Original Contribution

Prognosis of Ischemic Stroke With Newly Diagnosed Diabetes Mellitus According to Hemoglobin A1c Criteria in Chinese Population

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Background and Purpose—Hemoglobin A1c (HbA1c) was recommended to diagnose diabetes mellitus, but whether newly diagnosed diabetes mellitus (NDDM) according to the new criteria was associated with stroke prognosis was unclear. We aimed to investigate the prognosis of ischemic stroke with NDDM according to the new criteria.

Methods—Ischemic stroke without a diabetes mellitus history in the survey on Abnormal Glucose Regulation in Patients With Acute Stroke Across China were included in the analysis. NDDM was defined as fasting plasma glucose ≥7.0 mmol/L, 2-hour oral glucose tolerance test ≥11.1 mmol/L, or HbA1c ≥6.5%, and NDDM was divided into group 1, diagnosed by glucose criteria (fasting plasma glucose ≥7.0 mmol/L or 2-hour oral glucose tolerance test ≥11.1 mmol/L with/without HbA1c ≥6.5%), or group 2, diagnosed by single high HbA1c (fasting plasma glucose <7.0 mmol/L, 2-hour oral glucose tolerance test <11.1 mmol/L, and HbA1c ≥6.5%). The association between NDDM and 1-year prognosis (mortality, stroke recurrence, and poor functional outcome [modified Rankin scale score 3–6]) was estimated.

Results—Among 1251 ischemic stroke patients, 539 were NDDM and 141 of NDDM with single high HbA1c. NDDM was an independent risk factor for 1-year mortality (hazard ratio, 1.12; 95% confidence interval, 1.001–1.26), stroke recurrence (hazard ratio, 1.14; 95% confidence interval, 1.01–1.28), and poor functional outcome (odds ratio, 2.58; 95% confidence interval, 1.95–3.43) compared with non–diabetes mellitus. Nevertheless, NDDM with single high HbA1c was not significantly associated with 1-year prognosis for all end points (P>0.05 for all).

Conclusions—NDDM by new criteria was associated with poor prognosis at 1 year after ischemic stroke; however, NDDM with single high HbA1c did not predict a poor prognosis. **(*Stroke*. 2016;47:00-00. DOI: 10.1161/STROKEAHA.116.013606.)**

Key Words: diabetes mellitus ■ glucose ■ prognosis ■ risk factor ■ stroke

Diabetes mellitus (DM) and ischemic stroke are common disorders that often develop together and interact with each other. DM is an important risk factor for ischemic stroke; the reported hazard ratio (HR) for ischemic stroke was 2.3 (95% confidence interval [CI] 2.0–2.7) in individuals with DM versus those without DM.[1] Furthermore, ischemic stroke patients with DM have a poor prognosis,[2–4] and DM has been widely used to predict outcome after acute ischemic stroke or transient ischemic attack as an important risk factor.[5–7]

The traditional glucose-based criteria of DM are based on a fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) (FPG ≥7.0 mmol/L and/or 2-hour OGTT ≥11.1 mmol/L).[8,9] Recently, hemoglobin A1c (HbA1c) criteria (HbA1c ≥6.5%) have been proposed as an alternative to glucose-based criteria by the American Diabetes Association[10] and World Health Organization.[11] However, glucose-based and HbA1c-based criteria are frequently discordant regarding DM diagnosis,[12,13] but an increasing number of DM

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individuals have been supplementary diagnosed using HbA1c criteria as single high HbA1c which with abnormal HbA1c (HbA1c ≥6.5%) but normal glucose (FPG <7.0 mmol/L and 2-h OGTT <11.1 mmol/L). However, there are limited data on the prognosis of newly diagnosed diabetes mellitus (NDDM) using the newly proposed criteria in acute ischemic stroke patients without a history of DM. Furthermore, the relationship between NDDM with single high HbA1c and ischemic stroke prognosis is unclear.

We used the Abnormal Glucose Regulation in Patients with Acute Stroke across China (ACROSS-China) registry to characterize 1-year prognosis of NDDM using newly proposed criteria in acute ischemic stroke patients without a history of DM in Chinese population. We further investigated whether NDDM patients with single high HbA1cs have a poor prognosis compared with non-DM patients.

Methods

Standard Protocol Approvals, Registration, and Patient Consent

Ischemic stroke patients without a history of DM in the survey on ACROSS-China were included in our study. ACROSS-China is a well-designed, nationwide prospective cohort study that aimed to investigate the prevalence and distribution of abnormal glucose regulation in hospitalized patients (aged ≥18 years) with a first ischemic and hemorrhagic stroke (within 14 days after onset), the current condition of abnormal glucose regulation treatment in these patients with stroke, and the impact of abnormal glucose regulation on the outcome of these patients from 2008 to 2009 across China. The details of this study have been previously described.[14]

Acute ischemic stroke was diagnosed according to the World Health Organization criteria[15] combined with brain computed tomography or magnetic resonance confirmation. Patients were diagnosed as acute ischemic stroke when the following conditions were met: acute occurrence within 14 days of neurological deficit, focal or overall involvement of the nervous system; symptoms that lasted for >24 hours, and the exclusion of nonvascular causes (eg, primary and metastatic neoplasms, postseizure paralysis, or head trauma) that led to brain function deficit and of intracerebral hemorrhage by computed tomography or magnetic resonance imaging. The diagnostic criteria were consistent across all participating hospitals.

NDDM Evaluation

The first overnight fasting venous blood samples were drawn to measure the blood HbA1c. HbA1c was measured following admission using high-performance liquid chromatographic analysis, which is aligned with the Diabetes Control and Complications Trial and the National Glycohemoglobin Standardization Program standards.[16] A standard OGTT was performed in the ischemic patients without previous DM during the morning hours (range: 07:00–11:00) on day 14±3 after stroke onset or before discharge (if hospital stay <14 days) according to the World Health Organization criteria.[9] After overnight fasting (at least 8 hours), the patients drank 250 mL of a solution that included 75 g of glucose within 3 minutes. Immediately before administration of the drink and after 2 hours, venous blood samples were collected in sodium fluoride tubes to measure plasma glucose. Fasting and 2-hour OGTT plasma glucose levels were measured (mmol/L) via an automated glucose oxidation method.

NDDM was diagnosed as a FPG ≥7.0 mmol/L, 2-hour OGTT ≥11.1 mmol/L, or HbA1c ≥6.5%.[10,11] NDDM individuals were divided into 2 groups: group 1, NDDM diagnosed via traditional glucose-based criteria (FPG ≥7.0 mmol/L or 2-hour OGTT ≥11.1 mmol/L with/without HbA1c ≥6.5%), and group 2, NDDM diagnosed via a single high HbA1c (FPG <7.0 mmol/L, 2-hour OGTT <11.1 mmol/L and HbA1c ≥6.5%).

Data Collection and Risk Factors

Patient baseline information, such as sex, age, height, weight, waist circumference, hip circumference, blood pressure (mm Hg), admission fasting glucose level (mmol/L), hemoglobin (Hb), low-density lipoprotein (mmol/L), high-density lipoprotein (mmol/L), triglyceride (mmol/L), and body mass index (kg/m^2), were recorded within 24 hours after admission. The assessment of medical history included a history of hypertension, dyslipidemia, atrial fibrillation (confirmed by at least 1 ECG), coronary heart disease, DM, and current or previous smoking. The first overnight fasting venous blood samples were measured at admission.

The severity of neurological impairment was evaluated by the National Institutes of Health Stroke Scale within 24 hours after admission. The etiologic subtypes of ischemic stroke were classified according to the Trial of Org 10172 in Acute Stroke Treatment[17] as atherothrombotic infarction, cardiogenic embolism, lacunar infarction, undetermined type, and other type. The occurrence of pulmonary or urinary infection complications and medicine use during hospitalization were also recorded.

Patient Follow-Up and Outcome Evaluation

At 12 months after stroke onset, the prognoses of all patients were assessed through telephone follow-up. The telephone follow-up was centrally conducted for all included patients and was based on a shared standardized interview protocol. The outcomes included all-cause mortality, stroke recurrence, and poor functional outcome at 12-month follow-up. Stroke recurrence was defined as a new neurological deficit, including ischemic or hemorrhagic stroke, which was associated with rehospitalization. Poor functional outcome was defined as modified Rankin scale scores 3 to 6.

Statistical Analysis

The demographic and clinical characteristics of the stroke patients with NDDM were compared with patients without DM using the χ^2 test for categorical variables and *t* test or Wilcoxon rank-sum test for continuous variables, respectively. We also compared the subgroups of the NDDM patients with the non-DM group using χ^2 test for categorical variables and ANOVA or Kruskal–Wallis test for continuous variables, respectively. The age- and sex-adjusted or multivariate-adjusted HR with their 95% CI for stroke recurrence and death was estimated using a Cox regression model, whereas odds ratios with their 95% CI for the poor functional outcome at 12 months were estimated using a logistic regression model. The multivariate models adjusted for all the significant covariates in univariate analyses, including age, sex, body mass index, triglyceride level at admission, history of hypertension, and anticoagulation use during hospitalization. The data were analyzed with SAS version 9.4 statistical software (SAS Institute Inc, Cary, NC). All reported *P* values were 2 sided with $P<0.05$ considered significant.

Results

During the study period, 2639 patients exhibited a first acute ischemic stroke within 14 days after onset. Five hundred and thirty-four patients were excluded because of a history of DM. In the remaining 2105 patients, 312 patients without OGTT data (dysphagia or rejected) and 252 patients without HbA1c data were also excluded. After further exclusion of 290 patients without 12-month follow-up data, 1251 patients were included in the final analysis (Figure 1). There was no significant difference in baseline characteristics between the study patients and the excluded 854 ischemic stroke patients who did not undergo OGTT or HbA1c, or lost at follow-up, except history of hyperlipidemia, antihypertensive drug usage during hospitalization, and stroke subtype (Table I in the online-only Data Supplement).

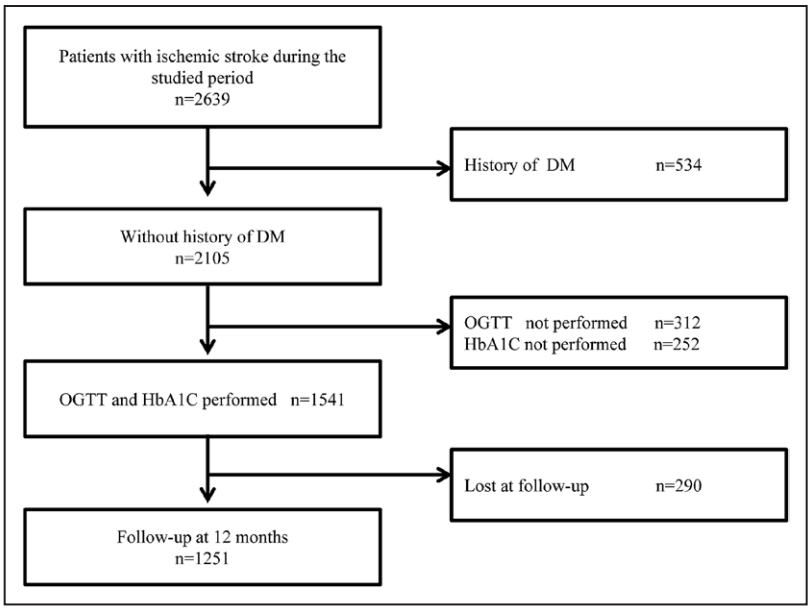

Figure 1. Flow chart showing the patient selection. DM indicates diabetes mellitus; HbA1c, hemoglobin A1c; and OGTT, oral glucose tolerance test.

Baseline Characteristics

The clinical characteristics of the included 1251 first ischemic stroke patients without a history of DM are shown in Table 1. The average age of the study subjects was 62.2±12.6 years, and 793 (63.4%) patients were men. Five hundred and thirty-nine patients (43.1%) with NDDM were detected by the newly proposed criteria (FPG ≥7.0 mmol/L, 2-h OGTT ≥11.1 mmol/L, or HbA1c ≥6.5%). The distribution of NDDM identified via different diagnostic criteria is illustrated in Figure 2. The patients with NDDM were older and less likely to be men compared with the non-DM patients (P<0.05 for all). The patients with NDDM were more likely to have an increased body mass index, admission fasting glucose level, HbA1c level, and triglyceride level, as well as an increased frequency of a history of hypertension compared with the non-DM patients (P<0.05 for all). The patients with NDDM were more likely to receive more oral hypoglycemic drugs and insulin during hospitalization compared with the non-DM patients (P<0.05 for all).

Of the 539 NDDM patients, 398 patients were diagnosed using traditional glucose-based criteria regardless of the level of HbA1c, and 141 patients were diagnosed with single high HbA1c. The patients who were diagnosed using traditional glucose-based criteria were older and more likely to have an increased systolic blood pressure, body mass index, admission fasting glucose level, and triglyceride level and to receive more oral hypoglycemic drugs and insulin during hospitalization compared with the other groups (P<0.05 for all). The NDDM patients with single high HbA1c were more likely men, exhibited an increased HbA1c level, and received more anticoagulation drugs during hospitalization compared with the other groups (P<0.05 for all).

Association Between NDDM and 12-Month Outcome

As shown in Table 2, the rates of mortality, stroke recurrence, and poor functional outcome were 16.3%, 22.2%, and 36.1%, respectively, in patients with NDDM at 12-month follow-up. After adjustment for age, sex, and potential confounders, patients with NDDM had a marginal significantly increased risk of mortality (HR, 1.12; 95% CI, 1.001–1.26; P=0.048), stroke recurrence (HR, 1.14; 95% CI, 1.01–1.28; P=0.03), and poor functional outcome (odds ratios, 2.58; 95% CI, 1.95–3.43; P<0.001) at 12 months compared with the non-DM patients.

After adjustment for age, sex, and potential confounders, the patients who were diagnosed using traditional glucose-based criteria regardless of the level of HbA1c had significantly increased risks of mortality (HR, 1.17; 95% CI, 1.03–1.33; P=0.02), stroke recurrence (HR, 1.19; 95% CI, 1.04–1.35; P=0.01), and poor functional outcome (odds ratios, 3.33; 95% CI, 2.45–4.51; P<0.001) at 12 months compared with the non-DM patients. Despite a tendency, the NDDM patients with single high HbA1c did not seem to exhibit a definite correlation with the risk of mortality (HR, 1.02; 95% CI, 0.85–1.22; P=0.85), stroke recurrence (HR, 1.03; 95% CI, 0.86–1.24; P=0.77), or poor functional outcome (odds ratios, 1.19; 95% CI, 0.74–1.91; P=0.47) compared with the non-DM patients after adjustment for potential risk factors.

Discussion

In our study, we demonstrated that NDDM according to the new criteria was associated with poor prognosis at 1 year after first acute ischemic stroke onset in Chinese patients. However, the patients with NDDM with single high HbA1c did not exhibit a definite correlation with poor prognosis compared with non-DM patients.

Previous studies have demonstrated that the prevalence of NDDM in stroke patients tested by OGTT ranged from 17.5 to 37.5%.[18–21] A European study had investigated the prevalence of NDDM using the newly proposed HbA1c criteria and indicated that the prevalence of NDDM was 25% in patients with stroke or transient ischemic attack.[20] In our study, 32% of the patients were diagnosed using the glucose-based criteria,

Table 1. Baseline Characteristics in Relation to the NDDM State

	Diabetes Mellitus			Non–Diabetes Mellitus (N=712)	*P* Value‡	*P* Value§
	Total (N=539)	Group 1* (N=398)	Group 2† (N=141)			
Sex (men), n (%)	316 (58.6)	220 (55.3)	96 (68.1)	477 (67.0)	0.002	<0.001
Age, y, mean±SD	64.2±11.9	64.3±12.1	64.2±11.6	60.6±12.8	<0.001	<0.001
NIHSS score at admission, median (IQR)	4 (2–8)	5 (2–8)	4 (2–7)	4 (2–8)	0.76	0.10
Body mass index, kg/m^2, mean±SD	25.1±3.8	25.3±3.9	24.3±3.2	24.7±3.8	0.03	0.002
Fasting glucose at admission, mmol/L, mean±SD	7.0±2.6	7.2±2.7	6.3±2.0	5.1±0.9	<0.001	<0.001
HbA1C, mean±SD	7.1±1.7	7.1±1.8	7.4±1.3	5.5±0.7	<0.001	<0.001
Triglyceride at admission, mmol/L, mean±SD	1.9±1.2	2.0±1.2	1.8±1.0	1.6±1.0	<0.001	<0.001
LDL at admission, mmol/L, mean±SD	3.2±1.5	3.2±1.5	3.3±1.4	3.1±1.4	0.054	0.08
HDL at admission, mmol/L, mean±SD	1.2±0.4	1.2±0.3	1.2±0.6	1.2±0.3	0.10	0.19
History of hypertension, n (%)	339 (62.9)	253 (63.6)	86 (61.0)	407 (57.2)	0.04	0.11
History of hyperlipidemia, n (%)	63 (11.7)	42 (10.6)	21 (14.9)	86 (12.1)	0.83	0.38
History of atrial fibrillation, n (%)	25 (4.6)	21 (5.3)	4 (2.8)	46 (6.5)	0.17	0.22
History of coronary heart disease, n (%)	70 (13.0)	49 (12.3)	21 (14.9)	84 (11.8)	0.53	0.59
Smoking, n (%)					0.54	0.79
Current smoker	173 (32.1)	127 (31.9)	46 (32.6)	250 (35.1)		
Ever smoker	54 (10.0)	38 (9.6)	16 (11.4)	68 (9.6)		
Nonsmoker	312 (57.9)	233 (58.5)	79 (56.0)	394 (55.3)		
Medicine use during hospitalization, n (%)						
Oral hypoglycemic drugs	175 (32.5)	146 (36.7)	29 (20.6)	11 (1.5)	<0.001	<0.001
Insulin	67 (12.4)	60 (15.1)	7 (5.0)	10 (1.4)	<0.001	<0.001
Antihypertensive drugs	254 (47.1)	184 (46.2)	70 (49.7)	308 (43.3)	0.17	0.31
Diuretics	11 (2.0)	9 (2.3)	2 (1.4)	18 (2.5)	0.57	0.72
β-blockers	21 (3.9)	17 (4.3)	4 (2.8)	27 (3.8)	0.93	0.75
Statin	277 (51.4)	203 (51.0)	74 (52.5)	360 (50.6)	0.77	0.92
Intravenous alteplase	11 (2.0)	7 (1.8)	4 (2.8)	27 (3.8)	0.07	0.17
Antiplatelet	332 (61.6)	249 (62.6)	83 (58.9)	459 (64.5)	0.30	0.43
Anticoagulation	36 (6.7)	21 (5.3)	15 (10.7)	39 (5.5)	0.38	0.047
Pulmonary infection, n (%)	43 (8.0)	35 (8.8)	8 (5.7)	50 (7.0)	0.52	0.39
Urinary infection, n (%)	17 (3.2)	13 (3.3)	4 (2.8)	33 (4.6)	0.19	0.41
TOAST subtypes, n (%)					0.15	0.11
Cardioembolism	25 (4.6)	20 (5.0)	5 (3.6)	46 (6.5)		
Large artery atherosclerosis	350 (65.0)	265 (66.6)	85 (60.3)	430 (60.4)		
Small artery occlusion	140 (26.0)	100 (25.1)	40 (28.4)	195 (27.4)		
Other/undetermined	5 (0.93)	3 (0.8)	2 (1.4)	17 (2.4)		
Undefined	19 (3.5)	10 (2.5)	9 (6.4)	24 (3.4)		

DM indicates diabetes mellitus; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; NDDM, newly diagnosed diabetes mellitus; NIHSS, National Institutes of Health Stroke Scale; OGTT, oral glucose tolerance test; and TOAST, Trial of Org 10172 in Acute Stroke Treatment.

*Group 1: DM diagnosed by glucose criteria (FPG ≥7.0 mmol/L or 2-h OGTT ≥11.1 mmol/L with/without HbA1c ≥6.5%).

†Group 2: DM diagnosed by single high HbA1c (FPG <7.0 mmol/L, 2-h OGTT <11.1 mmol/L and HbA1c ≥6.5%).

‡*P* value between DN (total) and non–DM.

§*P* value between subgroups of DM (groups 1 and 2) and non-DM.

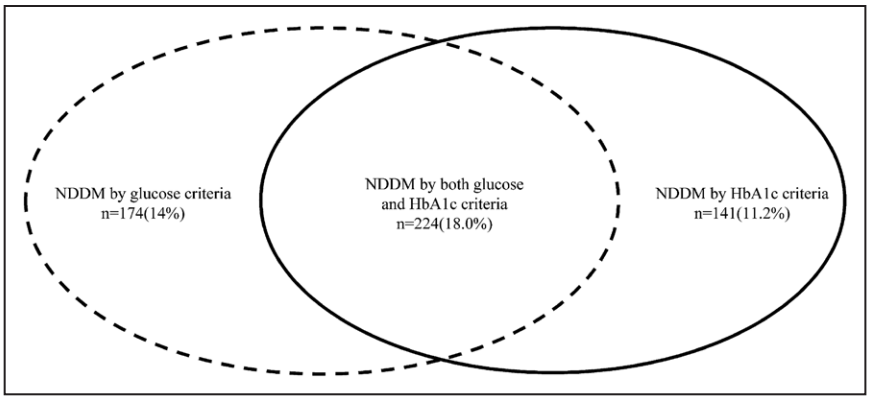

Figure 2. Distribution of newly diagnosed diabetes mellitus (NDDM) with different diagnostic criteria. Glucose criteria: fasting plasma glucose ≥7.0 mmol/L and/or 2-hour glucose ≥11.1 mmol/L in a standard oral glucose tolerance test. Hemoglobin A1c (HbA1c) criteria: HbA1c ≥6.5%.

and the percentage increased to 43%, which is higher than the former studies, via the addition of patients with single high HbA1c.[18–21] We infer that the most important reason was a high prevalence and low awareness of DM in China. A recent national-wide study showed that the prevalence of DM among Chinese aged 60 to 69 years was 25%,[22] and the proportion of those knowing of their DM was only 40%.[23] Also, some patients with stress hyperglycemia may be included in NDDM and this may lead to a higher rate of DM.

Glucose-based criteria and HbA1c-based criteria are frequently discordant regarding DM diagnosis[12]; thus, there were more NDDM patients by adding patients with single high HbA1c according to the HbA1c criteria. In the general population without a history of DM, 8% to 53% NDDM patients were found with single high HbA1c.[24–27] The proportion of NDDM with single high HbA1c in DM stroke patients in our study (25.6%) was not more than that in general population in previous studies (8% to 53%).

Ischemic stroke patients with DM or in-hospital hyperglycemia have exhibited poor clinical outcomes.[1,28–30] Our study indicated that NDDM according to the new criteria independently predicted poor prognosis in patients with ischemic stroke, as previously reported. In the subgroup analysis, we determined that NDDM with single high HbA1c did not exhibit a definite correlation with a poor prognosis compared with non-DM. Several studies have indicated that high HbA1c at admission was an independent significant predictor of poor prognosis in ischemic stroke patients without a DM history[31,32]; however, these studies did not exclude patients with in-hospital hyperglycemia. Thus, the results could not prove the relationships between single high HbA1c and stroke prognosis.

Table 2. Adjusted OR/HR of Poor Prognosis at 12-Mo According to NDDM State

Prognosis	Groups	N	N (%) of Events	Age and Sex Adjusted OR/HR (95% CI)†	Multivariate Adjusted* OR/HR (95% CI)†
Death	Non-DM	712	25 (3.5)	Ref.	Ref.
	DM group 1‡	398	78 (19.6)	1.16 (1.02–1.31)	1.17 (1.03–1.33)
	DM group 2§	141	10 (7.1)	1.02 (0.85–1.22)	1.02 (0.85–1.22)
	DM total‖	539	88 (16.3)	1.12 (1.001–1.25)	1.12 (1.001–1.26)
Stroke recurrence	Non-DM	701	52 (7.4)	Ref.	Ref.
	DM group 1‡	372	98 (26.3)	1.11 (1.03–1.33)	1.19 (1.04–1.35)
	DM group 2§	137	15 (10.9)	1.03 (0.86–1.24)	1.03 (0.86–1.24)
	DM total#	509	113 (22.2)	1.13 (1.01–1.27)	1.14 (1.01–1.28)
Poor functional outcome¶	Non-DM	698	121 (17.3)	Ref.	Ref.
	DM group 1‡	396	164 (41.4)	3.03 (2.26–4.05)	3.33 (2.45–4.51)
	DM group 2§	139	29 (20.9)	1.11 (0.70–1.77)	1.19 (0.74–1.91)
	DM total‖	535	193 (36.1)	2.40 (1.83–3.15)	2.58 (1.95–3.43)

CI indicates confidence interval; DM, diabetes mellitus; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HR, hazard ratio; NDDM, newly diagnosed diabetes mellitus; OGTT, oral glucose tolerance test; and OR, odds ratio.

*Adjusted for age, sex, body mass index, triglyceride at admission, history of hypertension, and anticoagulation use during hospitalization.

†HR for death and stroke recurrence, whereas OR for poor functional outcome.

‡Group 1: DM diagnosed by glucose criteria (FPG ≥7.0 mmol/L or 2-h OGTT ≥11.1 mmol/L with/without HbA1c ≥6.5%).

§Group 2: DM diagnosed by single high HbA1c (FPG <7.0 mmol/L, 2-h OGTT <11.1 mmol/L and HbA1c ≥6.5%).

‖DM total: DM group 1+DM group 2.

¶Poor functional outcome: modified Rankin scale score 3–6.

The reasons that NDDM patients with single high HbA1c did not exhibit a definite correlation with poor prognosis compared with the non-DM patients in ischemic stroke may be explained as follows. First, several factors can affect the HbA1c level,[10,33] particularly the red cell life span. A long erythrocyte lifespan will lead to increased HbA1c because of the increased duration of glucose exposure.[34,35] Thus, some non-DM patients with HbA1c ≥6.5% were diagnosed as DM. Second, the current cutoff point of HbA1c criteria for DM diagnosis was based on the correlation between the HbA1c level and the risk of developing diabetic retinopathy that represent small vessel disease[36,37]; however, it was not used to predict the prognosis of ischemic stroke patients, which mostly represent large vessel disease or cardioembolism disease. Although some research has demonstrated that an increased HbA1c at admission was an independent significant predictor for poor prognosis in ischemic stroke patients,[31,32] it is not clear which cutoff point for HbA1c is best fit to predict the prognosis regarding the prevention of a second stroke. Finally, there are racial and ethnic differences regarding HbA1c levels,[38] and the HbA1c levels tend to be increased in Asians compared with whites with impaired glucose tolerance.[39] Furthermore, the HbA1c criteria for DM diagnosis were based on non-Chinese populations; thus, whether this cutoff point is applicable to Chinese populations remains unclear.

DM is an important risk factor for the prediction of stroke prognosis. However, all DM patients have been diagnosed according to the glucose criteria rather than the HbA1c criteria in previous studies.[5–7] It is important to use HbA1c to predict long-term diabetic retinopathy and monitor metabolic control in DM; however, according to the results of our study, caution should be used in NDDM diagnosis with single high HbA1c without a DM history if we use DM as a risk factor to predict stroke prognosis, which would lead to overestimates of poor clinical prognosis in stroke patients and excessive hypoglycemic therapy. Using NDDM with single high HbA1c without a history of DM to predict prognosis in patients with stroke or other vascular diseases remains controversial. Additional studies should be conducted to investigate the mechanism and clinical characteristics of patients with single high HbA1c without a DM history in patients with cardiovascular disease.

Our study has several limitations. First, some ischemic stroke patients were excluded because of the lack of OGTT and HbA1c data in the hospital or were lost to follow-up at 1 year. However, no significant differences in sex, age, vascular risk factors, or medical history were identified between the included and excluded patients. Second, all OGTT were tested on days 14±3 after stroke onset or before discharge (if hospital stay <14 days) according to previous studies[18]; however, it is difficult to avoid mixed patients with stress hyperglycemia, which could lead to bias.[40] Third, the OGTT and HbA1c tests were not repeated according to the advice of the American Diabetes Association,[10] and NDDM may be overestimated in our study.

In conclusion, NDDM according to the new HbA1c criteria proposed by American Diabetes Association was associated with poor prognosis at 1 year after ischemic stroke onset in Chinese patients; however, single high HbA1c did not exhibit a definite correlation with poor outcome compared with non-DM. Future studies should consider patients with NDDM, especially patients with single high HbA1c.

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Disclosures

None.

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Prognosis of Ischemic Stroke With Newly Diagnosed Diabetes Mellitus According to Hemoglobin A1c Criteria in Chinese Population

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SUPPLEMENTAL MATERIAL

Table I. Baseline characteristics between the study patients and those excluded

	Patients excluded (N=854)	Patients included (N=1251)	p value
Gender (male), n(%)	573(67.1)	793(63.4)	0.08
Age (year), mean (SD)	62.6±13.3	62.2±12.6	0.37
NIHSS score at admission, median (IQR)	4(2-8)	4(2-8)	0.47
History of hypertension, n(%)	517(60.5)	746(59.6)	0.68
History of hyperlipidemia, n(%)	75(8.8)	149(11.9)	0.02
History of atrial fibrillation, n(%)	64(7.5)	71(5.7)	0.09
History of coronary heart disease, n(%)	105(12.3)	154(12.3)	0.99
Smoking, n(%)			0.48
Current smoker	503(58.9)	706(56.4)	
Ever smoker	83(9.7)	122(9.8)	
Non smoker	268(31.4)	423(33.8)	
Medicine use during hospitalization, n(%)			
Oral hypoglycemic drugs	105(12.3)	186(14.9)	0.09
Insulin	39(4.6)	77(6.2)	0.12
Antihypertensive drugs	338(39.6)	562(44.9)	0.01
Diuretics	19(2.2)	29(2.3)	0.89
Beta blockers	33(3.9)	48(3.8)	0.97
Statin	413(48.4)	637(50.9)	0.25
Intravenous alteplase	26(3.0)	38(3.0)	0.99
Antiplatelet	529(61.9)	791(63.2)	0.55
Anticoagulation	43(5.0)	75(6.0)	0.35
Pulmonary infection, n(%)	69(8.1)	93(7.4)	0.59
Urinary infection, n(%)	24(2.8)	50(4.0)	0.15
TOAST subtypes, n(%)			<0.001
Cardio embolism	65(7.6)	71(5.7)	
Large artery atherosclerosis	534(62.5)	779(62.3)	
Small artery occlusion	182(21.3)	335(26.8)	
Other/undetermined	35(4.1)	22(1.8)	
Undefined	38(4.5)	44(3.5)	

IQR indicates interquartile range; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; TOAST, Trial of Org 10172 in Acute Stroke Treatment.