Review Article: Terminal Delirium in Geriatric Patients With Cancer at End of Life
Deborah D. Moyer

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Terminal Delirium in Geriatric Patients With Cancer at End of Life

Deborah D. Moyer, MSN, CHPN

Abstract
Terminal delirium is a common symptom that is frequently underdiagnosed in geriatric patients with cancer at end of life and is a major cause of distress for the patient as well as their family. This article explores the hyperactive and hypoactive delirium subtypes as well as the pathophysiology of terminal delirium and the theory of acetylcholine deficiency and dopamine excess. The causes for terminal delirium underdiagnosis as well as the causes of terminal delirium itself are identified. The use of the Confusion Assessment Method (CAM) is discussed as a means of delirium diagnosis and the Memorial Delirium Assessment scale (MDAS) is presented as a tool to measure its severity. Lastly, nonpharmacologic and pharmacologic treatment measures are reviewed and an algorithm is presented to assist the clinician in the identification and management of terminal delirium.

Keywords
delirium, palliation, geriatric, oncology, end of life, cancer

Delirium is a common, if not inevitable, syndrome that occurs during the final 24 to 48 hours of life in the terminally ill patient with cancer. It occurs with a frequency of 85% to 90%. Morita et al. found that delirium not only occurs in the final days of life but can also occur up to 29 days before death with a median survival time of 10 days from delirium onset. Delirium is frightening and distressing to the patient, family, and staff. Bruera et al. found that the majority of patients with advanced cancer recalled their experience of delirium as causing them moderate-to-severe levels of distress. Delirium is the main contributing factor for a family’s inability to continue to care for patients in their home and a common reason for admission to an inpatient hospice unit.

Terminal delirium is divided into 4 types: hyperactive 21%, hypoactive 29%, mixed 43%, and unclassified 7%. Hyperactive delirium is characterized by increased psychomotor activity and is the type of delirium most commonly recognized by the casual observer. Patients frequently exhibit agitation, psychosis, and mood liability. In addition, they may refuse to cooperate with medical care, may demonstrate disruptive behaviors, and may sustain injuries from falling. Hyperactive delirium is often associated with the adverse effects of anticholinergic drugs, drug intoxication, and withdrawal states. Hyperactive delirium is classified by Meagher et al. as containing 3 or more of the following: hypervigilance, restlessness, fast or loud speech, anger or irritability, combative behavior, and delusions.

Another common form of delirium is hypoactive delirium which occurs in 29% of the cases and is characterized as having less psychomotor activity. This type of delirium is more common in elderly patients and is less frequently recognized by clinicians due to the absence of disruptive or bizarre behavior. Patients with hypoactive delirium may appear sluggish and lethargic as well as confused. Meagher et al. classify hypoactive delirium as containing 4 or more of the following: unawareness, decreased alertness, sparse or slow speech,}

### Definition
The term delirium comes from the Latin *delirare* which means to become “crazy or to rave.” Other synonyms for delirium are acute brain failure, acute organic brain syndrome, acute confusional state, and postoperative psychosis. Although there are other synonyms, delirium remains the preferred term. Pies defines delirium as an acute or subacute disturbance of consciousness characterized by the reduced ability to focus, sustain, or shift attention appropriately. The hallmark sign of delirium is a fluctuating level of consciousness, which can change from hour to hour. It is preceded by a prodrome of restlessness, insomnia, and nightmares and may include slowed or slurred speech, irritability, combative behavior, impaired short-term memory, sensory distortions, psychotic phenomena, and a reversed sleep—wake cycle. Typically, delirium worsens at night and is followed with lucid periods in the morning.

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lethargy, decreased motor activity, staring, and apathy. A study in nonactively dying cancer patients with delirium found that although hyperactive delirium was more distressing to caregivers, both hypoactive and hyperactive delirium were equally distressing to patients.  

Mixed delirium satisfies both hypoactive and hyperactive components and occurs in 43% of cases. Unclassified delirium has no motor component and patients meet neither hyper- nor hypoactive criteria as described by Meagher et al.

**Pathophysiology**

The pathophysiology of delirium is poorly understood. The most accepted theory of delirium focuses on the neurotransmitter system. This theory states that “relative acetylcholine deficiency and dopamine excess could mediate the characteristic symptoms of delirium.” This theory is supported by the fact that delirium can be evoked by dopamine agonists and anticholinergic medications and can be successfully treated with dopamine receptor antagonists and possibly by cholinesterase inhibitors. Pies found high serum anticholinergic activity in patients with delirium. Cholinesterase inhibitor therapy was found to be useful in a study done by Jacobson (2005) to treat various types of delirium as cited in Pies. Dopaminergic excess can also contribute to or precipitate delirium and can be a side effect of the dopaminergic drugs used to treat Parkinson’s disease whereas dopamine antagonists, such as antipsychotic drugs like haloperidol, can be used to treat delirium. There is also evidence that deregulation of the limbic—hypothalamic—pituitary—adrenal axis, with pathologically sustained high levels of cortisol occurring with acute stress can precipitate and/or sustain delirium.

The development of delirium is considered a consequence of the diffuse impairment of brain tissue function. Disturbances in the internal environment of the brain, particularly interference with oxygen and glucose metabolism, are thought to underlie most cases of delirium. In addition, delirium can develop in patients with brain cancer with space-occupying lesions and associated cerebral edema. Other causes of delirium can be metabolic encephalopathy from drug side effects (eg, opioids, steroids, or chemotherapeutic agents), sepsis, oxygen deprivation, fluid, and electrolyte imbalances (eg, hyponatremia, dehydration, or hypercalcemia), hypoglycemia, and hepatic failure. Other factors that may cause or contribute to delirium include sleep deprivation, fecal impaction, and urinary retention.

**Advanced Age and Delirium**

In a group of patients admitted to an inpatient hospice unit for the management of delirium with a cancer diagnosis, Cobb et al found that delirium is not only a phenomenon of the elderly patients but occurs in patients of all ages. They found that patients with chronic problems such as diabetes mellitus, chronic obstructive pulmonary disease, history of alcohol abuse, or any type of communication impairment increases their vulnerability to delirium at the end of life. Preexisting cognitive decline such as the presence of Alzheimer dementia (AD) is the most confirmed risk factor for delirium. Delirium may be superimposed on preexisting AD, and it is sometimes not appreciated in elderly patients. Often a sudden burst of yelling, agitation, or aggressive behavior will signal the demented patient’s new onset of delirium. Other risk factors for delirium include older age, frailty, severe illness or multiple comorbidities, polypharmacy, and hospital admission due to infection or dehydration. In older patients with these risk factors plus the addition of another trigger (eg, urinary tract infection or catheter, lower respiratory tract infection, electrolyte abnormalities, and/or constipation) may contribute to the onset of delirium.

**Why is Delirium Underdiagnosed?**

Delirium is often apparent but in many cases goes undetected by the clinician. Some studies have shown that delirium is not detected in 22% to 50% of cases. Factors that contribute to the underdetection of delirium include preexisting dementia, depression, older age, presence of sensorial alterations (eg, hearing and vision impairments) and the hypovolemic presentation of delirium. Other possible reasons for nondetection of delirium are its fluctuating nature and the lack of formal cognitive assessment as part of routine screening across care settings. Moreover, the lack of obtaining an adequate informant history regarding the patient’s premorbid level of cognition and function, and ageist attitudes toward older people with an expectation of confusion may all contribute to a missed diagnosis. For example, Bruera et al document that clinicians frequently misinterpret agitation as an expression of pain in patients with hyperactive delirium, even though pain was not an issue prior to the development of delirium or after resolution of delirium. The distinguishing hallmark that should alert the clinician to the diagnosis of delirium is the sudden onset and fluctuating changes in the patient’s ability to focus and sustain attention.

**Causes of Delirium**

Delirium is usually multifactorial and the patients’ vulnerability to delirium increases with the overall burden of terminal illness. The most common contributors of delirium in patients with advanced cancer include medication (eg, opioids, anticholinergic, steroids, and antidepressants), infection (eg, pneumonia, urinary tract infection), fluid imbalances (eg, dehydration, overload), and electrolyte imbalances (eg, hypercalcemia). Furthermore, Cobb et al cites poor pain management, constipation, hypoxia, and poor glycemic control as contributing factors in delirium presentation at end of life.

Brunnhuber et al suggests that medication is the most common cause of delirium. The most frequent category of medication is opioids, followed by anxiolytics with more than
half of the patients receiving both medications. Other drugs cited to precipitate delirium are metoclopramide, antihistamines, corticosteroids, quinolones, and anticonvulsants as well as antidepressants, H2 blockers, and antiemetics. In addition, delirium may be triggered by the withdrawal of psychoactive drugs.

The central cause of delirium, when it relates to opioids, is not the opioid itself but rather dehydration and the resulting opioid toxicity. Cobb et al finds that decreased renal and liver function with resulting poor metabolism and excretion lead to toxic levels of medications at end of life. From these findings, Morita et al recommend that clinicians not overlook dehydration, especially in preterminal patients with minimum fluid retention symptoms and large doses of morphine due to the accumulation of opioid metabolites, which accelerate the development of delirium. Lawlor et al found that in patients with advanced cancer, delirium was reversible in 50% of episodes, which were precipitated by opioids and other psychoactive medications and dehydration. This delirium is frequently reversed with change in opioid or dose reduction, discontinuation of unnecessary psychoactive medication, or hydration. Ganzini states that low-dose hydration is still controversial and is being reevaluated as a palliative care option for patients in their final weeks of life.

Diagnosis of Delirium

According to the American Psychiatric Association’s (APA) Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, DSM-IV), there are 4 essential features needed to make a diagnosis of delirium. They include inattention, a sudden change in cognition, an acute and fluctuating disturbance of the consciousness, and an underlying medical cause. Inattention is manifested in the patient repeating questions and responses, being easily distracted by noise, and being only able to respond to simple commands. The patient exhibits perceptual disturbance by calling out for family, climbing out of bed or huddling in a chair, being overly fearful of treatments, and may appear frightened and suspicious of others. In addition, the patient may have sleep/wake cycle disturbance as evidenced by being awake at night and being drowsy during the day. The patient’s sudden change in cognition presents with activities being out of sequence to time and verbal cues being inappropriate to location. Finally, the patient may have the inability to recognize family or staff.

Knowledge of the patient’s baseline cognitive status is essential for the assessment of delirium. In the earliest evaluation, data should be collected from the patients’ family or caregivers regarding their mental status prior to the onset of delirium. With the knowledge of prior cognitive status, clinicians are able to identify early signs of delirium such as anxiety, anger, depression, or psychosis rather than misdiagnose, misinterpret, and mismanage delirium. With early recognition comes the ability to promptly deal with the underlying medical causes, provide rapid implementation of interventions, and reduce the severity and the duration of the delirium episode. And contrary to common belief, delirium can then be improved significantly, sometimes up to full remission, in the patient with terminal cancer.

The Confusion Assessment Method (CAM; see Figure 1) was developed to help clinicians without a psychiatric background quickly identify delirium. It is a brief 9-item instrument that can be completed in less than 5 minutes. This tool helps to identify the syndrome’s essential features necessary for making a diagnosis of delirium and is useful in distinguishing the difference between delirium and dementia. The diagnosis of delirium requires the presence of 2 criteria (acute onset and fluctuating course and inattention) and of either disorganized thinking or altered level of consciousness. Although the CAM is useful in diagnosing delirium, the severity of delirium is measured using the Memorial Delirium Assessment scale (MDAS; see Figure 2). The MDAS is a 10-item scale used specifically to measure the severity of delirium in patients with cancer. It includes items that are representative of the many features of delirium, reflecting the DSM-IV criteria and enables detection of both hypoactive and hyperactive forms.

Management of Terminal Delirium

Nonpharmacologic Interventions

Nonpharmacologic interventions are an important aspect of care for the delirious patient at end of life. Nursing interventions should focus on promoting a therapeutic environment that fosters a balance between sensory deprivation and sensory overload. Macleod states “the failing brain, like an ailing heart, benefits from the reduction in workload; hence it is desirable to limit but not deprive sensory input.” This balance is achieved by keeping the physical environment consistent: avoiding room or bed changes, maintaining patient routines, and promoting continuity of staffing.

In addition to the physical environment consistency, the characteristics of the environment are equally important. Avoiding ambiguous lighting assists in preventing illusions and hallucinations, thus a well-lit room is preferable. The noise level should be below 45 dB during the day and less than 20 dB at night. Eyeglasses and hearing aids should be available to help correct the patient’s misperceptions and personal items such as comforters and pillows should be provided to help promote environmental familiarity. In addition, noxious stimuli should be removed (eg, urinary catheters, intravenous pumps) and medical testing (eg, blood pressure and temperature monitoring) should be avoided. If the patient has hyperactive delirium that is stimulated by visitors, reduction in visits is warranted. Furthermore, the use of a clock and calendar are effective orienting cues.

The clinician should communicate with the patient in a simple and reassuring manner. The clinician should use simple questions such as “do you feel confused?” or “do you feel disoriented?” With the use of these techniques, the patient may become aware of her own confusion and thereby be reassured. Furthermore, it is helpful to stimulate the patient to perform easy...
tasks, such as eating, but excessive demands should not be made due to the patient’s weakened emotional stability. 10

In addition, Gagnon et al 15 found that psychoeducational interventions with the use of guidelines on how to react when delirium happens should be offered to family caregivers to reduce the burden that they experience from delirium. Family members should be instructed not to contradict or challenge what the patient says but rather take advantage of the patients’ lucid periods and provide orientation, reassurance, explanation, and clarification. 10,20 Some families may aggravate, rather than, improve the patient’s delirious state if they are not provided with education on delirium. 20

### Identification of Causative Factors

Morita et al 3 found that delirium diagnosed on admission to a palliative care unit may be reversible in 50% of patients and an even higher percentage of cases are reversible when triggered by drugs, dehydration, or hypercalcemia. Identification of possible causes of terminal delirium begins with a thorough physical examination of the patient. The clinician needs to be alert for any neurological signs that would signal a central nervous system (CNS) event, fever, dehydration, unmanaged pain, hypoxia, and hypercalcemia, as well as signs of organ failure, urine retention, constipation, bowel obstruction, and/or fecal impaction. 10 Interventions designed to lessen the delirium and to improve the overall comfort of the patient include titrating of pain medication to achieve improved pain control, instituting a bowel regimen, providing supplemental oxygen, promoting daytime activity, and avoiding hypoglycemia. 3 Any underlying reversible causes should be treated. 21

Next, both prescription and over-the-counter drugs should be reviewed as potential delirium triggers and subsequently decreased or stopped. 7 Drugs most frequently cited as

<table>
<thead>
<tr>
<th>Feature 1: Acute Onset and Fluctuating Course</th>
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<tbody>
<tr>
<td>This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions: Is there evidence of an acute change in mental status from the patient’s baseline? Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?</td>
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<tr>
<th>Feature 2: Inattention</th>
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<tr>
<td>This feature is shown by a positive response to the following question: Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?</td>
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<th>Feature 3: Disorganized thinking</th>
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<tr>
<td>This feature is shown by a positive response to the following question: Was the patient’s thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?</td>
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<th>Feature 4: Altered Level of consciousness</th>
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<tr>
<td>This feature is shown by a positive response to the following question: Overall, how would you rate this patient’s level of consciousness? (Alert [normal]; Vigilant [hyperalert, overly sensitive to environmental stimuli, startled very easily]; Lethargic [drowsy, easily aroused]; Stupor [difficult to arouse]; Coma; [unarousable]; Uncertain)</td>
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Figure 1. The Confusion Assessment Method Instrument. CAM Instrument and Algorithm adapted from Ann Internal Med. 1990;113(12):941-948. 17
**INSTRUCTIONS:** Rate the severity of the following symptoms of delirium based on current interaction with subject or assessment of his/her behavior or experience over past several hours (as indicated in each item.)

**ITEM 1-REDUCED LEVEL OF CONSCIOUSNESS (AWARENESS):** Rate the patient’s current awareness of and interaction with the environment (interviewer, other people/objects in the room; for example, ask patients to describe their surroundings).

- **0:** none (patient spontaneously fully aware of environment and interacts appropriately)
- **1:** mild (patient is unaware of some elements in the environment, or not spontaneously interacting appropriately with the interviewer; becomes fully aware and appropriately interactive when prodded strongly; interview is prolonged but not seriously disrupted)
- **2:** moderate (patient is unaware of some or all elements in the environment, or not spontaneously interacting with the interviewer; becomes incompletely aware and inappropriately interactive when prodded strongly; interview is prolonged but not seriously disrupted)
- **3:** severe (patient is unaware of all elements in the environment with no spontaneous interaction or awareness of the interviewer, so that the interview is difficult-to-impossible, even with maximal prodding)

**ITEM 2-DISORIENTATION:** Rate current state by asking the following 10 orientation items: date, month, day, year, season, floor, name of hospital, city, state, and country.

- **0:** none (patient knows 9-10 items)
- **1:** mild (patient knows 7-8 items)
- **2:** moderate (patient knows 5-6 items)
- **3:** severe (patient knows no more than 4 items)

**ITEM 3-SHORT-TERM MEMORY IMPAIRMENT:** Rate current state by using repetition and delayed recall of 3 words [patient must immediately repeat and recall words 5 min later after an intervening task. Use alternate sets of 3 words for successive evaluations (for example, apple, table, tomorrow, sky, cigar, justice)].

- **0:** none (all 3 words repeated and recalled)
- **1:** mild (all 3 repeated, patient fails to recall 1)
- **2:** moderate (all 3 repeated, patient fails to recall 2-3)
- **3:** severe (patient fails to repeat 1 or more words)

**ITEM 4-IMPAIRED DIGIT SPAN:** Rate current performance by asking subjects to repeat first 3, 4, then 5 digits forward and then 3, then 4 backwards; continue to the next step only if patient succeeds at the previous one.

- **0:** none (patient can do at least 5 numbers forward and 4 backward)
- **1:** mild (patient can do at least 5 numbers forward, 3 backward)
- **2:** moderate (patient can do 4-5 numbers forward, cannot do 3 backward)
- **3:** severe (patient can do no more than 3 numbers forward)

**ITEM 5-REDUCED ABILITY TO MAINTAIN AND SHIFT ATTENTION:** As indicated during the interview by rambling, irrelevant, or incoherent speech, or by tangential, circumstantial, or faulty reasoning. Ask patient a somewhat complex question (for example, “Describe your current medical condition.”).

- **0:** none (patient’s speech is coherent and goal-directed)
- **1:** mild (patient’s speech is slightly difficult to follow; responses to questions are slightly off target but not so much as to prolong the interview)
- **2:** moderate (disorganized thoughts or speech are clearly present, such that interview is prolonged but not disrupted)
- **3:** severe (examination is very difficult or impossible due to disorganized thinking or speech)

**ITEM 6-DISORGANIZED THINKING:** As indicated during the interview by rambling, irrelevant, or incoherent speech, or by tangential, circumstantial, or faulty reasoning. Ask patient a somewhat complex question (for example, “Describe your current medical condition.”).

- **0:** none (patient’s speech is coherent and goal-directed)
- **1:** mild (patient’s speech is slightly difficult to follow; responses to questions are slightly off target but not so much as to prolong the interview)
- **2:** moderate (disorganized thoughts or speech are clearly present, such that interview is prolonged but not disrupted)
- **3:** severe (examination is very difficult or impossible due to disorganized thinking or speech)

**ITEM 7-PERCEPTUAL DISTURBANCE:** Misperceptions, illusions, hallucinations inferred from inappropriate behavior during the interview or admitted by subject, as well as those elicited from nurse/family/chart accounts of the past several hours or of the time since last examination.

- **0:** none (no misperceptions, illusions, or hallucinations)
- **1:** mild (misperceptions or illusions related to sleep, fleeting hallucinations on 1-2 occasions without inappropriate behavior)
- **2:** moderate (hallucinations or frequent illusions on several occasions with minimal inappropriate behavior that does not disrupt the interview)
- **3:** severe (frequent or intense illusions or hallucinations with persistent inappropriate behavior that disrupts the interview or interferes with medical care)

**ITEM 8-DELUSIONS:** Rate delusions inferred from inappropriate behavior during the interview or admitted by the patient, as well as delusions elicited from nurse/family/chart accounts of the past several hours or of the time since the previous examination.

- **0:** none (no evidence of misinterpretations or delusions)
- **1:** mild (misinterpretations or suspiciousness without clear delusional ideas or inappropriate behavior)

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**Figure 2.** Memorial Delirium Assessment Scale (MDAS) © 1996. J Pain Symptom Manage. 1997;13(3):128-137.
deliriogenic include anticholinergic medications such as tricyclic antidepressants, antiserotone agents such as scopolamine, antinausea drugs, benzodiazepines, and corticosteroids. In addition, opioids especially morphine in large doses given in the dehydrated patient with poor renal function, can cause terminal delirium through substantial accumulation of the drug metabolites. Agitation may be mistaken for pain and result in the administration of higher doses of opioids that may further exacerbate delirium. Morita et al strongly recommends that opioid toxicity should be aggressively managed with intensive palliative methods such as opioid rotation and treatable hydration. Hydration, especially in preterminal patients with minimum fluid retention symptoms and large doses of morphine may be helpful in the treatment of delirium. At the same time, Morita et al does not consider it justified to administer artificial hydration to extremely ill patients with dehydration-related hypoactive delirium, if they have severe fluid retention and require low doses of opioids.

Opioid rotation is defined as “a change in opioid drug or route of administration with the goal of improving outcomes.” Opioid rotation begins with the selection of a new drug at a starting dose that minimizes potential risks of overdose while at the same time maintains analgesic effectiveness. To reduce the risk of unintentional overdose, the conversion ratio of one opioid to another should be reduced to 25% to 50% of the calculated equianalgesic dose, by using an existing equianalgesic dose table as a starting point.

Moryl et al documented the use of methadone as part of an opioid rotation strategy in patients with uncontrolled pain and severe delirium that were admitted to a palliative care cancer unit. They found that methadone was effective in the treatment of both refractory pain and terminal delirium. Most patients in their group had a short-term improvement in mental status as well as significant and lasting improvement in analgesia. The safety of methadone has also been demonstrated in the presence of chronic liver and renal failure, common at end of life. In addition, the eventual worsening of the patient’s mental status in this study was devoid of agitation and hyperactive delirium. Consequently, patients and their families who may opt for sedation at the end of life, as a means to manage terminal delirium an uncontrolled pain, should be informed about the possible advantages of methadone.

### Pharmacological Interventions

According to Saxena and Lawley, the primary aim in the management of delirium is to treat the underlying cause, but if this fails, it may be necessary to prescribe medication to treat distressing or dangerous behavioral disturbances. Haloperidol is the drug of choice in treatment of terminal delirium and is effective in both hyperactive and hypoactive forms. Haloperidol does not induce severe sedation but helps to treat the agitation associated with hyperactive delirium and allows the patient to rest once response is achieved. The advantages of haloperidol are its wide therapeutic margin of safety, ease of administration by a variety of routes, and its relative lack of cardiopulmonary and anticholinergic effects.

<table>
<thead>
<tr>
<th>ITEM 9-DECREASED OR INCREASED PSYCHOMOTOR ACTIVITY: Rate activity over past several hours, as well as activity during interview, by circling (a) hypoactive, (b) hyperactive, or (c) elements of both present.</th>
</tr>
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<tbody>
<tr>
<td>0: none (normal psychomotor activity)</td>
</tr>
<tr>
<td>a b c 1: mild (hyperactivity is barely noticeable, expressed as slightly slowing of movement. Hyperactivity is barely noticeable or appears as simple restlessness.)</td>
</tr>
<tr>
<td>a b c 2: moderate (hypoactivity is undeniable, with marked reduction in the number of movements or marked slowness of movement; subject rarely spontaneously moves or speaks. Hyperactivity is undeniable, subject moves almost constantly; in both cases, exam is prolonged as a consequence.)</td>
</tr>
<tr>
<td>a b c 3: severe (hypoactivity is severe; patient does not move or speak without prodding or is catatonic. Hyperactivity is severe; patient is constantly moving, overreacts to stimuli, requires surveillance and/or restraint; getting through the exam is difficult or impossible.)</td>
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<tr>
<th>ITEM 10-SLEEP-WAKE CYCLE DISTURBANCE (DISORDER OF AROUSAL): Rate patient’s ability to either sleep or stay awake at the appropriate times. Utilize direct observation during the interview, as well as reports from nurses, family, patient, or charts describing sleep-wake cycle disturbance over the past several hours or since last examination. Use observations of the previous night for morning evaluations only.</th>
</tr>
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<tbody>
<tr>
<td>0: none (at night, sleeps well; during the day, has no trouble staying awake)</td>
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<tr>
<td>1: mild (mild deviation from appropriate sleepfulness and wakefulness states: at night, difficulty falling asleep or transient night awakenings, needs medication to sleep well; during the day, reports periods of drowsiness or, during the interview, is drowsy but can easily fully awaken him/her)</td>
</tr>
<tr>
<td>2: moderate (moderate deviations from appropriate sleepfulness and wakefulness states: at night, repeated and prolonged night awakening; during the day, reports of frequent and prolonged napping or, during the interview, can only be roused to complete wakefulness by strong stimuli)</td>
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<tr>
<td>3: severe (severe deviations from appropriate sleepfulness and wakefulness states: at night, sleeplessness; during the day, patient spends most of the time sleeping or, during the interview, cannot be roused to full wakefulness by any stimuli)</td>
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Figure 2. (Continued).
Utilization of Confusion Assessment Method

1. Acute onset and fluctuating course
2. Inattention
3. Disorganized thinking
4. Altered Level of consciousness

The diagnosis of delirium requires 1 + 2 and either 3 or 4.

Identify and Treat Possible Causes

- Uncontrolled pain—initiate pain medication
- Drug toxicity [e.g., opioid]—opioid decrease or opioid rotation
- Polypharmacy—discontinue unnecessary medications
- Dehydration—hydration if appropriate with oral, intravenous or subcutaneous route
- Poor glycemic control—management of hypoglycemia
- Hypoxia—supplemental oxygen
- Hypercalcemia (esp. with bone metastasis)
- Drug side effects (e.g., steroids, anticholinergics, benzodiazepines)—discontinue or decrease dose of offending medications
- Urinary retention—Foley catheter
- Constipation or impaction—bowel program and disimpact if indicated
- Bowel obstruction—medication and decompression management
- Infection—antibiotics
- End-of-Life—medication management. See pharmacologic treatment

Nonpharmacological Treatment

- Caregiver education and counseling to minimize distress
- Approach to patient—simple and reassuring
- Promote daytime activity
- Maintain quiet, well-lit environment
- Promote staff continuity
- Avoid room and bed changes
- Provide hearing aids and eyeglasses
- Encourage personal items such as comforters and pillows
- Limit visitors in hyperactive delirium patient
- Remove noxious stimuli—catheters and pumps
- Limit medical monitoring and testing—BP and Temperature / Blood work
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- Remove noxious stimuli—catheters and pumps
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- Remove noxious stimuli—catheters and pumps
- Limit medical monitoring and testing—BP and Temperature / Blood work

Pharmacological Treatment

First line agent
- Haloperidol 0.5-2 mg Q 1 hour prn

Alternatives
- Risperidone 0.5 to 1 mg bid
- Olanzapine 2.5-5 mg daily
- Quetiapine fumarate 50-100 mg bid.

Figure 3. Algorithm for identification and treatment of terminal delirium. Bid indicates twice daily.

at low doses. The major side effects of haloperidol, which are relevant to elderly patients at end of life, are drug-induced parkinsonism (DIP). Drug-induced parkinsonism, sometimes referred to as akathisia, is linked to discomfort, choking, falls in ambulatory patients, and decreased bed mobility in bed bound patients. Akathisia is a syndrome of motor restlessness and a feeling of muscular quivering that can cause significant discomfort and may be mistaken as worsened agitation. Akathisia can occur with the first dose of haloperidol or can appear as late as 3 to 5 days after haloperidol initiation. Contraindications to haloperidol in delirium include hepatic encephalopathy, delirium tremens (DTs), AIDS, and Lewy body dementia. In these situations, benzodiazepines are recommended, although they may aggravate delirium if administered in inadequate doses. Benzodiazepines such as lorazepam can be administered in large enough doses to settle and sedate the delirious patient. Saxena and Lawley found that the common selection of lorazepam to treat delirium is troubling because benzodiazepines themselves are implicated in causing delirium. It is usually best to avoid benzodiazepines in managing patients with delirium at end of life unless there are contraindications to other preferred medications.
2.5–5 mg daily), or quetiapine fumarate (Seroquel; 50–100 mg bid).\(^1\)\(^4\) The Cochrane Collaboration (2007)\(^2\)\(^5\) found no difference in the efficacy of low-dose haloperidol in comparison with olanzapine or quetiapine although haloperidol in high doses was associated with greater incidence of side effects, mainly DIP. These medication options are aimed at controlling agitated behaviors, psychosis, and cognitive dysfunction and are not intended to sedate the patient but rather to relieve the patient’s symptoms.\(^2\)\(^0\)

**Conclusion**

Delirium is a common symptom in the geriatric population with cancer at the end of life. The clinician needs to have the ability to recognize the early signs of delirium so that predisposing factors can be promptly eliminated. After that, early intervention can be initiated with the use of nonpharmacological approaches as well as with the use of the first-line pharmacologic agent haloperidol.\(^3\) More research is needed on the use of the atypical antipsychotics risperidone, olanzapine, and quetiapine to assess whether they may be more efficacious than haloperidol. In addition, although nonpharmacologic interventions may be useful in terminal delirium, no controlled studies have been conducted to verify their effectiveness.\(^6\) Lastly, there is conflicting and inconsistent data regarding the efficacy of pharmacological treatment for delirium prevention and no recommendation can be made for the routine clinical prophylactic use of any pharmacological agent in the prevention of delirium (Figure 3).\(^2\)\(^4\)

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