAMA 283 (7): 909-14, 2000. [PUBMED Abstract]
4. Billings JA, Krakauer EL: On patient autonomy and physician responsibility in end-of-life care. Arch Intern Med 171 (9): 849-53, 2011. [PUBMED Abstract]
5. The ethics of respect for persons: lying, cheating, and breaking promises and why physicians have considered them ethical. In: Veatch RM: The Basics of Bioethics. 3rd ed. Upper Saddle River, NJ: Pearson Education, Inc., 2012, pp 62-83.
6. Blinderman CD, Krakauer EL, Solomon MZ: Time to revise the approach to determining cardiopulmonary resuscitation status. JAMA 307 (9): 917-8, 2012. [PUBMED Abstract]
7. Swindell JS, McGuire AL, Halpern SD: Beneficent persuasion: techniques and ethical guidelines to improve patients' decisions. Ann Fam Med 8 (3): 260-4, 2010 May-Jun. [PUBMED Abstract]
8. Olsen ML, Swetz KM, Mueller PS: Ethical decision making with end-of-life care: palliative sedation and withholding or withdrawing life-sustaining treatments. Mayo Clin Proc 85 (10): 949-54, 2010. [PUBMED Abstract]
9. Huddle TS: Moral fiction or moral fact? The distinction between doing and allowing in medical ethics. Bioethics 27 (5): 257-62, 2013. [PUBMED Abstract]
10. Rhymes JA, McCullough LB, Luchi RJ, et al.: Withdrawing very low-burden interventions in chronically ill patients. JAMA 283 (8): 1061-3, 2000. [PUBMED Abstract]

11. Puchalski C, Ferrell B, Virani R, et al.: Improving the quality of spiritual care as a dimension of palliative care: the report of the Consensus Conference. J Palliat Med 12 (10): 885-904, 2009. [PUBMED Abstract]
12. Balboni MJ, Sullivan A, Enzinger AC, et al.: Nurse and physician barriers to spiritual care provision at the end of life. J Pain Symptom Manage 48 (3): 400-10, 2014. [PUBMED Abstract]
13. Phelps AC, Lauderdale KE, Alcorn S, et al.: Addressing spirituality within the care of patients at the end of life: perspectives of patients with advanced cancer, oncologists, and oncology nurses. J Clin Oncol 30 (20): 2538-44, 2012. [PUBMED Abstract]
14. Balboni TA, Vanderwerker LC, Block SD, et al.: Religiousness and spiritual support among advanced cancer patients and associations with end-of-life treatment preferences and quality of life. J Clin Oncol 25 (5): 555-60, 2007. [PUBMED Abstract]
15. Balboni TA, Balboni M, Enzinger AC, et al.: Provision of spiritual support to patients with advanced cancer by religious communities and associations with medical care at the end of life. JAMA Intern Med 173 (12): 1109-17, 2013. [PUBMED Abstract]
16. Balboni TA, Paulk ME, Balboni MJ, et al.: Provision of spiritual care to patients with advanced cancer: associations with medical care and quality of life near death. J Clin Oncol 28 (3): 445-52, 2010. [PUBMED Abstract]
17. Zimmermann C, Swami N, Krzyzanowska M, et al.: Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. Lancet 383 (9930): 1721-30, 2014. [PUBMED Abstract]
18. Boland E, Johnson M, Boland J: Artificial hydration in the terminally ill patient. Br J Hosp Med (Lond) 74 (7): 397-401, 2013. [PUBMED Abstract]
19. Bruera E, Hui D, Dalal S, et al.: Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. J Clin Oncol 31 (1): 111-8, 2013. [PUBMED Abstract]
20. Yamaguchi T, Morita T, Shinjo T, et al.: Effect of parenteral hydration therapy based on the Japanese national clinical guideline on quality of life, discomfort, and symptom intensity in patients with advanced cancer. J Pain Symptom Manage 43 (6): 1001-12, 2012. [PUBMED Abstract]
21. Del Río MI, Shand B, Bonati P, et al.: Hydration and nutrition at the end of life: a systematic review of emotional impact, perceptions, and decision-making among patients, family, and health care staff. Psychooncology 21 (9): 913-21, 2012. [PUBMED Abstract]
22. Malia C, Bennett MI: What influences patients' decisions on artificial hydration at the end of life? A Q-methodology study. J Pain Symptom Manage 42 (2): 192-201, 2011. [PUBMED Abstract]
23. McCann RM, Hall WJ, Groth-Juncker A: Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. JAMA 272 (16): 1263-6, 1994. [PUBMED Abstract]
24. Raijmakers NJ, Fradsham S, van Zuylen L, et al.: Variation in attitudes towards artificial hydration at the end of life: a systematic literature review. Curr Opin Support Palliat Care 5 (3): 265-72, 2011. [PUBMED Abstract]
25. Bozzetti F: Total parenteral nutrition in cancer patients. Curr Opin Support Palliat Care 1 (4): 281-6, 2007. [PUBMED Abstract]
26. McCallum PD, Fornari A: Nutrition in palliative care. In: Elliott L, Molseed LL, McCallum PD, eds.: The

Clinical Guide to Oncology Nutrition. 2nd ed. Chicago, Ill: American Dietetic Association, 2006, pp 201-7.

27. Orrevall Y, Tishelman C, Permert J: Home parenteral nutrition: a qualitative interview study of the experiences of advanced cancer patients and their families. Clin Nutr 24 (6): 961-70, 2005. [PUBMED Abstract]
28. Statement on Artificial Nutrition and Hydration Near the End of Life. Chicago, Ill: American Academy of Hospice and Palliative Medicine, 2013. Available online. Last accessed January 5, 2018.
29. Torelli GF, Campos AC, Meguid MM: Use of TPN in terminally ill cancer patients. Nutrition 15 (9): 665-7, 1999. [PUBMED Abstract]
30. Dy SM: Enteral and parenteral nutrition in terminally ill cancer patients: a review of the literature. Am J Hosp Palliat Care 23 (5): 369-77, 2006 Oct-Nov. [PUBMED Abstract]
31. Rosenberg JH, Albrecht JS, Fromme EK, et al.: Antimicrobial use for symptom management in patients receiving hospice and palliative care: a systematic review. J Palliat Med 16 (12): 1568-74, 2013. [PUBMED Abstract]
32. Albrecht JS, McGregor JC, Fromme EK, et al.: A nationwide analysis of antibiotic use in hospice care in the final week of life. J Pain Symptom Manage 46 (4): 483-90, 2013. [PUBMED Abstract]
33. Nakagawa S, Toya Y, Okamoto Y, et al.: Can anti-infective drugs improve the infection-related symptoms of patients with cancer during the terminal stages of their lives? J Palliat Med 13 (5): 535-40, 2010. [PUBMED Abstract]
34. Ford PJ, Fraser TG, Davis MP, et al.: Anti-infective therapy at the end of life: ethical decision-making in hospice-eligible patients. Bioethics 19 (4): 379-92, 2005. [PUBMED Abstract]
35. Hickman SE, Nelson CA, Moss AH, et al.: The consistency between treatments provided to nursing facility residents and orders on the physician orders for life-sustaining treatment form. J Am Geriatr Soc 59 (11): 2091-9, 2011. [PUBMED Abstract]
36. Lloyd-Williams M, Payne S: Can multidisciplinary guidelines improve the palliation of symptoms in the terminal phase of dementia? Int J Palliat Nurs 8 (8): 370-5, 2002. [PUBMED Abstract]
37. Niederman MS, Berger JT: The delivery of futile care is harmful to other patients. Crit Care Med 38 (10 Suppl): S518-22, 2010. [PUBMED Abstract]
38. LeGrand SB, Walsh D: Comfort measures: practical care of the dying cancer patient. Am J Hosp Palliat Care 27 (7): 488-93, 2010. [PUBMED Abstract]
39. Preston NJ, Hurlow A, Brine J, et al.: Blood transfusions for anaemia in patients with advanced cancer. Cochrane Database Syst Rev 2: CD009007, 2012. [PUBMED Abstract]
40. Uceda Torres ME, Rodríguez Rodríguez JN, Sánchez Ramos JL, et al.: Transfusion in palliative cancer patients: a review of the literature. J Palliat Med 17 (1): 88-104, 2014. [PUBMED Abstract]
41. Smith LB, Cooling L, Davenport R: How do I allocate blood products at the end of life? An ethical analysis with suggested guidelines. Transfusion 53 (4): 696-700, 2013. [PUBMED Abstract]
42. Wright AA, Zhang B, Ray A, et al.: Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. JAMA 300 (14): 1665-73, 2008. [PUBMED Abstract]

43. Miyashita M, Morita T, Sato K, et al.: Factors contributing to evaluation of a good death from the bereaved family member's perspective. Psychooncology 17 (6): 612-20, 2008. [PUBMED Abstract]
44. Zhukovsky DS, Hwang JP, Palmer JL, et al.: Wide variation in content of inpatient do-not-resuscitate order forms used at National Cancer Institute-designated cancer centers in the United States. Support Care Cancer 17 (2): 109-15, 2009. [PUBMED Abstract]

Dying in the Hospital or Intensive Care Unit

No Further Escalation of Care

Patients with advanced cancer are often unprepared for a decline in health status near the EOL and, as a consequence, they are admitted to the hospital for more aggressive treatments. This complicates EOL decision making because the treatments may prolong life, or at least are perceived as accomplishing that goal. At that point, patients or families may express ambivalence or be reluctant to withdraw treatments rather than withhold them.

One strategy to explore is preventing further escalation of care. The goal of this strategy is to provide a bridge between full life-sustaining treatment (LST) and comfort care, in which the goal is a good death. It has been suggested that clinicians may encourage no escalation of care because of concerns that the intensive medical treatments will prevent death, and therefore the patient will have missed the “opportunity to die.”[1] One study [2] described the care of 310 patients who died in the intensive care unit (ICU) (not all of whom had cancer). For 95 patients (30%), there was a decision not to escalate care. The average time from ICU admission to deciding not to escalate care was 6 days (range, 0–37), and the average time to death was 0.8 days (range, 0–5). The interventions most likely to be withheld were dialysis, vasopressors, and blood transfusions. Fifty-five percent of the patients eventually had all life support withdrawn. The transition to comfort care did not occur before death for the other decedents for the following reasons: waiting for family to arrive, change of family opinion, or waiting for an ethics consultation.

Conversely, some situations may warrant exploring with the patient and/or family a time-limited trial of intensive medical treatments. The patient or surrogates may choose to withdraw all LST if there is no improvement during the limited trial.[1] From an ethical standpoint, withdrawing treatment is equivalent to withholding such treatment. Both actions are justified for unwarranted or unwanted intensive care.

Withdrawal of Ventilatory Support

Two methods of withdrawal have been described: immediate extubation and terminal weaning.[3] Immediate extubation includes providing parenteral opioids for analgesia and sedating agents such as midazolam, suctioning to remove excess secretions, setting the ventilator to “no assist” and turning off all alarms, and deflating the cuff and removing the endotracheal tube. Gentle suctioning of the oral cavity may be necessary, but aggressive and deep suctioning should be avoided. In some cases, patients may appear to be in significant distress. Analgesics and sedatives may be provided, even if the patient is comatose. Family members and others who are present should be warned that some movements may occur after extubation, even in patients who have no brain activity. Such movements are probably caused by hypoxia and may include gasping, moving extremities, or sitting up in bed.[4] Immediate extubation is generally chosen when a patient has lost brain function, when a patient is comatose and unlikely to experience any suffering, or when a patient prefers a more rapid procedure.

Terminal weaning entails a more gradual process. Ventilator rate, oxygen levels, and positive end-expiratory pressure are decreased gradually over a period of 30 minutes to a few hours. A patient who survives may be placed on a T-piece; this may be left in place, or extubation may proceed. There is some evidence that the gradual process in a patient who may experience distress allows clinicians to assess pain and dyspnea and to modify the sedative and analgesic regimen accordingly.[5] In a study of 31 patients undergoing terminal weaning, most patients remained comfortable, as assessed by a variety of physiologic measures, when low doses of opioids and benzodiazepines were administered. The average time to death in this study was 24 hours, although two patients survived to be discharged to hospice.[6]

Paralytic agents have no analgesic or sedative effects, and they can mask patient discomfort. These neuromuscular blockers need to be discontinued before extubation. Guidelines suggest that these agents should never be introduced when the ventilator is being withdrawn; in general, when patients have been receiving paralytic agents, these agents need to be withdrawn before extubation. The advantage of withdrawal of the neuromuscular blocker is the resultant ability of the health care provider to better assess the patient’s comfort level and to allow possible interaction between the patient and loved ones. One notable exception to withdrawal of the paralytic agent is when death is expected to be rapid after the removal of the ventilator and when waiting for the drug to reverse might place an unreasonable burden on the patient and family.[7]

Regardless of the technique employed, the patient and setting must be prepared. Monitors and alarms are turned off, and life-prolonging interventions such as antibiotics and transfusions need to be discontinued. Family members should be given sufficient time to make preparations, including making arrangements for the presence of all loved ones who wish to be in attendance. They need to be given information about what to expect during the process; some may elect to remain out of the room during extubation. Chaplains or social workers may be called to provide support to the family.

References

1. Cochrane TI: Unnecessary time pressure in refusal of life-sustaining therapies: fear of missing the opportunity to die. Am J Bioeth 9 (4): 47-54, 2009. [PUBMED Abstract]
2. Morgan CK, Varas GM, Pedroza C, et al.: Defining the practice of "no escalation of care" in the ICU. Crit Care Med 42 (2): 357-61, 2014. [PUBMED Abstract]
3. Marr L, Weissman DE: Withdrawal of ventilatory support from the dying adult patient. J Support Oncol 2 (3): 283-8, 2004 May-Jun. [PUBMED Abstract]
4. Heytens L, Verlooy J, Gheuens J, et al.: Lazarus sign and extensor posturing in a brain-dead patient. Case report. J Neurosurg 71 (3): 449-51, 1989. [PUBMED Abstract]
5. Truog RD, Cist AF, Brackett SE, et al.: Recommendations for end-of-life care in the intensive care unit: The Ethics Committee of the Society of Critical Care Medicine. Crit Care Med 29 (12): 2332-48, 2001. [PUBMED Abstract]
6. Campbell ML, Bizek KS, Thill M: Patient responses during rapid terminal weaning from mechanical ventilation: a prospective study. Crit Care Med 27 (1): 73-7, 1999. [PUBMED Abstract]

7. Truog RD, Burns JP, Mitchell C, et al.: Pharmacologic paralysis and withdrawal of mechanical ventilation at the end of life. N Engl J Med 342 (7): 508-11, 2000. [PUBMED Abstract]

The Dying Person and Intractable Suffering

Suffering at the End of Life (EOL)

Patient perspectives: Published in 2013, a prospective observational study of 64 patients who died of cancer serially assessed symptoms, symptom intensity, and whether symptoms were unbearable.[1] Weakness was the most prevalent symptom (93% of patients). Fifty-one percent of patients rated their weakness as high intensity; of these, 84% rated their suffering as unbearable. Pain, loss of control over one's life, and fear of future suffering were unbearable when symptom intensity was high.

Informal caregiver perspectives: Caregiver suffering is a complex construct that refers to severe distress in caregivers' physical, psychosocial, and spiritual well-being. A number of studies have reported strong associations between patients' and caregivers' emotional states. In a systematic review of 19 descriptive studies of caregivers during the palliative, hospice, and bereavement phases, analysis of patient-caregiver dyads found mutuality between the patient's condition and the caregiver's response. Caregivers were found to be at increased risk for physical and psychological burden across studies, with caregiver distress sometimes exceeding that of the patient.[2]

Several studies have categorized caregiver suffering with the use of dyadic analysis. In a qualitative study involving 22 dyadic semistructured interviews, caregivers dealing with advanced medical illness, including cancer, reported both unique and shared forms of suffering. Suffering was characterized as powerlessness, threat to the caregiver's identity, and demands exceeding resources.[3] Because caregiver suffering can affect patient well-being and result in complicated bereavement, early identification and support of caregiver suffering are optimal.[4]

Palliative Sedation

Palliative sedation may be defined as the deliberate pharmacologic lowering of the level of consciousness, with the goal of relieving symptoms that are unacceptably distressing to the patient and refractory to optimal palliative care interventions. In considering a patient's request for palliative sedation, clinicians need to identify any personal biases that may adversely affect their ability to respond effectively to such requests. Several points need to be borne in mind:

- There is no evidence that palliative sedation shortens life expectancy when applied in the last days of life.[5]
- The goal of palliative sedation is to relieve intractable suffering.
- Discussions about palliative sedation may lead to insights into how to better care for the dying person. For example, requests for palliative sedation may create an opportunity to understand the implications of symptoms for the suffering person and to encourage the clinician to try alternative interventions to relieve symptoms.
- When dealing with requests for palliative sedation, health care professionals need to consider their own

cultural and religious biases and reflect on the commitment they make as clinicians to the dying person.[6]

The following questions may serve to organize discussions about the appropriateness of palliative sedation within health care teams and between clinicians, patients, and families:

- What are the indications for palliative sedation?
- Has the patient received optimal palliative care short of palliative sedation?
- What is the intended level of consciousness?
- Will the palliative sedation be maintained continuously until death or adjusted to reassess the patient's symptom distress?
- What are the plans for discontinuation or maintenance of hydration, nutrition, or other potentially life-sustaining treatments (LSTs)?

Indications for palliative sedation: The two broad indications for palliative sedation are refractory physical symptoms and refractory existential or psychological distress. A retrospective study at the MD Anderson Cancer Center in Houston included 1,207 patients admitted to the palliative care unit. Palliative sedation was used in 15% of admissions. The most common indications were delirium (82%) and dyspnea (6%).[7] The use of palliative sedation for refractory existential or psychological symptoms is highly controversial. In a survey of the attitudes and experiences of more than 1,000 U.S. physicians toward intentional sedation to unconsciousness until death revealed that 68% of respondents opposed palliative sedation for existential distress. Of note, only 10% of physician respondents had prescribed palliative sedation in the preceding 12 months.[8] A previous survey conducted by the same research group reported that only 18% of surveyed physicians objected to "sedation to unconsciousness in dying patients" without a specified indication.[9]

One potential objection or concern related to palliative sedation for refractory existential or psychological distress is unrecognized but potentially remediable depression. (Refer to the Requests for Hastened Death section of this summary for more information.)

Further objections or concerns include (1) whether the principle of double effect, the ethical basis for the use of palliative sedation for refractory physical distress, is adequate justification; and (2) cultural expectations about psychological or existential suffering at the EOL. The principle of double effect is based on the concept of proportionality. It states that the intended effect of palliative sedation (relief of suffering) may justify the foreseeable but unintended consequence (shortening of life expectancy or loss of ability to interact with loved ones) if the intended (positive) outcome is of greater value than the unintended (negative) outcome.[10] Thus, in the case of palliative sedation for refractory psychological or existential distress, the perception that palliative sedation is not justified may reflect a devaluation of the distress associated with such suffering or that other means with fewer negative consequences have not been fully explored.

Intended level of sedation: Another decision is whether the intended level of sedation is unconsciousness or a level associated with relief of the distress attributed to physical or psychological symptoms. In a survey of U.S. physicians,[8] two-thirds of respondents felt that unconsciousness was an acceptable unintended consequence of palliative sedation, but deliberate unconsciousness was unacceptable. This finding may relate to the sense of proportionality. A qualitative study of 54 physicians who had administered palliative sedation indicated that physicians who were more concerned with ensuring that suffering was relieved were more likely to administer palliative sedation to unconsciousness. Physicians who chose mild sedation were guided more by their assessment of the patient's condition.[11]

Intended duration of sedation: If the clinician anticipates that a distressing symptom will improve with time, then the clinician should discuss with the patient any recommendations about a deliberate reduction in the depth of sedation to assess whether the symptoms persist. In the published experience cited earlier,[7] palliative sedation for delirium or dyspnea was reversible in 23% of patients admitted to a palliative care unit. Furthermore, deliberate reductions in the depth of sedation may be appropriate if there is a desire for communication with loved ones.

Role of potentially LSTs during palliative sedation: The intent of palliative sedation is to relieve suffering; it is not to shorten life. The decision to discontinue or maintain treatments such as artificial hydration or nutrition requires a review of the patient's goals of care and the potential for benefit or harm. In general, the absence of evidence for benefit seems to justify recommendations to forgo LSTs in the context of palliative sedation. On the other hand, open lines of communication and a respectful and responsive awareness of a patient's preferences are important to maintain during the dying process, so the clinician should not overstate the potential risks of hydration or nutrition. There is consensus that decisions about LSTs are distinct from the decision to administer palliative sedation.

Requests for Hastened Death

Potential reasons for requests: Requests for hastened death or statements that express a desire to die vary from expression of a temporary or passive wish to a sustained interest in interventions to end life or a statement of intent to plan or commit suicide.[12] Reliable data on the frequency of requests for hastened death are not available.

Requests for hastened death provide the oncology clinician with an opportunity to explore and respond to the dying patient's experience in an attentive and compassionate manner. From the patient's perspective, the reasons for requests for hastened death are multiple and complex and include the following:

- Depression or a sense of hopelessness.[13]
- Uncontrollable pain or other physical symptoms, with decreased quality of life.[14]
- Loss of personal identity and social relations.[15]
- To avoid being a burden to others.[16]

The cited studies summarize the patient's perspectives. Surveys of health care providers demonstrate similar findings and reasons.

Responding to requests: Recommendations are based on principles of counseling and expert opinion. Specific studies are not available. The first and most important consideration is for health care providers to maintain awareness of their personal reactions to requests or statements. It is imperative that the oncology clinician expresses a supportive and accepting attitude. Providers who are too uncomfortable to engage in a discussion need to explain to a patient the need for a referral to another provider for assistance.[17] Other prudent advice includes the following:

- Be open to concerns.
- Assess other contributing factors.
- Respond to specific issues.
- Conclude the discussion with a summary and a plan.

References

1. Ruijs CD, Kerkhof AJ, van der Wal G, et al.: Symptoms, unbearability and the nature of suffering in terminal cancer patients dying at home: a prospective primary care study. BMC Fam Pract 14: 201, 2013. [PUBMED Abstract]
2. Williams AL, McCorkle R: Cancer family caregivers during the palliative, hospice, and bereavement phases: a review of the descriptive psychosocial literature. Palliat Support Care 9 (3): 315-25, 2011. [PUBMED Abstract]
3. Meeker MA, Waldrop DP, Schneider J, et al.: Contending with advanced illness: patient and caregiver perspectives. J Pain Symptom Manage 47 (5): 887-95, 2014. [PUBMED Abstract]
4. Hebert RS, Arnold RM, Schulz R: Improving well-being in caregivers of terminally ill patients. Making the case for patient suffering as a focus for intervention research. J Pain Symptom Manage 34 (5): 539-46, 2007. [PUBMED Abstract]
5. Maltoni M, Scarpi E, Rosati M, et al.: Palliative sedation in end-of-life care and survival: a systematic review. J Clin Oncol 30 (12): 1378-83, 2012. [PUBMED Abstract]
6. George R: Suffering and healing--our core business. Palliat Med 23 (5): 385-7, 2009. [PUBMED Abstract]
7. Elsayem A, Curry Iii E, Boohene J, et al.: Use of palliative sedation for intractable symptoms in the palliative care unit of a comprehensive cancer center. Support Care Cancer 17 (1): 53-9, 2009. [PUBMED Abstract]
8. Putman MS, Yoon JD, Rasinski KA, et al.: Intentional sedation to unconsciousness at the end of life: findings from a national physician survey. J Pain Symptom Manage 46 (3): 326-34, 2013. [PUBMED Abstract]
9. Curlin FA, Nwodim C, Vance JL, et al.: To die, to sleep: US physicians' religious and other objections to physician-assisted suicide, terminal sedation, and withdrawal of life support. Am J Hosp Palliat Care 25 (2): 112-20, 2008 Apr-May. [PUBMED Abstract]
10. Olsen ML, Swetz KM, Mueller PS: Ethical decision making with end-of-life care: palliative sedation and withholding or withdrawing life-sustaining treatments. Mayo Clin Proc 85 (10): 949-54, 2010. [PUBMED Abstract]
11. Swart SJ, van der Heide A, van Zuylen L, et al.: Considerations of physicians about the depth of palliative sedation at the end of life. CMAJ 184 (7): E360-6, 2012. [PUBMED Abstract]
12. Hudson PL, Kristjanson LJ, Ashby M, et al.: Desire for hastened death in patients with advanced disease and the evidence base of clinical guidelines: a systematic review. Palliat Med 20 (7): 693-701,

2006. [PUBMED Abstract]

13. Breitbart W, Rosenfeld B, Pessin H, et al.: Depression, hopelessness, and desire for hastened death in terminally ill patients with cancer. JAMA 284 (22): 2907-11, 2000. [PUBMED Abstract]
14. Wilson KG, Scott JF, Graham ID, et al.: Attitudes of terminally ill patients toward euthanasia and physician-assisted suicide. Arch Intern Med 160 (16): 2454-60, 2000. [PUBMED Abstract]
15. Coyle N, Sculco L: Expressed desire for hastened death in seven patients living with advanced cancer: a phenomenologic inquiry. Oncol Nurs Forum 31 (4): 699-709, 2004. [PUBMED Abstract]
16. Mak YY, Elwyn G: Voices of the terminally ill: uncovering the meaning of desire for euthanasia. Palliat Med 19 (4): 343-50, 2005. [PUBMED Abstract]
17. Hudson PL, Schofield P, Kelly B, et al.: Responding to desire to die statements from patients with advanced disease: recommendations for health professionals. Palliat Med 20 (7): 703-10, 2006. [PUBMED Abstract]

Grief and Bereavement

Family members are likely to experience loss at the death of their loved one. If left unattended, loss, grief, and bereavement can become complicated, leading to prolonged and significant distress for either family members or clinicians. Furthermore, clinicians are at risk for significant grief from the cumulative effects of many losses through the deaths of their patients. Burnout has also been associated with unresolved grief in health care professionals. (Refer to the PDQ summary on Grief, Bereavement, and Coping With Loss for more information.)

Challenges to the Professional Caregiver

Oncologists and nurses caring for terminally ill cancer patients are at risk for personal suffering, owing to the clinical intensity and chronic loss inherent in their work. Lack of training in advance care planning and communication can leave oncologists vulnerable to burnout, depression, and professional dissatisfaction.[1] One group of investigators studied oncologists' grief related to patient death and found strong impact in both the personal and professional realms. Negative effects included a sense of distraction and withdrawal from patients.[2]

One study made an important conceptual distinction, explaining that while grief is healthy for oncologists, stress and burnout can be counterproductive.[3] Other terms used to describe professional suffering are *moral distress*, *emotional exhaustion*, and *depersonalization*.[4] Moral distress was measured in a descriptive pilot study involving 29 physicians and 196 nurses caring for dying patients in intensive care units. Both groups of professionals experienced moral distress related to pressure to continue aggressive treatment they considered futile. Nurses experienced more moral distress than did physicians, and perceived less collaboration than did their physician colleagues.[5]

Several strategies have been recommended to help professionals manage the emotional toll of working with advanced and terminally ill cancer patients, including self-care, teamwork, professional mentorship, reflective writing, mindfulness techniques, and working through the grief process.[6]

References

1. Meier DE, Back AL, Morrison RS: The inner life of physicians and care of the seriously ill. JAMA 286 (23): 3007-14, 2001. [PUBMED Abstract]
2. Granek L, Tozer R, Mazzotta P, et al.: Nature and impact of grief over patient loss on oncologists' personal and professional lives. Arch Intern Med 172 (12): 964-6, 2012. [PUBMED Abstract]
3. Shayne M, Quill TE: Oncologists responding to grief. Arch Intern Med 172 (12): 966-7, 2012. [PUBMED Abstract]
4. Edmonds C, Lockwood GM, Bezjak A, et al.: Alleviating emotional exhaustion in oncology nurses: an evaluation of Wellspring's "Care for the Professional Caregiver Program". J Cancer Educ 27 (1): 27-36, 2012. [PUBMED Abstract]
5. Hamric AB, Blackhall LJ: Nurse-physician perspectives on the care of dying patients in intensive care units: collaboration, moral distress, and ethical climate. Crit Care Med 35 (2): 422-9, 2007. [PUBMED Abstract]
6. Sanchez-Reilly S, Morrison LJ, Carey E, et al.: Caring for oneself to care for others: physicians and their self-care. J Support Oncol 11 (2): 75-81, 2013. [PUBMED Abstract]

Changes to This Summary (04/08/2016)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Care Decisions in the Final Weeks, Days, and Hours of Life

Added text to state that patients who preferred to die at home were more likely to do so (56% vs. 37%; odds ratio [OR], 2.21).

Added text to state that patients were less likely to die at home (OR, <1) if there was moderate or severe pain (43% vs. 69%; OR, 0.56) or higher functional status as measured by the Palliative Performance Scale (OR, 0.53).

Forgoing Potentially Life-Sustaining Treatments

Revised text to state that a significant proportion of patients die within 14 days of transfusion, which raises the possibility that transfusions may be harmful or that transfusions were inappropriately given to dying patients.

Dying in the Hospital or Intensive Care Unit

Added text to state that it has been suggested that clinicians may encourage no escalation of care because of concerns that the intensive medical treatments will prevent death, and therefore the patient will have missed the “opportunity to die” (cited Cochrane as reference 1).

Added text to state that the patient or surrogates may choose to withdraw all life-sustaining treatment if there is no improvement during the limited trial. Also added text to state that from an ethical standpoint, withdrawing treatment is equivalent to withholding such treatment, and both actions are justified for unwarranted or unwanted intensive care.

The Dying Person and Intractable Suffering

Revised text to state that if the clinician anticipates that a distressing symptom will improve with time, then the clinician should discuss with the patient any recommendations about a deliberate reduction in the depth of sedation to assess whether the symptoms persist. Also added text to state that deliberate reductions in the depth of sedation may be appropriate if there is a desire for communication with loved ones.

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- be discussed at a meeting,
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The lead reviewers for Last Days of Life are:

- Joseph Bubalo, PharmD, BCPS, BCOP (Oregon Health and Science University Hospital)
- Larry D. Cripe, MD (Indiana University School of Medicine)
- Tammy I. Kang, MD (Texas Children's Pavilion for Women)

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