ORIGINAL CONTRIBUTION

A Clinicopathological Comparison of Community-Based and Clinic-Based Cohorts of Patients With Dementia

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Objectives: To compare the sensitivity and specificity of the clinical diagnosis of Alzheimer disease, the distribution of pathological causes, and the demographic and clinical characteristics of 2 different groups of patients with dementia.

Design: Retrospective clinicopathological study.

Setting: A memory disorder clinic in a university hospital and a multiethnic community.

Patients: Sixty-three patients from a memory disorder clinic and 26 patients from a large community-based study who underwent autopsy after clinical evaluation.

Main Outcome Measures: Differential distribution of clinical and pathological findings, with clinicopathological correlations.

Results: Clinic patients were younger at diagnosis, more educated, and more likely to be white. Of the 63 clinic patients we evaluated, 29 (46%) had a pathological diagnosis of definite AD, 15 (24%) had a diagnosis of mixed AD, and 19 (30%) had a diagnosis of another type of dementia. The pathological diagnoses in the community patients were distributed as follows: 6 (23%) had definite AD, 6 (23%) had mixed AD, 6 (23%) had cerebrovascular disease, and 8 (31%) had another type of dementia. The difference in distribution of pathological diagnoses between these 2 groups was only significant for cerebrovascular diseases. For patients seen at the clinic, the sensitivity of the clinical diagnosis of AD was 98% and the specificity was 84%; for the community group, the sensitivity was 92% and the specificity was 79%.

Conclusions: The difference in sensitivity and specificity of clinical diagnosis was not statistically significant between the groups of clinic patients and community patients. Dementia associated with cerebrovascular disease was more prevalent in the community sample. This difference may be attributable to clinical and demographic differences between the 2 groups.

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DEMENTIA IS a syndrome of cognitive impairment associated with functional and socioprofessional repercussions.[1] In the United States and Europe, the most common cause of dementia is considered to be Alzheimer disease (AD), followed by vascular dementia (VD).[2-6] However, in Japan[7,8] and some other countries[9] where stroke and its risk factors are prevalent, VD is the main cause of cognitive impairment. The diagnosis of probable AD is based on clinical criteria[1,10] but is proven only on neuropathological examination.[11,12] Similarly, clinical criteria have been developed for the diagnosis of probable VD, but definite diagnosis requires pathological confirmation.[13]

The accuracy of clinical diagnosis vs pathological confirmation varies widely in the literature.[14-17] Most of the clinical and clinicopathological studies on dementia were carried out in hospital-based or clinic-based populations. To our knowledge, no studies have correlated clinical and pathological diagnosis in a cohort of patients from the community. Hence, no information exists regarding the accuracy of clinical diagnosis in that setting. These patients may differ demographically and clinically from patients with dementia who were drawn from the clinic or hospital settings. These differences may in turn affect the causes of dementia and the clinical accuracy of diagnosis compared with pathological findings.

The purpose of this study was to compare the clinical and neuropathological diagnoses of 2 groups of patients with dementia. The first group was selected from a memory disorder clinic and the second from a community-based cohort of patients. Our main objectives were 3-fold:

POPULATION AND METHODS

STUDY POPULATION

The study population consisted of 2 groups of patients. The first group comprised 63 patients from the Memory Disorders Clinic that is associated with the federally supported Alzheimer's Disease Research Center, a tertiary referral facility for patients with cognitive complaints. The second group included 26 patients selected from a large community-based study of elderly individuals over the age of 65 years who were participating in an epidemiologic study of aging and dementia in northern Manhattan.

CLINICAL DIAGNOSIS

The diagnosis of dementia was based on the *Diagnostic and Statistical Manual, Revised Third Edition* (*DSM-III-R*), criteria.[18] Alzheimer disease was diagnosed according to the National Institute of Neurological Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria.[10] The National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria were used for the diagnosis of VD.[13] The clinical evaluation included a structured neurological and psychiatric examination, neuropsychological testing, and a series of laboratory tests. Each patient's complete blood cell count, serum electrolyte levels, serum vitamin B_{12} level, and folate level were measured. In addition, liver and renal function tests, Veneral Disease Research Laboratory tests, thyroid function tests, and brain imaging (either computed tomography or magnetic resonance imaging) were done. Findings on examination and laboratory studies were used to reach the final clinical diagnosis at a consensus conference of neurologists, psychiatrists, and neuropsychologists. While all patients in the clinic group received the entire workup, neuroimaging or laboratory data were not available for many in the community group. Both populations were evaluated by the same group of physicians.

The patients' characteristics included were sex, race/ethnicity (white, black, or Hispanic), education (years), stage of disease at entry and at the last visit as assessed by the Clinical Dementia Rating scale,[19] age at the time of entry into the study, age at the time of death, and vascular risk factors.

AUTOPSY CONSENT PROCEDURE

All patients and families in the Memory Disorders Clinic were given information about autopsy and gave nonbinding verbal consent if they wished to participate in the autopsy program. In the community, no recruitment effort was systematically attempted because of the concern that participation in the aging study might be adversely affected. Older patients with severe dementia who resided in nursing homes and had family members who were accessible or involved in their care were targeted for discussions about autopsy. Legal consent was obtained upon death for all patients.

NEUROPATHOLOGICAL DIAGNOSIS

Neuropathological examinations were performed at the Columbia Presbyterian Medical Center, New York, NY, and diagnosis was based on either the Consortium to Establish a Registry for Alzheimer's Disease criteria[11] or the Khachaturian criteria[12] for AD. Diagnoses of other dementias were made using standard published clinical and pathological criteria.[11,20-22]

STATISTICAL ANALYSIS

For purposes of statistical analysis, clinical and pathological diagnoses were classified as either AD or non-AD. The clinical and pathological diagnoses were used in 2×2 contingency tables to determine sensitivity (the number of patients with the clinical diagnosis of AD who met the pathological criteria for AD, or true positives, divided by the total number of patients with the neuropathologically definite diagnosis of AD) and specificity (the number of patients without the clinical diagnosis of AD who did not meet the pathological criteria for AD, or true negatives, divided by the total number of patients without a neuropathologically definite diagnosis of AD). Bivariate analyses were done to compare different subgroups of patients; t test and χ^2 analysis were used for continuous and discrete variables, respectively. Chi squared analysis was also used to compare the sensitivity and specificity of clinical diagnoses in the 2 groups. Logistic regression analyses, including variables of interest, were used to identify the determinants of brain autopsy and to further compare the 2 groups. Statistical analyses were performed using SPSS for Windows (version 8.0; SPSS Inc, Chicago, Ill).

(1) to compare the sensitivity and specificity of the clinical diagnoses of the 2 groups, (2) to determine whether the distribution of causes differs according to patient population, and (3) to evaluate the effects of different demographic and clinical characteristics on the final diagnosis.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

Compared with clinic patients who died but did not have autopsies, autopsied clinic patients were younger at the time of diagnosis ($P<.001$) and death ($P=.05$), more educated ($P=.001$), more likely to be white ($P=.009$), more likely to have been in the study for a longer period ($P=.008$), and more likely to have a diagnosis of probable AD ($P<.001$) (**Table 1**). Race lost its significance when we adjusted for age and education in a logistic regression model.

The same analyses were carried out in the community cohort of patients (**Table 2**). Community patients who underwent autopsies were more likely to have been in the study for a longer period ($P<.001$) and more likely to have a diagnosis of probable AD ($P<.001$).

Patients from the clinic and from the community who underwent autopsies were compared (**Table 3**). Bivariate analyses showed that clinic patients were younger

Table 1. Clinical Characteristics of Autopsied and Nonautopsied Clinic Patients*

Characteristic	Nonautopsied (n = 130)	Autopsied (n = 63)	P
Sex, No. (%)			
Male	65 (50)	36 (57)	.32†
Female	65 (50)	27 (43)	
Race, No. (%)			
White	83 (64)	52 (83)	.009
African American	31 (24)	5 (8)	
Hispanic	16 (12)	4 (6)	
Other	0	2 (3)	
Age at entry, y‡	75.5 (9.0)	68.3 (10.6)	.001
Age at death, y‡	76.3 (9.0)	72.9 (11.0)	.05
Education, y‡	12.1 (4.7)	14.9 (3.5)	.001
Time in study, y‡	2.2 (1.6)	3.4 (3.0)	.008
Clinical diagnosis, No. (%)			
No dementia	13 (10)	3 (5)	<.001
Probable AD	43 (33)	40 (63)	
Possible AD	54 (42)	6 (10)	
Other	20 (15)	14 (22)	

*AD indicates Alzheimer disease.
†P not significant.
‡Values are mean (SD).

Table 2. Clinical Characteristics of Autopsied and Nonautopsied Community Patients*

Characteristic	Nonautopsied (n = 318)	Autopsied (n = 26)	P
Sex, No. (%)			
Male	123 (39)	10 (38)	.83†
Female	195 (61)	16 (62)	
Race, No. (%)			
White	73 (23)	5 (19)	.37†
African American	131 (41)	10 (38)	
Hispanic	112 (35)	10 (38)	
Other	2 (1)	1 (4)	
Age at entry, y‡	79.6 (7.6)	81.5 (8.4)	.23†
Age at death, y‡	82.4 (7.7)	84.1 (8.4)	.14†
Education, y‡	8.5 (4.2)	8.4 (5.4)	.81†
Time in study, y‡	0.4 (1.0)	2 (1.7)	<.001
Clinical diagnosis, No. (%)			
No dementia	191 (60)	3 (12)	<.001
Probable AD	62 (19)	11 (42)	
Possible AD	50 (16)	3 (12)	
Other	15 (5)	9 (35)	

*AD indicates Alzheimer disease.
†P not significant.
‡Values are mean (SD).

at the time of entry into the study ($P<.001$), more educated ($P<.001$), and more likely to be white ($P<.001$). Community patients had more severe dementia at the time of intake ($P<.001$) and death ($P<.001$) (data not shown), had a shorter period of participation in the study ($P=.03$), and were older at the time of death ($P<.001$).

CLINICAL DIAGNOSIS

Of the 63 clinic patients who underwent autopsies, 3 (5%) did not have clinically diagnosed dementia, 40 (63%) had a diagnosis of probable AD, 6 (10%) had a diagnosis of possible AD, and 14 (22%) had another diagnosis (ie, chromosome 17–associated familial dementia [n = 2], frontal lobe dementia [n = 1], dementia associated with Creutzfeldt-Jacob disease [n = 4], Huntington disease [n = 2], amyotrophic lateral sclerosis with dementia [n = 1], adult polyglucosan disease [n = 1], Parkinson disease–associated dementia [n = 2], and dementia of unknown cause [n = 1]). In the community group of patients, the clinical diagnoses were distributed as follows: 3 (12%) had no dementia, 11 (42%) had probable AD, 3 (12%) had possible AD, and 9 (35%) had another diagnosis (Parkinson disease–associated dementia [n = 5], VD [n = 1], multisystem atrophy [n = 1], and dementia of unknown cause [n = 2]). The clinical diagnoses of the 2 groups of patients who had autopsies were compared and did not differ significantly.

Table 3. Clinical Characteristics of Autopsied Patients From the Clinic and From the Community*

	Clinic (n = 63)	Community (n = 26)	P
Sex, No. (%)			
Male	36 (57)	10 (38)	.11†
Female	27 (43)	16 (62)	
Race, No. (%)			
White	52 (83)	5 (19)	<.001
African American	5 (8)	10 (38)	
Hispanic	4 (6)	10 (38)	
Other	2 (3)	1 (4)	
Age at entry, y‡	68.2 (10.7)	81.5 (8.4)	<.001
Age at death, y‡	72.9 (11.0)	84.1 (8.4)	<.001
Education, y‡	14.9 (3.5)	8.4 (5.4)	<.001
Time in study, y‡	3.4 (3.0)	2 (1.7)	.03
Clinical diagnosis, No. (%)			
No dementia	3 (5)	3 (12)	.27†
Probable AD	40 (63)	11 (42)	
Possible AD	6 (10)	3 (12)	
Other	14 (22)	9 (35)	

*AD indicates Alzheimer disease.
†P not significant.
‡Values are mean (SD).

PATHOLOGICAL FINDINGS

Of the clinic patients (n = 63), 29 (46%) had a pathological diagnosis of definite AD (6 with Lewy bodies), 15 (24%) had a diagnosis of mixed AD (AD associated with cerebrovascular disease), and 19 (30%) had a diagnosis of some other type of dementia (Creutzfeldt-Jacob disease [n = 4], progressive degenerative disease [n = 3], diffuse Lewy body disease [n = 2], Huntington disease [n = 2], multisystem atrophy [n = 1], frontal lobe dementia [n = 1], progressive supranuclear palsy [n = 1], amyotrophic lateral sclerosis [n = 1], Parkinson disease [n = 1], multiple sclerosis [n = 1], adult polyglucosan disease [n = 1], and subcortical gliosis [n = 1]).

The pathological diagnoses in the community group were distributed as follows: 6 (23%) had definite AD; 6 (23%) had mixed AD (AD associated with cerebrovascular disease); 6 (23%) had cerebrovascular disease, including infarcts and hypertensive vasculopathy (5 were nonwhite); and 8 (31%) had a diagnosis of another type

Table 4. Correlation Between Clinical and Neuropathological Diagnoses in Clinic Patients*†

Clinical Diagnosis	Neuropathological Diagnosis, No.				
	Definite AD	Mixed AD	Vascular Dementia	Other	Total
Probable AD	27	11	0	2	**40**
Possible AD	1	4	0	1	**6**
Vascular dementia	0	0	0	0	**0**
Other	1	0	0	16	**17**
Total	**29**	**15**	**0**	**19**	**63**

*AD indicates Alzheimer disease.

†Sensitivity of the clinical diagnosis of AD was 98% (43/44); specificity of the clinical diagnosis of AD was 84% (16/19).

Table 5. Correlation Between Clinical and Neuropathological Diagnoses in Community Patients*†

Clinical Diagnosis	Neuropathological Diagnosis, No.				
	Definite AD	Mixed AD	Vascular Dementia	Other	Total
Probable AD	5	4	1	1	**11**
Possible AD	0	2	1	0	**3**
Vascular dementia	0	0	1	0	**1**
Other	1	0	3	7	**11**
Total	**6**	**6**	**6**	**8**	**26**

*AD indicates Alzheimer disease.

†Sensitivity of the clinical diagnosis of AD was 92% (11/12); specificity of the clinical diagnosis of AD was 79% (11/14).

of dementia (ie, Parkinson disease [n = 3], progressive supranuclear palsy [n = 2], Wernicke disease [n = 1], diffuse Lewy body disease [n = 1], and frontal lobe dementia [n = 1]). The difference in distribution of pathological diagnoses between the clinic group and the community group was significant only for cerebrovascular disease ($P<.001$). However, this significance disappeared when the distribution of pathological diagnoses was adjusted for differences in race, age, and education between the 2 groups. Vascular risk factors (ie, smoking, high blood pressure, atrial fibrillation, coronary artery disease, congestive heart failure, hyperlipidemia, and diabetes mellitus) were significantly more common in the community group (54% [n = 14]) than in the clinic group (27% [n = 17]) ($P = .02$). However, adding this variable to the logistic regression model did not alter the outcome of the analysis.

SENSITIVITY AND SPECIFICITY OF THE CLINICAL DIAGNOSIS OF AD

For patients who were seen at the clinic, sensitivity was 98% and specificity was 84% (**Table 4**). Four patients were incorrectly diagnosed in the clinic. Three with clinically diagnosed AD actually had diffuse Lewy body disease, subcortical gliosis, and multiple sclerosis, as determined at the time of the postmortem examination (false positives). One patient with clinically diagnosed dementia of unknown cause had AD on pathological examination (false negative). There was no change in the clinical diagnosis over time.

For patients in the community group, the sensitivity of the last clinical diagnosis of AD was 92% and the specificity was 79% (**Table 5**). Clinical and pathological diagnoses were different in 4 patients. Three patients with clinically diagnosed AD (false positives) had pathological diagnoses of cerebrovascular disease (n = 2) and frontal lobe dementia (n = 1), and 1 patient with a clinical diagnosis of dementia of unknown cause had typical changes of AD (false negative). The clinical diagnoses changed in 5 community patients (19%) over time (mean duration of follow-up, 2 years; SD, 1.7 years). When the clinical diagnosis at the time of the first visit was considered, sensitivity was 75% and specificity was 86%. The improvement in sensitivity was a result of the clinical reassignment of 2 patients who were initially not thought to have AD to a diagnosis of probable AD. Both of these patients had AD on pathological examination. The slight deterioration in specificity is explained by the changes in the clinical categories of 3 patients—2 patients who were initially considered not to have clinically diagnosed dementia were rediagnosed with AD (whereas pathological diagnosis indicated cerebrovascular disease), and 1 patient with a pathological diagnosis of non-AD who was initially diagnosed with AD was reassigned to the clinical non-AD category on follow-up.

The differences in sensitivity and specificity between the clinic and community patients were not statistically significant.

COMMENT

The aims of this clinicopathological study were to compare the sensitivity and specificity of the clinical diagnosis of AD, the distribution of pathological causes, and the demographic and clinical characteristics of 2 different groups of patients with dementia, 1 selected from a tertiary memory disorder clinic and the other selected from a community-based cohort.

We found that clinic patients who had autopsies were younger at the time of diagnosis and at the time of death, more educated, more likely to be white, and more likely to have been in the study for a longer period than patients who did not have autopsies. Community patients who had autopsies were more likely to have been in the study for a longer period. In accordance with our findings, Harrell et al[23] reported on 69 deceased patients in a memory clinic and found that those who underwent autopsies were more likely to be white and younger at the time of presentation and at the time of death. However, there were no major differences in clinical diagnoses for autopsied and nonautopsied patients. They concluded that ". . . the frequency of occurrence of various dementias obtained through autopsied series are representative of the demented population." In our experience, those who underwent autopsies were more likely to have received the diagnosis of probable AD as opposed to possible AD or other types of dementias. We believe this to be owing to the fact that patients with the diagnosis of probable AD represent our purest category of patients with AD clinically and are most frequently recruited into research studies. Consequently, they are examined more closely and

more frequently, which possibly enhances their relationship with the clinic staff and improves the odds of their families consenting to have an autopsy performed. Fillenbaum et al[24] found that out of 308 consecutively deceased patients with AD at 24 Consortium to Establish a Registry for Alzheimer's Disease sites, the 167 who had autopsies were more likely to be white, to be better educated, to have been in the study longer, and to have had a longer total duration of AD. The racial difference persisted even after adjustment for education and other demographic characteristics in a logistic regression model. In contrast, we found that when we adjusted for education, age, and clinical diagnosis in the clinic sample, race lost its significance, suggesting that race was confounded by these other variables, and that by itself it was a negligible factor in determining which patients had autopsies in this group. Because of the general demographic characteristics of the patients seen at our Memory Disorder Clinic, 18% of all autopsied patients were nonwhite. This proportion is higher than the 6%[24] and the 15%[23] reported in 2 previous studies.

WHEN CLINICAL and pathological diagnoses were compared, the sensitivity and specificity of the clinical diagnosis of AD were not significantly better in the group of patients from the clinic. This could be explained by the fact that the same group of clinicians evaluated the 2 samples. The sensitivity and specificity at our Memory Disorder Clinic are among the highest reported in the literature[14,15,25] and are enhanced by the reliance on rigorously established clinical criteria and the consensus process.[26] The lower values in the community-based sample were a result of 3 false positives and 1 false negative, reducing the specificity to 79%. There was a tendency to overdiagnose AD in the community group. One reason that may account for this finding is that clinical diagnosis in the community group was often made without the use of laboratory tests and neuroimaging procedures. Two of the 3 erroneously diagnosed patients with AD actually had vascular disease on pathological examination. This diagnosis might have changed if brain imaging had been available. However, in the absence of a clinical history suggesting an association between the cognitive symptoms and neuroimaging findings, these patients would have been classified at best as having mixed AD and VD (or possible AD, according to the NINCDS-ADRDA criteria), which would not have changed their clinical diagnoses. Furthermore, the patients in the community group were part of an epidemiological study on aging and were selected randomly from the general population, whereas the patients in the clinic group were all referred by primary care physicians because they had memory complaints. Nevertheless, the 92% sensitivity and 79% specificity achieved in the clinical diagnosis of AD in the community group seem quite good compared with the values for the clinic group. In fact, these values are better than those reported by several clinicopathological studies carried out in memory disorder clinics and in hospital settings that based their diagnoses on extensive clinical and laboratory workups.[14,16,27-29] This suggests that by doing a structured clinical evaluation that includes an extensive history, a detailed physical examination, and neuropsychological testing in a group of elderly patients in the community, very good clinical sensitivity and specificity can be achieved in the diagnosis of AD. A study evaluating the role of a neuropsychological paradigm similar to the one we used in the diagnosis of AD[30,31] showed it to be very useful in minimizing interobserver diagnostic variability over time and in contributing to the improved accuracy of diagnosis. Furthermore, the improvement in sensitivity with follow-up underscores the importance of repeated evaluations in reaching a correct diagnosis.

Comparison of clinic and community patients revealed significant demographic differences. Patients in the community cohort were older, less educated, and more likely to belong to a minority group, which can be explained by the characteristics of the population of our catchment area. Clinically, these patients were older at the time of death, had a shorter period of participation in the study, and had more severe dementia at the time of intake and death. These differences are owing in part to the fact that we focused our recruitment efforts in the community on older age, a more advanced stage of dementia, and admission to a nursing home.

A vascular cause for dementia on pathological examination was found more often in the community group than in the clinic group. In fact, none of our clinic patients who underwent autopsy was diagnosed with pure VD on clinical grounds or on pathological examination. The scarcity of VD in the pathological reports of patients with dementia from memory disorder clinics has been recently confirmed by several studies.[14,17,32-37] One reason for this finding is that clinicians are reluctant to diagnose VD in patients with obvious symptoms and signs of stroke.[38] Hence, this subgroup of patients is less likely to be referred to memory disorder clinics[39] and more likely to be referred to stroke clinics. These referral patterns may also vary between countries, since geriatric services in Europe seem to receive a higher proportion of patients with VD.[33,40] Some authors have criticized the NINDS-AIREN criteria for including all types of cerebrovascular disease and have suggested using the term *primary dementia* to describe VD and the term *stroke with secondary dementia* in patients with overt stroke and cognitive symptoms.[41] Pathological diagnosis of cerebrovascular disease was significantly more prevalent in the community-based cohort of patients. This is not surprising in light of the higher frequency of vascular risk factors in the community group. Five of the 6 patients with this diagnosis were nonwhite, and when pathological diagnosis was adjusted for differences in race, age, and education between the 2 groups, this significance disappeared. This suggests that demographic characteristics may play an important role in the etiology of certain types of dementias. Recent studies have shown that, in addition to the typical risk factors for cerebrovascular diseases (eg, older age, being male, hypertension, hyperlipidemia, diabetes mellitus, atrial fibrillation, congestive heart failure, coronary heart disease, carotid bruit, ciga-

rette smoking, and alcohol abuse[2]), being nonwhite[42] and having fewer years of education,[43] among other factors, predispose patients to VD.

In conclusion, our study shows that the sensitivity and specificity of clinical diagnoses differed only slightly between the clinic group and community group when structured clinical diagnoses were made and careful follow-up was maintained. The prevalence of different subtypes of dementias also differed between the 2 groups. These differences can be explained, at least in part, by the different demographic and clinical characteristics of these 2 populations and by the types of clinical evaluations they received.

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REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, DC: American Psychiatric Association, 1994.
2. Konno S, Meyer JS, Terayama Y, Margishvili GM, Mortel KF. Classification, diagnosis and treatment of vascular dementia. *Drugs Aging*. 1997;11:361-373.
3. Tomlinson BE, Blessed G, Roth M. Observations on the brains of demented old people. *J Neurol Sci*. 1970;11:205-242.
4. Jellinger K. Neuropathological aspects of dementias resulting from abnormal blood and cerebrospinal fluid dynamics. *Acta Neurol Belg*. 1976;76:83-102.
5. Schoenberg BS. Epidemiology of vascular dementia and multi-infarct dementia. In: Meyer JS, Lechner H, Marshall J, et al, eds. *Vascular and Multi-infarct Dementia*. Mt Kisco, NY: Futura Publishing Co; 1988:47-59.
6. Chui HC. Dementia: a review emphasizing clinicopathologic correlation and brain-behavior relationships. *Arch Neurol*. 1989;46:806-814.
7. Ueda K, Kawano H, Hasuo Y, Fujishima M. Prevalence and etiology of dementia in a Japanese community. *Stroke*. 1992;23:798-803.
8. Yoshitake T, Kiyohara Y, Kato I, et al. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. *Neurology*. 1995;45:1161-1168.
9. Skoog I, Nilsson L, Palmertz B, Andreasson LA, Svanborg A. A population-based study of dementia in 85-year-olds. *N Engl J Med*. 1993;328:153-158.
10. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34:939-944.
11. Mirra SS, Heyman A, McKeel D, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD), part II: standardization of the neuropathologic assessment of Alzheimer's disease. *Neurology*. 1991;41:479-486.
12. Khachaturian ZS. Diagnosis of Alzheimer disease. *Arch Neurol*. 1985;42:1097-1105.
13. Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies: report of the NINDS-AIREN International Workshop. *Neurology*. 1993;43:250-260.
14. Pearl GS. Diagnosis of Alzheimer's disease in a community hospital-based brain bank program. *South Med J*. 1997;90:720-722.
15. Rasmusson DX, Brandt J, Steele C, Hedreen JC, Troncoso JC, Folstein MF. Accuracy of clinical diagnosis of Alzheimer disease and clinical features of patients with non-Alzheimer disease neuropathology. *Alzheimer Dis Assoc Disord*. 1996;10:180-188.
16. Jellinger K, Danielczyk W, Fischer P, Gabriel E. Clinicopathological analysis of dementia disorders in the elderly. *J Neurol Sci*. 1990;95:239-258.
17. Mendez MF, Mastri AR, Sung JH, Frey WH. Clinically diagnosed Alzheimer disease: neuropathologic findings in 650 cases. *Alzheimer Dis Assoc Disord*. 1992;6:35-43.
18. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*. Washington, DC: American Psychiatric Association; 1987.
19. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412-2414.
20. Cummings JL, Benson D. *Dementia: A Clinical Approach*. 2nd ed. Newton, Mass: Butterworth-Heinemann; 1992.
21. Joachim CL, Morris JH, Selkoe DJ. Clinically diagnosed Alzheimer's disease: autopsy results in 150 cases. *Ann Neurol*. 1988;24:50-56.
22. McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. *Neurology*. 1996;47:1113-1124.
23. Harrell LE, Callaway R, Powers R. Autopsy in dementing illness: who participates? *Alzheimer Dis Assoc Disord*. 1993;7:80-87.
24. Fillenbaum GG, Huber MS, Beekly D, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD), part XIII: obtaining autopsy in Alzheimer's disease. *Neurology*. 1996;46:142-145.
25. Jellinger KA, Bancher C. Proposals for re-evaluation of current autopsy criteria for the diagnosis of Alzheimer's disease. *Neurobiol Aging*. 1997;18(suppl 4):S55-S65.
26. Blacker D, Albert MS, Bassett SS, Go RCP, Harrell LE, Folstein MF. Reliability and validity of NINCDS-ADRDA criteria for Alzheimer's disease. *Arch Neurol*. 1994;51:1198-1204.
27. Victoroff J, Mack WJ, Lyness SA, Chui HC. Multicenter clinicopathological correlation in dementia. *Am J Psychiatry*. 1995;152:1476-1484.
28. Todorov AB, Go RC, Constantinidis J, Elston RC. Specificity of the clinical diagnosis of dementia. *J Neurol Sci*. 1975;26:81-98.
29. Mayeux R, Saunders AM, Shea S, et al. Utility of the apolipoprotein E genotype in the diagnosis of Alzheimer's disease: Alzheimer's Disease Centers Consortium on Apolipoprotein E and Alzheimer's Disease. *N Engl J Med*. 1998;338:506-511.
30. Schofield PW, Tang M, Marder K, et al. Consistency of clinical diagnosis in a community-based longitudinal study of dementia and Alzheimer's disease. *Neurology*. 1995;45:2159-2164.
31. Stern Y, Andrews H, Pittman J, et al. Diagnosis of dementia in a heterogeneous population: development of a neuropsychological paradigm-based diagnosis of dementia and quantified correction for the effects of education. *Arch Neurol*. 1992;49:453-460.
32. Whitlock G, MacMahon S, Anderson C, Neal B, Rodgers A, Chalmers J, for the PROGRESS Management Committee. Blood pressure lowering for the prevention of cognitive decline in patients with cerebrovascular disease: Perindopril Protection Against Recurrent Stroke Study. *Clin Exp Hypertens*. 1997;19:843-855.
33. Nolan KA, Lino MM, Seligmann AW, Blass JP. Absence of vascular dementia in an autopsy series from a dementia clinic. *J Am Geriatr Soc*. 1998;46:597-604.
34. Thal LJ, Galasko D, Katzman R, et al. Patients clinically assessed at an Alzheimer's center generally have Alzheimer's pathology [abstract]. *Neurology*. 1991;41(suppl 1):323.
35. Boller F, Lopez OL, Moossy J. Diagnosis of dementia: clinicopathologic correlations. *Neurology*. 1989;39:76-79.
36. Galasko D, Hansen LA, Katzman R, et al. Clinical-neuropathological correlations in Alzheimer's disease and related dementias. *Arch Neurol*. 1994;51:888-895.
37. Ince PG, McArthur FK, Bjertness E, Torvik A, Candy JM, Edwardson JA. Neuropathological diagnoses in elderly patients in Oslo: Alzheimer's disease, Lewy body disease, vascular lesions. *Dementia*. 1995;6:162-168.
38. Millikan C, McDowell F, Easton J. *Stroke*. Philadelphia, Pa: Lea & Febiger; 1987:235.
39. Hulette CM, Nochlin D, McKeel D. Neuropathologic basis of vascular dementia related to cerebral infarction [abstract]. *Neurology*. 1996;46:A364.
40. Bucht G, Adolfsson R, Winblad B. Dementia of the Alzheimer type and multi-infarct dementia: a clinical description and diagnostic problems. *J Am Geriatr Soc*. 1984;32:491-498.
41. Drachman DA. New criteria for the diagnosis of vascular dementia: do we know enough yet? *Neurology*. 1993;43:243-245.
42. Desmond DW, Tatemichi TK, Paik M, Stern Y. Risk factors for cerebrovascular disease as correlates of cognitive function in a stroke-free cohort. *Arch Neurol*. 1993;50:162-166.
43. Tatemichi TK, Desmond DW, Paik M, et al. Clinical determinants of dementia related to stroke. *Ann Neurol*. 1993;33:568-575.