J Rehabil Med 2012; 44: 319–324

ORIGINAL REPORT

STROKE REHABILITATION IS ASSOCIATED WITH A REDUCTION IN DEMENTIA RISK: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

Yi-Chun Chou, MD[1]*, Chien-Chang Liao, PhD[2,3,4,5]*, Li-Ting Su, MS[4,5,6], Pei-Yu Yang, MD[1] and Fung-Chang Sung, PhD[4,5]

From the [1]Department of Physical Medicine and Rehabilitation, China Medical University Hospital, Taichung, [2]Department of Anesthesiology, Taipei Medical University Hospital, [3]School of Medicine, Taipei Medical University, Taipei, [4]Department of Public Health, China Medical University, [5]Management Office for Health Data, China Medical University Hospital and [6]Trauma and Emergency Center, China Medical University Hospital, Taichung, Taiwan.
**The first two authors contributed equally to this paper and should be considered as first authors.*

Objective: **Focusing on the relationship between physical activity and incident cognitive impairment, the aim of this study was to investigate whether stroke rehabilitation reduces the risk of dementia.**
Methods: **Claims data of 1,000,000 insured subjects randomly selected from the National Health Insurance programme of Taiwan were used to identify adults with a newly diagnosed ischaemic stroke in 1997–2002. Among them, 1,375 received rehabilitation and 3,722 did not. Both groups were followed up until the end of 2007 to measure the incidence of development of dementia.**
Results: **The incidence of development of dementia was lower in the rehabilitation cohort than in the non-rehabilitation cohort (1.22 vs 1.70 per 100 person-years), with an adjusted hazard ratio (HR) of 0.73 (95% confidence interval (CI) = 0.60–0.89) in the multivariate Cox proportional hazard regression analysis. Female gender (HR = 1.26, 95% CI = 1.07–1.50), older age (HR = 7.71, 95% CI = 3.36–17.7), low income (HR = 1.82, 95% CI = 1.42–2.33), and Parkinson's disease (HR = 1.64, 95% CI = 1.33–2.03) were risk factors associated with the development of dementia.**
Conclusion: **Post-stroke rehabilitation is associated with a reduction in dementia risk among ischaemic stroke patients.**

Key words: comorbidity; dementia; stroke; rehabilitation; cohort study.

J Rehabil Med 2012; 44: 319–324

Correspondence address: Fung-Chang Sung, China Medical University College of Public Health, 91 Hsueh-Shih Road, Taichung 404, Taiwan. E-mail: fcsung@mail.cmu.edu.tw

Submitted March 1, 2011; accepted November 14, 2011

INTRODUCTION

Stroke and dementia are major health concerns in the elderly population. Epidemiological studies have shown that patients with stroke are at an appreciably greater risk of developing dementia than those without stroke (1–5). Post-stroke dementia is one of the major determinants of dependency among stroke patients (4, 6). Given the decline in mortality after stroke, and the ageing population (4), it is important to prevent dementia among stroke survivors.

Physical activity programmes have been reported to be effective in slowing cognitive decline and improving quality of walking in elderly people with dementia (7). The population-based cohort study, INVADE, demonstrated that moderate or maximal physical activity reduces the incidence of cognitive impairment (8). Verghese et al. (9) also observed a beneficial effect of leisure activities on dementia in community-dwelling older people. Evidence has suggested that stroke rehabilitation may be helpful in improving motor function (10), but its effect on cognitive function is not clear (11). Further research is required into whether physical movement and activity can reduce the incidence of dementia among stroke patients.

Dementia is a common sequela of stroke among elderly people in developed and developing countries (6, 12). The prevalence rate of the sequel is higher in Taiwan (1.7–4.4%) than in Western countries (1.5%) (13, 14). Using the National Health Insurance (NHI) database, we conducted a population-based cohort study to investigate the association between stroke rehabilitation and risk of dementia occurrence among ischaemic stroke patients in Taiwan.

METHODS

Data sources

This retrospective cohort study used reimbursement claims data obtained from the Taiwan NHI programme. The NHI programme covers more than 99% of the population and contracts with 97% of the hospitals and clinics in Taiwan (15). The National Health Research Institute, which maintains and updates the NHI database. The institute has released a sub-dataset composed of claims data for 1,000,000 randomly selected insurance enrolees to the public for research and administrative purposes. This random subgroup represents approximately 5% of the entire insured population in Taiwan. We used this sub-dataset in this study after obtaining approval from the National Health Research Institute review committee. For data analysis, we retrieved information about patients' characteristics and medical care records by linking ambulatory claims, inpatients care claims, and the registry for beneficiaries, with scrambled personal identification numbers to ensure privacy protection.

Study subjects and study end-point

The primary discharge diagnosis of ischaemic stroke (International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 433 and 434) was used to identify patients in whom new-onset ischaemic stroke had been diagnosed during the period 1997–2002. Exclusion criteria were: patients <20 years old and those with a history of dementia at baseline. Rehabilitation recipients were identified according to NHI medical records as patients who had ever received post-stroke rehabilitation services. Rehabilitative programmes comprised facilitation of hemiplegic limbs, muscle strengthening, ambulation and balance training to achieve functional improvement.

ICD-9-CM codes 290.0, 290.1, 290.2, 290.3 and 331.0 were used to search for outpatients and inpatients with a new diagnosis of dementia during the follow-up period ending on 31 December 2007. Person-years of follow-up were determined by calculating the interval between the date on which stroke was diagnosed and whichever of the following dates was first: date of dementia diagnosis; date of withdrawal from the NHI programme; date of death, or the end of 2007.

Statistical analysis

A χ^2 test was used to compared differences in age, sex, occupation, urbanization levels of residential area, monthly income, hospital levels, and comorbidity, including diabetes, hypertension, hyperlipidaemia, Parkinson's disease, and incidence of dementia, between stroke patients with and without rehabilitation. The length of stay and in-hospital medical costs were also compared between the two groups. To determine the urbanization level of the patients' residential area, the population density (persons/km^2) was calculated by dividing the population by the area for each township and city district in which the study subjects were registered for insurance purposes. The levels of urbanization were classified as low, moderate, or high according to the tertile distribution of population density.

We calculated incidence density rates of dementia by sociodemographic characteristics subsequent to ischaemic stroke. The rate ratios of incident dementia for the rehabilitation group to non-rehabilitation group were also determined. The dementia-free survival rates were estimated using the Kaplan–Meier method, and the difference between survival curves was compared using the log-rank test. A time-dependent analysis was further performed to estimate the effect of dementia in the first and subsequent years. Univariate and multiple Cox proportional hazard regression analyses were conducted to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of risk of dementia in association with stroke rehabilitation. The multiple models were simultaneously adjusted for sociodemographic characteristics and comorbid conditions. Time-dependent analysis was performed using the Cox proportional hazard model to investigate the time-effect of rehabilitation on reduction in dementia risk. All analyses were performed using SAS statistical software (version 9.1 for Windows; SAS Institute, Inc., Cary, NC, USA), and the results were considered statistically significant when two-tailed *p*-values were less than 0.05.

RESULTS

We identified 5,097 patients with ischaemic stroke during the period 1997–2002; of these, 1,375 subjects received rehabilitation care and 3,722 did not (Table I). Compared with stroke patients who did not receive rehabilitation, patients who received rehabilitation services were younger (46.5% vs 42.0%, $p=0.0002$, for <65 years old) and tended to have lower income (68.5% vs 59.4%, $p<0.0001$, for <15,000 New Taiwan Dollars).

During the follow-up period, the overall incidence density rate of dementia was lower in patients who received rehabilitation than in those who did not (1.22 vs 1.70 per 100 person-years) (Table II). The incidence of dementia increased with age in both groups. The Kaplan–Meier model showed that the cumulative incidence of dementia over the follow-up period was 3.5% higher in stroke patients who received rehabilitation than in those who did not (log-rank $p=0.0008$) (Fig. 1). The incidence rate was

Table I. *Selected sociodemographic characteristics of patients with and without rehabilitation after ischaemic stroke diagnosed in 1997–2002*

	Rehabilitation			
	No (n=3,722) n (%)	Yes (n=1,375) n (%)	Total (n=5,097) n (%)	p-value[a]
Sex				0.07
Female	1,643 (44.1)	568 (41.3)	2,211 (43.4)	
Male	2,079 (55.9)	807 (58.7)	2,886 (56.6)	
Age				0.0002
20–44 years	188 (5.1)	76 (5.5)	264 (5.2)	
45–64 years	1,373 (36.9)	564 (41.0)	1,937 (38.0)	
65–79 years	1,817 (48.8)	656 (47.7)	2,473 (48.5)	
≥80 years	344 (9.2)	79 (5.8)	423 (8.3)	
Occupation				0.10
White-collar	975 (26.2)	373 (27.1)	1,348 (26.5)	
Blue-collar	1,745 (46.9)	600 (43.6)	2,345 (46.0)	
Others	1,002 (26.9)	402 (29.2)	1,404 (27.5)	
Urbanization				0.90
Low	212 (5.7)	82 (6.0)	294 (5.8)	
Moderate	1,359 (36.5)	495 (36.0)	1,854 (36.4)	
High	2,151 (57.8)	798 (58.0)	2,949 (57.9)	
Income				<0.0001
<15,000 NTD	2,210 (59.4)	942 (68.5)	3,152 (61.8)	
≥15,000 NTD	1,512 (40.6)	433 (31.5)	1,945 (38.2)	
Hospital levels				0.72
Medical centres	1,274 (34.2)	487 (35.4)	1,761 (34.6)	
Regional hospitals	1,507 (40.5)	548 (39.8)	2,055 (40.3)	
Community hospitals	941 (25.3)	340 (24.7)	1,281 (25.1)	

[a] Chi-square test for comparing characteristics between ischemic stroke patients with and without rehabilitation.
NTD: New Taiwan Dollar.

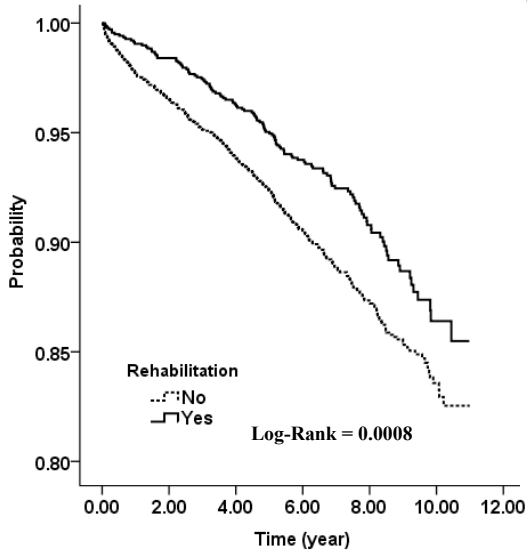

Fig. 1. Kaplan–Meier analysis for dementia development in patients with and without rehabilitation after ischaemic stroke.

Table II. *Incidence of dementia in patients with and without rehabilitation after ischaemic stroke and rate ratio by sociodemographic characteristic*

	Rehabilitation								
	No (*n*=3,722)				Yes (*n*= 1,375)				
	n	Cases *n* (442)	PY *n* (25,828)	Rate[a] (1.71)	*n*	Cases *n* (124)	PY *n* (10,111)	Rate[a] (1.23)	Rate ratio (0.72)
Sex									
Female	1,643	223	11,335	1.97	568	59	4,124	1.43	0.73
Male	2,079	219	14,493	1.51	807	65	5,987	1.09	0.72
Age									
20–44 years	188	6	1,452	0.41	76	0	590	0.00	0.00
45–64 years	1,373	83	9,997	0.83	564	30	4,339	0.69	0.83
65–79 years	1,817	274	12,358	2.22	656	76	4,714	1.61	0.73
≥80 years	344	79	2,021	3.91	79	18	469	3.84	0.98
Occupation									
White-collar	975	109	6,870	1.59	373	34	2,710	1.25	0.79
Blue-collar	1,745	184	12,155	1.51	600	45	4,464	1.01	0.67
Others	1,002	149	6,803	2.19	402	45	2,938	1.53	0.70
Urbanization									
Low	212	33	1,427	2.31	82	5	637	0.78	0.34
Moderate	1,359	146	9,478	1.54	495	49	3,643	1.35	0.87
High	2,151	263	14,922	1.76	798	70	5,831	1.20	0.68
Income									
<15,000 NTD	2,210	325	15,116	2.15	942	105	6,795	1.55	0.72
≥15,000 NTD	1,512	117	10,711	1.09	433	19	3,316	0.57	0.52
Hospital levels									
Medical centres	1,274	129	8,893	1.45	487	39	3,553	1.10	0.76
Hospitals	1,507	194	10,242	1.89	548	62	3,985	1.56	0.82
Community hospitals	941	119	6,693	1.78	340	23	2,572	0.89	0.50

[a]Per 100 person-years.

PY: person-years; NTD: New Taiwan Dollar.

Table III. *Comparison of baseline comorbidity and mortality in the follow-up period between patients with and without rehabilitation after ischaemic stroke*

	Rehabilitation						
	No (*n*=3,722)		Yes (*n*=1,375)		Total (*n*=5,097)		
	n	(%)	*n*	(%)	*n*	(%)	*p*-value
Diabetes, *n*							0.0002
No	2,134	(57.3)	708	(51.5)	2,842	(55.8)	
Yes	1,588	(42.7)	667	(48.5)	2,255	(44.2)	
Hypertension, *n*							<0.0001
No	459	(12.3)	95	(6.9)	554	(10.9)	
Yes	3,263	(87.7)	1,280	(93.1)	4,543	(89.1)	
Hyperlipidaemia, *n*							0.24
No	2,379	(63.9)	854	(62.1)	3,233	(63.4)	
Yes	1,343	(36.1)	521	(37.9)	1,864	(36.6)	
Parkinson's disease, *n*							0.12
No	3,349	(90.0)	1,216	(88.4)	4,565	(89.6)	
Yes	373	(10.0)	159	(11.6)	532	(10.4)	
Depression, *n*							0.038
No	3,585	(96.3)	1,306	(95.0)	4,891	(95.6)	
Yes	137	(3.7)	69	(5.0)	206	(4.0)	
Medical cost, USD, mean (SD)	1,070 (1753)		1,411 (1998)		1,162 (1829)		<0.0001
Length of stay, days, mean (SD)	12.5 (74.3)		14.7 (35.0)		13.1 (66.1)		0.291
Death							0.295
No	3,401	(91.4)	1,269	(92.3)	4,670	(91.6)	
Yes	321	(8.6)	106	(7.7)	427	(8.4)	

SD: standard deviation; USD: United States dollar.

much higher in the non-rehabilitation group in the first year, and then the rates become more similar in subsequent years.

Table III also shows that patients in the rehabilitation group were also more likely than those in the non-rehabilitation group to have diabetes mellitus, hypertension, and depression. Higher medical cost was found in the rehabilitation group than in the non-rehabilitation group. There was no significant difference in length of stay and in-hospital death.

Table IV shows the crude and adjusted HRs and 95% CIs of dementia in association with rehabilitation and other covariates. Stroke patients with rehabilitation had a 28% lower risk of dementia than stroke patients without rehabilitation (unadjusted model, HR = 0.72, 95% CI = 0.59–0.88). The beneficial effect was not weakened after adjusting for sociodemographic factors and comorbid conditions (HR = 0.74, 95% CI = 0.60–0.89). Female gender (HR = 1.27, 95% CI = 1.07–1.50), older age (HR = 7.84, 95% CI = 3.41–18.0), and low income (HR = 1.81, 95% CI = 1.42–2.32) were associated with increased risk of developing dementia. Stroke patients with Parkinson's disease were at higher risk of dementia than stroke patients who did not have Parkinson's disease (HR = 1.60, 95% CI = 1.29–1.98). Table V indicates that the greatest benefit of rehabilitation for reducing dementia risk among stroke patients was in the first year (HR = 0.43, 95% CI = 0.19–0.96). The benefit decreased with years after stroke.

Table V. *Annual change in hazard ratio (HR) of dementia associated with rehabilitation estimated for stroke patients relative to patients without rehabilitation*

	Rehabilitation			
	No		Yes	
Multiple model	HR	(95% CI)	HR	(95% CI)
f/u 6 months	1.00	(Reference)	0.43	(0.19–0.96)
f/u 1 year	1.00	(Reference)	0.43	(0.24–0.78)
f/u 2 year	1.00	(Reference)	0.48	(0.30–0.75)
f/u 3 year	1.00	(Reference)	0.53	(0.37–0.78)
f/u 4 year	1.00	(Reference)	0.61	(0.45–0.83)
f/u 5 year	1.00	(Reference)	0.65	(0.50–0.84)
f/u 6 year	1.00	(Reference)	0.66	(0.52–0.83)
f/u 7 year	1.00	(Reference)	0.74	(0.61–0.91)
f/u 8 year	1.00	(Reference)	0.69	(0.55–0.85)

f/u: follow-up time; CI: confidence interval.
The model was adjusted for sociodemographic characteristics, comorbidities, length of stay and death.

DISCUSSION

These findings suggest that post-stroke rehabilitation lowers the incidence of dementia in patients with ischaemic stroke. In addition, stroke rehabilitation was found to be associated with improvement in neuropsychiatric conditions in people with stroke.

Table IV. *Cox proportional hazard models measured crude and adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of dementia by associated factors*

Variable	Univariate HR (95% CI)	Multiple model 1 HR (95% CI)	Multiple model 2 HR (95% CI)
Rehabilitation			
No	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	0.71 (0.58–0.87)	0.73 (0.59–0.89)	0.73 (0.60–0.89)
Sex			
Female	1.32 (1.12–1.56)	1.20 (1.02–1.42)	1.27 (1.07–1.50)
Male	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age			
20–44 years	1.00 (ref)	1.00 (ref)	1.00 (ref)
45–64 years	2.71 (1.19–6.16)	2.19 (0.96–4.99)	2.16 (0.95–4.92)
65–79 years	7.14 (3.18–16.0)	5.28 (2.34–11.9)	4.56 (2.02–10.3)
≥80	13.9 (6.11–31.8)	9.75 (4.25–22.4)	7.84 (3.41–18.0)
Occupation			
White-collar	1.00 (ref)	1.00 (ref)	1.00 (ref)
Blue-collar	0.93 (0.75–1.14)	1.15 (0.90–1.47)	1.16 (0.90–1.48)
Others	1.34 (1.08–1.67)	1.10 (0.88–1.38)	1.11 (0.89–1.38)
Urbanization			
Low	1.15 (0.82–1.61)	1.32 (0.93–1.87)	1.23 (0.87–1.74)
Moderate	0.93 (0.78–1.10)	1.02 (0.84–1.24)	1.00 (0.87–1.22)
High	1.00 (ref)	1.00 (ref)	1.00 (ref)
Income			
<15,000 NTD	2.03 (1.67–2.46)	1.95 (1.52–2.49)	1.81 (1.42–2.32)
≥15,000 NTD	1.00 (ref)	1.00 (ref)	1.00 (ref)
Hospital levels			
Medical centres	1.00 (ref)	1.00 (ref)	1.00 (ref)
Regional hospitals	1.34 (1.10–1.63)	1.29 (1.06–1.57)	1.28 (1.05–1.56)
Community hospitals	1.13 (0.90–1.41)	1.11 (0.90–1.39)	1.05 (0.83–1.32)
Parkinson's disease			
No	1.00 (ref)		1.00 (ref)
Yes	2.13 (1.73–2.62)		1.60 (1.29–1.98)

Model 1 adjusted sociodemographic characteristics. Model 2 adjusted sociodemographic characteristics, significant comorbidity, length of stay and death.
NTD: New Taiwan Dollar.

Age is the most common risk factor, with the likelihood of dementia increasing from approximately 0.1% in subjects aged less than 65 years to 1.0% in elderly people. In people over the age of 85 years, however, the incidence increases to nearly 25% (1). Similarly, our results revealed that the incidence of dementia increased with age in both the rehabilitation and non-rehabilitation groups. However, the proportion of patients >80 years of age was only slightly lower in the rehabilitation group than in the non-rehabilitation group. This may be because patients ≥80 years of age tend to have a greater number of comorbidities than younger patients, thereby making it difficult for them to participate in a vigorous rehabilitation programme. In addition to older age, female sex and low income were associated with increased risk of dementia. These observations are consistent with findings reported by Verdelho et al. (11) and Ivan et al. (16), who found that dementia risk was elevated in women and subjects who were older and had lower levels of education. A possible explanation for the findings may be that the occurrence of stroke had a substantial deleterious impact on cognition in groups of individuals who were not at a lower baseline risk for dementia in the general population, including males, individuals younger than 80 years of age, and those who had completed a high-school education (17).

Parkinson's disease is a disabling, progressive condition that is predominantly thought of as a movement disorder. Cognitive impairment has been associated with Parkinson's disease (18, 19). Cognitive changes are not evident until the later stages of the disease. The disorder is often complicated by a spectrum of cognitive deficits that range from isolated cognitive impairment to severe dementia. The clinical manifestations of Parkinson's disease dementia generally overlap other disorders (18, 19). In our study, we found that stroke patients with Parkinson's disease were also at higher risk of dementia than stroke patients without Parkinson's disease. Further research is needed to determine whether the accelerated development of dementia resulted from the combined effect of stroke and Parkinson's disease.

Dementia is a common cause of cognitive decline. Vascular risk factors, transient ischaemic attacks, silent and clinically evident strokes, and ischaemic changes on brain imaging studies are all associated with the development of dementia. Prevention of post-stroke dementia involves the treatment of risk factors and the same measures used to prevent stroke (20). Physical activity has well-known beneficial effects for many chronic diseases, such as ischaemic heart disease, stroke, and diabetes. However, evidence showing that physical activity can prevent or delay cognitive decline is controversial. The results of some longitudinal studies and randomized trials have suggested that physical exercise enhances cognitive function in older adults (9, 20–22), whereas other studies could not demonstrate the benefit of physical exercise in preserving cognitive function (23). The results of the present study show that the protective effect of rehabilitation measured from multiple Cox proportional regression analysis was similar to that from univariate analyses. The results indicate that the comorbidities analysed in this study did not significantly influence the effect of stroke rehabilitation on reduction of dementia risk. We therefore propose that stroke rehabilitation plays an essential role in preventing post-stroke dementia.

This study has several limitations. First, we did not exclude baseline comorbidities, such as hypertension, diabetes mellitus and Parkinson's disease; factors that are associated with the development of dementia. However, all of those comorbidities were more prevalent in the rehabilitation cohort than in the non-rehabilitation cohort. Therefore, the beneficial effect of rehabilitation may have been underestimated in this study. Secondly, stroke and dementia may share a genetic component (23–25). However, confounding of genetic factors was not likely to occur because there is no reason that the genetic factors ought to differ between patients being selected to receive or not to receive rehabilitation therapy. In addition, stroke recurrence during the study period might increase the risk for incident dementia; however, further analysis revealed that there were fewer cases of recurrence in the rehabilitation cohort than in the non-rehabilitation cohort. Therefore, stroke recurrence after rehabilitation is not likely to be a confounding factor (11). In addition, undiagnosed dementia or cognitive impairment or dementia occurring immediately after stroke may have affected the provision of stroke rehabilitation, thereby biasing our study. The Kaplan–Meier analysis shows that the incidence rate is much higher in the non-rehabilitation group in the first year, and that the rates then become more similar in subsequent years. We performed a further analysis to estimate the annual HR during the follow-up period. The HR demonstrates a strong protective effect from rehabilitation in the first year and then protective association become more weaker, to near 0.70, in the subsequent 5^{th}–8^{th} years. Finally, we did not evaluate differences in stroke severity between patients who received and those who did not receive rehabilitation services. We adjusted for comorbidities in the regression models in an attempt to deal with confounding due to differences in health conditions coexisting with stroke between the two groups.

In summary, the present study used a large population-based representative data to investigate the risk of dementia for patients with stroke. We found that stroke rehabilitation is associated with a reduction in dementia risk. Effective dementia prevention strategies would have large public health implications through improving quality of life and reducing economic cost and social burden. Further research, with more complete information, including rehabilitation status, rehabilitation levels and other treatments, is required in order to clarify the dementia outcomes. A trial of stroke rehabilitation may be needed.

ACKNOWLEDGEMENTS

This study was supported partly by the National Science Council, Executive Yuan, Taiwan, Republic of China (grant number NSC 97-2625-M-039-003), China Medical University Hospital (grant number 1MS1, DMR-98-067) and Taiwan Department of Health Clinical Trial and Research Center for Excellence (grant number DOH99-TD-B-111-004).

REFERENCES

1. Zhu L, Fratiglioni L, Guo Z, Aguero-Torres H, Winblad B, Viitanen M. Associated of stroke with dementia, cognitive impairment, and

functional disability in the very old: a population-based study. Stroke 1998; 29: 2094–2099.
2. Zhu L, Fratiglioni L, Guo Z, Winblad B, Viitanen M. Incidence of stroke in relation to cognitive function and dementia in the Kungsholmen Project. Neurology 2000; 54: 2103–2107.
3. Savva GM, Stephan BCM. Epidemiological studies of the effect of stroke on incident dementia: a systematic review. Stroke 2010; 41: e41–e46.
4. Leys D, Henon H, Mackowiak-Cordoliani MA, Pasquier F. Post-stroke dementia. Lancet Neurol 2005; 4: 752–759.
5. Desmond DW, Moroney JT, Sano M, Stern Y. Incidence of dementia after ischemic stroke: results of a longitudinal study. Stroke 2002; 33: 2254–2262.
6. Melkas S, Okasala NK, Jokinen H, Pohjasvaara T, Vataja R, Oksala A, et al. Poststroke dementia predicts poor survival in long-term follow-up: influence of prestroke cognitive decline and previous stroke. J Neurol Neurosurg Psychiatry 2009; 80: 865–870.
7. Kemoun G, Thibaud M, Roumagne N, Carette P, Albinet C, Toussaint L, et al. Effects of a physical training programme on cognitive function and walking efficiency in elderly persons with dementia. Dement Geriatr Cogn Disord 2010; 29: 109–114.
8. Etgen T, Sander D, Huntqeburth U, Poppert H, Forsti H, Bickel H. Physical activity and incident cognitive impairment in elderly persons: the INVADE study. Arch Intern Med 2010; 170: 186–193.
9. Verghese J, Lipton RB, Katz MJ, Hall CB, Derby CA, Kuslansky G, et al. Leisure activities and the risk of dementia in the elderly. N Engl J Med 2003; 348: 2508–2516.
10. Gordon NF, Gulanick M, Costa F, Fletcher G, Franklin BA, Roth EJ, et al. Physical activity and exercise recommendations for stroke survivors. Circulation 2004; 109: 2031–2041.
11. Verdelho A, Hénon H, Lebert F, Pasquier F, Leys D. Depressive symptoms after stroke and relationship with dementia: a three-year follow-up study. Neurology 2004; 62: 905–911.
12. Jorm AF, Korten AE, Henderson AS. The prevalence of dementia: a quantitative integration of the literature. Acta Psychiatr Scand 1987; 76: 465–479.
13. Liu HC, Lin KN, Teng EL, Wang SJ, Fuh JL, Guo NW, et al. Prevalence and subtypes of dementia in Taiwan: a community survey of 5297 individuals. J Am Geriatr Soc 1995; 43: 144–149.
14. Liu CK, Lin RT, Chen YF, Tai CT, Yen YY, Howng SL. Prevalence of dementia in an urban area in Taiwan. J Formos Med Assoc 1996; 95: 762–768.
15. Chen HF, Lee SP, Li CY. Sex differences in the incidence of hemorrhagic and ischemic stroke among diabetics in Taiwan. J Womens Health (Larchmt) 2009; 18: 647–654.
16. Ivan CS, Seshadri S, Beiser A, Au R, Kase CS, Kelly-Hayes M, et al. Dementia after stroke: the Framingham study. Stroke 2004; 35: 1264–1269.
17. Kokmen E, Whisnant JP, O'Fallon WM, Chu CP, Beard CM. Dementia after ischemic stroke: a population-based study in Rochester, Minnesota (1960–1984). Neurology 1996; 46: 154–159.
18. Weintraub D, Comella CL, Horn S. Parkinson's disease – part 3: neuropsychiatric symptoms. Am J Manag Care 2008; 14: S59–S69.
19. Graham JE, Rockwood K, Beattie BL, Eastwood R, Gauthier S, Tuokko H, et al. Prevalence and severity of cognitive impairment with and without dementia in an elderly population. Lancet 1997; 349: 1793–1796.
20. Luck T, Riedel-Heller SG, Kaduszkiewicz H, Bickel H, Jessen F, Pentzek M, et al. Mild cognitive impairment in general practice: age-specific prevalence and correlate results from the German study on ageing, cognition and dementia in primary care patients (AgeCoDe). Dement Geriatr Cogn Disord 2007; 24: 307–316.
21. Abbott RD, White LR, Ross GW, Masaki KH, Curb JD, Petrovitch H. Walking and dementia in physically capable elderly men. JAMA 2004; 292: 1447–1453.
22. Weuve J, Kang JH, Manson JE, Breteler MM, Ware JH, Grodstein F. Physical activity, including walking, and cognitive function in older women. JAMA 2004; 292: 1454–1461.
23. Slooter AJC, Tang MX, van Duijn CM, Stern Y, Ott A, Bell K, et al. Apolipoprotein E-4 and the risk of dementia with stroke: a population-based investigation. JAMA 1997; 277: 818–821.
24. Joutel A, Corpechot C, Ducros A, Vahedi K, Chabriat H, Mouton P, et al. Notch3 mutations in CADASIL, a hereditary adult-onset condition causing stroke and dementia. Nature 1996; 383: 707–710.
25. Desmond DW, Moroney JT, Lynch T, Chan S, Chin SS, Shungu DC, et al. CADASIL in a North American family: clinical, pathologic, and radiologic findings. Neurology 1998; 5: 844–849.