Impaired Glucose Regulation Predicted 1-Year Mortality of Chinese Patients With Ischemic Stroke

Data From Abnormal Glucose Regulation in Patients With Acute Stroke Across China

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Background and Purpose—It remains uncertain if impaired glucose regulation (IGR) as a predictor for stroke outcomes. This study aimed at observing the effect of IGR on the 1-year outcomes in Chinese patients with ischemic stroke. Methods—Patients with acute ischemic stroke were recruited consecutively in multihospitals across China. Oral glucose tolerance test was performed to identify IGR. Cox proportion hazard model was performed to investigate the effect of IGR on 1-year mortality or stroke recurrence in patients with ischemic stroke. Results—The study recruited 2639 patients with ischemic stroke. IGR was shown as an independent risk factor for the mortality of patients with ischemic stroke (hazard ratio [95% confidence interval], 3.088 [1.386–6.884]; P=0.006). However, IGR showed no significant effects on the dependency or stroke recurrence of patients (P=0.540 and 0.618, respectively). Conclusions—IGR was an independent predictor for the mortality of patients with ischemic stroke. IGR should be highlighted and intervened actively in the patients with ischemic stroke. (Stroke. 2014;45:1498-1500.)

Key Words: cerebral infarction ■ prediabetes ■ mortality

Pre–diabetes mellitus (pre-DM) is an intermediate metabolic state between normal glucose metabolism (NGM) and DM, including impaired fasting glucose and impaired glucose tolerance. In Europe and America, the effect of pre-DM on outcomes of cardiovascular disease was reported controversial. Studies on pre-DM and stroke outcomes were scarce. The prevalence of DM or pre-DM was high in Chinese patients with stroke. This study investigated the effect of impaired glucose regulation (IGR) on the 1-year outcomes of Chinese patients with ischemic stroke.

Methods

The study of Abnormal Glucose Regulation in Patients With Acute Stroke Across China (ACROSS-China) was a nationwide prospective cohort study aimed at investigating the prevalence and effects of abnormal glucose regulation among hospitalized patients with acute stroke. Patients with acute ischemic stroke within 14 days after onset were recruited consecutively. Acute ischemic stroke was diagnosed according to World Health Organization criteria. Patient baseline information and medical history were recorded within 24 hours after admission. The severity of neurological defect was evaluated by the National Institutes of Health Stroke Scale and Glasgow Coma Scale. Dependency of patients was defined as modified Rankin Scale of 3 to 5 scores.

A standard oral glucose tolerance test was performed in all the patients without previous DM at day 14±3 after stroke onset or before discharge. The diagnosis of IGR was performed according to the World Health Organization criteria as having impaired fasting glucose (fasting plasma glucose, ≥6.1 mmol/L; meanwhile, <7.0 mmol/L) and impaired glucose tolerance (2 h plasma glucose, ≥7.8 mmol/L; meanwhile, <11.1 mmol/L). Patients were contacted over telephone by trained research personnel at Beijing Tiantan Hospital at 1 year after stroke onset. Telephone modified Rankin Scale scores were obtained to identify the dependency of patients. Stroke recurrences associated with rehospitalization were sourced to the attended hospitals to ensure a reliable diagnosis. Case fatality was either confirmed on a death certificate from the local citizen registry or from the attended hospital.

The Ethics Committees at all participating hospitals approved the procedures, and all patients or their designated relatives gave informed consents.

Statistical Analysis

In this article, proportions, means with SDs or medians together with the interquartile ranges were used for different variables. The effect of IGR on death and recurrence of stroke was analyzed in Cox proportional hazards model. We selected the adjusted variables according to the comparison of univariate analysis on the clinical characteristics between groups with and without outcome events, as well as those confirmed effect factors for stroke outcomes in previous studies. Data were analyzed with SAS version 9.1.3 statistical software.

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Results

This survey consecutively recruited 2639 patients with acute ischemic stroke. One-year follow-up information was available for 2167 patients (82.1%). Clinical characteristics of these patients (n=2167) were compared with those for 472 patients lost to 1-year follow-up. The average age showed similar results in the 2 groups (62.55±12.52 versus 63.48±12.55; \(P=0.142\)), as well as the similar male sex proportion (\(P=0.428\)) and severity of neurological functional defect (National Institutes of Health Stroke Scale score) at admission (\(P=0.115\)). The prevalence of IGR in patients available to 1-year follow-up information was lower than that in patients lost to 1-year follow-up (23.6% versus 28.9%; \(P<0.001\)).

Of the 2167 patients, 439 were recognized as having IGR, and NGM was found in 487 cases. Compared with patients having NGM (Table 1), patients with IGR were older, with higher waist circumference. Severity of stroke showed greater at baseline in those with IGR. History of hypertension, hyperlipidemia, atrial fibrillation, and smoking was more frequent in patients with IGR.

The 1-year poor outcomes of patients with IGR or NGM were compared (Table 2). Death was found in 6.8% of patients with IGR, which was significantly higher than patients with NGM (2.1%). The occurrence of dependency and stroke recurrence was comparable in the 2 groups. Additional analysis showed death relevant to stroke was the main death cause in both of the 2 groups, accounting for 86.21% (IGR group) and 81.25% (NGM group; \(P=0.107\)). The median time interval from stroke attack to death was 225 (51–306) days in IGR group and 180 (110–241) days in NGM group (\(P=0.6028\)).

Compared with NGM, the effects of IGR on the outcomes were shown in Table 3. IGR was a significantly independent risk factor for mortality of patients at 1 year after onset (hazard ratio, 3.088; 95% CI, 1.386–6.884; \(P=0.006\)). However, IGR showed no significant effects on the dependency or stroke recurrence of patients (\(P=0.540\) and 0.618, respectively).

Discussion

This study concluded that IGR was an independent risk factor for 1-year death of patients with ischemic stroke. Follow-up information at 1 year was available in 82.1% of all enrolled patients. The main variables, such as average age, National Institutes of Health Stroke Scale, Glasgow Coma Scale, were comparable between patients with and without 1-year follow-up, which indicated that patients with 1-year information were a good representation of all the patients enrolled in our survey. We acknowledged that the prevalence of IGR was higher in patients lost to 1-year follow-up (28.9% versus 23.6%), accordingly, the effect of IGR on stroke outcome might have been underestimated partly in this article.

Our study described characteristics of patients with IGR. Age, fasting glucose, glycosylated hemoglobin, etc, showed higher in patients with IGR than in patients with NGM, which

### Table 1. Clinical Characteristics of Patients With Impaired Glucose Regulation or Normal Glucose Metabolism After Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>Patients With Ischemic Stroke</th>
<th>Impaired Glucose Regulation</th>
<th>Normal Glucose Metabolism</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>2167</td>
<td>439</td>
<td>487</td>
<td>...</td>
</tr>
<tr>
<td>Sex (men, %)</td>
<td>63.70</td>
<td>66.10</td>
<td>68.40</td>
<td>0.4676</td>
</tr>
<tr>
<td>Age, mean±SD, year</td>
<td>62.55±12.52</td>
<td>63.17±12.62</td>
<td>59.37±12.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NIHSS at admission</td>
<td>4 (2–8)</td>
<td>4 (2–9)</td>
<td>4 (2–7)</td>
<td>0.0352</td>
</tr>
<tr>
<td>GCS at admission</td>
<td>14.3±1.69</td>
<td>14.19±1.79</td>
<td>14.5±1.24</td>
<td>0.0023</td>
</tr>
<tr>
<td>Fasting glucose at admission, mmol/L</td>
<td>6.66±2.85</td>
<td>5.45±1.21</td>
<td>5.13±1.01</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>6.67±1.86</td>
<td>6±1.04</td>
<td>5.57±0.97</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglyceride at admission, mmol/L</td>
<td>1.8±1.22</td>
<td>1.69±0.94</td>
<td>1.62±1.07</td>
<td>0.2614</td>
</tr>
<tr>
<td>BMI at admission</td>
<td>24.89±3.75</td>
<td>24.76±3.81</td>
<td>24.41±3.68</td>
<td>0.1673</td>
</tr>
<tr>
<td>Waist circumference at admission, cm</td>
<td>86.6±10.08</td>
<td>86.41±10.22</td>
<td>84.58±9.23</td>
<td>0.0048</td>
</tr>
<tr>
<td>History of hypertension, %</td>
<td>63.40</td>
<td>64.00</td>
<td>57.20</td>
<td>0.0384</td>
</tr>
<tr>
<td>History of hyperlipidemia, %</td>
<td>16.10</td>
<td>20.30</td>
<td>12.50</td>
<td>0.0047</td>
</tr>
<tr>
<td>History of atrial fibrillation, %</td>
<td>6.30</td>
<td>8.90</td>
<td>4.00</td>
<td>0.0026</td>
</tr>
<tr>
<td>History of current or ever smoking, %</td>
<td>66.30</td>
<td>68.70</td>
<td>61.50</td>
<td>0.0095</td>
</tr>
<tr>
<td>Fasting glucose at 14 d</td>
<td>5.57±1.64</td>
<td>5.15±0.78</td>
<td>4.8±0.58</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2-h glucose at 14 d</td>
<td>9.94±4.02</td>
<td>9.12±1.06</td>
<td>8.43±0.96</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pulmonary infection, %</td>
<td>8.10</td>
<td>9.20</td>
<td>5.20</td>
<td>0.019</td>
</tr>
</tbody>
</table>

\(P\) values refer to the comparisons between impaired glucose regulation and normal glucose metabolism groups. BMI indicates body mass index; GCS, Glasgow Coma Scale; HbA1c, glycosylated hemoglobin; and NIHSS National Institute of Health Stroke Scale.

### Table 2. The Comparison of 1-Year Outcomes Between Patients With IGR and NGM After Ischemic Stroke Onset

<table>
<thead>
<tr>
<th></th>
<th>Patients With Ischemic Stroke</th>
<th>IGR</th>
<th>NGM</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, %</td>
<td>11.80</td>
<td>6.80</td>
<td>2.10</td>
<td>0.0004</td>
</tr>
<tr>
<td>Dependency, %</td>
<td>18.20</td>
<td>15.70</td>
<td>11.90</td>
<td>0.105</td>
</tr>
<tr>
<td>Stroke recurrence, %</td>
<td>18.40</td>
<td>8.20</td>
<td>7.10</td>
<td>0.5088</td>
</tr>
</tbody>
</table>

IGR indicates impaired glucose regulation; and NGM, normal glucose metabolism.
reflected the nature of IGR as an intermediate stage between NGM and DM.

The total mortality rate was significantly higher in IGR group than in NGM group. Additional analysis of the differences in causes or timing of death in the 2 groups addressed that most of the death was because of death relevant to stroke, and there were no significant differences in either causes of death or timing of death between the 2 groups.

This is a new survey, which reported the association between IGR and mortality, dependency, or stroke recurrence of patients with ischemic stroke with a large sample of analysis population. Our findings highlight the concept of the clinical significance that early identification and treatment of IGR should be emphasized to improve the outcome of ischemic stroke in the Chinese population.

Several limitations need to be addressed. We acknowledged the possibility that residual confounding (ie, worse severity at baseline among patients with IGR that was not fully captured by statistical adjustment) might have influenced the finding of increased mortality among the patients with IGR. Oral glucose tolerance test results were not available for 307 of our analysis patients, which might influence the evaluation of association between IGR and outcomes of patients.

Conclusions

Our survey clarified that IGR increased the mortality risk of patients with ischemic stroke. IGR should be highlighted and intervened actively in the patients with ischemic stroke.

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Disclosures

None.

References

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