



MCI AND DEMENTIA

Diagnosis and treatment

▶WHO SHOULD READ THIS?

All primary care PAs should be able to recognize and treat mild cognitive impairment (MCI) and dementia.

▶WHAT IS DEMENTIA, AND HOW DOES IT DIFFER FROM MCI?

The diagnosis of dementia as described in the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition, text revision) requires that the patient have memory impairment plus aphasia, apraxia, agnosia, and/or a disturbance in executive functioning. These deficits must produce significant impairment in occupational or social functioning, represent a decline from a previously higher level of functioning, and be separate from other psychiatric or neurologic disorders.¹

Dementia typically manifests after age 50 years, becomes more common with advancing age, and is more prevalent in men than women after 80 years.² Approximately 5.3 million persons in the United States have Alzheimer's dementia (AD), and this population is growing.³ In persons 65 years and older, AD accounts for half of all forms of dementia, but only one-third of demented younger persons have AD.² The greatest risk factor for dementia is being 65 years or older. Other risk factors include lower level of education, family history of dementia, genetic mutations, and vascular disease.² While dementia affects 1% to 2% of the general population,⁴ the progression from MCI to dementia may

be 12% or more per year,^{4,5} suggesting that persons with MCI have an accelerated risk for dementia.

MCI represents a vague prodromal stage between normal cognitive function and dementia and it is often confused with normal age-related cognitive changes. Persons with MCI usually present with memory impairment that exceeds the changes seen with normal aging, although other cognitive domains may also be affected. These patients or their family members may describe changes from previous personal norms. MCI has been reported to have a population prevalence of 22% in persons 75 years or older.⁶ In 80% of patients, MCI progresses to dementia within 6 years of diagnosis.⁵ Only 5% of patients with MCI have a potential to improve to normal.⁵

▶HOW ARE MCI AND DEMENTIA DIAGNOSED?

The diagnostic criteria for MCI are described in **Figure 1**.⁴ MCI is subclassified into amnesic (memory-impairment) and nonamnesic (non-memory-impairment) types, each of

which is further subclassified based on the clinical presentation and cognitive domains involved.⁴ The purpose of MCI classification is related to the predictive nature of certain subclassifications. For example, amnesic MCI-single domain is associated with AD, whereas nonamnesic MCI-single domain tends to be associated with frontotemporal dementia.⁴

Numerous neuropsychological assessment tools are available to assist in the diagnosis of both dementia and MCI. The Mini-Mental State Examination is commonly used by PAs to screen for cognitive changes (MMSE, www.minimental.com). While reliable for dementia, however, the MMSE may be inadequate for MCI screening.^{7,8} For assessing MCI, the Montreal Cognitive Assessment (MoCA)⁹ is a validated test which is available free at www.mocatest.org (see **Table 1** for other useful Web sites). The MoCA was reported to have 90% sensitivity and specificity for identifying MCI, compared with only 18% for the MMSE.⁹ The MoCA distinguishes between normal age-related cognitive changes and MCI and requires approximately 10 minutes to administer, but it does not distinguish between MCI and dementia with certainty. PAs should become familiar with this screening tool and consider it for evaluating questionable cognitive changes in adult patients.

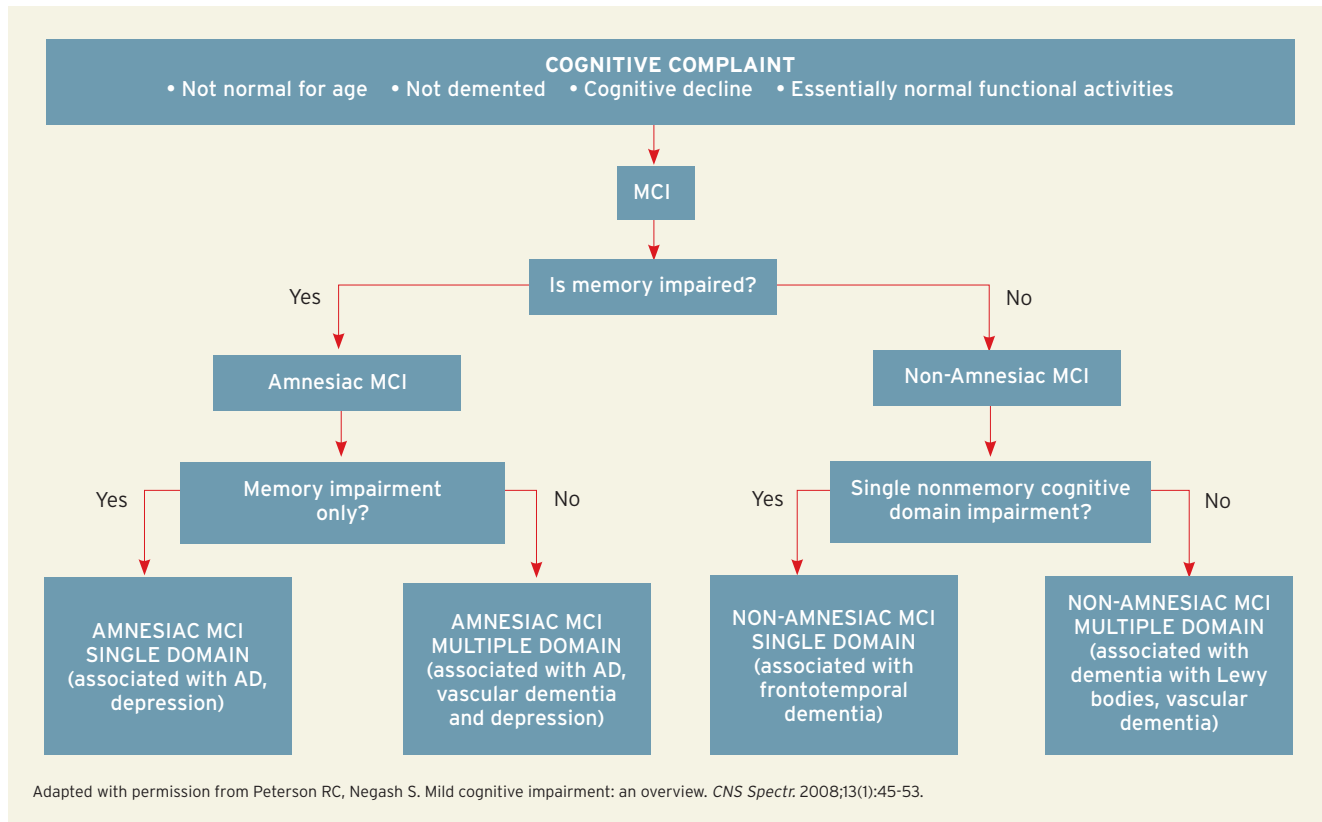
At the patient's first presentation with cognitive changes, laboratory testing may be useful for evaluating reversible causes of cognitive impairment, such as delirium.² Tests should include a CBC,

TAKE-HOME POINTS

- The best offense is a good defense: encourage physical, social, and intellectual engagement throughout the lifespan, and aggressively treat all chronic disorders.
- Consider implementing both the MoCA (Montreal Cognitive Assessment) and the MMSE (Mini-Mental State Examination) when evaluating possible cognitive disorders.
- Screen for mild cognitive impairment (MCI) and initiate treatment with cholinesterase inhibitors (donepezil has been demonstrated to produce the greatest improvement) as early as possible in the disease process.
- Educate patients and their family members on community services available to support patients with MCI and dementia.

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FIGURE 1. Algorithm for MCI diagnosis and subtyping



complete metabolic panel, ESR, and thyroid-stimulating hormone. Other tests that may be indicated based on the patient's history include measures of serum vitamin B₁₂, RPR/VDRL, HIV, and Lyme disease. Comorbid conditions such as diabetes, hyperlipidemia, and hypertension should be fully treated, and cognitive function should then be reassessed.

In the setting of neurologic or cognitive changes, neuroimaging may be helpful in assessing MCI and dementia. Brain MRI can demonstrate whole brain atrophy, increased relative ventricular volume, or atrophy of specific regions such as the frontal lobes, hippocampus, and entorhinal cortex, particularly in AD.^{2,3} Hippocampal and entorhinal cortex volumes may be affected in patients with amnesic MCI before AD develops.¹⁰ In addition,

vascular pathology that may be associated with vascular dementia may be apparent on MRI.² When available, positron emission tomography may be useful for assessing brain region functional activity³ as well as for quantifying brain amyloid distribution.¹¹

Several CSF biomarkers for AD are being studied for their predictive capability and may be available in the future.² In AD, CSF tau and phosphorylated tau protein concentrations increase and amyloid β -42 decrease compared with normal controls.^{10,12} Patients who have MCI that has progressed to AD have increased CSF tau concentrations, whereas CSF tau concentrations remain low in patients with MCI that has not progressed to AD.¹⁰ The genetic marker apolipoprotein E4 (ApoE4) allele is associated with increased risk for developing AD,

and screening for this allele may assist in prediction of disease progression.^{2,5} Mutations in genes for amyloid precursor proteins presenilin 1 and presenilin 2 are also associated with earlier symptom presentation and their detection.

HOW ARE MCI AND DEMENTIA TREATED?

MCI has multiple contributing causes, and there is no single effective treatment. The Alzheimer's Disease Cooperative Study demonstrated the cholinesterase inhibitor donepezil (Aricept, generics) to be effective at reducing risk for progressing from MCI to AD over the first 12 months of the study and was particularly effective in ApoE4 carriers; however, no significant benefits were noted at the end of the 3-year study.⁴ In two separate trials, the cholinesterase



TABLE 1. Helpful resources

Montreal Cognitive Assessment:
www.mocatest.org

Alzheimer's Disease Research Center
clinical dementia rating:
alzheimer.wustl.edu/cdr/

Free access to Neuropsychopharmacology -
5th Generation of Progress from the American
College of Neuropsychopharmacology:
[www.acnp.org/publications/neuro5thgen-
eration.aspx](http://www.acnp.org/publications/neuro5thgeneration.aspx)

inhibitor galantamine (Razadyne, generics) did not significantly slow progression from MCI to AD after 24 months and was associated with an increased death rate.⁴ Finally, the cholinesterase inhibitor rivastigmine (Exelon, generics) showed no significant benefits in conversion from MCI to AD after 4 years; however, mortality was not affected.⁴ Therefore, while not currently indicated for MCI, the cholinesterase inhibitors appear to be somewhat effective for delaying the cognitive changes associated with progression of MCI to dementia. Because of its association with an increased death rate, galantamine should be reserved for patients who do not tolerate donepezil or rivastigmine.

The N-methyl-D-aspartic acid receptor antagonist memantine (Namenda) was shown to have small but significant effects at improving cognition, behavior, and activities of daily living in patients with moderate to severe AD but not in those with vascular dementia for up to 6 months after initiating treatment.¹³ Reports on memantine's effectiveness in MCI are not presently available, and this medication is indicated only for patients with moderate to severe AD. Other proposed medical treatments, which have not demonstrated protective effects, include the cyclooxygenase inhibitor rofecoxib (Vioxx, withdrawn), vitamin E and other antioxidant nutrients, and omega 3 fatty acids.

Physical activity has been shown to improve multiple aspects of cognition, with the greatest effects on executive functions, even when activity is started later in life.¹⁴ Social and intellectual engagement are likewise beneficial¹⁴ and should be encouraged throughout the lifespan.

Clinicians should consider the social and familial impact of MCI, and particularly dementia, on patients and their support system. Patients and families should be referred to supportive social services to assist in meeting the escalating care requirements that follow progression to dementia. Clinicians should facilitate the patient's access to those services as a part of caring for the patient and family. **JAAPA**

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