

## **Urban-rural differences in risk factors for ischemic stroke in northern China**

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## Abstract

This study aims to investigate urban-rural differences in characteristics and risk factors of ischemic stroke in northern China. The present cross-sectional study was based on the High-risk Population Screening and Intervention Project for Stroke. The cluster sampling method was used to select urban and rural screening sites in northern China. By collecting information and screening the data, patients with ischemic stroke were obtained and a control group with similar gender, age, and regional distribution was selected among the nonischemic stroke patients. Then, the demographic and risk factors of patients with ischemic stroke were described and analyzed.

The prevalence of ischemic stroke in northern China was 2.88%, with a greater prevalence in rural areas than in urban areas (3.32% vs 2.43%), and a greater prevalence in males than in females (3.06% vs 2.73%). Furthermore, rural stroke patients were younger than urban stroke patients. Hypertension, family history of stroke, and smoking were the top 3 independent risk factors for ischemic stroke. Overweight/obesity and low education were associated with increased ischemic stroke in urban areas, while low education was associated with less ischemic stroke in rural areas. In addition, the prevalence of alcoholism, dyslipidemia, diabetes, and obvious overweight/obesity was greater in urban areas, while high-salt diet and low education and income were more prevalent in rural regions. Moreover, the smoking index was higher in rural areas than in urban areas.

The characteristics and risk factors of ischemic stroke differ between rural and urban areas, which could be used to design specific preventative measures.

**Abbreviations:** BMI = body mass index, CI = confidence interval, TIA = transient ischemic attack.

Keywords: ischemic stroke, north China, risk factors, rural, urban

## 1. Introduction

Stroke has become the main cause of death worldwide, and is the leading cause of disability and death of adults in China.<sup>[1-4]</sup> The latest national research revealed that rural areas experienced greater stroke changes, when compared with cities, and that the incidence, prevalence, and mortality of rural stroke all surpassed those in urban areas.<sup>[5]</sup> Ischemic stroke is the main subtype of stroke, and its medical cost is much higher, when compared with

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other cardiovascular and cerebrovascular diseases.<sup>[5–7]</sup> Hence, it has become one of the most important sources of economic burden, and a major public health problem in China.

Multiple genetic and environmental risk factors contribute to ischemic stroke. The common controllable risk factors include hypertension, diabetes, atrial fibrillation, hyperlipidemia, smoking, alcohol, high-salt diet, and lack of exercise.<sup>[8]</sup> For a disease with high disability and without effective treatment, it is particularly important to control its risk factors. The prevalence of stroke is undoubtedly attributed to the increased burden of vascular risk factors in developing countries.<sup>[9]</sup> Controlling risk factors can avoid the occurrence of most strokes and reduce economic burden.<sup>[10–12]</sup> Studies have found that the distribution of risk factors for ischemic stroke differ in urban and rural populations, which may be correlated to the differences in economic status, education, environmental status, and living habits.<sup>[5,13–15]</sup> Thus, studying the differences of risk factors for ischemic stroke between urban and rural areas is important for targeted prevention and control.

The latest survey revealed that the stroke burden is greater in north China than in south China.<sup>[5]</sup> However, there is a lack of large-scale epidemiological studies on cerebral infarction in northern China. The present study relied on the special medical reform project of the National Health and Family Planning Commission, the High-risk Population Screening and Intervention Project for Stroke. A large population at a high risk of stroke in northern China was obtained, and the characteristics and risk factors of ischemic stroke in urban and rural areas were compared. The aim of the present study was to provide evidence for the targeted control of risk factors for ischemic strokes in urban and rural areas.

## 2. Subjects and methods

## 2.1. Ethical statement

Ethical approval was obtained from the Ethics Committee of the First Hospital of Shanxi Medical University. A written informed consent was obtained from each participant.

## 2.2. Study areas

In 12 areas of northern China, including Liaoning, Jilin, Heilongjiang, Beijing, Hebei, Shanxi, Inner Mongolia, Shandong, Henan, Xinjiang, Shaanxi, and Gansu, a total number of 100 reasonably distributed urban and rural areas were selected as screening sites. These areas had convenient transportation, and was feasible for the long-term tracking of high-risk groups. A cluster sampling approach was used for each screening site to obtain the target screening populations, and  $\geq$ 2000 individuals were required per screening site. The sample size was estimated based on the national survey for the prevalence of ischemic stroke.

#### 2.3. Subject selection criteria

Inclusion criteria were residents who were aged  $\geq$ 40 years, who have lived in the area for at least 6 months (born before January 1, 1977), and volunteered to participate in the study. Exclusion criteria were subjects who were unable to complete screening for severe illness, or who do not meet the above criteria.

Additional criteria for patients with ischemic stroke were patients with a history of ischemic stroke and have available records (diagnosed by a secondary hospital or above) or on-site brain imaging data (necessary symptoms of neurological deficit); patients with strokes caused by tumors, poisoning, or trauma were excluded. Criteria for the control group were patients with similar gender, age, and location of ischemic stroke population, and were randomly selected among the noncerebral infarction populations.

## 2.4. Screening methods

The "2016 Comprehensive Cardiovascular and Cerebrovascular Risk Factors Communities and Township Populations Intervention Questionnaire" was used to conduct the face-to-face screening of the incorporated object. Individuals with ischemic stroke and controls, who have complete information, were screened. The data collection and technical route is presented in Fig. 1.

#### 2.5. Diagnostic criteria

The diagnostic criteria were as follows: hypertension: systolic blood pressure  $\geq 140 \text{ mm Hg}$  and/or diastolic blood pressure  $\geq 90 \text{ mm Hg}$ , or the use of anti-hypertensive medications<sup>[16]</sup>; Diabetes: fasting blood glucose  $\geq 7.0 \text{ mmol/L}$  or nonfasting time blood glucose  $\geq 11.0 \text{ mmol/L}$ , or the use of hypoglycemic drugs<sup>[17]</sup>; Dyslipidemia: total cholesterol  $\geq 6.22 \text{ mmol/L}$ , triglyceride  $\geq 2.26 \text{ mmol/L}$ , high-density lipoprotein cholesterol < 1.04 mmol/L, low-density lipoprotein cholesterol  $\geq 4.14 \text{ mmol/L}$ , one or more abnormalities, or the use of lipid-lowering drugs<sup>[18]</sup>; Physical exercise:  $\geq 3$  times per week, at least 30 minutes of moderate to intense exercises, or engaging in moderate to severe manual labor; Smoking: continuous or cumulative smoking for 6 months or more; Atrial fibrillation: definitive diagnosis at secondary hospitals and above, or with available electrocardiographic

support; Overweight or obesity: BMI  $\geq 26$  was considered obviously overweight, while BMI  $\geq 28$  was considered obese [BMI=weight (kg)/height (m<sup>2</sup>)]; Alcoholism: frequent heavy drinking was defined as drinking white wine  $\geq 3$  times/week, at  $\geq 100$  grams each time; Family history of stroke: parents or siblings in the family have stroke; Past transient ischemic attack (TIA): definitive diagnosis at secondary hospitals or above; Highsalt diet: daily salt intake  $\geq 6$ g; Educational level: secondary school/high school and above was considered as high education level, while junior high school and below was considered as low education level; Income level: an annual income >10,000 Y was considered as high income level, while an annual income <10,000 Y was considered as low income level.

## 2.6. Quality control

The investigators were required to be professionally trained and qualified, fully understand the contents of the questionnaire, be loyal to their original intentions, and conduct inquiries in easy-tounderstand languages. When the survey was completed, a certain number of questionnaires were randomly selected to verify the completeness and authenticity.

## 2.7. Statistical analysis

Excel was used to build the database, and the SPSS 24.0 statistical software (Statistical Product and Service Solutions, https://www.ibm.com/products/spss-statistics) was used for statistical analysis. The qualitative data were represented as numbers and percentages, and Chi-square test was used for comparisons between 2 groups. Quantitative data with a normal distribution were expressed as mean $\pm$  standard deviation, and comparisons between 2 groups were performed using independent-sample *t* test. Non-normal distribution data were expressed as median (interquartile range), and the Mann–Whitney *U* test was used for comparison. Multivariate logistic regression analysis was used to calculate the odds ratios (ORs) and 95% confidence interval (95% CI). A 2-tailed *P*<.05 was considered statistically significant.

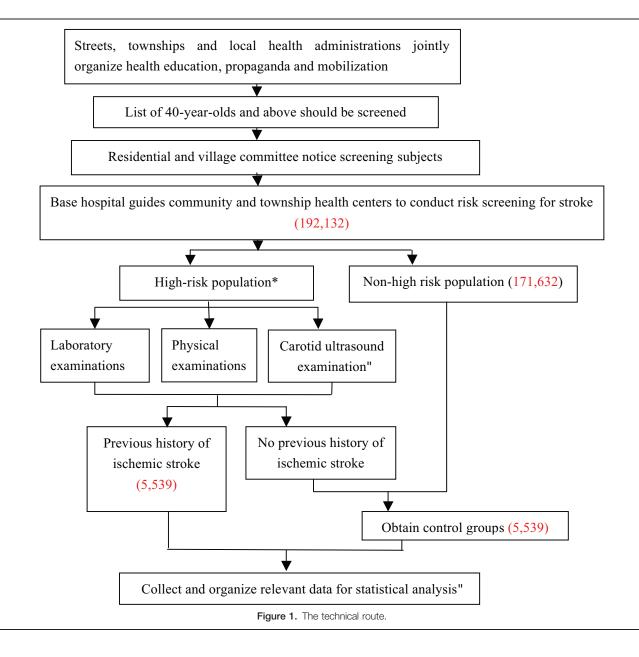
#### 3. Results

## 3.1. Basic information

A total of 192,131 subjects were screened, including 93,943 (48.90%) subjects in urban areas and 98,188 (51.10%) subjects in rural areas. Among these participants, 90,218 (46.96%) were males. Furthermore, 5539 (2.88%) patients had ischemic stroke. Among these patients, 2280 (2.43%) patients were from urban areas, while 3259 (3.32%) patients were from rural areas. There was a higher prevalence in urban areas than in rural areas (P < .001). Among these ischemic stroke patients, there were more male patients than female patients [2761 (3.06%) vs 2778 (2.73%); P < .001].

# 3.2. Baseline characteristics of the ischemic stroke population

The baseline characteristics of patients with ischemic stroke are presented in Table 1. Age was greater  $(66.19 \pm 9.09 \text{ vs } 65.47 \pm 8.95 \text{ years}, P=.003)$ , while low-education and low-income percentages (both, P < .001) were lower in urban patients with ischemic stroke, when compared with patients in rural areas. Among the 5539 patients with ischemic stroke, 2439 (44.03%)



patients were of working-age (<65 years). However, there was no difference in gender between urban and rural ischemic stroke patients (Table 1).

### 3.3. Exposure to risk factors for stroke in the population

Table 1

The stroke risk factors that urban and rural ischemic stroke patients and controls are exposed to are presented in Tables 2 to

4. Except for high-salt diet and low education, the exposure rates of risk factors were higher in the ischemic stroke group, when compared with the control group, in both urban and rural populations (Tables 2 and 3). Furthermore, the percentage of low-income patients was higher in urban stroke patients, when compared with urban controls (Table 2), while this percentage was lower in rural stroke patients, when compared with rural controls (Table 3). The multivariate regression analysis revealed

Demographic characteris	tics of the patients with ischemic	stroke in urban and rural areas in	n northern China.	
Items	Urban (n=2280)	Rural (n = 3259)	ť/X <sup>2</sup>	Р
Age (x $\pm$ SD)	$66.19 \pm 9.09$	65.47±8.95	2.946	.003
Male (n, %)	1159 (50.83)	1602 (49.16)	1.509	.219
Low education (n, %)	1606 (70.44)	3023 (92.76)	486.751	<.001
Low income (n, %)	966 (42.37)	2552 (78.31)	747.638	<.001

Table 2

Risk factors	Stroke patients (n=2280)	Controls (n=2280)	ť/X <sup>2</sup>	Р
Low education	1606, 70.4%	1536, 67.4%	5.0015	.025
Low income	966, 42.4%	851, 37.3%	12.1	.001
Smoking	611, 26.8%	296, 13.0%	136.562	<.001
Alcoholism	80, 3.5%	24, 1.1%	30.858	<.001
Lack of exercise	985, 43.2%	774,33.9%	41.205	<.001
High-salt diet	1154, 50.6%	1191, 52.2%	1.202	.273
Family history of stroke	869, 38.1%	165, 7.2%	619.88	<.001
Past TIA	107, 4.7%	39, 1.7%	32.719	<.001
Atrial fibrillation	63, 2.8%	23, 1.0%	18.962	<.001
Hypertension	1658, 72.7%	557, 24.4%	1064.199	<.001
Dyslipidemia	1017, 44.6%	283, 12.4%	579.69	<.001
Diabetes	609, 26.7%	181, 7.9%	280.468	<.001
Obvious overweight and obesity	941, 41.3%	612, 26.8%	105.694	<.001

that hypertension, family history of stroke, smoking, dyslipidemia, diabetes, and lack of exercise were common independent risk factors for ischemic stroke in both urban and rural areas (Table 4). Obvious overweight or obesity and low education were the risk factors for urban stroke patients, while atrial fibrillation was a risk factor for rural stroke patients (Table 4). In addition, low education was a protective factor for rural stroke patients (Table 4).

 Table 3

 Exposure of stroke risk factors in rural patients with ischemic stroke.

Risk factors	Stroke patients (n=3259)	Control (n = 3259)	ť/X2	Р
Low education	3023, 92.8%	3097, 95.0%	14.654	<.001
Low income	2552, 78.3%	2414, 74.1%	16.105	<.001
Smoking	810, 24.9%	463, 14.2%	117.544	<.001
Alcoholism	59, 1.8%	38, 1.2%	4.615	.032
Lack of exercise	1441, 44.2%	1080, 33.1%	84.299	<.001
High-salt diet	1954, 60.0%	1915, 58.8%	0.967	.325
Family history of stroke	1192, 36.6%	265, 8.1%	759.588	<.001
Past TIA	158, 4.8%	67, 2.1%	38.12	<.001
Atrial fibrillation	95, 2.9%	31, 1.0%	33.149	<.001
Hypertension	2385, 73.2%	822, 25.2%	1499.596	<.001
Dyslipidemia	1043, 32.0%	335, 10.3%	461.284	<.001
Diabetes	572, 17.6%	184, 5.6%	225.259	<.001
Obvious overweight and obesity	1212, 37.2%	873, 26.8%	81.042	<.001

Table 4

The multivariate analysis of risk factors in urban and rural patients with ischemic stroke.

Area	Factors	Р	OR	95% CI
Urban	Low education	.032	1.189	1.015–1.394
	Smoking	<.001	2.498	2.076-3.006
	Lack of exercise	.033	1.176	1.013-1.364
	Family history of stroke	<.001	5.149	4.219-6.284
	Hypertension	<.001	5.172	4.444-6.018
	Dyslipidemia	<.001	2.232	1.870-2.664
	Diabetes	<.001	2.079	1.687-2.562
	Obvious overweight and obesity	.012	1.218	1.044-1.421
Rural	Low education	.003	0.686	0.537-0.878
	Smoking	<.001	2	1.721-2.324
	Lack of exercise	<.001	1.571	1.393-1.771
	Family history of stroke	<.001	4.076	3.473-4.783
	Atrial fibrillation	.032	1.685	1.047-2.711
	Hypertension	<.001	5.845	5.185-6.590
	Dyslipidemia	<.001	1.719	1.464-2.019
	Diabetes	<.001	1.693	1.382-2.073

CI = confidence interval, OR = odds ratio.

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Ischemic stroke risk factors in urban and rural areas

Factors	Gender	Urban (n=2,280)	Rural (n = 3259)	t/X <sup>2</sup>	Р
High-salt diet	M+F	1154, 50.61%	1954, 59.96%	47.551	<.001
Smoking	M+F	611, 26.80%	810, 24.85%	2.658	.103
	Μ	546, 47.11%	689, 43.01%	4.574	.032
Alcoholism	M+F	80, 3.51%	59, 1.81%	15.817	<.001
	Μ	78, 6.73%	56, 3.50%	15.234	<.001
Lack of exercise	M+F	985, 43.20%	1441, 44.22%	0.561	.454
Family history of stroke	M+F	869, 38.11%	1202, 36.88%	0.869	.351
Atrial fibrillation	M+F	63, 2.8%	95, 2.9%	0.112	.738
Hypertension	M+F	1658, 72.72%	2385, 73.18%	0.146	.703
Dyslipidemia	M+F	1017, 44.61%	1043, 32.00%	20.636	<.001
	Μ	472,40.90%	448,27.97%	49.278	<.001
	F	545, 48.62%	595, 35.91%	44.634	<.001
Diabetes	M+F	609, 26.71%	572, 17.55%	67.084	<.001
Obvious overweight or obesity	M+F	941, 41.27%	1211, 37.16%	9.554	.002

## 3.4. Comparison of stroke risk factors in urban and rural ischemic stroke populations

A comparison of risk factors between urban and rural areas is presented in Tables 5 and 6. The top 3 risk factors for ischemic stroke in urban patients were hypertension (72.72%), high-salt diet (50.61%), and dyslipidemia (44.61%), while the top 3 risk factors in rural patients were hypertension (73.18%), high-salt diet (59.96%), and lack of exercise (44.22%). The exposure rates of diabetes mellitus, dyslipidemia, overweight or obesity, and heavy drinking were higher in urban areas, while the exposure

Table 6

### The multivariate analysis of exposed stroke risk factors in urban and rural areas.

Factors	Р	OR	95% CI
Age	<.001	0.987	0.981-0.994
Low education	<.001	3.147	2.643-3.747
Low income	<.001	3.800	3.346-4.315
Alcoholism	<.001	0.506	0.347-0.738
Dyslipidemia	<.001	0.631	0.556-0.716
Diabetes	<.001	0.645	0.557-0.747
Obvious overweight or obesity	.005	0.840	0.743-0.949
High-salt diet	.001	1.225	1.085–1.383

Note: The risks in urban areas were used as references. An odds ratio (OR) of <1 indicates that the risk factor is more common in urban areas.

CI = confidence interval, OR = odds ratio.

stratified study of gender revealed that smoking and alcoholism have an obviously higher exposure rate in male cerebral infarction groups, when compared with female cerebral infarction groups (Table 5). In the multifactor analysis, aging, alcoholism, dyslipidemia, diabetes, and obvious overweight or obesity were the more common stroke risk factors in urban areas, while low education, low income, and high-salt diet were more common in rural areas (Table 6).

rate of high-salt diet was higher in rural areas. In addition, the

## 3.5. Control of chronic disease in ischemic stroke patients

The chronic disease control in ischemic stroke patients is presented in Table 7. The control rates of hypertension, diabetes, and dyslipidemia were significantly higher in urban ischemic stroke patients, when compared with rural ischemic stroke patients. In addition, it was also found that the compliance rates of blood pressure and blood glucose were significantly higher in urban areas, when compared with rural areas.

## 4. Discussion

Stroke seriously endangers the lives and health of the people. The present study revealed that nearly half of the stroke patients were of the working age, which would undoubtedly cause heavy burden on families and the society. Furthermore, the incidence of stroke in China is lower in the south, when compared with the north, but this incidence is higher in the countryside, when

#### Table 7

Chronic disease control	in ischemic stroke patients.				
Diseases	Parameters	Urban (n1)	Rural (n2)	Х <sup>2</sup>	Р
Hypertension $n1 = 1658$ n2 = 2358	Control rates, n (%)	1341 (80.88)	1858 (77.90)	5.248	.022
	Compliance rates, n (%)	1033 (62.30)	1376 (57.69)	8.632	.003
Diabetes n1 = 609 n2 = 572	Control rates, n (%)	474 (77.83)	383 (66.96)	17.521	<.001
	Compliance rates, n (%)	362 (59.44)	300 (52.45)	5.857	.016
Dyslipidemia $n1 = 1017$ n2 = 1043	Control rates, n (%)	343 (33.73)	303 (29.05)	5.23	.022

compared with the cities.<sup>[5]</sup> Hence, it is of great significance to compare the characteristics and risk factors of stroke in high-risk populations between urban and rural areas in northern China.

The present study found that the prevalence of ischemic stroke in patients who were  $\geq 40$  years old in northern China was 2.88%, which was higher than the results (1.79%) of a national study.<sup>[3]</sup> Furthermore, the prevalence was higher in rural areas than in urban areas, and male patients were greater than female patients, which is consistent with previous results.<sup>[5]</sup> In addition, it was found that the control rates of hypertension and diabetes were significantly lower in the rural ischemic stroke population, when compared with those in urban areas. The risk of stroke increases with age. Furthermore, it was found that the average age of ischemic stroke was 65 years, and that rural stroke patients were slightly younger than urban patients. A previous study revealed that stroke occurred mainly in subjects who were greater than 60 years old in China.<sup>[3]</sup> A study in India reported that the median age of stroke was 67 years, and that the stroke patients in developing countries were younger than those in developed countries.<sup>[9]</sup> Therefore, an age of approximately 65 years is the key age for the prevention and treatment of ischemic stroke. Hypertension, as the most common risk factor for stroke, accounts for 88% of stroke patients, and results in 73% of the stroke burden.<sup>[5]</sup> Furthermore, its population attributable risk for stroke is 53.2%.<sup>[3]</sup> The present study also revealed that it is the most relevant independent risk factor for ischemic stroke in urban and rural areas (OR = 5.712/5.845), and the rate of exposure in an ischemic stroke population was slightly higher in the village, when compared with the city (72.72% vs 73.18%), which is consistent with the view reported in eastern China, Uganda, and Northern Sweden, in which hypertension is more common in rural stroke patients.<sup>[14,15,19]</sup> However, the specific reasons are yet to be clarified.

The prevalence of cardiovascular risk factors has been increasing each year in China.<sup>[13,20–22]</sup> It was found that dyslipidemia, obvious overweight or obesity, and diabetes were more prevalent in urban stroke patients, which is consistent with several national studies.<sup>[5,6,13,14]</sup> Furthermore, the prevalence of dyslipidemia was higher in female patients than in male patients, which might be due to the relatively high rate of dyslipidemia among postmenopausal women.<sup>[23]</sup> Studies have found that urban areas have more overweight or obese subjects, and the highest urban-rural difference was in subjects who are greater than 60 years old.<sup>[24]</sup> The Uganda study also reported a similar urban-rural difference.<sup>[15]</sup> These findings are similar to the present results. However, the correlation between socioeconomic status and overweight/obesity is reversed in developed countries.<sup>[19]</sup> Although the prevalence of overweight/obesity is higher in urban areas than in rural areas, the growth in the latter is accelerating.<sup>[24]</sup>

The relationship between drinking and stroke remains controversial. A recent meta-analysis on 27 prospective studies suggested that mild to moderate drinking may reduce the risk of cerebral infarction, while alcoholism is associated with an increased risk of all stroke subtypes.<sup>[25]</sup> The present study included heavy drinking as a risk factor, which is more specific than the drinking used in previous studies. However, the drinking habits of abstainers were not investigated in the present investigation, which could underestimate the true contribution of this risk factor to cerebral infarction. This is a possible reason why it was not identified as an independent risk factor for ischemic stroke in the whole study population. Nevertheless, it

was found that heavy drinking in the ischemic stroke population was more common in the city than in the village, and this was still the case after adjusting for other confounding factors. Studies have shown that low income can reduce alcoholism and the morbidity and mortality of alcoholism-related disease.<sup>[26]</sup> A Danish hospital-based study of ischemic stroke found that the stroke risk of individuals with the lowest education was 36% higher, when compared with individuals with the highest education, while for individuals in the lowest income group, this was almost twice of that in individuals in the highest income group.<sup>[27]</sup> In contrast, low education in the present study was identified as a protective factor for ischemic stroke in rural areas, which warrants further investigation. Furthermore, it was found that high-salt diet is a risk factor for ischemic stroke, especially in rural areas. This is consistent with the fact that there was a gradual increase in salt intake from south to north China,<sup>[28]</sup> and that people in less economically developed regions take more salt.<sup>[29]</sup>

Smoking is the second most important risk factor for stroke after hypertension.<sup>[30]</sup> It was found that smoking was a major risk factor for male stroke patients, and that the prevalence of smoking was higher in urban areas than in rural areas, which is consistent with the findings of a study conducted in India.<sup>[31]</sup> It was also found that the smoking index was significantly higher in rural areas, which was similar to a previous survey.<sup>[32]</sup> Furthermore, family history of stroke, atrial fibrillation, and lack of exercise are also important risk factors for ischemic stroke.<sup>[22,33-35]</sup> Although the present study did not reveal any difference between urban and rural areas, caution should still be taken. Atrial fibrillation has been a major risk factor for ischemic stroke.<sup>[36]</sup> However, the present study failed to identify atrial fibrillation as a risk factor, which is probably because the prevalence of atrial fibrillation was relatively low in the study population.

In summary, the distribution characteristics of risk factors for ischemic stroke in northern China were obtained. It was found that hypertension was the most common stroke risk factor. Furthermore, rural stroke patients were younger and associated with low income and education, and more salinity dietary, while urban stroke patients had a higher prevalence of diabetes, dyslipidemia, and overweight/obesity. More specific measures should be taken to control risk factors for ischemic stroke.

The strength of the present study was the large sample size and wide coverage. However, there were a few limitations. First, merely stroke survivors of cerebral infarction, who were >40 years old, were included. Second, the specific forms of physical exercise and actual salt intake were not specifically stratified. Third, other risk factors, such as air pollution, infections, nationalities, and psychological and social pressures, were not included. Lastly, this was a cross-sectional study.

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## **Author contributions**

Data curation: Hui Sang, Tingting Liu, Weidong Liu, Jian Li. Writing – original draft: Yang Li, Xin Zhang. Writing – review & editing: Xiaoyuan Niu.

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