

Silent Infarction in Patients with First-ever Stroke

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Abstract-

Background/Purpose: Silent infarcts (SIs) are commonly found in brain computed tomography (CT) or magnetic resonance imaging (MRI) of elderly subjects. However, the prevalence of this silent infarction (SI) and risk factors for this entity are not entirely known. This study was aimed to evaluate the prevalence of silent infarcts in brain CT and risk factors in patients admitted with first-ever ischemic stroke or transient ischemic attack (TIA).

Methods: From July 2003 to May 2005, a prospective study was performed for 446 patients admitted to our neurology service with a diagnosis of TIA or stroke. Two hundred and twenty-six patients did not have a history of stroke or TIA prior to the event. All patients received a brain CT on the day when they arrived at the hospital. Risk factors that are monitored included age, history of hypertension, diabetes mellitus, cardiovascular disease, stroke, smoking and alcohol use. Cholesterol and triglyceride levels were measured on the second day of admission.

Results: The results showed that the frequency of SI among 226 patients with first-ever stroke or TIA was 20%. Most of the SIs were small and deep. Small-artery disease was more frequently observed in patients with silent infarction. Age, hypertension, diabetes mellitus, hypercholesterolemia, hypertriglyceridemia, alcohol habit, smoking and atrial fibrillation were not significantly different between patients with silent infarct and patients without silent infarct.

Conclusions: The study shows small-artery disease is more frequent in patients with silent infarction. The clinical significance of silent infarct needs further study.

Key Words: Silent cerebral infarction, Stroke, Computed tomography, Magnetic resonance imaging, Transient ischemic attack

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INTRODUCTION

Silent cerebral infarction, brain infarct not associated with a stroke history, is a common finding in the

study of brain images including computed tomography (CT) and magnetic resonance imaging (MRI) of stroke patients. Silent infarcts (SIs) are also found in normal elderly subjects. The prevalence of silent infarct (SI) in

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CT scan was between 10% and 40%⁽¹⁻⁴⁾. The wide range is partly explained by the variation of age between different studies. The Rotterdam study reported that 20% of population aged 60 to 90 years old showed SI⁽¹⁾. The frequencies increased from 8% among 60 to 65 years old subjects to 35% in the oldest group (from 85 to 90 years old).

Most of the SIs observed in acute stroke patients were small and deep. Hisayama study showed that the prevalence of SI was 12.9% while 86% of them were small⁽⁵⁾. The infarct was not only found in ischemic stroke patients but also in patients with initial hypertensive brain hemorrhage⁽⁶⁾. A prospective study reported by Kobayashi et al. showed that individuals with silent subcortical infarct have a higher annual incidence of clinical stroke⁽⁷⁾. From these results, it has been suggested that SI is a risk factor for clinical brain infarct and brain hemorrhage. The risk factors of SI include aging, stenosis of carotid artery, hypertension, diabetes mellitus, and retinal artery stenosis. These are also similar risk factors for cerebrovascular disease. Smoking, male sex, and glucose intolerance were also found to be risk factors for SI^(4,8-10). Atrial fibrillation has been reported to be a risk factor of SI⁽¹¹⁾, but it has not been supported by other studies⁽¹²⁾.

Multiple small infarcts are common causes of dementia⁽¹³⁾. Although SIs do not produce neurological symptoms; they may increase the possibility of vascular dementia. Since repeated strokes can cause dementia and disabilities, it is reasonable to believe that the presence of one or more SI in stroke patients could affect the recovery and prognosis.

Because SI is associated with a higher rate of mortality and subsequent clinical cerebrovascular disease⁽⁷⁾, it is important to investigate the prevalence of silent stroke. The prevalence of silent infarct in CT scan varied in previous studies⁽¹⁻⁴⁾. It would be of interest to know whether the prevalence of silent infarct in the ischemic stroke patients in Taiwan is different from those in other countries. The purposes of this study were to investigate the prevalence of SI in the patients with first-ever stroke in Taiwan and to explore potential risk factors of SI.

SUBJECTS AND METHODS

From July 2003 to May 2005, this prospective study was performed on patients admitted to our neurology service with a diagnosis of stroke or TIA. Thirty-two patients were hemorrhagic stroke and 446 patients were ischemic stroke or TIA. Among the 446 patients, 220 had a history of stroke prior to the event. The other patients (226) without a history of stroke or TIA were included in the current study.

Silent stroke was defined as a focal hypodensity of presumably vascular origin on CT scans or MRI not related to the present event and was seen in patients without a history of stroke or TIA. The diagnosis of stroke was based on the definition given by the World Health Organization⁽¹⁴⁾. The symptoms of TIA include transient monocular blindness, supratentorial lacunar syndrome (pure motor, pure sensory and sensorimotor symptoms), and vertebrobasilar infratentorial TIA (ataxia, dysarthria, dysphasia, diplopia, and rotatory dizziness).

The information related to their clinical stroke and risk factors including onset of stroke, age, alcohol use, cigarette smoking, history of diabetes mellitus, hypertension, cardiovascular disease and family history of stroke were obtained from each patient. Hematocritic, biochemical parameters, chest X-ray, and EKG were performed on the day when patients arrived at the hospital. On the second day, levels of fasting blood sugar (glucose) and serum lipids (cholesterol and triglyceride) were determined. Systolic and diastolic blood pressures were measured with a sphygmomanometer and the mean of three measurements was used for the analysis. Hypertension was defined as systolic pressure ≥ 140 mmHg; diastolic pressure ≥ 90 mmHg, or by a reported regular treatment for hypertension. Diabetes mellitus was defined as fasting glucose ≥ 126 mg/dl or under treatment of diabetes mellitus. Hypercholesterolemia was defined as total serum cholesterol ≥ 200 mg/dl while hypertriglyceridemia was defined as serum triglyceride ≥ 160 mg/dl. One who smoked more than 10 cigarettes per day and more than 1 years was classified as a smoker, drank more than 25 g alcohol per day for more than 1

year was classified as an alcohol user.

Computed tomography of the brain was performed on the day of admission; follow up CT or MRI was again performed if necessary. One neurologist and one radiologist reviewed all scans. Infarcts were defined as hypodense lesions within a recognized vascular territory.

For the clinical information, infarcts were categorized as symptomatic infarcts, if lesions corresponded with the symptom of the events. The focal hypodensities that were not related to the qualifying events were categorized as an irrelevant infarct. Chi square was calculated for the assessment of risk factors. $p < 0.05$ was considered to be statistically significant.

RESULTS

The mean age of 226 patients with a first-ever stroke included in the current study was 68.76 ± 11.58 years. The distribution of age was as following: 4 under 40 years old; 11 were from 41 to 50; 51 to 60 were 29; 61 to 70 were 73; 71 to 80 were 54; 81 to 90 were 30; and 5 patients were over 90 years old. Results of the biochemical study and health history interview are shown in Table 1. Among these patients, 67.3% had hypertension, and 36.7% of the patients had diabetes mellitus. Hypercholesterolemia (cholesterol ≥ 200 mg/dl) and hypertriglyceridemia (triglyceride ≥ 160 mg/dl) were found in 27.4% of the patients. The frequency of patients with a history of smoking was 23.9% (41.5% were men and 2.9% were women). The proportion of patients with

a history of alcohol drinking was 2.6%. Atrial fibrillation and ischemic heart disease were found in 7.5% and 15.5% of patients, respectively.

Silent brain infarct was detected in 45 of the 226 (20%) patients with first-ever stroke (Table 1). Among these 45 patients, 27 (60%) had one, 9 (20%) had two, 8 (17.8%) had three and 1 had four SIs. The characteristics of symptomatic strokes are shown in Table 2. Small-artery occlusive disease was more frequent in the patients with silent infarction compared with those without silent infarction. ($p = 0.004$). Large-artery atherosclerosis was more frequent in patients without SI than in patients with SI (9% vs 17.1%); however there was no statistical significance. The brain CT of 161 (71.2%) patients showed that the infarct was the cause of present stroke and the brain CT of remaining 65 (28.8%) patients revealed no focal abnormality connected to the stroke.

As shown in Table 3, most SIs, 62.5% (45/73), were located in the basal ganglia or the internal capsule. Twenty-one (28.8%) were in the subcortical areas, four (5.5%) were cortical infarcts (3 in the frontal lobe and 1 in the parietal lobe), two (2.7%) were in the brain stem, and one (1.4%) was located in the cerebellum. The mean diameter of SIs was 7.3mm. About 93% of them were smaller than 15 mm and 83.3% of them were smaller than 10 mm. By definition, most SIs were lacunar infarcts. Patients with SI more often had hypertension (75.6% vs 65.2%), hypertriglyceridemia (33.3% vs 30%), cardiovascular disease (20% vs 14%) and smok-

Table 1. Baseline characteristics of patients with and without silent infarcts

	Silent infarction (+)		Silent infarction (-)		Total		p-value χ^2
	n= 45	%	n= 181	%	n= 226	%	
Age (Y)	68.3±13.3		68.9±11.2		68.8±11.6		0.61
Sex M	26	57.8	97	53.6	123	54.4	
Hypertension	34	75.6	118	65.2	152	67.3	0.19
Diabete mellitus	13	28.9	70	38.7	83	36.7	0.22
Hypercholesterolemia	10	22.2	52	28.7	62	27.4	0.38
Hypertriglyceridemia	15	33.3	47	30.0	62	27.4	0.32
Smoking	14	31.1	40	22.1	54	23.9	0.20
Alcohol	2	4.4	4	2.2	6	2.6	0.40
Atrial fibrillation	1	2.2	16	8.8	17	7.5	0.13
HCVD	9	20.0	26	14.4	35	15.5	0.35

HCVD: hypertensive cardiovascular disease.

Table 2. Subtype of stroke in patients with first-ever stroke

Subtype of stroke	SI (+)	SI (-)	p-value (χ^2)
Oxfordshires stroke classification			
Total anterior circulation	0	10	0.10
Partial anterior circulation	7	28	1.0
Lacunar infarction	33	116	0.25
Posterior circulation	5	27	0.50
TOAST stroke subtype			
Cardioembolic	9	33	0.80
Small-artery disease	25	59	0.004
Large-artery atherosclerosis	4	31	0.17
Unknown	7	58	0.03

SI: silent infarct.

Table 3. Location of silent cerebral infarction

	No
No of infarctions	73
L/R	48/25
Frontal	16
Temporal	5
Parietal	3
Occipital	1
Cerebellum	1
Brain stem	2
Basal ganglion+ internal capsule	45
Cortex/subcortex	7/66

L: left; R: right.

ing habit (31.1% vs 22.1%). Patients without SI more often had diabetes mellitus (28.9% vs 38.7%) and hypercholesterolemia (22.2% vs 28.7%). However, these differences did not reach statistical significance. The prevalence of SI was not related to age. However, 60% (3/5) had SI in the patients over 90 years old.

DISCUSSION

In this study, SI was found in 20% of patients with first-ever stroke. This is lower than that reported in other MRI studies for ischemic (33%) or hemorrhagic (47%) stroke patients. In the studies using brain CT for patients with first-ever stroke, the frequencies of SI ranged from 10 to 37%^(4,9,15-16). Differences in the frequencies may be related to age or other factors. The prevalence of SI reported by Jorgenson and coworkers⁽⁸⁾, was higher than

20%. However, the mean age of patients in their study (75.0±10.7 years) was higher than that in the current study (68.76±11.58 years). Their study also showed that the age-specific prevalence of SI rose from 16% in stroke patients younger than 55 years old to 33% in patients older than 75⁽⁸⁾.

Previous studies found that most SIs were generally small and located in the subcortical areas. These characteristics are more pronounced in the present study in which 91.3% of SIs were found in the white matter (internal capsule, corona radiata and centrum semiovale) and were in subcortical gray matter (basal ganglia). In the present study, patients with SI in the brain CT scan usually had hypertension, cardiovascular disease, and smoking habit. However, there was no statistical significance. The risk factors for stroke and SI appeared to be similar⁽¹⁷⁾. In regards to the risk factors for SI; there are contradictory findings among different studies. Herderschee and co-workers found that age, hypertension and current cigarette smoking were independent risk factors for SI⁽⁴⁾. Kase, however, found in the Framingham study that glucose intolerance, but not hypertension, cigarette smoking, cardiovascular disease or atrial fibrillation, was more frequent in patients with SI than in patients without SI⁽⁹⁾. Norris and Zhu reported that SI was more frequent in patients with both TIA and carotid stenosis than in patients with either TIA or carotid stenosis⁽¹⁸⁾. In a study of patients with asymptomatic carotid atherosclerosis, SI was found by Brott and co-workers in 15% of total patients with asymptomatic carotid atherosclerosis⁽¹⁹⁾.

The current study excluded patients with a previous stroke or TIA. The advantage of using first-ever stroke patients as study subjects was to avoid the bias of false SIs (for example, reversible ischemic neurological deficit). For the diagnosis of SI, CT scan might not be the best approach. The resolution of MRI is higher than CT scan; therefore, MRI is more sensitive than that of CT scan in detecting small infarctions. In this study, SI was found in 20% of patients with first-ever stroke, which is lower than the prevalence of silent infarction reported in the MRI study. Bernick et al reported the silent infarction was found in 28% of subjects without a

history of stroke⁽²⁰⁾. However, small hyperintense foci in basal ganglion or thalamus on MRI could be due to dilated perivascular spaces rather than lacunar infarct. Tokao et al. reported a pathological finding of silent infarct and small hyperintense foci in the basal ganglion and thalamus on MRI, and found that putaminal foci were mostly due to dilated perivascular space whereas most thalamic foci were lacunar infarction⁽²¹⁾.

In conclusion, it appears that small-artery disease is more frequent in the patients with silent infarction than those without silent infarction. The clinical significance of silent infarction is uncertain. Further prospective, controlled studies are necessary to clarify the influence of silent infarction on the outcome of stroke patients.

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