Austin Journal of Clinical Neurology

Open Access

Austin Publishing Group

Research Article

External Validation of Multiple Intravenous Thrombolysis Prediction Models

Yinglei-Li[1,3], Lingyun-Xi[2], Litao-Li[1]*, Tao-Qie[3], Bing-Dai[3], Shichao-Liu[3] and Feifei-Yu[3]

[1]Department of Hebei Medical University, Shijiazhuang, China

[2]Department of Laboratory Medicine, Chinese People's Liberation Army 82nd Army Group Hospital, Baoding, China

[3]Department of Emergency Medicine, Baoding First Central Hospital, Baoding, China

***Corresponding author: Litao-Li**
Department of Neurology, Hebei Provincial People's Hospital, Shijiia zhuang, China

Received: November 12, 2022; **Accepted:** December 19, 2022**; Published:** December 25, 2022

Abstract

Background and Purpose: ASPECTS, ASTRAL, DRAGON, THRIVE-c and START are predictive models that have been gradually developed in recent years to predict functional outcome after acute stroke in patients treated with intravenous thrombolysis, respectively. We aimed to externally validate these scores to assess their predictive performance in this advanced stroke center in China.

Methods: We examined the clinical data of 835 patients with AIS who were admitted to the emergency department for intravenous thrombolysis at the Advanced Stroke Center, First Central Hospital, Baoding, China, between January 2016 and May 2022, and scored the patients using the five scales. The 3-month modified Rankin Scale scores were observed for each score point, and patients with scores 3 to 6 were defined as having a poor prognosis and compared with the proportions predicted based on risk scores. The ROC curve was used to analyze the predictive value of each score for poor prognosis at 3 months.

Results: Finally, 728 patients were included, and 318 (43.68%) had a poor prognosis. roc curve analysis, the five scores corresponded to C values of 0.851, 0.825, 0.854, 0.809, and 0819 in the overall patients, respectively, and in the pre-circulation 0.853, 0.813, 0.833, 0.804, 0.807, and 0.848, 0.862, 0.909, 0.811, 0.857 in the posterior cycle, respectively (all P> 0.05).

Conclusions: The five scores predicted the 3-month adverse prognostic risk in AIS patients undergoing intravenous thrombolysis in both anterior circulation and posterior circulation lesions, but the DRAGON score had the highest predictive diagnostic value in the posterior circulation.

Keywords: Intravenous Thrombolysis Anterior Circulation and Posterior Circulation Lesions Prognosis Registries Roc Curve Stroke.

Introduction

The annual incidence of ischemic stroke accounts for 14 million, which is about 70-80% of stroke. It is the second leading cause of death worldwide after ischemic heart disease and has a very high disability rate, making it one of the major diseases that seriously threaten human life, health and quality of life [1-3]. In the acute symptoms of ischemic stroke, That is, timely application of tissue-type plasminogen activator intravenous thrombolysis within the time window is the only approved and effective pharmacological treatment and timely intravenous thrombolysis significantly improves the prognosis of patients with acute ischemic stroke [4]. However, A significant proportion of patients, even when treated with intravenous thrombolysis even, they did not fully benefit, and still had complications, left neurological disability, and even bleeding and death [5]. Urgent thrombolysis and beneficial treatment may lead to awesome complications; Entangled in the risk of thrombolysis, itmay delay revascularizationd, resulting in the worsening of the disease itself [6-7]. Therefore, Early prognostic assessment of patients with AIS within the time window of intravenous thrombolytic therapy is very helpful, thus reducing the time delays in patient

Citation: Yinglei-Li, Lingyun-Xi, Litao-Li, Tao-Qie, Bing-Dai, Shichao-Liu, et al. External Validation of Multiple Intravenous Thrombolysis Prediction Models. Austin J Clin Neurol. 2022; 9(2): 1160.

management [8] and preventing more serious complications.

In recent years, there are many studies on predictive models of scoring systems for prognosis of intravenous thrombolysis in patients with AIS [9-16]. The model [17] can predict the long-term prognosis of AIS patients early and accurately, which not only helps Doctors to diagnose and treat, but also can convey prognosis expectations to patients. However, most of the current prediction models have some limitations, for examples, many variables, difficult to obtain, cumbersome calculation, which have not been widely used in modern clinical practice. The establishment and validation [18] of prediction models are usually based on one or several specific cohorts. Small amount of verification in different geographical regions or ethnic groups is the main reasons limiting the application of these models in clinical. So, for the existing prediction model, it is very important to verify its prediction ability and the clinical influence in different areas [19].

Currently found, the ASPECTS, ASTRAL, DRAGON, THRIVE-c, and START models all use simple and easy to obtain available predictors in different ways, but they have the ability to predict clinical application. For the ASPECTS score, not only can the dichotomy of 0 to 7 and 8-10 be used, but also the trichotomous zones of 0-4, 5-7, 8-10 can be used [20-22]. DRAGON [10,23] was consisted of arterial CT high-density signs/early infarct signs, pre-stroke MRS score, age, baseline blood glucose, onset to time of administration OTT and baseline NIHSS score, with a total score of 10, calculated using multivariate logistic regression analysis, including imaging information [23]. ASTRAL [11] it does not require emergency imaging information and consists of six readily available clinical parameters: age, NIHSS score, time from onset to admission DNT, visual field range, blood glucose and level of consciousness [24-25] using multivariate logistic regression analysis. The original THRIVE score [12] was a categorical variable consisting of baseline NIHSS score, age, and chronic disease score (including hypertension, diabetes, and a trial fibrillation) with a total score of 9. And later, so as to predict the prognosis of every individual, the team modified this scoring system by converting the original variables (NIHSS score and age), which were transformed into a dichotomous calculation, the THRIVE-c score [26-27], into a continuous variable. The START [13,28] model were calculated as continuous variables for NIHSS score, age, MRS score (modified Rankin Scales) before this stroke and OTT time (onset-to-treatment time,). All these five models have been validated nationally and internationally as to predict the probability of adverse prognosis at 3 months in patients undergoing intravenous thrombolysis [22-28]. Although the respective variables vary, there is still a small of evidence regarding their respective clinical usefulness and the corresponding comparative validation. The intent of this study was to evaluate the prognostic predictive function of these five models in patients with AIS undergoing intravenous thrombolysis by independent external validation and comparison using patient data from our stroke center.

Research Materials and Methods

The design of this study was all in accordance with the guidelines established in the Declaration of Helsinki. And was approved by the ethics committee of Baoding first central hospital (ethics approval number: 2022-063). This study is a retrospective analysis, including patients with stroke who received intravenous thrombolytic therapy with alteplase in the national high-end stroke center of the first Central Hospital of Baoding city from January 1, 2016 to May 31, 2022.

Inclusion Criteria

(1) Age ≥18 years.

(2) Indication for intravenous thrombolysis.

(3) Obtain informed consent from patient and family and sign.

Exclusion Criteria

(1) Patients receiving further endovascular treatment.

(2) Patients with a final diagnosis of stroke-like disease.

(3) Patients with missing data on predictor variables for ASPECTS, ASTRAL, DRAGON, THRIVE-c and START models.

(4) Patients who were missed during the 3-month follow-up.

The responsible physician decided whether to thrombolyze the patient intravenously by referring to the international guidelines [4-5] at the early time for AIS patients. Patients receiving intravenous thrombolytic therapy were given written informed consent by themselves or their immediate family members. The dose of alteplase treatment was divided into a standard dose (0.9 mg/kg) or a low dose (0.6 mg/kg), and the maximum dose administered was 90 mg.

Research Methods

We retrospectively counted and analyzed the data of AIS patients in the thrombolysis database of the First Central Hospital of Baoding, which was continuously collected. Data collection personnel have been trained in relevant professions. We collected baseline characteristics, vascular risk factors, current and previous stroke severity, clinical examination and experimental examination results, information on current treatment, and so on.

Vascular risk factors include hypertension, coronary artery disease, diabetes mellitus, hyperlipidemia, history of previous stroke, a trial fibrillation, smoking, and alcohol consumption. Stroke severity in stroke patients is assessed by the National Institute of Health stroke scale (NIHSS) score, with the baseline NIHSS score indicating the NIHSS score before thrombolytic administration.

Hypertension [29] diabetes mellitus, coronary artery disease, hyperlipidemia, atrial fibrillation, smoking, and alcohol consumption were defined according to international standards for diagnosis; previous stroke history included previous ischemic stroke, hemorrhagic stroke, and transient ischemic attack history[31].

AIS patients were divided into anterior and posterior circulation groups based on different lesion infarct sites. The etiological diagnosis is based on the classical 1993 TOAST staging proposed by Adams et al. in the USA [32]forlarge artery atherosclerotic type, cardiogenic embolism, small artery occlusion, stroke of other known etiology and stroke of unknown cause.

Predictive Model Scoring Scale

AllAIS patients were scored using the five predictive model scales ASPECTS, ASTRAL, DRAGON, THRIVE-c and START, which were assessed by two senior stroke neurologists, and in case of inconsistent scoring, a third senior physician made the scoring decision.

ASPECTS Scores: Anterior circulation ASPECTS score: 10 regions in 2 levels of the middle cerebral artery blood supply area were selected on CT images.

(1) At the level of the nucleus accumbens (i.e., thalamus and striatum planes), which is divided into 7 regions: anterior cortical region of the middle cerebral artery, lateral cortical region of the insula of the middle cerebral artery, posterior cortical region of the middle cerebral artery, insula, nucleus accumbens, caudate nucleus, and posterior limb of the internal capsule.

(2) The level above the nucleus accumbens (2 cm above the level of the nucleus accumbens), including the middle cerebral artery cortex above the anterior middle cerebral artery cortical area, the middle cerebral artery cortex above the lateral middle cerebral artery insula cortical area, and the middle cerebral artery cortex above the posterior middle cerebral artery cortical area.

The boundary between the two is the head of the caudate nucleus, and any ischemic changes in the caudate nucleus and below are defined as the nucleus accumbens level in cross-sectional CT images, while ischemic changes above the head of the caudate nucleus are defined as the supranucleusaccumbens level.

These 10 regions were given the same weight of 1 point. The number of regions with EIC is subtracted from the score of 10, with a score of 10 indicating a normal CT scan and a score of 0 indicating extensive ischemia in the MCA blood supply area.

pc-ASPECTS scores the posterior circulation into 10 points.

A score of 1 is for the left or right thalamus, cerebellum, or posterior cerebral artery region; a score of 2 is for the midbrain or pontine brain.

ASTRAL Score: Six were included: age, NIHSS score, onset to admission time DNT, visual field range, glucose, and level of consciousness.

DRAGON Score: Six were included: arterial CT hyperdensity sign/early infarct sign, pre-stroke mRS score, age, baseline glucose, onset to time of administration OTT and baseline NIHSS score with a total score of 10.

THIRVE-cscore

The predictors of the model included two continuous variables (baseline NIHSS score, age) and one dichotomous variable, the Chronic Disease Scale (CDS), which was scored as 1 point each for hypertension, diabetes mellitus, and atrial fibrillation.

THRIVE-c model calculation formula (P is the probability of good prognosis):

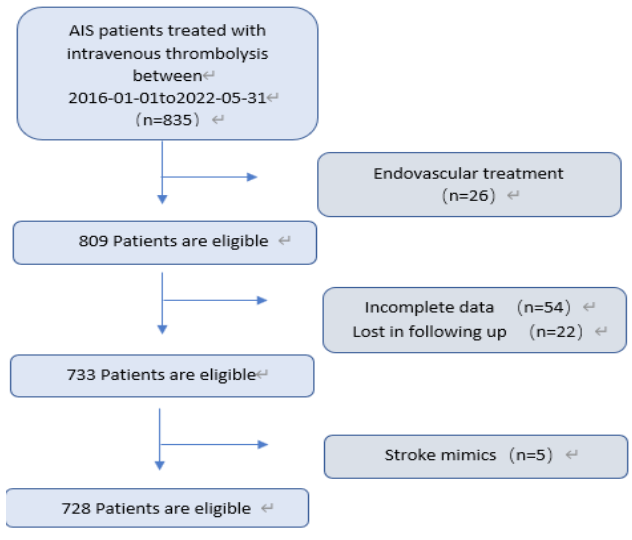

Figure 1: Study Flowchart.

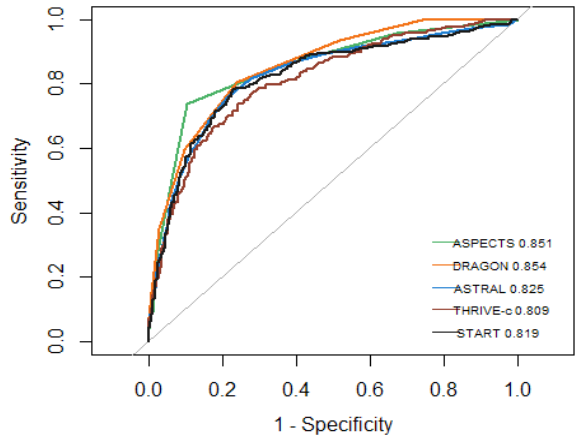

Figure 2: ROC curves for model-predicted 30-day prognosis of ASPECTS, ASTRAL, DRAGON, THRIVE-c and START.

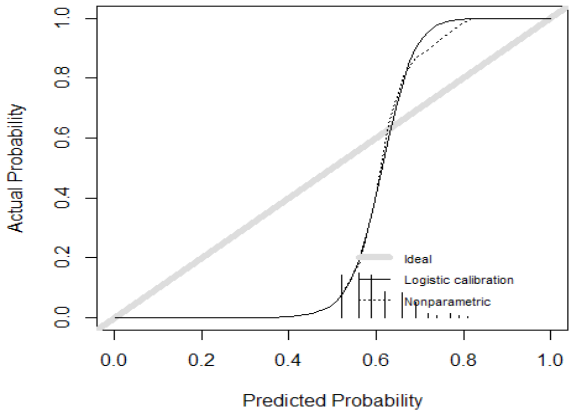

Figure 3: The calibration curve for the ASPECTS score.

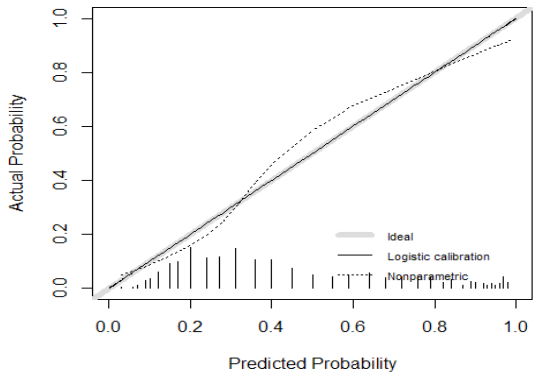

Figure 4: The calibration curve for the ASTRAL score.

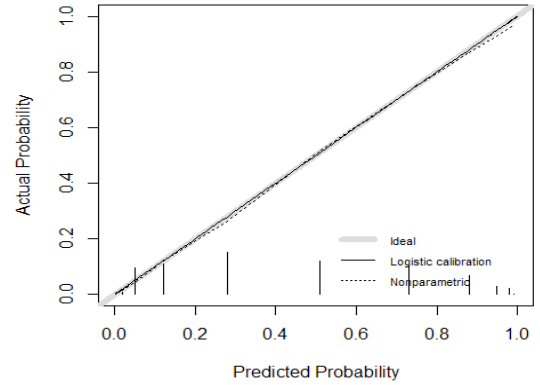

Figure 5: The calibration curve for the DRAGON score.

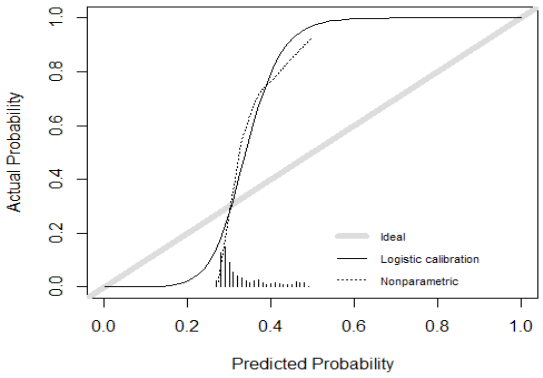

Figure 6: The calibration curve for the THRIVE-c.

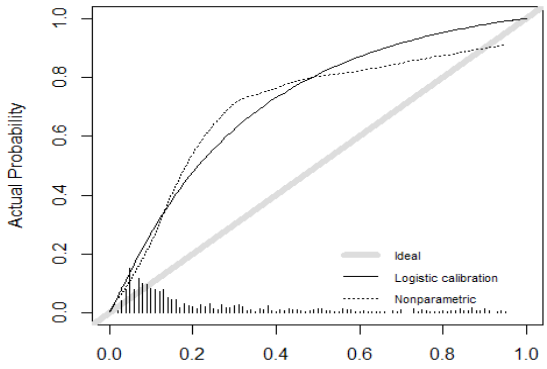

Figure 7: The calibration curve for the START score.

Table 1: Detailed baseline information for the validation cohort population is shown in the table 1.

	Total Queue (N=728)	Good prognosis group (N=410)	Poor prognosis group (N=318)	Z/χ^2	*P*
Age, [median, *M(Q)*]	66 (17)	64 (16)	66 (18)	-2.928	0.003*
Female (female/male)	245/483	130/280	115/203	1.593	0.207
Height[cm, *M(Q)*]	170 (11)	170 (11)	170 (11)	-0.174	0.862
Weight[kg, *M(Q)*]	70.00 (18)	70.00 (15.00)	70 (18)	-1.341	0.180
BMI *M(Q)*	24.97 (4.83)	25.26 (4.54)	24.55 (5.00)	-1.47	0.142
Smoke, n(%)	341 (46.97%)	204 (49.89%)	137 (43.22%)	3.180	0.075
Drinking, n(%)	236 (32.42%)	148 (36.19%)	88 (27.67%)	5.193	0.015*
Pre-cycle and post-cycle					
Pre-cycle, n(%)	553(75.96%)	296(72.2%)	257(80.8%)	7.292	0.007*
post-cycle, n(%)	175(24.04%)	114(27.8%)	61(19.2%)		

*$P<0.05$, The difference was statistically significant.

$$P = 1/e^{\left(\begin{array}{c}-(4.94+(-0.035*age)+(-0.19*NIHSS)+(-0.11*CDS1)+\\(-0.41*CDS2)+(-0.70*CDS3)\end{array}\right)}$$

3.4.4 START Score: Predictors of the model included baseline NIHSS score, age, mRS score before the current stroke and onset-to-treatment time (OTT).

START model calculation formula (P is the probability of poor prognosis).

$$Log\left[\frac{p(X)}{1}-p(X)\right]=-5.15+(0.429*pre-stroke\ mRS)+\left(\begin{array}{c}(0.188*NIHSS)+(0.030*age)+(0.002*OTT\end{array}\right)$$

$$P = 1/e^{\left(\begin{array}{c}-5.15+(0.429*pre-stroke\ mRS)+(0.188*NIHSS)+\\(0.030*age)+(0.002*OTT\end{array}\right)}$$

Ending events and follow-up

The evaluation index was a 3-month poor functional prognosis, evaluated by the mRS score, obtained by a 3-month face-to-face visit or telephone follow-up [33].

The mRS score [34-35] was evaluated as follows.

A score of 0 indicates complete absence of symptoms.

A score of 1 indicates no significant functional impairment despite symptoms and no assistance with daily living.

A score of 2 indicates a mild disability, unable to perform all previous tasks and activities, but able to manage personal matters without assistance from others.

A score of 3 indicates a moderate disability, requiring some assistance but walking without assistance

A score of 4 indicates a severe disability, unable to walk without the help of others and unable to care for his or her own physical needs

A score of 5 indicates severe disability, bedridden, incontinent and requiring constant care and attention

A score of 6 is death.

The mRS score of 0-2 in this study was defined as a good functional prognosis, and the mRS score of 3-6 was defined as a poor functional prognosis, which is consistent with the definition of the original study that developed these models.

Statistical Methods

For continuous variables in this study, we first evaluated the normality of the data using the Kolmogorov-Smirnov test. Those that conformed to a normal distribution were expressed as mean ± standard deviation, non-normally distributed continuous variables were expressed as median, and categorical variables were expressed as frequency and percentage. The t-test was used to make two-by-two comparisons for continuous-type variables conforming to a normal distribution, the Mann-Whitney U-test for variables with a non-normal distribution, and the chi-square test for categorical variables.

The ASPECTS, ASTRAL, and DRAGON models predicted 3-month adverse prognosis of AIS patients using respective scales, and the probabilities of the THRIVE-c and START models were calculated using their respective logistic formulas. Model

Table 2: Comparison of the predictive factors and prognostic distribution of the validation cohort with the original cohort for model building.

	ASPECTS			ASTRAL			DRAGON			START			HTRIVE-c		
Baseline Parameter	Mean or Proportion, %			Mean or Proportion, %			Mean or Proportion, %			Mean or Proportion, %			Mean or Proportion, %		
	Validation Cohort (N=728)	Original Cohort(N=156)	P Value	Validation Co-hort (N=728)	Original Cohort(N=1645)	P Value	Validation Cohort(N=728)	Original Cohort(N=1319)	P Value	Validation Cohort (N=728)	Original Cohort (N=10574)	P Value	Validation Cohort(N=728)	Original Cohort(N=6194)	P Value
Age, y	65	68	-	63.42	68.2	-	65	69(60-77)	-	65	71		65	70(60-76)	
sex(women)	33,70%	46.15%	<0.001	33.70%	42.80%	<0.001	33.70%	44.70%	<0.001	-	-		33.70%	42.50%	<0.001
NIHSS at baseline	-	-	-	7.48	8.9	-	5	9(5-14)	-	5	11		5	12(8-17)	
Visual field defect	-	-	-	0.40%	32.50%	<0.001	-	-	-	-	-			/	
Alertness	-	-	-	23.40%	88.90%	<0.001	-	-	-	-	-			/	
OTA,min	-	-	-	55.62	395.8	-	-	-	-	-	-			/	
Early infarct signs	79.67%	75%	<0.001	79.67%	-	-	79.67%	30.60%	<0.001	-	-			/	
Dense vessel	-	-	-	99.60%	-	-	99.60%	17.70%	<0.001	-	-			/	
OTT, min	-	-	-	137.78	-	-	133	118(88-158)	-	133	160			/	
Glucose, mmol/L	-	-	-	8.09	7.1	-	6.85	6.6(5.7-7.8)	-	-	-			/	
Systolic BP,mmHg	-	-	-	146.61	158.9	-	145	156(140-171)	-	-	-			/	
Diastolic BP,mmHg	-	-	-	81.77	96.9	-	85	83 (74-92)	-	-	-				
Hypertension	-	-	-	62.90%	-	-	62.90%	59.70%	0.15	-	-		62.90%	66.10%	0.087
DM	-	-	-	23.30%	-	-	23.30%	14.50%	<0.001	-	-		23.30%	19.30%	0.011
Hyperlipidemia	-	-	-	1.20%	-	-	1.20%	39.10%	<0.001	-	-			/	
Previous stroke	-	-	-	13.20%	-	-	13.20%	12.70%	0.771	-	-			/	
Atrial fibrillation	-	-	-	12.70%	-	-	12.70%	27.70%	<0.001	-	-		12.70%	24.60%	<0.001
Proportions of 3-mo outcome, mRS score,%															
3-6	43.68%	51.9%	<0.001	43.68%	34%	<0.001	-	39.50%	0.66	43.70%	39.10%	0.014	43.70%	50.30%	<0.001
0-2	56.32%	48.1%	<0.001	56.32%	66%	<0.001	-	60.50%	0.66	-	-		56.30%	49.70%	<0.001
3-4	-	-	-	23.20%	-	-	-	25.7	-	-	-				
5-6	-	-	-	20.50%	-	-	-	13.8	-	-	-				

*$P<0.05$, The difference was statistically significant.

Table 3: Predictors of the model of ASPECTS, ASTRAL, DRAGON, THRIVE-c, START.

		Optimal cut-off value	Sensitivity (%)	Specificity (%)	Yoden Index	AUC (95%CI)
Overall data	ASPECTS	7.5	89.5	73.6	0.631	0.851 (0.822,0.879)
	ASTRAL	19.5	78.8	75.8	0.546	0.825 (0.794,0.856)
	DRAGON	4.5	76.1	80.5	0.566	0.854 (0.828,0.880)
	THRIVE-c	-	75.6	73.6	0.492	0.809 (0.688,0.762)
	START	-	77.1	78.3	0.554	0.819 (0.787,0.851)
Pre-Cycle	ASPECTS	7.5	90.2	73.9	0.639	0.853 (0.822,0.885)
	ASTRAL	19.5	78	75.5	0.535	0.813 (0.776-0.850)
	DRAGON	4.5	72.6	80.5	0.531	0.833 (0.800-0.865)
	THRIVE-c	-	69.3	79.4	0.487	0.804 (0.767,0.840)
	START	-	76	78.2	0.542	0.807 (0.769,0.844)
Post-Cycle	ASPECTS	7.5	87.7	72.1	0.598	0.848 (0.876-0.910)
	ASTRAL	19.5	80.7	77	0.577	0.862 (0.803,0.921)
	DRAGON	4.5	85.1	80.3	0.654	0.909 (0.865-0.953)
	THRIVE-c	-	87.7	67.2	0.549	0.811 (0.743,0.885)
	START	-	86.8	73.8	0.606	0.857 (0.794,0.919)

Table 4: Hosmer-Lemeshow goodness-of-fit test for ASPECTS, ASTRAL, DRAGON, THRIVE-c, and START models.

		χ^2	*P*
Overall data	ASPECTS	57.881	<0.001
	ASTRAL	28.641	0.000365
	DRAGON	1.5119	0.8245
	THRIVE-c	181.03	<0.001
	START	278.81	<0.001
Pre-Cycle	ASPECTS	46.043	<0.001
	ASTRAL	21.857	0.005187
	DRAGON	8.1584	0.4182
	THRIVE-c	150.49	<0.001
	START	27.921	<0.001
Post-Cycle	ASPECTS	26.622	0.000821
	ASTRAL	8.9067	0.3502
	DRAGON	4.9352	0.7645
	THRIVE-c	41.305	<0.001
	START	27.921	<0.001

performance was evaluated in two ways: discrimination and calibration. The discrimination reflects the ability of the prediction model to discriminate between the occurrence and non-occurrence of outcome events, as assessed by the area under the receiver operating characteristic curve (AUROC). Good discriminative ability, and 1.0 indicates perfect discriminative ability [36]. Calibration refers to the agreement between the risk of occurrence of an outcome event predicted by the model and the probability of the actual observed outcome event, and this study used two indicators, calibration curve and Brier score, to evaluate the calibration of the model. The calibration curve was plotted based on the probability of predicted adverse prognosis and the probability of actual observed adverse prognosis, and the closer the curve was to a 45° straight line, the better the calibration of the model. The Hosmer-Lemeshow (H-L) goodness-of-fit [$\chi 2$ (*P*)] was applied to test the fit of each evaluation model to the actual outcome, and *P*> 0.05 suggested that the model was a good fit to the actual outcome. The lower the Brier score, the better the model calibration is indicated. In addition, because the Brier score can quantitatively evaluate the accuracy of the model, it can be used to compare the predictive ability of five models. Statistical analyses in this study were performed in R (Version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria), and a two-sided $P \leq 0.05$ was considered statistically different.

Results

Baseline Information of the Validation Cohort

A total of 835 patients with AIS treated with intravenous thrombolysis with alteplase were screened, of whom 107 were excluded. Of the excluded patients, 26 received bridging therapy, 54 had incomplete data, 22 were lost to follow-up, and 5 were diagnosed with stroke-like disease. The patient screening process is shown in Figure 1. Finally, we included data from 728 patients for statistical analysis.

The median age of the final included patients was 66 years, of which 245 (33.65%) were female patients and 96 patients (13.2%) had a previous history of stroke. The median baseline NIHSS score was 5, and the median onset-to-dose time was 133 min. 90.8% of patients received standard dose (0.9 mg/kg) intravenous thrombolysis with alteplase, and 9.2% received a low dose (0.6 mg/kg) of alteplase. The other 9.2% used a low dose (0.6 mg/kg) of alteplase. After thrombolytic therapy, 37 (5.08%) patients experienced bleeding conversion, and at 3-month follow-up, 318 patients (43.68%) had a poor functional prognosis. The difference in age was statistically significant between the good prognosis groups compared to the poor prognosis group, with a higher age level of 66 years in the poor prognosis group. The difference in drinking status between the two groups was statistically significant. The differences between the two groups of patients in the anterior and posterior circulation were statistically significant. Detailed baseline information for the validation cohort population is shown in the (Table 1).

Comparison of the Validation Queue with the Original Queue for Model Construction

We compared the predictors of the validation cohort with the predictors of each score and model, as shown in Table 2.

The mean of age in the validation cohort was 63.42, 33.70% female, and the mean of blood glucose was 8.09. The validation cohort had a relatively small percentage of females. The validation cohort had a lower proportion of poor MRS compared to the ASPECTS cohort, and the difference was statistically significant. The validation cohort had a higher proportion of poor MRS compared to the ASTRAL cohort, with a statistically significant difference and fewer visual field deficits. The differences in gender, early infarcts, diseased vessels, diabetes mellitus, hyperlipidemia, and atrial fibrillation were statistically significant in the validation cohort compared with the DRAGON group. The validation cohort had a higher proportion of poor MRS compared to the STRAT group, and the difference was statistically significant. The differences in the validation cohort compared with the HTRIVE-c group were statistically significant for gender, atrial fibrillation, and percentage of poor MRS.

Optimal Cutoff Values for Each Score, Model, and Discrimination Index

As shown in Table 3, the best cutoff value for the ASPECTS score in the overall data was 7.5, with an AUC value of 0.851 (0.822, 0.879) and the highest sensitivity of 89.5% among the five scores and models; the best cutoff value for the ASTRAL score was 19.5, with an AUC value of 0.825 (95% CI, 0.794, 0.856), the sensitivity was 78.8% and the specificity was 75.8%. Among the discrimination indexes, the DRAGON score had the largest AUC value of 0.854 (0.828, 0.880) and the largest specificity of 80.5%. The best cutoff value of ASPECTS score in the former cycle was 7.5, and the maximum AUC value was 0.853 (0.822, 0.885), with the highest sensitivity of 90.2% among the five scores and models; the best cutoff value of ASTRAL score was 19.5, and the AUC value was 0.813 (0.776-0.850), with the sensitivity of 78.0% and the specificity of 75.5%. Among the discrimination indexes, the AUC value of DRAGON score was 0.833 (0.800-0.865), and the specificity was the largest at 80.5%. The best cutoff value for the ASPECTS scores in the posterior cycle was 7.5, with an AUC value of 0.848 (0.876-0.910) and the highest sensitivity of 87.7% among the five scores and the THRIVE-c model; the best cutoff value for the ASTRAL score was 19.5, with an AUC value of 0.862 (0.803, 0.921) and a sensitivity of 80.7%, and the specificity was 77.0%. Among the differentiation indexes, the DRAGON score had a maximum AUC value of 0.909 (0.865-0.953) and a maximum specificity of 80.3%.

As shown in Figure 2, the ROC curves of the scoring models were relatively close. Among them, the area under the DRAGON curve is the largest and the area under the THRIVE-c scoring curve is the smallest.

Calibration Degree Evaluation for Each Score, Model In the Validation Cohort

The Calibration curve is used to evaluate the calibration of the prediction model. The ideal calibration curve is a curve with an intercept of 0 and a slope of 1 (Table 4).

It can be seen that the DRAGON score is well calibrated in the validation model, and the prediction model predicts the prognosis with good agreement with the actual probability.

The calibration curves (Figure 3-7) show that the ASPECTS score, THRIVE-c, and START models have a large gap from the middle diagonal and average calibration.

The Brier scores, 0.2406, 0.0264, 0.1691, 0.2938, and 0.2266 for ASPECTS, ASTRAL, THRIVE-c, DRAGON, and START, respectively.

Discussion

The AUROC of the ASPECTS, ASTRAL, DRAGON, THRIVE-c, and START models for predicting 3-month adverse prognosis in our cohort of patients receiving intravenous thrombolysis for AIS was found to be in the acceptable good range for differentiating patients with a 3-month adverse prognosis. The difference did not reach a statistically significant level, however. In addition, although all five had acceptable predictive discrimination, analysis of their pair wise calibration showed that only the DRAGON score model was well calibrated and the accuracy of the remaining four models in predicting prognosis was less than optimal. The discrimination reflects the ability of the prediction model to distinguish between the occurrence and non-occurrence of outcome events; if a model has good discrimination, it can correctly distinguish patients with a high incidence of outcome events from those with a low incidence, focusing on the classification of groups of patients. Calibration refers to the agreement between the risk of occurrence of an outcome event predicted by the model and the actual observed probability of occurrence of the outcome event, i.e., the accuracy of predicting the probability of occurrence of an outcome event in a given individual. An ideal prediction model should have both discrimination and calibration. In this study, we found that the five models had fairdiscrimination in predicting the 3-month adverse prognosis of AIS patients, but the models, except DRAGON, were poorly calibrated, suggesting that they are insufficient to provide accurate information about the likelihood of adverse prognosis at 3 months for individual patients and are difficult to use as a tool to guide clinical AIS patient treatment decisions [38]. This study is the first domestic and international study to validate five models simultaneously as well as to perform simultaneous pre- or post-loop classification validation. The aspects [9] scoring entity model was introduced in 2000. The very beginning, it was based on the results of preoperative head CT examination of 117 patients. This patient received intravenous thrombolytic therapy for internal reasons of middle cerebral artery supply area infarction within 3 hours after the onset of the disease in two teaching hospitals in North America, only involving the CT examination results. In the subsequent experiments, it was found that the actual effect of aspects score of AIS patients was basically very different from the NIHSS score used in clinical medicine. In 2008 [39] Kimura K et al. Clearly proposed in Okayama, Japan that DWI level reliably predicted improper conclusions within 3 hours after the onset of venous thrombolysis, and DWI level ≤ nezu t et al [40] found that baseline DWI level ≥ 7 was related to better clinical medical conclusions (*OR*= 1.85; 95% confidence interval: 1.07 to 3.24), The aspect is related to death (*OR*= 3.61; 95% confidence interval: in 2011, nezu t et al. [41] Further found that for patients with hyperacute stroke, dwi-aspects score is about 1 point lower than ct-aspects. Aspects is a useful predictor of symptomatic cerebral hemorrhage and consciousness 3 months after the recombining of institutional fibrin chaperone. In recent years, Cheng x, Su x [42] et al. Will base on deep learning (Edwi aspect) The DWI Alberta cerebral apoplexy advocate initial computed tomography score calculated by the automated technical tool software of the compared with the evaluation of acute apoplexy by neurology emergency department doctors, and found that the evaluation of Edwi was the same as that of senior neurology emergency department doctors. Although the uncertainty scoring rules and the influence of the center line movement cause weak to moderate consistency in M5, internal capsule and caudate nucleus regions. Sakai K et al. [43] found

in the experiment of intravascular therapy of the nervous system in Japan that according to the DWI interpretation of the join Smartphone Application and the DWI interpretation of the application platform PC monitor, the application of the smartphone application allows capillary neurologists to add .The diagnosis and treatment intelligent mobile phone application shows the huge market prospect of acute stroke management methods. Aspects score [44] has a high predictive analysis value for the recovery of patients with anterior and posterior circulation AIS patients after intravenous thrombolysis. It has been certified in China and other countries in the world.

The ASTRAL score [11] was developed in 2010 by Patrikk, a Swiss scholar, to predict the prognosis at 3 months after acute ischemic stroke by combining the patient's age, time from onset to admission, NIHSS score, blood glucose in the acute phase, visual field range deficit, and impaired level of consciousness, and does not require cranial imaging findings, making the scale much more useful. The ASTRAL score was first validated in China by Liu G [45] in 2013 as a reliable tool for predicting adverse outcomes at 3 and 12 months after AIS. 2013 Papavasileiou V et al [24] validated the ASTRAL score in the Athens Stroke Registry as a reliable predictor of 5-year functional prognosis and mortality in patients with acute ischemic stroke. In 2015 Vanacker [46] et al. developed the ASTRAL-R score in a cohort of patients from four stroke centers in Switzerland to predict 24-hour revascularization in patients undergoing intravenous thrombolysis, with 5 variables and a total score of 6 points, including 1 point each for glucose >7 mmol/l, severe extracranial stenosis, large artery occlusion,and visual field defects, and 2 points for reduced level of consciousness. A score of 2 was assigned to reduced level of consciousness. The Dragon [10] score (high-density artery, Mrs, age, blood sugar value, effect to treatment and NIHSS) was formulated in Germany in 2012. The predicted independent variables include high-density artery relative density / clinical symptoms of initial infarction, Mrs score before stroke, age, baseline blood sugar value, time from onset to use and baseline NIHSS score. In 2013, strbian d [23] and others found that in the innovative information of 12 stroke cores in Germany, Germany, Switzerland, Italy and Spain that continuously accept intravenous thrombolysis for the treatment of cerebral ischemic stroke, dragon score is well represented in the large collaborative sequence of anterior and posterior circulation stroke. In 2015, Zhang x [47] and others found that in China, the Dragon score showed a good predictive effect after the operation of institutional plasminogen chaperone protein. In order to use dragon for patients with MRI examination as baseline imaging data information, Turc [48] et al. Replaced the sign of high density of middle cerebral artery on CT with MRA proximal middle cerebral artery occlusion in France, and replaced the sign of initial infarction on CT with DWI ≤ 5 points in 2013. Other independent variables are saved. The total area under the ROC curve predicted by mri-dragon score for poor prognosis in AIS three months after intravenous thrombolysis was 0.83, which was higher than the Dragon score based on CT. In 2014 [49] Turc g et al. Of France clearly proposed and proved that mri-dragon score predicted the recovery of subacute cerebral ischemic stroke patients after receiving MRI treatment for 3 months after intravenous thrombolysis (IV tPA). 2020 lesenne a [50] et al found that ct-dragon score was used to predict the long-term effect of anterior circulation and posterior circulation after subacute stroke.

Thrive[12]score was formulated by flint et al in 2010 for patients with cerebral embolism (meci) and mechanical venous thrombosis elimination in multi meci experiments, which is composed of baseline NIHSS score, age and chronic disease score (including patients with high blood pressure, diabetes and atrial fibrillation). In the traditional thrive scoring system, NIHSS scores and age, which were continuous variables at the beginning, are converted into classification variables, and the risk of poor prognosis is determined by measuring the total score of each predictor. Thrive-c [27] model is a modification of the existing thrive score. This model converts all predictors into continuous variables and establishes a logical equation to accurately estimate the possibility of poor prognosis of individual patients in clinical treatment. Predicting the short-term or long-term adverse prognosis of AIS before and after the cycle time has the same prediction effect.

The START [13] model, developed and validated in 2018 from a national multicenter cohort in Italy (SITS-ISTR), consists of four non-categorical predictors (baseline National Institutes of Health (NIH) Stroke Scale score: 0-25, age 18 years, onset to treatment time: 0- 270 minutes and pre-stroke modified Rankin Scale score: 0-2,), can reliably predict the probability of poor prognosis in stroke patients receiving intravenous thrombolytic therapy. Also, the authors compared the START model with the DRAGON and ASTRAL models, both of which had higher predictive power (AUROC) than these two models.2019 Song B [28] et al. validated in China found that the START nomogram is a reliable and simple clinical tool to predict unfavorable.

Although all five models had acceptable AUROC values in distinguishing patients with different outcomes, the ideal calibration was not obtained when the five models were applied to our patient cohort. We guess the following possibilities. First, the most important factor may be the difference in the distribution of predictors and outcomes between the model building cohort and the prediction cohort, i.e., the case-mix effect [53]. Therefore, we compared the distribution of predictors and outcomes between the validation cohort and the original cohort. The proportion of patients with a 3-month adverse prognosis also differed. The distribution of predictors not included in the original prognostic model was also part of the impact of the case-mix. Second, studies have shown that more patients in Asia use 0.6 mg/kg alteplase [54]. In the cohort of this study, 67 (9.2%) patients used used low-dose alteplase, and the difference in the proportion of patients using low-dose alteplase may also be an important influencing factor. However, it is the difference in characteristics between the external validation cohort and the model development cohort that allows for validation of the generalizability of the model, and if the patient characteristics are extremely similar to those of the development model, it only reflects whether the predictive model is reproducible. In addition, the passage of time and changes in clinical practice, such as changes in current guidelines, patient management, and the increasing proportion of patients receiving endovascular therapy, may be another influencing factor on the predictive power of the model. Therefore, prediction models need to be continuously updated and improved to adapt to changes in clinical practice for better application and clinical service [55]. In addition to prediction accuracy, there are other influencing factors on whether a prognostic model can be applied in the clinic, such as convenience and validity in clinical practice, especially in the environment where AIS revascularization treatment is a matter of seconds. As a good early prognostic model, predictor variables need to be easily accessible and reliable, and the number of predictor variables should be minimized to facilitate clinical application. Models that are

overly complex or include variables that cannot be routinely used in emergency situations (e.g., complex neuroimaging parameters) will be limited in their clinical use, even if they have perfect predictive power [56]. In this regard, ASPECTS requires only imaging information, DRAGON requires a combination of imaging, other explicit variables of the patient, and explicit variables in ASTRAL, THRIVE-c model, and START model, and does not require imaging information in the acute phase. This study is the first national and international study to compare three types of models simultaneously: imaging score alone, inclusion of imaging model, and exclusion of imaging information. The current study has some limitations. First, because our validation data came from a single database of stroke centers with a single sample source, the results are not representative of the entire Chinese population. Further external validation of the five model types using multicenter observations from more geographic regions is needed. Secondly, some patients were followed up by telephone, which may bias the results in part, and future studies should evaluate patients in the field as much as possible to reduce the bias of follow-up information. The amount of missing data (3.02%) from the final 3-month MRS follow-up may have influenced the study results.

In summary, this study confirmed the validity of the ASPECTS, ASTRAL, DRAGON, THRIVE-c and START scoring models in predicting the prognosis of patients with AIS 90 d after intravenous thrombolytic therapy by ROC curve analysis, and also compared the differences between the five prediction models, and validated the differences between the five prediction models from the pre- and post-loop subgroups. The DRAGON score was found to be more effective than the other four groups in predicting the prognosis of AIS patients at 90 d after intravenous thrombolytic therapy. In addition, all five model scores could be used for the predictive assessment of 90-d prognosis after intravenous thrombolysis in AIS patients in the anterior and posterior cycles. In the anterior cycle, ASPECTS was better than the other four groups in predicting 90-d prognosis after intravenous thrombolysis in patients with AIS. In the post-loop, the DRAGON model score was better than the other four groups in predicting the 90-d prognosis after intravenous thrombolytic therapy in patients with AIS. Our validation study found that the calibration of the remaining four models, except for the DRAGON model, was less than optimal. More studies are needed in the future to validate the performance ability of these five models in more cohorts and further model optimization to propose simpler models suitable for prehospital healthcare workers' prediction [57].

Conclusions

All five score prediction models, ASPECTS, ASTRAL, DRAGON, THRIVE-c, and START, predicted 3-month adverse prognostic risk in patients with AIS treated with intravenous thrombolysis in both anterior and posterior circulation lesions, but the DRAGON score had the highest predictive diagnostic value in the posterior circulation. the probability of the DRAGON score predicting prognosis in the prediction models was in better agreement with the actual probability was in good agreement, and the calibration of the remaining four prediction models was less than ideal.

Conflicts of Interest

The authors declare no conflict of interests pertinent to this study. There is no conflict of interests to be declared.

References

1. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. Int J Stroke. 2022; 17: 18-29.
2. Jolugbo P, Ariëns RAS. Thrombus Composition and Efficacy of Thrombolysis and Thrombectomy in Acute Ischemic Stroke. Stroke. 2021; 52: 1131-1142.
3. Chen Y, Wright N, Guo Y, Turnbull I, Kartsonaki C, et al. Mortality and recurrent vascular events after first incident stroke: a 9-year community-based study of 0•5 million Chinese adults. Lancet Glob Health. 2020; 8: e580-e590.
4. Psychogios K, Tsivgoulis G. Intravenous thrombolysis for acute ischemic stroke: why not? CurrOpin Neurol. 2022; 35: 10-17.
5. Lees KR, Bluhmki E, von Kummer R, Brott TG, Toni D, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. Lancet. 2010; 375: 1695-703.
6. Mazya M, Egido JA, Ford GA, Lees KR, Mikulik R, et al. Predicting the risk of symptomatic intracerebral hemorrhage in ischemic stroke treated with intravenous alteplase: Safe Implementation of Treatments in Stroke (SITS) symptomatic intracerebral hemorrhage risk score. Stroke. 2012; 43: 1524-1531.
7. Coutts SB, Yu AYX. Tenecteplase for acute stroke: the thrombolysis puzzle. Lancet Neurol. 2022; 21: 496-497.
8. Wardlaw JM, Murray V, Berge E, Del Zoppo G, Sandercock P, et al. Recombinant tissue plasminogen activator for acute ischaemic stroke: An updated systematic review and meta-analysis. Lancet. 2012; 379: 2364–2372.
9. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet. 2000; 355: 1670-4.
10. Strbian D, Meretoja A, Ahlhelm FJ, Pitkäniemi J, Lyrer P, et al. Predicting outcome of IV thrombolysis-treated ischemic stroke patients: the DRAGON score. Neurology. 2012; 78: 427-32.
11. 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; 78: 1916-22.
12. Flint AC, Cullen SP, Faigeles BS, Rao VA. Predicting long-term outcome after endovascular stroke treatment: the totaled health risks in vascular events score. AJNR Am J Neuroradiol. 2010; 31: 1192-1196.
13. Cappellari M, Turcato G, Forlivesi S, Bagante F, Cervellin G, et al. The START nomogram for individualized prediction of the probability of unfavorable outcome after intravenous thrombolysis for stroke. Int J Stroke. 2018; 13: 700-706.
14. Kim YD, Nam HS, Yoo J, Park H, Sohn SI, et al. Prediction of Early Recanalization after Intravenous Thrombolysis in Patients with Large-Vessel Occlusion. J Stroke. 2021; 23: 244-252.
15. Wang F, Huang Y, Xia Y, Zhang W, Fang K, et al. Personalized risk prediction of symptomatic intracerebral hemorrhage after stroke thrombolysis using a machine-learning model. Ther Adv Neurol Disord. 2020; 13: 1756286420902358.
16. Fiehler J, Thomalla G, Bernhardt M, Kniep H, Berlis A, et al. ERASER. Stroke. 2019; 50: 1275-1278.
17. Whiteley WN, Thompson D, Murray G, Cohen G, Lindley RI, et al. Targeting recombinant tissue-type plasminogen activator in acute ischemic stroke based on risk of intracranial hemorrhage or poor

functional outcome: an analysis of the third international stroke trial. Stroke. 2014; 45: 1000-6.

18. Rosso C, Lamy JC. Prediction of motor recovery after stroke: being pragmatic or innovative? Curr Opin Neurol. 2020; 33: 482-487.

19. Rosso C, Lamy JC. Prediction of motor recovery after stroke: being pragmatic or innovative? Curr Opin Neurol. 2020; 33: 482-487.

20. Demchuk AM, Hill MD, Barber PA, Silver B, Patel SC, et al. Importance of early ischemic computed tomography changes using ASPECTS in NINDS rtPA Stroke Study. Stroke. 2005; 36: 2110-5.

21. Yoo AJ, Zaidat OO, Chaudhry ZA, Berkhemer OA, González RG, et al. Impact of pretreatment noncontrast CT Alberta Stroke Program Early CT Score on clinical outcome after intra-arterial stroke therapy. Stroke. 2014; 45: 746-51.

22. Puetz V, Sylaja PN, Coutts SB, Hill MD, Dzialowski I, et al. Extent of hypoattenuation on CT angiography source images predicts functional outcome in patients with basilar artery occlusion. Stroke. 2008; 39: 2485-90.

23. Strbian D, Seiffge DJ, Breuer L, Numminen H, Michel P, et al. Validation of the DRAGON score in 12 stroke centers in anterior and posterior circulation. Stroke. 2013; 44: 2718-21.

24. Papavasileiou V, Milionis H, Michel P, Makaritsis K, Vemmou A, et al. ASTRAL score predicts 5-year dependence and mortality in acute ischemic stroke. Stroke. 2013; 44: 1616-20.

25. Cooray C, Mazya M, Bottai M, Dorado L, Skoda O, Toni D, Ford GA, Wahlgren N, Ahmed N. External Validation of the ASTRAL and DRAGON Scores for Prediction of Functional Outcome in Stroke. Stroke. 2016 Jun;47(6):1493-9.

26. Flint AC, Faigeles BS, Cullen SP, Kamel H, Rao VA, et al. THRIVE score predicts ischemic stroke outcomes and thrombolytic hemorrhage risk in VISTA. Stroke. 2013; 44: 3365-9.

27. Flint AC, Rao VA, Chan SL, Cullen SP, Faigeles BS, et al. Improved ischemic stroke outcome prediction using model estimation of outcome probability: the THRIVE-c calculation. Int J Stroke. 2015; 10: 815-21.

28. Song B, Chen X, Tang D, Ibrahim M, Liu Y, et al. External Validation of START nomogram to predict 3-Month unfavorable outcome in Chinese acute stroke patients. J Stroke Cerebrovasc Dis. 2019; 28: 1618-1622.

29. Lei C, Wu B, Liu M, Chen Y, Yang H, et al. Totaled health risks in vascular events score predicts clinical outcomes in patients with cardioembolic and other subtypes of ischemic stroke. Stroke. 2014; 45: 1689–1694.

30. Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults. Chinese guidelines on prevention and treatment of dyslipidemia in adults. Zhonghua Xin Xue Guan Bing Za Zhi. 2007; 35: 390–419.

31. Liao S, Wu N, Gong D, Tang X, Yin T, Zhang H, Li X. Association of aldehydes exposure with obesity in adults. Ecotoxicol Environ Saf. 2020; 201: 110785.

32. Adams HJ, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993; 24: 35–41.

33. Saarijärvi M, Bratt EL. When face-to-face interviews are not possible: tips and tricks for video, telephone, online chat, and email interviews in qualitative research. Eur J Cardiovasc Nurs. 2021; 20: 392-396.

34. Wilson JT, Hareendran A, Grant M, Baird T, Schulz UG, et al. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. Stroke. 2002; 33: 2243-6.

35. Nguyen TN, Abdalkader M, Nagel S, Qureshi MM, Ribo M, et al. Noncontrast Computed Tomography vs Computed Tomography Perfusion or Magnetic Resonance Imaging Selection in Late Presentation of Stroke With Large-Vessel Occlusion. JAMA Neurol. 2022; 79: 22-31.

36. Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. JAMA. 1994; 271: 703-7.

37. Redelmeier DA, Bloch DA, Hickam DH. Assessing predictive accuracy: how to compare Brier scores. J Clin Epidemiol. 1991; 44: 1141-6.

38. Gallagher CA, Chudzinska M, Larsen-Gray A, Pollock CJ, Sells SN, et al. From theory to practice in pattern-oriented modelling: identifying and using empirical patterns in predictive models. Biol Rev CambPhilos Soc. 2021; 96: 1868-1888.

39. Kimura K, Iguchi Y, Shibazaki K, Terasawa Y, Inoue T, et al. Large ischemic lesions on diffusion-weighted imaging done before intravenous tissue plasminogen activator thrombolysis predicts a poor outcome in patients with acute stroke. Stroke. 2008; 39: 2388-91.

40. Nezu T, Koga M, Kimura K, Shiokawa Y, Nakagawara J, et al. Pretreatment ASPECTS on DWI predicts 3-month outcome following rt-PA: SAMURAI rt-PA Registry. Neurology. 2010; 75: 555-61.

41. Nezu T, Koga M, Nakagawara J, Shiokawa Y, Yamagami H, et al. Early ischemic change on CT versus diffusion-weighted imaging for patients with stroke receiving intravenous recombinant tissue-type plasminogen activator therapy: stroke acute management with urgent risk-factor assessment and improvement (SAMURAI) rt-PA registry. Stroke. 2011; 42: 2196-200.

42. Cheng X, Su X, Shi J, Liu Q, Zhou C, et al. Comparison of automated and manual DWI-ASPECTS in acute ischemic stroke: total and region-specific assessment. Eur Radiol. 2021; 31: 4130-4137.

43. Sakai K, Komatsu T, Iguchi Y, Takao H, Ishibashi T, Murayama Y. Reliability of Smartphone for Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Scores in Acute Ischemic Stroke Patients: Diagnostic Test Accuracy Study. J Med Internet Res. 2020; 22: e15893.

44. Deng PP, Wu N, Chen XJ, Chen FL, Xu HS, Bao GS. NIHSS-the Alberta Stroke Program Early CT Score mismatch in guiding thrombolysis in patients with acute ischemic stroke. J Neurol. 2022; 269: 1515-1521.

45. Liu G, Ntaios G, Zheng H, Wang Y, Michel P, et al. External validation of the ASTRAL score to predict 3- and 12-month functional outcome in the China National Stroke Registry. Stroke. 2013; 44: 1443-5.

46. Vanacker P, Heldner MR, Seiffge D, Mueller H, Eskandari A, et al. ASTRAL-R score predicts non-recanalisation after intravenous thrombolysis in acute ischaemic stroke. Thromb Haemost. 2015; 113: 1121-6.

47. Zhang X, Liao X, Wang C, Liu L, Wang C, et al. Validation of the DRAGON Score in a Chinese Population to Predict Functional Outcome of Intravenous Thrombolysis-Treated Stroke Patients. J Stroke Cerebrovasc Dis. 2015; 24: 1755-60.

48. Turc G, Apoil M, Naggara O, Calvet D, Lamy C, et al. Magnetic Resonance Imaging-DRAGON score: 3-month outcome prediction after intravenous thrombolysis for anterior circulation stroke. Stroke. 2013; 44: 1323-8.

49. Turc G, Aguettaz P, Ponchelle-Dequatre N, Hénon H, Naggara O, et al. External validation of the MRI-DRAGON score: early prediction of stroke outcome after intravenous thrombolysis. PLoS One. 2014; 9: e99164.

50. Lesenne A, Grieten J, Ernon L, Wibail A, Stockx L, et al. Prediction of Functional Outcome After Acute Ischemic Stroke: Comparison of the CT-DRAGON Score and a Reduced Features Set. Front Neurol. 2020; 11: 718.

51. Flint AC, Kamel H, Rao VA, Cullen SP, Faigeles BS, Smith WS. Validation of the Totaled Health Risks In Vascular Events (THRIVE) score for outcome prediction in endovascular stroke treatment. Int J Stroke. 2014; 9: 32-9.

52. Chen LL, Yan SM, Wang WT, Zhang S, Liu HM, et al. Cohort study of THRIVE predicting adverse outcomes in acute ischemic stroke of the anterior circulation and posterior circulation after 3 months and 1 year of follow-up. J Clin Neurosci. 2022; 96: 33-37.

53. Andrews R, Goel K, Corry P, Burdett R, Wynn MT, Callow D. Process data analytics for hospitalcase-mixplanning. J Biomed Inform. 2022; 129: 104056.

54. Zhou Z, Delcourt C, Xia C, Yoshimura S, Carcel C, et al. Low-Dose vs Standard-Dose Alteplase in Acute Lacunar Ischemic Stroke: The ENCHANTED Trial. Neurology. 2021; 96: e1512-e1526.

55. Becker DJ, Albery GF, Sjodin AR, Poisot T, Bergner LM, et al. Optimising predictive models to prioritise viral discovery in zoonotic reservoirs. Lancet Microbe. 2022.

56. Sandset EC, Ranhoff Hov M. Stroke is more than a hemiparesis: the pre-hospital detection of stroke. Med J Aust. 2022; 217: 140-141.

57. Psychogios K, Tsivgoulis G. Intravenous thrombolysis for acute ischemic stroke: why not? CurrOpin Neurol. 2022; 35: 10-17.