

Critical Care Medicine Section

Delirium in Critically Ill Emergency Patients

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In recent years delirium has been getting a lot of attention in critically ill patients and has been associated with increased risk of mortality, prolonged ICU stay, significant long-term effect and impairment. Delirium in any patient is daunting on

the patient, their families and to our health care system. Since the 2013 guideline for pain, agitation and delirium routine screening and monitoring has been recommended and can be facilitated using the delirium check list (see Figure 1).^{1,2,3} Delirium alerts providers to a perilous process that is associated with poor outcomes. While it is unclear if delirium itself is the cause for this elevated consequence, there is a connection.

| Patient | Description | Score |
|--|--|-------------------------------------|
| Level of Consciousness | A: No response | None |
| | B: Response to intense and persistent stimulation | None |
| | C: Respond to mild or moderate stimuli | 1 |
| | D: Normal wakefulness | 0 |
| | E: Exaggerated response to normal stimulation | 1 |
| | | + |
| Inattention | Difficulty following conversation or instructions; easily distracted by external stimuli, difficulty in shifting focuses | 1 |
| | | + |
| Disorientation | Any obvious mistake in person, place or time. | 1 |
| | | + |
| Hallucination/delusion/ Psychosis | Manifestation of hallucination, behavior due to hallucination or delirium. Gross impairment if reality testing | 1 |
| | | * Score >4 associated with delirium |

Figure 1: Intensive Care Delirium Screening Checklist

What is Delirium?

The American Psychiatric Association's fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) recently revised the diagnostic criteria for delirium. Delirium is a syndrome of an acute change in mental status from baseline, "alterations in the content (that is, attention) and/or level (that is, arousal) of consciousness are core to the diagnosis of delirium."⁴

In critically ill patients, such changes can be noted as: hypervigilance, inattention, disorganized thinking, altered level of consciousness. These can be temporary and often a reversible state of altered mentation, secondary to an acute process. Delirium is further divided into three subtypes:

1. Hyperactive (characterized by restlessness, agitated behaviors, confusion, hallucinations)
2. Hypoactive (characterized by sedation, motor slowness, lethargy withdrawal from interactions)
3. Mixed (fluctuation between hypoactive and hyperactive subtypes)⁵

Delirium should be categorized by suspected subtype etiology so that treatment can be catered. Hyperactive delirium is more easily recognized given its more outwardly visible presentation. Whereas hypoactive delirium is perhaps more occult given presentation of lethargy and hypoactivity. This can often be assumed as "resting", when in fact is a form of delirium and thereby undertreated. Mixed type delirium is more difficult to treat given that patients may experience elements of both previous noted subtypes in a short amount of time.

Vulnerable Populations

Special consideration should be taken for vulnerable patient populations such as the elderly and pediatric populations. Both have propensity for long term neurological effects and higher mortality.

Elderly patients are at highest risk for delirium due to concomitant confounders such as hearing and visual loss. Nearly 30 percent of admitted elderly patients will exhibit delirium at some point during a hospital stay.^{6,7} Incidence rises to 50 percent in elderly patients admitted for complex surgical procedures.⁸ One study suggested that patients with more severe delirium after hip surgery, including psychomotor agitation, had higher rates of mortality and nursing home placement. Furthermore, delirium that does not resolve before discharge is also a risk factor for nursing home placement.^{9,10}

Factors that increase the risk for delirium and confusion in all patients including traumatic brain injury; in the elderly, include dementia, stroke, Parkinson's. Extrinsic factors include medications, sepsis, drugs, dehydration, and situational changes.

Differential Diagnosis

A broad differential diagnosis in the emergency department is crucial and extensive. Workup should commence first foremost by ruling out catastrophic processes such as hypoglycemia, infection cerebral vascular accident, traumatic brain injury, sun-downing, non-convulsant seizure, psychosis, and delirium tremens, just to name a few.

Many medications can cause delirium and should be considered when attempting to identify cause of acute change in mentation. 30 percent of all cases of delirium are associated with drug toxicity.¹¹ In the ICU, worsening of the underline condition should be considered or complication related to the hospitalization, medication.

In admitted patients with established medical diagnosis who develop altered mentation, potential worsening of the underline process should be the priority focus. For example, avoiding the mistake of attributing new altered mention in a patient admitted for acute stroke to delirium when in fact, the cause is progression of ischemia or secondary injury.

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Delirium vs. Dementia

Delirium and dementia can be confused. Delirium disturbs attention versus dementia disturbs memory. Delirium typically has a sudden onset with a clear onset, whereas dementia typically has an uncertain onset, is slow to start and gradual in progression. Confusion can be due to either, especially in the acute phases of delirium or the onset of dementia. Evaluation to differentiate the two is crucial in order to appropriately treat and or mitigate long term effects.

Evaluation

Evaluation and examination are difficult in assessing delirium since the majority of history is dependent on secondary account. Family and friend provided history may elucidate a state of “just not right” or “just not himself/herself today”. Not eating or drinking as usual may also be a presenting sign. A thorough physical exam including a complete neurological exam is critical to rule out source of altered mentation as well as diagnose altered mentation in and of itself.

Clinical instruments such as the Intensive Care Delirium Screening Checklist (ICDSC) or the Confusion Assessment Method for ICU (CAM-ICU) tool should be incorporated in to emergency department workup and in ICU daily in-patient evaluation to aid in early and correct diagnosis of delirium.^{2,3} The ICDSC is a screening checklist of eight items and administered daily, with sensitivity 99 percent sensitivity and 64 percent specificity for early detection of delirium. Critics of the ICDSC tool, make note that the tool was studied in ICU patients with mainly medical, cardiovascular and surgical disease and not validated for emergency medicine use. The CAM-ICU score takes 5 minutes to assess and has a sensitivity of 94-100 percent and a specificity of 90-95 percent.^{12,13} A review of 11 bedside instruments used to identify the presence of delirium in adults supported the use of the CAM-ICU as the best, and the Mini Mental State Exam as the least accurate test.¹⁴ (Figure 1, Figure 2)

Laboratory tests may elucidate sources of acute altered mentation. Workup should include but not limited to thyroid functions, vitamin B12 level, urinalysis, CBC for evidence of acute infection, with known limitation in elderly who may or may not mount fevers or leukocytosis, lumbar puncture to identify meningitis when other sources of infection have not been identified.

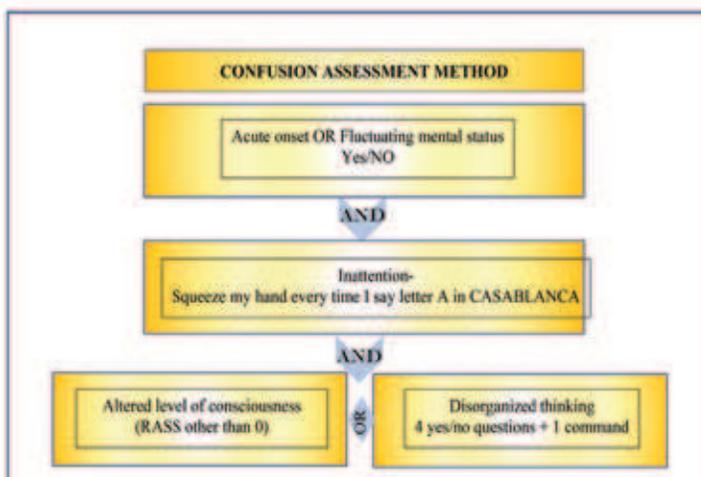


Figure 2: CAM-ICU Method

“Early recognition and treatment of both the underlying cause and outward presentation are paramount to reduce days of delirium and reduce the potential for long term affects.”

Treatment

While correct identification and classification is paramount, equally is treatment. There is no magic bullet to treat delirium, especially as each patient’s individual medical process is different, making broad recommendations for whole populations difficult.

First steps include treating the underlying cause of the delirium such as antibiotics for bacterial infections, mitigating agents for acute drug withdrawal, cessation of drug induced delirium, reduce location changes.

Non-pharmacological agents should be attempted as first line treatment; verbal reorientation, early ambulation, clock in visual field of patient, windows and good lighting, and avoiding sleep-wake cycle disturbances. Units that addressed these ambient factors have shown to have decreased incidence of delirium.¹⁵⁻¹⁸ More and more guidelines include “Family engagement/empowerment”. We too often discard or ignore family members by having restricted access to the department or the ICU. Family members can be trained in assisting, re-orientating, and participating in plan of care. Harnessing their bedside presence can be a useful way to limit medication use and time consumption/frustration by the medical team.

Current evidence does not support the use of any medications in order to prevent delirium. Haloperidol did not prevent delirium in ICU patients in the REDUCE trial.¹⁹ While Haloperidol remains the mainstay of treatment and can be given orally, intramuscular or intravenous, the current recommendation is to avoid routine treatment with Haloperidol and or other medication. Patients who are agitated and could potentially harm themselves or others may benefit from short term, low doses of Haloperidol. Of note, intravenous administration is associated with prolonged QT and should be monitored.

In one study, haloperidol and chlorpromazine showed improvement in delirium compared to lorazepam.²⁰ Risperidone (0.5 mg every 12 hours) was associated with a reduced incidence of clinical delirium in post cardiac surgery patients.²¹ Quetiapine, risperidone, ziprasidone, and olanzapine have fewer side effects compared to haloperidol, and in small studies they appear to have similar efficacy to the former.²²⁻²⁴

Cholinesterase inhibitors have been proposed to prevent delirium in selected patients, but these, too, have not shown efficacy towards prevention.²⁵⁻²⁷ Gabapentin and melatonin have shown some efficacy in reducing delirium namely by reducing pain and improving sleep cycles, respectively.^{28,29}

Whether in the ICU or the emergency department, mechanically ventilated patients are at high risk to develop delirium. The New Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/ Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU recommends avoidance of haloperidol, use of dexmedetomidine or propofol as a sedative agent that also reduces days of delirium and ventilator days.³⁰

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Benzodiazepines have a limited role in the treatment of delirium; they are primarily used as a sedative drug, treatment for alcohol withdrawal or when neuroleptic drugs are contraindicated. Benzodiazepines use is associated with poor outcomes in ICU patients and in elderly populations.^{20,31-34}

Physical restraints should only be used as last resort and in conjunction with pharmacological agents to mitigate symptoms. Isolated use of restraints increases likelihood of rhabdomyolysis, acute kidney injury, hyperthermia and death.

In general, symptomatic treatment is not used for hypoactive delirium. One study suggested that patients with hypoactive delirium have a similar response to treatment with haloperidol as those who were agitated.³⁵ Some case reports have attempted to show use of stimulants to mitigate hypoactive delirium with no avail.

Conclusion

Delirium has a significant impact on patients and is associated with poor outcomes, highest in older patient populations. Delirium is not only associated with higher mortality, it is also associated with prolonged hospital stays, likelihood for nursing home stays as opposed to discharge to home, overall functional and cognitive decline. Delirium impacts patients as well as family members. Early recognition and treatment of both the underlying cause and outward presentation are paramount to reduce days of delirium and reduce the potential for long term affects. Currently, there is no concrete treatment option for delirium; some are better than others, but none are ideal. More studies need to be done to better understand delirium and treatment options.

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References

- Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine: Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013; 41:263-306
- Ely EW, Inouye SK, Bernard GR, et al: Delirium in mechanically ventilated patients: Validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA* 2001;286:2703-2710
- Bergeron N, Dubois MJ, Dumont M, et al: Intensive care delirium screening checklist: Evaluation of a new screening tool. *Intensive Care Med* 2001; 27:859-864
- European Delirium Association; American Delirium Society. The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. *BMC Med*. 2014 Oct 8;12:141.
- Krewulak KD1 Stelfox HT, Leigh JP, Ely EW, Fiest KM. Incidence and Prevalence of Delirium Subtypes in an Adult ICU: A Systematic Review and Meta-Analysis. *Crit Care Med*. 2018 Dec;46(12):2029-2035
- Francis J. Delirium in older patients. *J Am Geriatr Soc*. 1992;40(8):829.
- Inouye SK, Rushing JT, Foreman MD, Palmer RM, Pompei P. Does delirium contribute to poor hospital outcomes? A three-site epidemiologic study. *J Gen Intern Med*. 1998;13(4):234.
- Dyer CB, Ashton CM, Teasdale TA Postoperative delirium. A review of 80 primary data-collection studies. *Arch Intern Med*. 1995;155(5):461.
- Marcantonio E, Ta T, Duthie E, Resnick NM, Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. *J Am Geriatr Soc*. 2002;50(5):850.
- McAvay GJ, Van Ness PH, Bogardus ST Jr, Zhang Y, Leslie DL, Leo-Summers LS, Inouye SK. Older adults discharged from the hospital with delirium: 1-year outcomes. *J Am Geriatr Soc*.
- Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990; 113:941.
- Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. *J Am Geriatr Soc* 2008; 56:823.
- Wong CL, Holroyd-Leduc J, Simel DL, Straus SE. Does this patient have delirium?: value of bedside instruments. *JAMA* 2010; 304:779.
- Francis J. Drug-induced delirium: Diagnosis and treatment. *CNS Drugs* 1996; 5:103.
- Clegg A, Siddiqi N, Heaven A, et al. Interventions for preventing delirium in older people in institutional long-term care. *Cochrane Database Syst Rev* 2014; :CD009537.
- Van Rompaey B, Elseviers MM, Van Drom W, et al. The effect of earplugs during the night on the onset of delirium and sleep perception: a randomized controlled trial in intensive care patients. *Crit Care* 2012; 16:R73.
- Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009; 373:1874.
- Landefeld CS, Palmer RM, Kresevic DM, Fortinsky RH, Kowal J. A randomized trial of care in a hospital medical unit especially designed to improve the functional outcomes of acutely ill older patients. *N Engl J Med*. 1995;332(20):1338)
- van den Boogaard M, Slooter AJC, Bruggemann RJM, Schoonhoven L, Beishuizen A, Vermeijden JW, Pretorius D, de Koning J, Simons KS, Dennesen PJW, et al. Effect of haloperidol on survival among critically ill adults with a high risk of delirium: The REDUCE randomized clinical trial. *JAMA* 2018, 319:680-690
- Breitbart W, Marotta R, Platt MM, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. *Am J Psychiatry* 1996; 153:231.
- Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. *Anesthesiology* 2012; 116:987.
- Parellada E, Baeza I, de Pablo J, Martinez G. Risperidone in the treatment of patients with delirium. *J Clin Psychiatry* 2004; 65:348.
- Skrobik YK, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. *Intensive Care Med* 2004; 30:444.
- Hawkins SB, Bucklin M, Muzyk AJ. Quetiapine for the treatment of delirium. *J Hosp Med* 2013; 8:215.
- Overshott R, Karim S, Burns A. Cholinesterase inhibitors for delirium. *Cochrane Database Syst Rev* 2008; :CD005317.
- Sampson EL, Raven PR, Ndhlovu PN, et al. A randomized, double-blind, placebo-controlled trial of donepezil hydrochloride (Aricept) for reducing the incidence of postoperative delirium after elective total hip replacement. *Int J Geriatr Psychiatry* 2007; 22:343.
- Liptzin B, Laki A, Garb JL, et al. Donepezil in the prevention and treatment of post-surgical delirium. *Am J Geriatr Psychiatry* 2005; 13:1100.
- Leung JM, Sands LP, Rico M, et al. Pilot clinical trial of gabapentin to decrease postoperative delirium in older patients. *Neurology* 2006; 67:1251.
- Sultan SS. Assessment of role of perioperative melatonin in prevention and treatment of postoperative delirium after hip arthroplasty under spinal anesthesia in the elderly. *Saudi J Anaesth* 2010; 4:169.
- Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, Watson PL, Weinhouse GL, Nunnally ME, Rochweg B, Balas MC, van den Boogaard M, Bosma KJ, Brummel NE, Chanques G, Denehy L, Drouot X, Fraser GL, Harris JE, Joffe AM, Kho ME, Kress JP, Lanphere JA, McKinley S, Neufeld KJ, Pisani MA, Payen JF, Pun BT, Puntillo KA, Riker RR, Robinson BRH, Shehabi Y, Szumita PM, Winkelman C, Centofanti JE, Price C, Nikayin S, Misak CJ, Flood PD, Kiedrowski K, Alhazzani W. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. *Crit Care Med*. 2018 Sep;46(9):e825-e873
- Loneragan E, Luxenberg J, Areosa Sastre A, Wyllier TB. Benzodiazepines for delirium. *Cochrane Database Syst Rev* 2009;
- Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006; 104:21.
- Riker RR, Shehabi Y, Bokesch PM, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. *JAMA* 2009; 301:489.
- Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. *JAMA* 2007; 298:2644.
- Platt MM, Breitbart W, Smith M, et al. Efficacy of neuroleptics for hypoactive delirium. *J Neuropsychiatry Clin Neurosci* 1994; 6:66.