ORIGINAL CONTRIBUTION

The Effect of Patient Attrition on Estimates of the Frequency of Dementia Following Stroke

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Background: Given that prevalence surveys may underestimate the magnitude of the association between an exposure and a disease with high morbidity or mortality, we investigated the effects of patient attrition on estimates of the frequency of dementia following ischemic stroke.

Patients and Methods: We examined 251 patients 3 months after stroke and diagnosed dementia in 66 (26.3%) based on the results of neuropsychological and functional assessments and modified criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*. Those 251 patients were drawn from a larger cohort of 297 patients, with the majority of the remaining 46 patients being unavailable for assessment due to death, severe stroke, or comorbid medical disorders. Using the coefficients in a logistic model of the clinical determinants of dementia based on the 251 patients who were examined, we calculated the probability of dementia for each of the 46 patients who were not examined. We considered a patient to have dementia when that probability was higher than the mean of the median probabilities of dementia in the groups of patients with and without dementia who completed the examinations.

Results: The sensitivity and specificity of our diagnostic method were 75.8% and 72.4%, respectively. We recognized dementia in 21 (45.7%) of the 46 unavailable patients, a significantly higher frequency than among examined patients. Additional analyses determined that the factors that increased the risk of becoming unavailable for follow-up, which included more severe stroke, left and right hemisphere infarct locations, and a history of prior stroke, are similar to the factors that increase the risk of dementia after stroke.

Conclusion: Our findings suggest that dementia is differentially associated with early patient attrition, potentially resulting in the underestimation of its frequency and underrecognition of its importance as an outcome of ischemic stroke.

Arch Neurol. 1998;55:390-394

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PREVALENCE surveys tend to underestimate the magnitude of the association between an exposure and an outcome, such as stroke and dementia, when it results in increased mortality and morbidity.[1] Numerous studies have reported that patients with dementia resulting from cerebrovascular disease are at an increased risk of early mortality compared with patients with dementia resulting from other causes, such as Alzheimer disease, as well as stroke patients without dementia.[2-5] Patients with dementia following stroke may also be at a higher long-term risk of recurrent stroke,[6] and, as a result, increased physical disability and reduced survival. Although studies performed in western countries have consistently reported that Alzheimer disease is a more frequent basis for dementia than cerebrovascular disease,[7] it is possible that the observed difference in prevalence is, at least in part, the result of the greater mortality and morbidity associated with vascular dementia, resulting in the unavailability of those patients for enumeration.

We performed the present study to determine whether stroke patients who become unavailable for in-person examinations due to death, severe stroke, significant comorbid illness, or other reasons have clinical features characteristic of stroke patients with dementia, potentially resulting in an artificially reduced estimate of the frequency of dementia after stroke. The secondary aim of this study was to illustrate the use of a logistic regression model of the clinical determinants of dementia to generate estimates of the probability of dementia for individual elderly patients following ischemic stroke.

PATIENTS AND METHODS

PATIENTS

As part of a prospective study of stroke and dementia,[8] we recruited 297 patients (mean [±SD] age, 72.0±8.4 years) within 30 days of ischemic stroke. Stroke was defined as the acute onset of a focal neurologic deficit attributable to cerebrovascular disease and supported by findings on computed tomographic scans (normal or relevant infarct). Eligibility criteria included an age of 60 years or older and the absence of any comorbid disorders that might limit survival or affect cognitive function, although patients were not excluded if a premorbid history of functional impairment suggested that they might also have Alzheimer disease. This study was approved by the Institutional Review Board of Columbia-Presbyterian Medical Center, New York, NY, and all patients provided informed consent.

PROCEDURES

Patients were seen for an initial assessment 7 to 10 days after stroke onset. They were administered a neurologic examination; functional scales, including the Barthel Index,[9] which assesses physical disability, and the Blessed Functional Activity Scale,[10] which assesses the cognitive aspects of activities of daily living; and the Mini-Mental State Examination (MMSE),[11] a popular mental status test. Based on the results of the neurologic examination and the Barthel Index, we also calculated a total score for each patient on the Stroke Data Bank Stroke Severity Scale.[12]

We performed our baseline dementia assessment 3 months after stroke to maximize the stability of each patient's course. As part of that assessment, we administered a battery of neuropsychological tests developed for use in epidemiological studies of dementia[13] in either English or Spanish and we repeated the examinations listed above. Based on modified criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*,[14] we required deficits in memory and 2 or more additional cognitive domains as well as functional impairment documented using the Blessed Functional Activity Scale for the diagnosis of dementia. Of the 297 patients who were initially enrolled in the study, 251 patients (84.5%) were available for that assessment and 66 (26.3%) of those 251 patients met our operationalized criteria for dementia.

STATISTICAL ANALYSES

To characterize their level of function immediately after stroke, we compared the 46 patients who were unavailable for dementia assessment with the 185 patients without dementia and the 66 patients with dementia with regard to the scores that they received on the MMSE, the Barthel Index, and the Stroke Severity Scale at the 7- to 10-day examination. We then performed χ^2 and logistic regression analyses to compare the group of unavailable patients with the groups of patients with and without dementia with regard to the clinical characteristics contained in a logistic model of the determinants of dementia that we presented previously[15] (**Table 1**). Next, we used that logistic model of the clinical determinants of dementia to calculate the median probabilities of dementia among examined patients with and without dementia based on the following standard formula[1]:

$$\text{Probability of Dementia} = \frac{1}{1+e^{-(a+b_1x_1+\ldots+b_rx_r)}},$$

where a represents the model intercept, b_1 through b_r represent the coefficients for each predictor variable in the model, x_1 through x_r represent an individual patient's values for each of the predictor variables, and r represents the number of predictor variables in the model. We calculated the probability of dementia for each of the 46 patients who were unavailable for assessment at the 3-month examination based on their clinical characteristics and diagnosed dementia in each of those patients when that probability fell above the mean of the median probabilities of dementia of the groups of examined patients with and without dementia. Finally, we compared the patients who were diagnosed as having dementia using this method with those who were determined to be free of dementia using this method with regard to their scores on the MMSE, the Barthel Index, and the Stroke Severity Scale at the 7- to 10-day assessment.

RESULTS

PATIENT CHARACTERISTICS BY EXAMINATION STATUS

Based on the results of *t* tests, we found that the 46 patients who were unavailable for examination were significantly more impaired than the 185 patients without dementia on the MMSE (mean [±SD] scores, 18.2±7.7 vs 24.2±4.8, respectively; $P<.001$), the Barthel Index (mean [±SD] scores, 54.0±35.2 vs 72.1±25.4, respectively; $P<.001$), and the Stroke Severity Scale (mean [±SD] scores, 8.0±3.0 vs 6.0±3.2, respectively; $P<.001$). Significant differences were not found between the 46 unavailable patients and the 66 patients with dementia, who received mean (±SD) scores of 18.4±5.7 on the MMSE ($P=.94$), 50.5±30.1 on the Barthel Index ($P=.61$), and 8.0±2.6 on the Stroke Severity Scale ($P=.97$).

Of the 46 patients who were unavailable for the 3-month examination, 26 patients had died (n=12) or were sick (n=8) or untestable due to disorders such as severe aphasia (n=6), while 20 patients refused that examination (n=10), had moved away from the area (n=8), or had become lost to follow-up (n=2). Among patients who died, the median time until death was 61.5 days. Based on the results of examinations performed 7 to 10 days after stroke, patients who died or were sick or untestable were significantly more impaired than patients who refused the 3-month examination, moved away from the area, or became lost to follow-up on the MMSE (mean [±SD] scores, 15.7±7.7 vs 21.4±6.6, respectively; $P=.02$), the Barthel Index (mean [±SD] scores, 45.0±33.9 vs 65.8±34.3, respectively; $P=.05$), and the Stroke Severity Scale (mean [±SD] scores, 8.9±2.3 vs 6.9±3.5, respectively; $P=.03$).

Table 1. Logistic Model of the Clinical Determinants of Dementia Based on a Sample of 251 Patients Examined 3 Months After Ischemic Stroke*

Variable	β	SE	OR	95% CI
Age, y				
≥80 vs 60-69	2.6752	0.5034	14.5	5.4-38.9
70-79 vs 60-69	1.0595	0.4055	2.9	1.3-6.4
Education, y				
≤8 vs ≥13	1.0733	0.5588	2.9	0.9-8.7
9-12 vs ≥13	1.2241	0.5299	3.4	1.2-9.6
Race, nonwhite vs white	0.8748	0.4295	2.4	1.0-5.6
Diabetes mellitus	0.9676	0.3613	2.6	1.3-5.3
Prior stroke	0.9976	0.3943	2.7	1.3-5.9
Lacunar infarction	1.0045	0.4053	2.7	1.2-6.0
Infarct location				
Left hemisphere vs brainstem or cerebellum	1.5501	0.5127	4.7	1.7-12.9
Right hemisphere vs brainstem or cerebellum	1.2024	0.5081	3.3	1.2-9.0
Major dominant hemispheral syndrome	1.3580	0.5464	3.9	1.3-11.3
Intercept	–5.8928	0.8914		

Adapted from Tatemichi et al.[15] SE indicates standard error; OR, odds ratio; and CI, confidence interval.

CLINICAL CHARACTERISTICS OF PATIENTS UNAVAILABLE FOR FOLLOW-UP

Table 2 presents the clinical characteristics contained in the logistic model shown in Table 1 for the 46 patients who were unavailable for follow-up as well as the 66 patients who were found to have dementia and the 185 patients who were found to be free of dementia in examinations performed 3 months after stroke. Results of χ^2 analyses demonstrated that patients with dementia differed significantly from patients who were unavailable for follow-up with regard to age and the occurrence of lacunar infarction as the index stroke. Both of those variables remained significant when they were entered into a logistic regression analysis, with dementia found to be associated with an age of 80 years or older vs 60 to 69 years (odds ratio [OR], 0.23; 95% confidence interval [CI], 0.07-0.73) and the occurrence of lacunar infarction as the index stroke (OR, 0.32; 95% CI, 0.12-0.84) relative to unavailability for examination. Results of χ^2 analyses also demonstrated that unavailable patients differed significantly from patients without dementia with regard to the frequency of presentation with a major dominant hemispheral syndrome, the location of the index stroke, the occurrence of lacunar infarction as the index stroke, and a history of prior stroke. Logistic regression analysis determined that unavailability for examination was associated with a major dominant hemispheral syndrome (OR, 2.67; 95% CI, 1.01-7.09), left hemisphere (OR, 3.16; 95% CI, 1.05-9.54) and right hemisphere (OR, 2.92; 95% CI, 1.02-8.34) infarct locations vs a brainstem or cerebellar infarct location, and a history of prior stroke (OR, 1.98; 95% CI, 0.95-4.11) compared with freedom from dementia.

FREQUENCY OF DEMENTIA AMONG PATIENTS UNAVAILABLE FOR FOLLOW-UP

To illustrate the use of a logistic regression model to estimate the probability of dementia, we describe the clinical characteristics of 2 hypothetical patients. First, a hypothetical high-risk patient would be an 82-year-old nonwhite person with 7 years of education and a history of prior stroke and diabetes mellitus who presents with a large left temporo-occipital infarction that has resulted in memory impairment, dysnomia, and a right homonymous hemianopia, consistent with a major dominant hemispheral syndrome. Using the standard formula presented earlier, those clinical characteristics would yield a probability of dementia of 97.4%. A hypothetical low-risk patient would be a 63-year-old white person with 16 years of education who has no history of prior stroke or diabetes mellitus and presents with a small right parietal infarction that has resulted in only a sensory disturbance, yielding a probability of dementia of 0.9%.

Based on the 251 patients who were examined 3 months after stroke, the median probabilities of dementia among patients with and without dementia were 42.4% and 13.9%, respectively. Using the mean of those values, or 28.2%, as a cutoff for the diagnosis of dementia, we cross-tabulated dementia diagnoses based on our probability method with dementia diagnoses based on formal in-person examinations of the 251 patients in our cohort and found that the sensitivity and specificity of our method were 75.8% and 72.4%, respectively. Using our probability method, we recognized dementia in 21 of the 46 patients who were unavailable for examination, or 45.7% of that sample. Thirteen (61.9%) of the 21 patients who were determined to have dementia using that method were unavailable for examination due to death, illness, or untestability, while 13 (52.0%) of the 25 patients who were determined to be nondemented using that method were unavailable for those reasons. Based on the results of examinations performed 7 to 10 days after stroke, the 21 unavailable patients who were determined to have dementia exhibited more severe cognitive, functional, and neurologic impairment than the 25 unavailable patients who were determined to be nondemented on the MMSE (mean [±SD] scores, 15.9±8.2 vs 19.9±7.0, respectively; P=.11), the Barthel Index (mean [±SD] scores, 40.7±33.4 vs 65.2±33.4, respectively; P=.02), and the Stroke Severity Scale (mean [±SD] scores, 9.3±2.0 vs 6.9±3.3, respectively; P=.004).

Table 2. Patients' Clinical Characteristics by Examination Status

Variable	Frequency (%)		
		Examined	
	Not Examined (n=46)	Demented (n=66)	Not Demented (n=185)
Age, y*			
≥80	6 (13.0)	23 (34.8)	21 (11.4)
70-79	21 (45.7)	26 (39.4)	66 (35.7)
60-69	19 (41.3)	17 (25.8)	98 (53.0)
Education, y			
≤8	21 (45.7)	27 (40.9)	60 (32.4)
9-12	15 (32.6)	32 (48.5)	76 (41.1)
≥13	10 (21.7)	7 (10.6)	49 (26.5)
Nonwhite race	32 (69.6)	51 (77.3)	118 (63.8)
Diabetes mellitus	14 (30.4)	31 (47.0)	57 (30.8)
Prior stroke†	16 (34.8)	21 (31.8)	38 (20.5)
Lacunar infarction*†	7 (15.2)	24 (36.4)	55 (29.7)
Infarct location†			
Left hemisphere	22 (47.8)	33 (50.0)	57 (30.8)
Right hemisphere	19 (41.3)	24 (36.4)	72 (38.9)
Brainstem or cerebellum	5 (10.9)	9 (13.6)	56 (30.3)
Major dominant hemispheral syndrome‡	11 (23.9)	12 (18.2)	15 (8.1)

*Based on χ^2 analysis, $P<.05$ for patients who were not examined compared with patients with dementia.
†Based on χ^2 analysis, $P<.05$ for patients who were not examined compared with patients without dementia.
‡Based on χ^2 analysis, $P<.01$ for patients who were not examined compared with patients without dementia.

COMMENT

Our results suggest that approximately half of the elderly patients in our cohort who were unavailable for follow-up would have received a diagnosis of dementia if they had been administered our baseline dementia assessment 3 months after stroke. This finding is consistent with our hypothesis that prevalence surveys tend to underestimate the frequency of dementia associated with stroke and suggests that studies of the incidence of dementia may provide more accurate estimates of effect size for use in public health planning. If we were to add the dementia diagnoses of patients who were unavailable for follow-up, as determined using the methods of the present study, to the dementia diagnoses of patients who were formally examined 3 months after stroke, the baseline frequency of dementia in our cohort would increase from 26.3% to 29.3%, a 3.0% increase in the absolute frequency of dementia and an 11.4% increase relative to the original estimate. It is interesting to note that patients who were unavailable for examination had more frequently experienced a major dominant hemispheral syndrome, left and right hemisphere infarctions, and prior stroke than patients who were found to be nondemented in our formal examinations, suggesting that the factors that increase the risk of becoming unavailable for follow-up are similar to those that increase the risk of dementia after stroke.

Although few formal epidemiological investigations of the frequency of dementia after stroke have been performed, their findings are consistent with those of the present study in suggesting that patients who have experienced more severe strokes, and who would thus be more likely to meet criteria for dementia, are frequently unavailable for dementia assessment. As part of the Stroke Data Bank study, for example, Tatemichi et al[16] recruited a consecutive series of 927 elderly ischemic stroke patients and found that 726 (78.3%) of those patients were assessable by neurologists for the purposes of dementia diagnosis 7 to 10 days after stroke. In a multivariate analysis, unassessability was associated with reduced alertness, aphasia, and hemineglect. Similarly, Censori et al[17] recruited a cohort of patients who were consecutively admitted to the medical center following ischemic stroke and found that 110 (75.3%) of 146 eligible patients were available for dementia assessment 3 months later, with 25 of the 36 unavailable patients having died prior to that assessment. Univariate analyses demonstrated that those 25 patients were significantly older, had more severe deficits, and had more frequently experienced "total anterior circulation infarcts" than the 121 patients who survived their presenting stroke.

Regarding the secondary aim of this study, we believe that the use of our logistic model of the clinical determinants of dementia can provide valuable information regarding the probability of dementia for individual elderly patients following ischemic stroke, particularly in the context of research programs that must determine dementia status but cannot complete formal neuropsychological and functional assessments due to patient death, untestability, or comorbid illness. For patients who become unavailable for in-person examinations by choice, due to refusal or relocation, a telephone-based dementia screening protocol can be attempted using instruments such as the Telephone Interview for Cognitive Status[18] and the Blessed Functional Activity Scale,[10] although the methodologic weaknesses inherent in such an approach are readily apparent.

Accepted for publication August 11, 1997.

This work was supported by grants R01-NS26179 and P01-AG07232 from the National Institutes of Health, Bethesda, Md.

Presented in part at the Regional North American Annual Meeting of the World Federation of Neurology–Research Group on Neuroepidemiology, Boston, Mass, April 18, 1997.

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REFERENCES

1. Kelsey JL, Thompson WD, Evans AS. *Methods in Observational Epidemiology*. New York, NY: Oxford University Press; 1986.
2. Katzman R, Hill LR, Yu ESH, et al. The malignancy of dementia: predictors of mortality in clinically diagnosed dementia in a population survey of Shanghai, China. *Arch Neurol*. 1994;51:1220-1225.
3. McGonigal G, McQuade CA, Thomas BM, Whalley LJ. Survival in presenile Alzheimer's and multi-infarct dementias. *Neuroepidemiology*. 1992;11:121-126.
4. Mölsä PK, Marttila RJ, Rinne UK. Long-term survival and predictors of mortality in Alzheimer's disease and multi-infarct dementia. *Acta Neurol Scand*. 1995;91:159-164.
5. Tatemichi TK, Paik M, Bagiella E, Desmond DW, Pirro M, Hanzawa LK. Dementia after stroke is a predictor of long-term survival. *Stroke*. 1994;25:1915-1919.
6. Moroney JT, Bagiella E, Tatemichi TK, Paik MC, Stern Y, Desmond DW. Dementia after stroke increases the risk of long-term stroke recurrence. *Neurology*. 1997; 48:1317-1325.
7. Desmond DW. Vascular dementia: a construct in evolution. *Cerebrovasc Brain Metab Rev*. 1996;8:296-325.
8. Tatemichi TK, Desmond DW, Mayeux R, et al. Dementia after stroke: baseline frequency, risks, and clinical features in a hospitalized cohort. *Neurology*. 1992; 42:1185-1193.
9. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. *Md Med J*. 1965;14:61-65.
10. Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiatry*. 1968;114:797-811.
11. Folstein MF, Folstein SE, McHugh PR. 'Mini-Mental State': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975; 12:189-198.
12. Foulkes MA, Wolf PA, Price TR, Mohr JP, Hier DB. The Stroke Data Bank: design, methods, and baseline characteristics. *Stroke*. 1988;19:547-554.
13. 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.
14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*. Washington, DC: American Psychiatric Association; 1987.
15. Tatemichi TK, Desmond DW, Paik M, et al. Clinical determinants of dementia related to stroke. *Ann Neurol*. 1993;33:568-575.
16. Tatemichi TK, Foulkes MA, Mohr JP, et al. Dementia in stroke survivors in the Stroke Data Bank cohort: prevalence, incidence, risk factors, and computed tomographic findings. *Stroke*. 1990;21:858-866.
17. Censori B, Manara O, Agostinis C, et al. Dementia after first stroke. *Stroke*. 1996; 27:1205-1210.
18. Desmond DW, Tatemichi TK, Hanzawa L. The Telephone Interview for Cognitive Status (TICS): reliability and validity in a stroke sample. *Int J Geriatr Psychiatr*. 1994;9:803-807.