The Role of Imaging in Clinical Stroke Scales That Predict Functional Outcome: A Systematic Review

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Abstract

Background and Purpose: Numerous stroke scales have been developed to predict functional outcomes following acute ischemic stroke. The goal of this study was to summarize functional outcome scores in stroke that incorporate neuroimaging with those that don't incorporate neuroimaging. **Methods:** Searches were conducted in Ovid MEDLINE, Ovid Embase, and the Cochrane Library Database from inception to January 23, 2015. Additional records were identified by employing the "Cited by" and "View References" features in Scopus. We included studies that described stroke prognosis models or scoring systems that predict functional outcome based on clinical and/or imaging data available on presentation. Score performance was evaluated based on area under the receiver operating characteristic curve (AUC). **Results:** A total of 3300 articles were screened, yielding 14 scores that met inclusion criteria. Half (7) of the scores included neuroimaging as a predictor variable. Neuroimaging parameters included infarct size on magnetic resonance diffusion-weighted imaging, infarct size defined by computed tomography hypodensity, and hemodynamic abnormality on perfusion imaging. The modified Rankin Scale at 3 months poststroke was the most common functional outcome reported (13 of 14 scores). The AUCs ranged from 0.64 to 0.84 for scores that included neuroimaging as a predictor and 0.64 to 0.94 for scores that did not include neuroimaging. External validation has been performed for 7 scores. **Conclusions:** Due to the marked heterogeneity in the scores and populations in which they were applied, it is unclear whether current imaging-based scores offer advantages over simpler approaches for predicting poststroke function.

Keywords

stroke, cerebrovascular disorders, neuroradiology, clinical specialty, outcomes, techniques

Introduction

Acute ischemic stroke is the second leading cause of death worldwide and a leading cause of long-term disability.^{1,2} A risk score that predicts functional outcomes after stroke has several potential uses. It could help guide realistic prognostic expectations for patients, families, and physicians and aid in the planning of long-term care. It could be used in nonrandomized studies to control for case-mix variation and in controlled clinical trials to define individual clinical end points, to select suitable patients, and to reduce required sample size.³⁻⁶ It could be used for risk adjustment when evaluating stroke providers. In order to be useful and applicable to clinical practice and management, a prognostic model must be validated, easy to implement, and contain variables that are readily available for all patients.

Many scores exist that aim to predict poststroke functional outcome. Some of these scores are simple, with the simplest including solely a scale of stroke severity (National Institutes

of Health Stroke Scale [NIHSS]), while others involve more inputs that require additional time and/or resources, such as neuroimaging. The added value of neuroimaging in predicting functional outcomes is important to critically evaluate, given the significant potential costs of imaging. These costs are both

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monetary and as potential harm to patients including possible treatment delays secondary to additional diagnostic imaging, radiation risks, and risk of contrast nephropathy. The goal of our study was to systematically review stroke scores that predict functional outcomes, with a focus on comparing clinical scores that incorporate imaging with those that do not incorporate imaging.

Methods

A systematic search was performed to comprehensively identify studies that use a clinical score/scale to predict functional outcome after ischemic stroke. We defined a score as a tool that could be administered during a patient's hospital admission in which various variables (including but not limited to clinical, physiologic, and/or imaging) were evaluated and given a numeric value, with these values being totaled to produce a final score that corresponded to the probability of a good or poor outcome. Risk discrimination performance was assessed using area under the receiver operating characteristics curve (AUC) based on the favorable or unfavorable functional outcome used to evaluate each score. This study was exempt from institutional review board approval because it only involved analysis of publicly available, published, aggregate data.

Systematic Literature Search Overview

A medical librarian (D.D.) performed comprehensive literature searches from inception to January 23, 2015, in Ovid MEDLINE, Ovid Embase, and the Cochrane Library. We conducted our search in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for systematic reviews.⁷ Relevant subject headings and keywords were used to capture stroke, a statistic or means of evaluating the predictive value of a score, as well as a standardized measure for assessing functional outcome. Results were limited to English. Additional records were identified by employing the "Cited by" and "View references" features in Scopus. Search methodology details for MEDLINE are provided in the Online Supplement. All records were imported into EndNote. The search initially identified 3936 studies. After duplicates were removed, 3330 studies remained. By examining the titles and abstracts (F.S.), the number of articles was reduced to 90. Two reviewers (F.S. and A.P.) independently examined these 90 articles to screen for articles for inclusion.

Inclusion/Exclusion Criteria

Studies were included only if a clinical score was used to predict functional outcome. Such scores needed to contain variables that could be obtained during the hospital admission of a patient with acute ischemic stroke. These variables were each assigned a numeric value which could be totaled to a final number or score that correlated with a probability of an

outcome. Studies that only identified predictors of functional outcome through logistic models or regression analysis were excluded. Studies that did not report AUC or c-statistic results were excluded. Functional outcome had to be assessed the earliest at a 3-month interval following the stroke using a validated scale such as the modified Rankin Scale (mRS) or other validated measures (including but not limited to Glasgow Outcome Scale [GOS], Barthel Index [BI], functional independence measure, and measures of instrumental activities of daily living). Scores that only evaluated mortality (mRS6) or clinical events (such as symptomatic intracerebral hemorrhage) were not included based on the functional outcome criterion. All patients had to have undergone an ischemic stroke. Patients who underwent thrombolysis or endovascular treatments were included as well as those who underwent no treatment measure. Studies were dated after 1996 and sample size had to be equal to or larger than 30 patients. Detailed systematic search methods are provided in the Online Supplement.

Results

Study Selection

We screened a total of 3330 abstracts from which 14 scores were ultimately deemed to meet all inclusion criteria for the systematic review. Study selection steps are summarized in Figure 1. Table 1 shows the risk scores included in this review and includes information regarding the study populations, components, and performance of each score. Most of the study populations were from clinical trials for acute stroke or regional stroke registries. Neuroimaging was included as a predictor variable in half (7 of the 14) of the scores included. The mRS score at 3 months was the most common functional outcome (predicted by 13 [93%] of these scores); the BI and GOS were also used as outcomes. The AUCs from the derivation studies ranged from 0.64 to 0.84 for scores that included imaging and 0.64 to 0.94 for scores without imaging predictors. We found that 7 scores (50%) were validated externally for functional outcome, while 2 additional scores were validated using the same population as the derivation cohort. Among these 7 scores, 4 scores (57%) that contained imaging variables were externally validated and 3 nonimaging scores (43%) were externally validated. Table 2 shows the scores grouped by ischemic stroke patient population, specifically referring to their treatment status with intravenous (IV) thrombolysis or endovascular therapy; we assumed the National Institutes of Health Stroke Scale (NIHSS) and Shortened versions of the National Institutes of Health Stroke Scale (sNIHSS) scores were derived in patient populations without either treatment, because these scores were derived before widespread use of these acute ischemic stroke treatments.

ASTRAL

The Acute Stroke Registry and Analysis of Lausanne (ASTRAL) score, which is an acronym of the derivation

Figure 1. The flow diagram of studies included in the review.

registry,³¹ as well as the covariates included in the score, was derived and validated in 2 separate European populations to predict the probability of an unfavorable outcome in patients with acute ischemic stroke (defined as mRS >2 at 3 months).⁸ It is a simple integer-based prognostic score that can predict ischemic stroke outcome at 3 months in patients arriving to the hospital setting within 24 hours, prior to any form of treatment. The ASTRAL score has been validated in the China National Stroke Registry for predicting poor functional outcome at 3 and 12 months.¹⁰

BOAS

The Bologna Outcome Algorithm for Stroke (BOAS) score was generated and then tested in a small number of patients admitted to the stroke unit at a hospital in Bologna, Italy¹¹ to predict functional outcome and death at 9 months. In

examining 415 variables related to vitals, laboratory values, imaging studies, treatment parameters, medical history, and stroke presentation, multivariable analyses were performed by multiple logistic regressions, with the final model yielding an additive score based on 5 variables (age, initial NIHSS, need of urinary catheter, oxygen administration, and persistence of paralysis in upper limb). The BOAS score is a prognostic assessment that can be provisionally established within the first 24 hours and updated during the stay in the stroke unit. When the NIHSS score exceeds a certain threshold, no other prognostic parameters are necessary, and outcome prediction can be immediate. Specifically, an initial NIHSS score ≥ 10 was sufficient to predict an unfavorable outcome, and with higher NIHSS values, the prognosis became even more unfavorable with 95% of patients with an mRS ≥ 5 at 9 months and 75% dead with an NIHSS >19 .

Table 1. Summary of Clinical Stroke Scores That Predict Functional Outcomes Included in This Review.

Score Name	Derivation Population	Predictors	Use of Imaging	Outcomes	AUC/Performance	Validation
ASTRAL ⁸	Patients with acute ischemic stroke having initial mRS <2, Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland, 2003 to 2010	Age, stroke severity based on NIHSS, time delay from onset to admission >3 hours, range of visual field defects, admission glucose, level of consciousness	None	3-Month mRS >2	AUC = 0.85 (derivation); AUC = 0.82 to 0.89 (validation range) ^{9,10}	External validation in Greek and Chinese populations
BOAS ¹¹	Patients with acute ischemic stroke having initial mRS <4, S. Orsola-Malpighi Hospital, Bologna, Italy, 2007 to 2008	Initial NIHSS score, age, need of urinary catheter, oxygen administration, persistence of paralysis in an upper limb	None	9-Month mRS >2	AUC = 0.89 (derivation); AUC = 0.84 (internal validation)	Internal validation on separate test population; no external validation
DRAGON ¹²	Patients with ischemic stroke treated with IV alteplase, Helsinki University Central Hospital, Helsinki, Finland, 1995 to 2010	Dense cerebral artery sign/early infarct signs on admission head CT, prestroke mRS score >1, age, blood glucose, onset to treatment time (OTT), NIHSS score	CT hypodensity and/or dense cerebral artery sign	3-Month mRS 3 to 6 (derivation and initial external validation); 3-month mRS 0 to 2 (external validation) or mRS 4 to 6 ¹³	AUC = 0.84 (derivation); AUC = 0.84 (validation for mRS 0-6); AUC = 0.79 (validation for mRS 0-2) ¹³	Internal validation with bootstrap; external validation in Swiss and Danish populations
MRI-DRAGON ¹⁴	Patients with ischemic stroke treated with IV alteplase, Hôpital Sainte-Anne, Paris, France, 2003 to 2012	DWI ASPECTS, prestroke mRS score >1, age, blood glucose, OTT, NIHSS score, MI (proximal middle cerebral artery) occlusion	MRI (DWI ASPECTS)	3-Month mRS 3 to 6	AUC = 0.83	Internal validation with bootstrap
HAT ¹⁵	tPA-treated group in the National Institute of Neurological Disorders and Stroke study, 2001 to 2007	NIHSS score, extent of hypodensity on CT scan, serum glucose at baseline, history of diabetes	CT hypodensity	3-Month mRS 0 to 2	AUC = 0.75	None for functional outcome
HIAT ¹⁶	Intra-arterial recanalization therapy (IAT)-treated patients with stroke at University of Texas Houston Stroke Center, Houston, Texas, 1998 to 2007	Age, baseline NIHSS score, admission glucose, diabetes, heart disease, previous stroke, absence of mismatch on the pretreatment MRI	Pre-IAT MRI (DWI lesion and perfusion deficit mismatch)	Hospital discharge mRS 4 to 6 (derivation); 3-month mRS 4 to 6 (validation)	None in derivation. AUC = 0.68 in external validation ¹⁷	External validation with Houston Stroke Center patients ¹⁷
HIAT2 ¹⁷	IAT-treated patients with stroke at University of Texas Houston Stroke Center, Houston, Texas, 2003 to 2011	Age, baseline NIHSS score, admission glucose, diabetes, hypertension, atrial fibrillation, clot-burden score, ASPECTS	CT ASPECTS	3-Month mRS 4 to 6	AUC = 0.70 (derivation)	External validation with US patients (Atlanta, GA)
iScore ¹⁸	Patients with acute ischemic stroke in Ontario, Canada, 2003 to 2008	Age, sex, stroke severity, stroke subtype, atrial fibrillation, congestive heart failure, cancer, renal dialysis, preadmission disability, glucose	None	30-Day mRS 3 to 6 (derivation); 3-month mRS 3 to 6 (validation)	AUC = 0.79 (derivation); AUC = 0.81 to 0.82 (external validation range) ^{19,20}	External validation in French and Korean populations

(continued)

Table 1. (continued)

Score Name	Derivation Population	Predictors	Use of Imaging	Outcomes	AUC/Performance	Validation
NAV ²¹	Patients with acute stroke treated with endovascular therapy, 2 US stroke centers, 2009 to 2011	Age, baseline NIHSS, decreased cerebral blood volume (estimated by CT perfusion)	CT perfusion	90-Day mRS 0 to 2	AUC = 0.77	None
NIHSS ²²	Patients with ischemic stroke, multiple North American sites, 1993 to 1994	NIHSS score	None	3-Month GOS = 3 or 4	AUC = 0.94	None
sNIHSS-4 ²³	Patients with ischemic stroke, multiple North American trial sites, 1997	sNIHSS-4 score (shortened version of NIHSS score)	None	3-Month mRS >3	AUC = 0.73 (left hemispheric stroke) and 0.75 (right hemispheric stroke)	None
SAD ²⁴	Patients with acute stroke having NIHSS ≥ 5 treated with endovascular therapy, multicenter prospective cohort, 2008 to 2013	Age, lesion volume on DWI	MRI (DWI)	3-Month mRS 4 to 6	AUC = 0.82 (derivation); AUC = 0.69 (external validation)	External validation (Massachusetts General Hospital)
SPAN ²⁵	Patients with acute ischemic stroke, multicenter IV alteplase trial (treatment and placebo patients), 1991 to 1994	Age, NIHSS score	None	3-Month "favorable outcome" (mRS 0-1, NIHSS ≤ 1 , BI ≥ 95 , GOS score = 1)	c-Statistic = 0.64	None
THRIVE ²⁶	Patients with acute stroke treated with endovascular therapy, multiple US trial sites, 2001 to 2003	NIHSS score, age, hypertension, diabetes, atrial fibrillation	None	3-Month mRS 0 to 3	AUC = 0.71 (derivation); AUC = 0.71 to 0.78 (external validation range)	Externally validated in other US clinical trial site ²⁷⁻³⁰

Abbreviations: AUC, area under the curve; ASPECTS, Alberta Stroke Program Early CT Score; ASTRAL, Acute Stroke Registry and Analysis of Lausanne; BI, Barthel Index; BOAS, Bologna Outcome Algorithm for Stroke; CT, computed tomography; DRAGON, (hyper)Dense cerebral artery sign/early infarct signs on admission CT scan, prestroke modified Rankin Scale (mRS) score, Age, Glucose level at baseline, Onset-to-treatment time, and baseline National Institutes of Health Stroke Scale score; DWI, diffusion-weighted imaging; GOS, Glasgow Outcome Scale; HAT, hemorrhage after thrombolysis; HIA T, Houston intra-arterial recanalization therapy; IV, intravenous; MRI, magnetic resonance imaging; mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; NAV, NIHSS, Age, and Volume; SAD, Stanford Age and Diffusion-Weighted Imaging; SPAN, Stroke Prognostication Using Age and NIHSS; THRIVE, Totalled Health Risk in Vascular Events; tPA, tissue plasminogen activator.

Table 2. Summary of Clinical Stroke Scores by Patient Population.

Ischemic Stroke Patient Population	Potentially Relevant Scores	Externally Validated Scores
Treated with intravenous thrombolysis	DRAGON, ^a MRI-DRAGON, ^a HAT, ^a SPAN	DRAGON ^a
Treated with endovascular therapy	HIAT, ^a HIAT2, ^a NAV, ^a SAD, ^a THRIVE	HIAT, HIAT2, SAD, THRIVE
Not treated with either intravenous thrombolysis or endovascular therapy	NIHSS, sNIHSS	
Not specific to treatment status	ASTRAL, BOAS, iScore	ASTRAL, iScore

Abbreviations: ASTRAL, Acute Stroke Registry and Analysis of Lausanne; BOAS, Bologna Outcome Algorithm for Stroke; HAT, hemorrhage after thrombolysis; HIAT, Houston intra-arterial recanalization therapy; MRI, magnetic resonance imaging; NIHSS, National Institute of Health Stroke Scale; SAD, Stanford Age and Diffusion-Weighted Imaging; SPAN, Stroke Prognostication Using Age and NIHSS; THRIVE, Total Health Risk in Vascular Events.

^aImaging as predictor.

DRAGON

In a population-based cohort from a hospital in Finland, several imaging and clinical factors were combined to create a 10-point score for predicting functional outcome in patients undergoing IV tissue plasminogen activator (tPA) within 4.5 hours of symptom onset following ischemic stroke (excluding basilar artery occlusion).¹² In this additive score, the higher the score, the higher the likelihood of poorer outcome. Specificity of the prediction at both extreme poles of the score reached up to 100%. The DRAGON score ([hyper]Dense cerebral artery sign/early infarct signs on admission head computed tomography [CT], prestroke mRS score >1, age, glucose level on admission, onset to treatment time, and NIHSS score on admission) was additionally externally validated in cohorts from Denmark and Spain treated with IV tPA,^{13,32} as well as a large multicenter cohort encompassing 12 European and Australian stroke centers³³ where the DRAGON score was once again shown to be able to predict good versus highly unfavorable outcome in IV thrombolysis patients. The DRAGON score was also shown to be effective in predicting unfavorable functional outcome when a proximal occlusion was present on CT angiography.¹³ In this large multicenter cohort, the DRAGON score was validated in both anterior and posterior circulation ischemic strokes and in women and men separately.³³

MRI-DRAGON

The DRAGON score was adapted to patients with anterior circulation strokes treated with IV tPA and imaged by magnetic resonance imaging (MRI), as opposed to CT. The MRI-DRAGON score was derived and internally cross-validated to predict outcome using the same 5 clinical variables and 2 MRI parameters.¹⁴ Sensitivity analyses using a score of ≤ 7 on the diffusion-weighted imaging (DWI) Alberta Stroke Program Early CT score (ASPECTS) demonstrated a similar AUC. All clinical parameters of the CT-DRAGON score were independently associated with 3-month outcome.

Hemorrhage After Thrombolysis

The hemorrhage after thrombolysis (HAT) score provides a grading scale that can be performed in the hyperacute phase to

predict the risk of intracranial hemorrhage (ICH) and 90-day prognosis after treatment with IV tPA.³⁴ The scale can predict the rate of any ICH after tPA including symptomatic ICH (sICH) and hemorrhage with final fatal outcome. It is a 5-point scale to predict the risk of ICH after tPA that was derived and evaluated in 2 independent cohorts (National Institute of Neurological Disorders and Stroke [NINDS] trial and patients treated at Beth Israel Deaconess Medical Center).³⁴ The HAT score was externally validated in patients from 2 phase II trials of ultrasound-enhanced thrombolysis (Combined Lysis of Thrombus in Brain ischemia using Transcranial Ultrasound and Systemic tPA and Transcranial Ultrasound in Clinical SONothrombolysis) with similar c-statistics for all outcome variables, including sICH, ICH, and 3-month favorable outcome.¹⁵

HIAT

The Houston intra-arterial recanalization therapy (HIAT) score was derived and validated to predict the outcome of intra-arterial recanalization therapy in patients with stroke having a large vessel occlusion, prior to the procedure.¹⁶ A higher HIAT score is associated with poorer outcome and mortality. The HIAT score predicts outcomes in both recanalizers and nonrecanalizers.¹⁶ In another study, the HIAT score demonstrated similar receiver operator characteristic properties in the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) 2 cohort.²⁴

HIAT 2

The HIAT2 score adds imaging features such as the ASPECTS obtained on CT to the clinical factors included in HIAT.¹⁷ Patients with HIAT2 score ≥ 5 had a 6 times greater odd of poor outcome at discharge compared to patients with a score < 5 . Additionally, the HIAT2 score could be translated to outcome at 90 days, with higher HIAT2 scores predicting poorer outcome. Furthermore, the HIAT2 score maintained the ability to predict poor outcome at 90 days after adjustment for recanalization, time from symptom onset to reperfusion, the use of general anesthesia, and the use of stent retrievers. The contribution of ASPECTS to the HIAT2 scoring system was

evaluated by removing it and creating a modified 0 to 7 scoring system.¹⁷ While the modified score continued to be a significant predictor of poor outcome, removing ASPECTS underestimated the patients' odds of having poor clinical outcome and resulted in a smaller AUC (0.6139). Similarly, adding the ASPECTS to the original HIAT to create a 0- to 4-point scale resulted in a score that better estimates poor outcome compared to the original HIAT score itself, with a larger AUC (0.6802).¹⁷

iScore

The iScore is a validated risk score that was developed in a Canadian cohort (Registry of the Canadian Stroke Network) that can be used to estimate the risk of short- and long-term mortality after an acute stroke.^{18,35} It categorizes patients with ischemic stroke into 5 risk categories using clinical parameters and comorbid conditions. It has been adapted to predict clinically relevant functional outcomes in patients admitted with an acute ischemic stroke when defined as death at 30 days or disability at discharge, death at 30 days or institutionalization at discharge, and functional outcome at 3 months. The iScore has also been validated in a French cohort (Dijon Stroke Registry), where it was shown to predict poor functional outcome defined as an mRS of 3 to 6 at discharge. The application of the iScore to a Korean cohort revealed good discrimination using AUC for poor functional outcome (mRS 3-6) at 3 months, despite significant differences in clinical presentation, risk factors, and stroke mechanisms between Asian and white (validation cohort from Canada) patients with strokes.¹⁹

NAV

The NAV score is a score named after the variables included in the score: NIHSS, age, and volume (ie, blood volume). It is simple in that it only includes the 3 aforementioned variables, but it also requires advanced imaging (CT perfusion) to estimate the percentage of ischemic tissue that has decreased cerebral blood volume (CBV).²¹ Points are assigned as follows: 2 points for an NIHSS score ≥ 15 , 1 point for age ≥ 70 years, and 1 point for decreased CBV $\geq 50\%$. All 3 variables were statistically significant predictors of good stroke outcome (90-day mRS 0-2) at a .05 α level. The score has not yet been externally validated in other settings/populations.

NIHSS

Although not designed to predict functional outcome, the NIHSS score was shown to predict GOS scores of 3 (severely disabled) and 4 (vegetative) with good accuracy.²² In the same study, the NIHSS score also predicted dependence (as defined by patients who were in a nursing home, chronic hospital, or substantially dependent on a caregiver) well. The NIHSS score ranges from 0 (no stroke symptoms) through 42 (scores of 21-42 indicate severe stroke, 16-20 moderate to severe stroke, 5-15 moderate stroke, 1-4 minor stroke). It is based on 11 clinical

and functional dimensions, including language, sensory, and motor items. Although the NIHSS is a common component of many clinical stroke scales included in this review, the use of NIHSS score as the sole predictor of functional outcome (assessed by AUC or c-statistic) was limited to this study.

sNIHSS-4

The sNIHSS-4 is a shorter version of the NIHSS score that only includes 4 components: strength in affected leg, gaze, visual fields, and language. Baseline sNIHSS-4 predicted poor functional outcome well in the United States and Canadian Lubeluzole in Acute Ischemic Stroke Study (AUC = 0.73-0.75 for left and right hemispheric stroke) and performed comparably to baseline NIHSS (AUC = 0.73-0.76).²³ Performance improved for sNIHSS-4 assessed at 2 and 5 days post-stroke (AUC = 0.81-0.83 and 0.86-0.90, respectively). The ability of the sNIHSS-4 to predict functional outcome has yet to be validated.

SAD

The Stanford Age and Diffusion-Weighted Imaging (SAD) score was derived in the DEFUSE 2 population and validated in Massachusetts General Hospital patients who had baseline MRI scans performed within 90 minutes of receiving endovascular therapy.²⁴ The SAD score assigns 0 to 3 points based on age (0 points for ≤ 55 years, 1 point for 56-69 years, 2 points for 70-79 years, 3 points for ≥ 80 years) and DWI volume (1 point for $>15 \text{ cm}^3$, 0 points for all other values). The SAD score performed similarly compared to the HIAT score in the external validation analysis.

SPAN

The Stroke Prognostication using Age and NIHSS (SPAN) index adds the NIHSS score to age; when this score is greater than 100, patients are considered SPAN-100 positive.²⁵ The SPAN score was evaluated using the NINDS tPA stroke trials and was found to predict function outcome (defined using mRS, NIHSS, BI, or GOS depending on study). The SPAN-100 cutoff was also found to be a significant predictor of risk of hemorrhagic complication after tPA. No internal or external validation analyses were conducted for the SPAN score.

THRIVE

The Totaled Health Risk in Vascular Events (THRIVE) score was constructed to predict outcome among patients undergoing endovascular stroke treatment from stroke patients in the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) and multi-MERCI trials, which evaluated recanalization using endovascular mechanical thrombectomy.²⁶ Higher values of the THRIVE score are associated with increased mRS values. Thus, patients with successful vessel recanalization (defined as a thrombolysis in cerebral

infarction grade of 2a or higher) and those with a lower THRIVE score had a higher probability of a good outcome and a decreased mortality rate. The relationship between THRIVE and good outcome was validated in an external data set, the Merci registry,³⁶ and also shown to have similar effects in the Thrombectomy REvascularization of Large Vessel Occlusions in Acute Ischemic Stroke (TREVO 2) trial where retrievable stents (the Trevo device) were used for endovascular stroke treatment.²⁷ The THRIVE score subsequently has been shown to predict long-term outcomes among patients receiving thrombolysis or no acute stroke treatment in the NINDS randomized control trial of tPA.²⁸ The THRIVE score has been validated across 3 major categories of patients with acute stroke: those receiving IV tPA, those receiving endovascular stroke treatment, and those receiving no acute recanalization therapy.

Discussion

There are several scores that aim to predict functional outcomes after ischemic stroke, but they have yet to be summarized in a systematic review. We found 14 scores that predicted functional outcomes (mRS, BI, or GOS) and found substantial variation across these scores in terms of patient population, complexity of predictors used, and risk discrimination performance. Half of the scores included neuroimaging as a predictor. We did not find an appreciable difference in terms of risk discrimination performance between these scores and scores without neuroimaging, although direct comparison is markedly limited due to heterogeneity in both patient population-specific factors (such as acute stroke severity and/or treatment status) and outcomes measured; for instance, ASTRAL discrimination performance was assessed using 3-month mRS > 2, while BOAS discrimination performance was assessed using 9-month mRS > 2. In those scales in which imaging was used, 3 used simple noncontrast head CT to evaluate core infarct extent while 3 used MRI DWI-defined core infarct for prognostication. Of note, only 1 score (HIAT) required the use of perfusion imaging to define MR DWI and MR perfusion mismatch; another score (NAV) requires CT perfusion. No other scores required IV contrast, perfusion-weighted techniques, or other methods besides widely available noncontrast CT and MR DWI. Additionally, while all scores looked at initial imaging, some scores also incorporated follow-up imaging parameters into the analysis leading to further variability and heterogeneity.

Our findings show that clinicians have multiple options for assessing poststroke functioning, but we did not find 1 score that is an obvious choice for all clinical situations. Most of the scores performed well in terms of risk discrimination and have been validated in internal or external populations (although only half of the scores were externally validated). Clinicians might consider the ease of calculating risk when choosing risk scores; the simplest scores are NIHSS alone, sNIHSS-4, and SPAN. Although they involve more inputs than the NIHSS-based scores, ASTRAL, BOAS, iScore, and THRIVE only

require clinical inputs and can be calculated quickly. Patient factors could guide choices among these scores. For instance, ASTRAL was derived from patients with stroke having mRS < 2, while BOAS was derived from more severe patients (mRS < 4). The availability of CT (DRAGON, HAT, HIAT2, NAV [CT perfusion]) versus MRI (MRI-DRAGON, HIAT [MR perfusion], SAD) can guide choices among scores that included imaging predictors.

Our systematic review has several limitations that should be noted. First, we found substantial heterogeneity in terms of patient demographics, stroke severity, and how the scores defined their inputs and outputs as well as how functional outcome was measured. Additionally, some patient populations received no treatment, while others received pharmaceutical treatment and other vascular intervention. Although such heterogeneity introduces bias and makes it difficult to directly compare studies, as mentioned above, this variation could allow clinicians to tailor their choice of risk score for their patient population and the most relevant outcome of interest. Additionally, we could not perform a meta-analysis of risk discrimination performance due to the heterogeneity in risk score inputs and functional outcomes reported. While the majority of studies assessed functional outcome using mRS, some scores used other measures such as BI and GOS, which are themselves inherently different. The BI has been widely used to measure outcomes and is useful for planning rehabilitative strategies as it is a scale that measures 10 basic aspects of activity related to self-care and mobility^{3,37,38}; the mRS assesses disability after stroke by measuring functional independence, incorporating the World Health Organization components of body function, activity, and participation^{3,39,40}; similar to mRS, GOS is another ordered scale to assess outcomes with a key difference compared to mRS being the lack of distinction among patients with good outcomes, since this group encompasses full recovery and mild disability.^{3,41} Furthermore, the mRS measure itself has been shown to have interobserver variability,⁴² which could further compound our analysis. Due to our selection criteria, there are some stroke studies that assessed functional outcome (such as but not limited to NIHSS from TOAST trial,⁴³ NIHSS-time score,⁴⁴ NIHSS-age score,⁴⁵ stroke thrombolytic predictive instrument,⁴⁶ 3-item scale,⁴⁷ six simple variables,⁴⁸ PLAN,⁴⁹ SEDAN⁵⁰) that were excluded as they were either operationalized as a statistical model as opposed to a score/scale that could be calculated at the bedside or they were not evaluated using the AUC/c statistic, but rather with disease association measures (such as odds ratios), which do not capture the full tradeoffs between sensitivity and specificity.

We found many studies (36 full-text papers reviewed, >50 other abstracts screened) that evaluated the use of imaging and clinical prognostic factors for poststroke functioning that were not included in our study because they did not include a score that could be calculated in a clinical setting. This discrepancy (>50 studies but only 7 scores that included neuroimaging) suggests that stroke imaging researchers ought to give more

consideration to incorporating their findings into single, composite risk scores that can be more easily integrated to guide clinical decision-making.

Conclusion

Numerous stroke scales have been developed to predict functional outcome following acute ischemic stroke. There is substantial variation and heterogeneity among these scores in terms of their development and adoptability, including the use of neuroimaging as a predictor of poststroke outcomes. It is unclear whether imaging-based scores should be favored over simpler approaches that do not include imaging for predicting poststroke function, although the appropriate choice of risk score could depend on the treatment status and other patient factors.

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