Impact of Risk Factors for Recurrent Ischemic Stroke in Prasat Neurological Institute

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Background: *Recurrent strokes are more likely to be more disabling or fatal than first-even strokes. The high frequency of recurrences underscores the importance of secondary prevention.*
Objective: *Investigate risk factors of recurrent ischemic stroke and to compare the outcomes after treatment following the Thai stroke guideline between patients with recurrent ischemic stroke and patients without recurrent ischemic stroke.*
Material and Method: *Sixty-seven patients with recurrent ischemic stroke and 167 patients without recurrent ischemic stroke were included in the present study. All patients were evaluated for demographic data, modifiable risk factors, and treatment.*
Results: *Patients without recurrent ischemic stroke had better controlled level of systolic blood pressure, diastolic blood pressure, and higher high-density lipoprotein level than patients with recurrent ischemic stroke. Carotid stenosis was higher in patients with recurrent ischemic stroke (43.3% vs. 28.7%, p = 0.032). Patients with recurrent ischemic stroke received statin therapy (67.2% vs. 86.8%, p = 0.001) and folic acid (61.2% vs. 78.4%, p = 0.007) less than patients without recurrent ischemic stroke. The multivariate analysis showed that well controlled diastolic blood pressure (p = 0.014), higher level of high-density lipoprotein (p = 0.010), and receiving of statin (p = 0.002) were associated with decreased incidence of recurrent ischemic stroke.*
Conclusion: *Well-controlled risk factors including blood pressure, fasting blood sugar, high-density lipoprotein, and low-density lipoprotein were crucial for the protection of recurrent ischemic stroke. Furthermore, the benefits of statin and folic acid therapies for the protection of recurrent ischemic stroke were emphasized.*

Keywords: *Recurrent ischemic stroke, Risk factors*

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Stroke is now the second leading cause of death after ischemic heart disease worldwide[1]. Two-thirds of all stroke deaths occur among people in developing countries[2]. According to Burden of disease and Injuries in Thailand: Ministry of Public Health November 2002, stroke is the first leading cause of death in Thai women and the third leading cause of death in Thai men[3]. Recurrent stroke is a major threat of stroke patients, especially in the early phase of stroke. Previous studies of recurrent strokes reported a first year recurrence rate between 6-14%[4-8] and 5-year recurrent rate between 20-37%[5,6,8].

Recurrent strokes are more likely to be disabling or fatal than first-even strokes[9]. Furthermore, recurrent stroke leads to severe complications, high mortality rate, and high cost of treatment[9]. The high frequency of recurrences underscores the importance of secondary prevention. Although a guideline for prevention of stroke in patients with ischemic stroke or transient ischemic attack has currently been published and used widely over the country, the incidence of recurrent ischemic strokes is still high[10]. To date, there is no report of the difference of control risk factors between patients with recurrent ischemic stroke and patients without recurrent ischemic stroke in Thailand. The aims of the present study, therefore, were to investigate risk factors of recurrent ischemic stroke and to compare the outcomes after treatment following the Thai stroke guideline[11] between patients with recurrent ischemic stroke and patients without recurrent ischemic stroke.

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Material and Method

Study design

A retrospective study was conducted at Prasat Neurological Institute, Bangkok, Thailand. All

patients with recurrent ischemic stroke who were admitted in Prasat Neurological Institute between October 1, 2006 and September 30, 2009 were consecutively recruited in the present study. Recurrent ischemic stroke was defined as an ischemic stroke that occurred for the second time. Control populations were selected based on each recurrent stroke patients in the present study group, by matching the date of first stroke event between the cases and control group. The present study was approved by the ethical committee of Prasat Neurological Institute.

Inclusion criteria

Inclusion criteria for the study group included the patients who had recurrent ischemic stroke[12], the second attack of an ischemic stroke, between October 1, 2006 and September 30, 2009 and having at least one CT scan or MRI of the brain during hospitalization. All the patients were aged 18 years or older.

Inclusion criteria for the control group included having the first-event ischemic stroke[12] during the same period as the study group, having at least one CT scan or MRI of the brain during hospitalization, being aged 18 years or older, and undertaking periodical follow-up at the outpatient clinic.

All patients in both study and control group were treated according to the Thai stroke guideline[11]. All patients in both study and control group had CT brain scan or MRI of the brain for confirming the diagnosis of ischemic stroke.

Exclusion criteria

The control patients who died during the period of follow-up or loss of follow-up were excluded.

Assessment of risk factors

All patients were evaluated for enrollment following recruitment criteria. The following variables were assessed: age, sex, underlying disease, time from the first-event ischemic stroke to the onset of recurrent in the present study group, time from the first-event ischemic stroke to the day of follow-up in the control group, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood sugar (FBS), HbA1C, lipid profile, complete blood count, VDRL, drug usage, and the subtype of ischemic stroke. The present study group was assessed at the time of admission of recurrent ischemic stroke. The control group was assessed as outpatients for the same duration as the present study group.

Hypertension (HT), diabetes mellitus (DM), and hyperlipidemia were diagnosed according to established criteria[13-15]. Modifiable risk factors for stroke and drugs were evaluated at admission for the study group and at the same time for the control group. Previously diagnosed hypertension was regarded as controlled, when blood pressure was lower than 140/90 mmHg[11]. DM was regarded as controlled, when fasting serum glucose level was lower than 130 mg/dl[11,16]. Hyperlipidemia was regarded as controlled, when plasma low-density lipoprotein (LDL) level was lower than 100 mg/dl[11]. Prevention of cardioembolism from atrial fibrillation (AF) was regarded as controlled, when the international normalized ratio (INR) of prothrombin time was kept in the range of 2.0-3.0. The diagnosis of carotid stenosis was made when there was 70 percent stenosis with the NASCET method[17]. The diagnosis of chronic kidney disease was made when the estimated glomerular filtration rate was less than 60 mL/min per 1.73 m^2[18]. First-event ischemic stroke was evaluated according to the clinical syndrome by Oxfordshire community stroke project classification (OCSP)[19] as total anterior circulation infarction, partial anterior circulation infarction, lacunar infarction, posterior circulation infarction and further classified according to TOAST criteria, as large vessel infarction, small vessel (lacunar) infarction, cardioembolic, and stroke of other determined or undetermined causes[20].

Sample size

Sixty-seven patients with recurrent ischemic stroke and having met the inclusion criteria were consecutively recruited during the present study period. The number of patients in the control group was three times more than the number of patients in the study group. However, 34 patients in the control group were excluded because they had loss of follow-up, resulting in 167 patients in the control group.

Statistical analysis

Statistical analysis was performed by utilizing SPSS 16.0. Continuous and categorical variables were expressed as mean and percentages respectively. Parametric and nonparametric comparisons of categorical and continuous variables were performed using the Chi-square test, Student t-test and Mann-Whitney test, as appropriate. Explanatory variables initially included in the model were those with a probability value < 0.15 from the univariate analysis. A p-value less than 0.05 was the threshold of statistical significance.

Results

Sixty-seven patients with recurrent ischemic stroke and 167 patients without recurrent ischemic stroke were included in the present study. The demographic characters of both groups are shown in Table 1. Male and female ratio of the present study group was 1.79 when compared to 1.32 of the control group. Mean age of the study group was 65.94 years (ranged from 44 to 92 years) and of the control group was 65.11 years (range from 34 to 90 years). There was no significant difference in terms of age, gender, and regional residency between the present study group and control group. The time since previous stroke occurred to the onset of recurrent ischemic stroke in the present study group was analyzed. The result showed that mean time since the previous stroke occurred to the onset of the recurrence was 13 months.

Comparison of risk factors between patients with recurrent ischemic stroke and patients without recurrent ischemic stroke was performed (Table 2). Prevalence of hypertension, DM, hyperlipidemia, AF, ischemic heart disease and chronic renal failure were not different between both groups. Incidence of carotid stenosis in patients with recurrent ischemic stroke was higher than patients without recurrent ischemic stroke (43.3% vs. 28.7%, p = 0.032).

The modifiable risk factors for stroke were then compared between patients with recurrent ischemic stroke and patients without recurrent ischemic stroke. Patients with non-recurrent ischemic stroke had significantly better controlled level of SBP, DBP, and higher HDL level than patients with recurrent ischemic stroke (Table 3). No significant differences were found in terms of fasting serum glucose level, HbA1C level, Cholesterol level, LDL level, Triglyceride level, CBC,

Table 1. Demographic characteristics of patients with recurrent stroke (Study group) and patients without recurrent ischemic stroke (Control group)

Characteristics	Study group (n = 67)	Control group (n = 167)	p-value
Age (yr)	65.94 (44-92)	65.11 (34-90)	0.616
Gender			
Male	43 (64.2%)	95 (56.9%)	0.305
Female	24 (35.8%)	72 (43.1%)	
Subtype of ischemic stroke (TOAST criteria)			
Large vessel infarction	21 (31.3%)	56 (34.4%)	0.149
Small vessel infarction	40 (59.7%)	103 (62.9%)	
Cardioembolic	6 (9%)	4 (2.5%)	
Clinical syndrome			
TICA	4 (6%)	20 (12%)	0.424
PICA	3 (4.5%)	7 (4.2%)	
Lacunar infarction	54 (80.6%)	119 (71.3%)	
Posterior circulation infarction	6 (9%)	21 (12.6%)	
Duration (mo)*	13	11	0.058

TICA = total anterior circulation infarction; PICA = partial anterior circulation infarction
* Duration, in control group, means the time from first ischemic stroke to follow-up

Table 2. Risk factors between study and control group

Risk factors	Study group (n = 67)	Control group (n = 167)	p-value
AF	5 (7.5%)	5 (3%)	0.127
DM	28 (41.8%)	67 (40.1%)	0.814
HT	56 (83.6%)	132 (79%)	0.430
Dyslipidemia	57 (85.1%)	151 (90.4%)	0.240
Carotid stenosis	29 (43.3%)	48 (28.7%)	0.032
Chronic renal failure	1 (1.5%)	9 (5.4%)	0.183

Table 3. Baseline status and treatments between study and control group

Status and treatments	Study group (n = 67)	Control group (n = 167)	p-value
Systolic blood pressure (mmHg)	142.75	134.63	0.013
Diastolic blood pressure (mmHg)	82.42	75.49	0.001
Fasting blood sugar (mg/dl)	113.25	111.47	0.263
HbA1C (mmols/l)	6.97 (n = 30)	7.08 (n = 13)	0.421
Cholesterol (mg/dl)	170.72	172	0.802
High density lipoprotein (mg/dl)	37.64	42.10	0.007
Low density lipoprotein (mg/dl)	107.43	101.54	0.244
Triglyceride (mg/dl)	127.61	126.55	0.651
Complete blood count			
Hematocrit (%)	38.77	39.57	0.961
White blood cell count	7,976.02	7,991.97	
Platelet count	248,227	281,373	
VDRL positivity	3 (4.5%)	4 (2.4%)	0.412
Antihyperglycemic drugs			
Sulfonylurea	12 (17.9%)	33 (19.8%)	0.745
Metformin	13 (19.4%)	37 (22.2%)	0.642
Thiazolidinedione	2 (3%)	3 (1.8%)	0.570
Folic acid	41 (61.2%)	131 (78.4%)	0.007
Antihypertensive drugs			
ACEI/ARB	26 (38.8%)	70 (41.9%)	0.662
Diuretic	8 (11.9%)	25 (15%)	0.547
Calcium channel blocker	27 (40.3%)	41 (24.6%)	0.016
Beta-blocker	10 (14.9%)	22 (13.2%)	0.742
Cardura	2 (3%)	2 (1.2%)	0.340
Lipid lowering drugs			
Statin	45 (67.2%)	145 (86.8%)	0.001
Gemfibrozil	2 (3%)	7 (4.2%)	0.664
Anti-platelet aggregation drugs			
Aspirin	49 (73.1%)	135 (80.8%)	0.194
Ticlopidine	2 (3%)	1 (0.6%)	0.142
Clopidogel	8 (11.9%)	17 (10.2%)	0.693
Aggrenox	1 (1.5%)	4 (2.4%)	0.666
Cilostazol 100 mg/d	4 (6.0%)	3 (1.8%)	0.900
Cilostazol 200 mg/d	1 (1.5%)	11 (6.6%)	0.110
Warfarin	5 (7.5%)	6 (3.6%)	0.206

ACEI/ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blockers; VDRL = veneral disease research laboratory test

and VDRL reactivity between patients with recurrent ischemic stroke and the controls.

The analysis of drugs usage in patients with recurrent ischemic stroke and control group including antihypertensive drugs, antihyperglycemic drugs, antiplatelet aggregated drugs and anticoagulant showed no difference between the present study group and control group except for calcium channel blocker. Calcium channel blockers were used in patients with recurrent ischemic stroke more than in controls (40.3% vs. 24.6%, p = 0.016). On the other hand, the patients with recurrent ischemic stroke received statin therapy (67.2% vs. 86.8%, p = 0.001) and folic acid (61.2% vs. 78.4%, p = 0.007) less than patients without recurrent ischemic stroke.

The authors specifically analyzed the amount of antihypertensive drug used in patients with recurrent ischemic stroke and patients without recurrent ischemic stroke. The result showed no statistical difference in the amount of antihypertensive drug used between both groups (mean, 1.1642 vs. 1.0299, p = 0.288).

All patients were classified according to subtype of ischemic stroke as small vessel infarction, large vessel infarction, cardioembolic and stroke of undetermined causes by using TOAST criteria. They were also classified according to clinical stroke syndrome (OCSP) as TICA, PICA, lacunar infarction, and posterior circulation infarction. The result showed no statistically significant differences in ischemic stroke subtype (p = 0.149) and clinical stroke syndrome (p = 0.424) between patients with recurrent ischemic stroke and patients without recurrent ischemic stroke.

The univariate analysis between patients with recurrent ischemic stroke and the control group demonstrated that nine factors such as SBP, DBP, HDL, carotid stenosis, statin usage, aspirin usage, folic acid usage, large vessel stenosis, and small vessel stenosis were statistically significant factors.

Then, the multivariate analysis of these factors was performed (Table 4). The results revealed that factors associated with decreased incidence of recurrent ischemic stroke were well control DBP (p = 0.014), higher level of HDL (p = 0.010), and receiving of statin (p = 0.002).

Furthermore, the association between the result of treatment following the American heart association stroke guideline and the decreased incidence of recurrent ischemic stroke was analyzed by comparing the modifiable risk factors between patients with and without recurrent ischemic strokes. The result is shown in Table 5. Well controlled BP and low LDL did not shown any protective effect in prevention of ischemic stroke. However, the level of fasting blood sugar in patients without recurrent ischemic stroke was statistically significantly lower than that of patients without recurrent ischemic stroke (p = 0.01).

Table 4. Factors for recurrent ischemic stroke (multivariate analysis)

Factors	p-value	Odds ratio (95% CI)
SBP	0.955	1.001 (0.98-1.021)
DBP	0.014	0.960 (0.930-0.932)
HDL	0.010	1.037 (1.009-1.066)
Carotid stenosis	0.067	1.930 (0.956-3.896)
Statin	0.002	3.524 (1.589-7.817)
Aspirin	0.350	1.804 (0.523-6.218)
Folic acid	0.172	1.648 (0.804-3.379)
Large vessel infarction	0.279	2.539 (0.470-13.708)
Small vessel infarction	0.321	2.297 (0.445-11.865)

SBP = systolic blood pressure; DBP = diastolic blood pressure; HDL = high density lipoprotein

Discussion

The present study of risk factors and recurrent strokes in Perth[21] has demonstrated that hypertension was not identified as a risk factor of recurrence, similar to the present findings. Even though hypertension was not demonstrated as a risk factor of recurrence in the present study, the data from the UK-TIA study[22] showed that the risk of recurrent stroke increased following increased SBP levels more than 130 mmHg and increased DBP levels more than 80 mmHg indicated that poor blood pressure control was the risk of recurrent stroke and blood pressure was 'the lower, the better'. Similarly, the present study revealed that patients with recurrent ischemic stroke had higher blood pressure than patients without recurrence. Another factor that is most constantly associated with recurrence is diabetes[23]. The present result showed that fasting blood sugar in patients without recurrent ischemic stroke after the treatment following the stroke guideline was lower than that of

Table 5. Result of treatment modifiable risk factors

Risk factors	Study group (n = 67)	Control group (n = 167)	p-value
Hypertension			
SBP < 140 mmHg	24/56 (42.9%)	74/132 (56.1%)	0.476
DBP < 90 mmHg	34/56 (60.7%)	115/132 (78.8%)	0.182
Diabetes mellitus			
FBS < 130 mg/dl	17/28 (60.7%)	42/67 (62.7%)	0.010
Hyperlipidemia			
LDL < 100 mg/dl	28/57 (49.1%)	83/151 (55%)	0.614

SBP = systolic blood pressure; DBP = diastolic blood pressure; FBS = fasting blood sugar; LDL = low density lipoprotein

patients with recurrent ischemic stroke, although not statistically significant. This result was in concordance with the notion that hyperglycemia was a risk factor of recurrent ischemic stroke[16]. Indeed, diabetes has been considered as a prothrombotic state. Hyperglycaemia is associated with endothelial dysfunction, increased platelet aggregation and adhesiveness and decreased fibrinolytic activity enhancing thrombogenesis[16].

Furthermore, the present study demonstrated that patients without recurrent ischemic stroke had better controlling in blood pressure, LDL, and HDL than that in patients with recurrent ischemic stroke despite not being statistically significant. These results suggested that well controlling of blood pressure, FBS, LDL and HDL would protect the occurrence of recurrent ischemic stroke. That the differences of mentioned factors were not statistically significant may be due to a small sample size of the present study or may be other factors that will affect the recurrences.

The strong association of carotid stenosis and recurrent ischemic stroke is illustrated in the present study. This result was in agreement with previous reports showing that 50% of ischemic strokes were caused by atherothrombo-embolism and the majority of cases were related to the atheroma in the extracranial vessels[24,25]. Atherosclerotic narrowing at, or around, the origin of the internal carotid artery (ICA) was the most frequently implicated cause of large-artery transient ischemic attack (TIA) or ischemic stroke[26]. Most of the strokes that occur within the first few years after a TIA or minor stroke in patients with carotid stenosis are ischemic and occur in the territory of the symptomatic artery[27]. All these evidences support the notion that the risk of recurrent stroke was carotid stenosis. An early detection and an immediate treatment of carotid stenosis are thus desired for the protection of recurrent ischemic stroke.

The association of antihypertensive drug with secondary stroke prevention has been demonstrated by several studies. The association of the secondary stroke prevention with thiazide from the Carter study[28], with indapamide from The Chinese PATS study[29], with perindopril combined with indapamide from The PROGRESS study[30,31,], with ramipril from HOPE study[32] with ACE inhibitors and diuretics from the meta-analysis of Rashid group[33] were well established. However, no significant difference of antihypertensive drug taking between patients with recurrent and patients without recurrent ischemic stroke was demonstrated in the present study. Surprisingly, the authors found that patients with recurrent ischemic stroke receiving calcium channel blocker more than patients without recurrent stroke with statistically significant difference. To date, no report has shown the association of calcium channel blocker usage with increased risk of ischemic stroke[34].

The benefit of anti-platelet aggregation drugs in patients with non-cardioembolic stroke, such as aspirin 50 to 1,300 mg, aspirin plus Dipyridamole[35], Ticlopidine[36], and Clopidogrel[37] for prevention of recurrent ischemic stroke have been demonstrated by several investigators. Contrarily, the authors found no association of anti-platelet aggregation drug and recurrent ischemic stroke. The anti-platelet aggregation drugs that were evaluated in the present study included aspirin 60 to 325 mg, aspirin plus Dipyridamole, aspirin plus Cilostazol 100 to 200 mg, Ticlopidine, and Clopidogrel. These conflicting results may be due to the treatment guideline of both studied and control groups in the present study. All patients with or without recurrent ischemic stroke were treated according to the Thai stroke guideline resulting in similarity of antiplatelet aggregation drug treatment. Several previous studies have shown that statin therapy can reduce the risk of stroke. The Medical Research Council Heart Protection Study (HPS)[38] showed that statin therapy was associated with a 25% reduction in the risk of stroke (risk ratio 0.75, 95% CI: 0.66-0.85, p - 0.0001) but the impact of statin therapy on recurrent stroke in the patient stroke subgroup was not reported. The SPARCL study showed 16% risk reduction in time to first occurrence of stroke with atorvastatin (adjusted hazard ratio = 0.84, 95% CI = 0.71-0.99; p = 0.03)[39]. Similarly, the present study showed that patients with non-recurrent ischemic stroke had significantly received statin therapy more than patients with recurrent ischemic stroke. Indeed, patients without recurrent ischemic stroke in the present study had higher mean of HDL level than that of patients with recurrence. Furthermore, the number of patients without recurrent ischemic stroke with LDL level less than 100 mg/dl was higher than that of patients with recurrence. The possible reason behind this benefit of statin was that statin-induced LDL reduction was significantly correlated to plaque volume reduction and inversely correlated with arterial reverse remodeling associated with plaque regression even after 3-6 months of treatment[40]. Although plaque regression is considered to be a significant determinant of statin-induced clinical benefits in both primary and secondary prevention[41], its mechanisms remain not clear.

Interestingly, the present study showed that folic acid was associated with the decreased risk of recurrent ischemic stroke. The present results were consistent with previous report showing that homocysteine concentrations in plasma have been related to the risk of stroke, with an odds ratio of 1.5 (95% CI: 1.3-1.9) for each increase of 5 umol/l[42]. A recent meta-analysis calculated that, in primary prevention, a reduction of 3 umol/l involved a 19% reduction in the risk of stroke[39]. This attracted interest because of the possibility of therapeutic modification of stroke risk via the reduction of homocysteine levels using dietary schedules or supplements of folic acid and vitamins B6 and B12.

Even though the present study provided substantial evidences regarding the risk factors of recurrent ischemic stroke, there are a few weaknesses of the present study. The major pitfalls of the present study were too few numbers of patients in the present study group and control group resulting in no association of some risk factors and the occurring of recurrent ischemic stroke. Besides, the investigation was performed retrospectively. Some data such as life style modification, smoking, alcohol drinking and BMI thus were missing because patients' medical records were not complete. Some information especially blood pressure collected at the time of admission in patients with recurrent ischemic stroke may be confounded by stress and autoregulation in the acute phase of stroke. These might result in higher blood pressure of patients with recurrent ischemic stroke than that of patients without recurrent ischemic stroke.

In conclusion, the present study built strong evidences that well-controlled risk factors including blood pressure, fasting blood sugar, HDL and LDL were crucial for the protection of recurrent ischemic stroke. Furthermore, the benefits of statin and folic acid therapy for the protection of recurrent ischemic stroke were underscored. That 30 to 60% of patients with recurrent ischemic stroke were unable to control risk factors despite following treatment according to guidelines emphasized the seriousness of controlling of the risk factors.

Potential conflicts of interest

None.

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ความสำคัญของปัจจัยเสี่ยงต่อการกำเริบซ้ำของภาวะสมองขาดเลือด

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ภูมิหลัง: *การกำเริบซ้ำของโรคหลอดเลือดสมองตีบตันมีผลให้เกิดความพิการ และเสียชีวิตมากกว่าการเกิดโรคหลอดเลือดสมองตีบตันครั้งแรก*

วัตถุประสงค์: *เพื่อศึกษาปัจจัยเสี่ยงต่อการการเกิดการกำเริบซ้ำของโรคหลอดเลือดสมองตีบตัน และเพื่อเปรียบเทียบผลการรักษาผู้ป่วยตามแนวทางการรักษาผู้ป่วยโรคหลอดเลือดสมองในประเทศไทย ระหว่างกลุ่มผู้ป่วยโรคหลอดเลือดสมองตีบตันที่ไม่มีอาการกำเริบซ้ำ และกลุ่มผู้ป่วยโรคหลอดเลือดสมองตีบตันที่มีการกำเริบซ้ำ*

วัสดุและวิธีการ: *ศึกษาในผู้ป่วยที่มีการกำเริบซ้ำของโรคหลอดเลือดสมองตีบตัน 67 ราย และผู้ป่วยที่มีโรคหลอดเลือดสมองตีบตันที่ไม่มีอาการกำเริบซ้ำ 167 ราย ข้อมูลที่ศึกษาได้แก่ด้านประชากรศาสตร์, ปัจจัยเสี่ยง และยาที่ใช้รักษา*

ผลการศึกษา: *พบว่ากลุ่มผู้ป่วยโรคหลอดเลือดสมองตีบตันที่ไม่มีอาการกำเริบซ้ำ มีการควบคุมระดับ systolic blood pressure (SBP), diastolic blood pressure (DBP) ดีกว่าและมีค่า high density lipoprotein (HDL) สูงกว่ากลุ่มผู้ป่วยที่มีการกำเริบซ้ำของโรคหลอดเลือดสมองตีบตัน พบภาวะ carotid stenosis ในกลุ่มผู้ป่วยโรคหลอดเลือดสมองตีบตันที่มีการกำเริบซ้ำสูงกว่ากลุ่มผู้ป่วยที่ไม่มีอาการกำเริบซ้ำ (43.3% vs. 28.7%, p = 0.032) และกลุ่มผู้ป่วยโรคหลอดเลือดสมองตีบตันที่มีการกำเริบซ้ำมีการใช้ยา statin (67.2% vs. 86.8%, p = 0.001) และ folic acid (61.2% vs. 78.4%, p = 0.007) น้อยกว่ากลุ่มผู้ป่วยโรคหลอดเลือดสมองตีบตันที่ไม่มีอาการกำเริบซ้ำ เมื่อวิเคราะห์แบบ multivariate พบว่าการควบคุม DBP ได้ดี (p = 0.014), การมีค่า HDL สูง (p = 0.010) และการได้รับยา statin (p = 0.002) สัมพันธ์กับอัตราการเกิดการกำเริบซ้ำของภาวะสมองขาดเลือด*

สรุป: *การควบคุมปัจจัยเสี่ยงได้แก่ ความดันโลหิต, ระดับน้ำตาล, HDL, LDL มีความสำคัญอย่างยิ่งในการป้องกันการกำเริบซ้ำของภาวะสมองขาดเลือด นอกจากนี้การได้รับยา statin และ folic acid มีประโยชน์อย่างยิ่งในการป้องกันการกำเริบซ้ำของภาวะสมองขาดเลือด*