

Evaluation and Management of Delirium in Hospitalized Older Patients

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Delirium is common in hospitalized older patients and may be a symptom of a medical emergency, such as hypoxia or hypoglycemia. It is characterized by an acute change in cognition and attention, although the symptoms may be subtle and usually fluctuate throughout the day. This heterogeneous syndrome requires prompt recognition and evaluation, because the underlying medical condition may be life threatening. Risk factors for delirium include visual impairment, previous cognitive impairment, severe illness, and an elevated blood urea nitrogen/serum creatinine ratio. Interventions that have been shown to reduce the incidence of delirium in at-risk hospitalized patients include repeated reorientation of the patient to person and place, promotion of good sleep hygiene, early mobilization, correction of dehydration, and the minimization of unnecessary noise and stimuli. The treatment of delirium centers on the identification and management of the medical condition that triggered the delirious state. Nonpharmacologic interventions may be beneficial, but antipsychotic agents may be needed when the cause is nonspecific and other interventions do not sufficiently control symptoms such as severe agitation or psychosis. Although delirium is a temporary condition, it may persist for several months in the most vulnerable patients. Patient outcomes at one year include a higher mortality rate and a lower level of functioning compared with age-matched control patients. (*Am Fam Physician*. 2008;78(11):1265-1270. Copyright © 2008 American Academy of Family Physicians.)

Delirium is characterized by an acute change in cognition and attention. It develops over hours to days and usually fluctuates during the course of the day. It is the most common complication in older patients who are hospitalized, affecting 20 percent of those older than 65 years.^{1,2} In 10 to 30 percent of older patients admitted to the hospital from the emergency department, delirium is the presenting symptom of a potentially life-threatening condition (e.g., a medication overdose or toxicity, hypoglycemia, hypoxia, sepsis).³ In patients with delirium, the average increase in length of hospital stay is eight days, and mortality rates are twice as high compared with similarly matched patients without delirium.⁴ Physical and cognitive recovery at six and 12 months is significantly worse in patients with delirium compared with age-matched control patients.⁴ Adverse outcomes from delirium include aspiration, prolonged immobility and its repercussions, and loss of independence.

Epidemiology

Although delirium occurs in 11 to 42 percent of hospitalized patients and may affect up to

50 percent of those at high risk,^{1,5} the condition is unrecognized in up to 70 percent of patients.⁶ Mortality rates of hospitalized patients with delirium are 22 to 76 percent, and the one-year mortality rate is 35 to 40 percent.⁴

Although dementia and delirium are thought to be two distinct entities, patients with dementia are prone to delirium; two thirds of cases of delirium occur in patients with underlying cognitive impairment or dementia.⁷ Patients with dementia are more likely to present to the hospital with delirium, whereas those with no underlying dementia tend to develop delirium during their hospitalization.⁸

Etiology and Pathophysiology

The pathophysiology of delirium is not well understood. However, it is likely that multiple mechanisms are involved, and research has shown that changes in cerebral perfusion pressure occur in patients with delirium. One small study using single-photon emission computed tomography suggests that perfusion abnormalities can occur in the frontal or parietal areas of the cerebral cortex.⁹ Therefore, the development of delirium is usually multifactorial and involves the interrelationship between

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
The Confusion Assessment Method is recommended for the bedside diagnosis of delirium.	C	18, 19
Antipsychotic medications may be considered for selected patients with delirium only when drug treatment is necessary to control delirium symptoms.	C	18, 23
A predictive model can accurately assess a patient's risk of developing delirium.	C	26
Addressing six risk factors (i.e., cognitive impairment, sleep deprivation, dehydration, immobility, vision impairment, and hearing impairment) in at-risk hospitalized patients can reduce the incidence of delirium by 33 percent.	B	27
Hospital staff educational programs have been shown to effectively reduce delirium duration and related mortality.	B	29, 34

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

a predisposed patient and exposure to triggering factors.¹⁰ Risk factors for developing delirium include underlying dementia, poor functional status, heavy alcohol use, presence of a urinary catheter, and use of multiple medications; metabolic disturbances or use of certain medications can precipitate delirium (Table 1^{11,12}). A relatively benign insult may lead to delirium in at-risk patients. In patients who are less vulnerable, delirium usually only develops with a major insult, such as major surgery requiring general anesthesia or a severe illness that requires admission to an intensive care unit.

Anticholinergics, narcotic medications, and sedative-hypnotics are common precipitants of delirium. There is substantial evidence that cholinergic deficiency is a factor in the development of delirium.¹³ The release of cytokines has been shown to increase the permeability of the blood-brain barrier, which may also play a role in the development of the condition.¹⁴ Table 2 lists medications that may contribute to the onset of delirium.¹⁵

Diagnosis DIFFERENTIAL DIAGNOSIS

Delirium must be differentiated from other conditions that may cause acute confusion. It is important to distinguish if the acute confusion is due to a primary neurologic condition, such as dementia, a psychotic disorder, or a neurovascular insult, or if it is a complication of a systemic illness. Focal neurologic signs are usually present if a neurovascular insult or other neurologic etiologies are the cause.

Dementia can usually be identified in a patient with a history of a progressive decline in memory over months to years. This may be difficult to determine, particularly if no family member is present when the patient is admitted to the hospital. In addition, dementia with Lewy bodies may have features similar to delirium, such as fluctuating symptoms and hallucinations.¹⁶ In general, patients with dementia have intact attention and alertness.¹⁶

Patients with psychosis usually maintain normal sleep-wake cycles, orientation to person and place, and attention.¹⁷ The orientation of patients with depression or severe anxiety is generally preserved, and cognitive performance usually improves with encouragement.¹⁷ Acute mania is similar to delirium in that patients may be hyperactive; however, hyperactivity persists throughout a manic episode, whereas patients with delirium usually have interspersed periods of somnolence. Patients with mania are generally oriented, unlike patients with delirium.¹⁷

Table 1. Risk Factors and Precipitants for Delirium

Risk factors	Precipitants
Age older than 65 years	Electrolyte abnormalities
Dehydration	Environmental factors (e.g., excessive noise, interrupted sleep, unnecessary stimuli)
Dementia	Hypoxia, hypoglycemia, or ischemia
Functional dependence or immobility	Medications (especially anticholinergics, narcotics, and sedative-hypnotics); see Table 2
Infection at hospital admission	Neurologic disorder (e.g., stroke, seizures)
Malnutrition	Pain
Multiple comorbidities	Sleep deprivation
Multiple medications	Surgery
Chronic renal or hepatic impairment	Urinary catheter
Severe illness, admission to intensive care unit	Withdrawal from alcohol, illicit drugs, or benzodiazepines
Vision or hearing impairment	

Information from references 11 and 12.

Table 2. Selected Medications That May Precipitate Delirium

Anticholinergics	Antipsychotics
Anticonvulsants	Barbiturates
Antidepressants	Benzodiazepines
Antihistamines	Histamine H ₂ blockers
Antiparkinsonian agents	Lithium
	Opioid analgesics

Adapted with permission from Zafraou B. Troubleshooting delirium in elderly inpatients. *Psychiatric Times*. 2007;24(7):64-67. <http://www.psychiatrictimes.com/display/article/10168/54886>. Accessed July 3, 2008.

CLINICAL DIAGNOSIS

The diagnosis of delirium is made clinically. American Psychiatric Association guidelines recommend use of the Confusion Assessment Method (CAM) for the detection of delirium.¹⁸ The CAM is a modified version of criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.¹⁹ The shorter, four-item CAM can be completed at bedside in less than five minutes and compares favorably to more complex assessments.¹⁹ A diagnosis of delirium using the CAM instrument requires an acute onset, a fluctuating course, the presence of inattention, and either disorganized thinking or an altered level of consciousness.¹⁹ Patients may exhibit a hyperactive, hypoactive, or mixed subtype of delirium. Patients with hypoactive delirium, which is the most common subtype,²⁰ may be subdued, lethargic, stuporous, or comatose; therefore, it is important to arouse a “sleeping” patient during hospital rounds to assess the level of consciousness. Patients with the hyperactive subtype may be agitated, anxious, disoriented, or delusional. These patients may insist that they are at home and that members of the hospital staff are intruders. The mixed subtype has both hypoactive and hyperactive features. Patients in all subtypes may also exhibit disorganized speech, impaired cognition, memory deficits, sleep-wake cycle disturbances, and labile emotions.

The Mini-Mental State Examination (MMSE) can be used to identify problems with attention and cognition (e.g., orientation to person, place, and date; spelling the word “world” backwards; serial-seven subtraction).¹⁶ Although it was developed for patients with dementia and is only 33 percent sensitive for the diagnosis of delirium,¹¹ the MMSE may be helpful in following patients over the course of delirium (scores improve as the condition resolves).¹⁶

DIAGNOSTIC TESTING

The following studies may be helpful, depending on history and physical examination findings: serum chemistries, thyroid studies, electrocardiography, serum

troponin level, pulse oximetry or arterial blood gas measurement, urinalysis with culture, complete blood count, chest radiography, and lumbar puncture. Neuroimaging is generally not indicated. However, a patient with focal neurologic signs, a history of head trauma, or fever associated with encephalopathy should receive computed tomography of the head. Patients presenting with encephalopathy who have no available history should receive imaging, and patients with fever should additionally receive lumbar puncture. Electroencephalography is rarely needed, unless the cause of delirium is unclear and occult seizure is a consideration.^{11,16} Table 3 addresses the evaluation of underlying medical conditions that may lead to delirium.^{21,22}

Management and Prevention

The treatment of delirium requires addressing the underlying causes. Initial treatment involves assessing respiratory status, providing adequate oxygenation, evaluating for the presence of acute myocardial or cerebrovascular ischemia, and maintaining hydration. Other general supportive measures should include initiating venous thromboembolism prophylaxis, repositioning the patient often to prevent decubitus ulcers, mobilizing the patient as early as possible, and removing urinary catheters. Physical restraints should be avoided whenever possible.

Drug treatment is used only when other interventions are ineffective in controlling agitation and an underlying cause of delirium has been identified, and treatment of the underlying cause has been initiated. Haloperidol (Haldol) has been the most studied antipsychotic drug for controlling delirium symptoms. Haloperidol and atypical antipsychotics are recommended if drug treatment is necessary^{18,23} (Table 4¹¹). However, there are no published randomized controlled trials to establish the safety and effectiveness of any antipsychotic drug for the management of delirium symptoms.²⁴ A recent systematic review recommended larger comparative trials to determine the safety and effectiveness of atypical antipsychotics in patients with delirium.²⁵ Future drug treatment for delirium may include the use of procholinergic agents to increase acetylcholine activity in the brain, selective dopamine antagonists, and drugs that enhance cerebrovascular flow (e.g., anti-inflammatory or antiplatelet agents).

The optimal treatment of delirium involves primary

Anticholinergics, narcotic medications, and sedative-hypnotics are common precipitants of delirium.

Table 3. Evaluation of Underlying Medical Conditions That May Lead to Delirium

<i>Condition</i>	<i>Evaluation</i>
Acid-base disorders	Basic metabolic panel; arterial blood gas measurement, if an acid-base disorder is suspected or suggested by serum electrolyte levels
Anemia (hemoglobin level < 10 g per dL [100 g per L])	Complete blood count
Dehydration	Physical findings (e.g., reduced skin turgor, dry mucous membranes), orthostatic blood pressure and pulse measurements, urine specific gravity test, serum osmolality measurement, blood urea nitrogen/serum creatinine ratio
Electrolyte abnormalities (especially sodium, magnesium, and calcium)	Serum chemistries
Endocrine abnormalities (e.g., hyper- or hypothyroidism, Cushing syndrome, adrenal insufficiency)	Thyroid-stimulating hormone level; serum cortisol level or adrenocorticotropic hormone stimulation test, as needed
Hyper- or hypoglycemia	Serum glucose level
Hyper- or hypothermia	Measurement of patient's core temperature
Hypercarbia or hypoxemia	Pulse oximetry; arterial blood gas measurement, as needed
Infection	As indicated: blood cultures, complete blood count, chest radiography, CT, lumbar puncture, urinalysis with culture
Liver failure or insufficiency	Liver function tests and transaminase levels; serum ammonia level, as needed
Medications (especially anticholinergics, narcotic medications, or sedative-hypnotics)	Review of outpatient and inpatient medication use
Myocardial ischemia	Electrocardiography; serum troponin and myoglobin levels, as needed
Pain	Use of pain assessment scales, review of hospitalization (noting recent falls or surgical procedures)
Renal failure or insufficiency	Blood urea nitrogen level, serum creatinine level, urinalysis, estimated glomerular filtration rate
Stroke, including intracerebral hemorrhage	Neurologic examination; CT of the head, as indicated
Surgery (especially orthopedic or cardiac procedures)	—
Toxicities (e.g., drug or alcohol intoxication or withdrawal, heavy metal poisoning)	Review of social history and occupational or other exposures; serum alcohol level or urine/serum toxicology, as needed
Vasculitis	As indicated: erythrocyte sedimentation rate, highly sensitive C-reactive protein level
Vitamin deficiencies	Serum B ₁₂ and folate levels

CT = computed tomography.

Information from references 21 and 22.

prevention, which includes the reduction of modifiable risk factors. A useful, validated predictive model for delirium (Table 5) incorporates four risk factors and places patients in low-, intermediate-, or high-risk groups.²⁶ Those in the high-risk category have an approximately 80 percent chance of developing delirium while hospitalized.²⁶ Hospital staff educational programs and patient interventional programs have been shown to successfully reduce delirium by up to 33 percent in at-risk patients.²⁷ Nonpharmacologic interventions for reducing the risk of delirium include regular daily activities that are cognitively stimulating; correction of dehydration; early mobilization (bedside range-of-motion exercises if patient is bedridden); minimization of unnecessary noise and stimuli; promotion of good sleep hygiene; removal of urinary catheters and physical

restraints, when indicated; repeated reorientation; and the use of eyeglasses or a magnifying lens.²⁷

A study of medically hospitalized patients found that, by addressing six risk factors, one third fewer cases of delirium occurred compared with the control group.²⁷ The six factors included cognitive impairment, sleep deprivation, immobility, dehydration, vision impairment, and hearing impairment.²⁷ However, for a multi-component intervention to be effective in reducing delirium frequency, it is essential that there is adherence to the strategies used in the intervention.^{28,29}

Studies on prevention using antipsychotics are limited in number and only involve postoperative patients. A recent Cochrane review noted that prophylactic haloperidol after hip surgery did not reduce the incidence of delirium, but reduced its severity and duration.³⁰

Table 4. Pharmacologic Treatment of Delirium

Medication	Dosage	Adverse effects	Comments
Conventional antipsychotics			
Haloperidol (Haldol; brand not available as an oral tablet in the United States)	0.5 to 1 mg orally, twice daily; additional doses every four hours, as needed	Extrapyramidal symptoms, particularly with dosages greater than 3 mg per day; prolonged corrected QT interval on electrocardiography	Agent of choice; avoid intravenous use due to short duration of action; avoid in patients with withdrawal syndrome, hepatic insufficiency, or neuroleptic malignant syndrome
Atypical antipsychotics			
Risperidone (Risperdal)	0.5 mg twice daily	Extrapyramidal effects equal or slightly less than with haloperidol; prolonged corrected QT interval on electrocardiography	Tested only in small, uncontrolled studies; associated with increased mortality in older patients with dementia
Olanzapine (Zyprexa)	2.5 to 5 mg daily		
Quetiapine (Seroquel)	25 mg twice daily		
Benzodiazepines			
Lorazepam (Ativan)	Initial 0.5- to 1-mg dose orally; repeat every four hours, as needed	Paradoxical excitation, respiratory depression, oversedation	Should not be used unless patient has alcohol or benzodiazepine withdrawal, Parkinson disease, or neuroleptic malignant syndrome

NOTE: Pharmacologic treatment of delirium should be short-term and considered in selected patients only when the cause is nonspecific and other interventions do not sufficiently control symptoms.

Adapted with permission from Inouye SK. Delirium in older persons [published correction appears in *N Engl J Med*. 2006;354(15):1655]. *N Engl J Med*. 2006;354(11):1164.

Prognosis

Prospective trials of patients older than 70 years who developed delirium while hospitalized found that approximately 12 percent had persistent delirium at discharge.³¹ The independent risk factors for persistent delirium were dementia, vision impairment, functional impairment, high comorbidity, and the use of physical restraints.³⁰ Persistent delirium may take weeks to resolve, and can take months or longer in some cases.³²

According to another prospective study, MMSE scores of patients with delirium at two months and at 12 months showed a decline of approximately three points (out of 30). Patients with baseline dementia and delirium had a five-point reduction in MMSE scores at 12 months. Almost 40 percent of these patients required placement in a skilled nursing facility.^{31,32} Functional status also had a greater decline at 12 months compared with similarly matched patients without delirium. At 12 months, the mortality rate was 38 percent for patients with delirium, compared with 12 percent for those in the control group.⁴ Another study found a similar one-year mortality rate of 41 percent.³³ Patients with the hypoactive subtype of delirium had the highest one-year mortality; this group was 1.62 times more likely to

die compared with patients who had the hyperactive or mixed subtype.³³

Hospital staff education programs and focusing on caregiver-patient interaction has been shown to significantly reduce the duration of delirium, length of

Table 5. Predictive Model for the Risk of Delirium in Hospitalized Older Patients

Risk factor	Points
Vision impairment	1
Cognitive impairment	1
Severe illness (APACHE score > 16, or nurse rating of severe)	1
Elevated blood urea nitrogen/serum creatinine ratio (> 18)	1
Total: _____	

NOTE: Risk stratification using the point total: low risk = 0 points, 10 percent risk of developing delirium; intermediate risk = 1 or 2 points, 25 percent risk; high risk = 3 or 4 points, 80 percent risk.

APACHE = Acute Physiology and Chronic Health Evaluation.

Information from reference 26.

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hospital stay, and mortality in patients with delirium.^{29,34} Patients who receive these interventions may still require placement in a skilled nursing facility, but have shorter lengths of stay in the facility, saving approximately 15 percent in medical costs.³⁵

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Author disclosure: Nothing to disclose.

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