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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 providers 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 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, as 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 though imaging and other laboratory tests may also contribute. While Alzheimer's 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's 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 in managing independently medications, finances or transportation, diagnosis and intervention are necessary to ensure the health and safety of the patient.

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INTRODUCTION

Cognitive impairment in the elderly is a common condition, and in most instances, primary care providers are the first point of contact for a patient and family. In persons over age 70 years, 14% have sufficient cognitive impairment to warrant a diagnosis of dementia¹, and an equal number have mild but unequivocal cognitive impairment short of dementia². Persons with moderate to severe dementia are generally brought to medical attention because their care needs demand it³. Milder forms of cognitive impairment, on the other hand, present formidable conceptual and practical challenges in detection by primary care providers.

Mild Cognitive impairment (MCI) is the term for individuals who fall 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}. While most of the MCI literature pertains to the earliest manifestations of Alzheimer's disease (AD), MCI is a syndrome that could be caused by many etiologies⁴. Mild dementia is also defined by cognitive impairment and poor performance on objective cognitive assessments that represents a decline from the past, but importantly, dementia requires evidence of significant difficulties in daily life that interfere with independence. In mild dementia, patients retain independence in simpler activities, in contrast to more severe forms of dementia where basic activities of daily living are compromised. Recently released criteria for the Diagnostic and Statistical Manual for Mental Disorders-5 (DSM-5) include criteria for a new diagnostic label "Mild Neurocognitive Disorder" that closely resembles MCI⁶. While mild dementia represents a clinically relevant step towards increasing impairment and worse prognosis, there are many similarities in 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. One of us has recently reviewed the topic of MCI elsewhere⁷.

PROGNOSIS

A diagnosis of MCI or mild dementia carries important prognostic implications (Figure). MCI and mild dementia represent markedly heightened risk for worsening over the ensuing several years⁸. For example, in Olmsted County MN, 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. In typical clinical settings, where a diagnosis of MCI is likely to be made 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. Owing to the inherent variability in the clinical diagnosis of MCI, some persons diagnosed with MCI may later appear cognitively normal. Yet, even when a diagnosis of MCI is made and later rescinded because of improvement in cognition, individuals once diagnosed with MCI are at greater risk for future decline compared to persons who never were considered to have MCI⁸⁻¹⁰. In contrast, persons with dementia almost invariably worsen over time^{11, 12}.

NATURE OF COGNITIVE IMPAIRMENT

Cognitive functioning is typically characterized into one of 5 domains: 1) learning and memory, 2) language, 3) visuo-spatial, 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 in order to make a diagnosis, whereas more than one domain must be impaired to make a diagnosis of dementia. 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. We may misplace a watch or keys occasionally. But 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 impairment¹³. The most common earliest manifestation of pathological 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 patient's case, he 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 amnesic disorder, in our patient's case, amnesic MCI.

Non-amnesic cognitive impairments are nearly as common as the amnesic forms. Non-amnesic 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^{8, 14}.

Loss of insight into one's own cognitive difficulties is a common, though not invariant part, of both MCI and mild dementia. In contrast to older clinical lore, persons who otherwise appear cognitively intact and who report cognitive difficulties have a slightly greater likelihood of experiencing decline in the future^{13, 15}. However, clinicians should be cautious in using subjective cognitive complaints as a prognostic factor, because secondary gain, depression or life-long personality traits can also produce cognitive complaints. However, in our patient, loss of insight was the issue: it was his wife and not the patient who brought the cognitive concerns to the physician. The loss of insight in our patient might suggest that his illness is somewhat more advanced; patients who are earlier in the MCI diagnosis 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 making a diagnosis of MCI or mild dementia. The medical history is the principal means by which the clinician establishes whether or not 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 two sources. The general neurological 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, though, 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^{16, 17} 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 very 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. Review of all of the patient's medications should also occur 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 the ones 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 a number of instruments designed for use in primary care settings, but even so, such examinations may take 10 minutes to complete. The Montreal Cognitive Assessment (MOCA)^{18, 19} and the Short Test of Mental Status (STMS)^{20, 21} are two 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, an abnormal 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 care providers suspect cognitive impairment, referral for neuropsychological testing²² – 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 provider and the accessibility of consultations with a neurologist, psychiatrist, geriatrician or neuropsychologist to obtain further expertise in diagnosis. The decision also depends upon 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 work 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 the laboratory tests can aid in establishing an etiological diagnosis of the cognitive disorder. The American Academy of Neurology recommended a very simple battery of laboratory tests and a brain imaging study as part of the initial evaluation

of someone with suspected dementia²³ or MCI²⁴. Non-contrast brain MR or a brain CT will provide sufficient evidence to rule out brain tumors, subdural hematoma and other brain structural lesions. Routine MR or CT scans may also show evidence of cerebrovascular disease, with the MR 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 a vitamin B12 level, a thyroid stimulating hormone level and a brain imaging study.

ETIOLOGY

In persons over age 65 years, AD is the most common etiology of MCI and mild dementia²⁵⁻²⁷. Amnesic 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 other diseases often co-occur with AD. Cerebrovascular disease that causes brain infarctions becomes more common with advancing age as well. Estimates vary widely as to the exact contribution that cerebrovascular disease makes, but it is likely clinically important²⁷. Brain imaging with MR scanning may reveal silent infarcts or extensive white matter changes thought to be ischemic in nature. Knowledge of these lesions in someone with vascular risk factors might be treated differently compared to persons lacking these imaging findings. Both amnesic and non-amnesic impairments occur with cerebrovascular disease. Parkinson's disease with concomitant cognitive impairment, what is 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 non-amnesic MCI²⁸. 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 in the future.

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 though modest benefits of physical exercise²⁹. While a review of non-pharmacologic interventions in MCI or dementia asserted that the evidence was weak³⁰, 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 factors³⁰, but management of vascular risk factors is a part of good general care.

Pharmacological treatment of MCI presumed 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 amnesic type MCI, the type most likely to be

due to underlying AD. The results have been disappointing^{31, 32}. Although a hint of treatment benefit in the form of delay of progression to dementia was documented in one study³¹, with 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 though modest benefits^{33, 34}. Our decision to treat our patient with a cholinesterase inhibitor would depend on the results of our bedside 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 independently medications, finances or transportation, diagnosis and intervention are necessary to ensure the health and safety of the patient. Acknowledging that we lack therapies that block 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 challenges³⁵. The critics point out the stigma associated with a diagnosis of cognitive impairment, the modest interventional opportunities and the occasional reversal MCI to cognitive normality. In our patient the first two 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 shown to be of clear benefit³⁶. However, 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.

THE FUTURE

Research on imaging and cerebrospinal fluid biomarkers is intense and accelerating, but most of the progress has not yet come to affect routine clinical practice. The introduction of positron emission tomography (PET) β-amyloid imaging³⁷ has made it possible in the research setting and in clinical practice (for a very high cost, not covered by insurance) to establish whether or not a person is harboring abnormal levels of brain β-amyloid. PET

imaging to detect tau protein is also being studied in the research setting³⁸. A combination of imaging or cerebrospinal fluid studies has been introduced for research purposes into the diagnostic criteria for MCI (and dementia)^{39, 40}. 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 MCI or mild dementia patients is not established.

CONCLUSIONS

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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ABBREVIATIONS

AD	Alzheimer's disease
CT	computerized tomographic imaging
MCI	mild cognitive impairment
MR	magnetic resonance imaging

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CASE PRESENTATION

Mr Smith, a 73 yo man, comes for his yearly check-up 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 the Mr. Smith whether 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 handy man."

What should a health care provider do in this situation?

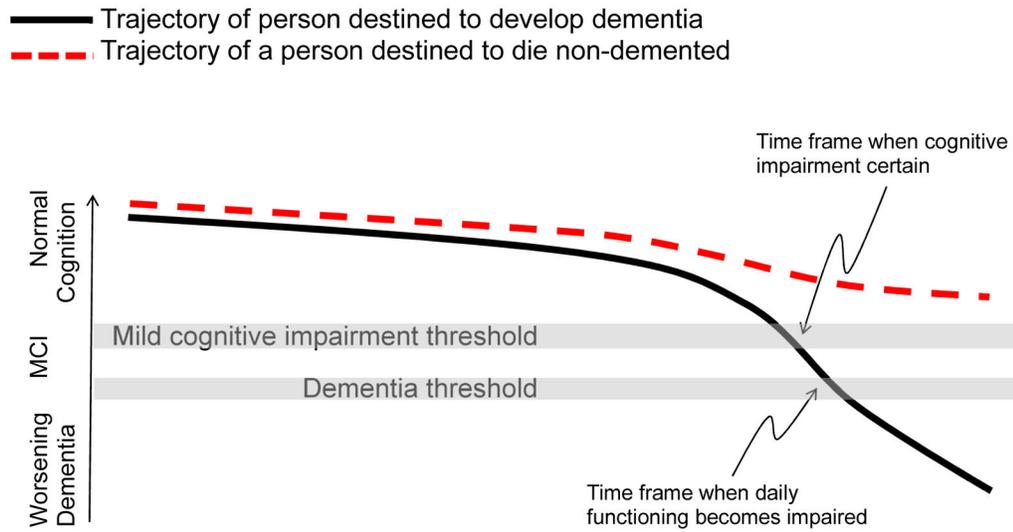


Figure. Graphic demonstration of the differences in cognitive trajectories between a person (red dashed line) destined to never become cognitively impaired during life and a person (solid black line) destined to develop dementia. The x-axis represents age, and the y-axis cognitive impairment. Thresholds for mild cognitive impairment and dementia are indicated by horizontal grey bands. The continuous nature of cognitive decline in persons destined to become demented defies simple algorithms; clinical judgment is needed to weigh information from the history and examination.

Table 1

The diagnosis of mild cognitive impairment and mild dementia. Adapted from^{5, 41}.

Mild Cognitive Impairment	Mild Dementia
Concern about a change in cognition, in comparison with the person's previous level	
Objective evidence of low performance in <i>one or more</i> cognitive domains that is greater than expected for the patient's age and educational background	Objective evidence of low performance in <i>more than one</i> cognitive domain that is greater than expected for the patient's age and educational background
Does not substantially interfere with daily activities, although complex functional previously tasks, such as paying bills, preparing a meal, or shopping may take more time or be performed less efficiently. Independence in daily life is preserved, with minimal aids or assistance.	Significant 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.
Not explained by delirium or major psychiatric disorder	

Table 2Functional Activities Questionnaire. Content from¹⁶ and form from⁴²

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 TV 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.
- 1 Have some difficulty, but can do this without help.
- 2 Need help with this.
- 3 Can't do this.
- 0 Never did (the activity)