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ORIGINAL COMMUNICATION

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Study on frequency and predictors of dementia after ischemic stroke

The Chongqing Stroke Study

Abstract *Objective* We studied a large hospitalized cohort of patients aged 55 years and over with acute ischemic stroke to identify the frequency and predictors of poststroke dementia. *Methods* A total of 434 consecutive patients with ischemic stroke were enrolled in this study. During admission, the demographic data, vascular risk factors, stroke features, and neurological status information were collected. All subjects were examined by a battery of neuropsychological tests during admission and 3 months after stroke. Logistic regression analysis was used to find the predictors of poststroke dementia. *Results* (1) The frequency of poststroke dementia was 27.2 %, that of stroke-related dementia was 21.6 %, and that of dementia after first-ever stroke was 22.7 % 3 months after stroke. (2) Univariate analysis indicated that older age, low educational level (≤ 6 years), everyday drinking, diabetes mellitus, atrial fibrillation, prior stroke, left carotid territory infarction, embolism, multiple stroke lesions, dysphasia, and gait impairment were more frequent in the patients with poststroke dementia. (3) Multivariate analyses demonstrated that age (OR 1.179, 95 %CI 1.130–1.230), low educational level (OR 1.806, 95 %CI 1.024–3.186), everyday drinking (OR 3.447, 95 %CI 1.591–7.468), prior stroke (OR 2.531, 95 %CI 1.419–4.512), atrial fibrillation (OR 3.475, 95 %CI 1.712–7.057), dysphasia (OR 5.873, 95 %CI 2.620–13.163), and left carotid territory infarction (OR 1.975, 95 %CI 1.152–3.388) were associated with poststroke dementia. *Conclusions* The frequency of dementia is about one-forth of patients with ischemic stroke 3 months after stroke. Independent predictors of poststroke dementia include age, low educational level, everyday drinking, prior stroke, dysphasia, atrial fibrillation, and left carotid territory infarction.

Key words frequency · stroke · dementia · predictors

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Abrreviations

AD	Alzheimer's disease
ADL	Activity of Daily Living
CI	Confidence Interval
CMMS	Chinese version of the Mini-Mental State Examination
CT	Computed Tomography
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
FOM	Fuld Object Memory Evaluation
IADL	Instrumental Activity of Daily Living
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
MRI	Magnetic Resonance Imaging
OR	Odds Ratio
POD	Pfeiffer Outpatient Disability Questionnaire
RVR	Rapid Verbal Retrieve
SD	Standard Error
TIA	Transient Ischemic Attack

Introduction

As the world population is aging, stroke and dementia become the major public health problems today, owing to their increasing incidence and high disability and mortality [11, 26]. The risk of dementia increases after stroke, stroke is considered to be the second most common cause of dementia [17, 32].

Some authors have considered that poststroke dementia was one of the rare preventable dementias [15, 16]. It is of great importance to identify predictors of poststroke dementia for its prevention. Despite the numerous studies on poststroke dementia, there has not been a consensus about its predictors. Reasons for a stroke patient to become demented are still insufficiently understood [2, 9, 31].

With a population of 1.3 billion, the frequency of dementia in the elderly is high in China [40]. Because of the differences in race, economic level, and lifestyle, the prevalence of and predictors for cognitive impairment after stroke in China might differ from those in western countries. There have been few studies specifically focusing on the predictors of poststroke dementia in China. We studied a large hospitalized cohort of patients aged 55 years and over with acute ischemic stroke to identify the frequency and predictors of poststroke dementia.

Methods

Patients

From May 8, 1999, to December 31, 2000, the consecutive patients with ischemic stroke admitted to Daping hospital were registered. Eligibility requirements included 1) the acute onset of ischemic stroke within 48 hours, 2) aged 55 years and over. The diagnosis of ischemic stroke was established on both clinical grounds when there were focal signs of cerebral dysfunction of acute onset lasting for > 24 hours, and brain CT or MRI. We excluded from the study patients 1) presence of a concomitant neurological disorder potentially affecting cognitive function (e. g., severe Parkinson's disease), 2) serious illness, severe hearing and visual impairment precluding a reliable assessment of cognitive function, 3) persistent impairment of consciousness, 4) previous long-lasting mental retardation, 5) severe aphasia (RVR score < 6), 6) without a reliable information, 7) with a history of severe head trauma or neurosurgery, 8) not living in Chongqing.

This study was approved by the Institutional Review Board of Third Military Medical University, and all subjects provided informed consent.

A total of 546 patients were registered in this study, 434 (79.5 %) were examined 3 months after stroke, a remaining 112 (20.5 %) patients were excluded: 23 (4.2 %) died, 21 (3.8 %) had severe dysphasia, hearing and visual impairment, and worsening illness precluding evaluation, 63 (11.5 %) refused examination or follow-up, 5 (0.9 %) moved away.

Clinical Assessment

During admission, all patients underwent a structured demographic data, medical history, neurological examinations and head imaging. We prospectively collected the following data: age, sex, handedness, educational level, cigarette smoking (never smoking, past smoking, and current smoking), alcohol drinking (everyday drinking, every week drinking, every month drinking, and occasionally drinking), prior stroke, prior transient ischemic attack (TIA), hypertension (previously diagnosed and treated or systolic pressure > 160 mm Hg and/or diastolic pressure > 90 mm Hg persistently observed during admission after the acute phase), diabetes mellitus (previously diagnosed and treated or fasting glucose > 7 mmol/L in 2 blood samples after the acute phase), atrial fibrillation (diagnosed and treated previously or during admission), heart failure (diagnosed and treated previously or during admission), stroke severity (NIH Stroke Scale), neurological sign, and stroke features.

Evaluation of prestroke cognitive function

During admission, the cognitive status before index stroke was assessed by inquiring close relatives of patients using a Chinese version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), previously validated in the Chinese population [12]. Functional status before stroke was assessed with the Activity of Daily Living (ADL) [6, 21].

Neuropsychological evaluation

At 7 to 10 days after stroke onset, we administered a battery of neuropsychological tests developed for use in epidemiological studies of dementia to all subjects [40, 41]. This neuropsychological battery includes: Chinese version of the Mini-Mental State Examination (CMMS) [20], Activity of Daily Living (ADL), Instrumental Activity of Daily Living (IADL) [24], Pfeiffer Outpatient Disability Questionnaire (POD) [30], Fuld Object Memory Evaluation (FOM) [13], Rapid Verbal Retrieve (RVR) [39], Wechsler Adult Intelligence Scale (DS and BD subtest) [40], and Hamilton Depression Rating Scale. The normative data for these tests had been previously established in a community group of elderly living in the same urban area with the same age, sex distribution, and cultural background [41]. The score < = 2 SD of normative value is judged as abnormality. To ensure reliability of the screening, correlating with participation of all interviewers was conducted. The K statistic reflecting interviewer reliability was estimated to be 0.91.

Follow-up

434 subjects were followed-up 3 months after the index stroke. 362 were assessed at the hospital, and 72 at home. The neuropsychological battery was the same as that used during admission.

Diagnosis of Dementia

Dementia was diagnosed based on criteria modified from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) [1]. Poststroke dementia was defined as dementia with concomitant stroke, stroke-related dementia was defined as dementia developing after index stroke, and dementia after first-ever stroke was defined as dementia with first-ever stroke.

The clinical diagnosis of dementia was made by senior neurologists and psychiatrists during admission and 3 months after stroke.

Statistical analyses

The univariate analyses were undertaken to compare the data of nondemented and demented patients after stroke, including demographic data, vascular risk factors, stroke features, and neurological

status. The Chi-square test was used for categorical variables and Student's t test for quantitative variables. All the variables with statistical significance ($p < 0.05$) in the univariate analyses were introduced into logistic regression analyses with a backward procedure and with $p > 0.05$ as the criterion for exclusion to find the independent predictors of dementia in 3 different patient groups: model A, poststroke dementia (n = 434, demented n = 118); model B, stroke-related dementia (n = 394, demented n = 87); model C, dementia after first-ever stroke (n = 321, demented n = 73). All these analyses were performed with SPSS for Windows, version 10.0(SPSS Inc) [33].

Results

The frequency of dementia was 118 (27.2 %) of 434 patients with ischemic stroke, 31 of 118 (7.1 %) were diagnosed as dementia during admission, 87 of 118 (21.6 %) were diagnosed as dementia 3 months after stroke, and 73 of 118 (22.7 %) were diagnosed as dementia after first-ever stroke.

Table 1 shows the comparison of demographic data between demented and nondemented patients. Mean age of demented patients was 8.5 years higher than nondemented patients ($p < 0.01$), and the proportion of low educational level (≤ 6 years) in the demented group was significantly higher than in the nondemented group (OR 2.757, 95 %CI 1.773–4.285). Demented patients did not differ in sex and handedness from the nondemented group, even after adjusting for educational level.

Table 2 indicates the vascular risk factors of demented and nondemented patients. All the vascular risk factors were more frequent in demented patients than in nondemented patients, but only diabetes mellitus (OR 1.659, 95 % CI 1.006–2.858), atrial fibrillation (OR 4.148, 95 % CI 2.325–7.398), prior stroke (OR 2.248, 95 % CI 1.422–3.555), and everyday drinking (OR 1.876, 95 % CI 1.022–3.443) reached statistical significance.

As shown in Table 3, stroke features associated with dementia included left carotid territory infarction (OR 1.593, 95 % CI 1.011–2.508), multiple stroke lesions (OR 2.189, 95 % CI 1.419–3.377), and embolism (OR 4.010, 95 % CI 2.151–7.474). The NIH stroke scale score in demented patients was slightly higher than in nondemented patients, but the difference was not significant ($p = 0.214$).

As seen in Table 4, demented patients more frequently had dysphasia (OR 5.833, 95 % CI 3.021–11.262) and gait impairment (OR 1.740, 95 % CI 1.132–2.673), than nondemented patients. The proportion of left carotid territory infarction in demented dysphasic patients was similar to that in nondemented dysphasic patients (78.6 % vs 75.0 %, $p = 0.786$).

All the variables with statistical significance ($p < 0.05$) in the univariate analyses were introduced into logistic regression analyses (Table 5). These variables included age, low educational level, diabetes mellitus, atrial fibrillation, prior stroke, everyday drinking, left carotid territory, multiple stroke lesion, embolism, dysphasia and gait impairment. Age, low educational level, everyday drinking, prior stroke, dysphasia, atrial fibrillation, and left carotid territory infarction were identified as independent predictors of dementia in

Table 1 Demographic Data of Demented and Nondemented Patients

	Demented (n = 118)	Nondemented (n = 316)	OR (95 % CI)
Age (y), mean ± SD	73.8 ± 7.5	65.3 ± 6.8	–
Females, n (%)	55 (46.6)	150 (47.5)	0.966 (0.632–1.476)
Right handed, n (%)	114 (96.6)	301 (95.3)	1.420 (0.462–4.369)
Education, n (%)	–	–	2.757 (1.773–4.285)
Illiterate	18 (15.3)	22 (7.0)	–
1–6y	39 (33.0)	58 (18.4)	–
7–9y	48 (40.7)	173 (54.7)	–
≥ 10y	13 (11.0)	63 (19.9)	–

Table 2 Vascular Risk Factors in Demented and Nondemented Patients

Vascular Risk Factor	Demented (n = 118)	Nondemented (n = 316)	OR (95 % CI)
Hypertension, n (%)	81 (68.6)	208 (65.8)	1.137 (0.723–1.788)
Diabetes Mellitus, n (%)	28 (23.7)	49 (15.5)	1.659 (1.006–2.858)
Heart failure, n (%)	24 (20.3)	57 (18.0)	1.160 (0.681–1.975)
Atrial fibrillation, n (%)	31 (26.3)	25 (7.9)	4.148 (2.325–7.398)
Myocardial infarction, n (%)	26 (22.0)	60 (19.0)	1.206 (0.718–2.025)
Prior stroke, n (%)	45 (38.1)	68 (21.5)	2.248 (1.422–3.555)
Prior TIA, n (%)	19 (16.1)	44 (13.9)	1.186 (0.661–2.130)
Current smoking, n (%)	22 (18.6)	51 (16.1)	1.191 (0.686–2.068)
Everyday drinking, n (%)	20 (16.9)	31 (9.8)	1.876 (1.022–3.443)

Table 3 Stroke Features in Demented and Nondemented Patients

	Demented (n = 118)	Nondemented (n = 316)	OR (95% CI)
Vascular territory, n (%)			1.593 (1.011–2.508)[a]
Left carotid	63 (53.4)	126 (39.9)	
Right carotid	46 (39.0)	149 (47.1)	
Vertebrobasilar	9 (7.6)	41 (13.0)	
Type of lesion, n (%)			2.189 (1.419–3.377)[b]
Single	64 (54.2)	237 (75.0)	
Multiple	54 (45.8)	79 (25.0)	
Mechanism of Stroke[c], n (%)			4.010 (2.151–7.474)[c]
Thrombotic	88 (74.6)	285 (90.1)	
Embolic	26 (22.0)	21 (6.6)	
Other	4 (3.4)	10 (3.2)	
NIH Stroke Scale (SD)	1.96 (3.1)	1.85 (3.0)	–

[a] Left vs Right; [b] Multiple vs Single; [c] Embolic vs Thrombotic

Table 4 Neurological Status of Demented and Nondemented Patients

Neurological Signs	Demented (n = 118)	Nondemented (n = 316)	OR (95% CI)
Dysphasia, n (%)	28 (23.7)	16 (5.1)	5.833 (3.021–11.262)
Dyskinesia, n (%)	51 (43.2)	130 (41.1)	1.089 (0.710–1.670)
Sensory disturbance, n (%)	19 (16.1)	54 (17.1)	0.931 (0.526–1.649)
Cranial nerve sign, n (%)	9 (7.6)	34 (10.7)	0.685 (0.318–1.475)
Cerebellum sign, n (%)	7 (5.9)	13 (4.1)	1.470 (0.572–3.779)
Bulb sign, n (%)	9 (7.6)	12 (3.8)	2.092 (0.858–5.101)
Gait impairment, n (%)	56 (47.5)	108 (34.2)	1.740 (1.132–2.673)

Table 5 Predictors of dementia after stroke in Multiple Logistic Regression

Variable	B	SE	Wald	OR	95% CI
Model A Poststroke dementia (n = 434,demented n = 118)					
Age	0.165	0.022	58.150	1.179	1.130–1.230
Low educational level	0.591	0.290	4.165	1.806	1.024–3.186
Everyday drinking	1.238	0.394	9.848	3.447	1.591–7.468
Prior stroke	0.929	0.295	9.904	2.531	1.419–4.512
Atrial fibrillation	1.246	0.361	11.883	3.475	1.712–7.057
Dysphasia	1.770	0.412	18.486	5.873	2.620–13.163
Left carotid territory	0.681	0.275	6.113	1.975	1.152–3.388
Constant	−13.816	1.576	76.881		
Model B Stroke-related dementia (n = 403,demented n = 87)					
Age	0.162	0.024	44.542	1.175	1.121–1.233
Low educational level	0.779	0.322	5.855	2.178	1.159–4.093
Everyday drinking	1.449	0.427	11.518	4.261	1.845–9.841
Prior stroke	1.181	0.327	13.075	3.258	1.718–6.180
Atrial fibrillation	1.238	0.397	9.726	3.450	1.584–7.512
Dysphasia	2.088	0.438	22.738	8.065	3.419–19.021
Left carotid territory	0.695	0.305	5.180	2.003	1.101–3.644
Constant	−14.147	1.791	62.424		
Model C Dementia after first-ever stroke (n = 321,dementia n = 73)					
Age	0.183	0.028	44.293	1.201	1.138–1.268
Low educational level	0.884	0.359	6.074	2.420	1.198–4.888
Everyday drinking	1.596	0.490	10.620	4.932	1.889–12.876
Dysphasia	1.945	0.473	16.897	6.996	2.767–17.687
Left Carotid territory	0.965	0.353	7.448	2.625	1.315–5.240
Constant	−15.319	2.204	57.294		

model A. Predictors in model B were the same as in model A. In model C, predictors included age, low educational level, everyday drinking, dysphasia, and left carotid territory infarction.

Discussion

Chongqing city is the municipality directly under the Central Government in China and has 31.000 thousands population, of which 93.6 % are Han people with the same lifestyle [41]. The catchment area of our hospital included about 1 million urban habitants, who can be considered to represent the urban population of China in demographic characters.

The our results showed that in patients with acute ischemic stroke aged ≥ 55 years, the frequency of dementia 3 months after stroke was 27.2 %, that of stroke-related dementia was 21.6 %, and that of dementia after first-ever stroke was 22.7 %. Our results were similar to other studies. In a large well defined stroke cohort of 337 patients aged ≥ 55 years with ischemic stroke, Pohjasvaara et al. [31] found that the proportion of dementia 3 months after index stroke was 31.8 %, that of stroke-related dementia was 28.4 %, and that of dementia after first-ever stroke was 28.9 %. Based on examinations performed 3 months after stroke onset in a cohort of 251 patients aged ≥ 60 years hospitalized with acute ischemic stroke, Tatemichi et al. [36] determined the frequency of dementia as 26.3 %. In a series of 251 consecutive unselected stroke patients aged ≥ 18 years, Barba et al. [2] found that the frequency of dementia 3 months after acute ischemic stroke was 30.1 %.

Compared with the dementia prevalence of 2.6 to 3 % in Chinese people aged ≥ 55 years [39, 40], the risk of poststroke dementia increased by a factor of 9 in our present study. These results were consistent with Tatemichi's study [36], in which ischemic stroke significantly increases the risk of dementia, the odds ratio for stroke patients compared with age-matched control subjects was 9.4. Kokmen et al. [22] suggested that the incidence of dementia in stroke patients in the first year was 9 times greater than controls. Desmond et al. [10] found that the risk of incident dementia increased 4-fold among ischemic stroke patients who were initially nondemented relative to clinically stroke-free elderly control subjects after adjustment for demographic factors and baseline level of cognitive function.

In this study, univariate analysis indicated that the demented patients more frequently had older age, low educational level (≤ 6 years), everyday drinking, diabetes mellitus, atrial fibrillation, prior stroke, left carotid territory infarction, embolism, multiple stroke lesion, dysphasia, and gait impairment than nondemented patients. Some investigators also demonstrated that these factors were more frequent in demented patients [9, 10, 18, 31].

There were no statistically significant differences of sex, handedness, prior TIA, heart failure, myocardial infarction, current smoking, stroke severity, dyskinesia, cerebellum sign, and bulb sign between dementia and nondementia patients in the present study. Our results did not accord with some studies [5, 14, 19, 38], in which sex (female), smoking, and stroke severity were more frequent in demented patients, and were predictors of poststroke dementia.

In the multivariate analyses, we demonstrated that age, low educational level, everyday drinking, prior stroke, atrial fibrillation, dysphasia, and left carotid territory infarction were predictors of dementia in both model A and model B. Compared with in model A and B, prior stroke and atrial fibrillation were excluded from predictors in model C.

In all of our three models, everyday drinking had a strong correlation with poststroke dementia, although other studies focusing on the poststroke dementia did not consider the alcohol drinking as a predictor [2, 9, 14, 18, 22, 31, 36]. This discrepancy with regard to the importance of alcohol drinking may result from difference in the drinking rate of the studied cohorts [2, 10, 31]. In our previous study, drinking rate was very high in the community population, and was proven to be a risk factor of cognitive impairment in the elderly [41]. Everyday drinking probably plays an important role in the development of poststroke dementia in this study.

Age and low educational level were independent predictors of poststroke dementia in the present study. This result was consistent with other series [2, 9, 14, 18, 22, 36]. In our previous study, age and low educational level were identified as an important risk factor of cognitive impairment in Chinese elderly people [41]. Dartigues et al. [8] demonstrated that lower education differed from higher education in many areas which were related to the cognitive function and health. Stern et al. [34, 35] studied the association between education and cognitive function in patients with Alzheimer's disease (AD), and concluded that high educational level might provide a reserve that compensated for the neuropathological changes of AD and delay the onset of its clinical manifestations.

Dysphasia was associated with dementia in all three models of our study, consistent with the findings of other authors [2, 5, 23, 38]. Ween et al. [42] tested 16 mildly aphasic patients on a variety of short- and long-term memory measures, and found that aphasia impaired both short- and long-term memory. Basso et al. [3] investigated 173 patients with left hemisphere disease and suggested that aphasia was also associated with deficits in intelligence.

Agreeing with other authors [2, 5, 14, 31, 37], we also found that left carotid territory infarction was an important predictor of poststroke dementia. Some studies found that unilateral left-sided damage could affect both

language and memory disturbance [3, 28, 37]. The results of our study and others support the hypothesis that left hemisphere is dominant for not only language but generalized cognitive function [3, 9, 25, 27, 28, 31, 37].

Prior stroke was identified as a predictor of poststroke dementia, in our study and other studies [9, 31, 37]. In a 10 years follow-up of ischemic stroke, Desmond et al. [10] suggested that previous stroke before baseline was a predictor of poststroke dementia, and of the 39 patients with recurrent stroke during follow-up, 17 (43.6 %) became demented. In another 2 years longitudinal study of poststroke dementia, prior stroke was considered as the most important predictor of dementia too [38]. In a population-based study, Kokmen et al. [22] also found that second stroke was a significant independent predictor of poststroke dementia in a multivariate Cox proportional hazards model.

Consistent with other studies [2, 5, 29, 38], our results demonstrated that atrial fibrillation was an independent predictor of poststroke dementia. In a large cross-sectional, population-based study focusing on the association between atrial fibrillation and dementia, Ott et al. [29] found the significant positive associations of atrial fibrillation with both dementia and impaired cognitive function, these associations were stronger in women, and the relation with dementia was more pronounced in the relatively younger elderly.

Although diabetes mellitus was more frequent in demented patients, it was not an independent predictor in this study. Diabetes mellitus as a predictor of poststroke dementia was reported by some authors [9, 5, 18, 37], other authors did not consider diabetes to be a predictor [2, 10, 14, 22, 23, 31, 36]. In the Fremantle Diabetes Study focusing on the association of dementia with diabetes, Bruce et al. [4] suggested that the high rate of dementia found in older people with diabetes might be due to the high rate of hypertension in the population but not diabetes. In a historical prospective cohort study of 3774 Japanese-American men, Curb et al. [7] found that diabetes was associated with the stroke-related dementia.

In conclusion, the frequency of poststroke dementia is about one-third of patients with ischemic stroke 3 months after stroke. Independent predictors of poststroke dementia include age, low educational level, everyday drinking, prior stroke, dysphasia, atrial fibrillation, and left carotid territory infarction.

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