



Official reprint from UpToDate®

www.uptodate.com © 2023 UpToDate, Inc. and/or its affiliates. All Rights Reserved.

Wolters Kluwer

Patients with cancer: Clinical features and diagnosis of cognitive impairment and delirium

AUTHORS: [Jacynthe Rivest, MD](#), [Jon Levenson, MD](#)**SECTION EDITORS:** [Jonathan M Silver, MD](#), [Susan D Block, MD](#)**DEPUTY EDITOR:** [David Solomon, MD](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

Literature review current through: **Oct 2023**.

This topic last updated: **Mar 28, 2023**.

INTRODUCTION

Cognitive impairment frequently occurs in patients with cancer and may negatively affect functioning and quality of life [1,2]. A subset of cancer patients with cognitive impairment can experience delirium, which is a neuropsychiatric syndrome [3,4]. Delirium is distressing for patients and families, can interfere with recognition and management of symptoms such as pain, and is associated with increased morbidity and mortality.

This topic reviews the clinical features of cognitive impairment in patients diagnosed with and treated for cancer, as well as the clinical features and diagnosis of delirium. Other topics discuss cognitive function after cancer treatment (ie, in cancer survivors), the clinical features and diagnosis of delirium in palliative care, the management of delirium in cancer patients, and the clinical features and diagnosis of other psychiatric disorders in cancer patients.

- (See "[Cognitive function after cancer and cancer treatment](#)".)
- (See "[Approach to symptom assessment in palliative care](#)", section on 'Delirium'.)
- (See "[Management of psychiatric disorders in patients with cancer](#)", section on 'Delirium'.)
- (See "[Patients with cancer: Overview of the clinical features and diagnosis of psychiatric disorders](#)".)

COGNITIVE IMPAIRMENT

Overview — Based upon multiple studies, patients with cancer, including cancer located outside of the central nervous system, often report cognitive decline [5,6]. However, the magnitude of the changes is typically modest, and functional impairment is usually minimal [5,7,8].

Standardized testing of patients with cancer indicates that cognitive dysfunction can occur in several domains, including [5,6]:

- Attention
- Concentration
- Executive functions (eg, planning, problem solving, and response inhibition)
- Information processing speed
- Memory

In addition, patient self-reports (rather than standardized tests) indicate that the prevalence of cognitive impairment is greater in patients with cancer than the general population and may adversely affect patient functioning and quality of life. Patient self-reports may provide information about subtle cognitive changes that are not detected by standard neuropsychological tests, but self-reports are generally nonspecific and influenced by beliefs and stress [6]. A nationally representative survey identified individuals with a history of cancer (n >1300) and individuals with no history of cancer; after controlling for potential confounding factors (eg, age, education, and self-rated general health), the analyses found that self-rated memory problems were present in more individuals with a history of cancer than controls (14 versus 8 percent) [9].

The duration of cognitive impairment in patients with cancer varies, and may extend beyond the acute illness and its treatment.

Prevalence — Although the prevalence of cognitive impairment in cancer patients varies due to differences in study populations and type of assessment [5,8], reviews estimate that impairment after diagnosis of cancer but prior to treatment occurs in approximately 20 to 30 percent of patients [5,6].

Cancer treatments are associated with neuropsychological deficits in up to 75 percent of patients [5,6]. However, in some cases, cancer-treatment related deficits are subtle and are associated with little or no functional impairment.

There are no established risk factors for cognitive impairment in patients with cancer, but increased age (eg, age \geq 65 years) and decreased baseline cognitive reserve (intellectual

capacity) appear to increase the risk [1,5,6,10]. In older patients, cancer-related cognitive decline may be more likely in those with fatigue, sleep problems, and frailty [1].

Pathogenesis — The neurobiologic mechanisms by which cognitive function declines in cancer patients have not been completely elucidated. Nonetheless, both structural and functional central nervous system changes have been correlated with cognitive impairment. It is likely that different mechanisms contribute and that cognitive dysfunction in some patients reflects an interaction between multiple factors [2].

Potential causes of cognitive impairment include [1,2,5,6,10,11]:

- Brain metastases – New-onset cognitive impairment in cancer patients should prompt brain imaging to look for brain metastases, especially in patients with primary tumors that have a relatively high rate of metastasizing to the brain. (See "[Epidemiology, clinical manifestations, and diagnosis of brain metastases](#)", section on 'Primary tumors'.)
- Dehydration.
- Electrolyte imbalances.
- Infection/sepsis.
- Major organ failure.
- Paraneoplastic syndromes.
- Cancer treatments – Many studies have focused upon chemotherapy's effect on cognition, which is commonly referred to as "chemobrain." As an example, a meta-analysis of five cross-sectional studies examined cognition in patients with breast cancer who were receiving or had received adjuvant chemotherapy (n = 208), and in controls (eg, breast cancer patients who did not receive adjuvant chemotherapy; n = 122) [12]. Executive functioning, language, memory, and spatial ability were each worse in patients treated with chemotherapy than controls, and the clinical differences were small to moderate.

However, it is often difficult to attribute adverse cognitive changes solely to chemotherapy because many patients in these studies received other cancer treatments that can affect cognition, such as hormonal therapy (eg, corticosteroids), or radiation therapy and surgery involving the use of general anesthesia.

Specific agents implicated in chemotherapy-related cognitive dysfunction include [2,11]:

- Asparaginase

- [Capecitabine](#)
- [Chlorambucil](#)
- [Cytarabine](#)
- Cytokines
- [Fluorouracil](#)
- [Ifosfamide](#)
- Interferon-alpha
- Interleukin-2
- [Methotrexate](#)
- [Procarbazine](#)
- [Vincristine](#)

Some data indicate that cognitive deficits related to cancer chemotherapy can become a long-term side effect that persists beyond treatment. (See "[Cognitive function after cancer and cancer treatment](#)".)

- Other medications such as anticholinergics, as well as medications used for anxiety, agitation, and pain (eg, benzodiazepines, and opioids).
- Comorbid psychiatric disorder – Patients with cancer often have psychiatric comorbidities that can lead to changes in cognition, including memory loss, impaired concentration, and decreased executive functioning. As an example, cognitive impairment may be a symptom of a depressive syndrome, such as major depression ([table 1](#)) or minor depression ([table 2](#)), if the impairment occurs in conjunction with other depressive symptoms like dysphoria, anhedonia, and suicidal ideation or behavior. In addition, cancer patients, especially those who are older (eg, age ≥ 65 years) can present with cognitive decline secondary to a neurodegenerative disorder. Substance intoxication or withdrawal can also contribute to impaired cognition.

Screening — Clinicians who want to screen patients with cancer for cognitive impairment can use either the Montreal Cognitive Assessment (MoCA) or the Mini Mental State Examination (MMSE) [[13,14](#)]. These standardized tests should be interpreted using age- and education-based normative values.

The MoCA is prone to yielding false positives. A prospective study of patients with brain tumors (n = 58) found that sensitivity for cognitive impairment was superior with the MoCA than the MMSE (62 versus 19 percent), but that specificity was superior with the MMSE (94 versus 56 percent) [[15](#)]. The MoCA is accessible online and in multiple languages at the [MoCA website](#). By contrast, the MMSE is copyrighted and must be purchased [[16](#)].

Additional information about the MoCA and MMSE is discussed separately. (See ["Mental status scales to evaluate cognition"](#), section on 'Scales with moderate assessment times (5 to 15 minutes)').

DELIRIUM

Overview — A subset of patients with cognitive impairment can experience delirium, which is a neuropsychiatric syndrome that involves a disturbance in attention resulting from another medical illness, a medication or drug of abuse, or exposure to a toxin [4]. Delirium is common in patients with cancer and can cause distress in patients, caregivers, and families, due to frightening symptoms that may prevent family members from communicating with their loved one. In addition, delirium is associated with poor outcomes that include prolonged hospitalizations, and increased morbidity and mortality [3,4]. As an example, a study of hospitalized cancer patients who developed delirium (n = 140) found that 30-day mortality was 25 percent [17]. Early recognition of delirium may enable clinicians to treat the cause and avert any adverse outcomes [11].

The subsections below discuss delirium in patients with cancer. The clinical features, causes, assessment, diagnosis, and differential diagnosis of delirium in general clinical settings are discussed in detail separately, and delirium in patients approaching the end of life is also discussed separately. (See ["Diagnosis of delirium and confusional states"](#) and ["Overview of managing common non-pain symptoms in palliative care"](#), section on 'Delirium'.)

Prevalence — The incidence of delirium in patients with cancer varies among different subgroups and hospital settings, such as general medical or oncology units and palliative care units [18]. In addition, some reported rates may be inaccurate because they were based upon screening tools that were not validated for case ascertainment.

Delirium is a common complication of cancer and its treatment, especially in patients who are hospitalized and patients with advanced disease [19,20]. Reviews suggest that at a minimum, the prevalence of delirium in hospitalized patients is approximately 10 to 30 percent [3,18]. However, higher rates have been reported; as an example, a prospective study of 90 patients undergoing hematopoietic stem cell transplantation found that during five weeks of hospitalization, delirium occurred in 50 percent [21].

Pathogenesis — Delirium is a neuropsychiatric disorder that is caused by physiologic disturbances and often involves multiple etiologies [3,4,11]. Among patients with cancer, the

potential causes of delirium overlap with those that can cause cognitive impairment in general. (See ['Pathogenesis'](#) above.)

Additional information about the pathogenesis of delirium is discussed separately. (See ["Diagnosis of delirium and confusional states", section on 'Pathogenesis'.](#))

Clinical features — The clinical features of delirium in patients with cancer can include the following [\[3,4\]](#):

- Sudden onset of symptoms that typically fluctuate in severity during the day
- Decreased level of consciousness (alertness or arousal)
- Attentional disturbances
- Cognitive impairment as manifested by:
 - Apraxia
 - Agnosia
 - Executive function (eg, planning) disturbances
 - Language disturbances
 - Memory impairment
 - Visuospatial dysfunction
 - Disorientation
- Delusions
- Mood symptoms (eg, dysphoria and lability)
- Neurologic findings (eg, asterixis, myoclonus, and tremor)
- Perceptual disturbances (illusions or hallucinations)
- Psychomotor activity is increased or decreased
- Sleep-wake cycle disturbances
- Speech is incoherent
- Thought process is disorganized

Screening — Screening tools can help clinicians diagnose delirium in medically ill patients. Among the instruments that have been validated in patients with cancer, we suggest the Confusion Assessment Method (CAM) ([table 3](#)), which has been used in hospitalized patients [\[3,18\]](#). Reasonable alternatives to the CAM include the Memorial Delirium Assessment Scale ([form 1A-B](#)) and the Delirium Rating Scale-Revised 98. Delirium in cancer patients is frequently missed and is often misdiagnosed as akathisia, anxiety, dementia, depression, or psychosis [\[11,22\]](#).

Diagnosis — According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR), the diagnosis of delirium requires each of the following criteria [4]:

- Disturbance in attention and awareness that develops quickly (usually hours to days) and tends to fluctuate each day.
- Disturbance in cognition (eg, memory, orientation, language, visual spatial ability, and/or perception).
- The disturbances in attention, awareness, and cognition are not better explained by another neurocognitive disorder and do not occur in the context of coma.
- Evidence from the history, physical examination, or laboratory findings indicate that the disturbances are caused by a general medical condition, substance intoxication or withdrawal, and/or medication side effect.

Subtypes of delirium have been delineated, based upon the patient's psychomotor behavior and level of arousal [4]:

- Hypoactive subtype – Psychomotor retardation, lethargy, and decreased level of arousal.
- Hyperactive subtype – Restlessness, agitation, and hypervigilance. Mood lability, failure to cooperate with care, and psychotic features may also be present.
- Mixed level of activity – Level of activity fluctuates.

In addition, delirium is classified as acute (lasting a few hour or days) or persistent (lasting weeks to months) [4].

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "[Patient education: Delirium \(confusion\) \(The Basics\)](#)")
- Beyond the Basics topic (see "[Patient education: Delirium \(Beyond the Basics\)](#)")

SUMMARY

- **Cognitive impairment**

- **Overview** – Patients with cancer, including cancer located outside of the central nervous system, often report cognitive decline. However, the magnitude of the changes is typically modest, and functional impairment is usually minimal. Cognitive dysfunction can occur in several domains, including attention, concentration, executive function, information processing speed, and memory. The duration of cognitive impairment in patients with cancer varies and may extend beyond the acute illness and treatment. (See '[Overview](#)' above.)
- **Prevalence** – Among patients with cancer, the prevalence of cognitive impairment after diagnosis of cancer but prior to treatment is approximately 20 to 30 percent. Cancer treatments are associated with neuropsychological deficits in up to 75 percent of patients. Increased age (eg, age ≥ 65 years) and decreased baseline cognitive reserve (intellectual capacity) appear to increase the risk of cognitive impairment in cancer patients. (See '[Prevalence](#)' above.)
- **Pathogenesis** – It is likely that different mechanisms contribute to cognitive impairment in patients with cancer and that cognitive dysfunction in some patients reflects an interaction between multiple factors. Potential causes include brain metastases, dehydration, electrolyte imbalance, infection, major organ failure, and paraneoplastic syndromes, as well as chemotherapy. (See '[Pathogenesis](#)' above.)
- **Screening** – Clinicians can screen patients with cancer for cognitive impairment with either the [Montreal Cognitive Assessment website](#) or the Mini Mental State Examination. (See '[Screening](#)' above.)

- **Delirium**

- **Overview** – A subset of patients with cognitive impairment can experience delirium, which is a neuropsychiatric syndrome that involves a disturbance in attention resulting from another medical illness, a medication or drug of abuse, or exposure to a toxin. Delirium can cause distress in patients, caregivers, and families and is associated with increased morbidity and mortality. (See '[Overview](#)' above.)
- **Prevalence** – At a minimum, the prevalence of delirium in patients hospitalized with cancer is approximately 10 to 30 percent. (See '[Prevalence](#)' above.)
- **Pathogenesis** – Delirium is due to a physiologic disturbance and often involves multiple etiologies. Among patients with cancer, the potential causes overlap with those that can cause cognitive impairment in general. (See '[Pathogenesis](#)' above.)
- **Clinical features** – The clinical features of delirium in patients with cancer include sudden onset of symptoms that typically fluctuate in severity during the day, decreased level of consciousness, attentional disturbances, cognitive impairment as manifested by disturbances in executive functions and memory, neurologic findings, perceptual disturbances, sleep-wake cycle disturbances, incoherent speech, and disorganized thought process. (See '[Clinical features](#)' above.)
- **Screening** – Screening tools can help clinicians diagnose delirium. Among the instruments that have been validated in patients with cancer, we suggest the Confusion Assessment Method ([table 3](#)). (See '[Screening](#)' above.)
- **Diagnosis** – The diagnosis of delirium requires each of the following criteria:
 - Disturbance in attention and awareness that develops quickly (usually hours to days) and tends to fluctuate each day.
 - Disturbance in cognition (eg, memory and/or orientation).
 - The disturbances in attention, awareness, and cognition are not better explained by another neurocognitive disorder and do not occur in the context of coma.
 - Evidence from the history, physical examination, or laboratory findings indicate that the disturbances are caused by a general medical condition, substance intoxication or withdrawal, and/or medication side effect.

(See '[Diagnosis](#)' above.)

Use of UpToDate is subject to the [Terms of Use](#).

Topic 109994 Version 8.0

