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PALLIATIVE CARE AND SYMPTOM MANAGEMENT IN OLDER CANCER PATIENTS

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SYNOPSIS

Older cancer patients are best served by a multidisciplinary approach with Palliative Care (PC) playing an integral role. PC focuses on symptom control irrespective of its cause and should not be associated only with terminal care. It provides an additional layer of support in the care of the cancer patient with an emphasis on quality of life. In this article, we discuss the evaluation and management of pain and other common non-pain symptoms that occur in the elderly cancer patient, as well as end of life care.

Keywords

Geriatrics; Cancer; Symptom management; Palliative care

A. PALLIATIVE CARE IN GERIATRIC ONCOLOGY

Medical care for older cancer patients 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 cancer patients benefit from a palliative approach which prioritizes the patient's individual goals, and strives to maintain the patient's independence and physical, emotional, and spiritual health. For the majority of 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 the older patient's cancer care throughout the

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trajectory of his/her 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 care givers may increase in importance. National organizations' guidelines recommend that PC be routinely integrated into comprehensive cancer care.(1,2)

B. SYMPTOM MANAGEMENT

Symptom management, whether related to the disease or to the treatment, influences the cancer patient's quality of life. For older adults, serious illness is frequently characterized by a high prevalence of untreated symptoms which result in progressive functional dependence. The focus on symptom management and maximization of function provide the patients and their caregivers, relief from one of the largest sources of stress. Advanced age is also associated with physiological 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.(4) 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 pharmacological properties of the drugs but also clinical, epidemiological, social, cultural and economic factors.(4)

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 cancer patients. These include cognitive and functional impairments, underreporting, bias in prescribing, comorbid conditions and polypharmacy, as well as drug administration in institutional living settings(6). The consequences of poorly managed pain extend to behavioral domains (i.e. depression, anxiety, and substance abuse), cardiovascular domains (i.e. HTN, increased incidence of DVTs due to impaired mobility), delirium, insomnia, functional impairment and increased health care utilization.

Pain is one of the most common symptoms experienced by cancer patients. Up to two-thirds of all older patients develop pain as a result of the cancer itself or as a consequence of its treatment (7). Treatment-related pain such as chemotherapy-induced peripheral neuropathy is more likely to affect the elderly. Pain may also be due to non-cancer related painful comorbidities more frequent in the elderly patient such as degenerative disk disease or osteoporosis-related fractures. The assessment of pain in cancer patients should involve a comprehensive evaluation with a thorough physical exam and pain review (Box 1). In addition, the clinician needs to be familiar with common cancer pain syndromes (e.g. plexopathies, peripheral neuropathy) in order to identify the correct etiology. (3)

There are a number of assessment tools for the evaluation of pain in the elderly (Table 1). Pain scales should be used even if they have mild or moderate cognitive impairment. As dementia progresses, the ability to self-report pain decreases. For these patients the clinician should anticipate the kinds of conditions that may cause pain, patient behaviors that may indicate pain (e.g. agitation, restlessness, irritability, facial expressions, labored breathing or

withdrawal) and could use surrogate reports of pain from care givers and nurses. If a patient shows behaviors that could be due to 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 upon The World Health Organization's (WHO) analgesic ladder (see Table 2). (8) 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 will eliminate the cause of pain. If this approach is not possible, is only partially successful or while the patient is awaiting treatment, non-pharmacological and/or pharmacological interventions are warranted.

1. Non-pharmacological Interventions—All treatment plans for older cancer patients should incorporate non-pharmacological interventions such as massage, relaxation techniques, exercise, and rehabilitation (3). Cognitive behavioral therapy may be helpful if the patient is cognitively intact. It is also important to ensure the involvement of a multidisciplinary team that includes a geriatrician, palliative care specialist, social worker, and chaplain.

2. Pharmacological Interventions

a. Non-opioid Therapy: Acetaminophen is used for the relief of mild to moderate pain and is the first line for pain control in the older cancer patient. However, due to potential liver toxicity, patients should be counseled not to consume more than 3000mg 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 (9).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are also effective for the treatment of mild to moderate pain, especially bone pain. However, NSAIDs are associated with increased risks in the older patient, and have been linked to gastrointestinal bleeds, renal toxicity, myocardial infarction, and stroke. Patients taking concomitant nephrotoxic agents and those with compromised renal function due to aging or other comorbidities are at higher risk of NSAIDs-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 (10). If NSAIDs are used, they should be prescribed in conjunction with a gastroprotective medication such as a proton pump inhibitor (11). Absolute contraindications for the use of NSAIDs include chronic kidney disease, active peptic ulcer disease and heart failure.

b. Opioid Therapy: Opioids are used in the treatment of moderate to severe cancer-related pain. These medications can be administered in any number of preparations (e.g. PO, IV, and transdermal) and compared to nonopioids, have no analgesic ceiling dose. (Table 3) 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 2). In the older cancer patient, oral administration is preferred because of

ease of use and affordability (10). Weak opioids (codeine, hydrocodone, tramadol, tapentadol and buprenorphine) are the second step in the WHO analgesic ladder and are recommended for mild-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.(12) In the table below with important considerations, it may be good to mention “consider starting stool softeners and laxatives to avoid opioid induced constipation”

Opioid Adverse Effects. The side effect profile of opioid pain medications is no different based on age, although older cancer patients are more likely to exhibit symptoms. (10) The most common opioid-related adverse effects include constipation, sedation, confusion, and hallucinations. Constipation in the older adult is multifactorial; opioid-induced constipation is likely caused by a combination of mu-receptor binding within the GI tract, delayed motility, and increased water resorption. **All patients prescribed opioids should be started on a prophylactic bowel regimen that includes a stimulant laxative.** (13) 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 as possible. (14) Other less common opioid-associated adverse effects seen in the older cancer patient include nausea, dry mouth, pruritus, myoclonus, and urinary retention.

c. Adjuvant Medications: Adjuvant medications are given to enhance the pain relief provided by an opioid. Some of them are used primarily for other indications (e.g. antidepressants, muscle relaxers, anticonvulsants, corticosteroids). Neuropathic cancer-related pain (such as chemotherapy-related pain) is best treated with adjuvant medications including tricyclic antidepressants and anti-epileptics. However, tricyclic antidepressants are rarely indicated in older cancer patients because of their association with significant anticholinergic side effects and subsequent cognitive changes. The most commonly prescribed anti-epileptics are gabapentin and pregabalin. In the older cancer patient, 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 NON-PAIN 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.(15) The prevalence of fatigue in patients receiving anti-cancer treatment has been estimated to be more than 80%.(16) 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.(17)

Management of Fatigue

1. Non-pharmacological interventions

- a. **Aerobic exercise-** is considered beneficial for individuals with CRF, specifically those with solid tumors during and post-cancer therapy.(18,19) 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.
- b. **Psychological interventions-** fatigue in terminally ill cancer patients is determined by both physical and psychological factors and it may be important to include psychological interventions.(20) Individual sessions during which participants were educated on fatigue and learned activity management have been found to be effective.(21)
- c. **Complementary therapies-** a wide range of practical interventions and complementary therapies are likely to be helpful. These include acupressure and acupuncture, stress management and relaxation, energy conservation measures, anticipatory guidance and preparatory information, and attention-restoring activities.(22)

2. Pharmacological interventions

- a. **Modafinil-** Recent studies and reviews show that Modafinil has no effect on CRF and should not be prescribed outside a clinical trial setting.(23)
- b. **Corticosteroids-** have been shown to improve fatigue in various studies. (24,25)
- c. **Methylphenidate-** Existing trials of methylphenidate on CRF provide limited evidence for its use.(26)
- d. **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.(27)
- e. **Cholinesterase inhibitors-** Donepezil has been studied. However, there is no evidence of a significant improvement in CRF.(28)
- f. **Other-** Traditional Chinese medicine (TCM) is widely used in the treatment of CRF in China. TCM appears to be effective in alleviating the fatigue in people with CRF.

However, due to the high risk of bias in the literature, larger, well-designed studies are needed to confirm the potential benefit.(29)

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 20–40% in the hospitalized patient and can be as high as 88% in the terminally ill patient with cancer. (30) The development of delirium may be an indicator of impending death in patients who are terminally ill.

The etiology of delirium is usually multifactorial, involving multiple medical conditions such as infections, organ failure or adverse reactions to medications. (Table 4) In cancer patients, its complexity is enhanced by the direct effects of cancer on the central nervous system (CNS) (i.e. brain metastatic disease) and the indirect CNS effects of the disease or its treatment. (31) 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 exam 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 (EEG) and/or lumbar puncture to rule out leptomeningeal carcinomatosis may be indicated. The diagnosis of delirium can be done using specific instruments such as the Confusion Assessment Method (CAM) (32) or the CAM-ICU for intubated patients (Box 3). (33)

Management of Delirium

1. **Non-pharmacological 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.(34)
2. **Pharmacological interventions:** When non-pharmacological interventions are not sufficient, treatment with psychotropic medications is necessary. To date, no medication has been approved by the US Food and Drug Administration (FDA) 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. (31)

ANXIETY and DEPRESSION

Anxiety and depression are the most common manifestations of psychological distress in cancer patients, 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 cancer patients, 47% have a formal psychiatric disorder. Approximately 85% of these patients have a disorder with depression or anxiety as the central symptom.(35) These symptoms tend to increase as death approaches.

Anxiety frequently invokes hopelessness and often causes patients to reject advice given by clinicians.(36) Goals of care conversations are a central component of cancer care.

Unfortunately, anxiety about death contributes to decreased communication between patients and family members regarding the patient's end-of-life care wishes.(37) Untreated anxiety is frequently detrimental to the patient's quality of life.

Terminally ill cancer patients experience progressive functional decline, accelerating symptom severity, deteriorating social support, and self-perceived burden to others, predisposing them to depressive symptoms.(38) Fatigue and confusion are associated with mild to moderate depressive symptoms and anxiety is very frequently associated with severe depressive symptoms.(39)

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.

1. Non-pharmacological Interventions: Non-pharmacological approaches for the treatment of anxiety should be tried first. Multidisciplinary assessments and short term psychotherapy can be employed 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, pharmacological and nonpharmacological interventions should be used concurrently.

2. Pharmacologic Interventions: Short 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 5)

For the treatment of depression in older adults with terminal cancer, initial dosing of antidepressants should be reduced due to 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 4–6 weeks. The tricyclics are the best studied and can be given as a single dose at bedtime. In some cases psychostimulants may be needed due to their rapid effect, but they may exacerbate anxiety and restlessness. (Table 6) 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 characterized by loss of muscle with or without loss of fat mass.(40) Anorexia is loss of appetite. While anorexia with weight loss is common among cancer patients, the profound weight loss suffered by 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 70–80% in advanced phases of the disease.(41) Anorexia and cachexia

may be more distressing to the families than to the patients themselves 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.

1. Non-pharmacological interventions

- a. Patients should be assessed and treated for causes interfering with appetite such as a dry mouth, uncontrolled pain, nausea and constipation.
- b. Encourage small, frequent meals and assist with feeding if needed.
- c. Oral nutritional supplementation may be beneficial

2. Pharmacological interventions: Many drugs including appetite stimulants, thalidomide, cytokine inhibitors, steroids, nonsteroidal anti-inflammatory drugs, branched-chain amino acids, eicosapentaenoic acid and anti serotonergic drugs have been proposed and used in clinical trials, while others are still under investigation in experimental animal models.(42) Appetite stimulants are not always successful, however some patients may benefit from them. When appetite stimulants are indicated Megestrol, Prednisone or Dronabinol(43) may be considered, but they have not been proven to extend life.

3. 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.(44) 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 the majority of terminally ill patients.(45) 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.(46)

NAUSEA AND VOMITING

Nausea and vomiting are common in advanced cancer patients.(47) The prevalence in cancer patients is estimated between 30–70% and the most common etiologies are chemotherapy-induced, radiation-induced, opioid-induced, bowel obstruction and constipation. As many factors may contribute to these symptoms, a history and physical focused on identification of specific causes is extremely important.

Management of Nausea and Vomiting

1. Non-pharmacological 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 cancer patients can be associated

with a significantly reduced intensity of nausea during chemotherapy and in the final phase of life.(48)

2. Pharmacological interventions: Drugs used to control nausea and vomiting include prokinetics, antihistamines, neuroleptics, serotonin receptor antagonists, benzodiazepines, corticosteroids, cannabinoids and others such as scopolamine. (Table 7)

DYSPNEA

Dyspnea is defined as an uncomfortable awareness of breathing and is a common symptom in PC patients. Acute dyspnea is the most frequent reason for an emergency admission in PC and severely impacts the quality of life.(49) In the terminally ill, dyspnea can have multiple etiologies. Common causes include effusions, bronchospasm, thick airway secretions and airway obstructions, anemia, anxiety and even unresolved emotional issues.

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

1. Non-pharmacological interventions

- a. Repositioning the patient usually to a more upright position
- b. Improving air circulation by opening windows or using fans,
- c. Relaxation techniques and breathing retraining
- d. 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.(50)

2. Pharmacological interventions

- a. Patients with specific diagnoses may benefit from treatments with diuretics, bronchodilators or corticosteroids.
- b. **Opioids** are recommended for emergency medical therapy of dyspnea in PC patients.(51) Opioids are the first choice treatment for most non-specific dyspnea as they suppress respiratory awareness effectively. Patients may report substantial relief of dyspnea with opiates without a change in respiratory rate. One of the most feared but infrequent side-effect is respiratory depression. Studies have shown that opioids are both safe and effective in the treatment of dyspnea in terminal cancer.(52). (Table 8) Oxycodone 5–10mg q 4 hours and PRN or morphine syrup 5–15mg q4 hours and PRN may be considered. In patients already on opioids and for those with high levels of anxiety, these doses may be increased by 50% every 4–12 hours until the patient experiences relief

- c. **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.(53) 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.(54) Many patients with endstage cancer are offered chemotherapy in an attempt to improve quality of life (QOL). Chemotherapy at the end of life has been shown not only to be futile in that it is not associated with improved patient survival, but also to be harmful by impairing the QOL near death of these patients.(55) 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. This 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 is particularly helpful where families plan 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 employed to provide relief from these refractory symptoms that are not controlled by other methods. It is aimed at inducing 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 4). The level of sedation can be easily maintained and the effect is reversible. In a systematic review, it was found that palliative sedation did not hasten death, which has been a concern of physicians and families in prescribing this treatment. (56)

Summary—Cancer patients can develop a number of symptoms that impair comfort and quality of life. They should be managed by a combination of non-pharmacologic 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.

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Box 1**Questions for the 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 cognitive status and functional ability.

Box 2**Important Considerations in the Treatment of Cancer Pain with Opioids**

- Strong opioids are the mainstay of the management of moderate-severe cancer pain
- The majority of patients tolerate Morphine quite well, including the elderly
- Occasional cancer-related pain can be managed with PRN opioid medications, but patients who require more than four PRN doses per day should be started on a long-acting scheduled medication.
- It is helpful to use the same drug for short and long acting doses (e.g. Morphine immediate and extended release). Rescue doses should be calculated at 10–15% of the total daily dose and should be scheduled based on the half-life of the medication (3).
- In the older cancer patient an ideal starting dose is 30–50% lower than the standard for younger patients and it is important to adhere to the ‘start low and go slow’ adage (5).
- Reduce dose of Morphine in patients with renal failure to avoid accumulation of the active metabolite morphine -6-glucuronide
- Dose titration in this population must be done carefully to balance any side effects with the level of analgesia.
- It is appropriate to increase the daily opioid dose by 25–50% every twenty-four hours until pain relief is achieved (6).
- Close follow-up is extremely important in order to evaluate for safe opioid storage, adherence, and frequency of use (3).
- Opioid rotation will be required in approximately 25% of patients started on Morphine who develop dose-limiting side effects.
- All patients prescribed opioids should be started on a prophylactic bowel regimen that includes a stimulant laxative to prevent opioid induced constipation.

Data from Refs 3, 5, 6.

Box 3**CAM criteria for a positive diagnosis of delirium**

1. Acute onset and fluctuating course of the mental status
2. Inattention: difficulty focusing and easily distracted
3. Disorganized thinking: disorganized or incoherent speech, and/or illogical flow of ideas
4. Altered level of consciousness, vigilant, hyper-alert, lethargic or stuporous.

1 and 2 plus 3 or 4 should be present for a positive diagnosis of delirium.

Adapted from Ely EW, Inouye SK, Bernard GR et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA: the journal of the American Medical Association 2001;286:2703–10; with permission.

Box 4**Four essential drugs needed for quality care of the dying cancer patient
(57)**

1. Morphine (i.e., an opioid),
2. Midazolam (a benzodiazepine),
3. Haloperidol (a neuroleptic),
4. Anticholinergic (i.e. glycopyrrolate)

KEY POINTS

- Palliative Care should be part of the older cancer patients' care 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 cancer patients, presents in the older cancer patient specific barriers for evaluation and treatment.
- Non-pain symptoms are multiple, frequent and debilitating. They need to be addressed comprehensively.
- Non-pharmacologic 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.

Table 1**Summary of Validated Pain Assessment Tools in the Elderly Population**

Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) (58)
Pain Assessment in Advanced Dementia (PAINAD) (59)
Doloplus-2 Scale (60)
Abbey Pain Scale (61)
Rotterdam Elderly Pain Observation Scale (REPOS) (62)
Pain Assessment Tool in Confused Older Adults (PATCOA) (63)
Pain Assessment in Non-communicative Elderly Persons (PAINE) (64)
Pain Assessment for the Demented Elderly (PADE) (65)
Mahoney Pain Scale (66)
Elderly Pain Caring Assessment-2 (EPCA-2) (67)
Discomfort Scale (DS-DAT) (68)
Certified Nurse Assistant Pain Assessment Tool (CPAT) (69)
Checklist of Non-verbal Pain Indicators (CNPI) (70)

Data from Refs 58–70.

Table 2

WHO analgesic ladder and recommendations for elderly patients

Step	Recommendations	Suggested Medications
Step 1- mild pain	Non-opioid +/- adjuvant	NSAIDs, Acetaminophen Neurontin, Pregabalin
Step 2- moderate pain	Weak opioid +/- Non-opioid +/- adjuvant	Codeine NSAIDs, Acetaminophen Neurontin, Pregabalin
Step 3- severe pain	Strong opioid +/- Non-opioid +/- adjuvant	Morphine, Oxycodone, Hydromorphone, Fentanyl, Methadone NSAIDs, Acetaminophen Neurontin, Pregabalin

WHO= World Health Organization

NAIDs= nonsteroidal anti-inflammatory drugs

Table 3

Opioid medications in older patients

Drug	Equianalgesic PO Dose	PO Starting Dose in Elderly*	Equianalgesic IV Dose	IV Starting Dose in Elderly*	Half-life	Duration of Action	Cautions
Morphine	30mg	2.5–7.5mg	10mg	1.25–2.5mg	1.5–3 hrs	3–7 hrs	Renal failure
Oxycodone	20mg	2.5mg		–	2–4 hrs	3–6 hrs	Patients with abuse potential
Hydromorphone	7.5mg	0.5–1mg	1.5mg	0.2mg	2–3 hrs	2–5 hrs	Renal failure
Methadone ‡	2mg	1.25–2.5mg	1mg	1.25mg	12–190 hrs	4–12 hrs	–
Fentanyl §	–	–	250mcg	12.5–25mcg	3–4 hrs	4–6 hrs	–

PO= by mouth; IV= intravenous, mg= milligrams, hrs= hours, mcg= micrograms

* = opioid-naïve patients

‡ = use restricted to experienced practitioner

§ = not for use in opioid naïve patients

Table 4**Etiology of Delirium Frequently Seen in the Cancer Patient**

Multiple medical etiologies (i.e. infections, organ failure, malignant hypercalcemia)
Uncontrolled Pain
Metastatic Brain Lesions
CNS effects of chemotherapeutic/immunotherapeutic agents (e.g. vincristine, interferon)
Medications used for supportive care (e.g. steroids, opioids, antiemetics, benzodiazepines)
Paraneoplastic syndromes
Constipation
Withdrawal from alcohol, illicit drugs, benzodiazepines
Sleep deprivation due to environmental factors
Strange/new environment

CNS= central nervous system

Table 5

Pharmacological Management of Anxiety in the Terminal Cancer Patient

Medication	Dosage	Route	Comments
Short acting benzodiazepines			
Lorazepam	0.5– 2 mg two to four times a day	PO	Available as PO, sublingual, rectal and IV preparations
Alprazolam	0.25– 2 mg three to four times a day	PO	Peaks in 30 minutes. Useful for quick relief of acute anxiety
Long acting benzodiazepines			
Clonazepam	0.25– 0.5 mg two to three times a day	PO	
Diazepam	2– 20 mg once to three times a day	PO	Parenteral form available
Others			
Haloperidol	0.5– 4 mg q4 hours PRN	PO	Parenteral forms available. Use in severe cases with psychotic features.

mg= milligram

PO= by mouth

IV= intravenous

q= every

Table 6

Pharmacological Management of Depression

Medication	Dosage (Max)	Route	Comments
SSRIs			
Citalopram	20–40 mg daily	PO	Taper when discontinuing. Dose adjustment in patient with severe renal impairment.
Escitalopram	10–20 mg daily	PO	Taper when discontinuing
Fluoxetine	10–60 mg daily	PO	
Tricyclic Antidepressants			
Amitriptyline	10–75 mg (150 mg)	PO HS	Sedating. Analgesic effects. Anticholinergic side effects.
Nortriptyline	10–25 mg (75 mg)	PO HS	Less side effects than amitriptyline
Psychostimulants			
Methylphenidate	2.5mg once to twice a day (60 mg daily)	PO	Adjuvant in patients with prognosis of days to weeks. Administer in morning and noon.
Modafinil	100–400 mg daily		Adjuvant in patients with prognosis of days to weeks
Miscellaneous			
Bupropion	100 mg BID (450 mg)	PO	Contraindicated with seizures
Mirtazapine	15mg (45 mg)	PO HS	Possible sedation, may improve oral intake
Venlafaxine	37.5 mg twice daily (375 mg)	PO	Available as extended release

mg= milligram

PO= by mouth

HS= at bedtime

bid= two times a day

Table 7**Pharmacological Management of Nausea and Vomiting in the Elderly Cancer Patient**

Medication	Dose (oral)	Route	Comments
Metoclopramide	5–15mg before meals	PO, SC or IV	May cause dystonia
Domperidone	Divided doses before meals to max of 80mg/day	PO	May cause dystonia
Diphenhydramine	1mg/kg/dose q4hours	PO, SC or IV	May cause drowsiness
Haloperidol	0.01–0.05mg/kg/dose q8hours	PO, SC or IV	May prolong QT interval. Can cause EPS.
Prochlorperazine	0.15mg/kg/dose q4hours	PO, PR or IV	May cause EPS and dystonias
Ondansetron	0.15mg/kg/dose q6hours	PO or IV	Used particularly in chemo induced nausea
Diazepam	0.05–0.2mg/kg/dose q6hours	PO or IV	Helpful in anticipatory nausea
Dexamethasone	2–4mg bid to qid	PO, SC or IV	Use for nausea with increased intracranial pressure
Dronabinol	2.5mg bid	PO	May cause dysphoria, drowsiness, hallucinations
Scopolamine	0.5mg transdermal q72hours	Transdermal	May cause dry mouth, blurred vision, confusion

mg= milligram

PO= by mouth

SC= subcutaneous

IV= intravenous

kg= kilogram

q= every

EPS= extrapyramidal symptoms

PR= by rectum

qid= four times a day

bid= two times a day

Table 8

Pharmacologic Management of Dyspnea in the End Stage Cancer Patient

Medication	Oral Dose	Comments
Mild dyspnea		
Hydrocodone	5mg q4 hours	Additional 5mg q2 hours PRN
Acetaminophen Codeine	1tab (30mg) q4 hours	Additional tab q2 hours PRN
Severe dyspnea		
Oxycodone	3–10mg q4 hours	Additional PRN doses
Morphine syrup	5–15mg q4 hours	
Hydromorphone	1–3mg q4 hours	

mg= milligram

q= every

PRN= as needed

tab= tablet