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Prevalence Features and Early Predictors of Symptomatic Lacunar Infarction in Villages and Towns in Northern China

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Abstract

Background: A higher incidence of symptomatic lacunar infarction (LI) was confirmed in metropolitan areas. The aim of this study was to determine the prevalence characteristics and early predictors of LI in a population of elderly outpatients in northern China.

Methods: From February 2011 to March 2012, a retrospective cohort of new patients was selected for study, all registered neurologic outpatients of the tertiary teaching hospital in northern China. A total of 453 outpatients, clinically only having had an initial visit and a magnetic resonance imaging study of the brain, were enrolled. The prevaleence characteristics and vascular risk factorsof LI were assessed.

Results: Of 453 symptomatic outpatients, 258(57.0%) patients had symptomatic LI. We found that the main types of symptomatic LI were nonfocal symptoms, such as dizziness and headache, dizziness/vertigo, and migraine/headache. Age, BMI, smoking, history of hypertension, duration of hypertension, existing hypertension, headache and dizziness, pure motor hemiparesis, blood glucose, hypercholesterolemia, systolic blood pressure, and ABCD2 score, were significantly higher in patients with LI than in those without LI (P<0.05). Multivariate logistic regression confirmed that hypertension ⩾3years in duration (odds ratio=1.092; 95% CI, 1.019 -1.170) and a median mABCD^2 score ⩾4 (odds ratio=3.912; 95% CI, 2.955- 5.180) were independent, early predictors of symptomatic LI.

Conclusions: The incidence of LI in Northern China was located at the higher end of range in northern China, and common type of symptomatic LI was nonfocal symptoms. Hypertension of long duration and high-risk ABCD^2 scores are early predictors of symptomatic LI.

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Introduction

The clinicopathologic features of lacunar infarct (ie, small, deep ischemic lesions, forming irregular cavities 0.2-20 mm in diameter) have appeared in the medical history in the twentieth century.[1] In such studies, small lacunes or lacunar strokes were usually ascribed to hypertensive small-artery disease (40 to 900 μm in diameter), so this is how it is currently viewed.[2]More recently, however, it has been shown that lacunar infarction (LI) may also result from atheromatous stenosis or occlusion of larger arteries (diameter >0.1mm), such as basilar or middle cerebral artery.[3-5]Some studies even suggest that small emboli from the heart may also be an important mechanism of LI.[6,7]Deep brain gray and white matter are typically involved, as well as white matter near cortex. The macrovascular complications of LI are often a consequence of cardiovascular damage and generally carry a worse prognosis than small-artery disease.[5]With increasing longevity, a higher incidence of symptomatic LI(31.4%-43%) was confirmed in metropolitan areas.[8,9]Pivotal work by Fisher (since 1965) cites 21 variants of lacunar syndrome, based on studies of neurology inpatients. However, very little information, particularly in terms of incidence and clinical characterization, has come from neurology outpatient sources in the villages and towns. The purpose of this study is to explore incidence, clinical features, and early predictors of symptomatic LI in neurology outpatients from a county town and villages in northern China.

Patients and Methods

A retrospective cohort of consecutive new patients was selected for study between February 2011 and February 2012. All were registered neurologic outpatients of the tertiary teaching hospital in northern Jiangsu, China. A total of 453 outpatients, clinically only having had their initial visit and having undergone a magnetic resonance imaging (MRI) study of the brain, were enrolled. The sample consisted of males and females, aged 40 years or older, 93% of subjects from 38 villages or towns and only 7% from one urban in Shuyang of northern China

The following risk factors were recorded by an experienced neurologist on two separate occasions (Weeks 1 and 5): gender, age, BMI, history of hypertension, diabetes mellitus, history of heart disease, snoring, alcohol use, smoking, systolic blood pressure, diastolic blood pressure, migraine/headache, dizziness/vertigo, dizziness and headache, numbness or pure sensory stroke, weakness or pure motor hemiparesis, and gait disturbances or ataxia.

All patients submitted to MRI of the brain within 24 hours of the first visit. The MRI was performed with 1.5 -T equipment (Siemens). MR sequences included conventional T2, fluid- attenuated inversion recovery (FLAIR) and diffusion-weighted images(DWI) on axial view, from medulla to cortex, at 5-mm section thickness. Select patients underwent MRA, CT, and color-coded Duplex sonography. All MR studies were reviewed by a neuroradiologist and a neurologist. The examiners looked specifically for hyperintense lesions on FLAIR or DWI, measuring maximum diameters when present and attempting to correlate MR findings with clinical status. The number and location of lesions were recorded in detail for each patient.

On MRI, diagnostic criteria of recent LI were as follows: (1) a round or ovoid lesion of increased signal relative to white or deep gray matter on DWI, FLAIR, or T2;(2) hypointensity on the apparent diffusion coefficient map (or decreased attenuation relative to white/gray matter on CT); (3) maximum diameter ⩽20 mm; and (4) location in cerebral hemispheric white matter, in basal ganglia, or in the brain stem.[10] LI was classified as single or multiple (>1) according to the number of lacunes. Leukoaraiosis was equated with bilateral, symmetrical, and diffuse abnormalities of parieto-

occipital white matter surrounding the lateral ventricles or hyperintense areas of the centrum semiovale. Exclusion criteria were as follows: (1) age <40 years; (2) previous history of stroke; (3) infarct size> 20 mm; (4) enlarged perivascular spaces.

To investigate potential early predictors of symptomatic LI, the study population was divided into two groups: those patients with LI and non-LI patients. The internationally accepted ABCD[2] scale was used to score clinical status. The NIHSS was also used to assess the severity of each LI group.

Related definition

Symptomatic LI was defined as a round or ovoid lesion of increased signal relative to white or deep gray matter and ≤ 20 mm in diameter on MRI-DWI and/or FLAIR. Clinically, diagnosis of symptomatic LI was on presenting with one of 21 lacunar syndromes classified by Fisher, or nonfocal or mixed symptoms which can be attributed to an acute LI.

We identified asymptomatic LI as sharply demarcated hyperintense lesions <20 mm on T2-weighted images with corresponding hypointense lesions with a hyperintense rim on FLAIR. In LI patients, the lesion could not be compatible with the clinical syndromes. One point was awarded when one or more asymptomatic LI were present.

The nonfocal symptoms such as isolated headache or dizziness which can be attributed to the LI, were defined as follow.

Migraine/headache: migraine/headache is a common risk factor for cerebrovascular disease [11-13] and is a common complaint (with or without aura) in neurologic outpatient clinics. The problem is usually recurring, affecting the forehead, temporal or occipital areas, or the entire head. Duration of symptoms can be from minutes to hours (generally <24 hours), although some may be recurrent or continuous for a few days or more.

Dizziness/vertigo: Dizziness or vertigo, also known as acute vestibular syndrome, [11] refers to the sudden onset of head movement can not be tolerated, masonic instability, nausea or vomiting, or nystagmus. Dizziness is a top-heavy feeling, but may encompass an element of spatial movement (tilting or shake). Vertigo can be described as the brain suddenly swinging back and forth like an obstruction, severe loss of balance, and the entire space itself greatly to the side of the rotation, and even fell to the ground. Dizziness or vertigo is often recurrent (lasting seconds to minutes; usually <24 hours) and may occur in continuous repeated episodes, of several days or longer, or persistent episodes, lasting more than a few days.

Dizziness/vertigo is a common cerebrovascular risk factor. [14-16] It is a posterior circulation symptom, but is also may be reflected a symptom of anterior circulation. Generally speaking, vertigo differs from dizziness only in terms of severity, but the boundaries here are blurred.

Dizziness and headache: dizziness and headache may develop alternately or together. This dual symptomology reflects a disorder of the anterior circulation, alone or in combination with a posterior circulatory problem. In an outpatient setting, patients'dizziness and headache are commonly linked with transient ischemic attacks (lasting minutes to hours; usually < 24 hours). Yet, dizziness and headache may persist for several days or longer.

Transient ischemic attack (TIA): a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.[17]

Vascular Risk Factors

Vascular risk factors were defined as follows: cigarette smoking (within the last 5 years); hypertension (prior or present use of antihypertensive agents or a systolic blood pressure [SBP] >140 mmHg and/or a diastolic BP [DBP] >90 mmHg, measured in a sitting position with least amount of antihypertensive medication); impaired fasting glucose (fasting plasma glucose of 5.6 -6.9

mmol/L; diabetes (fasting plasma glucose level ≥7.0 mmol/L, A1C ≥6.5%, or random plasma glucose >11.1 mmol/L , associated with symptoms of hyperglycemia); hypercholesterolemia (total venous plasma cholesterol level >5.0 mmol/L, LDL fraction >3.0 mmol/L, HDL fraction <1.0 mmol/L, triglyceride level >1.6 mmol/L); and a history of coronary and peripheral artery disease.

Statistical Analysis

All numeric variables were expressed as the mean ±SD or median (interquartile range [IQR]). Fisher's Exact test, Mann-Whitney *U* test, and Kruskal-Wallis test were used to explore the relationship between baseline patient variables. Univariate and multiple logistic regression analyses were used to determine the risk factors of LI. Data were analyzed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA), with level of significance set at $P<0.05$.

Results:

All 453 patients enrolled completed the study, with 258 (57.0%) symptomatic patients having LI and 195 (43.0%) symptomatic patients without LI (no abnormality besides of 3 benign tumors). All were diagnosed according to findings on brain MRI. Among 258 symptomatic patients with documented LI, 80% were released on antiplatelet therapy, for use at home or under the guidance of local community health centers. The rest (about 20%) were hospitalized. Baseline patient characteristics of LI in symptomatic patients LI are displayed in Table 1.

In our series, isolated dizziness or vertigo is the most frequent symptom LI patients (30.6%), transient symptoms with LI were observed in up to 86.1% of patients, persistent dizziness or vertigo is rare (13.9%).

Dizziness with headache in patients with LI occurred in the second (28.3%), and its temporary symptoms are observed 76.7%. The third most common types of symptoms is isolated migraine/ headache (21.7%), the transient symptoms were up to 91.0%. The others were followed by Fisher' several traditional LI types, including pure sensory stroke or TIA (12.8%), pure motor hemiparesis (3.9%), ataxic hemiparesis (0.8%), and so on.

Table 1. Clinical characteristics in patients with LI

Characteristic	Value (N=258)
Age, y	60.5±11.1
Female gender (%)	131(51.0)
Median episode duration, days (range)	8(1−110)
Dizziness/vertigo(%)	79(30.6)
Transient symptom	68(86.1)
Persistent symptom	11(13.9)
Migraine/headache(%)	56(21.7)
Transient symptom	51(91.1)
Persistent symptom	5(8.9)
Headache and dizziness(%)	73(28.3)
Transient symptom	56(76.7)
Persistent symptom	17(23.3)
Pure sensory stroke (%)	33(12.8)
Transient symptom	23(69.7)
Persistent symptom	10(30.3)
Pure motor hemiparesis(%)	10(3.9)
Sensorimotor syndrome(%)	1(0.4)
ataxic hemiparesis	2(0.8)
Other	4(1.6)
Median number of lesions on DWI or FLAIR (range)	8(1−110)
Single infarction on DWI or FLAIR(%)	21(8.1)
Multiple infracts on DWI or FLAIR(%)	237(91.9)
Recent LI in anterior circulation (%)	138 (53.5)
Recent LI in posterior circulation (%)	19 (7.4)
Recent LI in Anterior and posterior circulation (%)	101 (39.1)
Leukoaraiosis(%)	19 (7.4)
Chronic lacunes	4(1.6)
Initial median NIHSS score (range)	0.2(0-4)
Initial median ABCD2 score (range)	4(3-7)

DWI indicates diffusion-weighted imaging; FLAIR, fluid -attenuated inversion recovery; LI=Lacunar infarction; TIA=Transient ischemic attack; NIHSS=National Institutes of Health Stroke Scale;mRS=Rankin scale

In addition to a small number of patients (8.1%) were single LI, the remaining 91.9% of the symptomatic patients were multiple LI (median =7). The distributions of lesions were most common in the anterior circulation vascular areas (53.5%), but the anterior and posterior circulation involvements were not uncommon (39.1%). Pure posterior circulation LI accounted for only 7.4%.

Statistical analysis was conducted on 258 patients with LI and 195 patients without LI (Table 2). Univariate analysis indicated that the prevalence of older age, increased BMI, history of hypertension, hypertension of long duration, existing hypertension, smoking, dizziness and headache, pure motor hemiparesis, hyperglycemia, hypercholesterolemia, increased systolic blood pressure, and a higher ABCD2 score were more frequent in the LI group than in the non-LI group. However, only

Table 2. The results of univariate analysis in patients with or without LI

Episodes	Lacunar infarcts (N=258)	Non-lacunar infarcts (N=195)	P
Female gender (%)	131(51.0)	106(54.4)	0.500
Age (years,mean ±SD)	60.5±11.1	52.7±8.5	0.000
BMI (kg/m2, mean ±SD)	23.9±3.1	24.7±3.3	0.021
Hystory of hypertension(%)	155(60.1)	78(40.0)	0.000
Duration of hypertension (yrs, mean ±SD)	3.1±5.0	1.3±2.9	0.000
Actual hypertension(%)	220(85.3)	137(73.7)	0.000
Diabetes mellitus (%)	27(10.5)	11(5.6)	0.067
Heart disease(%)	9(3.5)	3(1.5)	0.201
Snorers habitually(%)	76(29.5)	69(35.4)	0.181
Smoking (%)	67(26.0)	34(17.4)	0.031
Alcohol drinker(%)	70(28.0)	46(23.6)	0.392
Migraine/headache(%)	56(21.7)	61(31.3)	0.021
Dizziness/vertigo(%)	79(30.6)	82(41.4)	0.012
Headache and dizziness(%)	73(28.3)	26(13.3)	0.000
Pure sensory stroke or TIAs(%)	33(12.8)	23(11.8)	0.750
Pure motor hemiparesis(%)	10(3.9)	0(0.0)	0.005
Sensorimotor syndrome(%)	1(0.4)	0(0.0)	0.384
ataxic hemiparesis	2(0.8)	0(0.0)	0.218
Miscellaneous(%)	4(1.6)	3(1.5)	0.992
Blood glucose (mmol/l, mean ±SD)	5.8±1.8	5.4±1.2	0.016
Hypercholesterolemia (%)	149(57.6)	89(45.6)	0.011
SBP, mm Hg (mean ±SD)	151.5±21.3	141.1±20.9	0.000
DBP, mm Hg (mean ±SD)	95.8±11.4	95.5±11.5	0.820
Median ABCD2score(renge)	4(1-6)	3(1-5)	0.000
ABCD2 score(mean ±SD)	3.3±0.82	2.2±0.81	0.000

BMI=Body mass index; SBP= systolic blood pressure;DBP=Diastolic blood pressure; ABCD2= Age, blood pressure, clinical features, duration of symptoms, and presence or absence of diabetes; scores range from 0 to 7, with higher scores indicating greater risk of stroke.

hypertension of long duration and high-risk ABCD2 scores were established by logistic regression as independent factors for early prediction of symptomatic LI (Table 3).

Discussions

Table. 3. Multivariate odds ratios for early predictors of LI

	OR	P Value	95% CI for OR
BMI	0.909	0.011	0.844-0.978
Hypertension duration of ≥3 years	1.092	0.013	1.019-1.170
ABCD2 score of≥4	3.912	0.000	2.955-5.180

BMI=Body mass index. ABCD2= Age, blood pressure, clinical features, duration of symptoms, and presence or absence of diabetes; scores range from 0 to 7, with higher scores indicating greater risk of stroke.

The earliest epidemiological data showed a 12% incidence of LI in the general population.[18]With increasing longevity in this century, existing clinical data indicate a 14%-33% incidence of LI in metropolitan areas in developed countries.[8,19] A higher incidence of LI (36.9%-43%) is currently being recorded in metropolitan areas in developing countries.[9,20] However, in an outpatient setting from a small county town and villages, our findings show a 57.0% rate of symptomatic LI in patients over the age of 40 years, with 82.5% in the older adults (>65 years of age). Our findings suggest that there is likely a higher prevalence of LI in the county town and villages of northern China. These figures may better represent the general population of the broad rural areas in northern Chinese. Therefore, the present study not only mean that the percentage rate of LI in developing countries is higher than in developed countries, but also in villages and towns is higher than in those metropolitan areas in Northern China. This condition may be related to differences in the intensity of intervention for their risk factors.

Although the 5 traditional types of LI and its 16 variants have been known and published, dizziness/vertigo or migraine/headache as common vascular risk factors has attracted wide attention. [11-16]The present study confirmed that such nonfocal symptoms, including dizziness/vertigo or migraine/headaches, were the most common clinical symptoms in patients with LI. Furthermore, dizziness and headache were seen routinely in the LI patients and occurred with significantly greater frequency in LI sufferers than in patient controls (without LI). Motor weakness accounted for only a small percentage of patients, which differs from cumulative inpatient records.[21] However, some epidemiological observations have confirmed a high prevalence of lacunar infarct or cerebral angiopathy in patients with headache or dizziness. [11-14,16,22] Therefore, our neurology outpatient series showed that clinical types of symptomatic lacunar infarction in northern China have had new variant.

LI with transient symptoms (including local and non-local transient symptoms) occurred in 76.7% of patients. In earlier studies, patients experiencing transient symptoms with DWI-positive LI prompted the phrase "transient symptoms with infarction" (TSI).[29] Small, acute infarcts that would otherwise go undiagnosed by CT or conventional MRI are detectable by DWI in approximately one-third of patients with TIAs.[23,24,30]

Current reports also specify that two-thirds of recent transient symptoms are accompanied by FLAIR-confirmed LI, which validates the TSI concept. In view of these findings, we offer two likely scenarios. Alternatively, it may be that either some lesions on FLAIR are asymptomatic LI, or the transient manifestation is triggered elsewhere in the vasculature of the brain, without demonstrable tissue change.

From our data, the full spectrum of variables analyzed, including history of hypertension, duration of hypertension, existing hypertension (proportionate), mABCD^2 scores, and more, were significantly higher in patients with LI than in those without LI (P <0.05). Multiple logistic regression, incorporating these risk factors, found that only hypertension ≥3 years in duration and ABCD^2 scores ≥4 were significantly and independently predictive of LI. Hypertension alone is a recognized risk factor for stroke,[18,19,20,31,32] but our data indicates that long-term hypertension specifically is an early predictor of LI.

Some limitations of our study are conceded. Instances of unexpected stroke are often routed directly from an ambulance or emergency room to the ICU, especially when the consciousness or motor weakness is involved (not uncommon).[33,34] This may account for the lower frequency of pure motor LI in our general neurology outpatients.

In conclusion, symptomatic lacunar infarcts have a very high prevalence in northern China and common type of symptomatic LI is nonfocal symptoms. Statistical analyses involving a host of variables established hypertension of long duration and high-risk ABCD^2 scores as early predictors of LI.

Disclosures

None.

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