Risks, Subtypes, and Hospitalization Costs of Stroke Among Patients with Systemic Lupus Erythematosus: A Retrospective Cohort Study in Taiwan

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ABSTRACT. ***Objective.*** To compare risks, subtypes, and hospitalization costs of stroke between cohorts with and without systemic lupus erythematosus (SLE).

Methods. From the catastrophic illnesses registry of Taiwan's universal health insurance claims data, we identified 13,689 patients with SLE diagnosed in 1997-2008 and selected 54,756 non-SLE controls, frequency-matched with age (every 5 years), sex, and index year. Age-specific and type-specific stroke incidence, hazard, and cost of stroke were compared between the 2 cohorts to the end of 2008.

Results. Compared with the non-SLE cohort, the risk of stroke was 3.2-fold higher in the SLE cohort (5.53 vs 1.74 per 1000 person-years) with an overall adjusted HR of 2.90 (95% CI 2.52–3.33). The age-specific risk was the highest in patients 1–17 years old (HR 163, 95% CI 22.2–1197) and decreased as age increased ($p = 0.004$). Hypertension and renal disease were the most important comorbidities in the SLE cohort predicting stroke risk (HR 1.75, 95% CI 1.28–2.39 and HR 1.66, 95% CI 1.32–2.10, respectively). There were more hemorrhagic strokes in the SLE cohort than in the non-SLE cohort, but not significantly (28.0% vs 23.4%; $p = 0.10$). The hospitalization cost for stroke patients was more than twice the cost for those with SLE than for those without ($p < 0.0001$).

Conclusion. Stroke risk and hospital care costs are considerably greater for patients with SLE than without. The relative risk of stroke is the highest in young patients with SLE. (First Release July 1 2012; J Rheumatol 2012;39:1611–18; doi:10.3899/jrheum.111510)

Key Indexing Terms:
HOSPITAL CARE COST
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Systemic lupus erythematosus (SLE) is an autoimmune disease occurring mainly in women, with various manifestations and prognoses. In spite of improved care leading to better survival in recent years, patients with SLE have up to a 5-fold higher mortality compared with the general population[1,2,3,4]. Cardiovascular disease (CVD) accounts for 20% to 40% of deaths in patients with SLE[1,2,3,4]. The risk of mortality from CVD, including stroke, is particularly high for young patients with SLE. A Swedish population-based study found that patients 20–29 years of age had a 16-fold increased risk of death from coronary heart disease[2]. A bimodal pattern of mortality has been reported. In a 10-year followup study, active SLE and infections were found to be the most common causes of death in the earliest 5 years of the followup period,

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whereas thrombosis was the most common cause of death in the latest 5 years[5]. CVD remained the major causes of deaths in patients with SLE in recent decades[2].

Patients with SLE tend to have premature atherosclerosis and thrombosis[6,7]. Atherosclerosis is 2.4-fold more prevalent (37.1% vs 15.2%, respectively) among patients with SLE than controls[7]. Compared with the general population, patients with SLE have a 2 to 50 times higher risk of myocardial infarction and 2 to 8 times higher risk of stroke[8,9,10,11]. Stroke is reported in 3% to 19% of patients with SLE, with a high recurrence rate[11,12,13,14]. In a recent study, 19% of patients with SLE developed ischemic stroke after a mean followup of 8 years[14]. From the US data of the Health Cost and Utilization Project-Nationwide Inpatient Sample, Krishnan found that younger patients with SLE were at a higher risk for ischemic stroke and intracerebral hemorrhage than the general population[15].

In a 5-year followup study of 625 patients with SLE from various ethnic groups, the Chinese (10.3%) were found to have a higher cumulative risk of arterial thromboembolism than African Americans (3.7%) and whites (6.6%)[16]. Unfortunately, no further analysis of stroke risk has been performed. It is not clear whether Chinese are also at a higher risk of stroke than any other ethnic group among patients with SLE. No population-based cohort study has compared the risks, subtypes, and costs of stroke between patients with SLE and the general population for Asians. Our study compares the risk of stroke in patients with SLE with that of the general population by sex, age, and type of stroke, using the claims data of a universal health insurance program. The cost for the care of the patients with stroke was also evaluated.

MATERIALS AND METHODS

Data source. Taiwan's National Health Insurance research database obtained from the National Health Research Institutes (NHRI) was used for our study. This insurance program has a coverage rate of 99% for 23 million people in Taiwan and features contracts with 90% of all healthcare institutions since 1996[17]. The NHRI managed the claims data and provided scrambled random identifications of insured subjects to secure patient privacy. Our study was exempt from the requirement of ethical review. The inpatient claims data were linked to the registry of catastrophic illnesses from 1996 to 2008. From the data, the diseases were identified according to the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM).

Study subjects. The diagnosis of SLE was made by rheumatology specialists according to clinical manifestations and laboratory data. Patients to be registered for catastrophic illnesses required the approval of the insurance authority, including both inpatient and outpatient cases. We identified 20,446 patients with the diagnosis of SLE (ICD-9-CM code 710.0) from the registry of catastrophic illnesses for 1996-2008 and linked to the inpatient claims data. Patients with SLE before 1997 were excluded (n = 6313). A total of 14,133 patients with SLE newly diagnosed from 1997 to 2008 were selected. SLE patients (n = 361) with stroke (ICD-9-CM code 430-438) at baseline or without information on age or sex (n = 83) were also excluded. The remaining 13,689 patients with SLE were included in the SLE cohort. The date of SLE diagnosis was used as the index date to estimate the followup time. For each identified SLE case, 4 comparison subjects were randomly selected from the whole insured population and linked to the inpatient claims database. The selection was frequency-matched with age (every 5 years), sex, and index year, excluding those with a history of SLE and stroke.

Variables. The sociodemographic characteristics including sex, age (1–17, 18–24, 25–34, 35–44, 45–54, 55–64, and ≥ 65 years), urbanization level, and income (< 15,000, 15,000–22,799, and ≥ 22,800 NT$) between the 2 cohorts were assessed. The urbanization level was categorized by the population density of the residential area into 5 levels, with level 1 as the most urbanized and level 5 as the least urbanized.

The baseline comorbidities that may be associated with stroke were identified before the index dates for subjects in both cohorts, i.e., by examining the comorbidity data of each study subject from the date of enrolling in the insurance plan through the index date. The inpatient claims were examined. Comorbidities included in our study were coronary artery disease (ICD-9-CM code 410-413, 414.0, 414.8, and 414.9), congestive heart failure (428, 398.91, and 402.x1), hypertension (401-405), diabetes (250), hyperlipidemia (272), hypercoagulability (289.81 and 286.9), renal disease (580-589), atrial fibrillation (427.31), and valvular heart disease (394-396, 424.0, and 424.1).

The person-years of followup were estimated for study subjects from the index date until the hospitalization for stroke (ICD-9-CM code 430-437) or censored because of death during hospitalization, loss to followup, withdrawal from the insurance plan, or December 31, 2008. The stroke cases were grouped into ischemic stroke (433-437) and hemorrhagic stroke, including subarachnoid stroke (430) and intracerebral stroke (431-432).

Statistical analysis. All statistical analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC, USA), with the significance level set to 0.05 on a 2-tailed test. The proportionate distributions of sociodemographic status and comorbidity between the cohorts with and without SLE were compared and tested using the chi-square test. The mean ages were also measured and tested using t-test. The sex- and age-specific incidence rates of stroke per 1000 person-years of followup for each cohort were calculated. The Cox proportional hazards regression was applied to measure the hazard ratio (HR) and 95% CI of stroke for the SLE cohort compared with the non-SLE cohort. Comorbidity-specific incidence rates of stroke and the related SLE cohort to non-SLE cohort HR were estimated with and without the comorbidity. Further analysis evaluated the occurrences of hemorrhagic stroke and ischemic stroke by sex. The incidence rates of hemorrhagic stroke and ischemic stroke by sex for both cohorts and associated HR with 95% CI of stroke were measured. The cost and length of stay for hospitalization and use of the intensive care unit (ICU) were calculated to compare the severity of stroke between the 2 cohorts. To assess the difference in the age-specific stroke-free rates between the 2 cohorts, the Kaplan-Meier analysis and log-rank test were applied.

RESULTS

Our study consisted of 13,689 patients in the SLE cohort and 54,756 subjects in the non-SLE cohort. Men accounted for 11.8% (Table 1) of each cohort. Both cohorts had a similar age distribution, with mean age of 35.0 (± 15.8) years. The SLE cohort was more prevalent with comorbidities than the non-SLE cohort (all $p < 0.0001$).

The mean followup periods were 5.47 ± 3.44 years in the SLE cohort and 5.77 ± 3.36 years in the non-SLE cohort (data not shown). The incidence of stroke was 3.2-fold greater in the SLE cohort than in the non-SLE cohort (5.53 vs 1.74 per 1000 person-years), with an adjusted HR of 2.90 (95% CI 2.52–3.33; Table 2). The lowest sex-specific and age-specific stroke incidence rates for patients with SLE were in women aged 18–24 years (3.44 per 1000 person-years) and in men aged 35–44 years (2.26 per 1000 person-years). However, the age-specific incidence rate ratio was the highest in the youngest groups and decreased with age. For both men and women combined, the comorbidities-adjusted HR compared

Table 1. Comparison of baseline characteristics between cohorts with and without systemic lupus erythematosus.

Characteristics	Systemic Lupus Erythematosus No, n = 54,756 n (%)	Yes, n = 13,689 n (%)	p
Men	6448 (11.8)	1612 (11.8)	1.00
Age, yrs			0.93
1–17	7166 (13.1)	1742 (12.7)	
18–24	9594 (17.5)	2448 (17.9)	
25–34	13,468 (24.6)	3367 (24.6)	
35–44	11,028 (20.1)	2757 (20.1)	
45–54	7148 (13.1)	1787 (13.1)	
55–64	3360 (6.1)	840 (6.1)	
≥ 65	2992 (5.5)	748 (5.5)	
Mean (SD)†	35.0 (15.8)	35.0 (15.8)	0.87
Income (NT$)			0.005
< 15,000	16,849 (30.8)	4299 (31.4)	
15,000–22,799	28,240 (51.8)	6856 (50.1)	
≥ 22,800	9667 (17.7)	2534 (18.5)	
Comorbidity			
CAD	398 (0.7)	224 (1.6)	< 0.0001
CHF	133 (0.2)	253 (1.9)	< 0.0001
Hypertension	865 (1.6)	927 (6.8)	< 0.0001
Diabetes	643 (1.2)	254 (1.9)	< 0.0001
Hyperlipidemia	284 (0.5)	267 (2.0)	< 0.0001
Hypercoagulability	8 (0.01)	41 (0.30)	< 0.0001
Renal disease	233 (0.43)	2564 (18.7)	< 0.0001
Atrial fibrillation	48 (0.09)	54 (0.4)	< 0.0001
Valvular heart disease	141 (0.3)	251 (1.8)	< 0.0001

† t-test, otherwise chi-square. Renal disease, ICD-9-CM code: 580-589. CAD: coronary artery disease; CHF: congestive heart failure; ICD-9-CM: International Classification of Diseases, 9th Revision, Clinical Modification.

with non-SLE groups for patients with SLE decreased from 163 (95% CI 22.2–1197) in children age 1–17 years to 0.80 (95% CI 0.56–1.12) in the elderly population.

Kaplan-Meier analysis showed that, during the 12-year study period, the overall stroke rate was 4.0% higher in the SLE cohort than that in the non-SLE cohort (log-rank test, $p < 0.0001$; Figure 1A). The gap decreased as age increased, and no difference was observed between the SLE cohort and the non-SLE cohort among the elderly population (Figures 1B-1E).

In general, the HR of stroke increased by 2% for the patients with SLE as age increased by 1 year (Table 3). SLE patients with the comorbidity of hypertension or renal disease were at a significantly higher risk for stroke than patients without the comorbidity within the cohort (HR 1.75, 95% CI 1.28–2.39 and HR 1.66, 95% CI 1.32–2.10, respectively). However, SLE patients without renal disease had a 3.06-fold risk of stroke (95% CI 2.65–3.53) compared to non-SLE subjects without renal disease. Among subjects with renal disease, the risks of stroke were not significantly different between the SLE cohort and non-SLE cohort. Similar patterns appeared for other comorbidities. Compared to the non-SLE group, both women and men in the SLE cohort had significantly higher risk of stroke, with adjusted HR of 3.06 and 2.39, respectively.

The stroke type-specific analysis revealed more ischemic stroke events in both cohorts. However, the SLE cohort had a higher portion of hemorrhagic stroke and less ischemic stroke, compared with the non-SLE cohort, but not significantly (28.0% vs 23.4%; $p = 0.10$). In contrast, the portion of ischemic strokes was lower in the SLE cohort compared to the non-SLE cohort, but this also was not significant (72% vs 76.6%; $p = 0.10$; Table 4). But the Cox model estimated risk of hemorrhagic stroke for the SLE cohort was significant compared with the non-SLE cohort, particularly for subarachnoid hemorrhage (HR 4.80, 95% CI 2.66–8.67; Table 5).

Patients with SLE had longer hospitalization stays than non-SLE subjects for stroke care (mean 19.9 ± 27.6 days vs 15.1 ± 36.4 days; $p < 0.0001$; Table 6). The mean cost for each case was more than double for the SLE cohort ($6815 ± 11,700 vs $3027 ± 6911 in USD; $p < 0.0001$). The mean inpatient care cost was about 3-fold higher for hemorrhagic stroke than for ischemic stroke for both cohorts. The difference in cost for hospitalization between the 2 cohorts was significant for intracerebral hemorrhagic stroke but not for subarachnoid hemorrhagic stroke. The patients with SLE were also more likely than non-SLE subjects to receive care at the ICU for stroke (12.6% vs 3.09%, respectively; $p < 0.0001$).

DISCUSSION

Our study demonstrated that patients with SLE are at increased risk of premature cerebrovascular disease, with an overall HR of 2.9. Compared to the non-SLE cohort, the age-specific HR of 163 is the highest in the youngest patients (< 18 years old), which reduces to 1.68 as age increases to the 55–64 years group after adjustment for comorbidity. This risk is much greater than the risk reported in previous studies. Ward found that young women with SLE (aged 18–44 years) are 1.75 times more likely to be hospitalized for stroke compared with young women without SLE after controlling for comorbidity[11]. However, among women aged ≥ 45 years, the risks of hospitalization for stroke were similar between those with and without SLE. Krishnan reported that patients with SLE (age ≤ 50 years) are also 1.7 times more likely to be hospitalized for stroke compared with the general population after adjustment for age and sex[15]. Only 1 study for the Asian population is available. A cohort study from Hong Kong has also shown a decreasing trend of relative risk for stroke with increasing age[10]. However, the Hong Kong study used a relatively small sample and did not adjust for any comorbidity.

The increased CVD risk in patients with SLE cannot be fully explained by traditional Framingham risk factors[8]. Inflammatory and autoimmune mechanisms are not likely to be involved in the pathogenesis of accelerating atherosclerosis among patients with SLE[18,19]. Immune complex-mediated endothelial damage, vasculitis, valvular heart disease, renal

Table 2. Sex-specific and age-specific incidence rates of stroke in subjects with and without systemic lupus erythematosus (SLE) and Cox model estimated hazard ratios of stroke for patients with SLE.

	Non-SLE		SLE		HR (95% CI)	
	Stroke Case	IR	Stroke Case	IR	Crude	Adjusted†
All††	551	1.74	414	5.53	3.17 (2.79–3.61)***	2.90 (2.52–3.33)***
1–17	1	0.02	49	4.92	213 (29.4–1540)***	163 (22.2–1197)***
18–24	7	0.12	55	3.80	31.1 (14.2–68.3)***	35.6 (15.2–83.4)***
25–34	21	0.28	78	4.17	15.1 (9.34–24.5)***	13.0 (7.89–21.5)***
35–44	59	0.89	74	4.74	5.35 (3.80–7.53)***	4.34 (2.99–6.29)***
45–54	111	2.78	59	6.36	2.29 (1.67–3.14)***	1.68 (1.18–2.39)**
55–64	118	6.19	55	13.5	2.20 (1.60–3.03)***	1.68 (1.18–2.40)**
≥ 65	234	17.1	44	16.3	0.97 (0.70–1.33)	0.80 (0.56–1.12)
p for trend					0.009	0.004
Women						
1–17	0	—	39	4.56	—	—
18–24	7	0.14	44	3.44	24.8 (11.2–55.1)***	29.7 (12.5–70.5)***
25–34	20	0.29	69	4.05	14.0 (8.51–23.0)***	12.2 (7.29–20.6)***
35–44	49	0.81	70	4.84	6.05 (4.20–8.72)***	5.09 (3.44–7.53)***
45–54	88	2.48	50	6.04	2.44 (1.72–3.45)***	1.80 (1.22–2.66)**
55–64	88	5.45	43	12.3	2.28 (1.57–3.29)***	1.82 (1.22–2.72)**
≥ 65	177	16.6	36	17.2	1.04 (0.73–1.49)	0.77 (0.51–1.14)
p for trend					< 0.0001	< 0.0001
Men						
1–17	1	0.16	10	7.16	43.5 (5.57–340)***	43.6 (5.34–356)***
18–24	0	—	11	6.36	—	—
25–34	1	0.14	9	5.39	37.2 (4.71–294)	39.2 (4.71–326)***
35–44	10	1.86	4	2.26	1.85 (0.58–5.89)	0.37 (0.04–3.70)
45–54	23	5.21	9	9.11	1.74 (0.81–3.77)	1.58 (0.62–4.01)
55–64	30	10.2	12	20.4	1.99 (1.02–3.88)*	1.44 (0.64–3.27)
≥ 65	57	18.6	8	13.4	0.74 (0.35–1.55)	0.78 (0.36–1.68)
p for trend					< 0.0001	< 0.0001

† Adjusted for sex, urbanization, income, coronary artery disease, congestive heart failure, hypertension, diabetes, hyperlipidemia, hypercoagulability, renal disease, atrial fibrillation, and valvular heart disease. †† Adjusted for age, sex, urbanization, income, coronary artery disease, congestive heart failure, hypertension, diabetes, hyperlipidemia, hypercoagulability, renal disease, atrial fibrillation, and valvular heart disease. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0001$. IR: incidence rate per 1000 person-years.

disease, corticosteroid-induced hypertension, dyslipidemia, obesity, and hyperglycemia may be factors. In addition, procoagulant factors, such as homocysteine and antiphospholipid antibodies, may also contribute to the increased risk of cardiovascular disease[20,21]. In our study, renal disease is an important risk factor for stroke, with an HR of 1.66 (95% CI 1.32–2.10). However, among subjects with renal disease, the risks of stroke were not significantly different between the SLE cohort and the non-SLE cohort. Therefore, renal disease might mediate the association between SLE and stroke.

We further analyzed data by age for comorbidity-specific incidence rates of stroke to investigate the contribution of comorbidity to stroke risk for young patients with SLE. No significant relationships were found because of small numbers of cases in the non-SLE groups (data not shown). Roman, *et al* reported in a case-control study that carotid arterial plaque was 5.6-fold more prevalent among young patients with SLE than their controls (13.4% vs 2.4%)[7]. Vasculopathy may be more common among younger-onset patients with SLE[22]. In addition, these younger-onset patients may have more severe diseases, which may be associated with a higher risk of CVD[23]. Further, CVD risk factors are more prevalent among young patients with SLE compared with the general population of the same age[12].

Our study demonstrated that the proportional distributions in stroke subtypes between SLE and non-SLE groups were not significantly different. In contrast, Krishnan reported that the risk of subarachnoid hemorrhage was lower in patients with SLE[15]. However, subarachnoid hemorrhage seems common among patients with SLE in Japan[24,25]. Given that diabetes, coronary artery disease, hyperlipidemia, and obesity were significantly more common in non-SLE subjects, these factors may explain the higher portion of ischemic strokes in this cohort, although it was nonsignificant.

Our study also demonstrated that the overall hospitalization cost and length of stay of patients with SLE were higher than those of patients without SLE ($p < 0.0001$). Patients with SLE are also more likely to stay in the ICU. These findings have not been reported previously, to our knowledge. Previous hospital-based studies correlated the hospitalization cost of

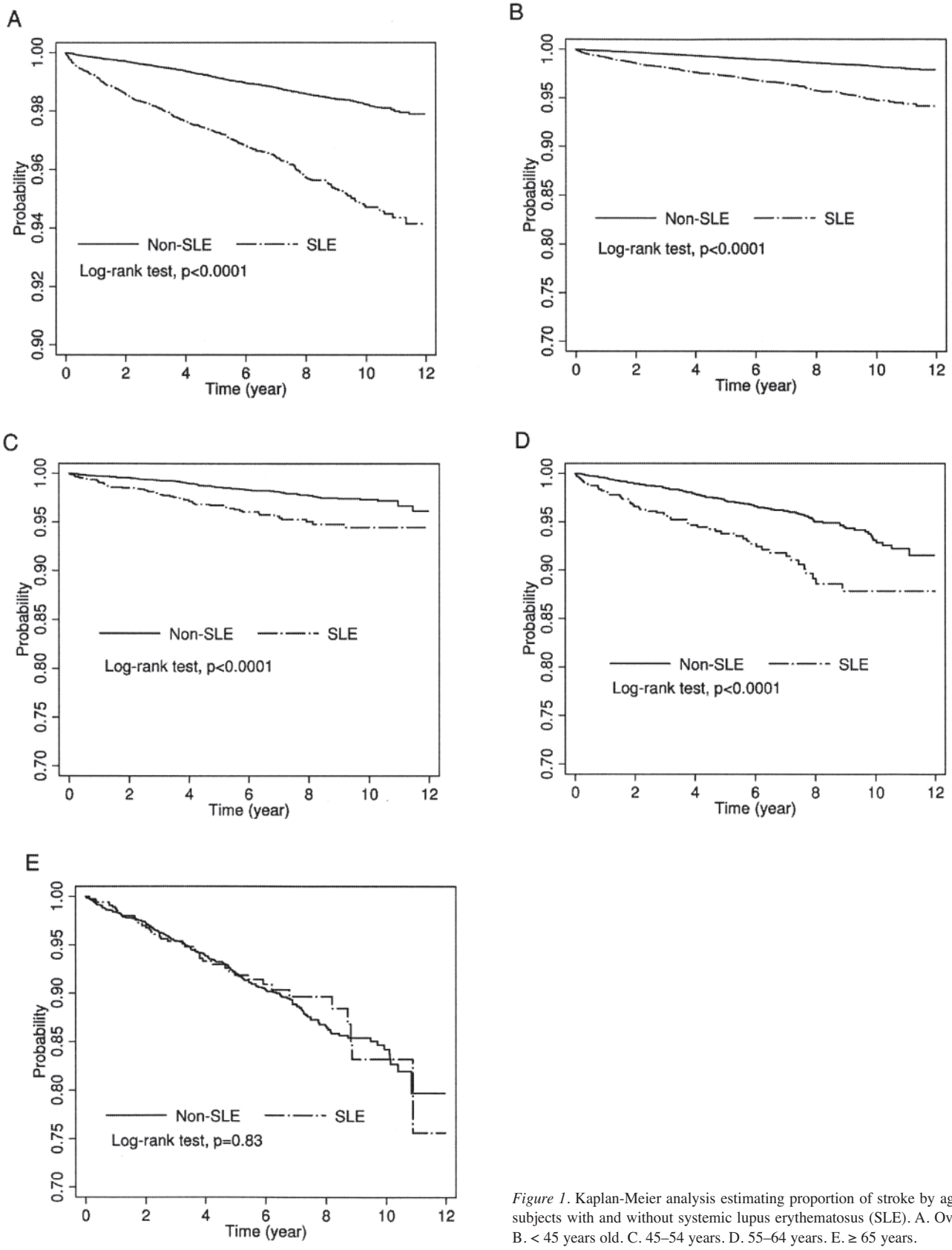

Figure 1. Kaplan-Meier analysis estimating proportion of stroke by age for subjects with and without systemic lupus erythematosus (SLE). A. Overall. B. < 45 years old. C. 45–54 years. D. 55–64 years. E. ≥ 65 years.

Table 3. Hazard ratios of stroke in multivariable Cox proportion regression analysis.

	Non-SLE		SLE			SLE to non-SLE
	Event	IR	Event	IR	HR (95% CI)	HR (95% CI)
Age	551	1.74	414	5.53	1.02 (1.02–1.03)***	—
Women	429	1.53	351	5.26	1.00 (reference)	3.06 (2.62–3.56)***
Men	122	3.39	63	7.74	1.28 (0.98–1.68)	2.39 (1.70–3.36)***
Comorbidity						
CAD						
No	524	1.67	398	5.38	1.00 (reference)	2.97 (2.57–3.43)***
Yes	27	16.53	16	18.14	1.43 (0.83–2.46)	1.25 (0.64–2.47)
CHF						
No	543	1.72	402	5.43	1.00 (reference)	2.93 (2.54–3.37)***
Yes	8	17.17	12	14.04	0.90 (0.48–1.69)	0.61 (0.17–2.16)
Hypertension						
No	498	1.59	352	4.96	1.00 (reference)	3.09 (2.67–3.59)***
Yes	53	16.59	62	16.06	1.75 (1.28–2.39)***	1.26 (0.80–1.98)
Diabetes						
No	502	1.60	404	5.47	1.00 (reference)	3.18 (2.76–3.68)***
Yes	49	19.01	10	10.68	0.79 (0.41–1.53)	0.52 (0.25–1.08)
Hyperlipidemia						
No	530	1.68	401	5.46	1.00 (reference)	2.97 (2.57–3.42)***
Yes	21	17.09	13	9.47	1.09 (0.62–1.91)	0.83 (0.31–2.22)
Hypercoagulability						
No	551	1.74	412	5.52	1.00 (reference)	2.88 (2.51–3.32)***
Yes	0	—	2	12.74	1.93 (0.48–7.85)	—
Renal disease						
No	529	1.68	300	4.84	1.00 (reference)	3.06 (2.65–3.53)***
Yes	22	27.43	114	8.89	1.66 (1.32–2.10)***	0.97 (0.54–1.74)
Atrial fibrillation						
No	551	1.74	411	5.50	1.00 (reference)	2.88 (2.50–3.11)***
Yes	0	—	3	20.69	1.12 (0.34–3.65)	—
Valvular heart disease						
No	549	1.74	400	5.44	1.00 (reference)	2.87 (2.49–3.30)***
Yes	2	3.47	14	11.24	1.35 (0.78–2.33)	7.31 (0.91–58.4)

SLE: systemic lupus erythematosus; IR: incidence rate per 1000 person-years; CAD: coronary artery disease; CHF: congestive heart failure.

stroke with stroke severity and subtype: that is, higher for hemorrhagic stroke than for ischemic stroke[26,27]. Although the National Institutes of Health Stroke Scales cannot be calculated using the claims data, stroke in the SLE group is likely more severe and complicated based on the hospitalization status. They require more intensive care, resulting in higher costs.

The strengths of our study include a large sample size, matched cohort, nationwide study, and longterm followup. However, our study has several limitations. First, the NHRI database provided limited information on sociodemographic characteristics. Some information was not available, such as marital status, education level, body mass index, smoking habits, disease activity, and laboratory data such as serum cholesterol levels and titers of antiphospholipid antibodies. These variables could not be adjusted for in the analysis. Information on income was used for the adjustment. Second, the information on chronic conditions such as hyperlipidemia was not accessible for some individuals. This happened in both groups. Third, stroke and other diseases were identified by ICD-9-CM codes. Patients with stroke in Taiwan are generally cared for at larger hospitals with adequate facilities. The codes were reviewed and validated by auditors for the insurance system to assure the accuracy of the claims. Fourth, calculation of the mortality ratio related to stroke was not possible because the date and causes of deaths for some patients could not be obtained from the database. Finally, the incidence rate of stroke may be underestimated because inpatient claims data were used. However, stroke cases without hospitalization are rare.

Patients with SLE have about a 3-fold higher risk for subsequent strokes. The age-specific relative risk decreases significantly as age increases, with younger patients at much higher relative risk. Both SLE and non-SLE cohorts have a higher incidence of ischemic stroke than hemorrhagic stroke. However, patients with SLE have a higher HR of hemorrhagic stroke than ischemic stroke. Renal disease is an important comorbidity associated with the risk of stroke in patients with SLE. The hospital care cost for stroke is considerably greater for patients with SLE than those without SLE. Close surveillance of risk factors and aggressive management of potentially reversible risk factors are necessary to reduce the occurrence of stroke.

Table 4. Proportional distribution of stroke subtypes compared between cohorts with and without systemic lupus erythematosus (SLE).

	Non-SLE Stroke Case (%)	SLE Stroke Case (%)	p*
All			
All strokes	551	414	
Hemorrhagic stroke			
All	129 (23.4)	116 (28.0)	0.10
Subarachnoid hemorrhage	23 (4.17)	28 (6.76)	0.08
Intracerebral hemorrhage	106 (19.2)	88 (21.3)	0.44
Ischemic stroke	422 (76.6)	298 (72.0)	0.10
Women			
All strokes	429	351	
Hemorrhagic stroke			
All	101 (23.5)	98 (27.9)	0.16
Subarachnoid hemorrhage	20 (4.66)	25 (7.12)	0.14
Intracerebral hemorrhage	81 (18.9)	73 (20.8)	0.50
Ischemic stroke	328 (76.5)	253 (72.1)	0.16
Men			
All strokes	122	63	
Hemorrhagic stroke			
All	28 (23.0)	18 (28.6)	0.40
Subarachnoid hemorrhage†	3 (2.46)	3 (4.76)	0.41
Intracerebral hemorrhage	25 (20.5)	15 (23.8)	0.60
Ischemic stroke	94 (77.0)	45 (71.4)	0.40

* Chi-square test. † Fisher's exact test.

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Table 5. Sex-specific incidence rates of stroke in subjects and Cox model estimated hazard ratio for patients with systemic lupus erythematosus (SLE).

Subjects	Non-SLE Stroke Case	Non-SLE IR	SLE Stroke Case	SLE IR	HR (95% CI) Crude	HR (95% CI) Adjusted†
All						
All strokes	551	1.74	414	5.53	3.17 (2.79–3.61)***	2.90 (2.52–3.33)***
Hemorrhagic stroke						
All	129	0.41	116	1.55	3.79 (2.95–4.88)***	3.23 (2.45–4.27)***
Subarachnoid hemorrhage	23	0.07	28	0.37	5.16 (2.97–8.95)***	4.80 (2.66–8.67)***
Intracerebral hemorrhage	106	0.34	88	1.18	3.50 (2.64–4.64)***	2.91 (2.12–3.99)***
Ischemic stroke	422	1.33	298	3.98	2.98 (2.57–3.46)***	2.79 (2.37–3.28)***
Women						
All strokes	429	1.53	351	5.26	3.44 (2.99–3.96)***	3.06 (2.62–3.56)***
Hemorrhagic stroke						
All	101	0.36	98	1.47	4.07 (3.09–5.38)***	3.39 (2.49–4.61)***
Subarachnoid hemorrhage	20	0.07	25	0.37	5.26 (2.92–9.47)***	4.88 (2.61–9.13)***
Intracerebral hemorrhage	81	0.29	73	1.09	3.78 (2.76–5.19)***	3.02 (2.12–4.32)***
Ischemic stroke	328	1.17	253	3.79	3.24 (2.75–3.82)***	2.98 (2.47–3.52)***
Male						
All strokes	122	3.39	63	7.73	2.27 (1.68–3.08)***	2.39 (1.70–3.36)***
Hemorrhagic stroke						
All	28	0.78	18	2.21	2.82 (1.56–5.10)**	2.79 (1.42–5.49)**
Subarachnoid hemorrhage	3	0.08	3	0.37	4.43 (0.89–21.9)	4.70 (0.79–27.9)
Intracerebral hemorrhage	25	0.69	15	1.84	2.63 (1.39–4.98)*	2.57 (1.23–5.38)*
Ischemic stroke	94	2.61	45	5.53	2.11 (1.48–3.01)***	2.30 (1.55–3.40)***

† Adjusted for sex, age, urbanization, income, coronary artery disease, congestive heart failure, hypertension, diabetes, hyperlipidemia, hypercoagulability, renal disease, atrial fibrillation, and valvular heart disease. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0001$. IR: incidence rate per 1000 person-years.

Table 6. Comparison of cost and length of stay for hospitalization between subjects with and without systemic lupus erythematosus (SLE). Data are mean ± SD (median) and no. (%).

Condition	Hospitalization Cost, US$			Length of Stay, days		
	Non-SLE	SLE	p	Non-SLE	SLE	p
All strokes	3027 ± 6911 (951)	6815 ± 11700 (2064)	< 0.0001	15.1 ± 36.4 (7.00)	19.9 ± 27.6 (10.0)	0.02
Hemorrhagic stroke						
All	6123 ± 7667 (3083)	13217 ± 15989 (8417)	< 0.0001	21.2 ± 19.9 (16.0)	26.1 ± 28.6 (17.0)	0.12
Subarachnoid	9867 ± 9973 (8720)	12289 ± 15249 (9165)	0.50	21.0 ± 19.1 (17.0)	24.4 ± 35.3 (14.6)	0.66
Intracerebral	5310 ± 6861 (2790)	13512 ± 16291 (7488)	< 0.0001	21.2 ± 20.1 (15.5)	26.7 ± 26.3 (19.5)	0.11
Ischemic stroke	2080 ± 6378 (804)	4323 ± 8315 (1469)	0.0001	13.3 ± 39.9 (6.00)	17.5 ± 26.8 (8.00)	0.09
Cases in ICU, n (%)	17 (3.09)	52 (12.6)	< 0.0001			

ICU: intensive care unit.

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