

ICU Delirium: An Expert Interview With E. Wesley Ely, MD, MPH

Better Assessment and Better Management of Intensive Care Unit Delirium Leads to Better Outcomes for Intensive Care Unit Survivors: An Expert Interview With E. Wesley Ely, MD, MPH

E. Wesley Ely, MD, MPH; Cayce L. Strength, BSN, RN

Medscape Critical Care. 2008; ©2008 Medscape
Posted 06/16/2008

Editor's Note:

Intensive care unit (ICU) clinicians have historically focused on short-term outcomes such as successful cardiopulmonary resuscitation, hemodynamic stability, and patient survival. During this decade, long-term neurocognitive outcomes in ICU survivors have been the subject of extensive investigation. Data from a number of studies and multiple disciplines have elucidated a chilling reality -- that cognitive dysfunction following critical illness is common, is associated with impairments in ability to perform normal everyday activities, decreased quality of life, and an inability to return to work, and may be permanent. ICU delirium, a form of acute brain dysfunction, is a life-threatening global disturbance of cognitive function that is highly prevalent in critically ill patients, especially the elderly and patients requiring mechanical ventilation. ICU delirium is reported to occur in up to 85% of critically ill patients.^[1,2] Although the exact mechanisms of ICU delirium are not fully understood, critical illness and its treatment has been shown to lead to de novo cerebral atrophy including white and grey matter abnormalities.^[3] ICU delirium is a strong, independent predictor of prolonged www.icudelirium.org hospitalization, reintubation, increased mortality, and increased cost of care. All ICU clinicians should be aware of risk factors for ICU delirium because some are modifiable. ICU nurses in particular play a key role in identifying delirium in critically ill patients. Validated tools for assessment of delirium and sedation level are available that are relatively easy to use. Incorporation of delirium assessment into clinical practice in the ICU may improve long-term patient outcomes.

Susan L. Smith, MN, PhD, Editorial Director for Medscape Critical Care, interviewed E. Wesley Ely, MD, MPH, and founder of Vanderbilt's ICU Delirium and Cognitive Impairment Study Group and Cayce Strength, BSN, RN, about brain dysfunction in critically ill patients and what physicians and nurses can do to prevent and ameliorate it.

Medscape: Why is it important for us to have this discussion today about ICU delirium?

Dr. Ely: ICU delirium has been identified over the past decade as an independent predictor of not only length of stay in the hospital and the ICU and cost of care, but also of a 3-fold higher rate of death by 6 months,^[1] and is likely associated with a higher risk for long-term cognitive impairment in ICU survivors.

Medscape: Could you comment a bit more about the cognitive impairment in ICU survivors?

Dr. Ely: We have previously reported that patients who had delirium were 10 times more likely to have cognitive impairment at hospital discharge than were patients who did not have delirium.^[4] Subse-

quently, we have been following patients out to 3 and 12 months and have found that the duration of delirium is related to the likelihood of long-term cognitive impairment. The cognitive impairment I am talking about is being measured using validated instruments for neurologic assessment,^[5-7] much the same as those you would use to test someone for dementia, meaning that this is commensurate with a mild-to-moderate and sometimes severe dementia that seems to be ICU-acquired or ICU-accelerated.

This is to say that patients come into the hospital with no previous detriment in their baseline cognitive status and then delirium develops amidst their critical illness and they end up with a dementia-like illness; or they may come in with mild dementia cognitive impairment and subsequently go on to have more pronounced, long-term cognitive impairment. This cognitive impairment appears permanent in one third to one half of these patients.

I should point out that this type of impairment interferes with activities of everyday life. These people have problems with executive function and memory, so that going back to work is often very difficult and consequently, many are forced to leave the workforce. In addition, those who previously functioned in family roles such as matriarch or patriarch, may no longer be able to do so because they cannot remember people's names, find their car in a parking lot, balance their checkbook, or help their kids with homework.

Medscape: What are the most common risk factors for ICU delirium, or what groups of patients are at the highest risk?

Dr. Ely: The highest-risk patients are those who have systemic illnesses such as severe sepsis or congestive heart failure that effect blood flow and exposure of the brain to oxygen and nutrients. In addition, there are baseline demographic factors, such as mild cognitive impairment, advanced age, and previous use of psychoactive medications, tobacco, or alcohol, to which they may not have access while in the ICU, which can lead to withdrawal symptoms. Patients who are sick enough to require mechanical ventilation are also at high risk for developing delirium. The ventilator itself introduces a host of therapeutic issues, such as high doses of sedatives and narcotics that may be delirigenic.

Medscape: Is sleep deprivation an important factor in ICU delirium?

Dr. Ely: Sleep deprivation in the ICU is a tremendous problem. Most ICU patients get only about 1 to 2 hours of real sleep a day. They may appear unconscious, but that is because we give them sedatives and analgesics such as benzodiazepines, propofol, and fentanyl that render them unconscious, but do not allow them to get normal sleep. In fact, most of the time patients are in stage 1 sleep or are not asleep at all, with multiple arousals per minute. This is a very catabolic state, contrary to sleep, which is an anabolic state. Ultimately, after days of such lack of sleep, the brain is adversely affected and patients are at high risk for developing delirium. Facilitating adequate and quality sleep requires doing things like keeping the lights on during the day and off at night, bathing patients during the day, and reducing noise at night. In addition, we should try to give these patients fewer sedatives and analgesics, which prevent them from getting real sleep.

Medscape: Are there pharmacologic agents that place patients at greater risk than others?

Dr. Ely: Yes, there are medications that may be less delirigenic. The benzodiazepines across class appear to be the worst offenders. My group has published 2 studies showing that lorazepam and midazolam are the most delirigenic drugs of the psychoactive

agents used to sedate patients.^[8,9] Propofol and fentanyl are not off the hook, however, and can be offenders when given in higher doses. Morphine or fentanyl can sometimes decrease delirium when used to treat pain, but when overused as sedatives we find that they increase delirium.

Two recent randomized, controlled trials, one published in JAMA^[10] and one as yet unpublished, have shown that dexmedetomidine, an alpha-2 agonist like clonidine, resulted in less acute brain dysfunction compared with benzodiazepines. What we do not yet know is whether this is because of the alpha-2 agonist mechanism of action vs the GABA (gamma-aminobutyric acid) agonism of benzodiazepines and propofol, or because of the very short half-life of dexmedetomidine. I need to disclose that I have received grant support and honoraria from Hospira, the manufacturer of dexmedetomidine.

Medscape: Are there tools that nurses and physicians can readily use to assess for and monitor ICU delirium?

Mrs. Strength: In the medical-surgical ICU, we monitor our patients for delirium using the Richmond Agitation-Sedation Scale (RASS)^[7] and Confusion Assessment Method for the ICU (CAM-ICU) at least twice a shift, sometimes every 4 hours. Nurses also actively participate in multidisciplinary rounds with physicians every morning and report the 4 important components of delirium monitoring: (1) current sedatives and amount/doses, (2) target RASS, (3) actual RASS, and (4) CAM-ICU scores. We also use RASS-targeted or goal-directed sedation, which the nurses report on every morning. We would like to emphasize that there are other viable and well-validated sedation scales and other delirium instruments such as the Intensive Care Delirium Screening Checklist^[11] that ICU clinicians can choose from for their patient monitoring. The important thing is to explore which ones you believe your group supports, implement them with compliance monitoring, and make sure over time to repetitively recalibrate your users (nurses and doctors) so that excellent patient monitoring is achieved.

Medscape: Is the RASS incorporated into a clinical pathway or the electronic medical record?

Mrs. Strength: Yes, RASS-targeted sedation is a physician order and is included in the patient's medication administration record and order set. The CAM-ICU is also incorporated into the computerized ICU flow sheet. In addition, documentation of RASS and CAM-ICU is being tracked as a quality improvement project.

Dr. Ely: The Society of Critical Care Medicine Clinical Practice Guidelines for the Sustained Use of Sedatives and Analgesics in the Critically Ill Adult recommend that a standardized, validated sedation scale and delirium monitoring be used for all ICU patients.^[12] These tools we are using have been translated into at least 14 languages and are being used in thousands of ICUs around the world. We recommend that every ICU use a 2-step approach to neurologic monitoring: (1) a sedation scale to clinically target administration of potent drugs and (2) assessment, early detection, and early treatment of delirium.

Medscape: What has changed since you began routine assessment and standardized monitoring of ICU delirium?

Mrs. Strength: Awareness of the problem has increased and communication among the members of the clinical team has improved, helping to achieve early detection of delirium. This model is now being incorporated into all ICUs at Vanderbilt University Medical Center.

Medscape: In your opinion, what mindset do clinicians need to change to provide better care for patients at risk for ICU delirium?

Mrs. Strength: Clinicians need to seriously think about the long-term impairments that patients can have as a result of ICU delirium. I realize that sometimes the focus is on issues that are more acute and clinically apparent. However, when a patient's critical illness has resolved, we don't want them to leave the ICU with serious cognitive impairment that might have been prevented by addressing the presence of delirium.

Dr. Ely: ICU delirium is a form of organ dysfunction. We attend to patients who have hypoxemia and who are in shock by focusing on the organs (ie, heart and lungs) that are not functioning normally. ICU delirium is another example of an organ (the brain) that is not working normally -- it is as simple as that -- and we need to treat it likewise, especially since we know that brain dysfunction has an adverse effect on length of stay, long-term cognitive function, and mortality. The problem is that this type of organ dysfunction is invisible unless you actively monitor for it. It is known that 80% to 90% of ICU delirium is hypoactive or mixed delirium.^[13] Hypoactive delirium is manifested by negative symptoms (vs positive symptoms such as pulling out intravenous lines or tubes that occur with hyperactive delirium); these patients sit or lie in bed with their brains turned off. You have to actually test the brain to see if the brain is on or not, which brings us back to the CAM-ICU. Clinicians also need to change their idea about what we can do about ICU delirium once it is diagnosed. A lot of things that cause it are iatrogenic and may be modifiable. Some of these modifiable causes include overuse of sedatives, unnecessarily restraining the patient, not getting patients out of bed, not letting patients sleep at night because of night shift routines (ie, baths are given at night), or not recognizing sepsis or congestive heart failure early enough. All of these things are manageable. I will close with the concept that the glass is half full, not half empty, meaning that while we do not have all the answers, we have a lot of answers. You cannot prevent or treat what you do not recognize in the first place.

References

1. Gunther ML, Jackson JC, Ely EW. The cognitive consequences of critical illness: practical recommendations for screening and assessment. *Crit Care Clin*. 2007;23:491-506.
2. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med*. 2007;33:66-73.
3. Gunther ML, Jackson JC, Ely EW. Loss of IQ in the ICU brain injury without the insult. *Med Hypotheses*. 2007;69:1179-1782.
4. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA*. 2004;291:1753-1762.
5. 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.
6. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). *Crit Care Med*. 2001;29:1370-1379.

7. Ely EW, Truman B, Shintani A, et al. Monitoring sedation status over time in ICU patients: the reliability and validity of the Richmond Agitation Sedation Scale (RASS). *JAMA*. 2003;289:2983-2991.
8. Pandharipande PP, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology*. 2006;104:21-26.
9. Pandharipande P, Cotton B, Shintani A, et al. Prevalence and risk factors for development of delirium in surgical and trauma ICU patients. *J Trauma*. In press.
10. 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;298:2644-2653.
11. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med*. 2001;27:859-864. Used with permission.
12. Jacobi J, Fraser GL, Coursin DB, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med*. 2002;30:117-141.
13. Peterson JF, Pun BT, Dittus RS, et al. Delirium and its motoric subtypes: a study of 614 critically ill patients. *J Am Geriatr Soc*. 2006;54:479-484.
14. Gunther NL, Morandi A, Ely EW. Pathophysiology of delirium in the intensive care unit. *Crit Care Clin*. 2008;24:45-65, viii.
15. ICU Delirium and Cognitive Impairment Study Group. Available at: <http://www.icudelirium.org>. Accessed May 16, 2008.
16. Masica AL, Girard TD, Wilkinson GR, et al. Clinical sedation scores as indicators of sedative and analgesic drug exposure in intensive care unit patients. *Am J Geriatr Pharmacother*. 2007;5:218-231.
17. Nelson JE, Tandin N, Mercado AF, et al. Brain dysfunction: another burden for the chronically critically ill. *Arch Intern Med*. 2006;166:1993-1999.
18. Soja SL, Pandharipande PP, Fleming SB, et al. Implementation, reliability testing, and compliance monitoring of the Confusion Assessment Method for the Intensive Care Unit in trauma patients. *Intensive Care Med*. 2008 Feb 23. [Epub ahead of print]
19. Pandharipande PP, Ely EW. Delirium and its motoric subtypes: a study of 614 critically ill patients. *J Am Geriatr Soc*. 2006;54:479-484.
- Nelson JE, Tandin N, Mercado AF, et al. Brain dysfunction: another burden for the chronically critically ill. *Arch Intern Med*. 2006;166:1993-1999.
- Soja SL, Pandharipande PP, Fleming SB, et al. Implementation, reliability testing, and compliance monitoring of the Confusion Assessment Method for the Intensive Care Unit in trauma patients. *Intensive Care Med*. 2008 Feb 23. [Epub ahead of print]
- Pandharipande PP, Ely EW. Delirium and its motoric subtypes: a study of 614 critically ill patients. *J Am Geriatr Soc*. 2006;54:479-484.

Wes Ely, MD, MPH, Professor of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University School of Medicine and Vanderbilt University Medical Center, Nashville, Tennessee

Cayce L. Strength, BSN, RN, Research Nurse Specialist II, Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, Tennessee

Susan L. Smith, RN, PhD, Editorial Director, Medscape Critical Care and Transplantation, Medscape LLC, New York, NY

Disclosure: Wes Ely, MD, MPH, has disclosed that he has received grants for clinical research and educational activities from Lilly, Pfizer, Hospira, and Aspect Medical. Dr. Ely has also disclosed that he has served as an advisor or consultant to Lilly, Hospira, and Healthways.

Disclosure: Cayce L. Strength, BSN, RN, has disclosed that she has received a grant from Aspect Medical and has served as an advisor or consultant to Hospira.

Disclosure: Susan L. Smith, RN, PhD, has disclosed no relevant financial relationships.

Suggested Readings

- Gunther NL, Morandi A, Ely EW. Pathophysiology of delirium in the intensive care unit. *Crit Care Clin*. 2008;24:45-65, viii.
- ICU Delirium and Cognitive Impairment Study Group. Available at: <http://www.icudelirium.org>. Accessed May 16, 2008.
- Masica AL, Girard TD, Wilkinson GR, et al. Clinical sedation scores as indicators of sedative and analgesic drug exposure in intensive care unit patients. *Am J Geriatr Pharmacother*. 2007;5:218-231.