ORIGINAL RESEARCH

Admission blood glucose and in-hospital clinical outcome among patients with acute stroke in Inner Mongolia, China

Ning Wang MPH¹
Dawei Qiao MD²
Weijun Tong MD¹
Fengshan Zhang MD²
Zhong Ju MD³
Tan Xu MD PhD¹
Erdunchaolu Jin MD⁴
Huan Zhang MPH¹
Yonghong Zhang MD PhD¹

¹ Department of Epidemiology, School of Radiation Medicine and Public Health, Medical College of Soochow University, Suzhou, China.

² Department of Neurology, Tongliao Municipal Hospital, Tongliao, Inner Mongolia, China.

³ Department of Neurology, First Hospital of Kerqin District, Tongliao, Inner Mongolia, China.

⁴ Department of Neurology, Teaching Hospital of Inner Mongolia University for Nationality, Tongliao, Inner Mongolia, China.

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Abstract

Purpose: There is still controversy about the association between admission blood glucose concentration and outcome of acute stroke. We studied the association between admission blood glucose and in-hospital death / dependency among acute stroke patients in Inner Mongolia, China.

Methods: 2,178 acute ischemic and 1,760 hemorrhagic stroke patients in six hospitals were included in the study. Blood glucose and other study variables were collected within the first 24-hr of hospital admission. Clinical outcomes were evaluated by neurologists during hospitalization. The associations between admission blood glucose and the risk of in-hospital death/dependency were analyzed using a multiple logistic model.

Results: There were associations between admission blood glucose and in-hospital death/dependency among patients with acute ischemic or hemorrhagic stroke. Compared with patients with blood glucose <6.1mmol/L, multivariate-adjusted odds ratio (95% confidence interval) of death/

dependency were 0.53 (0.23, 1.27), 2.22 (1.21, 4.11), 1.92 (1.12, 3.33) and 1.91 (1.00, 3.64) for ischemic stroke patients, and 0.93 (0.44, 1.96), 1.42 (0.65, 3.10), 1.98 (1.10, 3.55) and 2.93 (1.40, 6.11) for hemorrhagic stroke patients, with blood glucose 6.1-6.9, 7.0-7.7, 7.8-11.0 and ≥ 11.1 mmol/L, respectively.

Conclusion: Increased admission blood glucose was associated with death/dependency among patients with acute hemorrhagic and ischemic stroke

Stroke is the leading cause of death and long-term disability worldwide.¹ In China, Stroke is the third leading cause of death for males and the second for females.² The incidence and proportion of hemorrhagic stroke, especially, is much higher in the Chinese population than in western populations.³ Diabetes mellitus is one of the most important risk factors for stroke⁴⁻⁶, 20% to 50% of acute stroke patients are

hyperglycemic at presentation.⁷⁻⁹ Several studies have found a detrimental effect of acute hyperglycemia on outcome from ischemic and hemorrhagic stroke.¹⁰⁻¹⁴ Increased admission blood glucose (BG) concentrations in acute stroke have also been associated with longer in-hospital stay, increased cost, and mortality.¹² There are also studies¹⁵⁻¹⁶ that did not find an association between admission BG level and outcome after the onset of stroke when adjusted for other confounding factors. Therefore, there is still controversy about the association between admission BG level and outcome.

Although stroke is a leading cause of death and disability in China, there is no data on the relationship between admission BG level and short term clinical outcome among acute stroke patients in the Chinese population. The purpose of the present study is to examine the association between admission BG level and clinical outcomes, including death and dependency among acute ischemic and hemorrhagic stroke patients in Inner Mongolia, China.

Methods

Study Participants

The study was approved by Soochow University School of Public Health and Radiation Medicine Ethics Committee. Acute stroke patients were recruited from 6 hospitals (Tongliao Municipal Hospital, Teaching Hospital of Inner Mongolia University For Nationality, Kezuohou Banner (County) Hospital, Kezuozhong Banner Hospital, Zalute Banner Hospital, and First Hospital of Kerqin District) in Tongliao, a prefecture-level city in eastern Inner Mongolia, China. Written informed consent was obtained for all study participants. The 6 hospitals are the only western medicine facilities in this region and serve a population of 2.04 million; most of whom are of Han or Mongolian ethnicity. All patients with a clinical diagnosis of acute stroke admitted to the 6 hospitals from January 1, 2003 to December 31, 2005 were potentially eligible for the study. However, only those cases

confirmed by a computed tomography (CT) scan or magnetic resonance imaging (MRI) were included. All subtypes of stroke, including ischemic stroke (thrombosis, embolism, or lacunar infarction) and hemorrhagic stroke (intracerebral hemorrhage or subarachnoid hemorrhage) were included in this study. A team of investigators, including neurologists, reviewed the eligibility of study participants. Among 4,369 acute stroke patients admitted to the 6 hospitals during the study period, 3,938 had a CT scan or MRI confirming ischemic or hemorrhagic stroke and were included in this analysis. 431 patients were excluded from analysis because of a discharge diagnosis of transient ischemic attack or stroke of undetermined type (n=373) or lack of a CT scan or MRI test (n=58).

Data Collection

Baseline data were collected within the first 24-hr of hospital admission by in-person interview with patients or their family members, if patients were not able to communicate. Data on demographic characteristics, lifestyle risk factors, medical history, clinical laboratory tests, and imaging data (CT and MRI) were obtained using a standard questionnaire administered by trained staff. Cigarette smokers were defined as having smoked at least 1 cigarette per day for 1 year or more. The amount and type of alcohol consumed during the past year was collected. Alcohol consumption was defined as consuming one or more alcoholic drinks per day during the last year. Three BP measurements were taken within 30 min of admission while the study participants were in the supine position using a standard mercury sphygmomanometer according to a standard protocol.¹⁷

Blood glucose (BG) was measured using a modified hexokinase enzymatic method. Total cholesterol, HDL-cholesterol, and triglycerides were analyzed enzymatically on a Beckman Synchron CX5 Delta Clinical System (Beckman Coulter, Inc., Fullerton, CA, USA) using commercial reagents. LDL-

TABLE 1. Characteristics of stroke patients at hospital admission.

Characteristics	Ischemic	Hemorrhagic
N	2178	1760
Age (Mean±SD) (yr)	61.5±12.02	55.9±11.7
Male (%)	1351 (62.0)	1050 (59.7)
Ethnicity (Mongolian) (%)	512 (23.5)	473 (26.9)
Manual Labour Profession, n (%)	817 (37.5)	932 (53.0)
Hypertension (%)	1192(54.8)	1020(58.0)
Diabetes (%)	246 (11.3)	38 (2.2)
Cigarette smoking (%)	528(22.2)	358(20.3)
Alcohol drinking (%)	449(20.6)	382(21.7)
Dyslipidemia*, n (%)	896 (67.5)	400 (62.7)
Family History Hypertension, n (%)	109 (5.0)	117 (6.6)
Hyperglycemia (≥ 6.1 mmol/L) (%)	686 (40.1)	692 (55.0)
SBP (Mean±SD) (mmHg)	152.1±28.9	172.3±34.6
DBP (Mean±SD) (mmHg)	92.0±16.8	103.9±19.5
Median time onset to admission (hr)	11.1	8.8
Median duration of hospitalization (d)	7	10

* Total cholesterol ≥ 200 mg/dL or LDL ≥ 130 mg/dL or HDL < 40 mg/dL or triglyceride ≥ 150 mg/dL

cholesterol levels were calculated by use of the Friedewald equation for the participants.

The study outcomes included death and dependency during hospitalization. If a patient died in the hospital, a study staff member recorded the death on the event form and obtained the death certificate. If a patient survived the acute stroke, the study neurologists conducted a comprehensive clinical evaluation at discharge. Dependency was defined as moderate or severe disability using a Modified Rankin's scale > 2 .¹⁸

Statistical Analysis

The mean and standard deviation of continuous variables and proportion of categorical variables at hospital admission were calculated for both ischemic and hemorrhagic strokes. Patients were grouped by stroke subtype and BG concentration (< 6.1 , 6.1 - 6.9 , 7.0 - 7.7 , 7.8 - 11.0 , and ≥ 11.1 mmol/L). Multivariate logistic regression analysis was used to examine the association between BG and clinical outcome (death/dependency) adjusted for age, sex, ethnicity (Mongol vs. Han), education, alcohol consumption, cigarette smoking, physical activity, systolic blood pressure

(SBP), diastolic blood pressure (DBP), history of hypertension, history of diabetes, and dyslipidemia. Statistical analysis were conducted using SAS statistical software (version 9.1; SAS Institute Inc, Cary, North Carolina, USA).

Results

2,178 ischemic stroke and 1,760 hemorrhagic stroke patients were included in our analysis. Table 1 presents the demographic and clinical characteristics by stroke subtypes of stroke patients at admission. Those with acute ischemic stroke were more likely to be older, smoke cigarettes and have a history of diabetes or dyslipidemia; whereas those with acute hemorrhagic stroke were more likely to be of Mongolian ethnicity, have a profession involving manual labour, have both a personal and family history of hypertension, and have higher SBP and DBP level, and have hyperglycemia. There was no difference in sex or alcohol consumption between patients with acute ischemic and hemorrhagic strokes.

The median time from onset of symptom to admission was 9.3 hr (11.1 hr for ischemic, 8.8 hr for

TABLE 2. Odds ratio and 95% confidence intervals of clinical outcomes (death/dependency) associated with admission BG among acute stroke patients.

BG mmol/L	Unadjusted		Multivariate adjusted ^a	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
<6.1	1.00 (ref)		1.00 (ref)	
6.1-6.9	0.76 (0.45, 1.29)	0.306	0.73 (0.42, 1.26)	0.252
7.0-7.7	1.98 (1.26, 3.12)	0.003	1.84 (1.14, 2.97)	0.013
7.8-11.0	2.26 (1.57, 3.25)	<0.001	1.98 (1.34, 2.93)	0.001
≥11.1	2.75 (1.77, 4.28)	<0.001	2.30 (1.42, 3.71)	0.001

^aAdjusted for age, sex ethnicity (Mongol vs. Han), education, alcohol consumption, cigarette smoking, physical activity, SBP, DBP, history of hypertension, history of diabetes, and dyslipidemia.

hemorrhagic). The median duration of hospitalization was 7 days for ischemic stroke and 10 days for hemorrhagic stroke. 142 stroke patients (39 ischemic and 103 hemorrhagic) died during hospitalization and 1506 stroke patients (900 ischemic and 606 hemorrhagic) were disability on discharge. The in-hospital case-fatality rate was higher for acute hemorrhagic stroke (5.9%) than for acute ischemic stroke (1.8%). However, the disability rate was higher for those with acute ischemic stroke (41.3%) than those with acute hemorrhagic stroke (34.4%).

There was an association between BG on admission and death/dependency during hospitalization among patients with acute stroke (Table 2). Compared with those with BG<6.1mmol/L, multivariate-adjusted odds ratio (95% confidence interval) of death/dependency were 0.73 (0.42, 1.26), 1.84 (1.14, 2.97), 1.98 (1.34, 2.93), and 2.30 (1.42, 3.71), respectively, for patients with BG 6.1-6.9, 7.0-7.7, 7.8-11.0 and ≥11.1mmol/L. Furthermore, there was a positive association between BG on admission and death/dependency during hospitalization among ischemic or hemorrhagic stroke patients. Multivariate-adjusted odds ratio (95% confident interval) of death/dependency were 0.53 (0.23, 1.27), 2.22 (1.21, 4.12), 1.92 (1.12, 3.33) and 1.91 (1.00, 3.64), respectively, among ischemic stroke patients with BG 6.1-6.9, 7.0-7.7, 7.8-11.0 and ≥11.1 mmol/L. Multivariate-adjusted odds ratio (95% confidence interval) of death/dependency were 0.93 (0.44, 1.96), 1.42 (0.65, 3.10), 1.98 (1.11, 3.55) and 2.93 (1.40, 6.11), respec-

tively, among hemorrhagic stroke patients with BG 6.1-6.9, 7.0-7.7, 7.8-11.0 and ≥11.1 mmol/L.

Discussion

The overall mortality of acute stroke patients during hospitalization in the present study was 3.6%. The mortality of ischemic stroke and hemorrhagic stroke was 1.8% and 5.9%, respectively, which was lower than that of other reports.^{15,19,20} Our study showed the disability rates of ischemic stroke and hemorrhagic stroke were 41.3% and 34.4%, respectively, which was consistent with that of other reports in China.^{21,22} We have discussed mortality and disability rates during hospitalization among ischemic and hemorrhagic stroke patients in a previous report.²³ The purpose of this study is to examine the relationship between BG on admission and clinical outcome (death or dependency during hospitalization). We found that higher BG on admission correlated independently with clinical outcome during hospitalization among patients with acute ischemic or hemorrhagic stroke. For example, baseline BGs 7.0-7.7, 7.8-11.0 and ≥11.1mmol/L were associated with 1.84, 1.98 and 2.30-fold increase in the risk of death/dependency among acute stroke patients compared with BG <6.1mmol/L. We also found that the odds ratio of death /dependency associated with BG 7.0-7.7, 7.8-11.0 and ≥11.1mmol/L among ischemic stroke patients, and associated with 7.8-11.0 and ≥11.1mmol/L among hemorrhagic stroke patients were positive and significant. We have reported that BP on admission was associated with

TABLE 3. Odds ratio and 95% confidence intervals of clinical outcomes (death/dependency) associated with admission BG among acute patients with ischemic stroke and hemorrhagic stroke.

BG mmol/L	Unadjusted		Multivariate adjusted ^a	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Ischemic Stroke				
<6.1	1.00 (ref)		1.00 (ref)	
6.1-6.9	0.51 (0.22, 1.19)	0.119	0.53 (0.23, 1.27)	0.154
7.0-7.7	2.22 (1.22, 4.05)	0.009	2.22 (1.21, 4.11)	0.010
7.8-11.0	1.95 (1.16, 3.30)	0.012	1.92 (1.12, 3.33)	0.018
≥11.1	2.00 (1.08, 3.71)	0.027	1.91 (1.00, 3.64)	0.050
Hemorrhagic Stroke				
<6.1	1.00 (ref)		1.00 (ref)	
6.1-6.9	1.07 (0.52, 2.19)	0.854	0.93 (0.44, 1.96)	0.846
7.0-7.7	1.81 (0.89, 3.65)	0.100	1.42 (0.65, 3.10)	0.383
7.8-11.0	2.63 (1.53, 4.50)	<0.001	1.98 (1.11, 3.55)	0.022
≥11.1	4.11 (2.12, 7.95)	<0.001	2.93 (1.40, 6.11)	0.004

^aadjusted for age, sex, ethnicity (Mongol vs. Han), education, alcohol consumption, cigarette smoking, physical activity, SBP, DBP, history of hypertension, history of diabetes, and dyslipidemia.

death/dependency during hospitalization among acute hemorrhagic stroke patients (but not acute ischemic stroke patients).²³ Hence, in the present analysis, some factors including SBP/DBP were adjusted by using a multiple logistic model. These observational findings suggest that hyperglycemia on admission maybe predict the occurrence of poor outcome in short term for acute ischemic and hemorrhagic stroke patients. Our findings are consistent with previous reports^{20, 24} which demonstrated a positive association between hyperglycemia and poor outcome. A systematic review and meta-analysis by Capes²⁵ showed that acute hyperglycemia predicted an increased risk of in-hospital mortality and poor functional recovery after onset of ischemic stroke in non-diabetic patients. Alvarez-Sabin²⁶ showed that admission hyperglycemia was a powerful predictor of poor outcome in reperfused patients independently of possible confounders such as age, stroke severity, and diabetes mellitus. They believed that an elevated BG before reperfusion may partly counter-balance the beneficial effect of early restoration of blood flow, which lead to a lesser degree of neurological improvement, greater infarct size, and worse outcome in stroke patients. An MRI study²⁷ demonstrated that elevated BG was asso-

ciated with an increased progression of hypoperfused at-risk tissue to infarction and poor stroke outcome. Baird²⁸ showed that persistent hyperglycemia on serial glucose monitoring was an independent determinant of infarct expansion and was associated with worse functional outcome. Two studies^{10,29} suggested that hyperglycemia might worsen the clinical outcome in non-lacunar stroke, but not in lacunar stroke during acute ischemic stroke. One of the latest studies³⁰ found persistent hyperglycemia, hyperglycemia at baseline and at 24 hr was associated with poor outcomes in all the end points studied. A randomized trial³¹ demonstrated that lowering BG after onset improved long-term prognosis in diabetic patients with acute myocardial infarction. Pache's study³² also suggested that lowering BG with a glucose-insulin-potassium infusion may exert a positive effect on myocardial salvage in diabetic patients with acute myocardial infarction. There is also a study³³ showing that decreasing BG with glucose-insulin-potassium may also improve outcome in stroke patients. Our findings support the concept that acute stroke patients with hyperglycemia should be treated by lowering BG. We found that the effect of BG on death/dependency during hospitalization was different from BP among acute

stroke patients. Elevated BP was associated only with the risk of death/dependency among hemorrhagic stroke patients, but not ischemic stroke.²³ However, elevated BG was not only associated with the risk of death/dependency in hemorrhagic stroke patients, but also with ischemic stroke patients. Our findings imply that the mechanism of elevated BG increasing risk of poor outcome among acute stroke patients was different from elevated BP.

The mechanism of how hyperglycemia leads to poor outcome of stroke is currently unclear, but the findings of animal experiment³⁴ support the conclusion that hyperglycemia could cause further brain injury. Both moderate and severe hyperglycemia have been shown to be associated with worsening of mitochondrial function in the ischemic penumbra.³⁵ Parsons and his colleagues²⁷ suggested that acute hyperglycemia may increase brain lactate production and facilitate conversion of hypoperfused at-risk tissue into infarction, which might adversely affect stroke outcome. A rat experiment conducted by Shi et al³⁷ showed hyperglycemia aggravated the cerebral injury of ischemia-reperfusion, perhaps by its effect of inducing neuron apoptosis.

In summary, our study found that increased BG was associated with death/dependency among acute patients with ischemic stroke and hemorrhagic stroke. Blood glucose should be controlled in acute stroke patients during hospitalization.

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Correspondence to:

Yonghong Zhang, MD, PhD
 Department of Epidemiology
 School of Radiation Medicine and Public Health, Medical
 College of Soochow University
 199 Renai Road, Dushu lake high education Area,
 Suzhou, China.. 215123.
 Email: yhzhang@suda.edu.cn