Title

Prevalence and Classification of Mild Cognitive Impairment in the Cardiovascular Health Study Cognition Study: Part 1

Journal

JAMA Neurology, 60(10)

ISSN

2168-6149

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Publication Date

2003-10-01

DOI

10.1001/archneur.60.10.1385

ORIGINAL CONTRIBUTION

Prevalence and Classification of Mild Cognitive Impairment in the Cardiovascular Health Study Cognition Study

Part 1

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Objective: To examine the prevalence of mild cognitive impairment (MCI) and its diagnostic classification in the Cardiovascular Health Study (CHS) Cognition Study.

Design: The CHS Cognition Study is an ancillary study of the CHS that was conducted to determine the presence of MCI and dementia in the CHS cohort.

Setting: Multicenter population study.

Patients: We examined 3608 participants in the CHS who had undergone detailed neurological, neuropsychological, neuroradiological, and psychiatric testing to identify dementia and MCI.

Main Outcome Measures: The prevalence of MCI was determined for the whole cohort, and specific subtypes of MCI were examined in detail only at the Pittsburgh, Pa, center (n=927). Mild cognitive impairment was classified as either MCI amnestic-type or MCI multiple cognitive deficits–type.

Results: The overall prevalence of MCI was 19% (465 of 2470 participants); prevalence increased with age from 19% in participants younger than 75 years to 29% in those older than 85 years. The overall prevalence of MCI at the Pittsburgh center was 22% (130 of 599 participants); prevalence of the MCI amnesic-type was 6% and of the MCI multiple cognitive deficits–type was 16%.

Conclusions: Twenty-two percent of the participants aged 75 years or older had MCI. Mild cognitive impairment is a heterogenous syndrome, where the MCI amnestic-type is less frequent than the MCI multiple cognitive deficits–type. Most of the participants with MCI had comorbid conditions that may affect their cognitive functions.

Arch Neurol. 2003;60:1385-1389

OLDER PERSONS can develop demonstrable cognitive impairment, especially memory deficits, without crossing the threshold for dementia. This condition has been termed "mild cognitive impairment" (MCI), and these patients have an increased risk of developing dementia, especially Alzheimer disease.[1-3] Because memory deficits are the clinical hallmark of Alzheimer disease, most of the criteria

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developed to characterize MCI require the presence of memory deficits in isolation.[4-8] However, other researchers believe this to be too restrictive, as it does not capture other cognitive problems that often occur in elderly persons.[9,10] For example, age-associated cognitive decline describes those individuals with a wider range of cognitive deficits.[9]

The prevalence rates for MCI and related conditions have ranged from 3.2% to 53.8%,[6,11-15] reflecting differences in cohort characteristics, and the criteria used to define MCI. The prevalence of age-associated cognitive impairment seems higher than that of age-associated memory impairment. This is, in part, attributed to the fact that the concept of age-associated cognitive impairment involves a broader range of cognitive deficits, including isolated memory impairment.[14,16] In the present study, we report the prevalence of MCI in the Cardiovascular Health Study (CHS) Cognition Study using diagnostic criteria that encompass a range of clinical manifestations of MCI. The prevalence of MCI was determined after a multistage adjudication process.

METHODS

The characteristics of the 5888 CHS participants have been described previously.[17] Begin-

Author affiliations are listed at the end of this article.

ning in 1988-1989, all participants completed the Modified Mini-Mental State Examination (3MSE)[18] and the Digit Symbol Test[19] at their annual visits; the Benton Visual Retention Test was added for those tested between 1994 and 1998.[20] The Telephone Interview for Cognitive Status was used when participants did not come to the clinic.[21] Further information on cognition was obtained from proxies using the Informant Questionnaire for Cognitive Decline in the Elderly,[22] and the Dementia Questionnaire.[23] Symptoms of depression were measured with the modified version of the Center for Epidemiologic Studies–Depression Scale.[24] Between 1991 and 1994, 3608 participants underwent magnetic resonance imaging (MRI) of the brain. A second MRI of the brain was taken during the 1-year period of 1997-1998. The CHS staff also obtained information from participants and next-of-kin regarding the circumstances of the illness, the history of dementia, and the functional status, as well as information about pharmaceutical drug use and alcohol consumption.[25]

THE CHS COGNITION STUDY

In 1998-1999 the CHS attempted to identify all participants who had either prevalent dementia at the time of the MRI scan taken between 1991 and 1994, or subsequent incident dementia in 1998-1999; the sample was limited to the 3608 participants who had an MRI scan between 1991 and 1994.[25]

The participants were classified as high risk for dementia if they had any of the following characteristics: (1) a 3MSE score of less than 80 at 1 of their last 2 clinic visits, (2) a 5-point decline in the 3MSE from the time of MRI to last contact, (3) a Telephone Interview for Cognitive Status score less than 28, (4) an Informant Questionnaire for Cognitive Decline in the Elderly score of more than 3.6, (5) an incident stroke, (6) were currently residing in a nursing home, or (7) had a diagnosis of dementia found on medical record review.

In 3 of the clinics (Sacramento, Calif; Winston-Salem, NC; and Hagerstown, Md) only the high-risk white participants, but all of the African American participants, were evaluated for the diagnosis of dementia. This was done to increase the power of the analysis within the African American group, and to increase the overall power of the study. The examination of all Pittsburgh, Pa, participants allowed us to estimate the "misses" among the low-risk participants at the other centers.

CLINICAL EXAMINATION

Psychiatric Examination

In addition to the Center for Epidemiologic Studies–Depression Scale 10-item version, we administered the Neuropsychiatric Inventory[26] to expand the psychiatric information.

Neuropsychological Examination

The neuropsychological battery included tests of 6 cognitive domains: premorbid intelligence, memory, language, visuoconstructional/visuospatial, executive functions, and motor functions.[25] The results of the neuropsychological battery were classified as normal or abnormal (>1.5 SDs below individuals of comparable age and educational level) based on normative data collected from a sample of 250 unimpaired subjects in Pittsburgh. In 3 of the centers, participants with 2 abnormal test results were referred for a neurological examination and further clinical evaluation. In the Pittsburgh center, all of the available participants had a neurological examination regardless of the results of the neuropsychological battery.

Neurological Examination

The neurological examination included detailed assessments of motor and sensory functions,[25] as well as a mental status examination (ie, immediate and delayed recall of 3 words, verbal fluency, similarities, clock drawing test, and the Luria 3-hand test of sequencing). After the mental status examination, the neurologist asked the participant about his or her performance on these tests, and the response was graded on a 4-point scale of awareness of cognitive deficits.

DIAGNOSIS OF DEMENTIA

The diagnosis of dementia was based on a deficit in performance in 2 or more cognitive domains that were of sufficient severity to affect the participants' activities of daily living and on a history of normal intellectual function before the onset of cognitive abnormalities. An abnormal domain was present when the results of at least 2 tests of the same domain were abnormal. The dementia criteria were designed to identify subjects with syndromes that could include relatively preserved memory functions (eg, frontotemporal dementia), and, thus, a memory deficit, was not required for the diagnosis of dementia.[25]

CHS COGNITION STUDY MCI CRITERIA

MCI Amnestic-Type (MCI-AT)

These subjects had impairments in delayed verbal or nonverbal recall, and the cognitive deficits must represent a decline from a previous level of functioning, detected with the annual CHS neuropsychological testing, and normal performance in other cognitive function. This diagnosis did not exclude individuals with mild defects on instrumental activities of daily living.

MCI Multiple Cognitive Deficits–Type (MCI-MCDT)

These subjects had deterioration in at least 1 cognitive domain (not including memory), or 1 abnormal test result in at least 2 other domains, without sufficiently severe cognitive function impairment, or loss of instrumental activities of daily living to constitute dementia. These cognitive deficits may or may not affect instrumental activities of daily living and represent a decline from a previous level of functioning, detected with the annual CHS neuropsychological testing.

PROBABLE AND POSSIBLE MCI

The degree of certainty of the diagnosis of MCI was graded as probable or possible based on the amount of information available for the diagnosis and the presence of comorbid conditions.

Probable MCI

Participants were classified as having probable MCI if they met the following criteria: (1) participants or their families reported cognitive problems and (2) there were no neurological, psychiatric, or systemic illnesses that could explain their presence of cognitive deficits.

Possible MCI

Participants were classified as having possible MCI if they met the following criteria: (1) neither participants nor their families reported cognitive problems; or (2) there were neurological, psychiatric, or systemic illnesses that might explain the presence of cognitive deficits; or (3) there was an incomplete evaluation. We required that a minimum of 5 neuropsycho-

logical measures, encompassing 3 cognitive domains—one of which must be memory—be completed to consider the evaluation complete.

DIAGNOSTIC CLASSIFICATION

At the conclusion of the clinical evaluation, all information about the participant was sent to the Pittsburgh center and was reviewed by a single neurologist (O.L.L.) who made an initial classification: dementia, MCI, or normal. Neither the local neurologists nor the Pittsburgh neurologist had the MRI of the brain or the longitudinal neuropsychological data for review. The medical records of the first 200 participants with detailed evaluations were also reviewed by 2 other clinicians (J.B. and C.L.), who independently classified the cases. Agreement among the 3 clinicians was 87%.

Participants classified as having dementia or MCI were reviewed by an adjudication committee composed of experts in dementia diagnosis who first classified cases as having dementia, MCI, or as normal and then adjudicated the specific type of dementia or MCI. All participants classified as having MCI in the Pittsburgh center were later reviewed by the adjudication committee, that further classified the type of MCI.

The adjudication committee had access to the CHS data, the historical CHS cognitive test scores, vision and hearing test results, and the participant's history of alcohol intake, as well as all relevant CHS data, including medical record reviews. Based on the information available, the adjudication committee classified all CHS participants, including those who where dead in 1998-1999.

STATISTICAL ANALYSIS

The prevalence of MCI was estimated only among subjects alive in 1998-1999 who did not have dementia. Group differences were analyzed using the χ^2 test.

RESULTS

The CHS Cognitive Study identified 707 elderly participants who had dementia after adjudication, 577 were classified as having as MCI, and 2318 were considered normal. In Pittsburgh, 193 participants were classified as having dementia after adjudication, 159 were classified as having MCI, and 552 were considered normal. Of the 159 Pittsburgh participants who had MCI, 130 (82%) were alive in 1997-1998. Of these, 10 participants (8%) met criteria for probable MCI-AT, 26 (20%) for possible MCI-AT, 28 (22%) for probable MCI-MCDT, and 66 (51%) for possible MCI-MCDT.

Of the 26 participants who had the diagnosis of possible MCI-AT, 19 (73%) had MRI-identified ischemic lesions, 3 (11.5%) had depression, 1 (3%) had a history of alcohol abuse or dependence, and 4 (15%) received chemoradiotherapy. Of the 66 participants who had the diagnosis of possible MCI-MCDT, 29 (44%) had MRI-identified ischemic lesions, 3 (4.5%) had a history of clinical stroke without MRI correlates, 12 (18%) had a history of depression, 4 (6%) were taking psychiatric medication that can affect cognition, 4 (6%) received chemoradiotherapy, 4 (6%) had metabolic encephalopathy, 3 (4.5%) had neurological disorders (Parkinson disease, multisystem atrophy), 1 (1%) had learning disability, and 1 (1%) had a hereditary neurological disorder. There was more than 1 comorbid disorder per participant. Finally, 12 participants with possible MCI-AT (46%) and 19 participants with possible MCI-MCDT (29%) had insufficient clinical information. Of the participants with insufficient information, 8 (66%) with possible MCI-AT and 14 (74%) with possible MCI-MCDT also had systemic, neurological, or psychiatric illness that may have affected cognition.

In Pittsburgh, 12 (4%) of 319 participants were classified as low risk and were diagnosed as having dementia, and 42 (13.2%) as having MCI. This compared with 163 (27%) of 608 high-risk participants classified as having dementia and 181 (30%) classified as having MCI. Therefore, 7% of all participants having dementia and 19% of those having MCI in Pittsburgh were in this lower-risk stratum. Based on this initial classification of dementia in MCI, about 20% of the participants with MCI in the other 3 sites were not evaluated and consequently missed the adjudication process.

The prevalence of MCI in the entire CHS cohort was 18.8% and 21.7% in Pittsburgh. The prevalence in the CHS cohort, excluding Pittsburgh, was 15.3% (95% confidence interval, 13.7%-16.9%). The prevalence by age group, race, sex, and educational level is given in **Table 1**.

In Pittsburgh, the prevalence of MCI-AT was 6.0% and of MCI-MCDT was 15.7%. The prevalence of probable MCI and possible MCI is listed in **Table 2**. Because of the few participants, the estimates of prevalence by age in each MCI subgroup were dichotomized as younger or older than 80 years.

COMMENT

The identification and classification of MCI in population studies is a major challenge. In this study, we used the following 2 approaches: (1) we examined all participants classified as high risk at 3 sites and (2) we examined all participants at 1 site. The exclusion of dead subjects would have reduced the prevalence of MCI and would had biased the results toward a healthier subgroup. In addition, if we had examined only participants with abnormal global cognitive measures (ie, 3MSE score <80), we would have missed 88% of the MCI cases. Indeed, the mean 3MSE score was 88 in MCI cases. The availability of longitudinal clinical and neuropsychological information and the examination of high-risk participants allowed us to maximize the identification of MCI in this cohort. Based on estimates from the Pittsburgh sample, about 20% of the low-risk white population met criteria for MCI, suggesting that evaluation of lower-risk subjects is necessary to identify MCI in population studies. Nevertheless, data from all 4 sites together, and from the Pittsburgh center alone, are similar leading us to conclude that our population estimates are reliable.

The CHS MCI criteria were oriented to classify MCI subgroups based on their neuropsychological presentation, and to identify "pure" groups (probable vs possible), allowing us to better investigate the transition to dementia in future studies. These criteria were designed to capture different forms of cognitive impairment, with or without specific conditions that could themselves cause cognitive deficits. The group with possible MCI is particularly important because it includes participants

Table 1. Prevalence of Mild Cognitive Impairment Among CHS and Pittsburgh, Pa, Participants Without Dementia Who Were Alive in 1998-1999

Variable	Healthy Participants	Participants With MCI	Prevalence, %	95% CI
CHS Cohort				
No. of participants	2005	465	18.8	17.3-20.4
Age, y				
<75	315	73	18.8	14.9-22.7
75-79	1041	180	14.7	12.7-16.7
80-84	452	132	22.6	19.2-26.0
≥85	197	80	28.9	23.6-34.2
Sex				
Females	1223	282	18.7	16.8-20.7
Males	782	183	19.0	16.5-21.4
Race				
White	1804	297	14.1	12.7-15.6
African American*	201	168	45.5	40.5-50.6
Educational level				
Less than high school	974	300	23.5	21.2-25.9
High school or more	1027	165	13.8	11.9-15.8
Pittsburgh Cohort				
No. of participants	469	130	21.7	18.4-25.0
Age, y				
<75	69	18	20.7	12.2-29.2
75-79	253	55	17.9	13.6-22.2
80-84	114	36	24.0	17.2-30.8
≥85	33	21	38.9	26.0-51.8
Sex				
Female	289	68	19.0	15.0-23.1
Male	180	62	25.6	20.1-31.1
Race				
White	384	84	17.9	14.5-21.4
African American†	85	46	35.1	27.0-38.6
Educational level				
Less than high school	188	75	28.5	23.1-33.9
High school or more	181	55	16.4	12.4-20.3

Abbreviations: CHS, Cardiovascular Health Study; CI, confidence interval; MCI, mild cognitive impairment.
*Data include 16 participants of other races.
†Data include 2 participants of other races.

Table 2. Number of Subjects and MCI Subtype Prevalence Among Pittsburgh, Pa, Participants Without Dementia Who Were Alive in 1998-1999*

Diagnostic Type†	MCI Subtype, No. of Cases	Prevalence, %	95% CI
Probable MCI-AT	10	1.7	0.6-2.7
Age <80 y	5	1.3	0.2-2.4
Age ≥80 y	5	2.5	0.3-4.6
Possible MCI-AT	26	4.3	2.7-6.0
Age <80 y	16	4.1	2.1-6.0
Age ≥80 y	10	4.9	2.0-7.8
Probable MCI-MCDT	28	4.7	3.0-6.4
Age <80 y	16	4.1	2.1-6.0
Age ≥80 y	12	5.9	2.7-9.1
Possible MCI-MCDT	66	11.0	3.5-8.5
Age <80 y	36	9.1	6.3-11.9
Age ≥80 y	30	14.7	9.9-19.5

Abbreviations: AT, amnestic-type; CI, confidence interval; MCDT, multiple cognitive deficit–type; MCI, mild cognitive impairment.
*Data given for 1998-1999 age.
†For an explanation of the 2 diagnostic types see the "CHS Cognition Study MCI Criteria" subsection of the "Methods" section.

with disease processes that are known risk factors for dementia.[27,28] The group classified as having possible MCI-MCDT was the most frequent, and its prevalence increased with age, rising to 15% in participants older than 80 years. By contrast, the prevalence of probable MCI-MCDT was lower, although it also increased with age, up to 6% in participants older than 80 years.

Our findings showed that the proportion of participants with isolated memory deficits is small (prevalence, 5%), and the participants with the diagnosis of probable MCI-AT had a small representation across all age groups. In addition, the prevalence of possible MCI-AT was higher than that of probable MCI-AT, suggesting that a form of MCI-AT can occur in the context of comorbid conditions, which may be important determinants of cognitive deficits. Finally, the patterns of comorbidities, and changing prevalence lead us to hypothesize that both participants with probable MCI-AT and MCI-MCDT are more stable than those having a diagnosis of possible MCI and more likely to convert to dementia. By contrast, the participants having the diagnosis of possible MCI are more heterogeneous and subject to more variability in their prevalence.

Finally, these results showed that most of the participants with MCI have a greater range of cognitive impairment than simply memory loss. Future studies of MCI should be oriented to evaluate the full range of MCI that may represent a group of individuals at risk of dementia.

Accepted for publication May 28, 2003.

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This study was supported by contracts N01-HC-85079 through N01-HC-85086, N01-HC-35129, and N01-HC-15103 from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md, and grants AG15928 and AG 20098 from the National Institute on Aging, National Institutes of Health. Dr Becker is the recipient of a Research Scientist Development Award, Level II (K02-MH01077) from the National Institute of Mental Health, Bethesda.

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