ICU Delirium
Epidemiology, Monitoring, & Management

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DISCLAIMER

This slide set has been created by Dr. Ely and Ms. Truman of the Vanderbilt and VA ICU Delirium and Cognitive Impairment Study group to help you educate others regarding this very dangerous condition, which is experienced by so many millions of patients every year. Please contact us through the website if you have any suggestions or questions regarding this material.

Sincerely,

E. Wesley Ely, MD, MPH, FCCM, FACP
Brenda T. Pun, BSN, MSN, ACNP
Outline of Discussion

• **Background**  – the scope of the problem
• **Outcomes**  – important new data
• **Monitoring**  – now recommended as standard
• **Management**  – prevention and treatment
• **Call to action**  – act now, modify with new data
Background on ICU Delirium
• 50-80% of ventilated patients develop delirium
• 20-50% of lower severity ICU patients develop delirium
• Over 40,000 ventilated ICU patients in U.S are delirious every day
• 10% remain delirious at hospital discharge
Delirium is often ‘invisible’
(unless you look for it)

- The vast majority of delirium in the ICU is either hypoactive “quiet” subtype (35%) or mixed (64%)
- Very little (1%) is the pure hyperactive subtype
- Older age is a strong predictor of hypoactive delirium
- Onset: ICU Day 2 (+/-1.7)
- How long: 4.2 (+/-1.7) days

Ely EW et al. JAMA2001; 286, 2703-2710
Peterson J et al. JAGS 2006 in press
McNicoll L et al. JAGS 2003;51:591-98
Motoric Subtypes of Delirium

Admission Day in ICU

Cumulative Proportion with Delirium

- Hypoactive delirium
- Mixed-type delirium
- Hyperactive delirium

Peterson J JAGS, 2006;54 (April)
Delirium Pathophysiology

ICU Delirium and Clinical Outcomes
Delirium and Outcomes

- Increased ICU Length of Stay (8 vs 5 days)
- Increased Hosp Length of Stay (21 vs. 11 days)
- Increased time on the Ventilator (9 vs 4 days)
- Higher costs ($22,000 vs $13,000 in ICU costs)
- Estimated $4 to $16 billion associated U.S. costs
- 3-fold increased risk of death
- Possibly increased Long-Term Cognitive Impairment (aka, ICU accelerated dementia)

Delirium and Hospital LOS: pilot evaluation

- 39 of 48 patients (81.3%) developed delirium
- Duration of delirium was associated with ICU and hospital length of stay (P=0.0001)
- Using multivariate analysis, delirium was the strongest predictor of hospital stay (P=0.006) even after adjusting for severity of illness, age, gender, race, and benzodiazepine and narcotic administration

Ely et al, Intensive Care Med 2001; 27(12):1892-1900
Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit

Ely EW et al, JAMA 2004;291:1753-1762
## Patient Demographics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Ever Delirium (n=183)</th>
<th>Never Delirium (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (±SD)</td>
<td>56.4 (16.7)</td>
<td>53.6 (17.3)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>95 (51.9)</td>
<td>18 (43.9)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, %</td>
<td>145 (79.2)</td>
<td>32 (78.1)</td>
</tr>
<tr>
<td>Black, %</td>
<td>38 (20.8)</td>
<td>9 (22.0)</td>
</tr>
<tr>
<td>Charlson Co-morbidity, mean (±SD)</td>
<td>3.7(2.7)</td>
<td>3.2 (2.8)</td>
</tr>
<tr>
<td>APACHE II, mean (±SD)</td>
<td>25.6 (8.1)</td>
<td>23.2 (9.6)</td>
</tr>
<tr>
<td>SOFA Score, mean (±SD)</td>
<td>9.6 (3.4)</td>
<td>9.5 (3.0)</td>
</tr>
<tr>
<td>Dementia Scale, mean (±SD)</td>
<td>0.2 (0.8)</td>
<td>0.1 (0.57)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Ever Delirium (n=183)</td>
<td>Never Delirium (n=41)</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Sepsis / ARDS</td>
<td>95 (52.0)</td>
<td>24 (58.5)</td>
</tr>
<tr>
<td>MI</td>
<td>4 (2.2)</td>
<td>0</td>
</tr>
<tr>
<td>CHF</td>
<td>11 (6.1)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>Hepatic or renal failure</td>
<td>8 (4.4)</td>
<td>0</td>
</tr>
<tr>
<td>COPD</td>
<td>18 (9.8)</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>GI Bleeding</td>
<td>7 (3.8)</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>13 (7.1)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>Drug overdose</td>
<td>8 (4.4)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>Other</td>
<td>97 (53.0)</td>
<td>28 (68.3)</td>
</tr>
</tbody>
</table>

* More than one admission diagnosis listed for some patients.
## Univariate Clinical Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Never Delirium</th>
<th>Ever Delirium</th>
<th>RR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS in ICU</td>
<td>5.0 (4-6)</td>
<td>8.0 (7-9)</td>
<td>2.0 (1.5-3.1)</td>
</tr>
<tr>
<td>LOS in Ward</td>
<td>4.5 (3-6)</td>
<td>8.0 (6-11)</td>
<td>1.8 (1.2-2.5)</td>
</tr>
<tr>
<td>LOS in Hospital</td>
<td>11 (8-15)</td>
<td>21 (19-25)</td>
<td>2.1 (1.7-3.3)</td>
</tr>
<tr>
<td>6-mo mortality</td>
<td>15%</td>
<td>34%</td>
<td>2.4 (1.0-5.6)</td>
</tr>
</tbody>
</table>

6 Month Mortality

Survival (%) vs Time (Months)

- Normal (n=17)
- Mild (n=68)
- Moderate (n=69)
- Severe (n=70)
Greater Delirium Severity and Duration Associated with Increased Cost

Figure 2

Milbrandt E et al, Crit Care Med 2004;32:955-962
• After adjustment for age, gender, race, pre-existing comorbidity and cognitive impairment, ICU diagnoses, and severity of illness…delirium was associated with a 3-fold higher rate of death by 6 months and a 1.6-fold increase in ICU costs, and 10-fold higher rate of cognitive impairment at hospital discharge (p<0.001)

• National implications: Annual cost $7-20 billion

Milbrandt et al, Crit Care Med 2004;32:955-962
Delirium in Pneumonia

• “Altered mental status” was strongest independent predictor of mortality community-acquired pneumonia (O.R. 3.1, p<0.001)

• Relationship was stronger with advancing age

Waterer GW, Kessler LA, Wunderink R. AJRCCM 2004; 169:910-914
Mortality and Nursing Home Placement

- N=88 ICU survivors >65 years
- Delirium was independently associated with increased mortality or new nursing home placement (RR 3.4, 95% C.I. 1.0-11.3) after adjustment for age, dementia, comorbidities, and illness severity
- Trend towards higher rates of re-hospitalization (RR 1.6, 95% C.I. 0.8 to 3.4).

McNicoll L et al, JAGS 2004
Delirium and Higher Mortality in Taiwan

- Prospective cohort of 109 ventilated adults
- 13X higher likelihood of hospital mortality in delirious patients as compared to those without delirium after adjusting for relevant covariates
  (H.R. 13.0, 95% CI 2.7-62.9)

Lin SM, Crit Care Med 2004; 32: 2254-2259
Delirium in surgical ICU patients

- 100 non-elective surgical ICU patients
- Prevalence of delirium was 69%
- Average 4 days longer in the ICU (p=0.03)
- Fewer days alive and off ventilator (p=0.001)
- Midazolam use was strongest modifiable predictor

Pandharipande et al, 2006 SCCM
Delirium, Restraints, and Sedatives

- Barnes/Washington Univ study of 93 ventilated patients
- 47% developed delirium (CAM-ICU+)
- 29% persistent coma
- 24% normal cognition during study
- Continuous infusions of midazolam and fentanyl as well as restraints associated with delirium

Micek S et al, CCM 2005;33:1260-65
Cognitive Impairment and Patients’ Preferences

- The potential for being left cognitively impaired was the major determinant of patients’ treatment preferences at the end of life.

Fried, NEJM 2002;346:1061-1066
Monitoring ICU Delirium
Important yet under-diagnosed

• In a survey of 902 international healthcare professionals, we found that delirium was considered a very serious problem in the ICU by 92%
• Under-diagnosis was acknowledged by 80%

### Patient Comfort

<table>
<thead>
<tr>
<th>Pain</th>
<th>Sedation</th>
<th>Delirium</th>
</tr>
</thead>
</table>

Assessment of ICU Patients

<table>
<thead>
<tr>
<th>Patient Comfort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
</tr>
<tr>
<td>- 0-10 Scale VAS Scale</td>
</tr>
<tr>
<td>- Subjective/Physiologic indicators</td>
</tr>
</tbody>
</table>

The CAM-ICU takes ~30 seconds on average for either doctors or nurses to perform.

Why? Because most times delirium is diagnosed via just a few steps!
CAM-ICU

1. Acute onset of mental status changes or a fluctuating course

and

2. Inattention

and

3. Disorganized Thinking

or

4. Altered level of consciousness

= Delirium

Two Step Approach to Assessing Consciousness

Step 1 Level:
Arousal/Sedation Assessment (RASS, SAS)
(If pt opens eyes to voice then proceed to Step 2)

Step 2 Content:
Delirium Assessment (CAM-ICU)
### Feature 1: Acute Onset or Fluctuating Course
Positive if you answer ‘yes’ to either 1A or 1B.

<table>
<thead>
<tr>
<th>1A:</th>
<th>Is the pt different than his/her baseline mental status?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Or</td>
<td></td>
</tr>
<tr>
<td>1B:</td>
<td>Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation scale (e.g. RASS), GCS, or previous delirium assessment?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### Feature 2: Inattention
Positive if either score for 2A or 2B is less than 8.

Attempt the ASE letters first. If pt is able to perform this test and the score is clear, record this score and move to Feature 3. If pt is unable to perform this test or the score is unclear, then perform the ASE Pictures. If you perform both tests, use the ASE Pictures’ results to score the Feature.

#### 2A: ASE Letters: record score (enter NT for not tested)
**Directions:** Say to the patient, “I am going to read you a series of 10 letters. Whenever you hear the letter ‘A,’ indicate by squeezing my hand.” Read letters from the following letter list in a normal tone.

- S A V E A H A A R T

**Scoring:** Errors are counted when patient fails to squeeze on the letter ‘A’ and when the patient squeezes on any letter other than “A.”

Score (out of 10): ____

#### 2B: ASE Pictures: record score (enter NT for not tested) Directions are included on the picture packets.

Score (out of 10): __

### Feature 3: Disorganized Thinking
Positive if the combined score is less than 4

#### 3A: Yes/No Questions
(Use either Set A or Set B, alternate on consecutive days if necessary):

<table>
<thead>
<tr>
<th>Set A</th>
<th>Set B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Will a stone float on water?</td>
<td>1. Will a leaf float on water?</td>
</tr>
<tr>
<td>2. Are there fish in the sea?</td>
<td>2. Are there elephants in the sea?</td>
</tr>
<tr>
<td>3. Does one pound weigh more than two pounds?</td>
<td>3. Do two pounds weigh more than one pound?</td>
</tr>
<tr>
<td>4. Can you use a hammer to pound a nail?</td>
<td>4. Can you use a hammer to cut wood?</td>
</tr>
</tbody>
</table>

Score ___ (Patient earns 1 point for each correct answer out of 4)

#### 3B: Command
Say to patient: “Hold up this many fingers” (Examiner holds two fingers in front of patient) “Now do the same thing with the other hand” (Not repeating the number of fingers). *If pt is unable to move both arms, for second part of the command ask patient “Add one more finger”

Score ___ (Patient earns 1 point if able to successfully complete the entire command)

### Feature 4: Altered Level of Consciousness
Positive if the Actual RASS score is anything other than “0” (zero)

### Overall CAM-ICU (Features 1 and 2 and either Feature 3 or 4):
Large-scale implementation of sedation and delirium monitoring in the intensive care unit: A report from two medical centers

Objective: To implement sedation and delirium monitoring via a process-improvement project in accordance with Society of Critical Care Medicine guidelines and to evaluate the challenges of modifying intensive care unit (ICU) organizational practice styles.

Design: Prospective observational cohort study.

Setting: The medical ICUs at two institutions: the Vanderbilt University Medical Center (VUMC) and a community Veterans Affairs hospital (York-VA).

Subjects: Seven hundred eleven patients admitted to the medical ICUs for >24 hrs and followed over 4,163 days during a 21-month study period.

Interventions: Unit-wide nursing documentation was changed to accommodate a sedation scale (Richmond Agitation-Sedation Scale) and delirium instrument (Confusion Assessment Method for the ICU). A 20-min introductory in-service was performed for all ICU nurses, followed by graded, staged educational interventions at regular intervals. Data were collected daily for compliance, and randomly 40% of nurses each day were chosen for accuracy spot-checks by reference raters. An implementation survey questionnaire was distributed at 6 months.

Measurements and Main Results: The implementation project involved 64 nurses (40 at VUMC and 24 at York-VA). Sedation and delirium monitoring data were recorded for 711 patients (614 at VUMC and 97 at York-VA). Compliance with the Richmond Agitation-Sedation Scale was 94.4% (21,931 of 23,220) at VUMC and 99.7% (5,387 of 5,403) at York-VA. Compliance with the Confusion Assessment Method for the ICU was 90% (7,323 of 8,166) at VUMC and 84% (1,571 of 1,871) at York-VA. The Confusion Assessment Method for the ICU was performed more often than requested on 63% of shifts (5,146 of 8,166) at VUMC and on 8% (151 of 1,871) of shifts at York-VA. Overall weighted-k between bedside nurses and reference raters for the Richmond Agitation-Sedation Scale were 0.89 (95% confidence interval, 0.88 to 0.92) at VUMC and 0.77 (95% confidence interval, 0.72 to 0.83) at York-VA. Overall agreement (k) between bedside nurses and reference raters using the Confusion Assessment Method for the ICU was 0.92 (95% confidence interval, 0.90–0.94) at VUMC and 0.75 (95% confidence interval, 0.68–0.81) at York-VA. The two most-often-cited barriers to implementation were physician buy-in and time.

Conclusions: With minimal training, the compliance of bedside nurses using sedation and delirium instruments was excellent. Agreement of data from bedside nurses and a reference-standard rater was very high for both the sedation scale and the delirium assessment over the duration of this process-improvement project. (Crit Care Med 2005; 33:000–000)

Key Words: delirium; sedation; implementation; mechanical ventilation; protocols; monitoring; intensive care; nursing; quality improvement; process improvement; clinical practice guidelines
Can we achieve high compliance?

On 63% of shifts, the CAM-ICU was recorded by nurses more often than the once/shift requirement.
Will monitoring be done correctly?

CAM-ICU Agreement
Between Nurse and Ref Standard Rater
ICU Delirium and Management
This glass is half full. Even with many unanswered questions, there are many things one can do for our patients!
# Selected Delirium Risk Factors *

<table>
<thead>
<tr>
<th>Host Factors</th>
<th>Acute Illness</th>
<th>Iatrogenic or Environmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Sepsis *</td>
<td>Metabolic disturbances *</td>
</tr>
<tr>
<td>Baseline comorbidities</td>
<td>Hypoxemia *</td>
<td>Anticholinergic medications *</td>
</tr>
<tr>
<td>Baseline cognitive impairment</td>
<td>Global severity of illness score</td>
<td>Sedative and analgesic medications *</td>
</tr>
</tbody>
</table>

* Potentially modifiable factors; sleep deprivation likely huge but not studied to date
Risk factors you can’t control...

Age
Each year ↑ risk by 2%

Illness Severity
each APACHE point ↑ risk by 6%

Pandharipande, Anesthesiology 2006;104:21-26
Risk factors you can control...medications

Delirium Risk

Pandharipande, Anesthesiology 2006;104:21-26
1st prevent... 2nd treat ICU delirium

1. Consider developing protocolized approach, though most data are from non-ICU settings *
2. Treat underlying infection and CHF
3. Correct metabolic disturbances and hypoxemia
4. Frequent reorientation of patient by nurse and family
5. Goal-directed sedation/analgesia and/or daily wake-up
6. Stop the ventilator (SBT) each day to test readiness
7. Early mobilization and physical therapy
8. Attention to optimizing sleep patterns

* Inouye S, NEJM 1999;340:669-76
* Marcantonio E, JAGS 2001;49:516-22
Psychoactive Medications
Treatment of Delirium

1. Identify etiologies - usually multiple likely causes
2. Modify Risk Factors (e.g., reduce benzodiazepines)
3. No FDA approved therapies
4. Haloperidol (Haldol) 2-5mg IVP q 6h
5. Atypical antipsychotics are also used
6. Monitor side effects carefully: QTc prolongation, torsades de pointes, extrapyramidal symptoms *
7. Update approach as literature emerges from ongoing trials!

Hypotheses being tested by us and others in ongoing RCTs

1. Use standard sedatives and analgesics but change *quantity and delivery*
2. Use novel sedatives and analgesics with a *different mechanism*
3. Change drug class/paradigm to affect *different neurotransmitters* (*e.g.*, *antipsychotics*)
Conclusions on ICU Delirium

• ICU delirium is an under-recognized form of acute organ dysfunction in the critically ill
• It occurs in the majority of ventilated ICU patients, preferentially affecting older patients
• Delirium is an independent predictor of length of stay, cost of care, and mortality at 6 months
• Simple, quick, routine monitoring will help target patients for earlier interventions that may improve outcomes
• Management options are many and will become clearer with completion of ongoing trials
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• Gordon R. Bernard, MD Division Chief APCC, Critical Care Research
• Art P. Wheeler, MD Clinical Trialist in Critical Care
• Pratik Pandharipande, MD, MSCI Anesthesiology
• Bryan Cotton, MD; Bill Obremskey MD, MPH Trauma and Orthopedic Surgery
• Herbert Meltzer, MD; Paul Ragan, MD Psychiatry, Antipsychotics
• Sharon Gordon, PhD; Jim Jackson, PhD Geriatric Neuropsychology
• Howard S. Kirshner, MD Behavioral Neurology
• Paula Watson, MD Sleep Medicine, Critical Care
• Grant Wilkinson, PhD Clinical Pharmacology
• Rommel Tirona, MD; Usha Nair PhD Clinical Pharmacology
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• Ted Speroff, PhD Psychometrics, Safety
• Jennifer Thompson, BA, MPH Database, Biostatistics
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• Meredith Gambrell, BS Grants Specialist and Administrator
• Hope Campbell, PharmD and others Investigational Pharmacy
• Rasheeda Stephens, BS; Steve Cook, BS Medical Students