TITLE PAGE

Title: Prevalence of Recurrent Stroke and its related factors among Hypertension and Hypertension with type 2 Diabetes patients in Thailand.

Authors: Nitchamon Rakkapao

Affiliations:

   Faculty of Public Health, Khon Kaen University, Thailand

Corresponding authors:
   Name: Nitchamon Rakkapao

   Address: , Faculty of Public Health, Khon Kaen University, Khon Kaen, 40002, Thailand

   Telephone: +66-87-3203336
   Fax: +66-xxxxxxxxx
   e-Mail: Nitchamon_ph@hotmail.com

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Prevalence of Recurrent Stroke and its related factors among Hypertension and Hypertension with type 2 Diabetes patients in Thailand.

Nitchamon Rakkapao[1], Bandit Thinkamrop[2]

Abstract

Background: Recurrent stroke has been an important health problem. It has leaded to a high rate of mortality and disability. A few data of prevalence of recurrent stroke in developing countries has been reported. In Thailand, a study of recurrent stroke explored overall among hypertension and hypertension with type 2 Diabetes patients has not been shown.

Objective: To determine the prevalence of recurrent stroke and its related factors among hypertension and hypertension with type 2 diabetes patients in Thailand.

Methods: A nationally representative sample survey of type 2 diabetes and hypertension patients who visited 595 hospitals across Thailand during 2011-2012 was conducted. The complications of diabetes and hypertension patients were based on medical records and the recurrent stroke was the main focus of this study. Multiple logistic regressions were used for the data analysis.

Results: There are 3,439 stroke patients (54.4% of male) in this study. They were 65.1 ± 10.5 years old on average. The prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes patients was 1.5% (95%CI; 1.15-2.01).This study had found the prevalence of recurrent stroke in female greater than that in male. This disease decreased with the increasing of age, Moreover, we have found the higher rate in diabetes and hypertension patients than only hypertension. The prevalence of recurrent stroke had most found in hemorrhagic stroke (3.6%). The related factors of the recurrent stroke found in our analysis were HDL-cholesterol less than 40 mg/dL (OR_{adjust} =2.70 ,95%CI;1.29-5.65;p-value=0.008), diastolic blood pressure (OR_{adjust}=1.03,95%CI;1.01-1.06;p-value=0.009), type of cerebrovascular (OR_{adjust} =1.89,95%CI;1.08-3.33;p-value=0.026) and sex (OR_{adjust}=1.82,95%CI;1.05-3.18;p-value=0.033).

Conclusions: Prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes a patient in Thailand was lower than that of previous reports in Europe and in some countries of Asia. However, stroke patients should continually to focus on the medications, self-care, and usual check level of HDL-cholesterol. The preventive strategies still need to proceed in the future, to improve quality of the patient's stroke.

Keywords: prevalence, recurrent stroke, factor association, hypertension, type 2 diabetes, Thailand**.**

Introduction

Stroke has been a major health problem of worldwide and the trend still has been increasing continuously (1–3). It is a leading cause of mortality and disability.The Word Health Organization has estimated that every year stroke affects more than 15 million patients and of these, 5 million are permanently disabled, 5 million patients died and two thirds was found in developing countries(4). In the Southeast Asian region, stroke ranked first in number of years of life lost (1) In the United States, every year more than 795,000 people have stroke. About 610,000 of these are first or new strokes .One in four is recurrent stroke (5). While, in Thailand, stroke ranked second after ischemic heart diseases, the mortality rate was 20.8 per 100,000 people (6). Prevalence of stroke in the Thai population has been found to be between 1.8 percent (7) and 3.5 percent (8). While, most of those patients in a previous study had hypertension and type 2diabetes patients, and thus is considered to be an important in stroke patients

After stroke, rehabilitation and prevention, it is also an important concern .Despite recent advance in stroke prevention. The Word Health Organization has estimated that recurrent stroke constitutes about one quarter of all strokes (9). Many studies reported stroke patients suffer a recurrent stroke. In United States, it was reported that rate 5 to 14 percent will have a recurrent stroke within one year. Within five years, stroke will recurrence in 24 percent of woman and 42 percent of men(10) ,while in Spain was reported that rate 17.6 percent(11), in Scotland was reported 10.8 percent(12), in Australia was reported 19.8 percent(13) ,Japanese was reported 9.6 percent(14) and China was reported 11.2 percent(15), while no evidence were found in Thailand.

Recurrent stroke is a leading cause of serious long-term disability. It is an important factor in health care budgets as well as the burden of families (16–18). A few data of prevalence of recurrent stroke in developing countries has been reported. The aim of this study is to determine the prevalence of recurrent stroke and its related factors among hypertension and hypertension with type 2 diabetes patients in Thailand.

Primary outcome: Prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes patients in Thailand. (Stroke included cerebrovascular accident, ischemic, hemorrhagic, stroke of unknown type and Transient Ischemic Attack (TIA))
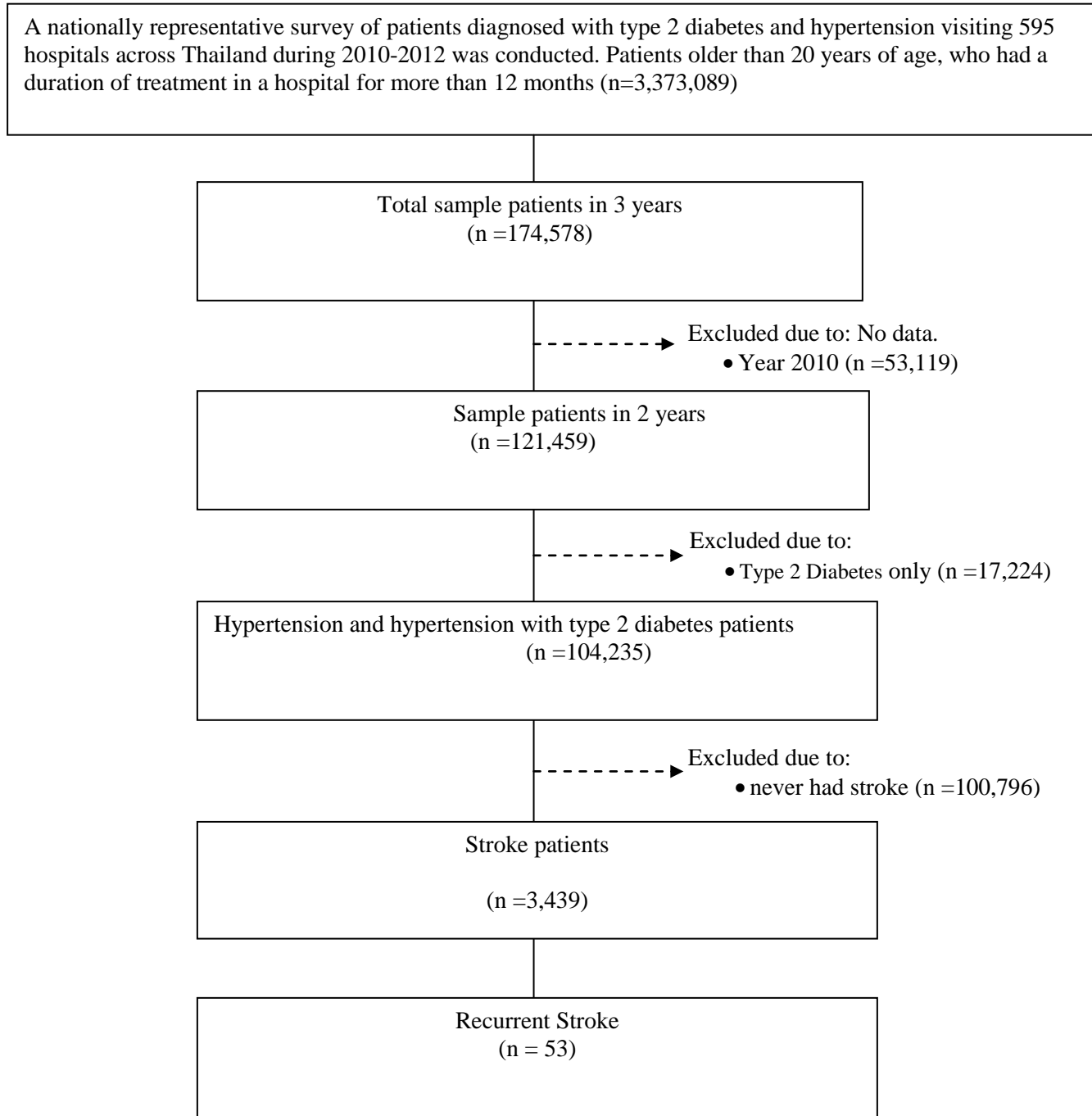
Methods

This study utilized data from an assessment on quality of care among diabetic patients diagnosed with type 2 diabetes and hypertension visiting hospitals in care of ministry of public health and Bangkok metropolitan administration in Thailand, 2010-2012 (DMHT) database. The DMHT was designed as cross-sectional study. In this study, 3,439 patients of 100, 235 patients from hypertension and hypertension with type 2 diabetic patients who used to have stroke were included.

For each patient, data was collected from medical records by health officer. The following variables were assessed: demographic characteristics (sex, age, body mass index, blood pressure, total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol, smoke, occupation, underlying diseases, duration of hypertension and type of cerebrovascular disease) Recurrent stroke was the main focus of this study. This project was approved by the Human Research and Ethics Committees of the Ministry of Public health of Thailand.

Demographic and other baseline characteristics of stroke patients were described using mean, standard deviation, median, minimum, and maximum for continuous data and frequency count, percentage for categorical data. Rate of recurrent stroke were estimated with 95% confidence interval (CI). Regarding investigation factors associated with recurrent stroke, multiple logistic regressions was used for the data analysis. This analysis was adjusted for the extraneous variables that were considered biologically and sociologically relevant or that showing a univariate relationship with the outcome. P-value less than 0.05 were considered as statistically significant. All analyses were performed using STATA version 12.0.

Results

Of 104,235 hypertension and hypertension with type 2 diabetes patients and 100,796 were excluded due to that they had never been stroke (Figure 1). A total of 3,439 patients with strokes were included in the study.

A nationally representative survey of patients diagnosed with type 2 diabetes and hypertension visiting 595 hospitals across Thailand during 2010-2012 was conducted. Patients older than 20 years of age, who had a duration of treatment in a hospital for more than 12 months (n=3,373,089)

Total sample patients in 3 years
(n =174,578)

Excluded due to: No data.
• Year 2010 (n =53,119)

Sample patients in 2 years
(n =121,459)

Excluded due to:
• Type 2 Diabetes only (n =17,224)

Hypertension and hypertension with type 2 diabetes patients
(n =104,235)

Excluded due to:
• never had stroke (n =100,796)

Stroke patients

(n =3,439)

Recurrent Stroke
(n = 53)

Figure1. Stages of algorithm of study investigating recurrent stroke

A total of 3,439 patients with stroke were enrolled, the mean age of the patients were 65.1 years (range from 22-94 years old). The majority of stroke patients were male (54.4%), the mean of body mass index were 24.4 (S.D. =4.2), the mean of systolic blood pressure was 131.3 (S.D. =16.9), the mean of diastolic blood Pressure was 75.7 (S.D.= 11.1). Total cholesterol less than 200 mg/dL (56.1%), Triglyceride readings more than or equal to 150 mg/dL (51.1), LDL-cholesterol more than or equal 100 mg/dL (60.5%) and HDL- cholesterol more than or equal 40 mg/dL (91.8%)

Most of stroke patients 57.3% did not smoke while 33.9 ever smoked. Occupation of stroke patients had been housekeeper, agricultural and employee (34.4%, 29.8% and 18.6%, respectively). The underlying diseases of stroke patients were only hypertension (67.4%), the mean of duration of hypertension were 6.1 years (range from 1-31 years old). Cerebrovascular disease of stroke patients was unknown (75.4%) and demographic of characteristics was presented in Table 1.

Table1. Demographic characteristics of stroke patients among hypertension and hypertension with type 2 diabetes patients (n =3,439)

Characteristics	Number	Percent
Sex		
male	1,869	54.4
Female	1,570	45.6
Age (years)		
Mean (SD)		65.1 (10.5)
Median (Min:Max)		65 (22-94)
Body mass index (n =3,122)		
Mean (SD)		24.4(4.2)
Median (Min:Max)		24.1 (15.2-48.9)
Blood Pressure		
Systolic BP Mean (SD)		131.3 (16.9)
Median (Min:Max)		130 (74-243)
Diastolic BP Mean (SD)		75.7 (11.1)
Median (Min:Max)		76 (40-94)
Total cholesterol		
<200 mg/dL	1,928	56.1
>=200 mg/dL	1,511	43.9

Characteristics	Number	Percent
Triglyceride		
<150 mg/dL	1,682	48.9
>=150 mg/dL	1,754	51.1
LDL-Cholesterol		
<100 mg/dL	1,358	39.5
>=100 mg/dL	2,081	60.5
HDL- Cholesterol		
>=40 mg/dL	3,157	91.8
<40 mg/dL	282	8.2
Smoke (n=2,756)		
Never	1,580	57.3
Ever	935	33.9
Currently	241	8.8
Occupation (n=3,358)		
Agricultural	1,002	29.8
Civil servant	121	3.6
Trade	216	6.4
Employee	623	18.6
Housekeeper	1,156	34.4
Other	240	7.2
Underlying diseases		
Hypertension	2,319	67.4
Hypertension with Diabetes type 2	1,120	32.6
Duration of Hypertension (years)		
Mean (SD)		6.1(4.1)
Median (Min:Max)		5 (1-36)
Type of cerebrovascular disease (the first time)		
Unknown stroke	2,314	75.4
Ischemic	302	9.8
Hemorrhagic	141	4.6
TIA	312	10.2

Prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes patients was 1.5 %(95%CI; 1.15-2.01), 1.8% were found in patients less than 60 years (95%CI; 1.07-2.76) and it decreased with age increased, while female had 2.0% more than male (95%CI; 1.34-2.79) 1.8% were found most in normal body mass index 95%CI; 1.03-2.81)

Patients of blood pressure more than 130/85 mg/dl were 2.0% (95%CI; 0.95-3.63), Total cholesterol less than 200 mg/dl were 1.7% (95%CI;1.07-2.43), Triglyceride readings more than or equal to 150 mg/dL were 1.6%(95%CI;1.06-2.29), LDL-cholesterol more than or equal 100 mg/dl were 1.6%(95%CI;1.13-2.27) and HDL- cholesterol less than 40 mg/dl were 3.2%(95%CI;1.46-5.97)

Prevalence of recurrent stroke has found in patients not smoke were 1.4% (95%CI; 0.87-2.10), Occupation of employee 2.6% (95%CI;1.47-4.13) , underlying diseases of hypertension with type 2 diabetes were 2.2% (95%CI;1.44-3.27), duration of hypertension less than 5 years have found 1.6%(95%CI;0.96-2.36) and the most cases were found in hemorrhagic patients 3.6 %(95%CI; 1.16-8.08). Prevalence of recurrent stroke were presented in Table 2.

Table 2. Prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes patients

subgroup	n	% recurrent stroke	95% CI
Overall	3,439	1.5	1.15-2.01
Sex			
male	1,869	1.2	0.73-1.77
Female	1,570	2.0	1.34-2.79
Age (years)			
<60	1,066	1.8	1.07-2.76
60-70	1,155	1.7	1.06-2.66
>=70	1,218	1.2	0.62-1.92
Body mass index			
<18	122	0.8	0.02-4.48
18-22.9	962	1.8	1.03-2.81
23-24.9	606	1.7	0.79-3.01
25-29.9	879	1.7	0.95-2.79
>=30	246	0.8	0.09-2.90

subgroup	n	% recurrent stroke	95% CI
Blood Pressure			
<=130/85	2,937	1.5	1.06-1.96
>130/85	502	2.0	0.95-3.63
Total cholesterol			
<200 mg/dL	1,928	1.5	0.96-2.09
>=200 mg/dL	1,511	1.7	1.07-2.43
Triglyceride			
<150 mg/dL	1,682	1.5	0.96-2.18
>=150 mg/dL	1,754	1.6	1.06-2.29
LDL-cholesterol			
<100 mg/dL	1,358	1.4	0.84-2.17
>=100 mg/dL	2,081	1.6	1.13-2.27
HDL- cholesterol			
>=40 mg/dL	3,157	1.4	1.01-1.86
<40 mg/dL	282	3.2	1.46-5.97
Smoke			
Never	1,580	1.4	0.87-2.10
Ever	935	1.1	0.51-1.95
Currently	241	0.8	0.10-2.96
Occupations			
Agricultural	1,002	1.3	0.69-2.20
Civil servant	121	2.5	0.51-7.07
Trade	216	0.9	0.11-3.30
Employee	623	2.6	1.47-4.13
Housekeeper	1,156	1.1	0.60-1.91
Other	240	2.1	0.67-4.79
Underlying diseases			
Hypertension	2,319	1.2	0.80-1.74
Hypertension with diabetes	1,120	2.2	1.44-3.27
Duration of Hypertension (years)			
< 5	1,351	1.6	0.96-2.36
5-10	1,364	1.5	0.95-2.34
>=10	724	1.5	0.76-2.70

subgroup	n	% recurrent stroke	95% CI
Type of cerebrovascular(first time)			
Unknown	2,314	1.4	0.98-1.99
Ischemic	302	2.7	1.15-5.15
Hemorrhagic	141	3.6	1.16-8.08
TIA	312	2.2	0.90-4.56

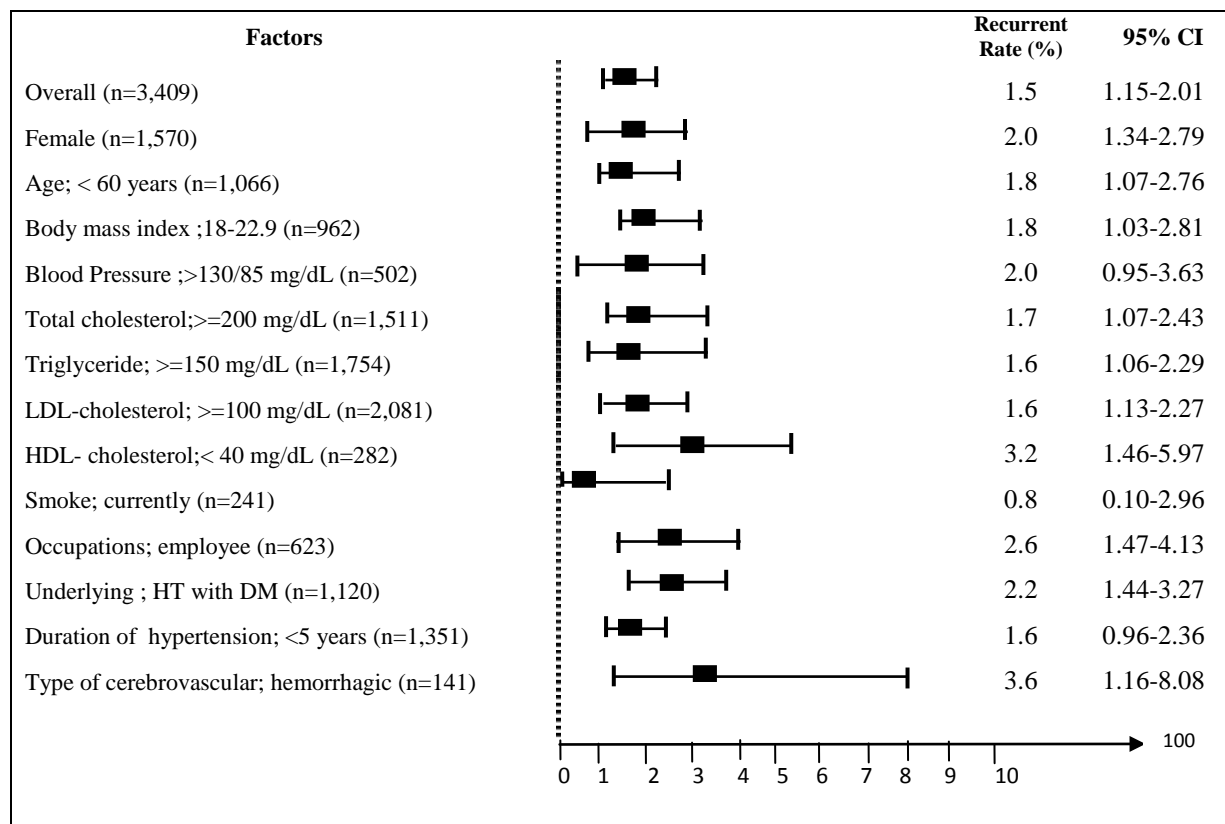| Factors		Recurrent Rate (%)	95% CI
Overall (n=3,409)		1.5	1.15-2.01
Female (n=1,570)		2.0	1.34-2.79
Age; < 60 years (n=1,066)		1.8	1.07-2.76
Body mass index ;18-22.9 (n=962)		1.8	1.03-2.81
Blood Pressure ;>130/85 mg/dL (n=502)		2.0	0.95-3.63
Total cholesterol;>=200 mg/dL (n=1,511)		1.7	1.07-2.43
Triglyceride; >=150 mg/dL (n=1,754)		1.6	1.06-2.29
LDL-cholesterol; >=100 mg/dL (n=2,081)		1.6	1.13-2.27
HDL- cholesterol;< 40 mg/dL (n=282)		3.2	1.46-5.97
Smoke; currently (n=241)		0.8	0.10-2.96
Occupations; employee (n=623)		2.6	1.47-4.13
Underlying ; HT with DM (n=1,120)		2.2	1.44-3.27
Duration of hypertension; <5 years (n=1,351)		1.6	0.96-2.36
Type of cerebrovascular; hemorrhagic (n=141)		3.6	1.16-8.08

Figure 2. Recurrent stroke rates

Results based on simple logistic regression of each factors on recurrent stroke had been found relevant variables included HDL- cholesterol less than 40 mg/dL (OR=2.33,95%CI;1.12-4.82;p-value=0.037), systolic blood pressure (OR=1.01,95%CI;1.01-1.03;p-value=0.036), diastolic blood pressure (OR=1.02 ,95%CI;1.01-1.05;p-value=0.023), underlying diseases hypertension with diabetes (OR=1.86,95%CI;1.08-3.21;p-value=0.026) and type of cerebrovascular diseases in the first time. (OR=1.88, 95%CI;1.07-3.29;p-value=0.032)

Table 3. Association of recurrent stroke between each category of factors based on simple logistic regression

Characteristics	number	% recurrent stroke	Odds ratio	95%CI	p-value
Sex					0.059
male	1,869	1.2	1		
Female	1,570	2.0	1.69	0.97-2.93	
Age (years)					0.157
>=70	1,218	1.2	1		
<70	2,221	1.8	1.53	0.83-2.84	
Body mass index					0.702
<=23	1,084	1.7	1		
>23	2,355	1.5	0.89	0.50-158	
Blood Pressure					
Systolic BP (every 1 mmHg)	3,439		1.01	1.01-1.03	0.036
Diastolic BP (every 1 mmHg)	3,439		1.02	1.01-1.05	0.023
Total cholesterol					0.633
<200 mg/dL	1,928	1.5	1		
>=200 mg/dL	1,511	1.7	1.14	0.66-1.96	
Triglyceride					0.798
<150 mg/dL	1,682	1.5	1		
>=150 mg/dL	1,754	1.6	1.07	0.62-1.84	
LDL-Cholesterol					0.582
<100 mg/dL	1,358	1.4	1		
>=100 mg/dL	2,081	1.6	1.17	0.66-2.06	
HDL- Cholesterol					0.037
>=40 mg/dL	3,157	1.4	1		
<40 mg/dL	282	3.2	2.33	1.12-4.82	

Characteristics	number	% recurrent stroke	Odds ratio	95%CI	p-value
Smoke (n=2,077)					0.639
Never	1,580	1.4	1		
Ever	935	1.1	0.76	0.36-1.62	
Currently	241	0.8	0.59	0.13-2.53	
Occupation					0.482
Housekeeper, Civil servant, Other	1,517	1.4	1		
Agricultural, Trade, Employee	1,841	1.7	1.22	0.69-2.13	
Underlying diseases					0.026
Hypertension	2,319	1.2	1		
Hypertension with Diabetes	1,120	2.2	1.86	1.08-3.21	
Duration of hypertension (every1 years)	3,439		0.98	0.91-1.05	0.579
Type of cerebrovascular (in first time)					0.032
Unknown stroke	2,314	1.4	1		
Ischemic, Hemorrhage, TIA	755	2.7	1.88	1.07-3.29	

Based on multivariable logistic regression, factors related to recurrent stroke had been found significant included HDL-cholesterol less than 40 mg/dL (OR_{adjust} =2.70 ,95%CI;1.29-5.65;p-value=0.008), diastolic blood pressure(OR_{adjust}=1.03,95%CI;1.01-1.06;p-value=0.009), type of cerebrovascular in first time (OR_{adjust} =1.89,95%CI;1.08-3.33;p-value=0.026) and sex (OR_{adjust} =1.82,95%CI;1.05-3.18;p-value=0.033) effect on recurrent stroke

Table 4. Association of recurrent stroke between each category of factors based on multiple logistic regressions (Multivariate)

Characteristics	number	% recurrent stroke	Crude Odds ratio	*Adjusted Odds ratio	95%CI	p-value
HDL- Cholesterol						0.008
>=40 mg/dL	3,157	1.4	1	1		
<40 mg/dL	282	3.2	2.33	2.70	1.29-5.65	
Diastolic BP (every 1 mmHg)	3,439		1.02	1.03	1.01-1.06	0.009
Type of cerebrovascular diseases						0.026
unknown stroke	2,314	1.4	1	1		
ischemic, hemorrhagic, TIA	755	2.7	1.88	1.89	1.08-3.33	
Sex						0.033
male	1,869	1.2	1	1		
female	1,570	2.0	1.69	1.82	1.05-3.18	

* Adjusted for baseline measurements and other covariates, including sex, HDL-cholesterol, diastolic blood pressure and type of cerebrovascular diseases
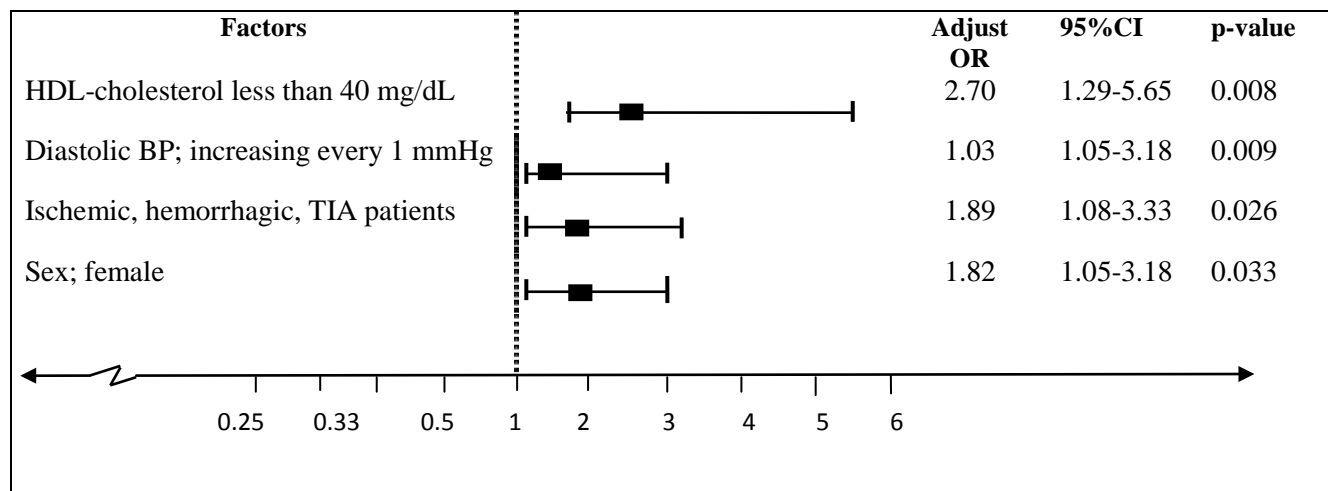

Factors		Adjust OR	95%CI	p-value
HDL-cholesterol less than 40 mg/dL		2.70	1.29-5.65	0.008
Diastolic BP; increasing every 1 mmHg		1.03	1.05-3.18	0.009
Ischemic, hemorrhagic, TIA patients		1.89	1.08-3.33	0.026
Sex; female		1.82	1.05-3.18	0.033

0.25 0.33 0.5 1 2 3 4 5 6

Figure 3 Association between recurrent stroke and factors based on Adjusted OR

Discussion

In this study, the prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes patients was 1.5 percent of 3,439 eligible participants. This prevalence was lower than previous reports from Europe and some countries of Asia while no evidence was found in Thailand. Prevalence of recurrent stroke in patient in Spain(11), Scotland(12),

Australia(13), Japanese(14) and China(15), was 17.6 percent, 10.8 percent, 19.8 percent, 9.6 percent,11.2 percent, respectively(19). In United States, it was reported that rate 5 to 14 percent will have a recurrent stroke within one year. Within five years, stroke will recurrence in 24 percent of woman and 42 percent of men(10) . Although the rate of recurrent stroke was only 1.5 percent, patients should continue to focus on the medications and self-care. This study may underestimate the problems, for examples, some patients with recurrent stroke may die before data was collected.

Regarding in this study, every 1 mmHg of diastolic blood pressure increased, HDL-cholesterol less than 40 mg/dL and having stroke and transient ischemic attack and being a female related with recurrent stroke. This finding was consistent with a study in 2012; lower HDL-cholesterol on admission was found to be independent risk factors for a recurrent of ischemic stroke within 12 months onset of stroke. (14). Elevated blood pressure is a well known risk factor for stroke, evidences have shown that most strokes occur in patients with uncontrolled hypertension and there is a positive and strong correlation between elevated blood pressure and stroke(20–22).The present result emphasizes the relationship between level of diastolic blood pressure and recurrent stroke. This study had found recurrent stroke among female more than male while inconsistent with reported from United States(10). However the cause of stroke recurrence can be caused by many factors, while the subtypes of recurrent strokes are often not identical. Most recurrences remain unexplained by risk factors. The best management method for recurrent stroke is prevention.

Limitation of this study is that some variables were not explored such as duration before occurred recurrence, lifestyle and self-care behaviors

In Conclusion: Prevalence of recurrent stroke among hypertension and hypertension with type 2 diabetes a patient in Thailand was lower than that of previous reports in Europe and in some countries of Asia. However, stroke patients should continually to focus on the medications, self-care, and usual check level of HDL-cholesterol. The preventive strategies still need to proceed in the future, to improve quality of the patient's stroke. The effect of improving HDL-cholesterol levels should be evaluated in preventing recurrent stroke in the future studies.

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