Palliative Care and Symptom Management in Older Patients with Cancer

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**KEYWORDS**

- Geriatrics
- Cancer
- Symptom management
- Palliative care

**KEY POINTS**

- Palliative care (PC) should be part of the care of older patients with cancer throughout the trajectory of the disease.
- Its focus on symptom management and maximization of function is essential in maintaining quality of life.
- Pain, a frequent symptom in all patients with cancer, presents specific barriers for evaluation and treatment in older patients with cancer.
- Nonpain symptoms are multiple, frequent, and debilitating. They need to be addressed comprehensively.
- Nonpharmacologic interventions should be considered first in the treatment of older adults in order to minimize drug-drug interactions and serious side effects.
- Timely referral to PC could decrease patient and caregiver distress.

**PALLIATIVE CARE IN GERIATRIC ONCOLOGY**

Medical care for older patients with cancer is complicated by many factors, including the heterogeneity of their health status, polypharmacy, frailty, dementia, delirium, and functional impairment. They are best served by a multidisciplinary approach with palliative care (PC) playing an integral role, primarily focusing on symptom control and quality of life. Older patients with cancer benefit from a palliative approach that prioritizes the patient’s individual goals, and strives to maintain the patient’s independence.

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and physical, emotional, and spiritual health. For most older patients living with cancer, both life-prolonging and palliative treatments can be necessary and appropriate. PC should not be associated only with terminal care, and should be part of older patients’ cancer care throughout the trajectory of their disease with various levels of involvement as the disease progresses. In some cases, introduction of PC may have an even greater impact at earlier time points when the focus is on cure. Closer to, during, and after death, attention to the caregivers may increase in importance. National organizations’ guidelines recommend that PC be routinely integrated into comprehensive cancer care.1,2

SYMPTOM MANAGEMENT

Symptom management, whether related to the disease or to the treatment, influences the quality of life of patients with cancer. For older adults, serious illness is frequently characterized by a high prevalence of untreated symptoms that result in progressive functional dependence. The focus on symptom management and maximization of function provide the patients and their caregivers with relief from one of the largest sources of stress. Advanced age is also associated with physiologic changes that affect the pharmacokinetics and pharmacodynamics of medications, further complicating the treatment of cancer-related symptoms. Age-related physiologic changes must be considered when making treatment decisions in older adults.3 In addition, cognitive impairment, functional difficulties, and caregiver issues play a role in errors and compliance. To prescribe appropriately for symptom management, clinicians must consider not only the pharmacologic properties of the drugs but also clinical, epidemiologic, social, cultural, and economic factors.3

ASSESSMENT AND MANAGEMENT OF PAIN

Pain is difficult to evaluate and manage. Many barriers exist to the optimal evaluation and adequate treatment of pain in older patients with cancer. These barriers include cognitive and functional impairments, underreporting, bias in prescribing, comorbid conditions, and polypharmacy, as well as drug administration in institutional living settings.4 The consequences of poorly managed pain extend to behavioral domains (ie, depression, anxiety, and substance abuse), cardiovascular domains (ie, hypertension, increased incidence of deep vein thrombosis caused by impaired mobility), delirium, insomnia, functional impairment, and increased health care use.

Pain is one of the most common symptoms experienced by patients with cancer. Up to two-thirds of all older patients develop pain as a result of the cancer or as a consequence of its treatment.5 Treatment-related pain, such as chemotherapy-induced peripheral neuropathy, is most likely to affect the elderly. Pain may also be caused by non–cancer-related painful comorbidities, which are more frequent in the elderly patients, such as degenerative disk disease or osteoporosis-related fractures. The assessment of pain in patients with cancer should involve a comprehensive evaluation with a thorough physical examination and pain review (Box 1). In addition, clinicians need to be familiar with common cancer pain syndromes (eg, plexopathies, peripheral neuropathy) in order to identify the correct cause.6

There are several assessment tools for the evaluation of pain in the elderly (Box 2). Pain scales should be used even if the patient has mild or moderate cognitive impairment. As dementia progresses, the ability to self-report pain decreases. For these patients clinicians should anticipate the kinds of conditions that may cause pain and patient behaviors that may indicate pain (eg, agitation, restlessness, irritability, facial expressions, labored breathing, or withdrawal), and possibly use surrogate reports
of pain from caregivers and nurses. If a patient shows behaviors that could be caused by pain, it should be assumed that the patient is experiencing pain and a trial of analgesics is appropriate. A decrease in those behaviors can be considered a positive response to the analgesics.

**Management of Pain**

The standard pain management algorithm is based on the World Health Organization (WHO) analgesic ladder (Table 1). The cause of pain should be identified and addressed properly in order to correct the underlying disease process causing the pain. Ideally the treatment of the cancer eliminates the cause of pain. If this approach is not possible, is only partially successful, or while the patient is awaiting treatment, nonpharmacologic and/or pharmacologic interventions are warranted.

**Box 1**

**Assessment of pain**

1. Questions about the onset, location, duration, quality, and any aggravating and alleviating factors of the pain.
2. Questions to determine the tolerable level of pain.
3. Questions about prior experiences with pain medications, their side effects, and barriers to use.
4. Assessment for medical comorbidities that may affect the perception and experience of pain.
5. Assessment of the patient’s cognitive status and functional ability.

**Box 2**

**Summary of validated pain assessment tools in the elderly population**

- Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC)
- Pain Assessment in Advanced Dementia (PAINAD)
- Doloplus-2 Scale
- Abbey Pain Scale
- Rotterdam Elderly Pain Observation Scale (REPOS)
- Pain Assessment Tool in Confused Older Adults (PATCOA)
- Pain Assessment in Noncommunicative Elderly Persons (PAINE)
- Pain Assessment for the Demented Elderly (PADE)
- Mahoney Pain Scale
- Elderly Pain Caring Assessment-2 (EPCA-2)
- Discomfort Scale-Dementia Alzheimer Type (DS-DAT)
- Certified Nurse Assistant Pain Assessment Tool (CPAT)
- Checklist of Nonverbal Pain Indicators (CNPI)

*Data from Refs. 7–19*
Nonpharmacologic interventions

All treatment plans for older patients with cancer should incorporate nonpharmacologic interventions such as massage, relaxation techniques, exercise, and rehabilitation. Cognitive behavior therapy may be helpful in patients who are cognitively intact. It is also important to ensure the involvement of a multidisciplinary team that includes a geriatrician, PC specialist, social worker, and chaplain.

Pharmacologic interventions

Nonopioid therapy

Acetaminophen Acetaminophen is used for the relief of mild to moderate pain and is the first line for pain control in older patients with cancer. However, because of potential liver toxicity, patients should be counseled not to consume more than 3000 mg of acetaminophen per day. It is also important to educate patients and their caregivers that many other medications, including over-the-counter medications, contain acetaminophen and require caution when used in combination.

Nonsteroidal antiinflammatory drugs

Nonsteroidal antiinflammatory drugs (NSAIDs) are also effective for the treatment of mild to moderate pain, especially bone pain. However, NSAIDs are associated with increased risks in older patients, and have been linked to gastrointestinal bleeds, renal toxicity, myocardial infarction, and stroke. Patients taking concomitant nephrotoxic agents and those with compromised renal function caused by aging or other comorbidities are at higher risk of NSAID-related renal toxicity. NSAID-associated side effects are dose and time dependent and therefore, in this population, NSAIDs should be used only for short intervals. If NSAIDs are used, they should be prescribed in conjunction with a gastroprotective medication such as a proton pump inhibitor. Absolute contraindications for the use of NSAIDs include chronic kidney disease, active peptic ulcer disease, and heart failure.

Opioid therapy

Opioids are used in the treatment of moderate to severe cancer-related pain. These medications can be administered in many preparations (eg, oral, intravenous, and transdermal) and, compared with nonopioids, have no analgesic ceiling dose (Table 2). Before initiating treatment it is important to evaluate the hepatic and renal function, cognitive ability, level of social support, and potential drug-drug interactions with other active medications (Box 3). In older patients with cancer, oral administration is preferred because of ease of use and affordability. Weak opioids (codeine, hydrocodone, tramadol, tapentadol, and buprenorphine) are the second

<table>
<thead>
<tr>
<th>Step</th>
<th>Recommendations</th>
<th>Suggested Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: mild pain</td>
<td>Nonopioid</td>
<td>NSAIDs, acetaminophen</td>
</tr>
<tr>
<td></td>
<td>± Adjuvant</td>
<td>Neurontin, pregabalin</td>
</tr>
<tr>
<td>Step 2: moderate pain</td>
<td>Weak opioid</td>
<td>Codeine</td>
</tr>
<tr>
<td></td>
<td>± Nonopioid</td>
<td>NSAIDs, acetaminophen</td>
</tr>
<tr>
<td></td>
<td>± Adjuvant</td>
<td>Neurontin, pregabalin</td>
</tr>
<tr>
<td>Step 3: severe pain</td>
<td>Strong opioid</td>
<td>Morphine, oxycodone, hydromorphone, fentanyl, methadone</td>
</tr>
<tr>
<td></td>
<td>± Nonopioid</td>
<td>NSAIDs, acetaminophen</td>
</tr>
<tr>
<td></td>
<td>± Adjuvant</td>
<td>Neurontin, pregabalin</td>
</tr>
</tbody>
</table>

Abbreviation: NSAIDs, nonsteroidal antiinflammatory drugs.

Table 1
WHO analgesic ladder and recommendations for elderly patients

Abbreviation: NSAIDs, nonsteroidal antiinflammatory drugs.
### Table 2
Opioid medications in older patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Equianalgesic PO Dose (mg)</th>
<th>PO Starting Dose in Elderly&lt;sup&gt;a&lt;/sup&gt; (mg)</th>
<th>Equianalgesic IV Dose</th>
<th>IV Starting Dose in Elderly&lt;sup&gt;a&lt;/sup&gt; (mg)</th>
<th>Half-life (h)</th>
<th>Duration of Action (h)</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30</td>
<td>2.5–7.5</td>
<td>10 mg</td>
<td>1.25–2.5 mg</td>
<td>1.5–3</td>
<td>3–7</td>
<td>Renal failure</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20</td>
<td>2.5</td>
<td>—</td>
<td>—</td>
<td>2–4</td>
<td>3–6</td>
<td>Patients with abuse potential</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>7.5</td>
<td>0.5–1</td>
<td>1.5 mg</td>
<td>0.2 mg</td>
<td>2–3</td>
<td>2–5</td>
<td>Renal failure</td>
</tr>
<tr>
<td>Methadone&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2</td>
<td>1.25–2.5</td>
<td>1 mg</td>
<td>1.25 mg</td>
<td>12–190</td>
<td>4–12</td>
<td>—</td>
</tr>
<tr>
<td>Fentanyl&lt;sup&gt;c&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
<td>250 μg</td>
<td>12.5–25 μg</td>
<td>3–4</td>
<td>4–6</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: IV, intravenous; PO, by mouth.

<sup>a</sup> Opioid-naive patients.

<sup>b</sup> Use restricted to experienced practitioners.

<sup>c</sup> Not for use in opioid-naive patients.
step in the WHO analgesic ladder and are recommended for mild to moderate pain. However, lower doses of stronger opioids have been shown to be more effective than weak opioids and many experts skip the second step of the ladder and use a strong opioid instead to treat cancer-related pain. At the same time consider starting stool softeners and laxatives to avoid opioid-induced constipation (see Box 3).

### Opioid adverse effects

The side effect profile of opioid pain medications is no different based on age, although older patients with cancer are more likely to show symptoms. The most common opioid-related adverse effects include constipation, sedation, confusion, and hallucinations. Constipation in older adults is multifactorial; opioid-induced constipation is likely caused by a combination of mu-receptor binding within the gastrointestinal tract, delayed motility, and increased water resorption. All patients prescribed opioids should be started on a prophylactic bowel regimen that includes a stimulant laxative to prevent opioid-induced constipation. The development of sedation, confusion, or hallucinations is usually managed with dose reduction or opioid rotation. The use of benzodiazepines should be avoided in this population if possible. Other less common opioid-associated adverse effects seen in older patients with cancer include nausea, dry mouth, pruritus, myoclonus, and urinary retention.

### Adjuvant medications

Adjuvant medications are given to enhance the pain relief provided by an opioid. Some of them are used primarily for other indications (eg,
antidepressants, muscle relaxers, anticonvulsants, corticosteroids). Neuropathic cancer-related pain (eg, chemotherapy-related pain) is best treated with adjuvant medications, including tricyclic antidepressants and antiepileptics. However, tricyclic antidepressants are rarely indicated in older patients with cancer because of their association with significant anticholinergic side effects and subsequent cognitive changes. The most commonly prescribed antiepileptics are gabapentin and pregabalin. In older patients with cancer, these medications should be renally dosed and escalated slowly. Serotonin-norepinephrine reuptake inhibitors (venlafaxine, duloxetine) have been shown to be effective and well tolerated.

ASSESSMENT AND MANAGEMENT OF NONPAIN SYMPTOMS

Fatigue

Fatigue is one of the most common and debilitating symptoms experienced by patients with cancer. Cancer-related fatigue (CRF) is characterized by feelings of tiredness, weakness, and lack of energy, and is distinct from that experienced by healthy individuals in that it is not relieved by rest or sleep. The prevalence of fatigue in patients receiving anticancer treatment has been estimated to be more than 80%. Fatigue has been found to be associated with distress, depression, anxiety, and low performance status, as well as other symptoms such as nausea, vomiting, lack of appetite, sleep disturbance, dyspnea, dry mouth, restlessness, and problems with concentration.

Management of fatigue

Nonpharmacologic interventions

1. Aerobic exercise: is considered beneficial for individuals with CRF, specifically those with solid tumors during and after cancer therapy. Combined aerobic and resistance exercise regimens with or without stretching should be included as part of rehabilitation programs for people who have been diagnosed with cancer.

2. Psychological interventions: fatigue in terminally ill patients with cancer is determined by both physical and psychological factors and it may be important to include psychological interventions. Individual sessions during which participants were educated on fatigue and learned activity management have been found to be effective.

3. Complementary therapies: a wide range of practical interventions and complementary therapies are likely to be helpful. These therapies include acupressure and acupuncture, stress management and relaxation, energy conservation measures, anticipatory guidance and preparatory information, and attention-restoring activities.

Pharmacologic interventions

1. Modafinil: recent studies and reviews show that modafinil has no effect on CRF and should not be prescribed outside a clinical trial setting.

2. Corticosteroids have been shown to improve fatigue in various studies.

3. Methylphenidate: existing trials of methylphenidate on CRF provide limited evidence for its use.

4. Antidepressants: paroxetine shows benefit in the treatment of fatigue, primarily when it is a symptom of clinical depression. Bupropion sustained release may have psychostimulant-like effects and, therefore, may be beneficial in treating fatigue.

5. Cholinesterase inhibitors: donepezil has been studied. However, there is no evidence of a significant improvement in CRF.
6. Other: traditional Chinese medicine (TCM) is widely used in the treatment of CRF in China. TCM seems to be effective in alleviating the fatigue in people with CRF. However, because of the high risk of bias in the literature, larger, well-designed studies are needed to confirm the potential benefit.\(^{41}\)

**Delirium**

Delirium is a fluctuating disturbance in attention and awareness that represents a decline from baseline status, accompanied by cognitive dysfunction. It is the most common serious neuropsychiatric complication in patients with cancer. It is associated with increased morbidity and mortality, increased length of hospitalizations, higher health care cost, and significant distress for patients, family members, and health professionals. The prevalence of delirium in cancer ranges from 20% to 40% in hospitalized patients and can be as high as 88% in terminally ill patients with cancer.\(^{42}\) The development of delirium may be an indicator of impending death in patients who are terminally ill.

The cause of delirium is usually multifactorial, involving multiple medical conditions, such as infections, organ failure, or adverse reactions to medications (Box 4). In patients with cancer, its complexity is enhanced by the direct effects of cancer on the central nervous system (CNS) (ie, brain metastatic disease) and the indirect CNS effects of the disease or its treatment.\(^{43}\) Delirium may interfere with the recognition of other symptoms such as pain. At times, agitation may be misinterpreted as uncontrolled pain and patients may be given increasing doses of opioids, which, in turn, can exacerbate the delirium state.

The work-up of delirium should always include a history and physical examination assessing for potentially reversible causes, with a thorough review of medications and doses. Laboratory tests may be necessary for the assessment of metabolic abnormalities, hypoxia, or other medical problems. Brain imaging to evaluate for brain metastasis, ischemia, or bleed as well as electroencephalography and/or lumbar puncture to rule out leptomeningeal carcinomatosis may be indicated. The diagnosis of delirium can be made using specific instruments such as the Confusion Assessment Method (CAM)\(^{44}\) (Box 5) or the CAM-ICU (CAM for the Intensive Care Unit) for intubated patients.\(^{45}\)

**Box 4**

**Causes of delirium frequently seen in the patients with cancer**

- Multiple medical causes (ie, infections, organ failure, malignant hypercalcemia)
- Uncontrolled pain
- Metastatic brain lesions
- CNS effects of chemotherapeutic/immunotherapeutic agents (eg, vincristine, interferon)
- Medications used for supportive care (eg, steroids, opioids, antiemetics, benzodiazepines)
- Paraneoplastic syndromes
- Constipation
- Withdrawal from alcohol, illicit drugs, benzodiazepines
- Sleep deprivation caused by environmental factors
- Strange/new environment

Abbreviation: CNS, central nervous system.
**Management of delirium**

**Nonpharmacologic interventions** The incidence of delirium can be reduced by minimizing exposure to known risk factors. Interventions are multifactorial and should include a thorough search for the underlying cause.46

**Pharmacologic interventions** When nonpharmacologic interventions are not sufficient, treatment with psychotropic medications is necessary. To date, no medication has been approved by the US Food and Drug Administration for the treatment of delirium. The main classes of medications studied in the treatment and prevention of delirium are antipsychotics, cholinesterase inhibitors, and alpha-2 agonists.43

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**Anxiety and Depression**

Anxiety and depression are the most common manifestations of psychological distress in patients with cancer, and the prevalence varies considerably depending on many factors, such as the type and stage of the disease, the patients’ coping abilities, and psychosocial support. Among patients with cancer, 47% have a formal psychiatric disorder. Approximately 85% of these patients have a disorder with depression or anxiety as the central symptom.47 These symptoms tend to increase as death approaches.

Anxiety frequently invokes hopelessness and often causes patients to reject advice given by clinicians.48 Goals of care conversations are central components of cancer care. However, anxiety about death contributes to decreased communication between patients and family members regarding the patient’s end-of-life care wishes.49 Untreated anxiety is frequently detrimental to patients’ quality of life.

Terminally ill patients with cancer experience progressive functional decline, accelerating symptom severity, and deteriorating social support, and perceive themselves to be a burden to others, predisposing them to depressive symptoms.50 Fatigue and confusion are associated with mild to moderate depressive symptoms and anxiety is frequently associated with severe depressive symptoms.51

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**Management of Anxiety and Depression**

A careful history and physical are important for determining effective interventions. Emphasis should be placed on identifying treatable conditions causing anxiety or depression, including pain and dyspnea, and managing them appropriately.

**Nonpharmacologic interventions** Nonpharmacologic approaches for the treatment of anxiety should be tried first. Multidisciplinary assessments and short-term psychotherapy can be used in managing
symptoms. Providing updated information on the prognosis, establishing short-term goals and expectations, identifying strengths and coping techniques, as well as the use of relaxation techniques can be helpful. In patients with depression and serious illness, pharmacologic and nonpharmacologic interventions should be used concurrently.

**Pharmacologic interventions**

Short-acting or long-acting oral benzodiazepines are the mainstay in treating anxiety symptoms in patients with serious illness. If the anxiety is severe and associated with paranoia or hallucinations, antipsychotics such as haloperidol may be needed (Table 3).

For the treatment of depression in older adults with terminal cancer, initial dosing of antidepressants should be reduced because of decreased drug clearance and potential side effects. Selective serotonin reuptake inhibitors (SSRIs) cause less sedation and fewer autonomic side effects than other antidepressant medications but may not show efficacy for 4 to 6 weeks. The tricyclics are the best studied and can be given as a single dose at bedtime. In some cases psychostimulants may be needed because of their rapid effect, but they may exacerbate anxiety and restlessness (Table 4). Patients should be referred to psychiatry when there is poor response to initial treatment and when there is a complex presentation with psychosis or suicidal ideation.

**Cachexia and Anorexia**

Cachexia is a complex metabolic syndrome associated with underlying illness and is characterized by loss of muscle with or without loss of fat mass. Anorexia is loss of appetite. Although anorexia with weight loss is common among patients with cancer, the profound weight loss in patients with cachexia cannot be entirely attributed to poor caloric intake. The overall prevalence of cancer anorexia-cachexia syndrome ranges from 40% at cancer diagnosis to 70% to 80% in advanced phases of the disease. Anorexia and cachexia may be more distressing to the families than to the patients, and treatment should include education of caregivers regarding the underlying disease.

**Management of cachexia and anorexia**

The best approach to the treatment of the cachectic syndrome is multifactorial. An improvement of cachexia may not be possible in all patients, but a reasonable goal could be to delay or prevent further decline.

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**Table 3**

Pharmacologic management of anxiety in patients with terminal cancer

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-acting Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5–2 mg 2–4 times a day</td>
<td>PO</td>
<td>Available as PO, sublingual, rectal, and IV preparations</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>0.25–2 mg 3–4 times a day</td>
<td>PO</td>
<td>Peaks in 30 min. Useful for quick relief of acute anxiety</td>
</tr>
<tr>
<td><strong>Long-acting Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.25–0.5 mg 2–3 times a day</td>
<td>PO</td>
<td>—</td>
</tr>
<tr>
<td>Diazepam</td>
<td>2–20 mg once to 3 times a day</td>
<td>PO</td>
<td>Parenteral form available</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.5–4 mg q4 h PRN</td>
<td>PO</td>
<td>Parenteral forms available. Use in severe cases with psychotic features</td>
</tr>
</tbody>
</table>

Abbreviations: PRN, as needed; q, every.
Nonpharmacologic interventions
1. Patients should be assessed and treated for causes interfering with appetite, such as a dry mouth, uncontrolled pain, nausea, and constipation.
2. Encourage small, frequent meals and assist with feeding if needed.
3. Oral nutritional supplementation may be beneficial.

Pharmacologic interventions Many drugs, including appetite stimulants, thalidomide, cytokine inhibitors, steroids, NSAIDs, branched-chain amino acids, eicosapentaenoic acid, and antiserotonergic drugs have been proposed and used in clinical trials, whereas others are still under investigation in experimental animal models. Appetite stimulants are not always successful; however, some patients benefit from them. When appetite stimulants are indicated, megestrol, prednisone, or dronabinol may be considered, but they have not been proved to extend life.

Artificial nutrition and hydration During the curative phase of cancer, optimal enteral or parenteral nutrition intake can reduce morbidity and mortality, and improve quality of life, but when the main goal of treatment becomes palliative, introduction of artificial nutrition is controversial. In patients at the end of life, artificial hydration and nutrition pose clinical, ethical, and logistical dilemmas. No strong evidence exists supporting the use of parenteral hydration or nutrition for most terminally ill patients. For patients with refractory cachexia, it is important to discuss the risks and benefits of parenteral nutrition and hydration with the patient, family members and health care team to set up realistic nutritional care goals. Previous studies on artificial hydration found no beneficial effects on terminal delirium, thirst, chronic nausea, and fluid
overload, but identified negative effects such as increased incidence of ascites and intestinal drainage.\textsuperscript{58}

**Nausea and Vomiting**

Nausea and vomiting are common in patients with advanced cancer.\textsuperscript{59} The prevalence in patients with cancer is estimated at between 30\% and 70\% and the most common causes are chemotherapy, radiation, opioids, bowel obstruction, and constipation. Because many factors can contribute to these symptoms, a history and physical focused on identification of specific causes is extremely important.

**Management of nausea and vomiting**

**Nonpharmacologic interventions** Small, frequent meals of the patient’s own choosing, providing adequate liquids, relaxation techniques, companionship, and a pleasant atmosphere during meals can be of help. Acupuncture in patients with cancer can be associated with a significantly reduced intensity of nausea during chemotherapy and in the final phase of life.\textsuperscript{60}

**Pharmacologic interventions** Drugs used to control nausea and vomiting include prokinetics, antihistamines, neuroleptics, serotonin receptor antagonists, benzodiazepines, corticosteroids, cannabinoids, and others such as scopolamine (Table 5).

**Dyspnea**

Dyspnea is defined as an uncomfortable awareness of breathing and is a common symptom in patients receiving PC. Acute dyspnea is the most frequent reason for an emergency admission in PC and severely affects the quality of life.\textsuperscript{61} In the terminally ill, dyspnea can have multiple causes. Common causes include effusions,
bronchospasm, thick airway secretions and airway obstructions, anemia, anxiety, and even unresolved emotional issues.

**Management of dyspnea**
Evaluation of patients complaining of dyspnea should include a thorough history and physical as well as imaging and/or other tests to rule out reversible causes.

**Nonpharmacologic interventions**
1. Repositioning the patient, usually to a more upright position
2. Improving air circulation by opening windows or using fans
3. Relaxation techniques and breathing retraining
4. Addressing anxiety issues and providing reassurance may be beneficial

Supplementary oxygen is often unnecessary in the PC setting. Oxygen delivered by a nasal cannula provides no additional symptomatic benefit for relief of refractory dyspnea in patients with life-limiting illness compared with room air.62

**Pharmacologic interventions**
1. Patients with specific diagnoses may benefit from treatments with diuretics, bronchodilators, or corticosteroids.
2. Opioids are recommended for emergency medical therapy for dyspnea in patients receiving PC.63 Opioids are the first-choice treatment of most nonspecific dyspnea because they suppress respiratory awareness effectively. Patients may report substantial relief of dyspnea with opiates without a change in respiratory rate. One of the most serious but infrequent side effects is respiratory depression. Studies have shown that opioids are both safe and effective in the treatment of dyspnea in terminal cancer64 (Table 6). Oxycodone 5 to 10 mg every 4 hours as needed or morphine syrup 5 to 15 mg every 4 hours as needed may be considered. In patients already on opioids and for those with high levels of anxiety, these doses may be increased by 50% every 4 to 12 hours until the patient experiences relief.
3. Benzodiazepines may also be helpful to relieve anxiety, which worsens dyspnea.

**END-OF-LIFE CARE**
Most referrals to PC and hospice occur late in the trajectory of the disease despite the fact that an earlier intervention could decrease patients’ symptoms of distress.65 Benefits are seen to extend to the caregivers as well; caregivers of patients referred early to PC had lower depression scores at 3 months and lower depression and stress burden in the terminal period.66 Many patients with end-stage cancer are offered chemotherapy in an attempt to improve quality of life. Chemotherapy at the end of life has been shown not

<table>
<thead>
<tr>
<th>Medication</th>
<th>Oral Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild Dyspnea</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>5 mg q4 h</td>
<td>Additional 5 mg q2 h PRN</td>
</tr>
<tr>
<td>Acetaminophen codeine</td>
<td>1 tab (30 mg) q4 h</td>
<td>Additional tab q2 h PRN</td>
</tr>
<tr>
<td><strong>Severe Dyspnea</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>3–10 mg q4 h</td>
<td>Additional PRN doses</td>
</tr>
<tr>
<td>Morphine syrup</td>
<td>5–15 mg q4 h</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1–3 mg q4 h</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviation: tab, tablet.*
only to be futile in that it is not associated with improved patient survival but also to be harmful by impairing the quality of life near death of these patients. Terminally ill patients experience a variety of symptoms in the last hours and days of life, including delirium, agitation, anxiety, restlessness, dyspnea, pain, vomiting, and psychological distress. Patients and families are usually unaware of the typical changes that occur in the last hours of life and at the moment of death, which can lead to last-minute confusion and panic. The purposeless movements and facial expressions that occur at this time can be misinterpreted as physical discomfort or emotional distress. The gurgling sounds of air passing over accumulated oropharyngeal secretions may be interpreted as choking. Caregiver education regarding what to expect in the final hours can help alleviate stress and prevent panic. This education is particularly helpful for families planning a home death.

Management of Refractory Terminal Symptoms and Agitation

In the terminal phase of life, symptoms may become refractory and poorly controlled by supportive and palliative therapies that specifically target these symptoms. Palliative sedation can be used to provide relief from these refractory symptoms that are not controlled by other methods. It is designed to induce a state of decreased awareness or in some cases, if necessary, unconsciousness. Sedative drugs, typically short-acting benzodiazepines, are administered in a monitored setting and titrated to achieve the desired level of sedation (Box 6). The level of sedation can be easily maintained and the effect is reversible. A systematic review found that palliative sedation did not hasten death, which has been a concern of physicians and families in prescribing this treatment.

**SUMMARY**

Patients with cancer can develop several symptoms that impair comfort and quality of life. They should be managed by a combination of nonpharmacologic and pharmacologic interventions. After initiation of treatment, patients should be reassessed frequently until the distressing symptoms are controlled while looking out for medication side effects. Caregiver education regarding what to expect in the final hours significantly alleviates stress.

**REFERENCES**


50. Tang ST, Chen JS, Chou WC, et al. Prevalence of severe depressive symptoms increases as death approaches and is associated with disease burden, tangible social support, and high self-perceived burden to others. Support Care Cancer 2015. [Epub ahead of print].


