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Prevalence and predictive factors of progression in pure motor, ataxic hemiparesis and mixed sensorimotor lacunar syndrome

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Abstract

Objectives: To explore the prevalence and predictive factors of progressive lacunar stroke (PLS). *Methods:* Consecutive patients with acute lacunar stroke, who were admitted at King Chulalongkorn Memorial hospital during 1st July 2015-30th June 2018, were retrospectively recruited. The clinical lacunar stroke was defined as acute motor deficit lasting more than 24 hours and clinical syndrome compatible with pure motor hemiparesis, ataxic hemiparesis or sensorimotor stroke. The patients with cardioembolism or imaging shown cortical involvement was excluded. PLS was considered if there was an increase in NIHSS more than 2 points during admission. Patient characteristics, clinical data, imaging findings and medical treatment during admission was statistically analyzed. Functional outcome was assessed based on the modified Rankin Scale at discharge and 3 months. *Results:* Of 302 patients, 70 (23.2%) had PLS. Multivariate logistic regression analysis revealed that age at stroke onset more than 60 years (adjusted odd ratio [aOR], 2.17; 95% confidence interval [CI], 1.16-4.06, p=0.016), initial systolic blood pressure (SBP) more than 165 mmHg (aOR 2.40, 95%CI 1.25-4.61, p=0.008), white blood cell (WBC) more than 8500/ microliters (aOR 1.95, 95%CI 1.05-3.62, p=0.034), pontine infarction (aOR 1.99, 95%CI 1.07-3.71, p=0.031), branch atheromatous disease (BAD) (aOR 2.47, 95%CI 1.37-4.48, p=0.003), and significant vessels stenosis relevant to infarction (aOR 2.41, 95%CI 1.09-5.36, p=0.031) were independent predictors of PLS.
Conclusion: Age more than 60 years, initial SBP more than 165mmHg, WBC more than 8500/microliters, pontine infarction, BAD and significant symptomatic artery stenosis are associated with PLS.

Keywords: Lacunar stroke, progressive stroke, predictive factors, prevalence

INTRODUCTION

Patients with lacunar stroke generally have better prognosis and higher survival rate than those with large vessels occlusive or cardioembolic stroke. However, some patients with lacunar stroke develop progressive motor deficit at acute phase leading to severe disability. The predictive factors for progression of lacunar stroke is not well established. Moreover, some patients with classic lacunar syndrome reveal large vessels stenosis which is more prevalent in Asian population. Since identifying presentation features that predict progression is important, the patients at risk should be monitored strictly and applied appropriate treatment as early as possible. Therefore, we investigated the prevalence of progressive lacunar stroke and predictive factors influencing progressive motor deficit of patients with lacunar stroke.

METHODS

Study population and patient selection

We retrospectively recruited consecutive patients,

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with acute ischemic stroke who were admitted to King Chulalongkorn Memorial Hospital (KCMH) between July 1, 2015 and June 30, 2018. The inclusion criteria included: (1) Aged more than 18 years old; (2) Admission within 72 hours after the stroke onset; (3) Clinical presentation of lacunar syndrome with motor deficit was defined as acute focal neurologic deficit that lasted more than 24 hours, consistent with one of the following three classic lacunar syndromes pure motor hemiparesis, ataxic hemiparesis and sensorimotor stroke. The exclusion criteria included: (1) Patients with cardiogenic embolism; (2) Patients with vasculitis, tumor, congenital disease and any type of arterial dissection; (3) Patients who presented with cortical dysfunction including aphasia, neglect, alteration of consciousness, visual field defect or apraxia; (4) CT or MRI brain revealed infarction in the territory of large vessel, multiple infarction or cortical infarction.

Information of patients

The patients' demographic data, stroke onset, systolic and diastolic blood pressure at first presentation was recorded. Medical history included hypertension, diabetes mellitus, dyslipidemia, and previous ischemic stroke was noted. Further, current antiplatelet usage and the episode of capsular warning sign were also collected.

We retrospectively reviewed laboratory testing, that was completely investigated following KCMH stroke protocol. Some laboratory parameters, including white blood cell count (WBC), hematocrit (Hct), random capillary blood glucose (CBG), blood urea nitrogen (BUN), creatinine (Cr), sodium (Na) and urine specific gravity were collected on admission day. Whereas, other laboratory tests including fasting blood glucose (FBG), hemoglobin A1C (HbA1C), low-density lipoprotein cholesterol (LDL), high sensitivity C-reactive protein (hs-CRP; mg/L) and erythrocyte sediment rate (ESR; mm/hr) were collected on the next morning.

All patients were treated with antiplatelets, high intensity statin and intravenous fluid, followed the acute stroke management protocol. In patients who were compatible with thrombolysis eligibility criteria, the information whether those patients received intravenous alteplase was collected.

Evaluation of progressive lacunar stroke and outcome measurement

Each patient was examined on admission and daily by neurology residents who were certified for National Institutes of Health Stroke Scale (NIHSS) examination. On admission, all patients were assessed about the patient's medical examination and classified to one of the following lacunar syndrome; pure motor, ataxic hemiparesis, sensorimotor stroke. The NIHSS and Medical Research Council (MRC) scale for muscle power of patients' four extremities were recorded daily during the admission. The NIHSS at discharge and 3 months after stroke onset were collected.

Progressive lacunar stroke was defined as an increase in NIHSS more than 2 points during the admission.

Functional outcome of the patients was assessed by the modified Rankin scale (mRS) and Bathel Indexes (BI) at discharge and 3 months after stroke onset.

Neuroimaging study and imaging measurement

CT brain was performed with Ingenuity Philips (USA) 128-slice scanning with a slice thickness of 6 mm or Revolution CT GE Medical System (USA) 256-slice scanning with a slice thickness of 6 mm. MRI was performed with Magnetom Skyra Siemens (Germany), 3 T, with slice thickness 5 mm or Ingenia Philips (USA) 1.5 T, with slice thickness 5mm or Discovery MR750 GE Medical System (USA) 3 T, with slice thickness 5 mm. The infarct size, location of infarction, old silent lacunar lesions, white matter hyperintensities and cerebral microbleeds were recorded. The infarct size was evaluated at maximal axial view diameter by diffusion-weighted imaging (DWI) (TR;1861 ms/TE: 69ms) of MRI or CT brain. The acquired infarct volume data were measured and analyzed by Olea Sphere version 2.3 Medical imaging software (USA). Concomitant silent lacunar infarcts were defined as 3-15 mm in diameter in horizontal sections with high intensity on both T2-weighted images (TR: 3500 ms/TE: 100 ms) or 3-20 mm in diameter of well-defined hypodensity lesion with sign of volume loss by axial view of CT brain. White matter hyperintensities were defined as diffuse hyperintensities on T2-weight imaging (TR:3500 ms/TE:100ms) or hypodensity lesion on CT brain that were located in the subcortical and periventricular white matter and were graded 0-3 by Frazekas scale. Cerebral microbleed was defined as round/ovoid 2-10 mm hypointense lesions on T2*-gradient-recalled echo (T2*-GRE) (TR:656 ms/ TE:26 ms) or susceptibility weighted imaging (SWI). The center of infarct location was classified into pons, midbrain, medulla oblongata, basal ganglia, internal capsule, thalamus and

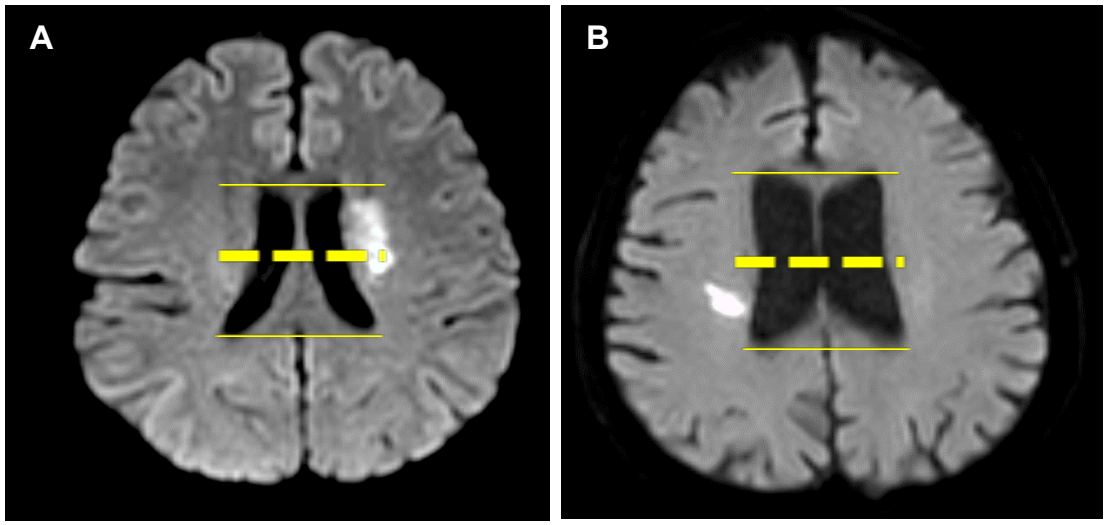

Figure 1. The type of corona radiate infarction in diffusion-weighted imaging. "Anterior type" (A) and "Posterior type" are classified by infarction's distribution.

corona radiata. Moreover, the corona radiata lesion was subcategorized into "anterior type" and "posterior type" using lesion's position related to the midline of imaginary tangential line to anterior and posterior horn of lateral ventricle (Figure1).

Intracranial and extracranial arteries were studied in all recruited patients by using magnetic resonance angiography (MRA) or computer tomography (CTA). The three-dimensional time-of flight images were acquired in the axial plane with a repetition time of 25 ms, echo time of 6.9 ms, flip angle of 18°, 210-mmfield of view, partition of 64, 219×512r acquisition matrix, and one signal average for a total imaging time of 4 min 33 s. The significant artery stenosis was defined if the stenosis exceeded 50% stenosis of the large vessels, according to the method of the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID trial) and Study Group and the North American Symptomatic Carotid Endarterectomy Trial (NASCET trial).

The "branch atheromatous disease" group was identified if the diameter in axial sections of acute infarction was more than 20 mm by MRI or 15 mm by CT scan or classically wedge-shaped paramedian infarction that extend to the surface of the pons without significant symptomatic large vessel stenosis (Figure 2).

Two neurologists (N.K. and T.K.) were blinded to the patient's clinical presentation and clinical outcomes, interpreted MRI brain, CT brain and angiographic features. Interobserver controversy was judged by final report of other radiologist.

Statistical analysis

Data was analyzed using SPSS (SPSS statistics for Windows, Version 17.0, SPSS Inc, USA). Descriptive data were analyzed using mean ± standard deviation or median ± inter-quartile range for continuous data and percentage for categorical data. The predictive factors were compared between patients with progressive stroke and stable stroke. For analytical statistics, we used Pearson Chi-square for qualitative variables and the Unpaired t-test for quantitative variables. The Mann-Whitney U test was used for ordinal scale data and non-parametric data. The logistic multiple regression model was analyzed and the algorithm used for computation included the enter method of the independent variables. The P-value <0.05 was considered statistically significant.

Ethical statement

This study was approved by the Local Ethics Committee from the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (COA No.141/2018, IRB no 741/2560).

RESULTS

From 2,077 consecutive patients, aged more than 18 years old, with acute ischemic stroke who were admitted in KCMH between July 1, 2015 and June 30, 2018, 302 patients with clinical presentation of acute lacunar syndrome with motor deficit were studied. There were 55.3% male. The mean age was 61.1±14.36 years (ranging from 29 to 91 years). One hundred and thirty-four patients

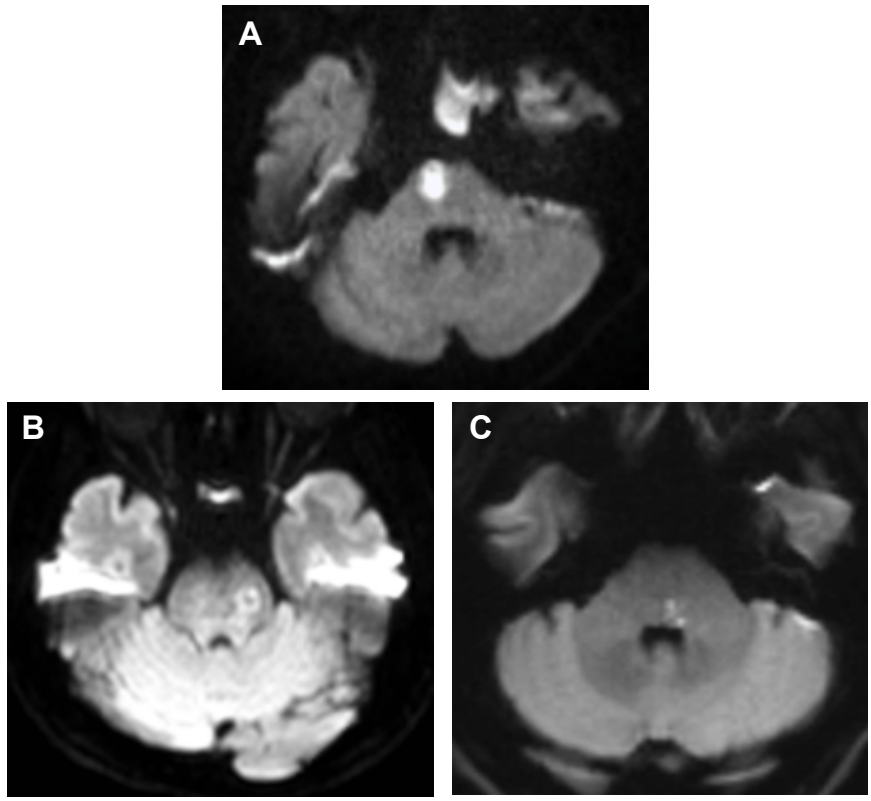

Figure 2. The distribution type of pontine infarction in diffusion-weighted imaging. Paramedian pontine infarction, starting at midline and extending to the surface of the ventral pons was caused by basilar branch atheromatous disease (A). Small deep infarction was round shape or not abut ventral surface of the pons (B,C).

(44.4%) had pure motor hemiparesis, 73 (24.1%) had ataxic hemiparesis and 95 (31.5%) had sensorimotor deficits. The median time interval between stroke onset and admission was 1 day. The median initial NIHSS was 4±2.

All the recruited patients had CT brain performed at admission to exclude the hemorrhagic stroke and identify the location of brain infarction, infarct size and previous silent lacunar lesions. According to the CT brain at admission, the index stroke site could not be identified in 198 patients (65.6%). All of those patients had MRI brain performed. The MRI brain was done in 248 patients (82.1%) with the median interval from the admission 3±4 days. In 78.1% of cases, CTA was performed. MRA was done in 16.6% of cases; and 5.3% of cases, both CTA and MRA were done. The infarction was located in corona radiate (39.7%), pons (25.4%), posterior limb of internal capsule (18.5%), basal ganglia (8.6%), thalamus (5.6%), medulla oblongata (1.7%) and midbrain (0.7%). The significant intracranial or extracranial artery stenosis which was relevant to infarct site was found in 11.9%.

From 302 patients, there were 36 patients who were performed transthoracic echocardiography; and the results revealed neither significant structural abnormality nor cardiac clot. All patients had continuous EKG monitoring for at least 48 hours before discharge that neither atrial fibrillation nor atrial flutter was captured. However, 36 patients also had 48-hours ambulatory Holter monitoring that neither atrial fibrillation nor atrial flutter was detected.

All patients received antiplatelet drugs. Forty-five patients (14.9%) received intravenous thrombolysis. The mean total amount of intravenous crystalloid fluid was 6,462±5,382 ml within 72 hours of admission.

Of the 302 patients, 70 patients (23.2%) had progressive lacunar stroke whereas 232 patients were classified into the stable group. The median onset time of clinical progression was 2±2 days from the stroke onset (range 0-9 days) (Figure 3). The median increased NIHSS score among patients with progressive lacunar stroke was 3±2 (range 3-8). The median initial NIHSS score was higher in patients with progressive lacunar stroke than in stable lacunar stroke (5 versus 4, P = 0.009).

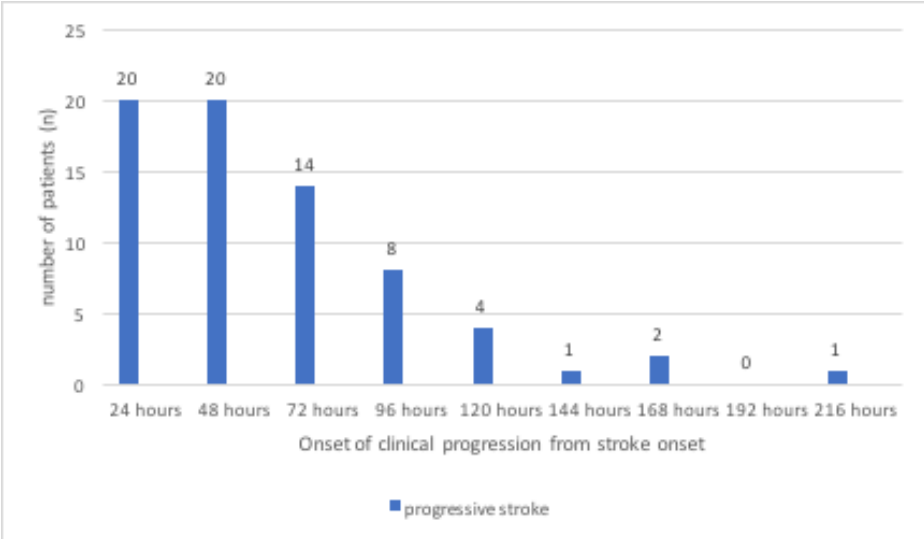

Figure 3. Onset of clinical progression from stroke onset

Repeated MRI or CT brain studies showed an extension of the infarct area, the mean increase of volume on infarction was 577.0±418.3 mm^3.

By univariate analysis (Table1), the following factors were significantly related to progressive lacunar stroke: higher mean age of stroke onset (64.8±4.2 years versus 61.0±3.1 years, P=0.011), higher mean systolic blood pressure on admission (175±26 mmHg versus 164±28 mmHg, P = 0.003), higher median diastolic blood pressure on admission (95±14 mmHg versus 90±22 mmHg, P = 0.017), higher median WBC (8,530±3240/ mcl versus 7,775±3463/mcl, P=0.031), larger infarct size => initial infarct size on arrival (1,395±1,540 mm^3 versus 880±1,055 mm^3, P<0.001), significant symptomatic artery stenosis (odd ratio [OR] 2.39, 95% confidence interval [CI] 1.15-4.96, P=0.017), branch atheromatous disease (OR 2.51, 95%CI 1.45-4.35, P<0.001), pontine infarction (OR 1.92, 95% CI 1.08-3.43, P=0.025).

For constructing the predictive model, we converted following parameters including age of stroke onset, systolic blood pressure and diastolic blood pressure on admission, WBC level and initial NIHSS into dichotomous data by cut-off point. By univariate analysis, those parameters including age equal or more than 60 years (OR1.83, 95% CI 1.03-3.25, P=0.037), initial systolic blood pressure equal or more than 165mmHg (OR2.82, 95%CI 1.59-5.01, P<0.001), initial diastolic blood pressure equal or more than 90 mmHg(OR 1.79, 95%CI 1.03-3.12, P=0.039), WBC equal or more than 8,500 / mcl (OR 1.90, P= 0.03, 95%CI 1.08-3.20), and NIHSS equal or less than 3 (OR 0.56, P= 0.046, 95%CI 0.30-0.98) were statistically significant.

All variables, except the volume of infarction, that statistically significant (P < 0.05) by univariate analysis were tested by logistic multiple regression analysis by enter method. As regard to the difference of supratentorial or infratentorial area of infarction, we excluded the volume of infarction to multivariate analysis.

Among these factors, age equal or more than 60 years, initial systolic blood pressure equal or more than 165mmHg, WBC equal or more than 8,500 / mcl, pontine infarction, branch atheromatous disease and significant symptomatic artery stenosis were demonstrated to be independent risk factors for progression by logistic multiple regression analysis (Table2).

In patients with progressive lacunar stroke, functional status at discharge and 3 months were statistically worse than the stable lacunar stroke (median mRS at discharge 3±2 versus 1±1, P<0.001 and median BI 64±31 versus 95±20, P<0.001), (median mRS at 90 days 2±1 versus 1±2, P<0.001 and median BI 80±40 versus 100±10, P<0.001). The patients with progressive lacunar stroke had significantly longer length of hospital stay (LOS) than patients with stable lacunar stroke (median LOS 8±5 versus 4±2, p<0.001)

DISCUSSION

In the present study, 23.2% of patients with acute lacunar syndrome exhibited progressive motor deficit, 28% of these had stroke progression within the first 24 hours and 77% within the

Table 1: Baseline clinical characteristics, laboratory parameters, radiographic findings and clinical outcomes of patients with progressive and stable lacunar stroke

	Progressive lacunar stroke (n=70)	Stable lacunar stroke (n=232)	P-value
Baseline characteristics			
Age (years), (mean±SD)	64.8±4.2	61.0±3.1	0.011*
Gender (male), n (%)	34 (48.6)	133 (57.3)	0.20
Hypertension, n (%)	49 (70.0)	136 (58.6)	0.087
Diabetes mellitus, n (%)	29 (41.4)	75 (32.3)	0.16
Dyslipidemia, n (%)	34 (48.6)	104 (44.8)	0.58
Previous ischemic stroke, n (%)	13 (18.6)	37 (15.9)	0.72
Prior antiplatelet, n (%)	20 (28.6)	47 (20.3)	0.14
- Aspirin	16 (80.0)	38 (80.9)	-
- Clopidogrel	2 (10.0)	5 (10.6)	-
- Cilostazol	1 (5.0)	0	-
- Aspirin with dipyridamole	1 (5.0)	0	-
- Aspirin with clopidogrel	0	4 (8.5)	-
Capsular warning signs, n (%)	7 (10.0)	10 (4.3)	0.72
Recurrent stroke within 3 years, n (%)	4 (5.7)	28 (12.7)	0.64
Initial SBP (mmHg), (mean±SD)	175±26	164±28	0.003*
Initial DBP (mmHg), (median±IQR)#	95±13	90±22	0.017*
Initial NIHSS (median±IQR)#	5±2	4±2	0.009*
Time to initial CT brain (days), (median±IQR)	1±1	1±1	-
Time to initial MRI brain (days), (median±IQR)	3±5	3±4	-
Clinical syndrome, n (%)			0.15
- Pure motor hemiparesis	36 (51.4)	98 (42.2)	-
- Ataxic hemiparesis	11 (15.7)	62 (26.7)	-
- Sensory motor stroke	23 (32.9)	72 (31.0)	-
Intravenous r-tPA, n (%)	12 (17.1)	33 (14.2)	0.51
Antithrombotic agents at progressive symptoms			0.25
- None	8 (11.4)	11 (4.7)	
- Single antiplatelet	46 (65.7)	135 (58.1)	
- Dual antiplatelet	15 (25.0)	86 (37.1)	
- Enoxaparin	1 (1.4)	0 (0)	
Laboratory parameters			
Hematocrit (%),(median±IQR)#	40.2±6.8	40.7±5.7	0.39
WBC (per mcl), (median±IQR)#	8,530±3,240	7,775±3,463	0.03*
Urine specific gravity, (median±IQR)#	1.006±0.006	1.010±0.014	0.05
CBG (mg/dL), (median±IQR)#	127±46	122±69	0.46
ESR (mm/hr), (median±IQR)#	13±20	14±17	0.54
hs-CRP (mg/L), (median±IQR)#	2.93±4.96	2.54±6.03	0.58
FBG (mg/dL), (median±IQR)#	112±45	105±50	0.12
LDL (mg/dL), (mean±SD)	135±50	130±45	0.41
Hemoglobin A1C (%),(median±IQR)#	5.9±2.5	5.9±1.9	0.82
BUN:Creatinine ratio ≥20, n (%)	14 (20.0)	46 (19.8)	0.95
Sodium (mmol/L), (median±IQR)#	139±4	138±4	0.91
Radiographic findings			
Location of infarction			
- Pontine infarction, n (%)	24 (34.2)	53 (22.8)	0.025*
- SI; Anterior type, n(%)	6 (8.6)	35 (15.1)	0.51
- SI; Posterior type, n(%)	52.9)	140 (60.3)	-
- Others, n(%)	4 (4.3)	4 (1.7)	-
Branch atheromatous disease, n (%)	28 (40.0)	59 (25.4)	<0.001*
Infarct volume (mm^3), (median±IQR)#	1,395±1540	880±1055	<0.001*
Silent lacunar infarction, n (%)	39 (55.7)	105 (45.2)	0.13
Cerebral microbleed, n (%)	18 (25.7)	57 (25.6)	0.96
White matter lesions (Frazekas ≥2), n (%)	23 (32.9)	70 (30.1)	0.67
Significant symptomatic artery stenosis, n (%)	14 (20.0)	22 (9.5)	0.017*

Functional outcomes			
NIHSS at discharge (median±IQR)[#]	6±4	2±3	<0.001*
NIHSS at 90 days after discharge (median±IQR)[##]	4±5	1±2	<0.001*
mRS at discharge (median±IQR)[#]	3±2	1±1	<0.001*
mRS at 90 days after discharge (median±IQR)[#]	2±2	1±2	<0.001*
BI at discharge (median±IQR)[#]	64±31	95±20	<0.001*
BI at 90 days after discharge (median±IQR)[#]	80±40	100±10	<0.001*
Length of hospital stay (days), (median±IQR)[#]	8±5	4±2	<0.001*

BI: Bathel index; CBG: capillary blood glucose; DBP: diastolic blood pressure; ESR: erythrocyte sediment rate; FBG: fasting blood glucose; NIHSS : National Institutes of Health Stroke Scale; IQR: interquartile range; mRS: modified Rankin Score; SBP: systolic blood pressure; SI: supratentorial infarction

* Statistically significant compared progressive lacunar stroke group with stable lacunar stroke group; P<0.05.

[#] Mann-Whitney U test compared progressive lacunar stroke group with stable lacunar stroke group.

subsequent 72 hours after stroke onset. The results are in accordance with other previously published studies (14-62%)[1-6], which suggest a high prevalence of progression in lacunar infarcts.

In the field of acute stroke, progressive lacunar stroke remains an important unresolved problem and the pathophysiology of progression is incompletely understood. Hemodynamic factors, extension of thrombosis, excitotoxity and edema have been proposed as possible mechanism of progression.[7] In our multivariate analysis, age more than 60 years, initial systolic blood pressure more than 165mmHg, WBC more than 8500 / mcl, pontine infarction, branch atheromatous disease and significant symptomatic artery stenosis were independent predictors of progressive motor deficits. Louis Caplan[2] first used the term branch atheromatous disease to describe an occlusion or stenosis at the origin of a deep penetrating artery of the brain, associated with a microatheroma or a junctional plaque, and leading to an internal capsule or pontine infarction. Imaging techniques in our study were unable to depict those small vessels changes, therefore we presumed branch atheromatous disease by indirect features that are produced by it; such as large lacunar infarction, paramedian pontine lesion extending to ventral pontine surface, infarction in the territory of lenticulostriate artery or anterior choroidal artery.[2]

Kitanaka and Teraoka[3] demonstrated that the risk of progressive lacunar infarction sharply increased in patients over 70 years old. Older patients are more likely to suffer from progressive lacunar infarction because neurons in the elderly decrease capacity in developing neuroplasticity after neural deterioration.

Takeuchi *et al.*[6] and Kim *et al.*[8] found that higher systolic blood pressure on admission was an independent predictor of stroke progression in penetrating artery infarction. High blood pressure (more than 140/90 mmHg) was seen in 75% of patients with acute ischemic stroke whose onset was within 72 hours.[9] The explanations of acute hypertensive response in lacunar stroke were increased plasma catecholamines after stress and physiological response to increased cerebral blood flow. Otherwise in a portion of these patients, the acute hypertensive response reflects undetected or inadequately treated chronic hypertension.[10] Impaired cerebral autoregulation and endothelial dysfunction in chronic hypertension, may predispose to progressive lacunar stroke in relation

Table 2: Multivariate logistic regression analysis of predictors for progressive lacunar stroke

	adjusted OR	95% CI	P-value
Age ≥ 60years	2.17	1.16-4.06	0.016*
Initial systolic blood pressure ≥ 165mmHg	2.40	1.25-4.61	0.008*
Initial diastolic blood pressure ≥ 90 mmHg	1.37	0.71-2.62	0.348
Minor stroke (Initial NIHSS ≤3)	0.65	0.35-1.22	0.182
WBC ≥8,500/ mcl	1.95	1.05-3.62	0.034*
Pontine infarction	1.99	1.07-3.71	0.031*
Branch atheromatous disease	2.47	1.37-4.48	0.003*
Significant vessels stenosis	2.41	1.09-5.36	0.031*

* Statistically significant compared progressive lacunar stroke group with stable lacunar stroke group; P<0.05.

to hemodynamic factors.[11]

In this study, the occurrence of progressive motor deficit was related to site and size of infarction but not the type of lacunar syndrome. Moreover, almost half of progressive lacunar stroke showed the expansion of the ischemic lesion.[3] Yamamoto *et al*. reported that branch atheromatous disease sometimes expressed with neurological worsening. Moreover, pontine infarction tends to progress compared with cerebral deep penetrating artery infarction.[12] Anterior pontine arteries are delicate vessels that branch acutely from the basilar artery and angle in a slightly caudal direction, therefore static blood could cause local thrombosis superimposed to the ostial atheroma. This could be the most plausible cause of expanding infarction in median pons. Furthermore, stepwise clot propagation of distal-to-proximal segment of perforating artery resulted in subsequent occlusion of other perforators, leading to enlargement of infarction. However, some progressive lacunar stroke occurred later than 72 hours, another etiology like delay neuronal damage independent from blood circulation is possible.[13] Basis pontis is anatomically unusual in having both gray and white matter, and this feature is presumed to account for the vulnerability of this area to perturbations in ionic and osmotic homeostasis.[14]

The role of extra or intracranial stenosis of relevant artery in the pathogenesis of lacunar stroke is still controversial. Therefore the presence of large vessels stenosis in patients with lacunar stroke is thought to represent opportunistic disease or to be a marker of diffuse atherosclerosis, including junctional plaque near the perforators.[15] Bang *et al*.[16] demonstrated that 28% patients with lacunar stroke had intracranial stenosis of the relevant artery and the stenotic lesion of intracranial artery was more prevalent on the ipsilateral side than on the contralateral side. This indicated that lacunar infarction could represent an intracranial type of large atherosclerotic disease. The factors that influence cerebral blood flow, such as fluctuating blood pressure or progressive formation of thrombus at the stenotic arteries may cause a progression in lacunar stroke.

Audebert *et al.*[4] proposed that progression in lacunar stroke which occurred within 24 hours of stroke onset, may be related to an acute inflammatory response. The higher leukocyte count, higher body temperature and a higher fibrinogen concentration on admission were associated with clinical deterioration. The inflammatory reaction may aggravate the damage to the ischemic tissue. This may be why the higher WBC is a contributing factor to worsening stroke.

Progressive lacunar stroke usually leads to poor outcome, our study confirmed that patients with progressive motor deficit were associated with significantly worse functional outcome at discharge and at 3 months. It was also related with significantly longer period of hospital admission. However, during 3 months follow-up, average patients with progressive lacunar stroke had improvement of their functional outcome and the disability decrease to the level of non-dependence, concordant with the natural history of lacunar stroke.

For future study, we plan to create a predictive model (age, blood pressure, branch atheromatous disease, pontine infarction, high WBC and large vessels stenosis [AB_2PWS score]) for predicting the risk of progression in patient with clinical symptoms of lacunar syndrome. This formula could help to identify patients at risk who should be monitored closely and applied appropriate treatment as early as possible.

In conclusion, prevalence of early motor deterioration in patients with pure motor, ataxic hemiparesis and mixed sensorimotor lacunar syndrome is not uncommon. Progressive lacunar stroke is associated with poor prognosis and substantial disability. Age more than 60 years, systolic blood pressure more than 165mmHg, WBC more than 8,500 / mcl, pontine infarction, branch atheromatous disease and significant symptomatic artery stenosis were found to be associated with the progressive motor deficit in patients with acute lacunar syndrome. We suggested patients with these predictive factors should receive close surveillance and further study is needed to establish appropriate management to prevent the progression for high risk patients.

DISCLOSURE

Conflict of interest: None

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