Diagnosis, pharmacologic management, non-pharmacologic management, and other considerations

This material is provided by UCSF Weill Institute for Neurosciences as an educational resource for health care providers.
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**Diagnosis**

**Definition**
Mild cognitive impairment (MCI) refers to cognitive decline that does not interfere with the person’s daily function.\(^1\)\(^,\)\(^,\)\(^2\) MCI is further classified into subtypes according to the cognitive domain most affected. For example, people with primarily memory impairment would be diagnosed with the amnestic subtype of MCI. Other subtypes include non-amnestic, executive, language, visuospatial and mixed.

**Etiology and differential diagnoses**
People with MCI form a heterogeneous group. The underlying etiology of the cognitive impairment can vary and includes among others:

1. Metabolic causes, such as vitamin B12 deficiency or thyroid disease
2. Infectious causes such as HIV or syphilis
3. Sleep disorders such as sleep apnea or sleep deprivation
4. Psychiatric illnesses such as depression, anxiety and adjustment disorders
5. Vascular disease of the brain and strokes
6. Brain tumors, or paraneoplastic syndromes from tumors elsewhere in the body
7. Multiple sclerosis or other inflammatory etiologies
8. Head trauma or its sequelae
9. Neurodegenerative illnesses that are in their prodromal stages such as Alzheimer’s disease or Lewy body disease
10. Medication side effect such as from anticholinergic medications.

**Course**
While some people with MCI may improve according to whether the underlying etiology is treatable (such as sleep apnea or vitamin B12 deficiency), others may continue to have MCI indefinitely, while some may progress to a symptomatic clinical dementia. For this latter group of patients, MCI can be considered to be a transitional stage between normal aging and the symptomatic predementia stage. Less than half of people with MCI progress to dementia. The conversion rate is slightly higher within specialist settings versus population studies.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\) The presence of multiple chronic conditions increases the risk of MCI and dementia.\(^2\) If an autosomal dominant form of AD is known to be present (i.e., mutation in APP, PS1, PS2), then the development of MCI is most likely the prodrome to Alzheimer’s disease (AD) dementia.\(^2\)

While MCI may precede any dementia etiology, it has been the most well-characterized in AD. Impairment in episodic memory (i.e., the ability to learn and retain new information) is most commonly seen in MCI patients who subsequently progress to a diagnosis of AD dementia. This type of MCI is referred to as amnestic MCI. The MCI patient who presents with an executive, spatial, or language impairment may still progress to AD dementia, to other types of dementia or may remain stable.\(^2\)

**Diagnostic Criteria**
A workgroup convened by the National Institute on Aging and the Alzheimer’s Association developed diagnostic criteria for MCI.\(^2\)

1. MCI—Criteria for the clinical and cognitive syndrome
1. Concern regarding a change in cognition
There should be evidence of concern about a change in cognition, in comparison with the person’s previous level. This concern can be obtained from the patient, from an informant who knows the patient well, or from a skilled clinician observing the patient.

2. Impairment in one or more cognitive domains
There should be evidence of lower performance in one or more cognitive domains that is greater than would be expected for the patient’s age and educational background. If repeated assessments are available, then a decline in performance should be evident over time. This change can occur in a variety of cognitive domains, including memory, executive function, attention, language, and visuospatial skills. Impairment in episodic memory (i.e., the ability to learn and retain new information) is seen most commonly in MCI patients who subsequently progress to a diagnosis of AD dementia.

3. Preservation of independence in functional abilities
Persons with MCI commonly have mild problems performing complex functional tasks that they used to perform previously, such as paying bills, preparing a meal, or shopping. They may take more time, be less efficient, and make more errors at performing such activities than in the past. Nevertheless, they generally maintain their independence of function in daily life, with minimal aids or assistance. It is recognized that the application of this criterion is challenging, as it requires knowledge about an individual’s level of function at the current phase of their life. However, it is noteworthy that this type of information is also necessary for the determination of whether a person is demented.

4. Not demented
These cognitive changes should be sufficiently mild that there is no evidence of a significant impairment in social or occupational functioning. It should be emphasized that the diagnosis of MCI requires evidence of intra-individual change. If an individual has only been evaluated once, change will need to be inferred from the history and/or evidence that cognitive performance is impaired beyond what would have been expected for that individual. Serial evaluations are of course optimal, but may not be feasible in a particular circumstance.

The Role of Biomarkers
There are 2 reasons to incorporate biomarkers in the assessment of MCI: (1) To establish support for the suspected etiology of the clinical syndrome in an individual with MCI and (2) To determine the likelihood of cognitive and functional progression for an individual MCI patient to a more severe stage of MCI or to dementia. Biomarkers are classified as to whether they reflect (1) amyloid beta (Aβ) deposition as assessed by decreased amyloid levels in cerebrospinal fluid (CSF) or amyloid deposition on amyloid tracer imaging, or (2) signs of neuronal injury as assessed by structural magnetic resonance imaging (MRI), functional imaging such as fluorodeoxyglucose (FDG) Positron Emission tomography (PET) or elevated tau levels in CSF. Evidence for both Aβ deposition and neuronal injury represents the highest likelihood of progression to Alzheimer’s disease. Because some biomarker results, such as CSF studies, can be inconclusive, the use and interpretation of biomarkers should always be used in conjunction with the clinical evaluation. Not all patients with MCI need biomarkers and this decision is best orchestrated with a behavioral and cognitive neurologist.

Categories of biomarkers:
1. Aβ deposition:
   a. CSF levels of Aβ42
   b. Positive PET scans using amyloid tracers
2. Signs of neuronal injury:
   a. Volume loss on structural MRI, such as in hippocampi
   b. Hypometabolism or hypoperfusion on functional brain imaging (fMRI, PET or Single-photon emission computed tomography (SPECT))
   c. Increased CSF levels of total tau and/or phosphorylated-tau (p-tau).

Pharmacologic Management

Medications to Use
A meta-analysis found little benefit in using cholinesterase inhibitors to prevent the progression of MCI to AD. However, most clinical trials were conducted without biomarker confirmation of the underlying etiology. It is anecdotally and practically accepted by most behavioral neurologist, that cholinesterase inhibitors are beneficial in patients with MCI that are suspected of being in the prodromal stage of Alzheimer’s disease. In that case, cholinesterase inhibitors are initiated and titrated following the same guidelines for patients with Alzheimer’s disease.

Medications to Avoid
Medications with strong anticholinergic side effects, such as sedating antihistamines, barbiturates, narcotics, benzodiazepines, gastrointestinal and urinary antispasmodics, Central nervous system (CNS) stimulants, muscle relaxants, and tricyclic antidepressants should be avoided. Antipsychotics should be used with caution. If used, carefully evaluate effectiveness of medication and consider discontinuing if there is no improvement in six weeks.

Non Pharmacologic Management

Healthy Lifestyle
There are lifestyle habits that promote health and well-being. Research suggests that the combination of good nutrition, physical activity, and mental and social engagement may provide benefit in promoting health although more study is needed to determine the actual mechanisms. A heart-healthy diet (lower in sugar and fat and higher in vegetables and fruit) is considered to be good for both the body and the brain. An example is the Mediterranean diet that promotes nutrition based on fruit, vegetables, nuts, and grains with limits on consumption of red meat and saturated fats.
Physical exercise has been associated with improvement of mood and mobility, and a decrease in the risk for falls. Physical activities that are socially engaging (walking or swimming with a friend and participating in exercise groups) can be especially enjoyable. Engagement in activities that are mentally stimulating (crossword puzzles, Sudoku, computer games) is encouraged as long as the activity is enjoyable.

The Alzheimer’s Association has more information on tips for maintaining your health: alz.org/we_can_help_brain_health_maintain_your_brain.asp

**Risk Factor Modification**

There are seven risk factors have been identified that are associated with Alzheimer’s disease and other causes of dementia. These risk factors can possibly be reduced or adjusted to help prevent changes in thinking skills and/or memory.13

- Type 2 diabetes
- High blood pressure
- Midlife obesity
- Smoking
- Depression
- Little or no mental activity
- Little or no physical exercise

There are multiple risk factors that contribute to the development of vascular dementia that include:14

- Hypertension
- Atrial fibrillation and other cardiac conditions
- High cholesterol
- Diabetes
- Metabolic syndrome
- Smoking
- Sleep-disordered breathing
- Sedentary lifestyle
- Hyperhomocysteinemia

**Sleep**

Disrupted sleep can negatively impact memory and thinking, though the mechanisms are not well understood.15

Components of sleep hygiene include:

- Avoid napping during the day
- Avoid stimulants such as caffeine, nicotine, and alcohol too close to bedtime
- Get regular exercise
- Avoid eating right before sleep
- Ensure adequate exposure to natural light
- Establish a regular relaxing bedtime routine
- Associate your bed with sleep. It’s not a good idea to use your bed to watch TV, listen to the radio, or read.

For more details on sleep hygiene, you can refer to the National Sleep Foundation at sleepfoundation.org/ask-the-expert/sleep-hygiene.

**Other Considerations**

**Support Resources**

- Family Caregiver Alliance: caregiver.org/mild-cognitive-impairment-mci
- UCSF Memory and Aging Center: memory.ucsf.edu/mild-cognitive-impairment
- Virginia Tech, Center for Gerontology: gerontology.vt.edu/docs/Gerontology_MCI_final.pdf

**Research and Clinical Trials**

The National Institutes of Health maintains an extensive listing of clinical trials at clinicaltrials.gov. Academic medical centers may be engaged in research and clinical trials.

**Safety**

If wandering or getting lost is a concern, refer the patient and family to the MedicAlert+Alzheimer’s Association Safe Return program (operated by the Alzheimer’s Association).

Other strategies for ensuring safety concerns may include door alarms and increased supervision.

**Legal Planning**

Provide information about advance directives and durable power of attorney while the patient is in the early stages of disease and able to articulate his or her wishes. Make referrals for legal and financial advice, especially if there are concerns about the patient’s judgment, decision-making, or vulnerability. A formal evaluation for capacity may be warranted. The Alzheimer’s Association provides a brochure that covers legal planning: alz.org/national/documents/brochure_legalplans.pdf.
• Advanced Directives
These documents allow individuals to state their preferences for medical treatments and to select an agent or person to make health care decisions in the event they are unable to do so or if they want someone else to make decisions for them.

• Power Of Attorney
A Power of Attorney (POA) is a legal document that gives someone of an individual’s choosing the power to act in their place. POAs can be for medical or financial matters.

• Living Will
A living will is a written, legal document that spells out medical treatments that an individual would and would not want to be used to keep them alive, as well as other decisions such as pain management or organ donation.

Teaching Video for Providers

References