Delirium in Older Adults: Differential Diagnosis and Appropriate Treatment

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Educational Objectives

By completing this educational activity, the participant should be better able to:

1. Discuss the predisposing and precipitating risk factors of delirium.
2. Recognize the different presentations of delirium.
3. Discuss how to evaluate, diagnose, and treat delirium.

Speaker Disclosure

Dr. Moquist disclosed that he has no financial relationships with any ineligible organizations or commercial interests.

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Dale C. Moquist, MD
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1

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3

3

Outline of Presentation

Incidence and Prognosis
Diagnosis and Spectrum
Neuropathophysiology
Risk Factors
Evaluation and Management
Quality Measures

4

4

Incidence and Prognosis

7

7

Case 1

- 76-year-old woman is admitted for elective R hip replacement. History includes HTN and DMII and takes enalapril and metformin.
- She complains of mild forgetfulness, often misplacing keys or where she has left the mail but otherwise, she has been healthy.
- She was swimming 3 miles a week until 3 months ago but her activities have been limited by R hip pain,
- Her vital signs are stable with a BMI of 22. On exam, she has decreased ROM of R hip with pain. Her SLUMS is 28/30.
- 32 hours postop, she pulls out her IV and wants to go home.

8

8

Audience Polling Question #1

Case 1: What is the MOST likely diagnosis?

A. Normal aging
B. Mild cognitive impairment
C. Major depression
D. Delirium
E. Alzheimer's Disease

9

9

Other Names for Delirium

- Acute confused state
- Acute mental status change
- Altered mental status
- Acute organic brain syndrome
- Reversible dementia
- Toxic or metabolic encephalopathy
- Delirium is the preferred term

10

10

Incidence

- Community Prevalence: 1-2%
- 1/3 of inpatients aged 70+ on general medical units
  - 1/2 on admission
  - Other 1/2 develop in the hospital
- Much higher in the ICU
  - 75% on mechanically ventilated patients
  - 35-50% among other ICU patients
- 15% in the ER
- Up to 85% at end of life

11

11

Morbidity

- Meta-analysis on 3,000 patients followed for 2 years showed increased risk:
  - 2-fold for death
  - 2.4-fold for institutionalization
  - 12.5-fold for new dementia
- Persistence of delirium poor long-term outcome: Attenuated delirium
  - Advanced age
  - Dementia
  - Multiple comorbidities
  - Functional impairment
- Persist > 6 months: Permanent cognitive decline

12

12

Prognosis

Independently associated with poor outcomes:

- Functional decline
- Cognitive decline
- Institutionalization
- Neurocognitive disorders
- Death

13

13

Diagnosis and Spectrum

14

14

DSM-V Delirium Diagnostic Criteria

- Disturbance of consciousness with reduced ability to focus, sustain, or shift attention
- Change in cognition or a perceptual disturbance NOT better accounted for by existing dementia
- Development over a short time (hours to days) and fluctuation during the day
- Evidence from history, physical, or labs that the disturbance is a direct physiologic consequence of a general medical condition or a drug
- Difficult to apply but use confusion assessment method
  - Clinically more useful
  - 95% sensitivity and specificity

15

15

Spectrum of Delirium

- Hyperactive, agitated, and or mixed delirium – 25% of all cases
  - "Classic" presentation
- Hypoactive delirium – 75% of all cases
  - "Quiet" delirium
  - Less often recognized and appropriately treated
  - Poorer prognosis
  - Special efforts to detect

16

16

Hyperactive Symptoms (≥3)

- Hypervigilance
- Restlessness
- Fast or loud speech
- Irritability
- Combativeness
- Impatience
- Swearing
- Singing
- Laughing
- Euphoria
- Anger
- Wandering
- Easy startling
- Fast motor responses
- Distractibility
- Tangentiality
- Nightmares
- Persistent thoughts
- Uncooperativeness

17

17

Hypoactive Symptoms (≥ 4)

- Unawareness
- Decreased alertness
- Sparse or slow speech
- Lethargy
- Slowed movements
- Staring
- Apathy

18

18

Delirium and Dementia

- Dementia = risk factor for delirium (SOE=A)
- Delirium in a patient *without* dementia:
  - Associated with incident dementia (SOE=B)
- Delirium in a patient *with* established dementia:
  - Less likely to be recognized → delirium persists → worse long-term outcomes (SOE=B)
  - Associated with accelerated cognitive decline (SOE=B)

19

19

Audience Polling Question #2

Which of the following is required for diagnosis of delirium using the confusion assessment method?

1. Acute change or fluctuating course in physical status
2. Hallucinations
3. Lethargy
4. Inattention
5. Delusions

20

20

Confusion Assessment Method (CAM)

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

Requires features 1 and 2 and either 3 or 4

21

21

Diagnostic Tools

- 3D-CAM: General medicine and surgery
- CAM-ICU: ICU
- UB-2: Sensitivity 93%, Specificity 64%
- 4AT: General medicine and surgery
- Use the right tool for the clinical situation
- 3D-CAM, CAM-ICU, and 4AT are on MDCalc app

22

22

CAM-ICU

- Version of CAM for non-verbal patients
- Uses same 4 features as CAM
  - Attention: Attention screening exam
  - Richmond agitation and sedation scale (RASS) for level of consciousness
  - Disorganized Thinking: Yes/No questions
- Excellent in ICU/non-verbal patients
- Available in MDCalc on iPhone

23

23

3D-CAM

1. Acute changes in mental status
   1. Being confused
   2. Thinking not in the hospital
   3. Seeing things that are not really there
2. Inattention
   1. Digit pan 3 digits and 4 digits backward
   2. Days of the week backward
   3. Months of the year backward
3. Disorganized thinking
   1. Current year
   2. Day of the week
   3. Type of place
4. Altered level of consciousness: None
5. Sensitivity 95% and Specificity 94%

24

24

3D-CAM

- 3-minute diagnostic assessment for CAM-defined delirium
- As soon as one item is "positive" move on to next feature:

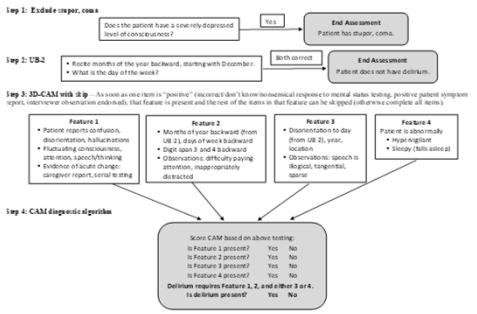
Feature 1	Feature 2	Feature 3	Feature 4
Patient reports confusion, disorientation, hallucinations Fluctuating consciousness, attention, speech/thinking Evidence of acute change: caregiver report, serial testing	Months of year backward, days of week backward Digit span 3 and 4 backward Observations: difficulty paying attention, inappropriately distracted	Disorientation to day, year, location Observations: speech is illogical, tangential, sparse	Patient is abnormally - Hypervigilant - Sleepy (falls asleep)

- Positive if features 1 *and* 2 plus 3 *or* 4 present
- Excellent sensitivity/specificity—95%

25

25

ULTRA-BRIEF CONFUSION ASSESSMENT METHOD (UB-CAM)



26

26

4AT

- Non-CAM based assessment
- Designed for general medicine patients
- Brief series of questions and observations
- Tally points → over threshold makes "diagnosis" of delirium
- Sensitivity/specificity near 90%

27

27

4AT

- Alertness
  - Normal: 0 points
  - Mild sleepiness <10 seconds: 0 points
  - Clearly abnormal: 4 points
- Age, date of birth, place, current year
  - No mistakes: 0 points
  - One mistake: 1 point
  - ≥ 2 mistakes or untestable: 4 points
- Attention
  - Lists ≥7 months correctly: 0 points
  - Starts but lists ≤ 7 months: 1 point
  - Untestable: 2 points
- Acute change or fluctuating course
  - No: 0 points
  - Yes: 4 points
- Sensitivity 90% and Specificity 84%
- Score of 4 or more suggests delirium
- Score of 1-3 suggests cognitive impairment
- Score of 0: More detailed testing may be needed

28

28

Neurophysiology

29

29

Pathophysiology

- Research is accelerating
- No identifiable biomarkers at this point
- No impact yet on clinical management
- Number and symptoms vary widely
- CAM-S derived from CAM
  - Long form 0-19
  - Short form 0-7
- Excellent predictive validity
- Two potential mechanisms

30

30

CAM-S DELIRIUM SEVERITY SCORING

The CAM can be used to determine both a CAM-S Long Form and CAM-S Short Form delirium severity score.

Feature	Severity Score		
Scoring the CAM-S: Rate each symptom of delirium listed in the CAM as absent (0), mild (1), marked (2). Acute onset or fluctuation is rated as absent (0) or present (1). Add these scores into a composite. Higher scores indicate more severe delirium.			
	Not Present	**Present (mild)**	**Present (marked)**
1. ACUTE ONSET & FLUCTUATING COURSE	0	1	
2. INATTENTION	0	1	2
3. DISORGANIZED THINKING	0	1	2
4. ALTERED LEVEL OFCONSCIOUSNESS	0	*vigilant/lethargic:* 1	*stupor or coma:* 2
5. DISORIENTATION	0	1	2
6. MEMORY IMPAIRMENT	0	1	2
7. PERCEPTUAL DISTURBANCES	0	1	2
8. PSYCHOMOTOR AGITATION	0	1	2
9. PSYCHOMOTOR RETARDATION	0	1	2
10. ALTERED SLEEP-WAKE CYCLE	0	1	2
Short Form SEVERITY SCORE:	Add the scores in rows 1-4. Range is 0-7. ☐		
Long Form SEVERITY SCORE:	Add the scores in rows 1-10. Range is 0-19. ☐		

31

31

Cholinergic Deficiency

- Acetylcholine is an important neurotransmitter for cognitive processes
- Anticholinergic drug overdose causes delirium; reversed by physostigmine
- Scales available to measure anticholinergic burden of drug regimens
- Cholinesterase inhibitors have <u>not</u> been effective in preventing/treating delirium (SOE = B)

32

32

Inflammation

- Especially important in postoperative, cancer, and infected patients
- Delirium is associated with ↑ C-reactive protein, ↑ IL-1β and IL-6, and ↑TNFα
- Inflammation can break down blood-brain barrier, allowing medications and cytokines access to CNS
- Neuroinflammation may damage neurons, leading to long-term cognitive effects

33

33

Risk Factors

34

34

Predisposing Factors

Consistent

- Advanced age
- Dementia
- Functional impairment in ADLs
- Multi-morbidity

Some Studies

- History of alcohol abuse
- Male gender
- Sensory impairment: Vision and hearing
- Depressive symptoms
- Laboratory abnormalities
- Mild cognitive impairment

35

35

Precipitating Factors

- Medications (3 meds added in 24 hours)
- Surgery
- Anesthesia
- Uncontrolled pain
- Low hematocrit level
- Bed rest
- Indwelling devices
- Infections: Resp & urinary
- Urinary retention
- Acute cardiac/pulmonary events
- Fecal impaction
- Fluid or electrolyte disturbances
- Drug withdrawal
- Physical restraints
- Restraints

36

36

Clinical Prediction Rule

Risk Factors	Points
• Age $\geq$ 70	1
• Alcohol abuse	1
• Cognitive impairment	1
• Physical functional impairment	1
• Abnormal serum chemistries	1
• Aortic aneurysm surgery	2
• Noncardiac thoracic surgery	1

37

37

Risks for Postoperative Delirium

- No risk factor points: 2%
- One or two risk points: 11%
- Three plus risk points: 50%
- Caused by SUM of predisposing factors and precipitating factors
- Greater the predisposing factors the fewer precipitating factors are needed
- Older & frail patients are more susceptible

Marcantonio E. A Clinical Prediction Rule for Delirium After Elective Noncardiac Surgery *JAMA*, January 12, 1994. Vol 271: 134-139

38

38

Key Facts of Postoperative Delirium

- Peak onset: First postoperative day
- Peak prevalence: Second postoperative day
- Incidence of delirium
  - Noncardiac surgery: 15%
  - Aortic aneurysm repair: 50%
  - CABG: 50%
  - Hip fracture repair: 50%
- Total dose of anesthetic agents

39

39

Postoperative Medication RX

- Do not use benzodiazepines
- Avoid use of meperidine
- Adequate pain management is important
  - High levels of pain associated with delirium
  - Use scheduled dosing
  - PCA
  - Regional anesthesia
  - Opioid sparing analgesics
  - Ice packs

40

40

More on Post OP Delirium

- Type or route anesthesia doesn't matter
- Dose of drugs matters: Reduce to lowest effect
- Minimize benzodiazepines and certain opioids
- Treat pain adequately with lowest possible dose

41

41

Evaluation & Management

42

42

Evaluation

- History focuses on the time course of changes and association with other symptoms or events
  - Fever
  - Shortness of breath
  - Change in medication
- Brown Bag Test: Do not forget OTCs
- Vital signs with oxygen saturation
- Careful general medical exam
- Neuro exam for new focal findings
- Identify acute medical problems or exacerbations of chronic medical problems

43

43

Laboratory Studies

- Selected based on history and exam findings
- Minimum: CBC, electrolytes, and kidney function
- Other tests in selected situations
  - Urine: UA, UC, and toxicology for drugs
  - Liver Function Tests
  - Serum Medication Tests
  - ABGs
  - CXR
  - EKG
  - Appropriate cultures
- Cerebral imaging is overused except for head trauma or new focal neurologic findings

44

44

What is the Source?

Drugs: Change in meds and OTC
Electrolyte disturbance
Lack of drugs including poorly controlled pain
Infections
Reduced sensory input: Hearing and vision
Intracranial
Urinary retention and fecal impaction
Myocardial/metabolic/pulmonary

45

45

Drugs to Reduce or Eliminate

- Alcohol
- Anticholinergics – Oxybutynin and benztropine
- Anticonvulsants – Primidone, phenobarbital, phenytoin
- Antidepressants – Amitriptyline, imipramine
- Antihistamines – Diphenhydramine
- H2 blocking agents
- Antiparkinsonian agents
- Barbiturates
- Benzodiazepines
- Zolpidem
- Opioids

46

46

Prevent or Manage CX

- Implement scheduled toileting program
- Avoid physical restraints
- Mobilize with assistance
- Use physical therapy
- Implement nonpharmacologic sleep regimen
- Avoid sedatives
- Minimize nighttime awakenings
- Assist with feedings with aspiration precautions
- Do not forget nutritional supplementation

47

47

Restore Function

- Reduce clutter and noise at night
- Provide adequate lighting
- Familiar objects from home
- Reorient at least three times a day
- With improvement match performance to ability: ADLs
- Educate family
- Discuss family's role in restoring function
- On discharge provide increased ADL support
- Follow mental status changes

48

48

Disruptive Behaviors

- Teach hospital staff appropriate interaction
- Encourage family visitation
- Pharmacologic intervention
  - Only necessary for disruptive behavior
  - Harm themself
  - Use low-dose high potency antipsychotics

49

49

What About Intervention With Meds?

- Antipsychotics have a more favorable risk benefit ratio than benzodiazepines or sedatives
- All use of antipsychotics for delirium is off-label
- Many studies are not blinded, and outcomes are difficult to interpret
- Use the lowest effective dose for the shortest duration
- Only use if agitated
- Do not use benzodiazepines as first-line RX
- Adding cholinesterase inhibitors does not work!

50

50

Antipsychotics in Delirium

Drug	Daily Dose	Adverse Events
Quetiapine	12.5-25 mg Max: 50 mg/24	Sedation, Hypotension, Eye Exam Q 6 Mo Can Be Used in Parkinson's, Fewer EPS
Ziprasidone	5-10 mg po/IM Max: 20 mg/24	Mild Sedation, Mild Hypotension
Haloperidol	.25-.50 mg	Relative Nonsedating, EPS, First Generation Agent
Olanzapine	2.5-5 mg Q12H No IV	Sedation, Falls, Gait Disturbance, Fewer EPS
Risperidone	.25-.5mg hs	Sedation, Hypotension, EPS With Doses > 1 mg/day

51

51

Care Transitions in Delirium

- Diagnosis requires knowledge of patient's baseline
- Presence of delirium at discharge to a SNF is risk factor for hospital readmission
- Prolonged cognitive and functional disability make care planning more difficulty: Increased resources
- Care transitions are risk factors for delirium particularly in highly vulnerable individuals
- Consider keeping in hospital extra day or two to allow discharge to home instead of SNF

52

52

Proactive Management

- Hospital elder life program: Decrease 40%
  - Cognitive impairment
  - Sleep deprivation
  - Immobility
  - Visual impairment
  - Hearing impairment
  - Dehydration
- Proactive geriatrics consultation in hip fracture
- Promote sleep hygiene
  - Melatonin
  - Warm milk
  - Back rubs
  - Soothing music
  - Avoid Diphenhydramine!

53

53

Quality Measures & Consensus Guidelines

54

54

Strong Guidelines for Postoperative DELIRIUM

Eight *strong* recommendations: Benefits clearly outweighed the risks, or the risks clearly outweighed the benefits.

- Multicomponent nonpharmacologic interventions delivered by an interprofessional team should be administered to at-risk older adults to prevent delirium.
- Ongoing educational programs regarding delirium should be provided for health care professionals.
- A medical evaluation should be performed to identify and manage underlying contributors to delirium.
- Pain management (preferably with nonopioid medications) should be optimized to prevent postoperative delirium.
- Medications with high risk of precipitating delirium should be avoided.
- Cholinesterase inhibitors should not be newly prescribed to prevent or treat postoperative delirium.
- Benzodiazepines should not be used as first-line treatment of agitation associated with delirium.
- Antipsychotics and benzodiazepines should be avoided for treatment of hypoactive delirium.

55

55

Weak Guidelines for Postoperative Delirium

Three *weak* recommendations: Current level of evidence or potential risks of the treatment did not support a strong recommendation.

- Multicomponent nonpharmacologic interventions implemented by an interprofessional team may be considered when an older adult is diagnosed with postoperative delirium to improve clinical outcomes.
- The injection of regional anesthetic at the time of surgery and postoperatively to improve pain control with the goal of preventing delirium may be considered.
- The use of antipsychotics (e.g., haloperidol, risperidone, olanzapine, quetiapine, or ziprasidone) at the lowest effective dose for the shortest possible duration may be considered to treat delirious patients who are severely agitated or distressed or who are threatening substantial harm to self and/or others.

56

56

Insufficient Evidence for Postoperative Delirium

One "insufficient evidence" recommendation: Current level of evidence or potential risks of the treatment did not support either a strong or weak recommendation.

- Use of processed electroencephalographic monitors of anesthetic depth during intravenous sedation or general anesthesia may be used to prevent delirium. (Two 2019 randomized trials did not show benefit of this approach.)

Insufficient evidence to recommend either for or against the following:

- Prophylactic use of antipsychotic medications to prevent delirium
- Specialized hospital units for inpatient care of older adults with postoperative delirium

Slide 57

57

Possible Future Treatments

- Ramelteon for Prevention of Delirium in Hospitalized Older Patients
  - Perkisas S. *JAMA Psychiatry* 2014;7(4):397-403
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Slide 58

58

Audience Polling Question #3

Case 2: Which of the following intervention has shown efficacy in reducing incident delirium in hip fracture patients?

1. Preoperative geriatric assessment
2. Melatonin 3 mg in the evening for the first 5 days of hospitalization
3. Early postoperative ambulation
4. Donepezil 5 mg preoperatively and continued for 30 days

Slide 59

59

Case 3

- A 79-year-old man is hospitalized after surgery for hip fracture. HX includes HTN and Mild cognitive impairment. On day 2 after surgery, he pull out an IV line and refuses meds. The nurse requests administration of Haldol. On Exam, he is oriented to self. He is somnolent, easily aroused, and has difficulty reciting days of the week backward.

60

60

Audience Polling Question #4

Case 3, Cont.: Which of the following is most liked to result from administering haloperidol?

1. Longer hospital stay
2. Increased short term mortality
3. Increased risk of drug interactions
4. Reduction in severity of symptoms

61

61

Case 4

- An 89-year-old man is admitted to a skilled-nursing facility for rehab after a 3-day hospitalization for pneumonia. He stays in bed and naps frequently during the day. He has a poor appetite and is slow to answer questions; when he responds he has difficulty staying focused on the conversation.
- Before hospitalizations he lived independently in the community with monthly visits from his daughter. HX includes HTN, BPH, chronic back pain, and anxiety. Meds are amlodipine, metoprolol, oxybutynin, tramadol, sertraline, & cefpodoxime.

62

62

Audience Polling Question #5

Case 4, Cont.: What is the most likely cause of his symptoms?

1. Depression
2. Delirium
3. Mild dementia
4. Sleep disorder

63

63

Case 5

- An 86-year-old woman is admitted to the hospital for heart failure. HX includes MCI. At baseline, she lives with her husband and independent in ADLs and some IADLs.
- On the evening of hospital day 2, the patient's daughter alerts the nurse her mother has been confused, speaking nonsensically about going to a grocery store. She undergoes evaluation using the CAM to determine whether she has delirium.

64

64

Audience Polling Question #6

Case 5, Cont.: What additional sign would support a diagnosis of delirium using CAM?

1. Disorientation to time and place but not person
2. Spatial planning deficit on the clock-drawing test
3. Inability to recite the months of the year backward
4. One out of three delayed recall

65

65

Case 6

- 79 y/o man comes in for geriatric assessment for total hip arthroplasty. History includes 3-vessel CAD, stoke with no residual deficits, HTN, hyperlipidemia, and depression
- On Exam: BP=156/84, other vital signs are normal. Whisper test result if normal and Vision Acuity if 20/30. MMSE is 27/30 and 7/15 of GDS. He uses a cane.
- Lab Findings
  - Electrolytes: Normal
  - BUN: 30
  - Creatinine: 1.4
  - Hematocrit: 35.1%
  - Albumin: 3.2

66

66

Audience Polling Question #7

Case 6, Cont.: In addition to history of stroke and HTN, which one of the following places this patient at increased risk of postop delirium?

1. Hypercholesterolemia
2. Cognitive status
3. Depression
4. BUN/Creatinine ratio

67

67

Case 7

- 70 u/o man comes to the office accompanied by his wife, who reports the has been confused & agitated for the last 3-4 days. HX of traumatic brain injury with frontal craniotomy 12 years ago. His MOCA score is 24. HX includes OSA, CAD, diabetes, & Chronic back pain. Meds are metformin 500 mg BID, Metoprolol 25 mg BID, ASA 81 mg Q d, atorvastatin 40 mg QD, & alprazolam 0.5 mg prn. He uses CPAP and is independent in ADLs. He receives help for IADLs. He is pleasant but appears anxious, startling when the nurse enters. He moves from the exam table to chair several times during the visit.
- On Exam: BP=150/90 with HR=100. All other vitals are normal. Chest is clear with regular heart sounds. Does not know the day of week and is unable to recite months of the year backward. Repeat MOCA score is 18.

68

68

Audience Polling Question #8

Case 7, Cont.: Which of the following is the most appropriate next step?

1. Obtain basic metabolic panel and CBC
2. Stop alprazolam
3. Refer to sleep medicine for adjustment of CPAP settings.
4. Start citalopram 10 mg QD

69

69

SUMMARY

- Very common geriatric problem in ER & hospitalized
- Predisposing & precipitating factors are important
  - Greater predisposing than fewer precipitating factors
  - Frail older adults are more susceptible
- Remember the mnemonic DELIRIUM
- Brown bag test to review ALL meds
- If needed use antipsychotics not benzodiazepines
- Anticipate complications
- Restore function
- Involve the family
- Be careful about transitions
- Remember AGS guideline recommendations

70

70

QUESTIONS?

73

73

Medications

Generic Name	Trade Name
Quetiapine	Seroquel
Ziprasidone	Geodon
Haloperidol	Haldol
Olanzapine	Zyprexa
Risperidone	Risperdal
Ramelteon	Rozerem
Dexmedetomidine	Igalmi
Propofol	Diprivan

74

74

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75

75

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76

76

Notes