Mild Cognitive Impairment and Mild Dementia: A Clinical Perspective

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Abstract

Mild cognitive impairment and mild dementia are common problems in the elderly. Primary care physicians are the first point of contact for most patients with these disorders and should be familiar with their diagnosis, prognosis, and management. Both mild cognitive impairment and mild dementia are characterized by objective evidence of cognitive impairment. The main distinctions between mild cognitive impairment and mild dementia are that in the latter, more than one cognitive domain is invariably involved and substantial interference with daily life is evident. The diagnosis of mild cognitive impairment and mild dementia is based mainly on the history and cognitive examination. The prognosis for mild cognitive impairment and mild dementia is an important motivation for diagnosis because in both, there is a heightened risk for further cognitive decline. The etiology of mild cognitive impairment and mild dementia can often be established through the clinical examination, although imaging and other laboratory tests may also contribute. Although Alzheimer disease is the most common cause of both, cerebrovascular disease and Lewy body disease make important contributions. Pharmacological treatments are of modest value in mild dementia due to Alzheimer disease, and there are no approved pharmacological treatments for mild cognitive impairment of any etiology. Nonetheless, new-onset cognitive impairment is a worrisome symptom to patients and families that demands answers and advice. If a patient is having difficulties managing medications, finances, or transportation independently, diagnosis and intervention are necessary to ensure the health and safety of the patient.
ILLUSTRATIVE CASE
Mr Smith, a 73-year-old man, comes for his yearly examination accompanied by his wife. After reviewing the conditions on his problem list, his wife mentions that she has had concerns about his forgetfulness. Mr Smith is quick to point out that he doesn’t feel that forgetfulness interferes with his activities. After asking Mr Smith if he would allow his wife to speak, the patient’s wife elaborates, “Over the past year, our children and I have noticed that Mr Smith often asks the same question over and over again. He didn’t used to do this. He doesn’t seem to be paying attention to what I am saying because he hardly ever remembers our conversations. If I ask him to go pick up some things in town, he usually comes back empty-handed or with only a few of the things I asked him to get. He doesn’t remember appointments. Yet, he has had no difficulties with driving or with directions, and he is still an excellent handyman.”

What should a health care professional do in this situation?

DEFINITION OF MILD COGNITIVE IMPAIRMENT AND MILD DEMENTIA
Cognitive impairment in the elderly is a common condition, and in most instances, primary care physicians are the first point of contact for a patient and family. Among persons older than 70 years, 14% have sufficient cognitive impairment to warrant a diagnosis of dementia,1 and an equal number have mild but unequivocal cognitive impairment short of dementia.2 Persons with moderate to severe dementia are generally brought to medical attention because their care needs demand it.3 Milder forms of cognitive impairment, however, present formidable conceptual and practical challenges in detection by primary care physicians.

Mild cognitive impairment (MCI) is the term used to describe the condition of individuals whose cognition lies between the cognitive changes of aging and early dementia4 (Table 1). They have objective evidence of cognitive impairment that represents a decline from the past, but they function independently or nearly so in their daily lives in a manner that is indistinguishable from the past.4,5 Although most of the MCI literature pertains to the earliest manifestations of Alzheimer disease (AD), MCI is a syndrome that could have many causes.4 Mild dementia is also defined by cognitive impairment and poor performance on objective cognitive assessments that represent a decline from the past, but importantly, dementia requires evidence of substantial difficulties in daily life that interfere with independence.5 In mild dementia, patients retain independence in simpler activities, in contrast to more severe forms of dementia in which basic activities of daily living are compromised. Recently released criteria for the Diagnostic and Statistical Manual of Mental Disorders: DSM-57 include criteria for a new diagnostic label, mild neurocognitive disorder, that closely resembles MCI. Although mild dementia represents a clinically relevant step toward increasing impairment and worse prognosis, there are many similarities in the diagnosis and recognition of MCI and mild dementia. Hence, this review will explore the bases for the diagnosis of MCI and mild dementia, the rationale for their timely recognition, the options for management, and a glimpse at future trends. Recently, the topic of MCI has also been reviewed elsewhere.8

<table>
<thead>
<tr>
<th>TABLE 1. Diagnosis of Mild Cognitive Impairment and Mild Dementia</th>
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<tr>
<td>Mild cognitive impairment</td>
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<tr>
<td>Concern about a change in cognition, in comparison with the person’s previous level</td>
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<td>Objective evidence of low performance in one or more cognitive domains that is greater than expected for the patient’s age and educational background</td>
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<td>Does not substantially interfere with daily activities, although complex functional tasks performed previously, such as paying bills, preparing a meal, or shopping, may take more time or be performed less efficiently.</td>
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<td>Independence in daily life is preserved, with minimal aids or assistance.</td>
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<td>Not explained by delirium or major psychiatric disorder</td>
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<tr>
<td>Mild dementia</td>
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<tr>
<td>Objective evidence of low performance in more than one cognitive domain that is greater than expected for the patient’s age and educational background</td>
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<td>Substantial interference with the ability to function at work or at usual activities but still able to carry out basic activities of daily living (bathing, dressing, personal hygiene) and participate in some pastimes, chores, and social functions</td>
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Adapted from Alzheimer’s Dementia.5,6
PROGNOSIS
A diagnosis of MCI or mild dementia carries important prognostic implications (Figure). Mild cognitive impairment and mild dementia represent markedly heightened risk for worsening over the ensuing several years.\textsuperscript{9} For example, in Olmsted County, Minnesota, the rate of progression to dementia among persons with MCI was 7.1% per year in contrast to the rate of progression among cognitively normal persons of 0.2% per year.\textsuperscript{9} In typical clinical settings in which MCI is likely to be diagnosed later in the course, the rate of progression to dementia may be even higher. These rates reflect averages of all ages over 70 years; in fact, the risk of incident dementia in persons with MCI increases with advancing age, so that a 90-year-old with MCI has a higher risk for progression to dementia than a 70-year-old who otherwise is similarly impaired. Because of the inherent variability in the clinical diagnosis of MCI, some persons diagnosed as having MCI may later appear to be cognitively normal. Yet, even when MCI is diagnosed and later rescinded because of improvement in cognition, individuals once diagnosed as having MCI are at greater risk for future decline compared with persons who never were considered to have MCI.\textsuperscript{9-11} In contrast, persons with dementia almost invariably worsen over time.\textsuperscript{12,13}

NATURE OF COGNITIVE IMPAIRMENT
Cognitive functioning is typically characterized into 1 of 5 domains: (1) learning and memory, (2) language, (3) visuospatial, (4) executive, and (5) psychomotor. These domains have a rough correspondence with their cerebral localization. For a diagnosis of MCI, only one of these areas must be impaired, whereas a diagnosis of dementia requires that more than one domain must be impaired. Evidence for involvement of individual domains can be obtained from the history, a brief mental status examination, or neuropsychological testing.

Forgetting is intrinsically human and increases with aging. It is part of normal experience to forget a name temporarily or an appointment rarely. However, when such events become frequent, suspicion should be high that there is more than just normal forgetting. Similarly, frequent re-asking of questions is much more likely to indicate substantial memory impairment.\textsuperscript{14} The most common earliest manifestation of pathologic cognitive impairment in the elderly is declining efficiency of memory, often exemplified by re-asking of questions. The challenge to clinicians is to appreciate where the boundary between normal and abnormal is for a particular patient. In our illustrative case, the patient was repeating himself in conversation, and his wife had taken over refilling his prescriptions because he was forgetting to do so. These symptoms strongly suggest an amnestic disorder, in our patient’s case, amnestic MCI.

Nonamnestic cognitive impairments are nearly as common as the amnestic forms. Non-amnestic impairment can involve word finding and speech difficulties, impaired geographic orientation, visual perception problems, and impaired mental agility. When there is dysfunction in more than one cognitive domain in persons with MCI, referred to as multidomain MCI, the risk for decline to dementia is much higher than when there are isolated memory problems or word finding problems.\textsuperscript{9,15}
Loss of insight into one’s own cognitive difficulties is a common, although not invariant, part of both MCI and mild dementia. Contrary to older clinical lore, persons who otherwise appear cognitively intact but report cognitive difficulties have a slightly greater likelihood of experiencing cognitive decline in the future. However, clinicians should be cautious in using subjective cognitive complaints as a prognostic factor because secondary gain, depression, or lifelong personality traits can also produce cognitive complaints. In our patient, loss of insight was the issue: it was his wife and not the patient who mentioned the cognitive concerns to the physician. The loss of insight in our patient might suggest that his illness is somewhat more advanced; patients in the earlier stages of MCI often have some preservation of insight into their cognitive decline.

**CLINICAL DIAGNOSIS OF MCI AND MILD DEMENTIA**

A medical history and a mental status examination are the principal tools for diagnosing MCI or mild dementia. The medical history is the primary means by which the clinician establishes whether the patient has impairment in daily functioning. The mental status examination is the means by which the clinician establishes whether there is objective evidence of cognitive impairment. Clinical judgment is required to integrate information from the 2 sources. A general neurologic examination should also be performed, but its role in the diagnostic process is largely in contributing to an understanding of the etiology of the cognitive disorder.

A thorough history from both the patient and someone who knows the patient well is essential. In the early stages of MCI, patients are aware of their cognitive difficulties and may themselves raise the concern with their physician. Generally, however, an informant who knows the patient well is necessary to corroborate the patient’s own observations. Finding such an individual and finding the time to interview an informant is one of the greatest challenges to diagnosis in the primary care setting. Several inventories of activities of daily living are available; for routine clinical use, the 10-item Functional Activities Questionnaire is a valid tool for characterizing daily functioning (Table 2). Even if the questionnaire is not administered verbatim, the content of the 10 items is a useful guide for surveying a person’s strengths and weaknesses in daily life. Understanding the patient’s other medical conditions, if any, is highly relevant to placing cognitive symptoms in perspective. For example, a patient with severe congestive heart failure or emphysema could have hypoxemia, hypercapnia, or markedly elevated hematocrit, all of which could affect cognitive functioning. All of the patient’s medications should also be reviewed when the diagnosis of cognitive impairment is being considered. Many widely used medications have the potential to impair cognition. Sedatives, narcotic pain medications, and medications with anticholinergic profiles are of greatest concern. In addition, anxiety or depression can contribute to cognitive difficulties.

The second tool for the diagnosis of cognitive impairment is the mental status examination. There are several instruments designed for use in primary care settings, but such examinations may take 10 minutes to complete. The Montreal Cognitive Assessment and the Short Test of Mental Status are 2 instruments we use. Mental status examinations are not perfect tools, but they are far more sensitive than casual conversations or ad hoc questions. In our patient, abnormalities on a mental status examination would provide important confirmation of the wife’s observations. A “normal” score would also be informative. Indeed, bedside examinations are known to be insensitive. Thus, if the patient, family, or physician suspect cognitive impairment, referral for

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**TABLE 2. Functional Activities Questionnaire**

In the past 4 weeks, does the patient have any difficulty or need help with:

1. Writing checks, paying bills, or balancing a checkbook
2. Assembling tax records, business affairs, or other papers
3. Shopping alone for clothes, household necessities, or groceries
4. Playing a game of skill, working on a hobby
5. Heating water; making a cup of coffee, turning off the stove
6. Preparing a balanced meal
7. Keeping track of current events
8. Following a television show, book, or magazine and being able to discuss them with acquaintances
9. Remembering appointments or remembering to take medications, keeping track of recent conversations, recent events, and the date
10. Driving, traveling out of the neighborhood, or arranging to take public transportation

Scoring guide: 0 = can do this without help or never did the activity; 1 = have some difficulty but can do this without help; 2 = need help with this; 3 = can’t do this

Adapted from J Gerontol and the United States Agency for Health Care Policy and Research.
neuropsychological testing—a far more sensitive method—should be considered.

More detailed evaluation of cognition would depend in part on the wishes of the patient and family, the experience of the health care professional, and the accessibility of consultations with a neurologist, psychiatrist, geriatrician, or neuropsychologist to obtain further expertise in diagnosis. The decision also depends on the severity of the cognitive impairment and the consequences of the diagnosis. When symptoms are mild or uncertain or when major life decisions are at stake, neuropsychological testing can be invaluable.

Imaging studies and blood tests are a necessary part of the evaluation of suspected cognitive impairment. Laboratory tests cannot answer the question of whether the patient has cognitive impairment, but they can aid in establishing an etiology of the cognitive disorder. The American Academy of Neurology recommended a simple battery of laboratory tests and a brain imaging study as part of the initial evaluation of someone with suspected dementia or MCI. Noncontrast brain magnetic resonance imaging (MRI) or brain computed tomography (CT) will provide sufficient evidence to rule out brain tumors, subdural hematoma, and other structural brain lesions. Routine MRI or CT may also show evidence of cerebrovascular disease, with MRI being much more sensitive than CT. These simple scanning techniques cannot be used to diagnose AD itself, however. Our patient should undergo laboratory studies such as measurement of his vitamin B12 and thyrotropin levels and a brain imaging study.

ETIOLOGY

In persons older than 65 years, AD is the most common etiology of MCI and mild dementia. Amnestic impairment is most typical for AD whether in the MCI or mild dementia stage. However, other diseases may also cause MCI and mild dementia, and comorbidities are often seen with AD. Cerebrovascular disease that causes brain infarctions becomes more common with advancing age as well. Estimates vary widely as to the exact contribution of cerebrovascular disease to MCI and mild dementia, but it is likely clinically important. Brain MRI may reveal silent infarcts or extensive white matter changes thought to be ischemic in nature. Patients with imaging evidence of these lesions who also have vascular risk factors might be treated differently than patients without these imaging findings. Both amnestic and nonamnestic impairments occur with cerebrovascular disease. Parkinson disease with concomitant cognitive impairment, now referred to as Lewy body disease, also becomes more common with advancing age. In its typical presentation, Lewy body disease may cause cognitive impairment and parkinsonism, prominent changes in personality, and alterations in sleep and wakefulness. Its typical mildest cognitive profile is that of a nonamnestic MCI. The frontotemporal degenerations are the least common of the degenerative dementias, but they too can produce an MCI syndrome. Depression, multiple medical comorbidities, and adverse effects of drugs can sometimes produce cognitive impairment; in principle, prognosis in these etiologies is more favorable than for neurodegenerative disease. In general, AD and other neurodegenerative diseases and cerebrovascular disease are inevitably progressive; hence, when they are the cause of MCI and mild dementia, worsening cognitive function can be anticipated.

TREATMENT

Treatment of patients with MCI and mild dementia should include strong encouragement to remain physically, socially, and mentally active. One study of persons with subjective memory impairment showed clear, although modest, benefits of physical exercise. Although a review of nonpharmacological interventions in MCI or dementia asserted that the evidence was weak, we believe that mental and physical stimulation should be encouraged. There are also no prospective studies of the impact of more aggressive treatment of vascular risk factors, but management of vascular risk factors is a part of good general care.

Pharmacological treatment of MCI presumed to be due to AD is quite limited, and treatment of MCI due to other neurodegenerative diseases is not available. There have been several trials of cholinesterase inhibitors in persons with amnestic-type MCI, the type most likely to be due to underlying AD. The results have been disappointing. Although a hint of treatment benefit in the form of delay of progression to dementia was documented in one study that
found a positive effect of donepezil for 12 months and up to 24 months in apolipoprotein ε4 carriers, the benefit did not persist over the 36-month duration of the study. Three cholinesterase inhibitors—donepezil, rivastigmine, and galantamine—are approved for the treatment of mild dementia due to AD. Treatment of patients with mild dementia due to AD has tangible but modest benefits.35,36 Our decision to treat our patient with a cholinesterase inhibitor would depend on the results of our clinical assessment and formal neuropsychological testing as well as our impression of the likelihood that AD was the underlying etiology. No treatments have been approved by the US Food and Drug Administration for MCI.

RATIONALE FOR DIAGNOSIS

New-onset cognitive impairment is common and is a worrisome symptom to patients and families. If a patient is having difficulties in managing medications, finances, or transportation independently, diagnosis and intervention are necessary to ensure the health and safety of the patient. Acknowledging that we lack therapies that block the progression of AD or other degenerative dementias, there are nonetheless important reasons to make a diagnosis. First, if family members sense that the patient is having cognitive difficulties, affirming the diagnosis through a rational evaluation enables them to come to grips with how the memory or cognitive difficulties interfere with daily life and what accommodations are needed. Second, the diagnosis of MCI enables families to plan for the future. Some patients and families may choose to discount future risk, but others might desire as much information as possible.

There are those who argue against making a diagnosis of MCI. Recent critical reviews highlight the benefits and challenges.37 The critics point out the stigma associated with a diagnosis of cognitive impairment, the modest interventional opportunities, and the occasional reversal of MCI to cognitive normality. In our patient, the first 2 criticisms are effectively refuted by the need for the patient and his family to know what is going on. The third point, the variable prognosis, can be conveyed to the patient and family through discussion and education. We acknowledge that cognitive screening of the elderly in the absence of a clinical concern has not been found to be of clear benefit.38 However, cognitive assessments pay off in the long run. Almost all clinicians would appreciate the added certainty for making a diagnosis when prior documentation exists that verifies a genuine change in condition. Our patient’s situation should not be viewed as an example of screening for cognitive impairment; in our patient, the spouse asked the physician for help with the problem.

FUTURE TRENDS

Research on imaging and cerebrospinal fluid biomarkers is intense and accelerating, but most of the progress has not yet affected routine clinical practice. The introduction of positron emission tomographic imaging of brain β-amyloid39 has made it possible in the research setting and in clinical practice (for a very high cost, not covered by insurance) to establish whether a person is harboring abnormal levels of brain β-amyloid. Positron emission tomography for detection of tau protein is also being studied in the research setting.40 A combination of imaging or cerebrospinal fluid studies has been introduced for research purposes into the diagnostic criteria for MCI (and dementia).41,42 Future clinical trials are likely to benefit from the enhanced antemortem diagnostic accuracy offered by the new imaging and fluid biomarker studies. As of 2014, however, the clinical value of biomarker characterization of patients with MCI or mild dementia has not been established.

CONCLUSION

Mild cognitive impairment and mild dementia are common problems in our aging society. Proper and timely diagnosis can minimize the dysfunction that accompanies cognitive loss.
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