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Is diabetes a predictor of worse outcome for spontaneous intracerebral hemorrhage?

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ABSTRACT

Background and purpose: Diabetes is common in acute stroke and is associated with worse outcome in ischemic stroke, but its influence on intracerebral hemorrhage (ICH) remains controversial. We examined the association between diabetes and clinical outcome in a large hospitalized population of Chinese patients with ICH.

Methods: We prospectively enrolled patients with ICH who were admitted within 3 days of stroke onset from March 2002 to December 2010. Data were analyzed on demographic and clinical characteristics such as age, gender, vascular risk factors, Glasgow Coma Scale (GCS) score at admission, site of hemorrhage and surgical treatment. Patient characteristics, functional outcome according to the modified Rankin scale (mRS) and mortality were compared between patients with and without diabetes.

Results: Of the 1438 ICH patients included, 118 (8.2%) had diabetes and this subgroup showed a significantly higher proportion of hypertension (OR = 1.98, 95% CI 1.33–2.96, P = 0.001) and hyperlipidemia (OR = 3.22, 95% CI 1.16–8.89, P = 0.024). Patients were followed up for a mean of 147.48 ± 3.59 days. Cox regression suggested that diabetes was not a significant predictor of mortality in our cohort (P > 0.05), and repeated-measures ANOVA showed that variance in mRS over the course of follow-up was similar between patients with and without diabetes (P = 0.463).

Conclusion: Our data suggest that diabetes in Chinese patients with ICH is not associated with increased mortality or functional outcome. Future studies are needed to clarify possible confounders affecting prognosis after ICH.

1. Introduction

Intracerebral hemorrhage (ICH) is a significant cause of morbidity and mortality throughout the world [1], accounting for approximately 20% of all strokes [2–5]. The incidence of ICH is higher in China than in many other countries [6]. ICH can result in significant functional deterioration within the first few hours after onset, with more than 20% of patients experiencing a decrease in the Glasgow Coma Scale (GCS) score [7,8]. As a result, even patients with relatively mild conditions can have poor prognosis in the long term [9].

Diabetes is a risk factor of ICH, occurring in approximately one-third of all patients [10]. It has been associated with poor outcomes [10–14] in ischemic stroke, but whether it influences prognosis after ICH remains controversial. In a rat model of ICH, brain edema and perihematomal cell death were more extensive in hyperglycemic animals than in normoglycemic ones [15]. Limited clinical studies have linked diabetes with higher in-hospital mortality in patients with ICH [16]. Hyperglycemia, often without an established diagnosis of diabetes, has also been linked to poor outcomes in such patients [10–12,14]. Whether the true risk factor for poor outcomes is diabetes, hyperglycemia or another confounder is unclear since some studies suggest that the poor outcomes in hyperglycemic patients does not reflect a direct harmful effect of glucose on neurons but rather stress induced by severe stroke [15,17].

These findings highlight the need to define better the role of diabetes and its interaction with other factors on prognosis after ICH. Therefore we conducted this prospective study to investigate

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whether diabetes is an independent predictor of worse outcome in Chinese patients with ICH.

2. Subjects

This study was approved by the Scientific Research Department of our hospital, and it complied with local ethics criteria. We prospectively and consecutively included stroke patients admitted to West China Hospital at Sichuan University within 3 days of symptom onset between March 2002 and December 2010. All patients had a clinical diagnosis of stroke according to the most recent definition recommended by the American Heart Association and American Stroke Association [18]. Diagnosis was confirmed by rapid computed tomography (CT) or magnetic resonance imaging (MRI) in order to distinguish ICH from ischemic stroke [7]. Patients diagnosed with subarachnoid hemorrhage or traumatic ICH were excluded from our study.

3. Data collection and definitions

Data were collected on demographic and clinical patient characteristics, including initial hemorrhagic stroke severity, site of hemorrhage, vascular risk factors, and the final decision whether to undergo surgery. Initial hemorrhagic stroke severity was measured using the Glasgow Coma Scale (GCS) score at admission; these scores are categorized as severe (3–8), medium (9–12), or mild (≥13) [19]. Site of hemorrhage was defined as lobar, deep in brain, ventricle, brainstem, cerebellum or other [20]. Vascular risk factors included history of hypertension, diabetes, hyperlipidemia, current smoking and current drinking. Hypertension was defined as one of the following: systolic blood pressure ≥140 mmHg, and/or diastolic blood pressure ≥90 mmHg at discharge, based on at least two measurements; patient self-report of hypertension; or self-report of use of antihypertensive drugs. Diabetes was defined as one of the following: fasting plasma glucose ≥126 mg/dl on repeated measurement; postload plasma glucose >198 mg/dl; patient self-report of diabetes; or history of anti-diabetic therapy. Hyperlipidemia was defined as serum cholestrol levels ≥5.2 mmol/l, serum triglycerides ≥1.7 mmol/l or patient self-report of hyperlipidemia. Patients who had smoked at least 1 cigarette/day for the preceding 3 months were defined as current smokers, while current drinkers were those who reported alcohol intake ≥60 g/day or ≥420 g/week [21].

3.1. Outcome assessment

Patients were followed up by telephone after discharge from our hospital, and either patients or their relatives gave us information about mortality and functional outcome. Mortality was calculated in patients who died within 1 month (early mortality) and in those 1 month survivors (long-term mortality). Functional outcome was classified as good, defined as a modified Rankin scale (mRS) score of 0–2, or poor, defined as an mRS score of 3–5. Patients who died were classified as having poor functional outcome. Disability, and death/disability were calculated at 90 days after admission. Disability was defined as an mRS score of 3–5.

3.2. Statistical analysis

The chi-squared test or Fisher's exact test were used to compare categorical data, while Student's *t* test was used to compare continuous data. Repeated-measures ANOVA was used to compare functional outcomes at different times during follow up, while Cox regression was used to identify significant predictors of outcome. The threshold of statistical significance was defined as a two-sided $P < 0.05$. All statistical analyses were performed using SPSS 20.0 for Windows (IBM, Chicago, IL, USA).

4. Results

4.1. Baseline characteristics

We enrolled 1438 patients with ICH (34.3% female; mean age, 59.6 ± 14.2 yr), of whom 118 (8.2%) had diabetes (35.6% female). Among those with diabetes, diagnosis was made before stroke in 80 patients (67.8%), and mean age at stroke onset was 61.5 ± 12.7 years.

Baseline characteristics of stroke patients with or without diabetes are shown in Table 1. The proportion of hypertension was significantly higher among patients with diabetes (OR = 1.98, 95% CI 1.33–2.96, $P = 0.001$), as was the proportion of hyperlipidemia (OR = 3.22, 95% CI 1.16–8.89, $P = 0.024$). The two subgroups were similar in terms of gender distribution, age, the final decision whether to undergo surgery, current smoking, current drinking, GCS score at admission, and site of hemorrhage ($P = 0.757$, 0.129, 0.270, 0.769, 0.711, 0.801, 0.867).

4.2. Early and long-term mortality

Patients were followed-up for a mean of 147.48 ± 3.59 days. Compared to patients without diabetes, those who had diabetes were prone to living through 1 month, and died in the follow up (Chi-squared test, $P = 0.001$, OR = 3.063, 95% CI 1.724–5.442).

In patients died within 1 month (early mortality), we found that diabetes was not an independent predictor of early mortality (Cox model, $P = 0.661$, HR = 0.93, 95% CI 0.67–1.30) (Table 2). In terms of those 1 month survivors (long-term mortality), the possible factors that would affect the prognosis wassite of hemorrhages (Cox model, $P = 0.011$, HR = 1.02, 95% CI 1.00–1.03) and surgical treatment (Cox model, $P = 0.003$, HR = 1.34, 95% CI 1.10–1.62). Similarily, diabetes was not a predictor of mortality in these patients ($P = 0.591$, HR = 0.99, 95% CI 0.69–1.41) (Table 2).

4.3. Outcomes at 90 days

The 90-day mortality rate was 22.0% among patients with diabetes and 22.2% among patients without it (Table 3). This mortality rate was found to be similar between the two subgroups after adjusting for gender distribution, age, site of hemorrhage, the final decision whether to undergo surgery, and GCS score at admission (OR = 0.933, 95% CI 0.499–1.745, $P = 0.966$).

The 90-day disability rate was 35.2% among patients with diabetes and 40.5% among those without it. The rate was similar in the two subgroups after adjusting for the above confounders (OR = 0.708, 95% CI 0.400–1.252, $P = 0.380$).

The combined rate of death and disability at 90 days was 49.5% in the presence of diabetes and 53.7% in its absence. There was no significant difference between the subgroups after adjusting for the above confounders (OR = 0.725, 95% CI 0.433–1.215, $P = 0.434$).

4.4. Functional outcome during follow-up

A total of 1169 patients completed the follow-up, including 91 (7.8%) with diabetes. Repeated-measures ANOVA showed that variance in mRS scores at 1, 3, 6 and 12 months was similar between patients with and without diabetes ($P = 0.463$, after adjusting the degrees of freedom based on $P < 0.001$ for Mauchly's test of sphericity).