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Estimation of expected years of life lost for patients with ischemic stroke and intracerebral hemorrhage

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Abstract

Purpose – The purpose of this paper is to estimate the mean life expectancy (LE) and the expected years of life lost (EYLL) for ischemic stroke and intracerebral hemorrhage.
Design/methodology/approach – This retrospective cohort study included 5,210 patients with a diagnosis of first ischemic stroke or intracerebral hemorrhage between 2005 and 2013 from Ramathibodi Hospital, Bangkok, Thailand. The survival of each case was followed until December 31, 2016. A semiparametric extrapolation method was applied to estimate the lifetime survival function relative to an age and sex-matched reference population.
Findings – Of 5,210 patients, 74.2 percent experienced ischemic stroke. About 54.3 percent were men. Mean age at diagnosis was 64.3 years. The mean LE was 12.5 years for ischemic stroke and 12.0 years for intracerebral hemorrhage. The EYLL among patients with intracerebral hemorrhage was significantly higher than among those with ischemic stroke (10.1 vs 5.7). Women were expected to lose more LE than men for both types of stroke (p-value < 0.05), while younger aged patients were expected to lose more years of life than older ones.
Originality/value – This study fulfilled an identified need to estimate LE and EYLL among patients with ischemic stroke and intracerebral hemorrhage.

Keywords Ischemic stroke, Intracerebral hemorrhage, Mean life expectancy, Expected years of life lost
Paper type Research paper

Background

Non-communicable diseases (NCDs) accounted for 71 percent of all deaths worldwide in 2016[1]. Of these, cardiovascular diseases and stroke are the two leading causes of death and premature death[1]. The years of life lost (YLL), an indicator of premature death, due to cardiovascular diseases increased 16 percent and stroke increased 12 percent from 2000 to

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2012 worldwide[2]. Although YLL attributed to cardiovascular diseases is ranked first worldwide, YLL attributed to stroke is ranked first in Southeast Asia[2].

Strokes have become a major public health burden. A report on the disease burden in Thailand, 2004, revealed that 267,000 YLL among Thai women and 282,600 YLL among Thai men were attributed to stroke[3]. The study reported the total stroke cases in Thailand in terms of premature death, but lacked YLL statistics for specific subtypes of stroke and lifelong estimation[3]. The expected years of life lost (EYLL) statistical model was developed taking lifelong estimation into account[4, 5]. Using the lifelong estimation method, the average years of life remaining after stroke and the average EYLL after stroke for each subtype of each individual in a Thai population can be estimated.

The purposes of this study included: to estimate age and sex-specific life expectancy (LE) for patients with ischemic stroke and intracerebral hemorrhage and to estimate EYLL for patients with ischemic stroke and intracerebral hemorrhage relative to age and sex in a specific Thai reference population. The more refined method of LE and EYLL estimation used in this study provided precise and clear evidence on long-term survival regarding stroke. The up-to-date information on lifelong stroke burden could be beneficial to generate appropriate interventions and evaluate the benefits of stroke programs.

Methods

This study received ethical approval from the Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University, No. MURA2015/759/S1 dated August 27, 2018. The target population comprised patients with ischemic stroke and intracerebral hemorrhage aged 18 years and above. The lifetime survival estimation is summarized in Figure 1.

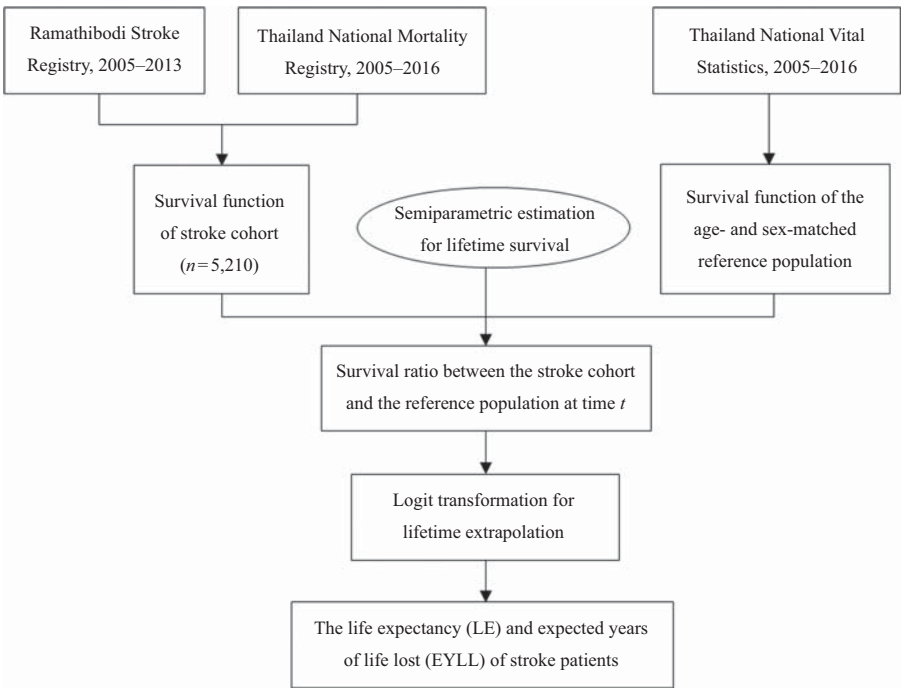

Figure 1.
Flow diagram of the inclusion of subjects and the estimation process

Ramathibodi Hospital stroke registry for survival

This study used data of patients with ischemic stroke (ICD-10 code: I63) and intracerebral hemorrhage (ICD-10 code: I61) from the database of Ramathibodi Hospital between January 2005 and December 2013. A total of 5,348 stroke cases were abstracted, with 138 patients excluded due to comorbidities that might shorten LE including lung cancer (47 cases), liver cancer (31 cases), pancreatic cancer (6 cases), leukemia (36 cases) and heart failure (18 cases). A total of 5,210 stroke cases remained to be analyzed. The survival of each case was followed until December 31, 2016. The survival status and date of death were ascertained from the National Mortality Registry. The study cohort was linked to the Thailand National Mortality Registry using patients' identification numbers. The identification information was encrypted before analyzing data to maintain confidentiality.

Generating an age- and sex-matched reference population

The life tables of the Thailand National Vital Statistics, acquired from Department of Provincial Administration, Ministry of Interior and Unit of Health Information, Bureau of Policy and Strategy, Ministry of Public Health, Thailand were applied to generate the age- and sex-matched reference population. Interpolating standard model life tables of the reference population from 2005 to 2016, set as one-year intervals by sex, were calculated using the following formula[4]:

$$ {}_{n}e_{x}^{s} = e_{x}^{s} + ({}_{n}a_{x} - x)\frac{e_{x+n}^{s} - e_{x}^{s}}{(x+n) - x}, $$

where x is the age in years; n the age interval length; e_x^s the standard life expectancy at age x; ${}_{n}e_{x}^{s}$ the standard life expectancy for age interval x to $x+n$; and ${}_{n}a_{x}$ the average age of death for age interval x to $x+n$.

Extrapolating the survival function to a lifetime

After ascertaining the survival status of all cases based on the 2005–2013 follow-up stroke data, the Kaplan–Meier estimator (nonparametric method) was used to generate the survival function for different stroke subtypes from the onset of stroke diagnosis up to the end of follow-up (December 31, 2016). Likewise, the same nonparametric method was used to estimate the survival function for the reference population. Next, the survival ratio between the stroke cohort and the reference population at each time was calculated, and a logit transformation of the ratio was performed and fitted with a simple linear regression (parametric method). This semiparametric method was combined to extrapolate the survival function throughout life after the culmination of the follow-up period of the stroke cohort. A semiparametric extrapolation method only requires an assumption of constant excess hazards in estimating the lifetime survival function. By choosing a negative slope closest to 0, we can project the long-term survival of this cohort from the available survival function to reference the population matched by age and sex. The estimates were carried out using the iSQoL statistical package[5].

Estimating mean life expectancy (LE) and expected years of life lost (EYLL)

The mean LE is the average life that an individual expects to survive after presenting with a specific condition. Correspondingly, the remaining LE conditional on survival at time t can be defined as:

$$ m(t) = E(T - t | T > t) \text{ for } t \geqslant 0, $$

where T is the time of failure or death[6].

X is a vector of covariates condition and β is a parameter of interest, so a semiparametric LE model was defined as the following formula[7]:

$$m(t|\mathrm{X}) = m(t) + \mathrm{X}^T\beta.$$

The area under the curve of survival function $m(t|X)$ throughout life for patients with stroke obtained using the extrapolation method represents the mean LE after experiencing an ischemic stroke or intracerebral hemorrhage. The EYLL was calculated by subtracting the area under the survival curve of patients with stroke from that of the age- and sex-matched reference in this study. The area under the survival curve of reference represents the LE of the Thai population in general, while the area under the survival curve of patients represents the LE of patients with ischemic stroke or intracerebral hemorrhage. The difference in area between these two curves is the estimation of EYLL.

Validating the extrapolation method

Validating the semiparametric extrapolation method for patients with stroke was performed on the data of patients with a diagnosis of stroke during the first four years. Then, the survival function was extrapolated to 12 years using the semiparametric extrapolation method. The survival data were actually followed until the end of 2016. The mean survival duration within the 12-year follow-up was calculated using the Kaplan–Meier method, which was considered the gold standard of survival analysis. The relative bias was computed to compare the differences in values between the Kaplan–Meier method and the semiparametric extrapolation method.

Results

A total of 5,210 patients with first stroke were eligible for the lifetime survival estimation. Table I shows the comparison and frequency distribution of general characteristics. About 54.3 percent were male. Of the 5,210 participants, 74.2 percent were patients with ischemic stroke and the rest were those with intracerebral hemorrhage. Within the stroke registry data, patients with intracerebral hemorrhage were about six years younger than those with ischemic stroke.

	Number (%)			
	All	IS	ICH	*p*-value[a]
Total cases	5,210 (100.0)	3,868 (74.2)	1,342 (25.8)	
Sex				
Male	2,830 (54.3)	2,046 (52.9)	784 (58.4)	< 0.001
Female	2,380 (45.7)	1,822 (47.1)	558 (41.6)	
Age at diagnosis, years, mean (SD)	64.32 (15.01)	65.95 (14.01)	59.64 (16.71)	< 0.001[b]
18–34	197 (3.8)	96 (2.5)	101 (7.5)	< 0.001
35–49	667 (12.8)	394 (10.2)	273 (20.3)	
50–64	1,548 (29.7)	1,140 (29.5)	408 (30.4)	
> 64	2,798 (53.7)	2,238 (57.9)	560 (41.7)	
Median stroke duration (years)	4.38	4.65	3.45	< 0.001[c]
Comorbidities[d]				
Diabetes mellitus	1,510 (29.0)	1,250 (32.3)	260 (19.4)	< 0.001
Hypertension	3,132 (60.1)	2,370 (61.3)	762 (56.8)	0.004
Dyslipidemia	1,773 (34.0)	1,482 (38.3)	291 (21.7)	< 0.001
Atrial fibrillation	811 (15.6)	681 (17.6)	130 (9.7)	< 0.001
Coronary artery disease	560 (10.7)	476 (12.3)	84 (6.3)	< 0.001

Notes: [a]χ^2 test; [b]independent *t*-test; [c]Mann–Whitney *U* test; [d]multiple responses

Table I. Comparison of the frequency distribution of patients registered in Ramathibodi Hospital as ischemic stroke and intracerebral hemorrhage, year 2005 and 2013

Interestingly, 27.8 percent of patients with intracerebral hemorrhage were below 50 years of age. The median stroke duration among patients with ischemic stroke was significantly higher than that among patients with intracerebral hemorrhage.

The mean LE of patients with ischemic stroke and intracerebral hemorrhage was estimated to be 12.51 years and 12.05 years, respectively (Figure 2). When compared with a reference population of the same age and sex, the EYLL among patients with intracerebral hemorrhage was significantly greater than that of patients with ischemic stroke. On average, the EYLL of patients with intracerebral hemorrhage was 10.07 years and the EYLL of patients with ischemic stroke was 5.70 years.

We also conducted stratified analysis by sex and age groups (Table II). The results showed that female patients were expected to lose more years of life than male patients (p-value < 0.05). The younger the age of patients with stroke, the more the expected years of life were lost (p-value < 0.05). It was quite obvious that intracerebral hemorrhage brought about poorer outcomes than ischemic stroke.

All 1,518 patients received a diagnosis of ischemic stroke and 585 patients of intracerebral hemorrhage during the first four years, between 2005 and 2008, of which the survival functions were extrapolated to 2016. The Kaplan–Meier estimate of a 12-year follow-up was used as the gold standard. The relative biases of those extrapolated using the

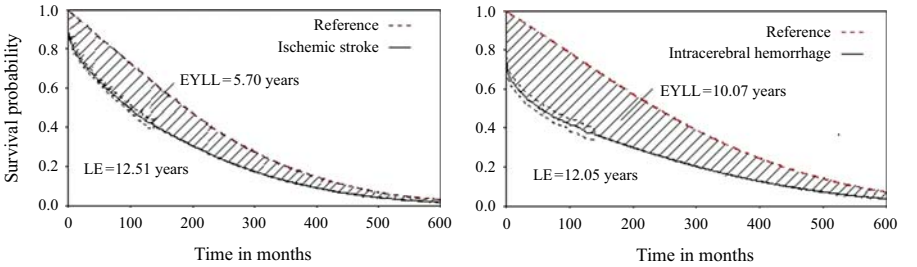

Figure 2.
Survival curves of patients with ischemic stroke and intracerebral hemorrhage and their corresponding referents

Notes: The solid line represents the survival curves of patients with stroke, while the dotted line represents the survival curve of the general population in Thailand that was age- and sex-matched. The area under the solid line represents the mean life expectancy (LE) and the shaded area between the two survival curves is the expected years of life lost (EYLL)

	Sex		Age			
	Male	Female	18–34 y	35–49 y	50–64 y	⩾65 y
All patients ($n = 5,210$)						
LE	12.67 ± 0.09	12.14 ± 0.13	34.94 ± 0.33	24.12 ± 0.14	16.11 ± 0.12	7.04 ± 0.10
EYLL	6.57 ± 0.06	6.98 ± 0.10	14.10 ± 0.28	9.96 ± 0.10	6.93 ± 0.09	4.89 ± 0.08
p-value	0.017			< 0.001		
IS patients ($n = 3,868$)						
LE	12.70 ± 0.11	12.21 ± 0.12	39.31 ± 0.36	25.64 ± 0.21	17.08 ± 0.13	7.48 ± 1.14
EYLL	5.24 ± 0.08	6.25 ± 0.09	9.30 ± 0.41	8.42 ± 0.21	5.92 ± 0.13	4.50 ± 0.10
p-value	< 0.001			< 0.001		
ICH patients ($n = 1,342$)						
LE	12.78 ± 0.16	10.62 ± 0.24	33.83 ± 0.49	21.97 ± 0.37	13.76 ± 0.26	5.00 ± 0.19
EYLL	9.97 ± 0.13	10.68 ± 0.21	15.69 ± 0.49	12.02 ± 0.36	9.55 ± 0.26	7.05 ± 0.19
p-value	0.023			< 0.001		

Table II.
Estimation of life expectancy (LE) and expected years of life lost (EYLL) due to stroke stratified by sex and age, years (y) and mean ± S.E.

Note: p-values from z-statistic test

semiparametric method compared with the Kaplan–Meier gold standard method were −3.18 percent for ischemic stroke and −2.27 percent for intracerebral hemorrhage. The censoring rates were lower than 50 percent (Table III).

Discussion

Related studies have reported on the burden of stroke in terms of mortality and prevalence[3, 8]. However, these studies did not stratify the types of stroke nor did they identify the loss of LE after stroke. To the best of our knowledge, this study is the first to quantify the EYLL of average patients with different types of stroke in Thailand by incorporating the LE information from that of the age- and sex-matched reference population in the estimation process. The EYLL is a measure of the disease overall burden on individuals and society that was widely used in several studies[9–11]. The EYLL reflects the social and economic impact of a disease given the mortality. It may be used as a basis for allocating appropriate interventions in the health sectors. In this study, we calculated the survival probability of the reference population from the average number of Thai national life tables, unlike one related study that applied internationally chosen life tables to calculate the disease burden using the YLL[3]. The relative biases of the extrapolation method based on four years of data to project eight years onward were all less than 5 percent. Thus, it could be concluded that our estimation of survival function throughout the lifetime of patients with stroke was valid and acceptable (Figure 2).

This study revealed that, on average, a patient was expected to lose 10.07 years of LE due to intracerebral hemorrhage and 5.70 years from ischemic stroke. Although the patients with ischemic stroke had more comorbid diseases than those with intracerebral hemorrhage, the EYLL due to ICH turned out to be almost two times that of the EYLL from ischemic stroke. This finding is consistent with a previous study from Taiwan[12]. Even though intracerebral hemorrhage accounted for only 25 percent of all strokes in this study, it was significantly associated with a higher loss of LE compared with ischemic stroke. The difference could be explained by the reason that intracerebral hemorrhage leads to death during the early periods of the disease more than ischemic stroke[13]. The lower rate of survival during the early period of patients with intracerebral hemorrhage directly affects the estimation of the EYLL. Moreover, the differences in pathophysiology and appropriate interventions between ischemic stroke and intracerebral hemorrhage may affect EYLL estimation. Ischemic stroke is caused by blood clot blocked blood vessels that damage brain tissues. However, the penumbra could be salvaged by thrombolysis, antiplatelet or anticoagulant agents[14]. However, intracerebral hemorrhage is caused by the rupture of blood vessels resulting in cutting off the connecting pathways to the brain tissue. The biochemical substances released during and after hemorrhage also adversely affect nearby vascular and brain tissues. For these reasons, intracerebral hemorrhage often led to worse outcomes than ischemic stroke[13, 14]. Furthermore, this study found that patients with intracerebral hemorrhage were about six years younger than those patients with ischemic stroke. This suggested that intracerebral

Table III. Estimate of mean survival durations in 12-year follow-up using the extrapolation method based on the first four years of follow-up data compared using the Kaplan–Meier (KM) estimates based on the full 12 years of follow-up data

		12-Year follow-up KM estimate		Estimate using extrapolation based on the first 4 years of follow-up			
	Cohort size	Mean	SE	Mean	SE	Relative bias (%)	Censoring rate[a] (%)
All patients with stroke	2,103	6.76	0.07	6.45	0.07	−4.59	41.61
Ischemic stroke	1,518	7.08	0.08	6.85	0.07	−3.18	43.61
Intracerebral hemorrhage	585	5.84	0.13	5.71	0.11	−2.27	36.41

Note: [a]The censoring rates were computed at the end of the first four years of follow-up

hemorrhage may occur more often among younger people than ischemic stroke, as reported in other studies[15, 16]. Therefore, stroke prevention programs should target young people.

Stratified analysis indicated that female patients had significantly greater levels of EYLL. This finding contradicted one study conducted in Singapore[15]. They reported that female patients had better survival rates than male patients for ischemic stroke, while no evidence was found concerning the difference in survival rates between sexes for intracerebral hemorrhage[15]. The different survival rates between sexes found in this study could have been due to the age at the first diagnosis wherein males were more likely to have a stroke at a younger age allowing them to live longer than female patients. Post-stroke survival time depends on the quality of care. In addition, there may have been a difference in care based on sex in the study samples. Further studies should explore disparities in acute stroke management and quality of post-stroke care by comparing male and female patients to improve survival time among female patients. The mean LE significantly declined with increasing age. This finding was consistent with related studies[15, 17]. Nevertheless, the longer period of survival could not guarantee a healthy or a happy life because most stroke patients had varying levels of neurological deficits[18, 19]. Moreover, the long-term living status after stroke should be further studied. The finding indicated that stroke risk at a younger age leads to the greatest EYLL.

This study had the advantages of a large cohort with a 12-year study period, but some limitations must be explained in this study. First, we used all-cause mortality rather than stroke-associated mortality. This could have led to underestimating stroke survival rates, because some patients may have died from other diseases. We mitigated this limitation by excluding stroke patients who also had other life-threatening diseases before performing data analysis[20]. Second, due to the limitation of secondary data, we could calculate the disease burden using stroke subtypes, sex and age groups but could not do so for other factors related to death, i.e., the severity of the stroke and the quality of post-stroke care[21]. Third, the results of this study could represent only patients with stroke in a tertiary hospital, not the general population due to patients' socioeconomic characteristics and quality of medical care, which is likely to differ across the country[8]. Further studies in different settings are recommended to gain wider knowledge regarding the burden of stroke in terms of EYLL in different areas. With such information, we would be able to compare the EYLL among health centers and implement appropriate programs to improve the quality of care and health outcome for patients with stroke.

This study successfully estimated the EYLL due to ischemic stroke and intracerebral hemorrhage, in terms of life years gained by preventing ischemic stroke and intracerebral hemorrhage with regard to different sex and age groups. Loss of LE data may be used as basic information to inform people how much of a burden a stroke would cost and encourage them to be more aware of factors leading to a stroke. Health personnel should use this information to advocate Thai populations to be more aware of a stroke's consequences using social networks and mass media. The results indicated that disparities existed in post-stroke survival time as observed using stroke subtypes, sex and age groups. These disparities may be due to differences in stroke management and post-stroke care. The study findings provided detailed information that could likely assist policymakers to prioritize policy agenda and motivate policymakers to mobilize resources and design appropriate preventive interventions both for acute and long-term stroke management. To provide better evidence on stroke, further studies on EYLL focusing on economic evaluation, different interventions and comparing with other diseases are suggested.

Conclusion

This retrospective cohort study applied the semiparametric extrapolation method to estimate the survival function throughout the lifetime of patients with strokes. The results revealed intracerebral hemorrhage caused more loss of LE than ischemic stroke and the female patients had poorer survival rates after stroke than male patients.

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