Diabetes and Poor Outcomes Within 6 Months After Acute Ischemic Stroke
The China National Stroke Registry

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Background and Purpose—Diabetes mellitus (DM) is an independent risk factor for ischemic stroke. However, controversy exists with regard to the impact of DM on prognosis after ischemic stroke in the Chinese population. We investigated the associations between DM and death, dependency, and stroke recurrence in patients after ischemic stroke onset in a nationwide, prospective registry, the China National Stroke Registry.

Methods—The China National Stroke Registry consecutively recruited patients hospitalized for acute ischemic stroke in 2007 to 2008 and who were prospectively followed up for clinical and functional outcomes (death, dependency, and stroke recurrence) at 3 and 6 months after disease onset. Multivariable logistic regression was performed to analyze the association between DM and stroke outcomes after adjusting for potential confounding including age, sex, National Institutes of Health Stroke Scale score, glucose level at admission, hypertension, coronary heart disease, smoking, urinary tract infection, and other factors.

Results—DM was identified in 3483 (27.0%) of stroke patients. Compared with stroke patients without DM, patients with DM had a significantly higher incidence of death or dependency and of recurrent stroke at 3 and 6 months after stroke onset. DM was an independent risk factor for death or dependency (adjusted odds ratio: 1.23; 95% confidence interval, 1.10 to 1.37) in patients with ischemic stroke at 6 months after onset.

Conclusions—DM independently predicted poor outcomes in Chinese patients after acute ischemic stroke. (Stroke. 2011; 42:00-00.)

Key Words: diabetes mellitus ■ ischemic stroke ■ death ■ dependency ■ recurrent stroke.

Diabetes mellitus (DM) is an independent risk factor for ischemic stroke, with an increased relative risk in patients with DM ranging from 1.8 to nearly 6.0.1 The prevalence of DM ranges from 21% to 44.4% among patients with acute ischemic stroke.2-4 However, evidence for an association between DM and prognosis after acute ischemic stroke still remains controversial. In Western populations, several studies suggested that DM was associated with a higher mortality from stroke,3,5,6 whereas some have not.7-9 Although abundant studies have indicated that DM is a predictive factor for dependency5,10 or recurrent stroke,6,11,12 several studies have shown no association between DM and disability9,13 or recurrence of stroke after ischemic stroke onset.3,7

DM is a major public health problem in China, with an age-standardized prevalence 9.7%.14 However, data for the impact of DM on outcomes of patients with ischemic stroke in China are limited and conflicting. Some studies have suggested that DM is a predictive factor for early- or long-term death after ischemic stroke,15-17 but several studies have not.12,18,19 The literature on the associations between DM and dependency and recurrent stroke in patients with ischemic stroke remains scarce.

In this study, we systematically investigated the effect of DM on mortality, dependency, and stroke recurrence in a large, nationwide, prospective cohort of Chinese patients with acute ischemic stroke at discharge, 3 months, and 6 months.

Subjects and Methods
The China National Stroke Registry is a well-designed, nationwide, prospective, cohort study aimed at observing vascular risk factors, clinical characteristics, diagnosis, treatment, and prevention for patients with acute stroke and for following up the outcomes of acute
stroke prospectively. Acute stroke included acute ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage.

Acute ischemic stroke was diagnosed according to World Health Organization criteria combined with brain computed tomography or magnetic resonance imaging. Patients were diagnosed as having acute ischemic stroke when the following conditions were met: acute occurrence within 14 days of neurologic deficit, with focal or overall involvement of the nervous system, lasting for >24 hours and after excluding nonvascular causes (primary and metastatic neoplasms, postseizure paralysis, head trauma, etc) that led to brain function deficit, and excluding intracerebral hemorrhage by computed tomography or magnetic resonance imaging. The diagnostic criteria were consistent across all participating hospitals.

Patients were classified as having DM when any of the following criteria were met: a self-reported physician diagnosis of DM, use of hypoglycemic medications (for example, insulin or sulfonylureas) during hospitalization, or hypoglycemic medication use at discharge. DM in this study included types 1 and 2. The ethics committees at all participating hospitals approved the procedures, and all patients or their designated relatives gave informed consent.

Patient baseline information was recorded at admission, including sex, age, height, weight, blood pressure (in mm Hg), random glucose level at admission (in mmol/L), and others, as described elsewhere. Assessment of baseline vascular risk factors included history of stroke (defined as a medical chart–confirmed history of stroke), hypertension (history of hypertension or hypertensive drug use), dyslipidemia (history of dyslipidemia or lipid-lowering drug use), atrial fibrillation (history of atrial fibrillation confirmed by at least 1 ECG, or the presence of the arrhythmia during hospitalization), coronary heart disease, peripheral artery disease, history of DM, current or previous smoking, moderate or heavy alcohol consumption (≥2 standard alcoholic beverages consumed per day), and body mass index (calculated as measured weight [kg] divided by the square of measured height [m²]).

The severity of neurologic impairment was evaluated by the National Institutes of Health Stroke Scale (NIHSS) and Glasgow Coma Scale within 24 hours after admission and at discharge. The clinical subtypes of ischemic stroke were classified according to Oxfordshire Community Stroke Project criteria. The occurrence of pneumonia or urinary tract infection complications during hospitalization was also recorded.

At 3 and 6 months after stroke onset, the outcomes of all patients were assessed through telephone follow-up, including death (or modified Rankin Scale [mRS] score=6), dependency (defined by mRS=3 to 5), recurrence of stroke (aggravated primary neurologic deficit; new signs; or rehospitalization with a diagnosis of ischemic stroke, intracerebral hemorrhage, or subarachnoid hemorrhage), other vascular events (including myocardial infarction, angina, pulmonary embolism, or peripheral artery disease), and the corresponding dates of onset. Poor outcomes were defined as death or dependency (mRS=3 to 6). The telephone follow-up was conducted centrally for all included patients and was based on a shared standardized interview protocol. The interviewers were trained centrally with the interview protocol and were blinded to a DM history for all patients.

**Statistical Analysis**

Demographic and clinical characteristics in stroke patients with DM were compared with those without DM by the χ² and t test for categorical and continuous variables, respectively. The associations between DM and death, dependency, or recurrence of stroke were analyzed in multivariate logistic-regression models, after adjusting for potential confounders including age, sex, prestroke mRS, body mass index, NIHSS score at admission, glucose level at admission, history of stroke, hypertension, dyslipidemia, coronary heart disease, smoking, alcohol, atrial fibrillation, Oxfordshire Community Stroke Project subtypes of ischemic stroke, antiplatelet agents use, management of DM during hospitalization, and urinary tract infection. Data were analyzed with SAS version 9.1.3 statistical software.

**Results**

This project consecutively recruited 22,216 hospitalized patients with acute stroke within 14 days after onset among 132 participating hospitals throughout China in 2007 to 2008. Of the 22,216 patients, 14,526 were diagnosed as having had acute ischemic stroke. At 6 months after stroke onset, follow-up information was available for 12,907 patients (88.9%) with acute ischemic stroke, who were then included in the present study.

Clinical characteristics of the analyzed population (N=12,907 patients) were compared with those for 1,619 patients who did not have 6-month follow-up information and thus were excluded from the analyzed population. The prevalence of DM was similar in the 2 groups (P=0.756), and the random glucose concentration at admission was also comparable (P=0.059). The severity of neurologic functional defect (expressed as NIHSS score) at admission showed similar results in the 2 groups (P=0.107). Patients with 6-month follow-up information seemed more likely to have a history of hypertension (P=0.0001) and coronary heart disease (P=0.0002), compared with the patients who were lost to follow-up.

A total of 3,483 stroke patients had DM, of whom 2,758 (79.2%) had a history of DM, and 725 (20.8%) were newly diagnosed during hospitalization. Compared with stroke patients without DM, patients with DM were older and had a higher proportion of females but had fewer moderate or heavy alcohol drinkers and fewer smokers (Table 1). Lacunar infarction presented more frequently in patients with DM compared with patients without DM, whereas the other 3 stroke subtypes did not. Hypertension, dyslipidemia, coronary heart disease, urinary tract infection, antiplatelet agents use, and history of stroke also presented more frequently in stroke patients with DM, whereas atrial fibrillation showed an opposite trend.

Table 2 shows that stroke patients with DM had a significantly longer hospital stay than those without DM. At discharge, death or dependency (mRS=3 to 6) in stroke patients with DM was significantly more frequent than in the group without DM (P<0.0001). At 3 months after stroke onset, the occurrence of death or dependency and of recurrent stroke was significantly higher in patients with DM compared with those without DM. A similar pattern was also observed at 6 months after stroke onset.

Furthermore, multivariate logistic-regression analyses (Table 3) suggested that, after adjusting for potential confounders, DM was an independent risk factor for death or dependency at discharge (odds ratio=1.18; 95% CI, 1.05 to 1.32), at 3 months (odds ratio=1.21; 95% CI, 1.08 to 1.35), and at 6 months (odds ratio=1.23; 95% CI, 1.10 to 1.37) but had no significant association with stroke recurrence at 3 months (odds ratio=1.07; 95% CI, 0.95 to 1.21) or 6 months (odds ratio=1.09; 95% CI, 0.98 to 1.22) after onset.

**Discussion**

In this study, we prospectively and systematically investigated the associations between DM and outcomes of acute ischemic stroke. To our knowledge, this study is the first nationwide stroke registry in China. DM was diagnosed in
27.0% of our population with acute ischemic stroke, which is consistent with the prevalence range of 21% to 44.4%, as suggested in the literature.2–4 Follow-up information at 6 months after stroke onset was available in 88.9% (12,907/14,526) of all enrolled patients at admission. The main variables, such as prevalence of DM and NIHSS score at admission, were comparable between patients with and without 6-month follow-up information, indicating that the analyzed population was a good representation of the patients enrolled in our registry.

Our results indicated that patients with DM were more likely to have a history of stroke, which contrasts with the majority of previous studies.6,12 We found that patients with DM more frequently had a history of handicap (mRS 2 to 5) before stroke onset, which was probably caused by previous stroke events. Complications of urinary tract infection were more frequent in our patients with DM but were rarely reported in previous studies, which might be explained by the fact that individuals with DM are at higher risk for urinary tract infection.27

We also found that the occurrence of death or dependency in stroke patients with DM was significantly more frequent than in those without DM, which indicates that DM is a strong determinant for death or dependency in ischemic
The potential confounding factors adjusted for in the multivariable logistic-regression analysis were selected as either confirmed effect factors for stroke outcomes in previous studies or important confounding variables related to DM, for example, glucose level at admission and urinary tract infection. Our findings confirmed that DM remained an independent predictor for poor outcomes in stroke patients, even after adjusting for admission hyperglycemia, in contrast with the previous studies reporting no significant outcome differences between patients with and without DM when adjusted for admission glucose levels. Our findings highlight the concept of the clinical significance that early identification and treatment of DM should be emphasized to improve the outcome of ischemic stroke in the Chinese population.

Several limitations need to be addressed. The selection of participating hospitals, though covering all areas of China, was done for convenience. All of the hospitals participating in the registry were from urban regions of China. These study sites may represent institutions with more resources and expertise than county-level or even more grassroots-level hospitals. It is not known what proportion of stroke patients in China currently have access to levels of hospital care similar to those who participated in our study. In the present study, we did not consider the possibility that diabetic patients could have had persistent poststroke hyperglycemia during the first days after onset, which could have an influence on stroke outcome, as has been demonstrated in a recently published study. Moreover, we performed the analysis based on a yes or no diagnosis of DM at admission or during hospitalization and did not collect information on new cases of DM at 3 and 6 months after stroke onset. Consequently, we could not analyze its impact on the final results.

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### Disclosures
None.

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