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# The Art of Estimating Outcomes and Treating Patients With Stroke in the 21st Century.

Gustavo Saposnik



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## The Art of Estimating Outcomes and Treating Patients With Stroke in the 21st Century Gustavo Saposnik

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## The Art of Estimating Outcomes and Treating Patients With Stroke in the 21st Century

Gustavo Saposnik, MD, MSc, FRCPC

*Will the future bring your wisdom to me? Or will darkness rule the kingdom for all eternity?...*

—Michel de Nostredame, known as Nostradamus (1503–1566)

Clinicians, patients, and their families usually inquire about an expected outcome after an acute event, the response to thrombolysis, and endovascular therapy. Some clinicians use their past experience or weight risk factors known to influence stroke outcomes. These factors can be categorized as follows: (1) patient-level factors (eg, age, stroke severity, comorbid conditions), (2) physician-level factors (eg, specialty, years of experience), and (3) institutional-level factors (eg, Joint Commission on Accreditation of Healthcare Organizations affiliation, stroke center, annual volume of stroke admissions).<sup>1,2</sup>

The development of novel diagnostic tests (ie, computed tomographic perfusion, assessment of collateral flow, MRI perfusion), risk prognostic scores (ie, ischemic stroke risk score [iSCORE], stroke prognostication using age and NIHSS-100 [SPAN-100], totaled health risks in vascular events [THRIVE], sugar, early infarct signs, dense cerebral artery sign, age, and NIH stroke scale [SEDAN], among others; Table), and therapeutic opportunities (ie, new agents for intravenous/intra-arterial thrombolysis, new catheters for endovascular treatment) provide relevant information when discussing and counseling patients with stroke and their families. Currently, there are several stroke risk prognostic scores to predict different outcome measures, including early- and long-term mortality, disability, discharge disposition, response to tissue-type plasminogen activator, and risk of intracerebral hemorrhage after thrombolysis (Figure).<sup>3–8</sup> When applied to large populations, risk scores can provide useful prognostic estimates.

Similar to other risk scores, the THRIVE is a clinical scoring system (range, 0–9) designed to help clinicians better understand a patient's chances of having a good outcome after

an acute ischemic stroke.<sup>9</sup> It assigns points for age (+1 for age 60–79, +2 for age >80 years), stroke severity (0 if National Institutes of Health Stroke Scale score <10, +2 if National Institutes of Health Stroke Scale score=11–20; +4 if National Institutes of Health Stroke Scale score ≥21), and history of hypertension (+1), diabetes mellitus (+1), and atrial fibrillation (AF; +1). In previous studies, scores ≥5 were associated with unfavorable outcomes.<sup>9</sup>

In the present study, Dr Lei et al<sup>10</sup> analyzed the relationships between THRIVE score and clinical outcomes in patients with (n=505) and without (n=3374) cardioembolic stroke. The authors found that a higher THRIVE score was independently associated with decreasing likelihood of favorable outcome (modified Rankin Scale score of 0–2) and an increased likelihood of death (cardioembolic stroke: odds ratio, 1.48; 95% confidence interval, 1.28–1.70; noncardioembolic stroke: odds ratio, 1.95; 95% confidence interval, 1.76–2.16). However, there was a low sensitivity associated with good outcome (68.3%), death (63.2%), and hemorrhagic transformation (62.5%) among patients with cardioembolic stroke. Slightly higher values were observed for patients with noncardioembolic stroke. The areas under the curves were similar between both groups of patients for good clinical outcome (0.729 versus 0.708;  $P=0.39$ ), but lower for hemorrhagic transformation (0.602 versus 0.608;  $P=0.45$ ). The authors concluded by saying that the THRIVE score is a simple tool that helps clinicians estimate good outcome and death after ischemic stroke.

### What Have We Learned From This Article and the Current Available Literature Using Stroke Risk Prognostic Scores?

1. Stroke risk prognostic scores may improve clinicians' accuracy when predicting clinical outcomes. For example, in Clinician Judgment vs Risk Score to Predict Stroke Outcomes (JURaSSiC), 111 clinicians with expertise in acute stroke care were randomly assigned to predict the outcomes of 5 ischemic stroke case scenarios.<sup>11</sup> Of 1661 predictions, clinicians had an overall accuracy of 16.9% for death or disability at discharge, 46.9% for 30-day mortality, and 33.1% for death or institutionalization at discharge. In contrast, 90% of the iSCORE-based estimates were within the 95% confidence interval of observed outcomes.<sup>11</sup> Less than 50% of clinicians were able to predict the probability of the primary outcome accurately in any of the 5 rated cases, and <1% provided an accurate prediction in 4 of the 5 cases (none accurately predicted all 5 cases). In summary, clinicians with expertise in stroke performed poorly compared with a validated tool (iSCORE) in

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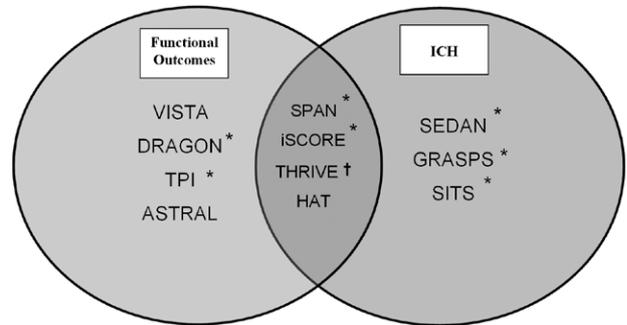
**Table. Variables Included in Stroke Prognostic Risk Scores (for Functional Outcomes)**

	SPAN-100	iSCORE	DRAGON	THRIVE	ASTRAL	TPI
Age, y	•	•	•	•	•	•
Sex		•				•
Clinical parameters						
Stroke severity	•	•	•	•	•	•
Visual field defect						•
Systolic blood pressure						•
Glucose on admission		•	•			•
Time of onset to treatment			•			•
Vascular risk factors						
Hypertension				•		
Diabetes mellitus				•		•
Atrial fibrillation		•		•		
Heart failure		•				
Coronary artery disease		•				
Previous TIA/stroke						•
Comorbid conditions						
Cancer		•				
Renal failure		•				
Prestroke mRS >2		•	•			
Imaging parameters						
HDMCA/early CT findings			•			

ASTRAL indicates Acute Stroke Registry and Analysis of Lausanne; CT, computed tomography; DRAGON, score based on (hyper) dense cerebral artery sign (HDMCA)/early infarct signs on admission CT prestroke modified Rankin Scale (mRS), age, glucose level, onset-to-treatment time, and National Institutes of Health stroke scale; iSCORE, ischemic stroke risk score; SPAN-100, stroke prognostication using age and NIHSS-100; THRIVE, totaled health risks in vascular events; TIA, transient ischemic attack; and TPI, thrombolytic predictive instrument.

predicting the outcomes of patients with an acute ischemic stroke.<sup>11</sup> Other studies also showed better clinician's performance by applying risk scores (eg, Hunt-Hess, Glasgow coma scale, Acute Physiology and Chronic Health Evaluation (APACHE) II) for other medical conditions.<sup>12,13</sup> Together, these findings are likely true for other stroke risk prognostic scores.

- External validation of prognostic scores is challenging. For example, in the present study, the authors found a THRIVE score of 2 as the most sensitive cutoff point (compared with a cutoff of 5 in the original publication). This was likely attributable to the small number of patients with higher THRIVE scores (as seen in Table 2 of the article). Moreover, the sensitivity of the THRIVE score in the studied population was modest at best. These findings may suggest the THRIVE score may have a poor classification (discrimination) in a wide spectrum of patients or just being undermined in the present cohort.
- Discrimination of risk scores: Should clinicians really care? Discrimination is a measure of how well a model/risk score can identify those with and without the event of interest. The most popular measure of discrimination is the c-statistic, also known as the area under the receiving operating characteristic curve. However, the



**Figure.** Venn diagram showing different stroke risk prognostic scores. Note the stroke prognostication using age and NIHSS (SPAN)-100, ischemic stroke risk score (iSCORE), totaled health risks in vascular events (THRIVE), and hemorrhage after thrombolysis (HAT) were validated to predict both functional outcomes and intracerebral hemorrhage (ICH). Risk scores were only validated for mortality not included. ASTRAL indicates Acute Stroke Registry and Analysis of Lausanne; DRAGON, score based on (hyper) dense cerebral artery sign (HDMCA)/early infarct signs on admission CT prestroke modified Rankin Scale (mRS), age, glucose level, onset-to-treatment time, and National Institutes of Health stroke scale; GRASPS, glucose race age sex pressure stroke severity score; SEDAN, sugar, early infarct signs, dense cerebral artery sign, age, and NIH stroke scale; SITS, safe implementation of thrombolysis in stroke-SICH risk score; TPI, thrombolytic predictive instrument; and VISTA, score derived from the Virtual International Stroke Trials Archive. \*Stroke risk prognostic score evaluated to estimate the response to intravenous tissue-type plasminogen activator. †The THRIVE score was validated in the Thrombectomy Revascularization of Large Vessel Occlusions in Acute Ischemic Stroke (TREVO) trial to determine the prognosis after endovascular therapy.

c-statistics may not be optimal in assessing models that predict future risk or stratify individuals into risk categories. Some good examples are well known in the literature.<sup>14</sup> Clinicians should care more about how well a risk score would be able to identify their patients with a specific condition (eg, favorable outcome, death, disability). Reclassification tables are usually required by reviewers and journals to assess the accuracy and predictive value of risk scores.

- Definition of cardioembolic stroke: The authors defined cardioembolic stroke as the presence of AF, cardiac failure, rheumatic valve disease, and acute myocardial infarction in the absence of a lacunar syndrome.<sup>10</sup> Although AF and cardiac failure are major risk factors for a cardioembolic event, AF is not a synonym of cardioembolic stroke. Stroke among patients with AF and cardiac failure may be caused by other mechanisms.<sup>15</sup> Moreover, AF developed after stroke (called poststroke AF) may be an epiphenomenon after the event rather than its cause.<sup>16</sup>

In summary, the present study provides confirmatory evidence of the potential value of risk prognostic scores (eg, iSCORE, SPAN-100, THRIVE, SEDAN, preadmission dependence, level of consciousness, age, and neurologic focal deficit (PLAN), among others) to assist clinicians in estimating outcomes when counseling patients with stroke and their families.

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## Disclosures

None.

## References

1. Saposnik G, Hill MD, O'Donnell M, Fang J, Hachinski V, Kapral MK; Registry of the Canadian Stroke Network for the Stroke Outcome Research Canada (SORCan) Working Group. Variables associated with 7-day, 30-day, and 1-year fatality after ischemic stroke. *Stroke*. 2008;39:2318–2324.
2. Lichtman JH, Jones SB, Wang Y, Watanabe E, Leifheit-Limson E, Goldstein LB. Outcomes after ischemic stroke for hospitals with and without Joint Commission-certified primary stroke centers. *Neurology*. 2011;76:1976–1982.
3. O'Donnell MJ, Fang J, D'Uva C, Saposnik G, Gould L, McGrath E, et al; Investigators of the Registry of the Canadian Stroke Network. The PLAN score: a bedside prediction rule for death and severe disability following acute ischemic stroke. *Arch Intern Med*. 2012;172:1548–1556.
4. Strbian D, Engelter S, Michel P, Meretoja A, Sekoranja L, Ahlhelm FJ, et al. Symptomatic intracranial hemorrhage after stroke thrombolysis: the SEDAN score. *Ann Neurol*. 2012;71:634–641.
5. Strbian D, Meretoja A, Ahlhelm FJ, Pitkaniemi J, Lyrer P, Kaste M, et al. Predicting outcome of IV thrombolysis-treated ischemic stroke patients: the DRAGON score. *Neurology*. 2012;78:427–432.
6. König IR, Ziegler A, Bluhmki E, Hacke W, Bath PM, Sacco RL, et al; Virtual International Stroke Trials Archive (VISTA) Investigators. Predicting long-term outcome after acute ischemic stroke: a simple index works in patients from controlled clinical trials. *Stroke*. 2008;39:1821–1826.
7. Saposnik G, Guzik AK, Reeves M, Ovbiagele B, Johnston SC. Stroke Prognostication using Age and NIH Stroke Scale: SPAN-100. *Neurology*. 2013;80:21–28.
8. Ntaios G, Faouzi M, Ferrari J, Lang W, Vemmos K, Michel P. An integer-based score to predict functional outcome in acute ischemic stroke: The astral score. *Neurology*. 2012;8:1916–1922.
9. Flint AC, Xiang B, Gupta R, Nogueira RG, Lutsep HL, Jovin TG, et al; TREVO-2 Trialists. THRIVE score predicts outcomes with a third-generation endovascular stroke treatment device in the TREVO-2 trial. *Stroke*. 2013;44:3370–3375.
10. Lei C, Wu B, Liu M, Chen Y, Yang H-I, Wang D, et al. Totalled Health Risks in Vascular Events score predicts clinical outcomes in patients with cardioembolic and other subtypes of ischemic stroke. *Stroke*. 2014;45:xxx–xxx.
11. Saposnik G, Cote R, Mamdani M, Raptis S, Thorpe KE, Fang J, et al. JURASSIC: accuracy of clinician vs risk score prediction of ischemic stroke outcomes. *Neurology*. 2013;81:448–455.
12. Navi BB, Kamel H, McCulloch CE, Nakagawa K, Naravetla B, Moheet AM, et al. Accuracy of neurovascular fellows' prognostication of outcome after subarachnoid hemorrhage. *Stroke*. 2012;43:702–707.
13. Knaus WA, Harrell FE Jr, Lynn J, Goldman L, Phillips RS, Connors AF Jr, et al. The SUPPORT prognostic model. Objective estimates of survival for seriously ill hospitalized adults. Study to understand prognoses and preferences for outcomes and risks of treatments. *Ann Intern Med*. 1995;122:191–203.
14. Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation*. 2007;115:928–935.
15. Weir NU. An update on cardioembolic stroke. *Postgrad Med J*. 2008;84:133–142, quiz 139.
16. Sposato LA, Riccio PM, Hachinski V. Poststroke atrial fibrillation: cause or consequence?: critical review of current views. *Neurology*. 2014;82:1180–1186.

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# Stroke

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