Delirium in the Older Emergency Department Patient – A Quiet Epidemic

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Synopsis

Delirium is defined as an acute change in cognition that cannot be better accounted for by a preexisting or evolving dementia. This form of organ dysfunction commonly occurs in older emergency department (ED) patients and is associated with a multitude of adverse patient outcomes. Consequently, delirium should be routinely screened for in older ED patients. Once delirium is diagnosed, the ED evaluation should focus on searching for the underlying etiology. Infection is one of the most common precipitants of delirium, but multiple etiologies may exist concurrently.

Keywords

delirium; emergency department; epidemiology; diagnosis; management

Introduction

Delirium is an under recognized public health problem that affects 7% – 10% of older emergency department (ED) patients.[1–3] This form of organ failure has devastating consequences for older patients and poses a significant threat to their quality of life. It has been associated with higher death rates,[4, 5] accelerated functional and cognitive decline,[6–8] and longer hospital length of stays.[9, 10] Delirium also places a tremendous financial burden on the United States health care system, costing over an estimated $100 billion in direct and indirect charges.[11, 12]

Despite its negative consequences, delirium is frequently missed by emergency physicians,[1, 3] and this is a serious quality of care issue.[13] Currently, 20 million older Americans visit the ED each year,[14–16] and are the fastest growing users.[14, 17] With the elderly population expected to grow exponentially over the next several decades, delirium's burden on EDs will intensify.[18] Therefore, the Society for Academic Emergency Medicine Geriatrics Task Force has recommended that delirium screening in the ED be one of the key quality indicators for emergency geriatric care.[19] Given this urgency, the purpose of this

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review is to discuss delirium's definition, risk factors, and consequences in older ED patients, and also discuss its diagnosis and management in the ED setting.

Definition of Delirium

Delirium is defined as an acute change in cognition that cannot be better accounted for by preexisting or evolving dementia.[20] This change in cognition is rapid, occurring over a period of hours or days, and is classically described as reversible. Patient's with delirium typically have inattention, disorganized thinking, altered level of consciousness (somnolent or agitated), and perceptual disturbances.[20]

Delirium is classified into three psychomotor subtypes: hypoactive, hyperactive, and mixed.[21] Hypoactive delirium is described as "quiet" delirium and is characterized by decreased psychomotor activity. These patients can appear depressed, sedated, somnolent, or even lethargic. Conversely, patients with hyperactive delirium have increased psychomotor activity and they appear restless, anxious, agitated, and even combative. Patients with mixed-type delirium exhibit fluctuating levels of psychomotor activity (hypoactive and hyperactive) over a period of time. Several epidemiological studies have investigated the frequency in which different psychomotor subtypes occur in a wide variety of settings (Table 1); hypoactive delirium and mixed-type delirium appear to be the predominant subtypes in older patients.[22–27] In the ED setting, Han et al. observed 96% of older patients with delirium exhibited the hypoactive or mixed subtype.[3]

Each psychomotor subtype is hypothesized to have a different underlying pathophysiological mechanism and underlying etiology.[21, 28] For example, delirium caused by alcohol withdrawal is more likely to be the hyperactive subtype, whereas delirium caused by a metabolic derangement is more likely to be the hypoactive subtype.[29] Not surprisingly, the various psychomotor subtypes of delirium have a differential effect on clinical course and outcomes,[30, 31] and also affect recognition by health care providers. Hyperactive delirium is more easily recognized. On the contrary, hypoactive delirium is often undetected because of its subtle clinical presentation, [32] and is often ascribed to other etiologies such as depression or fatigue.[33]

The Distinction between Delirium and Dementia

Delirium and dementia both cause cognitive impairment, and health care providers often confuse these two distinct clinical entities. This confusion is exacerbated by the high frequency in which delirium is superimposed upon dementia,[34] which is why delirium is often missed in these patients.[35] However, there are several key distinguishing features between delirium and dementia (Table 1), and most delirium assessments capitalize upon these differences. Unlike delirium, dementia is characterized by a gradual decline in cognition occurring over months or years, and is usually irreversible. Altered level of consciousness, inattention, perceptual disturbances and disorganized thinking are not commonly observed in patients with dementia.

However, there are some instances when the clinical features of delirium and dementia overlap, making them difficult to distinguish from each other. This is especially the case in patients with severe or end-stage dementia, where they can exhibit symptoms of inattention, perceptual disturbance, disorganized thinking, and altered level of consciousness even in the absence of delirium. When these patients develop delirium, an acute change in mental status is usually observed and any pre-existing abnormalities with inattention, disorganized thinking, or level of alertness may worsen. This is why establishing their baseline mental status is crucial to diagnosing delirium in patients with severe dementia.

Though classically thought of as irreversible, there are certain circumstances in which dementia may be reversible. Hypothyroidism, vitamin B12 deficiency, normal pressure hydrocephalus, and depression are examples of illnesses that can cause reversible dementia or a dementia-like illness (pseudodementia). However, the cognitive decline observed in reversible dementia is usually gradual as opposed to the rapid cognitive decline seen in delirium. Conversely, there is also a proportion of patients whose delirium is not transient; their symptoms can persist for months or even years.[36, 37]

Dementia with Lewy bodies (DLB) deserves special mention because it can be very difficult to distinguish from delirium. DLB is the second most common subtype of dementia (after Alzheimer's) and affects 15–25% of elderly demented patients.[38] Similar to delirium, DLB is characterized by a rapid decline and fluctuation in cognition, attention, and level of consciousness. Such fluctuations can be observed over several hours or days. Like delirium, perceptual disturbances are frequently observed in patients with Lewy body dementia. In contrast to delirium, however, patients with DLB have Parkinsonian motor symptoms, such as cog wheeling, shuffling gait, stiff movements, and reduced arm-swing during walking. Nevertheless, differentiating between DLB and delirium can be difficult in the ED and may require a detailed evaluation by a psychiatrist or neurologist.

Etiology of Delirium

Delirium is often the initial manifestation of an underlying acute illness and can be present before fever, tachypnea, tachycardia, or hypoxia.[39] The etiology of delirium is multifactorial and involves a complex interrelationship between patient vulnerability and precipitating factors (Figure 1).[40, 41] Patients who are highly vulnerable may be older, have severe dementia, and have multiple comorbidities. In these patients, a relatively benign insult, such as a small dose of narcotic medication, can precipitate delirium. Patients who are less vulnerable to developing delirium, like those who are younger and have little comorbidity burden, require higher doses of noxious stimuli (e.g. severe sepsis) to develop delirium.[42] Because older patients are more likely to have multiple vulnerability factors, they are disproportionately more susceptible to becoming delirious compared to younger patients. For this reason, nursing home patients are especially vulnerable.[43]

Most of what is known about delirium vulnerability factors is from studies performed in hospitalized patients (Table 3).[44–46] There are limited data from the ED, but one study identified dementia, premorbid functional impairment, and hearing impairment as independent risk factors for delirium in the ED.[3] Similar observations have been made in the medical and surgical inpatient population.[10, 40, 47–49] Dementia is probably the most consistently observed independent vulnerability factor for delirium across different clinical settings.[40, 48–55] As the severity of dementia worsens, the risk of developing delirium also increases.[56] Other vulnerability factors have also been reported in the hospital literature and include old age,[48, 51, 54] high comorbidity burden,[55] visual impairment,[40] baseline psychoactive drug use such as narcotics, benzodiazepines,[10, 48] and medications with anticholinergic properties,[51] history of alcohol abuse,[50, 55] and malnutrition.[41, 57]

Numerous precipitating factors of delirium have also been reported in the hospital literature (Table 3). Regardless of what the precipitating factors are, patients with higher severities of illness have a higher likelihood of developing delirium.[10, 40, 47, 54] It is important to keep in mind that multiple delirium precipitants can exist concurrently and on occasion, no obvious etiologic agent can be found.[58] Infections, such as a urinary tract infection or pneumonia, are one of the most common causes of delirium (34 – 43% of cases).[48, 52–54, 59, 60] Dehydration,[40] electrolyte abnormalities,[10, 61] organ failure,[10, 61] drug withdrawal, central nervous system insults,[52, 53, 59] and cardiovascular illnesses such as congestive heart

failure[54] and acute myocardial infarction[62] have all been implicated as delirium precipitants. Poorly controlled somatic pain may also cause delirium,[48, 63, 64] and pain control with non-narcotic or narcotic analgesia may help resolve delirium in this case.[64] Delirium can also be precipitated by iatrogenic events. Inouye et al. observed that the use of physical restraints or bladder catheters, or the addition of more than three medications were associated with delirium development.[41]

Psychoactive Medications as Risk Factors for Delirium

Medications with anticholinergic properties, benzodiazepines, and narcotics are notorious for precipitating and exacerbating delirium. Such medication risk factors are particularly relevant to the older patient population because polypharmacy is highly prevalent.[49] Medications with anticholinergic properties are more frequently associated with delirium than any other drug class.[65–67] Over 600 medications with anticholinergic properties exist, and of these, 11% are commonly prescribed to the elderly.[68] Some examples of commonly prescribed medications with anticholinergic properties are promethazine, diphenhydramine, hydroxyzine, meclizine, lomotil, and heterocyclic antidepressants (e.g. amitriptyline, doxepin).

Benzodiazepines have also been implicated as common delirium precipitants in hospitalized patients.[69–72] However, it is important to emphasize that delirium is heterogeneous and benzodiazepines can have a protective effect in a subgroup of delirious patients. For example, patients who are withdrawing from alcohol or sedatives have improved mortality and morbidity when given benzodiapezpines.[73] Narcotic medications are also deliriogenic, [48] and meperidine is a consistently observed culprit.[70, 72, 74–76] Similar to benzodiazepines, there is a subgroup of delirious patients who may benefit from narcotic medications. In patients with poor pain control, narcotic analgesia can reduce delirium severity. [64, 65]

To illustrate this point, we present a hypothetical case scenario. Mr. B is an 83 year old patient with a past history of dementia, hearing impairment, and depression who presents to an urgent clinic for nausea, vomiting, and diarrhea. He takes amitriptyline for his depression and donezepil for his dementia. The patient has normal vital signs, normal physical examination, and unremarkable laboratory workup. The urgent care clinician diagnoses Mr. B with gastroenteritis and prescribes promethazine 25mg tablets for symptomatic relief. Mr. B takes the medication as prescribed and develops a change in acute change mental status 24 hours later, which is subsequently diagnosed as delirium at the local ED.

In this scenario, this was a patient who was highly susceptible to developing delirium and possessed two vulnerability factors (dementia and hearing impairment). In addition, he was already on a medication with anticholinergic properties (amitriptyline) and the addition of promethazine increased the patient's anticholinergic burden, enough to precipitate delirium. This case illustrates how seemingly benign medications can precipitate delirium in a high risk patient.

The Negative Consequences of Delirium

There is an abundance of hospital-based studies which have investigated delirium's deleterious effects. From these studies, delirium is a powerful prognostic marker and has been associated with in-hospital and long-term mortality.[4, 5, 77–79] Though some have argued that delirium is simply a surrogate for severity of illness and comorbidity burden,[80] the relationship between delirium and death has been shown to be independent of these factors.[4, 5]

Delirium also has a profound impact on the older patient's quality of life. The trajectory of cognitive decline is accelerated in delirious patients compared non-delirious patients, and this effect is evident in patients with and without preexisting dementia.[6, 10, 78, 81, 82] Delirium is also associated with accelerated functional decline,[8, 81, 83] which can lead to subsequent loss of independent living and future nursing home placement.[8, 77]

Hospitalized patients with delirium are more prone to developing urinary incontinence, decubitus ulcers, and malnutrition.[11, 12, 51, 84] This can then lead to prolonged hospital stays and increased health care costs.[10, 55, 84, 85] Once discharged from the hospital, delirious patients are more likely to be rehospitalized, further adding to the financial burden.[8, 60, 77, 84] Moreover, there is also a huge emotional cost. Many patients are able to recall their experiences with delirium, causing patients and their families significant emotional distress.[86, 87]

To date, only four delirium outcome studies have been conducted in the ED setting. In 385 older ED patients, Lewis et al. observed that patients with delirium were significantly more likely to die at 3-months (14% versus 8%), but their analysis did not adjust for potential confounders.[2] Kakuma et al. studied 107 older patients discharged from the ED and reported that delirium was independently associated with 6-month mortality,[88] but this study excluded patients who were admitted to the hospital. Han et al. studied 303 older ED patients that were both admitted and discharged.[89] They found that patients who were delirious in the ED were more likely to die at 6-months compared to non-delirious patients (36% versus 10%). This relationship was independent of age, comorbidity burden, and severity of illness.[89] However, they did not incorporate other important confounders such as dementia and functional impairment in the multivariable model. Only one ED study has investigated the relationship between delirium and long-term functional outcomes. Vida et al. reported that delirium in the ED was associated with accelerated functional decline at 18-months in patients without pre-existing dementia only.[90] However, this association disappeared after adjusting for potential confounders.[90] Even with the relatively small number of ED studies and the limited external validity of hospital studies, delirium in the ED appears to be a marker for adverse patient outcomes.

Unrecognized Delirium in the Emergency Department

Despite delirium's negative consequences, emergency physicians miss 57% to 83% of cases due to lack of appropriate and routine screening. [1–3, 88, 91–93] This quality of care issue extends beyond the ED as similar miss rates have been observed in the hospital setting.[32, 94–97] Delirium is more commonly missed in patients with hypoactive symptomotology, who are aged 80 years and older, have visual impairment, or have dementia.[32, 35]

The consequences of missing delirium in the ED are unclear. However, Kakuma et al. reported that discharged ED patients in whom delirium was missed by the emergency physician were more likely to die at 6-months compared to patients in whom delirium was recognized (30.8% versus 11.8%).[88] Though the mechanism for this is uncertain, ED patients with undetected delirium may receive inadequate diagnostic workups, and an underlying life-threatening illness may remain undiagnosed. They may also receive inappropriate interventions such as medications with anticholinergic properties or benzodiazepines. Lastly, delirious patients who are discharged from the ED are less likely to understand their discharge instructions,[98] which may lead to non-compliance, recidivism, and increased mortality and morbidity.[99, 100]

Diagnosing Delirium in the ED

Several delirium assessments exist, but the Confusion Assessment Method (CAM) is probably the most widely accepted by clinicians. The CAM was developed for non-psychiatrists and is based upon the *Diagnostic and Statistical Manual of Mental Disorders, Revised 3rd Edition* criteria.[101] It consists of four features: 1) acute onset of mental status changes and a fluctuating course, 2) inattention, 3) disorganized thinking, and 4) altered level consciousness.[101] A patient must have both features 1 and 2 and either feature 3 or 4 to meet criteria for delirium (Figure 2). The CAM training manual recommends using a cognitive screening test such as the Mini-Mental State Examination and the Digit Span Test to help determine the features of the CAM.[102]

An acute change in mental status and fluctuating course (feature 1) is a cardinal feature of delirium and must be present for a patient to be CAM positive. In the ED, this feature is determined from interviewing a proxy such as a family member. Feature 1 can be difficult to ascertain if a proxy is not readily available in the ED. If a patient comes from a long-term care facility, contacting the patient's nurse or physician at that facility can often help establish the patient's baseline mental status. Similarly, the patient's primary care provider, if available, is another potential resource. In some patients, an acute change and fluctuation in mental status can be observed first hand during the ED stay.

Features 2, 3, and 4 are assessed during the patient interview and cognitive screen. Similar to feature 1, inattention (feature 2) is considered another cardinal feature of delirium and is described as a patient who is easily distractible and has difficulty maintaining focus. A patient with disorganized thinking (feature 3) may ramble, display tangential thoughts, or demonstrate an illogical flow of ideas. Patients with altered level of consciousness (feature 4) may exhibit drowsiness, lethargy, anxiety, hypervigilance, or combativeness (hyperactive).

Inouye et al. found the CAM to have excellent sensitivity (94% – 100%) and specificity (90% – 95%) in hospitalized patients.[101] Subsequent validation studies have shown more variability in diagnostic performances with sensitivities ranging from 46% to 94% and specificities ranging from 63% to 100%.[103] However, this variability is most likely attributable to the level of training.[104] The CAM has excellent interobserver reliability (kappa 0.70 – 1.00) when performed by trained personnel.[103] Thus far, the CAM is the only delirium assessment validated for use in the ED. Using lay interviewers to perform the CAM and a geriatrician's assessment as the reference standard, Monette et al. observed that the CAM was 86% sensitive and 100% specific in ED patients. They also reported that the CAM had excellent interobserver reliability (kappa = 0.91) in this setting.[105]

However, the CAM takes up to 10 minutes to perform,[102] which can be challenging in a highly demanding ED environment. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) may be more feasible in the ED because it takes less than two minutes to perform. The CAM-ICU primarily uses the same the same four features as the CAM: 1) acute onset of mental status changes or a fluctuating course, 2) inattention, 3) altered level of consciousness, and 4) disorganized thinking. Similar to the CAM, a patient must have both features 1 and 2, and either feature 3 or 4 to meet criteria for delirium. However, there are several notable differences between these two assessments. The CAM-ICU uses brief neuropsychiatric screening assessments to test for inattention and disorganized thinking. These screening assessments help minimize subjectivity and improve its ease of use. The CAM-ICU also slightly modifies the original CAM's feature 1, requiring either an acute change in mental status or fluctuating course.[106] In the latest iteration, the CAM-ICU also reorders features 3 and 4 of the CAM; the CAM-ICU's feature 3 is altered

level of consciousness and feature 4 is disorganized thinking. The rationale for this change is detailed in the next paragraph. Lastly, the CAM-ICU also uses the Richmond Agitation and Sedation Scale to help determine altered level of consciousess.[106]

Testing all four features of the CAM-ICU typically takes less than two minutes to perform. However, using the algorithm provided in Figure 3, the CAM-ICU can take less than 1 minute to perform in many cases. This algorithm provides a stepwise approach to performing the CAM-ICU and allows the rater to stop the assessment early, especially if either feature 1 (acute change in mental status or fluctuating course) or feature 2 (inattention) is negative. Disorganized thinking (CAM-ICU's feature 4) is performed only if features 1 and 2 are both positive, and there is no evidence of any altered level of consciousness (CAM-ICU's feature 3). Because the majority of CAM-ICU positive patients has altered mental status or a fluctuating course, inattention, and altered level consciousness, disorganized thinking (CAM-ICU's feature 4) is usually not assessed in the clinical setting. For this reason, the latest version of the CAM-ICU reverses the order of the original CAM's features 3 and 4 as described in the previous paragraph.

The CAM-ICU has been validated in mechanically ventilated and non-mechanically ventilated intensive care unit patients. Ely et al. reported that the CAM-ICU was highly sensitive (93% – 100%) and specific (89–100%) with excellent interrater reliability (kappa= 0.84 to 0.96) between nurses and physicians.[107, 108] However, the CAM-ICU has not been validated in the ED patients and spectrum bias may exist. A validation study in the ED setting is currently ongoing.

Several other delirium instruments exist in the literature (Table 4). Similar to the CAM, these instruments require subjective assessments and many take up to 10 minutes to complete, making them difficult to perform in the ED.[109–122] However, the Nursing Delirium Screening Scale (NuDESc) may be potentially useful in the ED because it takes less than two minutes to perform. The NuDESc is a checklist that asks nurses about the presence of disorientation, inappropriate behavior, inappropriate communication, hallucinations, and the presence of psychomotor retardation over an 8-hour shift.[113] However, the NuDESc does not assess for an acute change in mental status or fluctuating course and inattention, which are cardinal to the diagnosis of delirium. Despite this, the NuDESc appears to have excellent diagnostic characteristics. Using the CAM as the reference standard, Gaudreau et al. reported the NuDESc to be 86% sensitive and 87% specific.[113] Radtke et al. observed that the NuDESc was 95% sensitive and 87% specific compared to a research assistant's assessment using the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* criteria.[112] The NuDESc's interrater and interobserver reliability are unknown and will be important to elucidate given its use of subjective observations. Similar to the CAM-ICU, the NuDESc still requires validation in the ED setting.

Diagnostic Evaluation for Delirium in the ED

Once delirium is detected in the ED, the diagnostic evaluation should be focused on uncovering the underlying etiology. Though infection is the most common etiology of delirium in the older ED patient, life threatening causes should initially be considered and can recalled using the mnemonic device "WHHHHIMPS" (Table 5).[123] After these life threatening causes have been considered, the ED evaluation can focus on ruling out other causes of delirium listed in Table 3.

The ED evaluation of the delirious patient is summarized in Table 6. If available, obtaining a detailed history from a proxy is crucial. A careful review of the patient's home medication list should also be performed, including eliciting a history of any recent changes or additions

to the patient's home medication regimen. Because alcohol and benzodiazepine abuse can still occur in elderly patients, a careful social history should also be obtained.

The physical examination should look for any vital sign abnormalities, although they will be normal in most cases. A neurological examination should be performed looking for any focal neurological findings suggestive of a central nervous system insult. Laboratory and radiologic tests are commonly performed in all patients with delirium (Table 6). A urinalysis should be performed in all patients as urinary tract infections are common amongst delirious patients.. Electrolytes should be obtained to rule out hyper- or hyponatremia, or hypercalcemia. Because organ failure can precipitate delirium, a blood urea nitrogen and serum creatinine should be obtained to rule out uremia. Liver function tests and ammonia levels can also be considered, especially in patients with physical findings of end stage liver disease. Because thyroid dysfunction can cause delirium,[124] thyroid stimulating hormone should also be considered. An arterial or venous blood gas may be obtained if hypercarbia is suspected, especially in patients with chronic obstructive pulmonary disease. Rarely, patients with acute myocardial infarction can also present with delirium as the sole manifestation;[62] a 12-lead electrocardiogram and cardiac biomarkers can be considered, but their diagnostic yield in ED patients with delirium remains unknown. A lumbar puncture, though not routinely performed, should be considered if there is a clinical suspicion for meningitis/encephalitis and especially if no other etiologies for delirium are found.

A chest x-ray should also be considered to rule out pneumonia, especially in the setting of hypoxemia, tachypnea, or a history of cough and dyspnea. Performing computed tomography (CT) of the head in all delirious patients is controversial as it may have low diagnostic yield.[125] However, it may be ordered when no other cause for delirium is found. Based upon two studies, the head CT's diagnostic yield is increased when performed in patients with impaired level consciousness, a focal neurological defecit, or a recent history of a fall or head trauma.[125, 126] However, these studies were retrospective in nature and have yet to prospectively validated. Regardless, clinical judgment should be used when deciding if a delirious patient needs a head CT.

Disposition

There is little evidence based guidance regarding the disposition of older ED patients with delirium. However, admission of delirious patients is likely warranted in most cases. Older delirious patients who are discharged from the ED have higher death rates compared to non-delirious patients, and this effect is magnified when delirium is unrecognized by the emergency physician.[88] In addition, delirious patients may be more likely to return to the ED and be hospitalized.[1] For a small minority, ED discharge can be considered, particularly if close home supervision and follow-up can be arranged. For example, a patient who accidentally overdoses on a narcotic medication can be discharged home if the delirium resolves and if the patient remains delirium free after a period of ED observation. If admitted to the hospital, admission to an inpatient unit that specializes in geriatric care is preferable as it may improve patient outcomes.[127] Regardless of the patient's disposition, if delirium is detected in the ED, this should be communicated to the physician at the next stage of care.

Pharmacologic Management of Delirium

The single most effective treatment for delirium is to diagnose and treat the underlying etiology. Adjunct pharmacologic treatments have been investigated for delirium, but most studies are limited by their non-blinded trial design, poor randomization, or inadequate power. The American Psychiatry Association recommends avoiding benzodiazepines as monotherapy in delirious patients, except in the setting of alcohol and benzodiazepine

withdrawal.[45] As previously mentioned, benzodiazepines can precipitate and exacerbate delirium in most cases and they also have relatively high side effect profiles. One randomized trial attempted to compare the efficacy of antipsychotic medications and lorazepam in delirious patients, but was prematurely terminated because the lorazepam arm showed a higher prevalence of treatment limiting side effects such as over-sedation, disinhibition, ataxia, and increased confusion.[128]

Instead, antipsychotic medications should be used, especially in delirious patients with behavioral disturbances, agitation, and overt psychotic manifestations (i.e. visual hallucinations and delusions). Haloperidol is a commonly used typical antipsychotic and has been shown to improve delirium severity; Hu et al. compared haloperidol to placebo, and reported that 70.4% of patients who received haloperidol showed improvement in their delirium severity at the end of one week compared to 29.7% of the placebo group.[129] Intravenous haloperidol should be used cautiously because torsades de point has been reported when given in this formulation.[130]

Atypical antipsychotic medications such as olanzapine and risperidone are also frequently used to treat patients with delirium.[131] Compared to typical antipsychotics, this class of medications have a lower incidence of extrapyramidal side effects.[132] Olanzapine has been shown to improve delirium severity compared to placebo in one randomized control trial,[129] but it's efficacy may be attenuated in patients aged 70 years and older.[133] Risperdone has also been used to treat delirium, but only one clinical trial has been conducted to date. Han et al. compared risperidone to haloperidol and they observed that 75% of the haloperidol group versus 42% of the risperidone group showed improvement in their delirium severity. However, this difference was non-significant and the trial was underpowered.[134] Some studies have used quetiapine to treat delirium,[131, 135, 136] but no randomized control trials have been performed.

There are limited data on the effectiveness of typical and atypical antipsychotic medications in patients with different delirium subtypes; their use in patients with hypoactive delirium is controversial. However, a significant proportion of patients with hypoactive delirium will have some element of psychosis.[23] For many psychiatrists, when delirium is detected, an antipsychotic is initiated regardless of the subtype.[137]

Similar to benzodiazepines, medications with anticholinergic properties should be avoided. Narcotic medications should not be used to sedate an agitated patient and should only be used to treat acute pain. Although rare, there are reports of histamine-2 blockers, such as famotidine, ranitidine, and cimetidine, causing delirium.[138, 139] These should be avoided in delirious patients if at all possible.

Non-Pharmacologic Management of Delirium

Several non-pharmacologic delirium interventions have been developed for the in-hospital setting and may be tailored for the ED. Most of these non-pharmacologic interventions contain multiple components and involve a multidisciplinary team of physicians, nurses, and social workers or case managers.[140, 141] Moreover, geriatricians or geriatric psychiatrists are commonly consulted for these interventions.[140–142]

These interventions usually emphasize decreased use of psychoactive medications, increased mobilization by reducing the use of physical restraints and bladder catheters, and minimized disruptions in normal sleep-wake cycles. Many also encourage reorienting the patient by placing a large white board with the day and date, large clocks, or calendars in the patients' rooms. Cognitive stimulation, placing familiar objects in the patient's room as well as encouraging the presence of family members are also advocated. Though these delirium

interventions have shown to be beneficial in the post-operative setting,[141, 143] their efficacy in medical patients is equivocal.[140, 144] In medical inpatients, Pitkala et al. did find that their non-pharmacologic intervention improved delirium resolution during hospitalization and cognition at six months, but no improvement in nursing home placement or mortality was observed.[145] Additional research is required to determine if non-pharmacologic interventions are feasible and cost-effective in the ED setting.

Conclusion

Delirium is common in older ED patients and its etiology is multifactorial, involving a complex interplay between patient vulnerability and precipitating factors. Based upon numerous hospital studies and a limited number of ED studies, delirium has devastating effects on the patient's well being. As a result, delirium surveillance should be routinely performed in older ED patients, especially those at high risk. The CAM is the only delirium assessment validated for the ED and it has excellent diagnostic characteristics. However, it can take up to 10 minutes to complete and may be difficult to perform in the demanding ED environment. The CAM-ICU and NuDESc take less than two minutes to perform and may be more feasible to perform in the ED. However, they still require validation in the ED population. Once delirium is detected in the ED, the primary goal is to find and treat the underlying cause. Other adjunct pharmacological and non-pharmacological interventions have been studied in the hospital setting, but their efficacy is equivocal and their usefulness in the ED setting is unknown. Indeed, significant knowledge gaps exist in regards to the optimal diagnostic evaluation, disposition, and management of delirious ED patients. Given the impending exponential growth of the elderly patient population, intense research efforts to ameliorate these deficiencies are needed.

Acknowledgments

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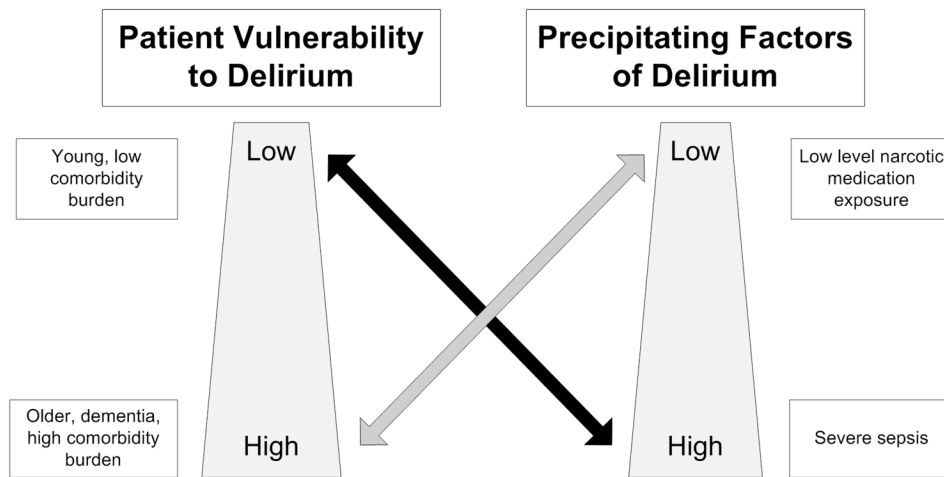
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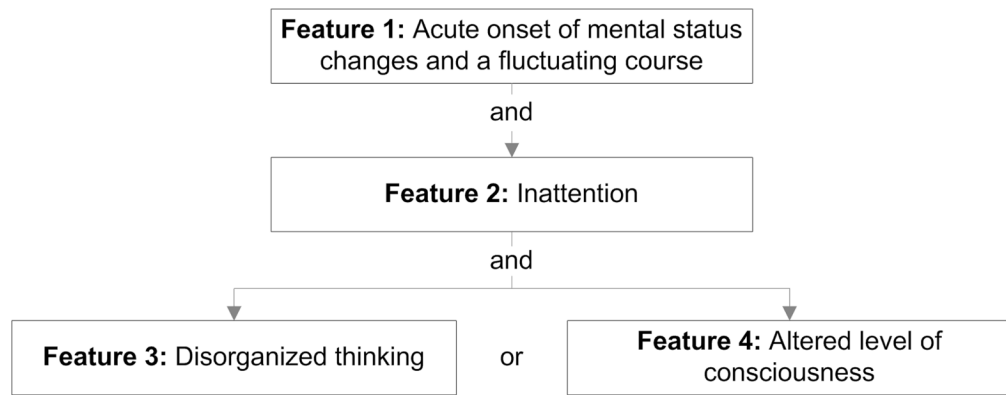
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Patient Vulnerability to Delirium

Precipitating Factors of Delirium

Young, low comorbidity burden

Low

Low

Low level narcotic medication exposure

Older, dementia, high comorbidity burden

High

High

Severe sepsis

Figure 1.
The interrelationship between patient vulnerability and precipitating factors in the development of delirium.[41] Patients who have little vulnerability require significant noxious stimuli to develop delirium (black arrow). Conversely, patients who are highly vulnerable require only minor noxious stimuli to develop delirium (gray arrow).

Feature 1: Acute onset of mental status
changes and a fluctuating course

and

Feature 2: Inattention

and

Feature 3: Disorganized thinking   or   **Feature 4:** Altered level of
consciousness

Figure 2.
Features of the Confusion Assessment Method. A patient must have both features 1 and 2,
and either 3 or 4 to meet criteria for delirium.
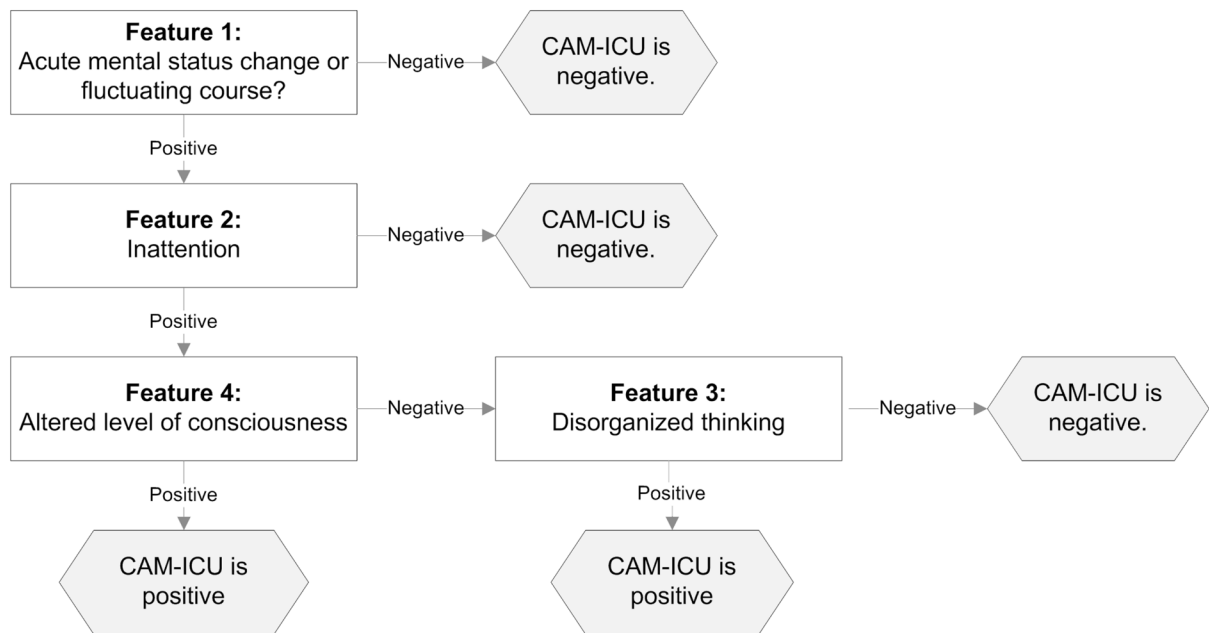
Figure 3.
Algorithm for performing the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) in the clinical setting. The shaded hexagons indicate a stopping point for the CAM-ICU.

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Table 1

Studies that have evaluated the psychomotor subtypes of delirium.

Author	Age Inclusion	Setting	Psychomotor Subtype		
			Hypo	Hyper	Mixed
Han 2009[3]	65	ED	92%	4%	4%
Liptzkin 1992[23]	>65	Inpatient, medical	19%	15%	52%
O'keefe 1999[24]	Not reported	Inpatient, geriatrics	29%	21%	43%
Marcanontio 2002[26]	65	Inpatient, hip fracture repair	71%	-	29%
Kelly 2001[25]	Nursing Home	Inpatient, geriatrics	56%	3%	41%
Peterson et al. 2006[22]	None	Inpatient, Medical ICU	44%	2%	55%
Pandharipande et al. 2009[27]	Non	Inpatient, Surgical ICU	64%	9%	0%
		Trauma ICU	60%	6%	1%

Hypo, hypoactive; hyper, hyperactive; ICU, intensive care unit; ED, emergency department.

Table 2

Differences between delirium and dementia.

Characteristic	Delirium	Dementia
Onset	Rapid over a period of hours or days	Gradual over a long period of time
Course	Fluctuating	Stable
Is cognitive decline reversible?	Yes	No
Altered of level of consciousness?	Yes	*No
Inattention present?	Yes	*No
Disorganized thinking present?	Yes	*No
Altered perception present?	Yes	*No

*
May be present in patients with severe dementia.

Table 3

Predisposing and precipitating factors for delirium.

Predisposing Factors

Demographics

- Advanced age
- Male gender

Comorbidity

- Dementia
- # of comorbid conditions
- Severity of comorbid conditions
- Chronic kidney disease
- End stage liver disease
- Terminal illness

Medications and Drugs

- Polypharmacy
- Baseline psychoactive medication use
- History of alcohol or other substance abuse

Functional Status

- Functional impairment
- Immobility

Sensory Impairment

- Hearing impairment
- Visual impairment

Decreased oral intake

- Dehydration
- Malnutrition

Psychiatric

- Depression

Precipitating Factors

Systemic

- Infection
- Inadequate pain control
- Trauma
- Dehydration
- Hypo- or Hyperthermia

Metabolic

- Thiamine deficiency (Wernicke's encephalopathy)
- Hepatic or renal failure

- Electrolyte disturbances

- Hypoglycemia/hyperglycemia

- Thyroid dysfunction

Medications and Drugs

- Medications and medication changes

- Recreational drug use or withdrawal

CNS

- Cerebrovascular accident

- Intraparenchymal hemorrhage

- Subdural/epidural hematoma

- Seizures and postictal state

- Meningitis/encephalitis

Cardiopulmonary

- Acute myocardial infarction

- Congestive heart failure

- Respiratory failure

- Shock

Iatrogenic

- Procedures or surgeries

- Indwelling urinary catheters

- Physical restraints

Modified from Pun et al, Fearing et al., and the American Psychiatry Association Delirium Guidelines.[44–46]

Table 4

Other delirium assessments.

Delirium Instrument	Duration or items	Interrater reliability	Reference Standard	Validated in ED?
Delirium Rating Scale – Revised 98[118]	15 – 30 minutes	Excellent	DSM-IV by psychiatrist	No
Delirium Symptom Interview[119]	15 minutes	Excellent	Psychiatrist or Neurologist	No
Memorial Delirium Assessment Scale[120]	10 items	Excellent	DSM-IIIR/IV by psychiatrist	No
Confusional State Examination[122]	22 items	Moderate to excellent	Psychiatrist	No
*Confusion Rating Scale[110, 111]	2 minutes	Unknown	CAM, SPMSQ	No
*Nursing Delirium Screening Scale[112, 113]	2 minutes	Unknown	CAM, DSM-IV by research assistant	No
*NEECHAM Confusion Scale[114–116]	10 minutes	Excellent	DSM-III by research nurse/ CAM	No

*
These instruments were developed specifically for nurses.

Table 5

Life-threatening causes of delirium.[123]

Wernicke's disease
Hypoxia
Hypoglycemia
Hypertensive encephalopathy
Hyperthermia or hypothermia
Intracerebral hemorrhage
Meningitis/encephalitis
Poisoning (whether exogenous or iatrogenic)
Status epilepticus

Table 6

Evaluation of the older emergency department patient with delirium.

History	Careful review of home medications Recent changes in home medications History of drug and alcohol abuse
Physical Examination	Vital signs Signs of infection Toxidromes Volume status Neurologic examination
Laboratory tests to consider	Urinalysis Blood glucose Electrolytes Blood urea nitrogen and serum creatinine Liver function tests and/or ammonia Thyroid stimulating hormone Arterial blood gas if hypercarbia is suspected Cardiac biomarkers if AMI is suspected Lumbar puncture if meningitis is suspected Urine drug screen
Radiological Tests to Consider	Chest x-ray Computed tomography of the head
Other Tests to Consider	12-lead electrocardiogram

AMI, acute myocardial infarction.