Validation of the DRAGON Score in 12 Stroke Centers in Anterior and Posterior Circulation

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Background and Purpose—The DRAGON score predicts functional outcome in the hyperacute phase of intravenous thrombolysis treatment of ischemic stroke patients. We aimed to validate the score in a large multicenter cohort in anterior and posterior circulation.

Methods—Prospectively collected data of consecutive ischemic stroke patients who received intravenous thrombolysis in 12 stroke centers were merged (n=5471). We excluded patients lacking data necessary to calculate the score and patients with missing 3-month modified Rankin scale scores. The final cohort comprised 4519 eligible patients. We assessed the performance of the DRAGON score with area under the receiver operating characteristic curve in the whole cohort for both good (modified Rankin scale score, 0–2) and miserable (modified Rankin scale score, 5–6) outcomes.

Results—Area under the receiver operating characteristic curve was 0.84 (0.82–0.85) for miserable outcome and 0.82 (0.80–0.84) for good outcome. Proportions of patients with good outcome were 96%, 93%, 78%, and 0% for 0 to 1, 2, 3, and 8 to 10 score points, respectively. Proportions of patients with miserable outcome were 0%, 2%, 4%, 89%, and 97% for 0 to 1, 2, 3, 8, and 9 to 10 points, respectively. When tested separately for anterior and posterior circulation, there was no difference in performance (P=0.55); areas under the receiver operating characteristic curve were 0.84 (0.83–0.86) and 0.82 (0.78–0.87), respectively. No sex-related difference in performance was observed (P=0.25).

Conclusions—The DRAGON score showed very good performance in the large merged cohort in both anterior and posterior circulation strokes. The DRAGON score provides rapid estimation of patient prognosis and supports clinical decision-making in the hyperacute phase of stroke care (eg, when invasive add-on strategies are considered). (Stroke. 2013;44:2718-2721.)

Key Words: ischemic stroke ■ outcome ■ prognosis ■ thrombolysis

Intravenous thrombolysis (IVT) with alteplase is the only approved clot-busting medical therapy in acute ischemic stroke, yet approximately half of the patients treated achieve recanalization in acute setting.1 Regarding functional benefit, a similar percentage of patients achieve good outcome (independence in activities of daily life; modified Rankin scale [mRS] score, 0–2).2,3 For patients who do not benefit from thrombolysis, alternative treatment strategies may be considered. In such cases, it is of utmost importance to predict the benefit of IVT as soon as possible after patient admission, because its efficacy decreases substantially with increasing onset-to-treatment time.2 We recently described such a
of CT as the first-line imaging modality, reporting performance score was recently adapted for patients undergoing MRI instead. Local study investigators developed the DRAGON score, which severe symptoms persist, despite thrombolytic treatment, as a rescue strategy. It reliably identifies patients who will very likely benefit from IVT but also those with high likelihood of miserable outcome, despite IVT. In the latter group, an invasive endovascular procedure can be an alternative treatment of choice, although currently that is not evidence-based. Such an approach is an alternative in some centers in situations in which severe symptoms persist, despite thrombolytic treatment, as a rescue strategy.

The DRAGON score showed very good performance in the original derivation and validation cohorts: area under the receiver operating characteristic curve (AUC-ROC) 0.84 (0.80–0.87) and 0.80 (0.74–0.86), respectively. Furthermore, the DRAGON score was recently adapted for patients undergoing MRI instead of CT as the first-line imaging modality, reporting performance score was recently adapted for patients undergoing MRI instead. Local study investigators developed the DRAGON score, which severe symptoms persist, despite thrombolytic treatment, as a rescue strategy.

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Table 2. Numbers of included patients per center are as follows: Barcelona (n=226), Basel (n=694), Bern (n=79), Box Hill (n=455), Erlangen (n=688), Helsinki (n=467), Lausanne (n=463), Lille (n=277), Melbourne (n=336), Perugia (n=58), St. Gallen (n=153), and Tampere (n=623). Proportions of patients per each cut-off of each parameter of the score are outlined in Table 1 in the online-only Data Supplement together with adjusted odds ratios for miserable and good outcomes per each parameter of the score.

Distributions of 3-month outcome per increasing points of the DRAGON score are outlined in Figure 1. The Hosmer–Lemeshow test showed good calibration of the model in the merged cohort ($\chi^2=1.2$; degrees of freedom=5; $P=0.94$). Predicted risk of miserable and good outcomes per categories of the DRAGON score and observed percentages are depicted in Figures I and II in the online-only Data Supplement. Performance of the DRAGON score in the entire cohort as judged with AUC-ROC was 0.84 (0.82–0.85; Figure 2) for miserable outcome and 0.82 (0.80–0.83) for good outcome, without statistical difference between them ($P=0.10$). The majority of patients had stroke in anterior circulation (n=3944; 87.3%). There was no difference in AUC-ROC ($P=0.55$) between anterior and posterior circulation strokes: 0.84 (0.83–0.86) and 0.82 (0.78–0.87), respectively. The same held true for sex-related analysis: AUC-ROC was 0.85 (0.82–0.87) in women and 0.82 (0.81–0.84) in men ($P=0.25$).

Proportions of patients with miserable outcomes (mRS score, 5–6) were 0%, 2%, 4%, 89%, and 97% for 0 to 1, 2, 3, 8, and 9 to 10 points, respectively. For mRS score 5 to 6 and DRAGON score 9 to 10, positive likelihood ratio was 45.4 (13.9–147.6), negative likelihood ratio was 1.0 (0.9–1.0), positive predictive value was 91.7% (77.5–98.2), negative predictive value was 81.1% (79.9–82.2), specificity was 99.9% (99.8–100), and sensitivity was 3.7% (2.6–5.2). In case of DRAGON score 8 to 10, the corresponding numbers were as follows: positive likelihood ratio was 24.9 (16.3–38.1), negative likelihood ratio was 0.8 (0.8–0.9), positive predictive value was 85.8% (79.6–90.7), negative predictive value was 83.1% (81.9–84.2), specificity was 99.3% (99.0–99.6), and sensitivity was 16.4 (14.1–19.1).

Proportions of patients with good outcome (mRS score, 0–2) were 96%, 93%, 78%, and 0% for 0 to 1, 2, 3, and 8 to 10 score points, respectively. For mRS score 0 to 2 and DRAGON score 0 to 2, positive likelihood ratio was 8.3 (6.6–10.5), negative likelihood ratio was 0.7 (0.7–0.7), positive predictive value was 91.5% (89.4–93.3), negative predictive value was 51.8% (50.2–53.4), specificity was 96.4 (95.4–97.1), and sensitivity was 30.3 (28.5–32.1).

**Discussion**

In a large multicenter cohort of 4519 patients, we successfully validated the DRAGON score, which accurately predicts outcome of IVT-treated ischemic stroke patients. Performance of the score was similarly good (AUC-ROC=0.85) in the original derivation cohort and in the multicenter-merged cohort (Figure 2). Baseline characteristics were similar between original derivation cohort and the current merged cohort (Table 2). Advantages of the DRAGON score are manifold: (1) it is simple, (2) does not require any computer calculations, (3) consists of parameters that are available immediately after patient admission, (4) is very fast to calculate, and (5) is cost-free. In this multicenter study, we improved the generalizability of the DRAGON score by validating it in patients with both anterior and posterior circulation ischemic strokes and in women and men separately.

The score estimates which patients have a very high likelihood of miserable outcome (bedridden incontinent patient in institutional care or death; mRS score, 5 and 6, respectively), despite administration of the only approved recanalization treatment for acute ischemic stroke, IVT with alteplase. Such patients are, in some centers, offered rescue add-on therapy (eg, endovascular procedure). These procedures are, however, not currently evidence-based. In case the use of such add-on rescue strategies is in line with local institutional protocols, the clinicians must act promptly to not lose time. In such situations, rapid arrangements of the endovascular procedures can be based on the DRAGON score, which is calculated even before IVT administration.

Based on the performance of the DRAGON score in the derivation and validation cohorts, patients with scores 0 to 3 have very high likelihood for good recovery after IVT. For patients with scores 7 to 10, the chances for good recovery are very...
low. In institutions where rescue endovascular procedures are not performed because of a lack of randomized trial data, these patients may be recruited into randomized controlled trials testing endovascular procedures or other add-on experimental treatments. Naturally, not all patients with high DRAGON scores would be suitable candidates for endovascular procedures (eg, a patient >80 years with extensive early infarction, high glucose, previous disability, and late presentation). Hence, institutional inclusion criteria for endovascular approach have to be considered in individual cases after obtaining informed consent from patients or their caregivers. Finally, because thrombosis treatment has a risk of intracranial hemorrhage that can influence patient outcome, the final decision can be based on both the DRAGON score (predicting functional outcome) and a score predicting risk of symptomatic intracranial hemorrhage after IVT (eg, the SEDAN score).

There are some limitations of this study. The datasets include mostly white patients. Also, assessments of early ischemic changes on pretreatment CT (eg, posterior circulation ASPECTS score) and the role of hyperdense signs in the basilar artery or posterior cerebral artery are warranted. The strength of the study is the large number of included patients. Furthermore, baseline characteristics and the outcome distribution in our dataset were similar to those of the Safe Implementation of Thrombolysis registry, with somewhat different baseline National Institutes of Health Stroke Scale scores (median, 10 in our database and 12 in the SITS database).

In conclusion, the DRAGON score provides an accurate and immediate estimation of functional outcome in IVT-treated ischemic stroke patients. Validation in a large multicenter cohort and in prespecified subgroups confirms its generalizability.

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References
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Supplementary Table I. Analysis of selected parameters per NIHSS and OTT category

<table>
<thead>
<tr>
<th>Parameter</th>
<th>no (%)</th>
<th>adjusted OR (95% CI)</th>
<th>adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>miserable outcome</td>
<td>good outcome</td>
</tr>
<tr>
<td>hyperDense cerebral artery sign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>1075 (23.8%)</td>
<td>1.64 (1.34-2.00)</td>
<td>0.69 (0.58-0.83)</td>
</tr>
<tr>
<td>no</td>
<td>3444 (76.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>early infarct signs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>1187 (26.3%)</td>
<td>1.30 (1.07-1.58)</td>
<td>0.64 (0.54-0.75)</td>
</tr>
<tr>
<td>no</td>
<td>3332 (73.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre-stroke mRS&gt;1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>278 (6.2%)</td>
<td>1.94 (1.44-2.62)</td>
<td>0.14 (0.09-0.20)</td>
</tr>
<tr>
<td>no</td>
<td>4241 (93.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 80 years</td>
<td>1166 (25.8%)</td>
<td>1.06 (1.05-1.07)</td>
<td>0.965 (0.960-0.970)</td>
</tr>
<tr>
<td>65-79 y</td>
<td>1954 (43.2%)</td>
<td>1.06 (1.03-1.08)</td>
<td>0.95 (0.93-0.98)</td>
</tr>
<tr>
<td>&lt; 65 y</td>
<td>1399 (31.0%)</td>
<td>1.06 (1.03-1.08)</td>
<td>0.95 (0.93-0.98)</td>
</tr>
<tr>
<td>Glucose on admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 8 mmol/L (144 mg/dL)</td>
<td>1106 (24.5%)</td>
<td>1.06 (1.03-1.08)</td>
<td>0.95 (0.93-0.98)</td>
</tr>
<tr>
<td>≤ 8 mmol/L (144mg/dL)</td>
<td>3413 (75.5%)</td>
<td>1.06 (1.03-1.08)</td>
<td>0.95 (0.93-0.98)</td>
</tr>
<tr>
<td>Onset-to-treatment time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 90 min</td>
<td>3766 (83.3%)</td>
<td>1.001 (1.000-1.002)</td>
<td>0.999 (0.998-1.000)</td>
</tr>
<tr>
<td>≤ 90 min</td>
<td>753 (16.7%)</td>
<td>1.001 (1.000-1.002)</td>
<td>0.999 (0.998-1.000)</td>
</tr>
<tr>
<td>NIHSS on admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 15</td>
<td>1286 (28.5%)</td>
<td>1.16 (1.14-1.17)</td>
<td>0.86 (0.85-0.87)</td>
</tr>
<tr>
<td>10-15</td>
<td>1113 (24.6%)</td>
<td>1.16 (1.14-1.17)</td>
<td>0.86 (0.85-0.87)</td>
</tr>
<tr>
<td>5-9</td>
<td>1431 (31.7%)</td>
<td>1.16 (1.14-1.17)</td>
<td>0.86 (0.85-0.87)</td>
</tr>
<tr>
<td>0-4</td>
<td>689 (15.2%)</td>
<td>1.16 (1.14-1.17)</td>
<td>0.86 (0.85-0.87)</td>
</tr>
</tbody>
</table>
Supplementary Figure I

Legend: Predicted risk of miserable outcome (mRS 5-6) per categories of the DRAGON score and observed percentages.

Supplementary Figure II

Legend: Predicted risk of good outcome (mRS 0-2) per categories of the DRAGON score and observed percentages.