Update on Alzheimer's Disease

Clinical Implications of the New Diagnostic Guidelines for Dementia

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ABSTRACT

New criteria have been proposed for diagnosing Alzheimer's disease. These emphasize that this illness exists on a continuum and begins early on. This article reviews the pros and cons of these criteria. It also provides practical guidelines for psychiatrists whose patients may be affected by these new criteria. Particular attention is given to patients who, as opposed to their wanting to know whether they are likely to have AD, want to deny this possibility.

KEY WORDS

Alzheimer's disease, diagnostic guidelines, mild cognitive impairment, dementia, biomarkers, plaques, neurofibrillary tangles, independence, capacity, memory, behavior, denial

INTRODUCTION

Experts recently have proposed new clinical and research guidelines for diagnosing Alzheimer's disease (AD).[1] The new criteria better reflect how AD exists on a continuum. AD is now viewed as starting earlier and progressing over a longer period of time compared to how it was previously viewed as emerging more rapidly and primarily in patients' later years.[2,3] This progression of AD is now seen as involving three stages: a pre-clinical or pre-symptomatic stage; a symptomatic, pre-dementia phase called "mild cognitive impairment (MCI) due to AD," and the AD or dementia phase. The criteria for the diagnosis of both AD and MCI may be made "at the bedside," allowing psychiatrists to diagnose the disease on clinical grounds alone.[4] To diagnose AD, a patient must be cognitively impaired in at least two of several domains that will be reviewed in this article. In order to diagnose AD, the impairments must be getting worse in the patient and interfere significantly with the patient's everyday functioning.

Research criteria involving biomarker findings now exist for AD that were not known when the prior diagnostic criteria were established in 1984. As a result of the discovery of biomarkers, the diagnoses of AD and MCI due to AD are both, under the current guidelines, more accurate.

The findings of plaques and neurofibrillary tangles on autopsy have, like these clinical diagnoses

and biomarkers, been "disentangled" from one another.[5] Thus, though usually parallel, the clinical and autopsy findings may be discrepant in some cases. An "occasional" patient reported to have dementia, for example, may have autopsy findings that provide no "obvious neuropathologic explanation."[5]

The criteria within the guidelines involving biomarkers are designed at this time for research purposes only. It is hoped that as early AD biomarkers are identified, researchers will be better able to identify patients at high risk.[6] Researchers may then "target" these patients for early experimental treatments that hopefully, due in part to being started early, may be more effective than those available now.[7] They may even be able to prevent AD from occurring.

For now, however, these new guidelines may affect what patients "clinically" want. The new guidelines may provide greater access to early biomarker testing in order to find out the degree to which a patient is at risk to develop AD. This testing may only be available to patients who participate in research. If a patient finds that he or she is at high risk for developing AD, the patient may want to participate in research in order to receive experimental treatments early in the disease. Because the treatments are experimental, they may not be effective, and psychiatrists discussing research with their patients should be sure that the patients understand this.

Patients choosing to participate in research can be based on a sound rationale. Even though the treatments patients receive are not evidence-based (and may never be), the treatments could be beneficial. As new treatments prove more effective than established treatments, as hopefully will be the case, the soundness of this rationale may decrease. Thus, psychiatrists may choose to encourage patients who want to participate in research to do so. Psychiatrists can encourage their patients by referring them to organizations, such as www.alz.org and "Trial Match" 1-800- 272- 3900.

While psychiatrists may help some patients pursue specific kinds of studies (a caregiver of one of my patients, for instance, sought information regarding research on deep brain stimulation),[8,9] they should keep in mind that other patients may not want to know whether they have or are likely to develop AD. These patients may be particularly challenging from a treatment standpoint, especially with the new guidelines, and the psychiatrist may find him- or herself between Scylla and Charybdis, so to speak.

In this article, I shall focus on the unique challenges psychiatrists may face with new guidelines. First I will review the new guidelines, and then I shall discuss how psychiatrists might best help patients who want to enter research. Finally, I will discuss how psychiatrists might best meet the needs of those patients who do not want to know whether they have AD or are likely to develop it.

In my opinion, psychiatrists can meet the needs of both of these highly diverse types of patients, and through this article, I will suggest how they might do so.

THE NEW GUIDELINES

Principles underlying the new guidelines. Lyketsos, a leader in this field, states that the new guidelines are based on the following three principles:[10] 1) The guidelines make it clear that psychiatrists can diagnose AD and MCI based on clinical findings alone. For example, a psychiatrist can test a patient for immediate and delayed memory in the office by using the measures in the Mini Mental Status Exam (MMSE) or by hiding objects around the room. In order to make a diagnosis of AD or MCI, the psychiatrist must also find evidence of a decline in the cognitive areas that are impaired as well as impairment in the patient's daily functioning. This is best to do over more than one visit, but it may be possible to infer this from the history provided by the patient or caregiver. 2) These guidelines allow psychiatrists to diagnose AD when it presents in atypical ways (e.g., impaired capacity to plan; impaired visual/spatial abilities, such as the ability to recognize faces or dress; impaired language; and altered behavior). This change in guidelines may allow psychiatrists to diagnose and treat patients more effectively when their dementia presents in unusual ways. In other words, the patient may not have impaired memory but exhibits other impaired cognitive functioning. 3) The new guidelines include findings regarding biomarkers that now can be used for research purposes. Lyketsos points out that the clinical and research criteria provide parallel, progressive developments of AD in the clinical as well as the physiological, biochemical, and anatomical realms. In other words, as a patient progresses clinically from pre-symptomatic to end-stage disease, a concomitant progression of brain disease from amyloid plaques alone to plaques with neurodegeneration but no symptoms to plaques and neurodegeneration with symptoms occurs. When symptoms have become severe enough to impair a patient's daily functioning, a diagnosis of AD can be made.

Lyketsos points out, however, that despite these parallels, the amyloid hypothesis still remains unproven.[10,11]

The new clinical and research guidelines. According to the new guidelines, AD involves a progression from a pre-clinical or pre-symptomatic stage to a symptomatic, pre-dementia phase (MCI due to AD) to the dementia phase (AD). The pre-clinical phase is intended for research purposes only.[12] In this phase, patients are wholly or almost wholly asymptomatic, though they may have underlying, "latent" brain disease, such as amyloid plaques. These plaques may be identified in positron emission tomography (PET) and cerebrospinal fluid (CSF) findings. Neurodegenerative findings or those of brain nerve injury that occur "downstream" become evident in tau, fluoro-deoxyglucose (FDG), and magnetic resonance imaging (MRI) biomarkers.

In the second phase, patients have symptoms, but the symptoms are not so significant that they impair the patient's everyday functioning.[13] In other words, the patient may have difficulty with his or her memory and/or with one or more other cognitive functions, but the impairment does not go beyond what would be expected of people who are in the same age and education bracket.

In the third phase, the patient is cognitively impaired in two or more areas, the impairments are worsening, and the individual is functionally impaired.[14] Making the distinction between MCI and AD may be clinically difficult for several reasons. There are, for instance, no established testing cut-off points. On tests such as the MMSE, patients usually score beyond 1 or 1½ standard deviations. It also may be difficult to determine what counts as a sufficient decline in memory or another cognitive function. Norms also are less well standardized for so-called "old, old" patients, meaning patients over 90.[15] The determination that may be the most difficult for psychiatrists to make, however, may be whether the cognitive problems a patient is having are interfering significantly with the patient's daily functioning.

A CRITICISM OF THESE GUIDELINES

The critical determination that differentiates MCI due to AD from AD is that patients with "only" MCI can still function independently. This difference may be profoundly important to patients because, although MCI due to AD usually progresses to become AD, this is not always the case. Thus, patients with "only" MCI may have hope, slight though this may be, that they will not develop AD.[16]

Morris criticizes this requirement of making independence the critical factor here, since care providers making this determination may reasonably differ.[17,18] Some psychiatrists, for instance, may interpret a patient needing help with "shopping, paying bills, or cooking," as only "mild" and, thus, not significant impaired, whereas others may see this as a significant impairment in a patient's independent, everyday functioning.

Another example that is not uncommon is, according to one study, that approximately 34 percent of patients with MCI have some difficulty performing tasks such as handling their money, whereas for those without MCI, this figure was only about five percent.[17] This difficulty in financial planning, in particular, has practical implications for psychiatrists clinically seeing these patients in that when patients have MCI or early AD, they are still capable of issuing legal documents, such as wills.[19] Psychiatrists seeing these patients might document in their chart notes that these patients have the legal capacity required for these tasks. This may prevent extraordinary and unnecessary legal problems later on.

This inherent difficulty of discerning whether a patient's signs and symptoms affect his or her functional independence is compounded by a common reluctance by the psychiatric community to diagnose a patient with AD or even MCI.[17] This reluctance may be due to a fear of how this diagnosis may adversely affect the patient. Thirty to 60 percent of clinicians, according to one source, may not disclose to patients that they have AD. The comparable figure from this same source for clinicians disclosing to their patients that they have "terminal cancer" is 94 percent.[17] I should note here that according to one study, less than 0.1 percent of patients committed suicide after being diagnosed with AD or MCI.[21]

The reluctance to diagnose a patient with AD or MCI may be more reasonably based on the fear that this information may have the effect of placing a "dark cloud" over the remainder of the patient's life. It is perhaps worth remarking that in Belgium, legislators are currently considering allowing dementia to be a ground for requesting active euthanasia.[22]

TWO OPPOSING CLINICAL CONCERNS RAISED BY THE NEW GUIDELINES

A clinical goal of the psychiatrist is to help patients achieve what it is they want. This is the case even when the psychiatrist sees a patient's outcomes as sub-optimal.

Patients and psychiatrists, or patients with the help of their psychiatrists, share the goal of learning of a diagnosis as soon as possible. While most patients would want to know their diagnosis as early as possible, these two goals may be incompatible if a patient diagnosed with MCI does not want to know if he or she later has or is likely to develop AD. What should a psychiatrist do in this case?

Helping patients have access to predictive testing and experimental treatments. The new criteria reflect our new awareness that AD develops over a much longer time. Thus, there are many potential gains from earlier diagnosis, and patients may want to know as much as they can. Usually, they learn this by participating in research.

These gains are well-acknowledged. If patients start anti-dementia medication early, they may do better. Some psychiatrists start patients on these medications as soon as they are diagnosed.

Patients also may better plan for their futures and make different choices if they are aware of their AD. Participation in research for altruistic reasons may add meaning to a patient's life. For these reasons, psychiatrists may want to take the initiative to raise these issues with their patients.[23] Clinicians taking somewhat analogous initiatives (e.g., by involving a patient's church, going to the patient's home, changing the words they use from "dementia" to "memory loss") have helped patients seek screening and treatment for AD.[24] Clinicians have helped these patient decide to decline life-sustaining treatments when the patients would have what, in their view, would be too poor a quality of life. Clinicians have shown them visual materials specially designed for this purpose, as opposed to just giving them verbal explanations that previously "failed."[25,26]

Principal investigators (PIs) of research protocols can also further a patient's access and equity. PIs can anticipate the needs of several different patient groups and build into their protocols such provisions as providing money for travel for patients who live far away and babysitters for parents (or grandparents) with small children.

Psychiatrists should continue to exhaust all treatments currently available, including nonpharmacological interventions (since current anti-AD drugs have slight benefits). Increasing equity may be difficult, especially because these treatments may work best when tailored to a patient's individual needs, but guidelines have been developed to help psychiatrists reach and treat larger numbers of patients effectively.[27] Psychiatrists should pursue greater equity for these patients at the end stage of AD and of their lives (e.g., hospice), discussion of which is outside the scope of this article.[28–30]

Helping patients who do not want to know that they have or are at risk of developing AD. Patients informed that they have MCI, often and somewhat counter-intuitively, report that they feel better. This may be because they now understand why they have been having the problems and thus have a greater sense of control. Not everyone is affected in this way, however. Some patients feel despair at even the thought that they may develop AD, and some may say that they would end their lives if they knew they had AD. They may believe that they would lead better lives not knowing whether they had AD. Examples of such patients have been provided in the medical literature well over a decade ago and also more recently.[31,32] Clare reported that some of these patients have tried to minimize the significance of early AD changes in such ways as telling themselves "It's nothing major" or "It's just got to do with age."[31] Others are less successful and say they want to end their lives, whether they actually ever do or do not.[31]

I recall such a patient. When I first saw her, her husband said he feared every moment of every day when she was out of his sight that she would kill herself by swallowing lye, since she had said that this was the way that she would end her life. She did better and, in fact, outlived him, though he had hoped that this would not happen.

Clare asserts, accordingly, that she believes such patients' responses to learning that they have AD lie along a spectrum. Bahro et al[33] shares this concept. Those at one end of the spectrum try to maintain a view of themselves as they were. They deny. Others, namely those at the other end of this spectrum seek to "self-adjust" or adapt. They accept that they have AD and try to do the best that they can.

Clare sees these patients' "central dynamic" as a "tension" between their attempting to protect themselves from the effects of this threat (of having AD) and their integrating this "new experience" into who they are becoming and will become.[31]

Some patients may try to remain in the former "self-maintaining" category by staying "unaware." Like Clare, other authors see these efforts to deny as "a motivated attempt at adaptive coping."[31] Clare sees this "denial" as a way to retain self-esteem. She, accordingly, recommends to clinicians "… to be sensitive to such patients'

psychological needs" and to be "ready to respond" in whatever way enhances the patients' well-being.[31]

Practical implications. The patients to whom Clare and Bahro et al refer, may want to and be able to remain feeling genuinely optimistic, at least for a time, even though they may know consciously that they are choosing to engage in denial. Consequently, they may not want to be tested for any memory deficits. They may not want to be tested for other reasons also. For example, one of my patients feared that if he was screened and the screening showed "deficits," his daughter would use this to "put him in an institution" against his will. She thought, he said, he lived "too alone." This problem requires another "solution." (He incidentally still shows no signs of dementia today).

If a psychiatrist wishes to maximally support those patients who want to wholly deny the possibility that they have AD, the psychiatrist must go along with them and do no testing, though this may go against what they see as the "main" tenet of their practice: "First, diagnose. Then, go from there."

Why might they even consider this? Psychiatrists have a duty to respect their patients' preferences, as well as more generally to do what they believe is best for them. Psychiatrists have this former duty even when a patient's cognitive capacity is somewhat impaired and even when under this same condition what the patient wants is not what the psychiatrist thinks is best.

A patient's capacity for decision-making may be somewhat impaired, when he or she "only" has MCI. This patient not receiving the proper information early in the AD disease process may go against the patient's best interests. Still, the case for the psychiatrist respecting what this patient wants, namely to be able to continue to "stay maximally able to deny," is substantial. What then could a psychiatrist do? The psychiatrist could avoid seeking a diagnosis of AD initially, even when the psychiatrist believes that AD (or MCI due to AD) might exist! First, the psychiatrist would inform the patient that if he or she is tested for AD, there may be harm from this testing the patient may first wish to consider. For example, this testing could make it more difficult for the patient to deny that he or she has a possibly significant memory problem. The psychiatrist could then not test. The psychiatrist would not even ask the few basic memory questions on the MMSI in order to test the patient's immediate and delayed memory. This is legal. A patient can say that he or she does not want to know. Clinicians over-riding this may be sued.

The psychiatrist may then offer to discuss the pros and cons of testing if the patient wants. The psychiatrist could say that the testing may support the patient's notion that the memory problems are simply due to normal aging. This is, of course, true. But there is the unavoidable downside: Even saying this may suggest to some patients that a diagnosis of AD is likely or that their memory problems are worse than they thought. These patients might fear having AD more than they otherwise would. This fear, in turn, might dampen their capacity to enjoy their remaining life as much as they would have.

CONCLUSION

New guidelines have been issued for diagnosing AD. These criteria emphasize that this disorder begins early and progresses over a long time.[34] Patients, as a result of this new knowledge and criteria, may seek greater access to prognostic findings and possibly effective treatments earlier. Both may be possible only in research contexts.

Psychiatrists should facilitate these research opportunities, while also taking into account the concomitant possibility that under these new conditions, more patients might be harmed. Patients who might deny that they have early AD or could later have AD might be harmed to a greater extent because the psychiatrist urging their participation in research might inadvertently make it harder for these patients to engage in denial.

Psychiatrists might consider avoiding the "first diagnose" protocol. They might instead inform all their patients initially of this risk and leave when and whether the patients want more information regarding their risk of having AD, at least for a time, up to them.

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