Clinical Diagnosis of Mild Cognitive Impairment

ADC Administrators’ Meeting
Boston, MA

Ronald C. Petersen, Ph.D., M.D.
Alzheimer’s Disease Research Center
Mayo Clinic College of Medicine
Rochester, MN
Disclosures

**Consultant:** GE Global Research
Elan Pharmaceuticals
Servier

**Research Support:** Pfizer, Inc. and Eisai, Inc.
through the ADCS
Cognitive Continuum

Normal

Mild Cognitive Impairment

Alzheimer's Disease
Clinical Features
MILD COGNITIVE IMPAIRMENT
Original Criteria

• Memory complaint
• Memory impaired for age
• Normal general cognitive function
• Normal activities of daily living
• Not demented
Components of the Diagnosis

- Interview with subject and informant
- Neuropsychological evaluation
- Neurological exam
Mild Cognitive Impairment
Clinical Characterization and Outcome

Ronald C. Petersen, PhD, MD; Glenn E. Smith, PhD; Stephen C. Waring, DVM, PhD; Robert J. Ivnik, PhD; Eric G. Tangalos, MD; Emre Kokmen, MD

From the Departments of Neurology (Dr Petersen and Kokmen), Health Sciences Research (Dr Petersen and Waring), and Psychiatry and Psychology (Dr Smith and Ivnik), and the Division of Community Internal Medicine (Dr Tangalos), Mayo Clinic, Rochester, Minn.

Mild cognitive impairment (MCI) is an evolving condition that has received several descriptors including mild cognitive impairment (MCI), incipient dementia, and isolated memory impairment. Reviews of several studies have indicated that these individuals are at an increased risk for developing AD ranging from 1% to 25% per year. The variability in these rates likely reflects differing diagnostic criteria, measurement instruments, and small sample sizes.

Questions can be raised as to the diagnostic criteria for MCI. Some investigators believe that virtually all these patients with mild disease have AD neuropathologically, and, therefore, this may not be a useful distinction. Others note that while many of these patients...
The image contains four bar graphs comparing the performance of different conditions across various cognitive tasks:

1. **MMSE**
   - Controls: High score
   - MCI: Moderate score
   - AD: Low score
   - CDR: 0, 0.5, 1

2. **Full Scale IQ**
   - Controls: High score
   - MCI: Moderate score
   - AD: Low score
   - CDR: 0, 0.5, 1

3. **Logical Memory II**
   - Controls: High score
   - MCI: Moderate score
   - AD: Low score
   - CDR: 0, 0.5, 1

4. **Visual Reproductions II**
   - Controls: High score
   - MCI: Moderate score
   - AD: Low score
   - CDR: 0, 0.5, 1
Mild Cognitive Impairment

MCI → AD 12%/yr

Control → AD 1-2%/yr

Current Classification Scheme for MCI
Amnestic MCI

Single domain

Multiple domain

• Alzheimer’s disease
• Depression
• Vascular cognitive impairment

Non-amnestic MCI

Single domain

Multiple domain

• Frontotemporal dementia
• Dementia with Lewy bodies
• Vascular cognitive impairment
Mild Cognitive Impairment

Cognitive complaint

- Not normal for age
- Not demented
- Cognitive decline
- Essentially normal functional activities

MCI

Memory impaired?

Yes

- Amnestic MCI
  - Memory impairment only?
    - Yes: Amnestic MCI Single domain
    - No: Amnestic MCI Multiple domain

No

- Non-amnestic MCI
  - Single non-memory cognitive domain impaired?
    - Yes: Non-amnestic MCI Single domain
    - No: Non-amnestic MCI Multiple domain

Cognitive complaint

- Not normal for age
- Not demented
- Cognitive decline
- Essentially normal functional activities

MCI

Memory impaired?

Yes

- Amnestic MCI
  - Memory impairment only?
    - Yes: Amnestic MCI Single domain
    - No: Amnestic MCI Multiple domain

No

- Non-amnestic MCI
  - Single non-memory cognitive domain impaired?
    - Yes: Non-amnestic MCI Single domain
    - No: Non-amnestic MCI Multiple domain

Petersen: J Int Med, 2004
Mild Cognitive Impairment

Cognitive complaint

Not normal for age
Not demented
Cognitive decline
Essentially normal functional activities

MCI

Memory impaired?

Yes: Amnestic MCI

Memory impairment only?

Yes: Amnestic MCI (Single domain)
No: Amnestic MCI (Multiple domain)

No: Non-amnestic MCI

Single non-memory cognitive domain impaired?

Yes: Non-amnestic MCI (Single domain)
No: Non-amnestic MCI (Multiple domain)

Petersen: J Int Med, 2004
Mild Cognitive Impairment

Cognitive complaint

Not normal for age
Not demented
Cognitive decline
Essentially normal functional activities

MCI

Memory impaired?

Yes
Amnestic MCI

Memory impairment only?

Yes
Amnestic MCI
Single domain

No
Amnestic MCI
Multiple domain

No
Non-amnestic MCI

Single non-memory cognitive domain impaired?

Yes
Non-amnestic MCI
Single domain

No
Non-amnestic MCI
Multiple domain

Petersen: J Int Med, 2004
MCI Outcomes

Clinical classification

Amnestic MCI
Single domain
AD
Non-amnestic MCI
Single domain
FTD
Multiple domain
DLB
Multiple domain

Etiology
Degenerative
Vascular
Psychiatric
Med Cond

AD
VCI
Depr
Depr

## MCI Outcomes

<table>
<thead>
<tr>
<th>Clinical classification</th>
<th>Single domain</th>
<th>Multiple domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnestic MCI</td>
<td>AD</td>
<td>AD</td>
</tr>
<tr>
<td>Non-amnestic MCI</td>
<td>FTD</td>
<td>VCI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Degenerative</th>
<th>Vascular</th>
<th>Psychiatric</th>
<th>Med Cond</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>Depr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCI</td>
<td></td>
<td></td>
<td>Depr</td>
<td></td>
</tr>
<tr>
<td>DLB</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Breadth of MCI Research

• Epidemiology
• Clinical
• Imaging
• Biomarkers
• Mechanism of disease
• Neuropathology
• Clinical trials
Publications on MCI
** Impairment in any 2 or more cognitive domains and sufficiently severe to affect function

*** Does not fit a known dementia syndrome
Function

Mild cognitive impairment

Probable AD

Definite AD

Age
aMCI criteria, degenerative
APOE status
MRI structural
FDG-PET
CSF tau, Aβ
Amyloid imaging
MCI SUMMARY

• USEFUL CONCEPT
• CRITERIA AVAILABLE
  – CLINICIAN INVOLVED
  – ALGORITHM
• OUTCOME DEPENDENT
• NEUROPATH TRANSITIONAL
• CLINICAL TRIALS FEASIBLE
MAYO ALZHEIMER’S DISEASE RESEARCH CENTER

- **Rochester**
  - Brad Boeve
  - David Knopman
  - Eric Tangalos
  - Joe Parisi
  - Cliff Jack
  - Walter Rocca
  - Bob Ivnik
  - Glenn Smith
  - Rosebud Roberts
  - Shane Pankratz
  - Yonas Geda
  - Dana Swenson-Dravis

- **Jacksonville**
  - Steve Younkin
  - Dennis Dickson
  - Neill Graff-Radford
  - Shu-Hui Yen
  - Todd Golde
  - Mike Hutton
  - John Lucas
  - Tanis Ferman
  - Floyd Willis
  - Francine Parfitt