The iScore Predicts Functional Outcome in Korean Patients With Ischemic Stroke

Tai Hwan Park, MD*; Gustavo Saposnik, MD, MSc, FAHA*; Hee-Joon Bae, MD; Soo Joo Lee, MD; Kyung Bok Lee, MD; Jun Lee, MD; Jong-Moo Park, MD; Jay Chol Choi, MD; Dong-Eog Kim, MD; Yong-Jin Cho, MD; Joon-Tae Kim, MD; Jae-Kwan Cha, MD; Junyeong Lee, PhD; Kyung-Ho Yu, MD; Byung-Chul Lee, MD; Byung-Woo Yoon, MD

Background and Purpose—Several stroke risk scores for prediction of functional outcome have been developed, but rarely validated in Asian populations. We assessed the validity of the iScore, recently developed from Canadian stroke population, in an Asian stroke population from Korea.

Methods—We applied the iScore to 4061 eligible participants with acute ischemic stroke in the nationwide multicenter stroke registry in Korea. The main outcome was poor functional outcome defined as having a modified Rankin Scale 3 to 6 at 3 months after stroke onset. The secondary outcome was death at 3 months. C-statistics were calculated to assess performance of the iScore.

Results—Poor functional outcome was found in 1496 patients (36.8%), whereas death at 3 months occurred in 294 patients (7.2%). C-statistics were 0.819 (95% confidence interval, 0.805–0.833) for poor functional outcome and 0.861 (95% confidence interval, 0.840–0.883) for death. Overall, there was a high correlation between observed and expected outcomes for poor functional outcome (Pearson correlation coefficient, $r=0.990$) and for death ($r=0.969$) according to risk score.

Conclusions—The iScore reliably predicts poor functional outcome or death at 3 months after stroke in Korean patients. (Stroke. 2013;44:1440-1442.)

Key Words: ischemic stroke ■ outcome ■ prediction ■ risk score

Accurate estimations of functional outcomes in patients with stroke may help clinicians provide effective stroke care, anticipate the discharge planning, and support patients and family having realistic expectations to plan long-term care.

Risk scores were developed to overcome the challenges of estimating outcomes. This is certainly more difficult in the stroke field, considering the variability of stroke syndromes, mechanisms, and the interrelation of factors influencing stroke outcomes. Several prediction tools have been developed to predict functional outcomes in patients with stroke. However, most of the published prediction tools were largely derived from white populations, neglecting the variability of stroke mechanisms, risk factors, and outcomes in Asian populations.

The iScore, recently developed and validated to predict death in acute ischemic stroke in Canadian population, also showed its usefulness to estimate functional outcomes. We sought to determine whether the iScore could predict functional outcomes at 3 months in Korean patients with ischemic stroke.

Study Population

We applied the iScore to patients with ischemic stroke participating in the multicenter prospective observational study on recurrence and its determinants after acute ischemic stroke in Korea. Clinical and laboratory data of consecutive patients with stroke admitted to 12 nationwide university or regional stroke centers are being collected using a standardized web-based data collection form (http://www.stroke-crc.or.kr). Functional outcome measured by the modified Rankin Scale at 3 months after stroke is obtained by direct assessment or by telephone interview. We identified patients with ischemic stroke 18 years and older admitted within 7 days after stroke.
onset between January 2011 and December 2011. Variables included in the iScore are captured in the MOSAIC database. History of cancer and renal dialysis were collected by chart review if undetermined in the database. Although baseline stroke severity was assessed by the National Institutes of Health Stroke Scale in the MOSAIC database, the iScore allows the application of either the National Institutes of Health Stroke Scale or the Canadian Neurological Scale.

Poor functional outcome, the primary outcome measure, was defined as a modified Rankin Scale 3 to 6 at 3 months after stroke onset. Secondary outcome was death at 3 months.

Statistical Analysis
We assessed performance of iScore using the C-statistic for discrimination and the Hosmer–Lemeshow test for calibration. Further details are provided in the online-only Data Supplement.

Results
Overall, there were 4061 patients eligible for the study (Figure in the online-only Data Supplement). Korean patients were younger and had milder stroke than participating patients in the derivation cohort from the Canadian Stroke Registry (Table).

Poor functional outcome (modified Rankin Scale, 3–6) was found in 1496 patients (36.8%), whereas death at 3 months occurred in 294 patients (7.2%). There was a graded increase of poor functional outcome or death by quartiles of the iScore (Figure 1). Poor functional outcome was 11.7% for quartile 1; 19.4% for quartile 2; 36.3% for quartile 3; and 79.7% for quartile 4.

The application of the iScore to the Korean cohort revealed a good discrimination: the C-statistics for poor functional outcome 0.819 (95% confidence interval, 0.805–0.833) and 0.861 (95% confidence interval, 0.840–0.883) for death at 3 months (see receiver operating characteristic curve in the online-only Data Supplement). The calibration was also good for primary (Hosmer–Lemeshow test, \( P = 0.624 \)) and secondary outcomes (Hosmer–Lemeshow test, \( P = 0.757 \)). There was a high correlation between observed and expected outcomes predicted by the iScore for both poor functional status (Pearson correlation coefficient, \( r = 0.990 \); Figure 2) and death at 3 months (\( r = 0.969 \); Figure in the online-only Data Supplement).

Discussion
There are substantial differences in clinical presentation, risk factors, and stroke mechanisms between Asian and white patients with stroke, thus affecting stroke outcomes.

Our results showed that the iScore provided accurate estimations for poor functional outcome (modified Rankin Scale, 3–6) or death at 3 months in Korean patients with an acute ischemic stroke. Despite differences in baseline characteristics of the Korean cohort (compared with the validation cohort from Canada), the C-statistics of the iScore for the primary and secondary outcomes were >0.81.

Together, these findings have practical clinical implications. First, limited information is available on the performance of risk scores when applied to ethnically different populations/groups other than white. A prediction model developed from the Get With the Guidelines-Stroke has been validated to predict in-hospital mortality in Chinese patients with stroke. Although in-hospital mortality is also a valuable prognostic measure, clinical outcomes at 3 months after stroke as measured in our study are more widely used in randomized trials and routine clinical practice. Second, although the iScore was developed to predict 30-day mortality, our study showed
a good performance in prediction of outcomes at 3 months without any modification of the original elements. The current study has a limitation. It is possible that variables not included in the iScore, known to influence stroke outcomes (eg, imaging findings), may improve discrimination power of the iScore.

In conclusion, our results show that the iScore can be reliably applied to Asian patients with an ischemic stroke to estimate clinical outcomes at 3 months. Other prognostic scores may be useful in estimating stroke outcomes, but remain to be validated in other ethnic groups having different risk factors, mechanisms, and stroke subtypes.

Sources of Funding
This work was supported by a grant of the Korea Healthcare Technology R&D Project, Ministry for Health, Welfare & Family Affairs, and the Republic of Korea (A102065).

Disclosures
None.

References
The iScore Predicts Functional Outcome in Korean Patients With Ischemic Stroke
Tai Hwan Park, Gustavo Saposnik, Hee-Joon Bae, Soo Joo Lee, Kyung Bok Lee, Jun Lee, Jong-Moo Park, Jay Chol Choi, Dong-Eog Kim, Yong-Jin Cho, Joon-Tae Kim, Jae-Kwan Cha, Juneyoung Lee, Kyung-Ho Yu, Byung-Chul Lee and Byung-Woo Yoon

Stroke. 2013;44:1440-1442; originally published online March 28, 2013; doi: 10.1161/STROKEAHA.111.000748

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/44/5/1440

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2013/03/28/STROKEAHA.111.000748.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/
Supplemental file

Statistical analysis

Continuous variables were compared by using Student t-test or Wilcoxon rank-sum test.
Categorical variables were compared by using chi-square test.
The National Institutes of Health Stroke Scale (NIHSS) score of Korean patients was converted to the CNS by following formula as reported in the previous study\(^1\): a CNS of 1-4 = an NIHSS score of 14-22 (severe), a CNS of 5-7 = an NIHSS score of 9-13 (moderate), a CNS of ≤8 = an NIHSS score of ≤8 (mild), and a CNS of 0 = an NIHSS score of >22.
Details of the analytic approach for the creation of the iScore have been published elsewhere.\(^2\) We used quartiles of risk score to divide the validation cohort into 4 risk categories and compared distribution of modified Rankin Scale between them. Performance of iScore was assessed using C-statistic for discrimination, and the Hosmer-Lemeshow (HL) test for calibration. We also assessed the calibration by using plot of observed versus predicted outcomes according to predicted risk score, in which Pearson correlation coefficient was used to compare the observed and predicted outcomes. Data were analyzed with SPSS version 15.0 (Chicago, Ill). A two-sided probability values <0.05 were generally considered a minimum level of statistical significance. The study protocol was approved by the institutional review boards of all participating hospitals, and informed consent for follow-up was obtained from patients or their relatives.
eFigure 1. Patients flow

2011.1.1 ~ 2011.12.31
All registered stroke patients
n= 5401

- Outside of the inclusion time window (n= 187)
- Age < 18 yrs (n=2)
- ICH or SAH (n=118)
  TIA (n=334)

Eligible ischemic stroke
n= 4760

- No consent (n= 161)
- Lost follow-up (n= 276)
- Missing TOAST (n=121)
  Missing initial glucose (n=141)

Final analytic cohort
n=4061
Figure 2. The receiver operating characteristic (ROC) curve for poor functional outcome

Legend of figure: The area under the ROC curve was 0.819.
eFigure 3. Observed and predicted death at 3 month after stroke onset according to the risk score group in Korean stroke patients (n=4061).

<table>
<thead>
<tr>
<th>iScore</th>
<th>n</th>
<th>Observed outcome, %</th>
<th>Predicted outcome, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>4</td>
<td>59.5</td>
<td>62.0 (58.5-65.4)</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>57.2</td>
<td>60.7 (56.8-64.7)</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>55.2</td>
<td>56.9 (53.1-60.7)</td>
</tr>
<tr>
<td>1</td>
<td>28</td>
<td>53.3</td>
<td>56.0 (52.2-59.9)</td>
</tr>
<tr>
<td>0</td>
<td>34</td>
<td>51.3</td>
<td>53.5 (49.3-57.7)</td>
</tr>
<tr>
<td>1-60</td>
<td>72</td>
<td>49.4</td>
<td>52.0 (47.6-56.4)</td>
</tr>
<tr>
<td>61-110</td>
<td>605</td>
<td>47.5</td>
<td>50.7 (47.3-54.3)</td>
</tr>
<tr>
<td>111-120</td>
<td>644</td>
<td>45.6</td>
<td>48.7 (45.2-52.3)</td>
</tr>
<tr>
<td>121-130</td>
<td>420</td>
<td>43.8</td>
<td>46.9 (43.2-50.6)</td>
</tr>
<tr>
<td>131-140</td>
<td>226</td>
<td>42.2</td>
<td>46.1 (42.4-49.9)</td>
</tr>
<tr>
<td>141-150</td>
<td>117</td>
<td>41.1</td>
<td>45.2 (41.4-49.0)</td>
</tr>
<tr>
<td>151-160</td>
<td>142</td>
<td>40.1</td>
<td>44.2 (40.3-48.2)</td>
</tr>
<tr>
<td>161-170</td>
<td>151</td>
<td>39.1</td>
<td>43.2 (39.3-47.1)</td>
</tr>
<tr>
<td>171-180</td>
<td>146</td>
<td>38.2</td>
<td>42.3 (38.3-46.3)</td>
</tr>
<tr>
<td>181-190</td>
<td>141</td>
<td>37.2</td>
<td>41.4 (37.2-45.6)</td>
</tr>
<tr>
<td>191-200</td>
<td>111</td>
<td>36.3</td>
<td>40.5 (36.3-44.7)</td>
</tr>
<tr>
<td>201-210</td>
<td>74</td>
<td>35.4</td>
<td>39.6 (35.2-44.0)</td>
</tr>
<tr>
<td>211-220</td>
<td>26</td>
<td>34.6</td>
<td>38.8 (34.2-43.4)</td>
</tr>
<tr>
<td>221-230</td>
<td>24</td>
<td>33.0</td>
<td>37.3 (32.8-41.8)</td>
</tr>
<tr>
<td>≥231</td>
<td>42</td>
<td>31.3</td>
<td>36.5 (31.7-41.3)</td>
</tr>
</tbody>
</table>

Legend of figure: Pearson correlation coefficient was 0.969, indicating excellent calibration.
eFigure 4. ROC curve for death at 3 months

Legend of figure: The area under the ROC curve was 0.861
eTable 1. Outcome analysis according to baseline iScore <200 and ≥200

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>iScore &lt;200 (n=3881)</th>
<th>iScore ≥200 (n=180)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor outcome (mRS 3-6)</td>
<td>1325 (34.1)</td>
<td>171 (95.0)</td>
<td>2.78 (2.63-2.94)</td>
</tr>
<tr>
<td>Death at 3 months</td>
<td>211 (5.4)</td>
<td>83 (46.1)</td>
<td>8.48 (6.91-10.41)</td>
</tr>
<tr>
<td>Death at 30 days</td>
<td>116 (3.0)</td>
<td>59 (32.8)</td>
<td>10.97 (8.33-14.44)</td>
</tr>
<tr>
<td>Death in hospital</td>
<td>74 (1.9)</td>
<td>44 (24.4)</td>
<td>12.82 (9.11-18.04)</td>
</tr>
<tr>
<td>Catastrophic outcome (mRS 4-6)</td>
<td>855 (22.0)</td>
<td>162 (90.0)</td>
<td>4.09 (3.78-4.41)</td>
</tr>
<tr>
<td>Favorable outcome (mRS 0-2)</td>
<td>2556 (65.9)</td>
<td>9 (5.0)</td>
<td>0.08 (0.04-0.14)</td>
</tr>
<tr>
<td>Good outcome (mRS 0-1)</td>
<td>1933 (49.8)</td>
<td>6 (3.3)</td>
<td>0.07 (0.03-0.15)</td>
</tr>
</tbody>
</table>

mRS indicates modified Rankin Scale; RR, relative risk; CI, confidential interval.

We compared various outcomes rates in patients with iScore ≥200 with those in patients with iScore <200 based on the previous report showing no apparent benefit of thrombolytic therapy in patients with iScore ≥200. Values in parentheses are column percentages, unless indicated otherwise. All mRS were measured at 3 months after stroke.
References

