Comprehensive Care of Delirious Patients

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Disclosures

None
Objectives

• Identify medical and surgical patients at highest risk for developing delirium in the hospital
• Articulate the outcomes linked to hospital-associated delirium
• Describe how to implement a multi-disciplinary strategy for the prevention of delirium at your hospital

Delirium

DEFINITION & PATHOPHYSIOLOGY
Delirium: DSM V

A. A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).

B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.

C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).

D. The disturbances in Criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.

E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

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Model of Delirium

- **Risk Factors**
- **Specific Insults**
- **Delirium**

- Increases in risk factors lead to specific insults, which result in delirium.
Risk Factors

- Age
- Pre-existing cognitive dysfunction
- Functional impairment
  - Mobility, vision, hearing
- Malnutrition
- Depression
- Alcohol abuse

Images from Wikimedia Commons

Altered Mental Status Mnemonic

Metabolic – hepatic encephalopathy, hyper/hypoglycemia, Wernicke’s encephalopathy, B12 deficiency, pancreatitis, porphyria
Oxygen – hypoxia/anoxia, hypercarbia/acidosis
Vascular – stroke, hemorrhage, hypertensive emergency, MI
Electrolytes/Endocrine – hypo/hypernatremia, hypo/hypercalcemia, hypo/hypermagnasemia, hyper/hypothyroidism, adrenal insufficiency
Structural – subdural hematoma, hydrocephalus
Seizure – non-convulsive or complex partial status, post-ictal confusion
Trauma/Tumor – head trauma, brain tumor
Uremia
Psychiatric
Infectious – any infection (sepsis, meningitis, UTI, pneumonia)
Drugs – intoxication and withdrawal
Altered Mental Status Mnemonic

**Metabolic** – hepatic encephalopathy, hyper/hypoglycemia, Wernicke’s encephalopathy, B12 deficiency, pancreatitis, porphyria

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**Seizure** – non-convulsive or complex partial status, post-ictal confusion

**Trauma/Tumor** – head trauma, brain tumor

**Uremia**

**Infectious** – any infection (sepsis, meningitis, UTI, pneumonia)

**Drugs** – intoxication and withdrawal

Iatrogenic Precipitants

- Medications (3 or more)
- Sleep deprivation
- Restraints
- Urinary catheters
- Frequent procedures
- Surgery (thoracic, vascular, and hip)
- Untreated pain
Even Demented Mice Get More Delirious

Murray et al, Neurobiology of Aging 2012

Ascending Arousal System

Saper et al, Nature 2005
Functional Connectivity in Subcortical Areas During Delirium

Choi et al, Am J Psychiatry 2012

Microglial Priming

Murray et al, Neurobiology of Aging 2012
Acetylcholine and Microglial Activation

Van Gool et al, Lancet 2010

Delirium

INCIDENCE & OUTCOMES
How Often Does Delirium Occur?

- Medical patients:
  - Prevalence (present on admission): 18-35%
  - Incidence (develops in the hospital): 11-14%
- Surgical patients:
  - Incidence: 11-51%
- ICU patients
  - Prevalence + Incidence: 80-85%

Inouye et al, Lancet 2013

What Are the Consequences of Delirium?

- Expensive:
  - Increased length of stay

Siddiqi et al, Age Aging 2006
Delirium: A Stress Test for the Brain

- Mortality (22 months)
  - Controls
  - Episode of Delirium
  - n=2957

- Institutionalization (14 months)
  - Controls
  - Episode of Delirium
  - n=2579

- Dementia (4 years)
  - Controls
  - Episode of Delirium
  - n=241

Witlox et al, JAMA 2010

Delirium and Accelerated Cognitive Decline

Davis et al, Brain 2012
Delirium Accelerates Cognitive Decline in Alzheimer Dementia

Global Cognition Scores in Survivors of Critical Illness.
ICU Delirium and Cognitive Decline

- ICU survivors have diminished cognitive function at 12 months
- 34% are similar to moderate TBI
- 24% are similar to mild AD
- Delirium is associated with lower cognitive function

![Chart showing cognitive function decline](chart1.png)

Pandharipande et al, *NEJM* 2013

Functional Outcomes and Delirium in Ventilated Patients

- Scale measures impairment in limb movement, eyesight, coordination, and hearing
- Adjusted for age, severity of illness, sepsis, duration of coma

![Chart showing functional outcomes](chart2.png)

Brummel et al, *Crit Care Med* 2014
Delirium

PREVENTION

Prevention: Pharmacologic

• Medications studied in randomized trials for prevention of delirium (mostly post-op):
  – Haloperidol (both ICU and non-ICU), risperidone, olanzapine
  – Donepezil, rivastigmine (113 patients)
  – Diazepam
  – Gabapentin
  – Epidural vs. halothane anesthesia
  – Ketamine

Melatonin

- 145 medical inpatients 65 and older; p=0.014
- 444 hip fracture patients 65 and older; p=0.4

Al-Aama et al, Int J Geriatr Psychiatry 2011; De Jonghe et al, CMAJ 2014

Ramelteon

- 67 (24 ICU) medical patients 65 – 89 years old randomized to ramelteon 8mg nightly vs. placebo
- 3% vs. 32% delirium rate (p=0.003)

Hatta et al, JAMA Psychiatry 2014
Dexmedetomidine and Delirium

Riker et al, *JAMA* 2009

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ICU Delirium: Dexmedetomidine vs. Morphine

Shehabi et al, *Anesthesiology* 2009
Prevention: Non-pharmacologic

• Pro-active geriatric consultation in hip-fracture patients reduced post-operative delirium from 50% to 32% (p = 0.04; NNT 5.6)
• Multicomponent intervention reduced delirium incidence from 15% to 9.9% (p=0.02; NNT 20)

**Early Mobilization**

Delirium reduced from 4 days to 2 days in 104 randomized ICU patients

Delirium reduced from 53% to 21% (p=0.003) among 27 patients before and 30 patients after intervention


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**Meta-analysis of Nonpharmacologic Delirium Prevention**

![Meta-analysis of Nonpharmacologic Delirium Prevention](image)

Hshieh et al, JAMA Int Med 2015
Hospital Elder Life Program

Length of stay reduced from 8.8 to 7.0 days among patients with delirium.

Rubin et al, JAGS 2011

Delirium

TREATMENT
HOPE-ICU:
Haloperidol vs. Placebo

- 141 mechanically ventilated ICU patients randomized to haloperidol 2.5 mg IV q8 hours or placebo
- Treated until CAM-ICU negative on 2 consecutive days or for 14 days


Pharmacologic Treatment

- Critical Care Guidelines (2013): “There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients.”
- Lancet 2013: “Because of the preponderance of evidence, pharmacological approaches to prevention and treatment [of delirium] are not recommended at this time.”

Pharmacologic Treatment

- Reserved for situations where a patient poses a danger to self or staff

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>1.25 mg to 2.5 mg daily</td>
<td>Better than placebo and equivalent to haloperidol in one RCT in reducing delirium severity</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>12.5 mg to 25 mg BID</td>
<td>Reduced delirium duration in one small RCT compared to placebo; no effect in another small RCT</td>
</tr>
</tbody>
</table>

All are off-label; see black box warning. Lonergan et al, Cochrane Database Syst Rev 2007

Treatment

- Treat the underlying cause
- Remove unnecessary medications
- Remove bladder catheters
- Early mobilization
- Normalize sleep-wake cycles
- Sitters instead of restraints
Delirium

CASES

When Do You Need to do a Head CT?

• 294 patients admitted to a hospital with acute confusion without clear etiology on admission
• 178 received head imaging

<table>
<thead>
<tr>
<th>Table 4: Predictive values of clinical markers for the absence of relevant diagnostic findings in cerebral imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical marker</td>
</tr>
<tr>
<td>------------------------------------</td>
</tr>
<tr>
<td>No focal signs</td>
</tr>
<tr>
<td>No focal signs + fever or dehydration</td>
</tr>
<tr>
<td>No focal signs + fever or dehydration + age &gt;65 years</td>
</tr>
<tr>
<td>No focal signs + fever or dehydration or urinary tract infection</td>
</tr>
<tr>
<td>No focal signs + fever or dehydration or urinary tract infection or pneumonia</td>
</tr>
<tr>
<td>No focal signs + pre-diagnosed dementia</td>
</tr>
<tr>
<td>No focal signs + pre-diagnosed dementia + no drowsiness</td>
</tr>
<tr>
<td>No focal signs + pre-diagnosed dementia + fever or dehydration</td>
</tr>
</tbody>
</table>

Hufschmidt et al, Acta Neurol Scand 2008
What About MRI?

• 67 y/o man with diabetes, hypertension, coronary artery disease is brought to the hospital for acute decline in mental status.

• Exam shows he is oriented to month but not date, hospital but not floor, and he can’t spell WORLD backwards. There is a mild pronator drift on the left.

• Head CT is negative.

Multifocal Strokes

![Brain MRI images]
Another Case...

• 65 y/o man has sudden onset fluctuating disorientation, forgetfulness, and strange behaviors such as attempting to turn the television on with his cell phone. He has a history of medically refractory epilepsy s/p right temporal lobectomy but still has one complex partial seizure per month.
• Neuro exam is nonfocal.

Thalamic Stroke
Strokes Masquerading as Delirium

- Basilar occlusion
- Medial and anterior thalamus
- Non-dominant parietal lobe
- Inferior division left MCA
- Diffuse shower of emboli

Lumbar Puncture in the Evaluation of AMS

- Hospital acquired delirium:
  - Unlikely to be helpful
    - No cases of meningitis in two series of 121 inpatients
  - Consider if:
    - fever, meningismus, headache are also present
    - immunocompromised, head trauma, or neurosurgery
- “Community acquired” delirium:
  - Low threshold to perform LP
  - Even in absence of fever and meningismus

When Should You Consider EEG?

- 74 y/o man with history of liver transplant and end stage renal disease presents after an episode of loss of consciousness and shaking with persistent confusion. Medications include tacrolimus.
- On exam he is alert and oriented but perseverates with some disorganized thinking. The degree of perseveration fluctuates over time.
- Basic labs and a non-con head CT are normal except for creatinine = 4.0 (baseline)

Nonconvulsive Status Epilepticus

- 7 - 10% of patients with unexplained encephalopathy have non-convulsive seizures – 12% for spells; 3% for AMS

Delirium

PREDICTION, SCREENING & DIAGNOSIS

Opportunities for Intervention

Day 1: Admit with pneumonia
- Identify high risk patients

Day 2: Dehydration, acute kidney injury
- Prevent dehydration; maintain sleep/wake cycle

Day 3: Drowsy all day
- Detect earlier with screening

Day 4: Pulls out IV, Fall
- Delirium typically diagnosed

## Prediction Rules

<table>
<thead>
<tr>
<th>Population</th>
<th>Components of Prediction Rule</th>
<th>Score</th>
<th>Rate of Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical patients ≥70</td>
<td>Cognitive impairment, poor visual acuity, high APACHE score, high BUN/Cr ratio</td>
<td>0</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-2</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-4</td>
<td>32%</td>
</tr>
<tr>
<td>AWOL Tool: medical patients ≥50</td>
<td>Age ≥80, unable to spell WORLD backward, orientation to place, illness severity</td>
<td>0</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>64%</td>
</tr>
<tr>
<td>Delirium Prediction Score: medical patients ≥65</td>
<td>Barthel index and BUN/Cr ratio: DPS = (1370 x BUN/Cr) – 4(Barthel Index)</td>
<td>≤-240</td>
<td>LR− = 0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;-240</td>
<td>LR+= 3.39</td>
</tr>
</tbody>
</table>


## Prediction Rules

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<tr>
<td>Elective non-cardiac surgery patients &gt;50</td>
<td>Age ≥70, alcohol abuse, cognitive impairment, high SAS class, abnormal pre-op electrolytes, AAA and thoracic surgery</td>
<td>0</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥3</td>
<td>50%</td>
</tr>
<tr>
<td>Elective cardiac surgery patients ≥60</td>
<td>MMSE ≤23 = 2 points; MMSE 24-27 = 1 point, prior stroke or TIA, Geriatric depression scale &gt;4, abnormal albumin</td>
<td>0</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥3</td>
<td>87%</td>
</tr>
</tbody>
</table>

Identifying Delirious Patients: CAM

1. Acute change in mental status and fluctuating course
2. Inattention
3. Disorganized thinking
4. Altered level of consciousness

94-100% sensitive and 90-95% specific compared to psychiatrist
High interobserver reliability

Inouye et al, Ann Int Med 1990

Clinical Validation of Delirium Screening Tests

• 2013 meta-analysis of CAM:
  – 9 studies
  – Sample size 52 – 280
  – Study design:

  \[ \text{CAM performed by trained RA or physician} \rightarrow \text{Delirium diagnosed by geriatrician or psychiatrist (gold standard)} \rightarrow \text{Test characteristics calculated} \]
Inattention: Hallmark of Delirium

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months of the Year Backward</td>
<td>83% (70-93)</td>
<td>90.8% (86.1-94.3)</td>
</tr>
<tr>
<td>[82% (65-93)]</td>
<td>[66% (58-73)]</td>
<td></td>
</tr>
<tr>
<td>MOTYB/evidence of confusion (either positive)</td>
<td>94% (83-99)</td>
<td>85% (79 -89)</td>
</tr>
<tr>
<td>Spatial Span Forward 5</td>
<td>92% (80-98)</td>
<td>69% (63-75)</td>
</tr>
<tr>
<td>Digit Span Forward (&lt;8)</td>
<td>58%</td>
<td>72%</td>
</tr>
<tr>
<td>Digit Span Backward (&lt;3)</td>
<td>81%</td>
<td>63%</td>
</tr>
<tr>
<td>Vigilance “A”</td>
<td>82% (65-93)</td>
<td>60% (52-68)</td>
</tr>
<tr>
<td>Serial Sevens (unable to do ≥4 subtractions; reach 72)</td>
<td>91% (75-98)</td>
<td>46% (38-54)</td>
</tr>
</tbody>
</table>

O’Regan et al, JNPP 2014; Leung et al, Int Psychogeriatrics 2011; Adamis et al, Ger & Geront 2015; **This slide meets cultural/linguistic competency requirement

Nursing Delirium Screening Scale

1. **Disorientation:** Verbal or behavioral manifestation of not being oriented to time or place or misperceiving persons in the environment.
2. **Inappropriate behavior:** Behavior inappropriate to place and/or for the person; e.g., pulling at tubes or dressings, attempting to get out of bed when that is contraindicated, and the like.
3. **Inappropriate communication:** Communication inappropriate to place and/or for the person; e.g., incoherence, noncommunicativeness, nonsensical or unintelligible speech.
4. **Illusions/Hallucinations:** Seeing or hearing things that are not there; distortions of visual objects.
5. **Psychomotor retardation:** Delayed responsiveness, few or no spontaneous actions/words; e.g., when the patient is prodded, reaction is deferred and/or the patient isunarousable.

Gaudreau et al, J Pain and Symptom Mgmt 2005
Delirium Prevention and Management Care Pathway

- Complete AWOL (1x) to assess delirium risk
  - **High Risk**: Score 2-4 (or, unable to assess)
  - **Low Risk**: Score 0-1
- Implement Delirium Care Plan (for prevention)
- Complete NuDESC Screen (Q shift)* on all patients
  - NuDESC ≥ 2 = Delirium
  - NuDESC < 2 = Delirium not present
- **Initiate Delirium Care Plan** (if not already done)
- Standard nursing assessment and care

* Best to complete screen toward end of shift; Communicate NuDESC score during all shift handoffs

- **NEW ADMISSION**
  - **TRANSFER**
- **Standard nursing assessment and care**
- **Communication**
  - Notify primary team of positive screen
  - Implement delirium care plan together with PCA
  - Provider to implement delirium order set and w/u causes
  - Floor pharmacist to review med list; note in EMR
Summary

• Definition and pathophysiology
• Epidemiology and outcomes
• Prevention and treatment
• Prediction, screening, and a multicomponent, interdisciplinary care pathway