

Smoking, Hypertension, and Their Combined Effect on Ischemic Stroke Incidence: A Prospective Study among Inner Mongolians in China

Xinfeng Huangfu, MD,* Zhengbao Zhu, MD,* Chongke Zhong, MD,*
Xiaoqing Bu, MD, PhD,* Yipeng Zhou, MD,* Yunfan Tian, MD,* Buren Batu, MD,†
Tian Xu, MD, PhD,*‡ Aili Wang, MD, PhD,* Hongmei Li, MD, PhD,*
Mingzhi Zhang, MD, PhD,* and Yonghong Zhang, MD, PhD*

Objective: We intended to investigate the combined effect of smoking and hypertension on ischemic stroke incidence based on a 10-year prospective study among Inner Mongolians in China. *Methods:* A prospective cohort study from June 2003 to July 2012 was conducted among 2589 participants aged 20 years and older from Inner Mongolia, China. We categorized the participants into 4 subgroups according to the status of smoking and hypertension. The cumulative incidence rates of ischemic stroke among the 4 subgroups were estimated using Kaplan–Meier curves and compared by log-rank test. Cox proportional hazard model was used to compute hazard ratios of ischemic stroke across the 4 subgroups after adjusting for important confounding factors. *Results:* The cumulative incidence rates of ischemic stroke were .85%, 2.05%, 3.19%, and 8.14% among non-hypertension/non-smokers, non-hypertension/smokers, hypertension/non-smokers, and hypertension/smokers, respectively. The multivariable-adjusted hazard ratios [95% confidence intervals] of ischemic stroke for hypertension and smoking were 1.84 [1.05-3.23] and 1.89 [1.11-3.22], respectively. The hazard ratios [95% confidence intervals] of ischemic stroke for non-hypertension/smokers, hypertension/non-smokers, and hypertension/smokers were 1.37 [.56-3.33], 1.34 [.54-3.29], and 2.93 [1.26-6.83], respectively, compared with the non-hypertension/non-smokers. Significant interaction was detected between smoking and hypertension on the risk of ischemic stroke. *Conclusions:* Our study indicated that participants with coexistence of smoking and hypertension were at the highest risk for ischemic stroke.

From the *Department of Epidemiology, School of Public Health and Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, Medical College of Soochow University, Suzhou, China; †Department of Epidemiology, Tongliao Center for Disease Prevention and Control, Tongliao, China; and ‡Department of Neurology, Affiliated Hospital of Nantong University, Nantong, Jiangsu, China.

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Address correspondence to Yonghong Zhang, MD, PhD, Department of Epidemiology, School of Public Health, Medical College of Soochow University, 199 Renai Road, Industrial Park District, Suzhou, Jiangsu Province, 215123, China. E-mail: yhzhang@suda.edu.cn.

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There was a significant interaction between smoking and hypertension on the risk of ischemic stroke. **Key Words:** Smoking—hypertension—ischemic stroke—interaction—prevention.

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Introduction

Stroke is a major cause of long-term disability and the second leading cause of death worldwide.¹ Among all stroke deaths, 85.5% are from developing (low and middle-income) countries,² and ischemic stroke accounts for nearly 87% of stroke.³ Thus, ischemic stroke remains an important public health challenge.⁴

More than 90% of stroke burden is attributable to modifiable risk factors, and control of behavioral and metabolic risk factors can avert about three-quarters of the global stroke burden.⁵ Further studies on risk factors are still needed to better understand the effects of these risk factors and to develop more appropriate strategies to prevent ischemic stroke. Hypertension is a strong determinant of risk for ischemic stroke and smoking is also widely considered as an important risk factor.^{6,7} Recently, it has caused some concerns that hypertension and smoking may act synergistically to elevate the risk of stroke,^{8,9} cardiovascular disease (CVD) and all-cause mortality.¹⁰ However, there was no report in Chinese stroke belt¹¹ about the combined effects of the 2 factors on ischemic stroke incidence in the general populations. This study aimed to analyze smoking, hypertension, and their combined effect on ischemic stroke incidence based on a 10-year prospective study among Inner Mongolians, a population from Chinese stroke belt.

Methods

Study Population

This prospective cohort study was conducted from June 2003 to July 2012 in 2 adjacent townships located in the counties of Kezuohou Banner and Naiman Banner in Inner Mongolia, an autonomous region in north China. The methods for study participants recruitment and baseline data collection have been described elsewhere.¹² Briefly, study participants aged 20 years and older were recruited from 32 villages in the 2 townships. There were a total of 3475 local residents aged 20 years and older who had lived there for several generations and maintained a traditional diet and lifestyle in these 32 villages. Among them, 886 persons were excluded from the study for the reasons of refusing to participate in the study or already having CVDs or endocrine diseases, including hyper/hypothyroidism. Thus, 2589 individuals were finally included in the study. Written informed consents were obtained from all study participants. This study was approved by the ethics committee at Soochow University in China.

Data Collection and Laboratory Tests

The information on demographic characteristics, medical history, and lifestyle risk factors were collected for all participants by trained staff with a standard questionnaire. The data about average amount (number) of cigarette smoking per day and the duration (number of year) of smoking were collected for the participants at baseline. Cigarette smoking was defined as having smoked at least 1 cigarette per day for 1 year or more.¹² Alcohol consumption was defined as consuming any type of alcoholic beverage containing at least 25 g alcohol per day on average for 1 year or more during the past years. Blood pressure (BP) measurements were taken 3 times while each participant was seated using a mercury sphygmomanometer and 1 of 4 cuff sizes (pediatric, regular adult, large adult, or thigh) based on participant arm circumference according to a standard protocol¹³ between 06:00 and 09:00 in the morning in the village halls. The first and fifth Korotkoff sounds were recorded as systolic and diastolic BP, respectively. The mean of these 3 BP measurements was used for data analysis. Hypertension was defined as systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg. Body weight and height were measured using standard methods, and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Waist circumference (WC) was measured at the level of 1 cm above the umbilicus.

Overnight fasting blood samples were obtained to measure total cholesterol (TC), high-density lipoprotein cholesterol, and triglycerides (TG). TC, high-density lipoprotein cholesterol, and TG were analyzed enzymatically using a Beckman Synchron CX5 Delta Clinical System (Beckman Coulter, Inc, Fullerton, CA) with commercial reagents.¹⁴ Low-density lipoprotein cholesterol levels were calculated using the Friedewald equation for participants who had < 400 mg/dL TG.¹⁵ A modified hexokinase enzymatic method was applied to test fast plasma glucose (FPG) levels.¹⁶

Follow-Up and Outcome Assessment

Our study followed all participants from June 2003 to July 2012, and the occurrence of ischemic stroke during the follow-up period was the primary outcome. Four county hospitals with modern diagnostic facilities, including computed tomography and magnetic resonance imaging, provided participants with medical service. Household surveys for all participants were conducted every

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