Evaluation of Memory Loss and Mild Cognitive Impairment

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Geriatrics Grand Rounds
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Objectives
1. Describe recommendations and tools for evaluation of cognitive impairment
2. Define mild cognitive impairment (MCI) and subtypes
3. Explore the clinical implications of mild cognitive impairment for patients and clinicians

Clinical Questions
• What are the benefits/harm of cognitive screening for patients?
• What does a diagnosis of Mild Cognitive Impairment (MCI) mean for our patients?
• How does this affect clinical care and practices?

Medicare Wellness Visit...
• Mandate released 2011
• Describes “detection of any cognitive impairment” in comprehensive exam details
• No specification of screening tool
Meet “Lou”

- 68 yo woman; 13 years of education
- Lives alone, independent with all IADLs/ADLs
- Osteoarthritis is her only medical condition
- Travels often, is involved in many activities
- Minor memory complaints
- MOCA=25/30

The Gray Zone

Why Specific Evaluation?

- Routine history and physical exam may miss up to 75% of patients with dementia
- Ideally allow care and guidance to improve planning and future decision making

Current Guidelines/Recommendations

- **USPSTF**: I statement: insufficient evidence to recommend for or against screening
- **Alz Assoc**: Recommends evaluation only when complaints/concerns are present
- **VA**: same as USPSTF
More on USPSTF recommendations...

- Released Nov 2013
- Based on Lin et. al, “Screening for Cognitive Impairment in Older Adults: A Systematic Review for the US Preventative Services Task Force” *Annals of Internal Medicine*
- Re-eval of 2003 recommendations

5 Key questions

1. Does *screening* for cognitive impairment in *community dwelling* older adults *improve decision making or patient/caregiver or societal outcomes*
2. What is the *test performance of screening instruments* to detect cognitive impairment?
3. What are the *harms of screening*?
4. *Do interventions* for MCI or mild to moderate dementia *improve outcomes*?
5. What are the *harms of intervention* for cognitive impairment

Screening and Decision Making/Outcomes (#1)

- No trials or published research on key question #1
- One fair quality study showed 50% of patients with positive screening results declined formal work up

Tools for Evaluation (#2)

- 46 studies, tests administered in <10 mins or self administered
- Community dwelling/primary care settings; most with high school education
- Most tools had limited for evaluation for review
• MMSE most extensively studied (25)
  – Sensitivity 88%/Specificity 86%
  – Dementia detection with cut off at 23-25

• Other tools studied: mini-cog, clock drawing test, IQCODE, Memory Impairment Screen,

• Detection of MCI:
  – MMSE: 80 sensitivity/70 spec
  – SLUMS: 92 sens/81 spec
  – MOCA: 80/76

### Potential Harms of Evaluation (#3)

• **No studies addressing adverse effects** of false test results or early diagnosis

• Detection of asymptomatic or pre-clinical disease...without effective treatment

• Preventative/Routine Screening—not recommended!

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**Do people want to know?**

- 220 vignette/surveys on patient preference
- at PCP, no demographic markers
- 90% want to be told
- Several said felt suicidal
- Negative reaction to not being told

Erde EL, Nadal EO, Schell TD*

**Do people want to know?**

- 200 patients complete questionnaire
- Told Alzheimer's or cancer
- 92% vs 86.5%, p=0.06
- If personal experience did not want to know
- 1.7% considered suicide

Attitudes of elderly subjects toward "truth telling" for the diagnosis of Alzheimer's disease.
Tanzella N, Walt AJ, Hanil S.
Mental Health Center of Greater Manchester, New Hampshire, USA.*
Benefits of Intervention (#4)

- Pharmacologic:
  - AchEI: 1-3 points on ADAS-cog
  - Memantine: same as above
  - Most differences non significant after one year follow up
- Non Pharmacologic:
  - Caregiver Interventions:

Harms of Intervention (#5)

- Attrition rate averaging 20% in most studies, more commonly in AchEI
- GI side effects, bradycardia
- No harms associated with non-pharmacologic or caregiver interventions
The Gray Zone

Normal

MCI

Dementia

Memory Complaints

<table>
<thead>
<tr>
<th>AAMI (Age associated memory impairment)</th>
<th>MCI</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective memory complaint</td>
<td>Multi-tasking, remote history, Transient minor lapse</td>
<td>Frequent forgetfulness, Difficulty/slowing of complex tasks</td>
</tr>
<tr>
<td>IADLs/ADLs</td>
<td>Independent</td>
<td>Independent to minor disruption</td>
</tr>
<tr>
<td>Formal testing</td>
<td>Normal</td>
<td>Normal to 1 SD below normal</td>
</tr>
</tbody>
</table>

Diagnosis

- **MCI criteria**
  - No/minimal dependence
  - Subjective memory complaints
  - “Lower than expected” performance
  - **MMSE 22-24**
  - **MoCA 22-26**
  - **SLUMS: 21-26 or 20-24 (high school)**

Epidemiology of MCI

- **Prevalence**: 3-19% in >65yo
- **Incidence**: 8-58/1,000 pt yrs
- Dementia at one year: **11-33%**
- **40% revert to normal**
MCI Sub-types

- Amnestic vs Non-amnestic (a vs na)
- Single vs Multi-Domain (SD vs MD)
- Abbreviations: MD-aMCI, SD-naMCI, etc.

DSM-V: Mild Neurocognitive Disorder (MNCD)

- Acquired and progressive
- MODERATE(?) cognitive decline
- Does not interfere with independence
- 1-2 SD below control on testing
- Previously: Cognitive Disorder NOS

Progression from MCI to Dementia

- Study setting influences prevalence/rates of progression:
  - Community dwelling vs specialty clinic
- Inconsistent follow up after diagnosis
**Higher risk of progression to dementia in mild cognitive impairment cases who revert to normal**  
*Neurology* 2014;82:317-325 Published Online before print December 18, 2013

- Mayo Clinic Study of Aging (MCSA)
- Prospective study from larger cohort of volunteer community dwelling older adults  
  - N=1,969
- Total prevalent/incident MCI n=534 cohort studied  
  - average age 75

**Other risk factors for progression**

- Woman > men
- Age
- APOE4 allele
- More cognitive dysfunction (*delayed recall/executive*)
- Lower functional independence

**Prevention of Progression?**

- Limited studies
- Diverse outcomes, measurements and designs
- Hold minimal clinical meaning
**Effect of Physical Activity on Cognitive Function in Older Adults at Risk for Alzheimer Disease**

A Randomized Trial

- Fitness for the Aging Brain Study (FABS)
- Community dwelling participants from advertisement and memory clinics
  - Initial telephone screen
- Excluded: significant cognitive impairment, depression, physical limitations
- Included: subjective memory complaints with or without objective decline in scoring
- 18 month follow up for analysis

**Results**

- Significant decrease in ADAS-Cog
  - 1.5 at 6 months, 0.69 at 18 months
  - Better than donepezil
- Delayed Recall
- APOE4
- No improvement in: depression ratings or QOL scores

**Control of vascular risk factors?**

- Mixed results on multiple trials
- Few with dementia as primary outcome
- Statin trials overall negative
Forette et. Al.“The Prevention of Dementia with Antihypertensive Therapy.” *Arch Intern Med* 2002

- No dementia, at least 60 years old
- Nitrendipine + add on
- 7.0 mmHg reduction
- 55% reduction in
- Dementia
- \( 7.4 \rightarrow 3.3/1\text{K} \) patient years

A “Pre-clinical” AD?

- Can we narrow down subtypes most likely to progress?
- Future research and therapeutic implications?
- Further support for the heterogeneity of AD, dementias and MCI

Risk scoring/stratification

- Biochemical Markers: CSF and serum
- Imaging: MRI and PET
- Neuropsychological Testing:

D.E Barnes et. Al, *Alzheimer’s & Dementia (2014) 1-10*

- Alzheimer’s Disease Neuroimaging Initiative (ADNI at UCSF)
  - N=382 with diagnosis of MCI
- 9 point scale: prospective prediction for AD diagnosis (30+ markers \( \rightarrow \) p-value of <.20 studied)
- Scores:
  - Function (FAQ) 0-3
  - Medial temporal cortical thickness 0-1
  - Hippocampal volume 0-1
  - ADAS-cog score 0-3
  - Clock draw 0-1
National Institute on Aging-Alzheimer’s Association workgroup recommendations

- Aim to further define MCI clinically and biochemically for narrowing of pre-clinical AD
- Stress importance of preserved functional dependence, decline over time
- Warn against use of biomarkers/imaging for clinical diagnosis but find utility for future research and therapeutic interventions

Meet “JoAnn”

- 68 yo woman 13 year education
- Lives with daughter who assists with finances and transportation— independent in other IADLs/ADLs
- COPD, DMII, CAD
- MOCA 25/30
- “forgets words” often
- Daughter also has concerns about decline

How (and *how not*) to evaluate?

- Subjective Memory Complaints + independence/functional screen
- Screening tools: choice based on clinical suspicion, patient education, language needs
- Biomarkers
- Imaging
Clinical Management

- Lifestyle modifications
- Advance Care Planning/Anticipatory Guidance
- Medication Review
- Follow up testing

Additions to the timeline?

- Normal
- MCI
- Dementia

Back to the Wellness visit

- Choice of screening based on patient history
- A focus on function and safety
- Careful attention to counseling and potential harms
Future Directions

• Studies to identify those most at risk for progression

• Understanding harms/benefits of early diagnosis

• Continued research on underlying pathophysiology

On a positive note….

We may be doing something right as primary care physicians!

• Decreasing Incidence in several population based studies

• Attributed to better education, socioeconomics and potential lifestyle changes related to vascular disease
Preventative *counseling* not screening??

Individual and public health education

Counseling families regarding healthy lifestyles

Questions/Comments?

Thank you for your time!