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Post-stroke dementia is associated with increased subsequent all-cause mortality: A population-based cohort study

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HIGHLIGHTS

- The subsequent mortality rate in patients with PSD is increased compared to those without.
- Average hospital day and frequency of medical visit would be increased in patients with PSD.
- Our findings provide crucial information for clinicians and the government to improve survival of patients after stroke.

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ABSTRACT

Background and aims: We aimed to determine whether patients with post-stroke dementia (PSD) have increased mortality risk in Taiwan.

Methods: We included ≥40-year-old patients who received a stroke diagnosis between 2000 and 2012 from a subset of the National Health Insurance Research Database of Taiwan. These patients were divided into PSD (International Classification of Diseases, Ninth Revision, Clinical Modification codes 290, 294.1, and 331.0) and post-stroke non-dementia (PSN) cohorts. Furthermore, we propensity score (PS) matched the PSD and PSN groups. PS was calculated through logistic regression to estimate the probability of stroke status assignment given the baseline variables, namely age, sex, and comorbidity. We calculated the adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for death in the PSD and PSN cohorts after adjustments for age, sex, and comorbidities.

Results: Overall incidence density rates of death were 148.7 and 106.7 per 1,000 person-years in the PSD and PSN PS-matched cohorts, with the aHR of 1.42 (95% CI = 1.34–1.50). Average hospital days increased by 9.03 days and frequency of medical visits increased by 15.8 times per year in the PSD cohort compared with the PSN cohort.

Conclusions: The subsequent mortality rate in patients with PSD is increased compared with those without PSD. Moreover, the average hospital days and frequency of medical visit are increased in patients with PSD. Our findings provide crucial information for clinicians and the government to improve survival of patients after stroke.

1. Introduction

Stroke is a serious sudden-onset neurovascular disorder with a global prevalence. The treatment priority for both ischemic and hemorrhagic strokes is to improve acute-stage and long-term-survival outcomes. Patients who survive the acute stage of a stroke usually have

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disability or restricted ability to perform daily activities and thereby have a reduced quality of life on the long term. To our knowledge, stroke is the most common cause of disability in the adult population [1–3]. Compared with patients in the developed Western countries, those in the developing Asian countries are more tolerant to their disability and daily-life dependency owing to certain ethnic and cultural differences [4,5].

The prevalence of dementia, a common neurological degenerative and debilitating disorder, gradually increases with age. The pathogeneses of dementia and stroke involve some common vascular risk factors [6–8]. Patients who survive a stroke may experience post-stroke dementia (PSD), which may be a predisposing factor for another stroke episode [9]. PSD prevalence is 10% in patients surviving the first stroke, and more than one-third of patients experiencing recurrent strokes develop PSD [10]. The strong association between PSD and multiple strokes indicates their common pathogenesis: the central causal role of stroke itself.

Here, we further investigated the correlated risk factors and mortality risk in Taiwanese patients with PSD and without PSD (denoted as "post-stroke non-dementia [PSN]") to develop future prevention strategies for stroke recurrence and reduce the burden of post-stroke care, particularly in patients with PSD. The mortality rates of patients with PSD and PSN may differ from those of the general population. We used a nationwide population-based database to investigate the subsequent mortality rates in the two groups of patients. Therefore, this study investigated the influence of PSD on long-term survival outcome after a stroke. The findings of this study may aid the future development and implementation of effective treatment strategies in Taiwan and other developing Asian countries.

2. Materials and methods

2.1. Data source

We conducted a population-based retrospective cohort study using the Longitudinal Health Insurance Database (LHID) of citizens enrolled in the Taiwan National Health Insurance (NHI) program. This NHI program began in March 1995 and has enrolled more than 99% of the 23 million citizens living in Taiwan [11]. The details of the LHID and NHI program have been given in previous studies [12,13]. This study was approved by the Research Ethics Committee of China Medical University and Hospital in Taiwan (CMUH104-REC2-115-CR2).

2.2. Study population

Patients aged ≥40 years with a diagnosis of stroke (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 430–438) were included in the total stroke cohort. The patients in the total stroke cohort were further divided into two cohorts based on their dementia status: the PSD group included patients who had new-onset dementia (ICD-9-CM codes 290, 294.1, and 331.0) after a stroke between January 1, 2000, and December 31, 2012; the PSN group included patients who did not receive a dementia diagnosis after stroke during follow-up. Patients aged < 40 years, having a dementia diagnosis before the stroke, or missing information for age or sex were excluded. The date of the first PSD diagnosis was defined as the index date, and the index date for the PSN group was a random month, day, and index year after the stroke diagnosis. The index date in the PSN group was assigned as the date of PSD cases. Furthermore, we propensity score (PS) matched PSD and PSN groups. This PS was calculated using a logistic regression to estimate the probability of the stroke status assignment given the baseline variables, namely age, sex, and comorbidities of chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), diabetes, hypertension, hyperlipidemia, recurrent stroke, aspiration pneumonia, and fall-related injury in the study cohorts.

2.3. Outcome definition

Follow-up period began on the index date and continued until death, withdrawal from the NHI program, or the end of December 31, 2013.

2.4. Statistical analysis

The baseline distributions of demographic characteristics and comorbidities in the PSD and PSN cohorts were compared (regardless of whether PS was matched). The categorical and continuous variables (i.e., baseline characteristics) were analyzed using chi-square and *t* tests. The Kaplan–Meier method was used to estimate the cumulative incidence of death between the two cohorts (PSD and PSN) with PS matching, and the significance was determined based on a log-rank test.

The incidence densities of death were calculated overall and stratified by age, sex, and comorbidity between the PSD and PSN cohorts. Univariable and multivariable Cox proportional hazards models were performed to estimate the hazard ratio (HRs) and 95% confidence intervals (CIs) for death associated with the PSD cohort and compared with the PSN cohort. The multivariable models were adjusted for age, sex, COPD, CAD, diabetes, hypertension, hyperlipidemia, recurrent stroke, aspiration pneumonia, and fall-related injury. Multivariable regression analysis was used to estimate the average hospital days per year for all-cause admission and the frequency of all-cause medical visits per year; their association with related risk factors between the two cohorts with PS matching was evaluated using the stepwise selection method. All statistical analyses were performed using SAS statistical software (version 9.4 for Windows; SAS Institute, Inc., Cary, NC, USA). A two-tailed p of < 0.05 was considered statistically significant.

2.5. Data availability statement

The dataset used in this study is held by the Taiwan Ministry of Health and Welfare (MOHW). The MOHW must approve our application to access this data. Any researcher interested in accessing this dataset can submit an application form to the MOHW requesting access. For further assistance, please contact the staff of MOHW (Taiwan MOHW, No.488, Sec. 6, Zhongxiao E. Rd., Nangang Dist., Taipei City 115, Taiwan (R.O.C.); Tel.: ?2-8590-6848; E-mail: stcarolwu@mohw.gov.tw). All relevant data are included within the paper.

2.6. Ethics approval and consent to participate

The National Health Insurance Research Database (NHIRD) encrypts patient personal information to protect privacy and provides researchers with anonymous identification numbers associated with relevant claims information, including sex, date of birth, medical services received, and prescriptions. Therefore, patient consent is not required to access the NHIRD. This study was approved to fulfill the condition for exemption by the Institutional Review Board (IRB) of China Medical University (CMUH104-REC2-115-CR3). The IRB also specifically waived the consent requirement.

3. Results

Table 1 lists the baseline demographic factors and comorbidities of the patients in the two cohorts with and without PS matching. Compared with the PSN cohort (mean age, 68.3 years), patients with PSD had a higher mean age (76.4 years) in the non-matched cohorts. In the two cohorts, slightly more than one-half of the cohorts comprised men. Comorbidities of COPD, CAD, diabetes, hypertension, hyperlipidemia, aspiration pneumonia, and fall-related injury were more prevalent in the PSD cohort than in the PSN cohort (all $p < 0.001$; Table 1). In the PS-matched cohorts, the distribution of age was similar, and ≥75 years patients were predominant (approximately 61% of patients were aged

Table 1
Distribution of age, sex, and comorbidity in the stroke and comparison cohorts with and without propensity score matching.

	Propensity score matched									
	Post-stroke non-dementia N = 11165		Post-stroke dementia N = 4441		*p*-value[b]	Post-stroke non-dementia N = 4411		Post-stroke dementia N = 4411		*p*-value[b]
	n	%	n	%		n	%	n	%	
Age, year					< 0.001					0.90
40-64	4303	38.5	503	11.3		490	11.1	503	11.4	
65-74	3281	29.4	1216	27.4		1215	27.5	1216	27.6	
≥75	3581	32.1	2722	61.3		2706	61.4	2692	61.0	
Mean (SD)[a]	68.3	11.9	76.4	9.29	< 0.001					
Sex					0.001					0.36
Female	4765	42.7	2021	45.5		1962	44.5	2005	45.5	
Male	6400	57.3	2420	54.5		2449	55.5	2406	54.6	
Comorbidity										
Chronic obstructive pulmonary disease	3109	27.9	1851	41.7	< 0.001	1823	41.3	1824	41.4	0.98
Coronary artery disease	5191	46.5	2445	55.1	< 0.001	2410	54.6	2425	55.0	0.75
Diabetes	3103	27.8	1363	30.7	< 0.001	1363	30.9	1356	30.7	0.87
Hypertension	9688	86.8	4079	91.9	< 0.001	4079	92.5	4052	91.9	0.28
Hyperlipidemia	5108	45.8	1813	40.8	< 0.001	1816	41.2	1809	41.0	0.88
Recurrent stroke	4930	44.2	1988	44.8	0.49	2075	47.0	1986	45.0	0.06
Aspiration pneumonia	325	2.91	262	5.90	< 0.001	185	4.19	261	5.92	0.001
Fall-related injury	43	0.39	37	0.83	< 0.001	19	0.43	36	0.82	0.36

Chi-square test
[a] *t*-test.
[b] Total stroke *vs*. comparison.

≥75 years). No significant differences were observed for age, sex, and comorbidity between the PSD and PS-matched PSN cohorts (Table 1).

The Kaplan–Meier analysis of a 12-year follow-up revealed a significant difference in the cumulative incidence of mortality between the PSD and PS-matched PSN cohorts. The overall incidence density rates of death were 149.7 and 67.2 per 1,000 person-years in the PSD and non-PS-matched PSN cohorts. The adjusted HR (aHR) of death was 1.42 (95% CI = 1.34–1.50) in the PSD cohort relative to the PSN cohort. Further PS-matched analysis revealed that the overall incidence density rates of death were 148.7 and 106.7 per 1,000 person-years in the PSD and PSN cohorts, with the aHR of 1.42 (95% CI = 1.34–1.50; Table 2).

When we stratified groups based on age, sex, and comorbidity, regardless of whether PS was matching, we observed that both PSD cohorts exhibited significantly higher mortality risks than did the PSN cohorts (Table 3).

Table 4 presents the results of the stepwise regression analysis for evaluating the risk factors associated with average hospital days per year between the two PS-matched cohorts. Average hospital days in the PSD cohort increased by 9.03 days compared with those in the PSN cohort. The comorbidities of COPD, CAD, hypertension, hyperlipidemia, and diabetes and the male sex were the following positive predictors of average hospital days of all-cause admission per year.

Table 5 illustrates the stepwise regression analysis in evaluating the risk factors for the frequency of medical visits per year between the two PS-matched cohorts. Aspiration pneumonia and PSD increased 22.1 and 15.8 times all-cause medical visit frequency. COPD, male sex, recurrent stroke, and aging (increase in every 1 year) were the following positive predictors of the frequency of all-cause medical visits per year.

4. Discussion

Taiwanese patients with PSD aged ≥40 years demonstrated a higher subsequent all-cause mortality risk than patients without PSD, regardless of the patients' sex and comorbidity status. In this study, we enrolled patients with both first-time and recurrent stroke to estimate the correlation of dementia development with overall post-stroke survival outcome. We noted that PSD development - often noted in patients with stroke - can be a specific predictor for poor long-term survival outcomes. Moreover, PSD highly increases the average hospital days and frequency of medical visits per year in post-stroke long-term care. All these post-stroke factors directly increase the burden of patient care on families, societies, and the government. PSD is an essential monitoring marker in health care systems in Taiwan and other developing Asian countries.

Table 2
Overall incidence (per 1,000 person-years) and hazard ratio of mortality with and without PS matching.

	Propensity score matched			
	Post-stroke non-dementia	Post-stroke dementia	Post-stroke non-dementia	Post-stroke dementia
	(N = 11165)	(N = 4441)	(N = 4411)	(N = 4411)
Mortality				
Person-years	54106	17305	19237	17225
Follow-up time (y)	4.85 ± 3.30	3.90 ± 2.97	4.36 ± 3.17	3.91 ± 2.97
No. of event	3637	2591	2053	2562
Incidence rate	67.2	149.7	106.7	148.7
cHR (95% CI)	1(Reference)	2.21 (2.10, 2.32)***	1(Reference)	1.39 (1.31, 1.47)***
aHR[a] (95% CI)[a]	1(Reference)	1.42 (1.34, 1.50)***	1(Reference)	1.42 (1.34, 1.50)***

[a] Adjusted for age, sex, chronic obstructive pulmonary disease, coronary artery disease, diabetes, hypertension, hyperlipidemia, recurrent stroke, aspiration pneumonia, and fall-related injury. ***$p < 0.001$.

Table 3
Incidence and hazard ratio for mortality stratified by age, sex, and comorbidity for patients with stroke compared with those without stroke or dementia.

	Propensity score matched											
	Post-stroke non-dementia N = 11165		Post-stroke dementia N = 4441				Post-stroke non-dementia N = 4411		Post-stroke dementia N = 4411			
	Event no.	rate	Event no.	rate	Crude HR (95% CI)	Adjusted HR[a] (95% CI)	Event no.	rate	Event no.	rate	Crude HR (95% CI)	Adjusted HR[a] (95% CI)
Age, year												
40-64	736	30.3	169	62.0	2.04 (1.73, 2.41)***	1.55 (1.31, 1.84)***	114	41.6	169	62.0	1.48 (1.17, 1.88)**	1.49 (1.17, 1.89)***
65-74	1086	65.2	660	120.5	1.86 (1.69, 2.05)***	1.56 (1.41, 1.72)***	480	74.0	660	120.5	1.64 (1.46, 1.85)***	1.57 (1.40, 1.77)***
≥75	1815	137.8	1762	193.7	1.41 (1.32, 1.50)***	1.35 (1.27, 1.45)***	1459	145.8	1733	192.1	1.32 (1.23, 1.42)***	1.34 (1.24, 1.43)***
Sex												
Female	1373	57.6	1108	133.3	2.30 (2.13, 2.49)***	1.43 (1.32, 1.55)***	820	92.0	1093	132.3	1.44 (1.31, 1.57)***	1.42 (1.29, 1.55)***
Male	2264	74.8	1483	164.9	2.18 (2.04, 2.33)***	1.48 (1.38, 1.58)***	1233	119.4	1469	163.9	1.36 (1.26, 1.47)***	1.41 (1.31, 1.52)***
Comorbidity												
None	83	28.3	33	141.2	4.62 (3.08, 6.94)***	2.17 (1.39, 3.37)***	20	53.6	32	137.0	2.30 (1.31, 4.02)***	2.23 (1.27, 3.91)**
With any one	3554	69.5	2558	149.8	2.14 (2.04, 2.25)***	1.51 (1.44, 1.60)***	2033	107.8	2530	148.9	1.38 (1.30, 1.46)***	1.40 (1.32, 1.49)***

Rate, per 1,000 person-years; HR, relative hazard ratio.
**$p < 0.01$, ***$p < 0.001$.
[a] Adjusted for age, sex, chronic obstructive pulmonary disease, coronary artery disease, diabetes, hypertension, hyperlipidemia, recurrent stroke, aspiration pneumonia, and fall-related injury.

In this study, 4,441 (28.5%) of the 15,606 patients developed PSD after stroke. When considering the known mortality rate in 2013 was 435.3 per 100,000 of the general population according to the Taiwan NHI database [14], the mortality risks in the PSN and PSD cohorts were evidently increased by 106.7 and 148.7 mortality events per 1,000 person-years in post-stroke patients aged ≥40 years in this study. Several researchers have studied PSD in developed Western countries for more than a decade and have recognized PSD as a negative marker for the long-term survival after a stroke [15–18]. The major risk factors for PSD and subsequent mortality are stroke severity and advanced age. In general, various cerebrovascular injuries from hypoxia, hypoperfusion, metabolic dysfunction, and altered cerebrovascular hemodynamics lead to dementia development [19]. The developing pathology may take years before manifesting its cognitive, behavioral, and functional impairments. Several postmortem studies including elderly people have reported silently mixed cerebrovascular and neuropathological findings before a definite diagnosis of dementia or stroke was made [20,21]. Macrovasculature and microvasculature changes and pathological remodeling after a stroke may further disrupt blood vessel integrity and blood–brain barrier permeability, thus resulting in hypoxia, oxidative stress, mitochondrial bioenergetics, neuroinflammation, and neurodegeneration. Although the post-stroke changes in brain histopathophysiology may not totally be reflected in clinical symptoms of cerebral hypoperfusion and neuronal function. Therefore, PSD might be considered a combination of vascular lesions, Alzheimer pathology, and white-matter changes developed even before the stroke episode.

Although the confounding effects of ethnic, cultural, and socioeconomic differences in the developed Western countries are involved, our study revealed a similar prevalence of PSD and its negative effects of long-term post-stroke survival in the developing Asian society of Taiwan. Furthermore, aspiration pneumonia, PSD, COPD, male sex, recurrent stroke, and advanced age were all positive predictors of frequency of medical visits for patients after stroke in our study cohorts. We also observed some common trends between the increase in average all-cause hospitalization per year and higher mortality risks in the cohorts. PSD considerably increased medical visits, average hospital days per year, and subsequent post-stroke mortality. However, among the various comorbidities in our patients, pulmonary disorders such as aspiration pneumonia and COPD could be considered the second leading factor to increase subsequent hospitalization and frequency of medical visit in post-stroke patients. Thus, in Taiwan, once a patient experiences a stroke, the pulmonary conditions play more critical roles for the long-term care than the cardiovascular factors do. In addition, although women are considered to use more medical services and spend more on health care than men do [22,23], our results revealed that male and female post-stroke patients in Taiwan have nearly the same mortality risk even if male post-stroke patients consumed more medical services in medical visit and admission per year. Further research is required to confirm this hypothesis in Taiwan and evaluate its applicability globally.

Because this study included a nationwide, population-based sample with little risk of recall and selection bias, our findings are accurate for Taiwan and can be used as a reference for other developing Asian countries with a heritage similar to that of Taiwan. However, this study has several limitations. First, we could not directly contact the patients because their identities are anonymized in the LHID. Therefore, the study design did not include details regarding the type and severity score of stroke, the psychological burden and severity score of

Table 4
Stepwise regression analysis for average hospital days of all-cause admission per year with propensity score matching.

Variable	Parameter estimate	Standard error	95% CI
Intercept	20.3	1.11	(18.1, 22.5)***
Post-stroke dementia *vs.* post-stroke non-dementia	9.03	0.55	(7.95, 10.1)***
Chronic obstructive pulmonary disease	7.85	0.57	(6.73, 8.97)***
Coronary artery disease	6.22	0.57	(5.10, 7.35)***
Hyperlipidemia	4.42	0.58	(3.28, 5.56)***
Diabetes	4.31	0.61	(3.11, 5.51)***
Hypertension	5.12	1.04	(3.08, 7.17)***
Sex (male *vs.* female)	2.26	0.56	(1.16, 3.36)***

***$p < 0.001$.

Table 5
Stepwise regression analysis for the frequency of all-cause medical visits per year with propensity score matching.

Variable	Parameter estimate	Standard error	95% CI
Intercept	−32.7	5.36	(-43.3, −22.2)***
Post-stroke dementia *vs.* post-stroke non-dementia	15.8	1.11	(13.7, 18.0)***
Chronic obstructive pulmonary disease	11.1	1.16	(8.85, 13.4)***
Aspiration pneumonia	22.1	2.56	(17.1, 27.1)***
Age (every one year)	0.57	0.06	(0.45, 0.70)***
Sex (male *vs.* female)	7.35	1.14	(5.10, 9.59)***
Recurrent stroke	6.05	1.15	(3.81, 8.30)***
Hyperlipidemia	−4.90	1.15	(-7.16, −2.65)***
Hypertension	−2.39	2.09	(-6.50, 1.71)

***$p < 0.001$.

dementia, and how the stroke and PSD were treated. Second, our dataset only included post-stroke all-cause mortality of patients who died at inpatient facilities due to the limitations of the NHI database. The individual mortality causes and deaths occurring outside the hospital were not included in the scope of our study, which may have introduced some possibility of estimation bias into the results. Third, although the NHI administration performs thorough quarterly reviews to ensure that the files are accurate and false claims are heavily sanctioned, miscoding may have occurred in the LHID. Considering the aforementioned limitations, our results did indicate that the sample size was sufficient to statistically demonstrate the increased subsequent mortality risk in patients with PSD.

4.1. Conclusions

The subsequent mortality rate was higher in patients with PSD than in patients without PSD. Moreover, average hospital day and frequency of medical visit are increased in the patients with PSD. Our findings provide crucial information for clinicians and the government to improve survival of patients after stroke.

Conflicts of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Author contributions

Conception/Design: Tomor Harnod, Chia-Hung Kao; provision of study material and patients: Chia-Hung Kao; collection and assembly of data: all authors; data analysis and interpretation: all authors; manuscript writing: all authors; final approval of manuscript: all authors.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2019.03.007.

References

[1] S. Howard-Wilsher, L. Irvine, H. Fan, T. Shakespeare, M. Suhrcke, S. Horton, et al., Systematic overview of economic evaluations of health-related rehabilitation, Disabil Health J 9 (2016) 11–25.
[2] F. Di Rienzo, C. Collet, N. Hoyek, A. Guillot, Impact of neurologic deficits on motor imagery: a systematic review of clinical evaluations, Neuropsychol. Rev. 24 (2014) 116–147.
[3] V.Y. Ma, L. Chan, K.J. Carruthers, Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain, Arch. Phys. Med. Rehabil. 95 (2014) 986–995.
[4] K.L. Chen, M.H. Tseng, F.C. Hu, C.L. Koh, Pediatric evaluation of disability inventory: a cross-cultural comparison of daily function between Taiwanese and American children, Res. Dev. Disabil. 31 (2010) 1590–1600.
[5] P.M. Greenfield, L.K. Suzuki, Culture and human development: implications for parenting, education, pediatrics, and mental health, fifth ed., in: W. Damon, I.E. Sigel, K.A. Renninger (Eds.), Handbook of Child Psychology: Child Psychology in Practice, vol. 4, John Wiley & Sons Inc, Hoboken, NJ, 1998, pp. 1059–1109.
[6] H. Gardener, C.B. Wright, T. Rundek, R.L. Sacco, Brain health and shared risk factors for dementia and stroke, Nat. Rev. Neurol. 11 (2015) 651–657.
[7] F.C. Goldstein, A.V. Ashley, Y. Endeshaw, J. Hanfelt, J.J. Lah, A.I. Levey, Effects of hypertension and hypercholesterolemia on cognitive functioning in patients with Alzheimer disease, Alzheimer Dis. Assoc. Disord 22 (2008) 336–342.
[8] A.C. Nooyens, B.M. van Gelder, W.M. Verschuren, Smoking and cognitive decline among middle-aged men and women: the Doetinchem Cohort Study, Am. J. Public Health 98 (2008) 2244–2250.
[9] G. Sibolt, S. Curtze, S. Melkas, J. Putaala, T. Pohjasvaara, M. Kaste, et al., Poststroke dementia is associated with recurrent ischemic stroke, J. Neurol. Neurosurg. Psychiatry 84 (2013) 722–726.
[10] S.T. Pendlebury, P.M. Rothwell, Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis, Lancet Neurol. 8 (2009) 1006–1018.
[11] N.H.I.R. Database, Taiwan (cited in 2017), http://nhird.nhri.org.tw/en/index.html.
[12] S.Y. Lin, C.L. Lin, C.C. Lin, I.K. Wang, W.H. Hsu, C.H. Kao, Risk of acute coronary syndrome and peripheral arterial disease in chronic liver disease and cirrhosis: a nationwide population-based study, Atherosclerosis 270 (2018) 154–159.
[13] H.M. Li, F.C. Sung, S.C. Li, Y.K. Huang, Y. Chang, C.C. Chang, et al., The effect of antibiotic prophylaxis for acute pelvic inflammatory disease after hysterosalpingography: a retrospective cohort study, Curr. Med. Res. Opin. 10 (2018) 1–6.
[14] Ministry of Health and Welfare, Taiwan, https://www.mohw.gov.tw/lp-3267-2.html.
[15] S. Melkas, N.K. Oksala, H. Jokinen, T. Pohjasvaara, R. Vataja, A. Oksala, et al., Poststroke dementia predicts poor survival in long-term follow-up: influence of prestroke cognitive decline and previous stroke, J. Neurol. Neurosurg. Psychiatry 80 (2009) 865–870.
[16] S. Melkas, J.V. Laurila, R. Vataja, N. Oksala, H. Jokinen, T. Pohjasvaara, et al., Post-stroke delirium in relation to dementia and long-term mortality, Int. J. Geriatr. Psychiatry 27 (2012) 401–408.
[17] D. Leys, H. Hénon, M.A. Mackowiak-Cordoliani, F. Pasquier, Poststroke dementia, Lancet Neurol. 4 (2005) 752–759.
[18] S. Moulin, J. Labreuche, S. Bombois, C. Rossi, G. Boulouis, H. Hénon, et al., Dementia risk after spontaneous intracerebral haemorrhage: a prospective cohort study, Lancet Neurol. 15 (2016) 820–829.
[19] L. Raz, J. Knoefel, K. Bhaskar, The neuropathology and cerebrovascular mechanisms of dementia, J. Cereb. Blood Flow Metab. 36 (2016) 172–186.
[20] K.A. Jellinger, J. Attems, Neuropathology and general autopsy findings in non-demented aged subjects, Clin. Neuropathol. 31 (2012) 87–98.
[21] J.A. Sonnen, K. Santa Cruz, L.S. Hemmy, R. Woltjer, J.B. Leverenz, K.S. Montine, et al., Ecology of the aging human brain, Arch. Neurol. 68 (2011) 1049–1056.
[22] S. Kaur, K.M. Stechuchak, C.J. Coffman, K.D. Allen, L.A. Bastian, Gender differences in health care utilization among veterans with chronic pain, J. Gen. Intern. Med. 22 (2007) 228–233.
[23] G.M. Owens, Gender differences in health care expenditures, resource utilization, and quality of care, J. Manag. Care Pharm. 14 (2008) Supp l:2–6.