# Metabolic Syndrome, Its Components, and Diabetes on 5-Year Risk of Recurrent Stroke among Mild-to-Moderate Ischemic Stroke Survivors: A Multiclinic Registry Study

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*Objectives:* The pieces of evidence regarding whether metabolic syndrome (MetS) is a better predictor than its individual components, especially diabetes, for recurrent stroke are limited. This study aimed to examine these associations. *Methods:* A total of 1087 ischemic stroke patients were recruited consecutively from 2003 to 2004. They were followed up until the end of 2008. Baseline clinical and laboratory characteristics and new stroke event during follow-up were recorded. MetS was defined by the definition issued by the Chinese Medical Association/Chinese Diabetes Society. *Results:* One hundred forty-three new stroke cases were recorded. After adjusting for baseline age, gender, education, marriage status, subtype stroke, length of index stroke to baseline assessment, history of cardiac diseases, smoking status, drinking status, clinics, aspirin treatment, and fibrinogen by Cox regression models, the risk of recurrent stroke was 43% higher in MetS patients than in non-MetS patients (hazard ratio [HR] = 1.43, 95% confidence interval [CI]: 1.01-2.01). The strength of this association is weaker than MetS individual components such as elevated glycemia (adjusted HR = 1.78, 95% CI: 1.26-2.52), elevated blood pressure (adjusted HR = 1.91, 95% CI: 1.11-3.30), or low high-density lipoprotein cholesterol (adjusted HR = 1.57, 95% CI: 1.08-2.51). Compared with the group with neither MetS nor diabetes, the adjusted risk of recurrent stroke was highest in the group with diabetes (HR = 2.77, 95% CI: 1.66-4.63), followed by those with both MetS and diabetes (HR = 1.91, 95% CI: 1.25-2.94). The risk of recurrent stroke in patients with MetS in the absence of diabetes was similar to those with neither. *Conclusion:* MetS is not superior to its individual components in predicting future recurrent stroke

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The paper has 6 authors, all of whom have made substantial contributions to the work. Dr. Xiang-Hua Fang and Dr. Xunming Ji are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Xiang-Hua Fang, the first author, also helped run the study, analyzed and interpreted the data, and drafted this paper. Dr. Xun-ming Ji and Dr. Xin-qing Zhang have made major contributions to the conception, design, and implementation of the study. Drs. Hong-Jun Liu, Hong-mei Zhang, and Xiao-ming Qin collected the data and visited patients. Drs. Xin-Qing Zhang, Xiao-Ming Qin, and Xun-Ming Ji diagnosed and classified stroke subtypes. Drs. Xiang-hua Fang and Xun-ming Ji provided the final approval of this revision.

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in patients who experience mild-to-moderate ischemic stroke. **Key Words:** Metabolic syndrome—diabetes—recurrent stroke—prognosis—follow-up study.


## Introduction

Death from stroke has been ranked as the second or third leading cause of death in the Chinese population for decades.[1,2] Data from a long-term epidemiological study indicated that the incidence of stroke has increased in China and one third of stroke cases were recurrent stroke.[3] Patients who experience 2 or more strokes are generally at higher risk of cardiovascular diseases (CVDs), and the clinical sequelae that follow a recurrent stroke event can be debilitating. Recurrent stroke patients carry greater risks of disability and death.[4-6] Secondary prevention of stroke continues to be a challenge and is of great concern to clinicians. Studies have shown that comprehensive modification of stroke-related risk factors in combination with antiplatelet therapy may prevent recurrent stroke.[7]

Metabolic syndrome (MetS) is mainly characterized by impaired glucose tolerance, elevated blood pressure, dyslipidemia, and central obesity. This cluster of highly interrelated risk factors is strongly associated with incidence of stroke in healthy individuals.[8-11] However, when dealing with patients with prior ischemic stroke, the roles of MetS and its individual components on long-term prognosis of stroke survivors are uncertain. Limited reports within 1 or 2 years' observation among stroke survivors are inconsistent in the Eastern Asia poststroke population.[12-14] In addition, whether the MetS is equivalent to or is a better predictor for second cardiovascular events than its individual components or traditional risk factors is also in controversy.[8,15,16]

Diabetes is now considered equivalent to coronary heart disease and is strongly associated with the occurrence of stroke.[17,18] In post-ischemic stroke patients in China, half of them have both Mets or diabetes.[12,19] Now it is generally accepted that both MetS and diabetes share a common underlying pathophysiological mechanism, insulin resistance. The result from Framingham Offspring study showed that diabetes appears to be a greater hazard for stroke than MetS.[20] Currently, there is paucity in the literature regarding the effects of MetS and diabetes on the outcome of patients who experience a mild-to-moderate stroke in the postacute stage after being treated in the outpatient setting or discharged from the hospital.

In the present study, we performed a 5-year prospective observational study in mild-to-moderate ischemic stroke patients in clinics. The objective of the current study was to examine if MetS would provide incremental risk information above its individual components in predicting the long-term risk of recurrent stroke; special attention has been paid to patients with both MetS and diabetes.

## Methods

This study was initiated in December 2003 and the details of the design, setting, sampling technique, and contents of the survey have been described elsewhere.[21] Briefly, in China, hospitals are classified into 3 grades: primary clinics (community hospitals) are defined as grade I; hospitals that serve several communities are defined as grade II; and central hospitals for a certain district or city are defined as grade III and are usually teaching hospitals. There are 600 primary clinics in the Beijing municipality in 2003. We performed a prospective registry study in 18 primary clinics that were selected randomly from locations in eastern, southern, western, northwestern, and northeastern regions of urban Beijing, China. The study was approved by the ethics committee of Xuanwu Hospital, Capital Medical University, and written informed consent was obtained from the study subjects. A total of 1371 stroke patients were recruited consecutively between December 2003 and December 2004. Patients eligible for enrollment were those who presented with a symptomatic stroke event, were diagnosed by a neurologist, and underwent examinations of computed tomography or magnetic resonance imaging. Patients with any silent stroke or who experienced an acute stroke within 3 months were excluded from the study. Of the 1371 patients, 1308 had experienced an ischemic stroke and 63 hemorrhagic stroke. Of the 1308 ischemic stroke patients, a total of 134 of patients did not meet enrollment criteria, and 87 patients refused to take part in the study as well as to provide written consents. Therefore, 1087 consented to participate in the study and were enrolled.

All enrolled patients underwent a standardized assessment by a multidisciplinary stroke care research team, including physicians, neurologists, epidemiologists, and nurses. To ensure uniformity of research methods, a manual of operations was compiled to standardize the research methods and procedures across the clinics. All of the people who participated in the study were trained before the start of the study (see Supplementary file 1). The assessment included gathering information on demographic characteristics, all known risk factors for cerebrovascular diseases, including hypertension, diabetes, and dyslipidemia. Smoking and drinking practices were characterized as never, current, or quit.

After the baseline assessment, the patients were interviewed every 6 months until the end of December 2008. At each follow-up interview, physicians in clinics spoke directly with the patients or their family members to document any acute events pertaining to cardiovascular events