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ORIGINAL RESEARCH

Novel Prehospital Triage Scale for Detecting Large Vessel Occlusion and Its Cause

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BACKGROUND: Patients with large vessel occlusion stroke (LVOS) need to be rapidly identified and transferred to comprehensive stroke centers. However, current prehospital evaluation and strategies still remain challenging.

METHODS AND RESULTS: We retrospectively reviewed our prospectively collected database of patients with acute ischemic stroke (AIS). Based on the items of National Institutes of Health Stroke Scale and medical history that had a strong association with LVOS, we designed the 4-item Stroke Scale (4I-SS) and validated it in multi-centers. The 4I-SS incorporated gaze, level of consciousness, arm weakness, and atrial fibrillation. Receiver operating characteristic analysis was used to compare the 4I-SS with previously established prehospital prediction scales. Finally, 1630 and 11 440 patients were included in the derivation and validation cohort, respectively. In the validation cohort, Youden Index, area under the curve, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the 4I-SS≥4 to predict LVOS were 0.494, 0.800, 0.657, 0.837, 0.600, 0.868, and 0.788, respectively, and that of the 4I-SS≥7 to predict basilar artery occlusion were 0.200, 0.669, 0.229, 0.971, 0.066, 0.974, and 0.899, respectively. Youden Index and area under the curve were higher than previously published scales for predicting LVOS. Further analysis showed that for predicting whether cardiogenic embolism was the cause, its accuracy was 0.922 when the 4I-SS score, including atrial fibrillation, was ≥6, and its accuracy of predicting the occluded vessel was intracranial internal carotid artery or M1 segment of the middle cerebral artery when it was ≥7 was 0.590.

CONCLUSIONS: The 4I-SS is an effective and simple tool that can identify LVOS and its cause.

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Key Words: 4I-SS ■ cardiogenic embolism ■ LVOS ■ NIHSS

Large vessel occlusion stroke (LVOS) often leads to severe disability and mortality. Although the current guideline for the early management of patients with acute ischemic stroke (AIS) regarding endovascular treatment recommends that endovascular procedures provide clinical benefit in selected AIS patients, the operation is highly time-dependent.[1–3] Several clinical scales to predict LVOS in the prehospital setting have been developed to facilitate emergency medical services transfer of selected LVOS patients directly to an endovascular treatmentcapable comprehensive stroke center (CSC) to avoid secondary transfers and delays in reperfusion. However, only a few scales have been tested and evidence for their utilities is weak; meanwhile some are too complex to perform in the complicated prehospital setting; and furthermore, the current assessment tools need to improve basilar artery occlusion (BAO) recognition.[4,5] The current issue to be urgently solved is to establish a tool with easy operation, good prediction performance, and large sample verification. The aim of this study was to propose and validate a novel prehospital triage scale, the 4-item Stroke Scale (4I-SS), for detecting LVOS by exploring the clinical characteristics.

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CLINICAL PERSPECTIVE

What Is New?

- This new prediction tool was developed and validated in the largest cohort to date.
- The tool includes 4 predictors, 3 symptoms and the medical history, and has excellent predictive performance for large vessel occlusion and cardiogenic embolism.

What Are the Clinical Implications?

- This new prediction tool can effectively and accurately identify large vessel occlusion and provide etiological information by simple assessments in the prehospital setting.
- Consequently, patients can be properly triaged, transported to a stroke center if needed, and receive targeted treatment.

Nonstandard Abbreviations and Acronyms

4I-SS	4-item Stroke Scale
AIS	acute ischemic stroke
BAO	basilar artery occlusion
CSC	comprehensive stroke center
FAST	face–arm–speech–time test
FAST-ED	Field Assessment Stroke Triage for Emergency Destination scale
FPSS	Finnish Prehospital Stroke Scale
G-FAST	gaze–face–arm–speech–time test
LAMS	Los Angeles Motor Scale
LVOS	large vessel occlusion stroke
mNIHSS	modified NIHSS
NIHSS	National Institutes of Health Stroke Scale
NPV	negative predictive value
PASS	Prehospital Acute Stroke Severity scale
PPV	positive predictive value
RACE	Rapid Arterial Occlusion Evaluation Scale
ROSIER	Recognition of Stroke in the Emergency Room
sNIHSS	shortened versions of the NIHSS
sNIHSS-EMS	shortened NIHSS for emergency medical services
TOF-MRA	time of flight magnetic resonance angiography
VAN	stroke vision, aphasia, neglect assessment

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

4I-SS Scale Design and Retrospective Validation

We retrospectively reviewed our prospectively collected database for acute stroke patients (hemorrhagic or ischemic stroke) within 8 hours of onset in our center during period from June 2009 to September 2020 (derivation cohort). We enrolled patients who (1) underwent computed tomography angiography or time of flight magnetic resonance angiography (TOF-MRA) within 8 hours of onset, (2) had a detailed National Institutes of Health Stroke Scale (NIHSS) score and medical history at admission, (3) had a diagnosis of AIS confirmed by diffusion-weighted imaging or computed tomography at 24 hours after symptom onset. Patients with poor image quality due to motion artifacts were excluded. Demographic, clinical, laboratory, and imaging data were recorded, including age, sex, blood pressure; prior antiplatelet therapy, prior anticoagulant therapy; medical history (smoking, hypertension, atrial fibrillation [AF], diabetes mellitus, hyperlipidemia, hyperhomocysteinemia, coronary heart disease, congestive heart failure, history of stroke/ transient ischemic attack, and family history of cardiovascular disease).

LVOS was defined as unilateral occlusion of intracranial internal carotid artery, or M1/M2 segments of the middle cerebral artery, or basilar artery (BA) on baseline computed tomography angiography or TOF-MRA. Two experienced neurologists blinded to the patient's information assessed the occlusion with rater discrepancies settled by consensus.

First, those items of the NIHSS and medical history with the association with LVOS were identified in a χ^2 test. Second, the associations of the NIHSS and medical history elements with LVOS were examined by computing odds ratios using binary logistic regression analysis. Based on the prehospital clinical practice and expert consensus, the screening tool needs to be simple and easy-operation, therefore, the maximum elements of new scale are 4.[6,7] Then, the predictive value of different combinations of these items with the highest association with LVOS was determined by receiver operating curve analysis. Some items were excluded to avoid difficulties and inconsistencies in the assessment by paramedic personnel although they had a high association with LVOS (eg, visual fields, facial paresis, limb ataxia, sensory, agnosia, and extinction/ inattention).[6–9] Based on previous studies and odds ratios, each item was scored using a simple grading

system.[6,7,9–13] Finally, a high global accuracy was obtained with the combination of 4 items that finally built the easy-operation 4I-SS: gaze (0, 2), level of consciousness (0, 1, 2), arm weakness (0, 1, 3), and AF (0, 1), as shown in Table 1.

Validation of the 4I-SS

After derivation, the tool performance was assessed using the MISSION data set (Improving In-hospital Stroke Service Utilization [MISSION] in China: A Cluster Randomized Trial of Interventions to Shorten Door to Needle Times; https://www.clinicaltrials.gov; unique identifier: NCT03317639) from January 2016 to January 2021 (validation data set). Demographics, clinical, imaging, laboratory data, and NIHSS were prospectively recorded in detail; therefore, the score of the 4I-SS was calculated. We selected patients for validation according to the inclusion and exclusion criteria of the design stage. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for the prediction of LVOS. The main objective of this study was to assess the accuracy of the 4I-SS for detecting real LVOS candidates in the validation cohort.

The study was approved by the human ethics committee of the second affiliated hospital of Zhejiang University, School of Medicine. Written informed consent was obtained from each patient or an appropriate family member. Clinical investigation had been conducted according to the principles expressed in the Declaration of Helsinki.

Table 1. The 4I-SS and Its Correspondence to the NIIHSS

Item	4I-SS	NIHSS
Gaze		
Normal	0	0
Partial or forced deviation	2	1–2
LOC		
Normal	0	0
Mild disturbance	1	1
Severe disturbance	2	2–3
Arm weakness		
No drift	0	0
Drift but does not hit bed	1	1
Some effort against gravity, no effort against gravity or no movement	3	2–4
AF		
Yes	1	
No	0	

4I-SS indicates 4-item Stroke Scale; AF, atrial fibrillation; LOC, level of consciousness; and NIHSS, National Institutes of Health Stroke Scale.

Statistical Analysis

Patients were dichotomized into the LVOS and non-LVOS group. Clinical characteristics were summarized by computing the median (interquartile range), and differences between 2 groups were tested by the t-test or Mann-Whitney U-test if they were continuous variables. Categorical or binary datum was summarized by proportion (n); and differences between 2 groups were tested by the Pearson χ^2 test. The AUCs of different models were compared by used Delong tests. Goodness of fit test was performed to check the fit of the 4I-SS scale. Sensitivity, specificity, PPV, NPV, and accuracy of the published prehospital scales were calculated for the prediction of LVOS in the validation cohort, and the cutoff values of the published scales were used which were reported in the previous literatures. All comparisons were 2-sided, with statistical significance defined as $P<0.05$. Analyses were calculated using SPSS version 22.0 (IBM, Armonk, New York) and SAS version 9.4 (SAS Institute Inc.).

RESULTS

A total of 1630 patients were finally included in the derivation cohort, and 11 440 in the validation cohort. Of the included patients in the derivation cohort, mean age was 70 (60–79) years and 661 (37.5%) were men; median NIHSS on admission was 10 (4–16); among them, 836 (51.3%) patients had LVOS. Of the included patients in the validation cohort, mean age was 70 (60–79) years and 4368 (38.2%) were women; median NIHSS on admission was 6 (3–12); among them, 3244 (28.4%) patients had LVOS.

In the derivation cohort, Table S1 showed the baseline characteristics of patients. The incidence of AF, the scores of LOC, gaze and arm weakness were significantly higher in the LVOS group. Figure and Table 2 showed different cutoff values of the 4I-SS for predicting LVOS, and the highest Youden Index (0.344) was achieved for score ≥4, with AUC, sensitivity, specificity, PPV, NPV, and accuracy of 0.693, 0.661, 0.683, 0.687, 0.657, and 0.672, respectively. The highest Youden Index (0.304) was achieved for the 4I-SS score ≥7 to predict BAO, with AUC, sensitivity, specificity, PPV, NPV, and accuracy of 0.644, 0.407, 0.897, 0.189, 0.962, and 0.869, respectively (Table 3).

In the validation cohort, Table S1 showed the baseline characteristics of patients. Consistent with the derivation cohort, the incidence of AF and the scores of LOC, gaze and arm weakness were significantly higher in the LVOS group. Figure S1 and Table 2 showed that Youden Index, AUC, sensitivity, specificity, PPV, NPV, and accuracy of the 4I-SS ≥4

Table 2. Sensitivity, Specificity, PPV, and NPV of Different Cutoff Values of the 4I-SS in Detecting LVOS

	Derivation cohort (n=1630)						Validation cohort (n=11 440)						
4I-SS score	Youden index	Sensitivity	Specificity	PPV	NPV	Accuracy	4I-SS score	Youden index	Sensitivity	Specificity	PPV	NPV	Accuracy
≥1	0.140	0.886	0.254	0.556	0.680	0.579	≥1	0.233	0.933	0.300	0.332	0.923	0.472
≥2	0.216	0.800	0.416	0.591	0.664	0.613	≥2	0.413	0.848	0.565	0.421	0.909	0.642
≥3	0.238	0.771	0.467	0.604	0.660	0.623	≥3	0.436	0.825	0.611	0.442	0.904	0.670
≥4	0.344	0.661	0.683	0.687	0.657	0.672	≥4	0.494	0.657	0.837	0.600	0.868	0.788
≥5	0.310	0.544	0.766	0.710	0.615	0.652	≥5	0.434	0.545	0.889	0.647	0.840	0.796
≥6	0.256	0.403	0.853	0.742	0.607	0.622	≥6	0.323	0.385	0.938	0.699	0.804	0.788
≥7	0.119	0.178	0.941	0.760	0.521	0.550	≥7	0.278	0.307	0.971	0.797	0.790	0.791
≥8	0.032	0.051	0.981	0.741	0.496	0.504	≥8	0.083	0.089	0.994	0.843	0.745	0.748

4I-SS indicates 4-item Stroke Scale; LVOS, large vessel occlusion stroke; and NPV, negative predictive value; PPV, positive predictive value; SEN, Sensitivity; and SPE, Specificity.

were 0.494, 0.800, 0.657, 0.837, 0.600, 0.868, and 0.788, respectively. The goodness of fit test showed the 4I-SS had a good fit ($\chi 2$=0.307, *P*=0.580). The diagnostic parameters of the 4I-SS were compared with preexisting scales including the 3-item Stroke Scale (3I-SS),[14] gaze–face–arm–speech–time test (G-FAST),[10] Conveniently-Grasped Field Assessment Stroke Triage (CG-FAST),[15] Cincinnati Prehospital Stroke Severity scale (CPSSS),[7] face–arm–speech–time test (FAST),[16] Field Assessment Stroke Triage for Emergency Destination scale (FAST-ED),[11] Finnish Prehospital Stroke Scale (FPSS),[13] Los Angeles Motor Scale (LAMS),[17] Prehospital Acute Stroke Severity scale (PASS),[6] Rapid Arterial Occlusion Evaluation Scale (RACE),[9] Recognition of Stroke in the Emergency Room (ROSIER),[4]stroke vision, aphasia, neglect assessment (VAN),[12] National Institutes of Health Stroke Scale (NIHSS),[1,18] abbreviated NIHSS (aNIHSS), modified NIHSS (mNIHSS), shortened versions of the NIHSS (sNIHSS), shortened NIHSS for emergency medical services (sNIHSS-EMS).[19] The AUC and the highest Youden index of the 4I-SS were higher than all scales, as well as NIHSS (Table 4). Delong test showed there was no statistically significant difference between the AUCs of 4I-SS and NIHSS (*Z*=−0.117, *P*-value=0.907). However, the accuracy of the 4I-SS was significantly higher than NIHSS (*P*<0.001).

The Youden Index, AUC, sensitivity, specificity, PPV, NPV, and accuracy of the 4I-SS for predicting BAO were 0.200, 0.669, 0.229, 0.971, 0.066, 0.974, and 0.899, respectively. The AUC was still higher than 12 published scales (FAST-ED, RACE, s-NIHSS-1, PASS, CPSSS, CG-FAST, ROSIER, LAMS, FPSS, G-FAST, aNIHSS, FAST) (Table 3).

Further analysis showed that when the 4I-SS score, including AF, was ≥6, the accuracy of the 4I-SS for predicting cardiogenic embolism (CE) of LVOS was 0.922, and sensitivity, specificity, PPV, and NPV were 0.564, 0.966, 0.669, and 0.948, respectively (Table 5). Subgroup analysis showed the accuracy of 4I-SS for predicting LVOS in patients of smoking, hypertension, AF, diabetes mellitus, hyperlipidemia, coronary heart disease was 0.585, 0.592, 0.636, 0.612, 0.644, 0.584, respectively. Furthermore, the analysis showed that the 4I-SS could moderately predict the occluded vessel was intracranial internal carotid artery or M1 when it was ≥7. The accuracy of the 4I-SS for predicting intracranial internal carotid artery or M1 was 0.590, meanwhile to predict M2 and BA was 0.111, 0.07, respectively (*P*<0.05), when the 4I-SS score was ≥7.

DISCUSSION

The study demonstrated that the 4I-SS could effectively and accurately identify LVOS in AIS patients, provide LVOS-related cause information and moderately

Table 3. Comparison of Various Published Clinical Scales With the 4I-SS to Predict Basilar Artery Occlusion

Scale	Cutoff	AUC (95%CI)	Youden index	Sensitivity	Specificity	PPV	NPV	Accuracy	*P* value*
4I-SS	≥7	0.644 (0.575–0.713)	0.304	0.407	0.897	0.189	0.962	0.869	<0.001
NIHSS	≥16	0.701 (0.670–0.732)	0.300	0.456	0.844	0.080	0.981	0.832	<0.001
s-NIHSS-8	≥12	0.699 (0.669–0.730)	0.278	0.368	0.910	0.109	0.980	0.894	<0.001
mNIHSS	≥12	0.692 (0.660–0.723)	0.295	0.473	0.822	0.073	0.981	0.812	<0.001
s-NIHSS-EMS	≥13	0.692 (0.660–0.723)	0.283	0.444	0.839	0.076	0.981	0.827	<0.001
s-NIHSS-5	≥6	0.691 (0.661–0.724)	0.268	0.469	0.799	0.065	0.981	0.789	<0.001
3I-SS	≥3	0.681 (0.651–0.711)	0.289	0.544	0.745	0.060	0.982	0.739	<0.001
VAN	≥3	0.673 (0.643–0.704)	0.250	0.326	0.924	0.114	0.979	0.907	<0.001
4I-SS	≥7	0.669 (0.639–0.698)	0.200	0.229	0.971	0.066	0.974	0.899	<0.001
FAST-ED	≥3	0.662 (0.632–0.692)	0.211	0.577	0.634	0.045	0.981	0.632	<0.001
RACE	≥4	0.654 (0.624–0.684)	0.242	0.640	0.602	0.046	0.982	0.604	<0.001
PASS	≥2	0.647 (0.619–0.647)	0.254	0.540	0.714	0.053	0.981	0.709	<0.001
CPSSS	≥2	0.643 (0.613–0.672)	0.272	0.552	0.720	0.056	0.982	0.715	<0.001
CG-FAST	≥3	0.643 (0.614–0.672)	0.222	0.623	0.599	0.044	0.982	0.600	<0.001
s-NIHSS-1	≥2	0.638 (0.609–0.667)	0.227	0.715	0.512	0.042	0.984	0.518	<0.001
ROSIER	≥3	0.621 (0.591–0.651)	0.156	0.770	0.386	0.036	0.983	0.397	<0.001
LAMS	≥3	0.619 (0.590–0.649)	0.183	0.686	0.497	0.039	0.982	0.503	<0.001
FPSS	≥3	0.616 (0.587–0.645)	0.171	0.644	0.527	0.039	0.980	0.530	<0.001
G-FAST	≥3	0.594 (0.566–0.623)	0.136	0.582	0.554	0.037	0.978	0.555	<0.001
aNIHSS	≥2	0.585 (0.536–0.615)	0.122	0.757	0.365	0.034	0.981	0.377	<0.001
FAST	≥2	0.579 (0.550–0.608)	0.102	0.799	0.303	0.033	0.981	0.317	0.001

3I-SS indicates 3-item Stroke Scale; 4I-SS, 4-item Stroke Scale; aNIHSS, abbreviated NIHSS; AUC, area under the curve; CG-FAST, Conveniently-Grasped Field Assessment Stroke Triage; CPSSS, Cincinnati Prehospital Stroke Severity scale; FAST, face–arm–speech–time test; FAST-ED, Field Assessment Stroke Triage for Emergency Destination scale; FPSS, Finnish Prehospital Stroke Scale; G-FAST, gaze–face–arm–speech–time test; LAMS, Los Angeles Motor Scale; mNIHSS, modified NIHSS; NIHSS, National Institutes of Health Stroke Scale; NPV, negative predictive value; PASS, Prehospital Acute Stroke Severity scale; PPV, positive predictive value; RACE, Rapid Arterial Occlusion Evaluation Scale; ROSIER, Recognition of Stroke in the Emergency Room; sNIHSS, shortened versions of the NIHSS; sNIHSS-EMS, shortened NIHSS for emergency medical services; and VAN, stroke vision, aphasia, neglect assessment.

*The hypothesis testing of these *P* values is AUC.

predict the occluded vessel. The AUC of the 4I-SS for predicting LVOS was higher than preexisting scales, as well as NIHSS. It also improved the recognition of BAO, could predict whether the cause of LVOS was CE and moderately predict the occluded vessel was intracranial internal carotid artery or M1.

We noted that some clinical data were different between 2 cohorts. For example, in the derivation cohort, the prevalence of hyperlipidemia and hyperhomocysteinemia was lower in LVOS patients. However, this was no difference between 2 groups in the validation cohort. In addition, the proportion of LVOS (51.3%) was higher in the derivation cohort, which may be due to the characteristics of CSC of derivation cohort, while the MISSION data set includes several CSCs and primary stroke centers, the proportion of LVOS (28.4%) is close to the actual prehospital situation (21.3%-35.9%).[7,9–11,20] Importantly, the AUC and the highest Youden index in the validation cohort were higher than those of derivation cohort, suggesting that the 4I-SS had a strong predictive ability in the prehospital setting.

Compared with published scales, the 4I-SS was simply consisted of 4 items which makes the operation easier and less time-consuming, and had a higher predictive power of LVOS.[18,21,22] Additionally, the 4I-SS is the only scale containing AF. Studies have shown that AF was an independent risk factor of LVOS, and could be quickly obtained before hospitalization for judgment of LVOS.[23–25] Studies have also shown that gaze had a higher predictive value than other neurological symptoms for LVOS.[12,24] These may explain the relatively high predictive ability of the 4I-SS.

The 4I-SS had a predictive power for the cause of LVOS. By far, there was only 1 scale for predicting the cause of LVOS, $BOCS_2$ scale,[26] and there were some predictive signs of LVOS' cause, including delayed-contrast filling sign (DCFS),[27] overestimation ratio of Susceptibility Vessel Sign,[28] the histologic features of thrombus.[29] Although the sensitivity of the 4I-SS was lower than $BOCS_2$ scale (93.5%), DCFS (83.2%) and overestimation ratio of Susceptibility Vessel Sign (97.1%), the specificity was higher than DCFS (70.8%) and overestimation ratio of Susceptibility Vessel Sign (91.3%), only lower than $BOCS_2$ scale (100%). Additionally, the 4I-SS was the only scale that could conveniently and accurately predict the cause of LVOS

Table 4. Comparison of Various Published Clinical Scales With the 4I-SS to Predict LVOS in the Validation Cohort

Scale	Cutoff	AUC (95%CI)	Youden index	Sensitivity	Specificity	PPV	NPV	Accuracy	*P* value*
4I-SS	≥4	0.800 (0.789–0.811)	0.494	0.657	0.837	0.600	0.868	0.788	<0.001
NIHSS	≥6	0.797 (0.787–0.806)	0.445	0.834	0.611	0.444	0.908	0.672	<0.001
s-NIHSS-8	≥6	0.794 (0.785–0.803)	0.479	0.699	0.780	0.541	0.874	0.758	<0.001
RACE	≥5	0.791 (0.781–0.800)	0.473	0.672	0.801	0.557	0.868	0.766	<0.001
mNIHSS	≥7	0.790 (0.781–0.800)	0.482	0.716	0.766	0.533	0.879	0.753	<0.001
s-NIHSS-EMS	≥6	0.790 (0.780–0.799)	0.451	0.816	0.635	0.455	0.903	0.684	<0.001
CG-FAST	≥4	0.790 (0.780–0.799)	0.424	0.538	0.886	0.638	0.837	0.792	<0.001
FAST-ED	≥4	0.788 (0.779–0.798)	0.471	0.715	0.756	0.521	0.877	0.744	<0.001
s-NIHSS-5	≥4	0.784 (0.774–0.793)	0.474	0.699	0.775	0.536	0.873	0.754	<0.001
CPSSS	≥2	0.780 (0.771–0.790)	0.452	0.617	0.835	0.582	0.854	0.776	<0.001
3I-SS	≥4	0.779 (0.769–0.789)	0.359	0.443	0.916	0.662	0.815	0.787	<0.001
LAMS	≥4	0.767 (0.757–0.777)	0.441	0.626	0.815	0.558	0.854	0.764	<0.001
PASS	≥2	0.765 (0.755–0.775)	0.452	0.623	0.829	0.576	0.855	0.773	<0.001
FPSS	≥5	0.761 (0.752–0.771)	0.357	0.459	0.898	0.625	0.817	0.779	<0.001
G-FAST	≥3	0.759 (0.749–0.769)	0.406	0.746	0.660	0.450	0.875	0.683	<0.001
s-NIHSS-1	≥2	0.755 (0.745–0.766)	0.402	0.788	0.614	0.432	0.886	0.662	<0.001
ROSIER	≥4	0.730 (0.720–0.740)	0.386	0.689	0.697	0.459	0.858	0.695	<0.001
VAN	≥2	0.718 (0.708–0.728)	0.372	0.834	0.538	0.402	0.897	0.618	<0.001
FAST	≥3	0.709 (0.699–0.719)	0.370	0.684	0.686	0.448	0.854	0.685	<0.001
aNIHSS	≥1	0.695 (0.684–0.705)	0.305	0.549	0.756	0.456	0.818	0.700	<0.001

3I-SS indicates 3-item Stroke Scale; 4I-SS, 4-item Stroke Scale; aNIHSS, abbreviated NIHSS; AUC, area under the curve; CG-FAST, Conveniently-Grasped Field Assessment Stroke Triage; CI, confidence interval; CPSSS, Cincinnati Prehospital Stroke Severity scale; FAST, face–arm–speech–time test; FAST-ED, Field Assessment Stroke Triage for Emergency Destination scale; FPSS, Finnish Prehospital Stroke Scale; G-FAST, gaze–face–arm–speech–time test; LAMS, Los Angeles Motor Scale; LVOS, large vessel occlusion stroke; mNIHSS, modified NIHSS; NIHSS, National Institutes of Health Stroke Scale; NPV, negative predictive value; PASS, Prehospital Acute Stroke Severity scale; PPV, positive predictive value; RACE, Rapid Arterial Occlusion Evaluation Scale; ROSIER, Recognition of Stroke in the Emergency Room; sNIHSS, shortened versions of the NIHSS; sNIHSS-EMS, shortened NIHSS for emergency medical services; and VAN, stroke vision, aphasia, neglect assessment.

*The hypothesis testing of these *P*-values is AUC.

before hospital, but above-mentioned scale and signs involved complex analysis. At present, different devices and combined therapies were introduced for LVOS with different causes, the 4I-SS could provide etiological information by simple assessments, and thus might be helpful to decision-making of endovascular procedure in future.

Table 5. Sensitivity, Specificity, PPV, NPV, and Accuracy of Different Cutoff Values of the 4I-SS in Detecting CE in the Validation Cohort

Validation cohort (n=11 440)					
4I-SS score	Sensitivity	Specificity	PPV	NPV	Accuracy
≥4	0.752	0.928	0.560	0.968	0.909
≥5	0.609	0.959	0.645	0.953	0.921
≥6	0.564	0.966	0.669	0.948	0.922
≥7	0.340	0.983	0.713	0.924	0.913
≥8	0.191	0.991	0.725	0.910	0.904

4I-SS indicates 4-item Stroke Scale; CE, cardiogenic embolism; NPV, negative predictive value; and PPV, positive predictive value.

The sample size of our study was very large. It was a scale that had been validated by the maximum sample size of multi-centers by far, larger than the sample size of 3I-SS,[14] G-FAST,[10] CG-FAST,[15] CPSSS,[7] FAST,[16] FAST-ED,[11] FPSS,[13] LAMS,[17] PASS,[6] RACE,[9] ROSIER,[4] and VAN,[12] so its predictive ability was convincing.

The prediction value of the 4I-SS for BAO has also been improved, and was stronger than 12 scales (FAST-ED, RACE, s-NIHSS-1, PASS, CPSSS, CG-FAST, ROSIER, LAMS, FPSS, G-FAST, aNIHSS, and FAST). Compared with the preexisting scales, its predictive power of LVOS in the anterior and posterior cerebral circulation was higher. A hallmark of BAO is reduced consciousness.[30] The 4I-SS incorporated the assessment of LOC, while most scales did not evaluate the consciousness level of patients.[4,6,7,9–13,15–17] In addition, patients with BAO have a high incidence of gaze, especially in patients with occlusions of the proximal or middle segments of the basilar artery.[30] The 4I-SS contained both items, which may explain its relatively high predictive value for BAO.

We noted that the accuracy and specificity of the 4I-SS was higher than NIHSS, while the sensitivity of the

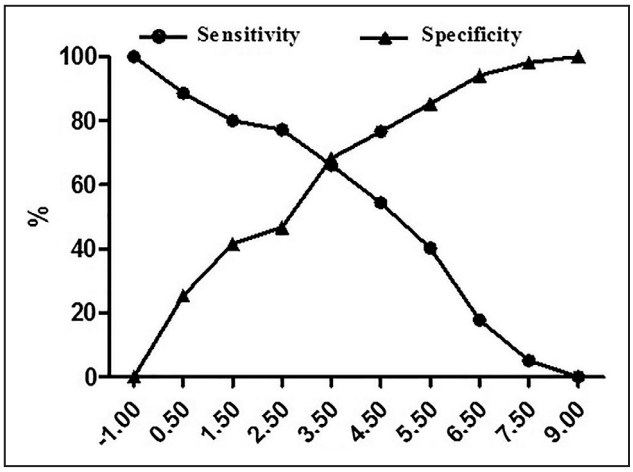

Figure. Sensitivity and specificity of different cutoff values of the 4-Item Stroke Scale in detecting large vessel occlusion stroke in the derivation cohort.

4I-SS was lower than NIHSS. Especially for BAO, we noted sensitivity of scales for screening BAO is generally low. Due to a relatively higher specificity, the finding that the 4I-SS had higher accuracy than NIHSS could be exaggerated or diluted. However, statistical analysis further confirmed that 4I-SS exactly had higher accuracy than NIHSS. There are some potential reasons. The signs and symptoms of stroke are variable, especially for BAO patients, who often present with several symptoms. However, scales cannot include many items for the aim of prehospital simple assessment, which would enhance the difficulty to design the scale and reduce the detection efficiency of the scale.[30–32] Recently, prehospital suspected LVO screening scales with high sensitivity and low specificity were reported to lead to interfacility transfer-related delays,[33] so-called "short cuts make long delays," especially for patients with non-LVO. For scales with high sensitivity, too many non-LVO patients would be transferred to CSCs, which would lead to CSCs being overburden and delays for thrombolytic therapy, too. Therefore, the 4I-SS with slightly low sensitivity and high specificity is rational to reduce the non-LVO population mistakenly identified as LVO, and potentially reduce the interfacility transfer-related delays for non-LVO patients. Additionally, from clinical practice, 4I-SS, with a relatively high specificity, can not only shunt patients, but also make patients get targeted treatment specifically.

Our study had some limitations. First, although the 4I-SS had a high predictive value of the cause of LVOS, this was based on the understanding of patient's medical history and accurate evaluation of the patient's neurological symptoms. Its predictive ability would be reduced, especially for the cause, when the information of AF was not clear. Second, we only developed and verified the 4I-SS in AIS patients, however, we may encounter patients with cerebral hemorrhage, non-stroke patients and so on in the actual prehospital environment. In the future, we need to further improve and develop a scale that can identify ischemic stroke, cerebral hemorrhage and other conditions. Third, although the predictive power of BAO of the 4I-SS has been improved, its sensitivity still needs to be elevated. The incidence of BAO accounts for about 1% of all strokes, but has a higher mortality and disability rate,[30] and early recognition and interventions can help improve the prognosis of these patients.

CONCLUSIONS

The 4I-SS is an effective and simple tool that can identify LVOS and its cause, and moderately predict the occluded vessel.

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Disclosures

None.

Supplementary Material

Table S1
Figure S1

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Supplemental Material

Table S1. **Comparison of baseline variables between LVOS and non-LVOS patients.**

Variable	DERIVATION COHORT (N=1630)			VALIDATION COHORT (N=11440)		
	LVOS (n=836)	Non-LVOS (n=794)	P-value	LVOS (n=3244)	Non-LVOS (n=8196)	P-value
Female, n (%)	327 (39.1%)	284 (35.8%)	0.163	1351(41.6%)	3017 (36.8%)	<0.001
Age, year, median (IQR)	71 (62-80)	69 (59-78)	0.001	73 (63-81)	69 (59-77)	<0.001
AF, n (%)	387 (46.3%)	219 (27.6%)	<0.001	1181(36.4%)	1147 (14.0%)	<0.001
Family history of cardiovascular disease, n (%)	37 (4.4%)	85 (10.7%)	<0.001	28 (0.9%)	115 (1.4%)	0.021
Hyperlipidemia, n (%)	276 (33.0%)	334 (42.1%)	<0.001	173 (5.3%)	475 (5.8%)	0.346
Hyperhomocysteinemia, n (%)	121 (14.5%)	165 (20.8%)	0.001	215 (6.6%)	563 (6.9%)	0.679
Congestive heart failure, n (%)	34 (4.1%)	50 (6.3%)	0.042	126 (3.9%)	114 (1.4%)	<0.001
Diabetes mellitus, n (%)	161 (19.3%)	181 (22.8%)	0.080	489 (15.1%)	1353 (16.5%)	0.063
History of stroke/TIA, n (%)	157 (18.8%)	126 (15.9%)	0.121	418 (12.9%)	1019 (12.4%)	0.512
Hypertension, n (%)	553 (66.1%)	543 (68.4%)	0.336	2030 (62.6%)	5280 (64.4%)	0.066
Smoking, n (%)	281 (33.6%)	282 (35.5%)	0.419	916 (28.2%)	2585 (31.5%)	0.001
Prior anticoagulation therapy, n (%)	62 (7.4%)	48 (6.0%)	0.270	111 (3.4%)	106 (1.3%)	<0.001
Prior antiplatelet therapy, n (%)	158 (18.8%)	138 (17.3%)	0.423	474 (14.6%)	1122 (13.7%)	0.208
Coronary heart disease, n (%)	87 (10.4%)	89 (11.2%)	0.602	261 (11.7%)	450 (7.5%)	<0.001
Systolic blood pressure, mmHg, median (IQR)	151 (135-168)	156 (140-172)	<0.001	153 (137-167)	155 (140-168)	<0.001
Diastolic blood pressure, mmHg, median (IQR)	83 (73-94)	86 (76-95)	0.002	84 (75-92)	85 (77-94)	<0.001
ONT,min, median (IQR)	206 (135-281)	215 (155-266)	<0.001	152 (110-202)	161 (115-215)	<0.001
DNT, min, median (IQR)	62 (42-88)	72 (48-102)	0.723	50 (38-69)	50 (37-66)	0.036
NIHSS sum, median (IQR)	13 (7-17)	7 (3-12)	<0.001	13 (8-19)	4 (2-8)	<0.001
A) LOC, median (IQR)	0 (0-1)	0 (0-0)	<0.001	0 (0-2)	0 (0-0)	<0.001
B) LOC questions, median (IQR)	1 (0-2)	0 (0-2)	<0.001	0 (0-2)	0 (0-0)	<0.001
C) LOC commands, median (IQR)	0 (0-2)	0 (0-0)	<0.001	0 (0-2)	0 (0-0)	<0.001
Gaze deviation, median (IQR)	1 (0-2)	0 (0-1)	<0.001	0 (0-1)	0 (0-0)	<0.001
Visual field test, median (IQR)	0 (0-0)	0 (0-0)	0.010	0 (0-0)	0 (0-0)	<0.001
Facial palsy, median (IQR)	1 (1-2)	1 (0-1)	<0.001	1 (1-2)	1 (0-1)	<0.001
Motor left arm, median (IQR)	0 (0-4)	0 (0-1)	<0.001	1 (0-4)	0 (0-1)	<0.001
Motor right arm, median (IQR)	0 (0-4)	0 (0-2)	<0.001	0 (0-4)	0 (0-1)	<0.001
Motor left leg, median (IQR)	0 (0-4)	0 (0-1)	<0.001	1 (0-4)	0 (0-1)	<0.001

Motor right leg, median (IQR)	0 (0-3)	0 (0-2)	<0.001	1 (0-4)	0 (0-1)	<0.001
Limb ataxia, median (IQR)	0 (0-0)	0 (0-0)	0.001	0 (0-0)	0 (0-0)	0.009
Sensory, median (IQR)	0 (0-1)	0 (0-1)	0.001	0 (0-1)	0 (0-1)	<0.001
Aphasia, median (IQR)	1 (0-3)	0 (0-2)	<0.001	1 (0-3)	0 (0-1)	<0.001
Dysarthria, median (IQR)	1 (0-2)	1 (0-1)	<0.001	1 (0-2)	0 (0-1)	<0.001
Extinction and inattention, median (IQR)	0 (0-0)	0 (0-0)	<0.001	0 (0-0)	0 (0-0)	<0.001
INFARCTION LOCALIZATION						
Anterior circulation, n (%)	744 (89.0%)	755 (95.1%)	<0.001	2890 (89.1%)	7786 (95.0%)	<0.001
Posterior circulation, n (%)	91 (10.9%)	20 (2.5%)	<0.001	347 (10.7%)	205 (2.5%)	<0.001
Both involved, n (%)	1 (0.1%)	2 (2.4%)	<0.001	7 (0.2%)	205 (2.5%)	<0.001
OCCLUSION SITES						
ICA, n (%)	248 (29.7%)	-	-	809 (24.9%)	-	-
M1, n (%)	427 (51.1%)	-	-	1631 (50.3%)	-	-
M2, n (%)	85 (10.2%)	-	-	704 (21.7%)	-	-
BA, n (%)	92 (11.0%)	-	-	353 (10.8%)	-	-

AF, atrial fibrillation; BA, basilar artery; DNT, door-to-needle time; ICA, intracranial internal carotid artery; LOC, level of consciousness; LVOS, large vessel occlusion strokes; M1, M1 segment of the middle cerebral artery; M2, M2 segment of the middle cerebral artery; NIHSS, national institutes of health stroke scale; ONT, onset-to-needle time; TIA, transient ischemic attack.

Figure S1. Sensitivity and specificity of different cutoff values of the 4-item stroke scale (4I-SS) in detecting large vessel occlusion stroke in the validation cohort.