Toted Health Risks in Vascular Events Score Predicts Clinical Outcome and Symptomatic Intracranial Hemorrhage in Chinese Patients After Thrombolysis

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Background and Purpose—The performance of the Toted Health Risks in Vascular Events (THRIVE) score in predicting clinical outcomes in Chinese patients with acute ischemic stroke post intravenous thrombolysis is unknown.

Methods—Data from the Thrombolyis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China) study was used to compare the THRIVE score with other scores used to predict clinical outcomes and symptomatic intracranial hemorrhage after intravenous thrombolysis.

Results—Among the 1128 patients with acute ischemic stroke who were included in this study, areas under the curve of the THRIVE score for symptomatic intracranial hemorrhage, 3-month poor functional outcomes, and death rate were 0.69, 0.71, and 0.78, respectively. The increased THRIVE score was related to the higher risk of developing symptomatic intracranial hemorrhage, poor functional outcomes, or death in patients with acute ischemic stroke at 3 months after thrombolysis.

Conclusions—The THRIVE score predicted reliably the risks of developing symptomatic intracranial hemorrhage, poor functional outcome, or death after intravenous thrombolysis therapy in Chinese patients with acute ischemic stroke. (Stroke. 2015;46:864-866. DOI: 10.1161/STROKEAHA.114.007979.)

Key Words: prognosis ■ stroke ■ thrombolytic therapy

Symptomatic intracranial hemorrhage (SICH) after intravenous thrombolysis with recombinant tissue-type plasminogen activator for patients with acute ischemic stroke (AIS) is a major concern in clinical practice. Assessment of the outcome of these patients after thrombolysis would be inadequate if only 1 prognostic factor is studied, such as age, stroke severity, or clinical presentation. A tool to predict clinical benefit and the risk of developing SICH could help clinicians decide if thrombolysis should be offered. The Toted Health Risks in Vascular Events (THRIVE) score was shown to be a useful tool in predicting the outcome in Western patients with AIS after thrombolysis. However, its usefulness in Chinese patients with AIS after thrombolysis is still unknown.

Methods
We applied the THRIVE score to patients enrolled in the national prospective stroke registry study—Thrombolyis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China). Consecutive patients who received intravenous recombinant tissue-type plasminogen activator (Actilyse; Boehringer Ingelheim, Germany) within 4.5 hours after AIS onset were recruited from 67 hospitals in China.

The THRIVE point was assigned according to the following criteria: 1 point, aged between 60 and 79 years; 2 points, age ≥80 years; 2 points, National Institutes of Health Stroke Scale (NIHSS) score between 11 and 20; 4 points, NIHSS score ≥21; and 1 point each for hypertension, diabetes mellitus, and atrial fibrillation. The THRIVE score was compared with 5 other scales: (1) Sugar, Early Infarct Signs, Dense Artery Sign, Age, and NIHSS (SEDAN), (2) Stroke Prognostication using Age and NIHSS (SPAN-100), (3) Houston Intrarterial Therapy 2 score (HIAT2), (4) Dense Artery Sign, Rankin Score, Age, Glucose, Onset to Treatment Time, and NIHSS (DRAGON), and (5) NIHSS/age (a model with NIHSS and age).

The 3-month outcome data included SICH after thrombolysis, functional outcomes, and mortality. SICH was defined according to the criteria of the National Institute of Neurological Disorders and Stroke recombinant tissue-type plasminogen activator stroke study. Poor functional outcome was defined as a modified Rankin Scale score of 3–6. Mortality included death from all causes.

Statistical Analysis
The continuous and categorical variables of patients’ baseline characteristics were presented as means±SD or median (interquartile range) and percentages, respectively. Odds ratios with 95% confidence intervals were calculated using logistic regression analysis. The discriminatory power of the THRIVE score was assessed by the area under the receiver-operator curve (AUC) and 95% confidence

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The Z test was used to compare the AUCs of different scores. Calibration was assessed using the Pearson correlation coefficient and Hosmer–Lemeshow test. The α level of significance was determined as $P<0.05$, 2-sided. All analyses were performed with SAS 9.3 software.

Results

From May 2007 to April 2012, 1128 patients were entered into the TIMS-China registry. The baseline characteristics of all the patients are summarized in Table I in the online-only Data Supplement.

The increased THRIVE score was associated with a higher risk of developing SICH, poor functional outcome, or death after thrombolysis (Table; Figure I in the online-only Data Supplement). Incidences of these poor outcomes in patients with 0 to 2, 3 to 5, and 6 to 9 points of the THRIVE score are listed in Table II in the online-only Data Supplement.

The AUC of the receiver operating characteristic curve of the THRIVE score was significantly greater than or similar to that of other scores (Table; Figure). For predicting post-thrombolytic SICH, the AUC of the THRIVE score was 0.69, compared with 0.61 of the SEDAN ($P=0.01$), 0.50 of the SPAN-100 ($P<0.001$), and 0.69 for NIHSS/age model ($P=0.74$), respectively. For poor outcome prediction, the AUC of the THRIVE score was 0.71, compared with 0.73 of the DRAGON ($P=0.02$), 0.66 of the HIAT2 ($P=0.001$), 0.51 of the SPAN-100 ($P<0.001$), and 0.76 for NIHSS/age ($P<0.001$), respectively. For predicting mortality, the AUC of the THRIVE score was 0.78, compared with 0.74 of the DRAGON ($P=0.009$), 0.71 of the HIAT2 ($P<0.001$), 0.54 of the SPAN-100 ($P<0.001$), and 0.79 for NIHSS/age ($P=0.59$), respectively.

Calibration analysis of the THRIVE score showed a high correlation between the predicted and observed probabilities of SICH ($r=0.93; P<0.001$), poor outcome ($r=0.99; P<0.001$), and death ($r=0.98; P<0.001$). The significance levels of the Hosmer–Lemeshow test for the prediction of SICH, poor outcome, and death were 0.37, 0.33, and 0.64, respectively (Figure II in the online-only Data Supplement).

Discussion

Our study showed that the THRIVE score performed well in predicting the risks of SICH, poor functional outcomes, and death in Chinese patients with AIS after thrombolysis. This score was superior or similar to other prediction models when AUCs of the receiver operating characteristic curves were compared.

The THRIVE score can be easily calculated as soon as the patient’s medical history is available and physical examination is completed. It is a better scoring model than Hemorrhage After Thrombolysis score and SPAN-100 for predicting post-thrombolytic SICH. Our study demonstrated that the THRIVE score was also superior to the SEDAN score, which required serum glucose levels. The THRIVE score was reported to be inferior to the DRAGON score and NIHSS/age in predicting other outcomes.

Table. Predictive Value of the Totaled Health Risks in Vascular Events Score for Symptomatic Intracranial Hemorrhage, 3-Month Poor Outcome, and Mortality

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n/N</th>
<th>% (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
<th>AUC (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SICH</td>
<td>61/1128</td>
<td>5.4 (4.2–6.9)</td>
<td>1.42 (1.24–1.64)</td>
<td>0.69 (0.62–0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Three-month poor outcome*</td>
<td>462/1105</td>
<td>41.8 (38.9–44.8)</td>
<td>1.56 (1.45–1.69)</td>
<td>0.71 (0.68–0.74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Three-month mortality</td>
<td>115/1107</td>
<td>10.4 (8.7–12.3)</td>
<td>1.80 (1.60–2.04)</td>
<td>0.78 (0.74–0.82)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AUC indicates area under the receiver-operator curves; CI, confidence interval; and SICH, symptomatic intracranial hemorrhage.

*Poor outcome was defined as a modified Rankin Scale score of 3–6.

A

B

C

Figure. Receiver operating characteristic (ROC) curve analysis comparing Totaled Health Risks in Vascular Event (THRIVE) score with other scores. ROC curves for prediction of symptomatic intracranial hemorrhage (A), 3-month poor outcome (B), and 3-month death (C). DRAGON indicates Dense Artery Sign, Rankin Score, Age, Glucose, Onset to Treatment Time, and NIHSS; HIAT2, Houston Intra-Arterial Therapy 2; NIHSS, National Institutes of Health Stroke Scale; SEDAN, Sugar, Early Infarct Signs, Dense Artery Sign, Age, and NIHSS; and SPAN-100, Stroke Prognostication using Age and NIHSS.
poor outcome. However, we found that the THRIVE score was better than the DRAGON score in predicting mortality.

Furthermore, our study showed that the THRIVE score was better in predicting mortality than developing SICH at 3 months. The possible explanation is that the patients’ profiles were rather complete in predicting poor outcomes and death, whereas some important risk factors were absent in predicting SICH (pretreatment blood pressure, usage of antiplatelets, and statins).1

Our study has several limitations. First, most of the participating hospitals in TIMS-China were urban hospitals. Second, changes in medical services during the 5-year study period might have influenced the study results. Third, the AUC of the THRIVE score in our study did not reach the threshold of 0.8, which was required for using on individuals. A previous study reported that the predictive scores were inaccurate when selecting patients with AIS for intravenous recombinant tissue-type plasminogen activator therapy in routine clinical practices because of its modest discriminatory power of scores.4 However, the THRIVE score is a more accurate model than most other scoring systems in predicting clinical outcome in patients with AIS after intravenous thrombolysis.

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Disclosures
None.

References
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http://stroke.ahajournals.org/content/suppl/2015/02/03/STROKEAHA.114.007979.DC1

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**SUPPLEMENTAL MATERIAL**

**Table I. Characteristics of Patients in the TIMS-China Registry (N= 1128)**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>440 (39.0)</td>
</tr>
<tr>
<td>Age, y (mean±SD)</td>
<td>63.5±11.3</td>
</tr>
<tr>
<td>NIHSS, median (IQR)</td>
<td>11 (7-16)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>667 (59.1)</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>196 (17.4)</td>
</tr>
<tr>
<td>Atrial Fibrillation, n (%)</td>
<td>202 (17.9)</td>
</tr>
<tr>
<td>THRIVE, median (IQR)</td>
<td>3 (2-4)</td>
</tr>
<tr>
<td>SEDAN, median (IQR) *</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>SPAN-100 positive, n (%)</td>
<td>29 (2.6)</td>
</tr>
<tr>
<td>HIAT2, median (IQR) †</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>DRAGON, median (IQR) ‡</td>
<td>4 (3-5)</td>
</tr>
<tr>
<td>NIHSS/age (for poor outcome)</td>
<td>-0.0 (-0.9-1.1)</td>
</tr>
<tr>
<td>NIHSS/age (for mortality)</td>
<td>-2.0 (-2.5- -1.5)</td>
</tr>
</tbody>
</table>

NIHSS indicates National Institutes of Health Stroke Scale; THRIVE, Totaled Health Risks in Vascular Events; SEDAN, Sugar, Early Infarct Signs, Dense Artery Sign, Age, NIH Stroke Score; SPAN-100, Stroke Prognostication using Age and NIH Stroke Scale; HIAT2, Houston Intra-Arterial Therapy 2 score; DRAGON, Dense Artery Sign, Rankin Score, Age, Glucose, Onset to Treatment Time, NIHSS; NIHSS/age, a model with National Institutes of Health Stroke Scale and age.  
* 67 missing values; †102 missing values; ‡67 missing values.
Table II. Odds Ratio for SICH, 3-Month Poor Outcome and Mortality by Trichotomized THRIVE Score

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Trichotomized THRIVE score</th>
<th>n/N</th>
<th>% (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SICH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>12/506</td>
<td>2.4(1.2-4.1)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5</td>
<td>35/516</td>
<td>6.8(4.8-9.3)</td>
<td>3.00 (1.54-5.84)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>6-9</td>
<td>14/106</td>
<td>13.2(7.4-21.2)</td>
<td>6.27(2.81-13.98)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>3-month poor outcome*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>118/495</td>
<td>23.8(20.2-27.8)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5</td>
<td>267/505</td>
<td>52.9(48.4-57.3)</td>
<td>3.58(2.74-4.70)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>6-9</td>
<td>77/105</td>
<td>73.3(63.8-81.5)</td>
<td>8.79(5.44-14.19)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>3-month mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>12/496</td>
<td>2.4(1.3-4.2)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5</td>
<td>65/506</td>
<td>12.9(10.1-16.1)</td>
<td>5.94(3.17-11.15)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>6-9</td>
<td>38/105</td>
<td>36.2(27.0-46.2)</td>
<td>22.87(11.39-45.95)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

SICH indicates symptomatic intracranial hemorrhage by National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Trial definition; THRIVE, Toted Health Risks in Vascular Events; CI, Confidence Interval.

*Poor outcome was defined as modified Rankin Scale 3-6.
Figure I. Percentage of patients in the TIMS-China with (A) symptomatic intracranial hemorrhage, (B) poor outcome, and (C) death at each point of the totaled health risks in vascular events (THRIVE) score. Patients with THRIVE score of 8 was merged into score of 7 for small sample size (n=8). There is no patient in our study with THRIVE score of 9.
Figure II. Calibration plot of THRIVE score for (A) symptomatic intracranial hemorrhage, (B) poor outcome and (C) death at 3 months. The vertical lines indicate the 95% confidence intervals of predicted rates of clinical outcome. Patients with THRIVE score of 8 was merged into score of 7 for small sample size (n=8). There is no patient in our study with THRIVE score of 9.