2025 Summer Virtual CME Series

Early Dementia Screening and Evaluation

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MOACOFP
MISSOURI SOCIETY OF
THE AMERICAN COLLEGE OF
OSTEOPATHIC FAMILY PHYSICIANS

DEMENTIA SCREENING AND EVALUATION

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NO CONFLICTS TO DECLARE

OBJECTIVES

- Understand the distinction between clinical dementia and Alzheimer's diagnosis according to a new guideline.
- Be aware of the literature on screening benefits and how new treatments might change benefits or not.
- Understand strengths and limitations of screening tests for dementia.
- Be aware of the diagnostic evaluation and its relevance to different types of dementia.

OVERVIEW

- What is dementia
- Why might we screen? Why is it still controversial?
- Biomarkers and the new Alzheimer Disease definition
- Screening tests and dementia evaluation
- What's important about dementia types
- Considerations about monoclonal antibodies aimed at amyloid

A BRIEF AND ELEGANT DEFINITION OF DEMENTIA

A decline of intellectual function in comparison to a previous level of performance causing an altered pattern of activity in a setting of unimpaired consciousness.

Source: Norman Foster, Univ. Michigan

DSM5: MAJOR NEUROCOGNITIVE DISORDER

- Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on:
  - Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and
  - A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

MAJOR NCD (CONT)

- The cognitive deficits interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).
- The cognitive deficits do not occur exclusively in the context of a delirium.
- The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).

MILD COGNITIVE IMPAIRMENT

- DSM5: Mild neurocognitive disorder
- Cognitive loss not severe enough to interfere with usual activities

WHY SCREEN?

- Preparation for the future
  - Advance care planning
  - Financial plans/financial power of attorney
  - Caregiver preparation
- Component of Medicare Wellness Evaluation
- Possibility of early therapy with anti-Amyloid agents

QUESTION OF WHETHER BENEFITS ARE SUFFICIENT

- USPSTF rating of I for screening for cognitive impairment (2020)
- One large randomized trial found no benefit for health-related quality of life
- Option of assessing when there are clues suggesting impairment
  - Family concerns, vague answers, deterioration in function

BIOMARKERS FOR ALZHEIMER'S DISEASE

- New definition from Alzheimer's Association workgroup defines Alzheimer's disease in terms of biomarkers
  - Distinguishing underlying disease and dementia syndrome
- Amyloid markers:
  - Positive Amyloid PET scan
  - Amyloid β in CSF
- Tau makers in plasma or CSF or Amyloid/ Tau ratios in CSF
  - Plasma markers not yet widely available; one recently FDA approved test: Lumipulse G pTau217/ β-Amyloid1-42 Plasma ratio

SCREENING TESTS

- Mini-Cog cutoff <3, 76% sensitive, 73% specific
  - 3 memory items and clock drawing
- Minimental State Exam cutoff 23 or 24, 89% sensitive, 89% specific
  - Pooled estimate; most widely studied test
  - Now technically proprietary but widely available

SCREENING TESTS (2)

- MOCA cutoff 22 or 24, sensitivity 91%, specificity 81%
  - Technically requires registration and fee but also widely available
- SLUMS: cutoff varies by education
  - <18-20 for education <12 years
  - <21 for education12 years or more;
  - Sensitivity 84-100% , Specificity 87-100%

EVALUATION OF PATIENT WITH COGNITIVE IMPAIRMENT

- History
  - Often input from family or other close contact is critical
- Mental Status Testing
- Often depression testing in dementia
- PE and Lab

HISTORY

- Time Course and Progression
- Other illnesses and conditions
- Medications
- ADL/IADL
- Safety issues
- Caregiver or family stress

PE, LAB, IMAGING

- Careful general and neurological examination with focused lab testing
- CBC, CMP, TSH, and B12; HIV and Syphilis serology if considered higher risk
- Neuroimaging
- Reversible dementia unfortunately uncommon

NEUROPSYCHOLOGICAL TESTING

- 5 hour process
- Areas of strength and weakness in multiple domains
- Preserved achievement with decline in intelligence
  - Inverse of Learning disability
- Potentially helpful in equivocal cases

DEMENTIA PRESENTATION

- Dementia uncommon < age 75 (e.g., 1% ages 60-64) but increases rapidly with age
  - Up to 40% of those over age 85
- Often a family member raises the issue and input from others essential in many cases
- Patients themselves complaining of memory loss frequently have depression with difficulty concentrating rather than dementia

PRINCIPAL CAUSES OF DEMENTIA

- Alzheimer's Disease (50-75%)
- Vascular Dementia (10-20%)
- Other degenerative conditions
  - Frontotemporal
  - Dementia with Lewy bodies
  - Parkinson's plus syndromes
- Potentially reversible dementias

Clues to Dementias other than Alzheimers

Feature	**Diagnostic consideration**
Abrupt onset	Vascular dementia
Stepwise deterioration	Vascular dementia
Prominent behavior changes	Frontotemporal dementia
Profound apathy	Frontotemporal dementia
Prominent aphasia	Frontotemporal dementia, vascular dementia
Progressive gait disorder	Vascular dementia, hydrocephalus

More Clues

Feature	Diagnostic consideration
Prominent fluctuations in levels of consciousness or cognitive abilities	Delirium due to infection, medications, or other causes; dementia with Lewy bodies; seizures
Hallucinations or delusions	Delirium; dementia with Lewy bodies
Extrapyramidal signs or gait	Parkinsonian syndromes, vascular dementia
Eye-movement abnormalities	Progressive supranuclear palsy, Wernicke's encephalopathy

From Kawas CH. Early Alzheimer's disease. N Engl J Med 2003;349:1058.

DISTINGUISHING DEMENTIA AND DELIRIUM

- Dementia is typically slowly progressive, pts have no alteration of consciousness, and pts usually only have episodic agitation
- Delirium is of acute onset and involves difficulty focusing attention and often an alteration in the level of consciousness
- Both may be associated with delusions or hallucinations

IMPORTANCE OF SPECIFIC DEMENTIA DIAGNOSIS

- Drugs to delay cognitive decline mostly for Alzheimer's Disease
  - Cholinesterase inhibitors also helpful with Lewy Body dementia
- With Lewy Body or Parkinson's dementia avoid most antipsychotics
  - Quetiapine preferred

AMYLOID-TARGETED THERAPIES

- 2 FDA-approved and available monoclonal antibody treatments directed against amyloid β plaques: Lecanemab and Donanemab
- Approved for mild cognitive impairment or mild Alzheimer dementia with confirmed brain amyloid pathology
  - For example, MMSE ≥ 22 or MOCA ≥ 17
- Slows but does not stop decline (on average 25-30%)
  - Not clear whether this is clinically meaningful or not

ISSUES WITH AMYLOID-TARGETED THERAPIES

- IV infusions required once monthly (donanemab) or twice monthly (lecanemab)
  - Infusion reactions are common but usually not serious
- Requirement for frequent MRI monitoring for Amyloid-related imaging abnormalities (ARIA)
  - Edema and microhemorrhages
  - 21% with Lecanemab and 37% with donanemab
  - Appear to be higher risk with patients who are APOE ε4 homozygotes

ISSUES WITH AMYLOID-TARGETED THERAPIES (2)

- Multiple contraindications
  - Bleeding disorders or anticoagulation
  - Prior stroke or TIA within last year
  - Prior significant cerebral hemorrhage
  - Autoimmune or immunologic disease or immunosuppression
  - Brain tumor other than meningioma or arachnoid cyst
  - BMI > 35 or <17
  - Relative contraindications include unstable medical or psychiatric condition or major depression

ISSUES WITH AMYLOID-TARGETED THERAPIES (3)

- Limited number of Black people, and very old people in studies of these drugs; participants were generally healthy
  - Likely this means only a small percentage of patients would be good candidates (one estimate 10%)
- Need for shared decision-making

SUMMARY

- Dementia is characterized by cognitive deficits sufficient to interfere with usual activities
  - Usually identified by others
- New definition focuses on biomarkers but relevance for primary care still limited
- Unclear if screening is of benefit
  - May benefit planning and possibly treatment
- Newer anti-amyloid drugs probably useful for few Pts

SUMMARY (2)

- Important to identify probable Alzheimer's Disease and Lewy Body Dementia
- History, physical and neurological examination, and cognitive evaluation are the most important components of the evaluation

QUESTIONS?