Validation of the National Institutes of Health Stroke Scale-8 to Detect Large Vessel Occlusion in Ischemic Stroke

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Background: Patients with acute ischemic stroke and large vessel occlusion (LVO) may benefit from prehospital identification and transfer to a center offering endovascular therapy. *Aims:* We aimed to assess the accuracy of an existing 8-item stroke scale (National Institutes of Health Stroke Scale-8 [NIHSS-8]) for identification of patients with acute stroke with LVO. *Methods:* We retrospectively calculated NIHSS-8 scores in a population of consecutive patients with presumed acute stroke assessed by emergency medical services (EMS). LVO was identified on admission computed tomography angiography. Accuracy to identify LVO was calculated using receiver operating characteristics analysis. We used weighted Cohen's kappa statistics to assess inter-rater reliability for the NIHSS-8 score between the EMS and the hospital stroke team on a prospectively evaluated subgroup. *Results:* Of the 551 included patients, 381 had a confirmed ischemic stroke and 136 patients had an LVO. NIHSS scores were significantly higher in patients with LVO (median 18; interquartile range 14-22). The NIHSS-8 score reliably predicted the presence of LVO (area under the receiver operating characteristic curve .82). The optimum NIHSS-8 cutoff of 8 or more had a sensitivity of .81, specificity of .75, and Youden index of .56 for prediction of LVO. The EMS and the stroke team reached substantial agreement ($\kappa = .69$). *Conclusions:* Accuracy of the NIHSS-8 to identify LVO in a population of patients with suspected acute stroke is comparable to existing prehospital stroke scales. The scale can be performed by EMS with reasonable reliability. Further validation in the field is needed to assess accuracy of the scale to identify patients with LVO eligible for endovascular treatment in a prehospital setting. **Key Words:** Acute stroke therapy—ischemic stroke—endovascular therapy—thrombectomy—large vessel occlusion—emergency medical services.

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Introduction

When compared with intravenous thrombolysis (tissue plasminogen activator, alteplase), endovascular treatment (EVT) for acute ischemic stroke has been shown to be more effective in improving the outcome of selected patients with ischemic stroke due to large vessel occlusion (LVO).[1-7]

To date, only a limited number of centers are capable of offering EVT for acute ischemic stroke and function as a comprehensive stroke center, of which most are situated in a metropolitan area. To address the inequity in access to EVT for patients with ischemic stroke located in rural, regional, and outer metropolitan areas, a "drip and ship" strategy can be used. In this model, patients with acute stroke are transported to the nearest hospital, where thrombolysis is administered to eligible patients. If computed tomography (CT) angiography shows an LVO, patients are then shipped to the nearest center providing EVT. The time taken to provide local hospital thrombolysis and to transfer the stroke patient to a comprehensive stroke center might, however, result in significant delays that can jeopardize potential reperfusion benefit.[8-10] If sufficiently accurate and reliable identification of LVO could occur before hospital arrival, direct triage of patients in outer metropolitan and regional areas to a comprehensive stroke center might help avoid time delays due to secondary hospital transfers.

Aims

We aimed to assess the accuracy of an existing, cut-down National Institutes of Health Stroke Scale-8 (NIHSS-8) for identification of patients with LVO, to validate the scale in a general cohort of patients suspected with acute ischemic stroke assessed by emergency medical services (EMS), and to test the inter-rater reliability of the NIHSS-8 between the EMS and the hospital stroke team.[11]

Methods

Patient Cohort

The study population consisted of consecutive patients with suspected acute stroke for whom the hospital acute stroke team was activated by EMS between 2012 and 2016 in a single center in Australia. Patients who were assessed by either EMS or the hospital stroke team only were excluded from the analysis. The center functions as the only comprehensive stroke center providing care for a population of 800,000 across an area of 29,145 km^2. At the time of data collection, the stroke team was activated only for patients with acute ischemic stroke within a 4.5-hour window from stroke symptom onset. The hospital stroke team was notified either by local ambulance paramedics prior to hospital arrival or by emergency physicians if a patient arrived at the emergency department without prior ambulance transport. Ethics approval for the use of the NIHSS-8 by EMS in our local health district was granted by the Hunter New England Health Human Research Ethics Committee (Ref number: 09/02/18/4.04).

Development of the NIHSS-8

The scale consists of 8 NIHSS items selected by stroke expert consensus to be more likely affected in large strokes underpinned by LVO (Fig 1).[11] The scale had been in use since 2010 and initially served the purpose of identifying patients eligible for thrombolytic therapy. Investigators (A.G., N.S., M.P., and C.L.) trained regional EMS in the use of the scale using the publically available online NIHSS training resources during a 1-week training session. Training was thereafter continued outside of the regional EMS control centers. Items regarded to be difficult to perform reliably by EMS after the initial training phase (e.g., assessment of visual field deficits, ataxia, or aphasia) were excluded from the final 8-item scale.

Data Collection

Admission NIHSS and imaging data were retrospectively analyzed. NIHSS data were collected upon patient admission to the emergency department by the hospital stroke team. All stroke team members maintain annual NIHSS certification and are highly experienced stroke clinicians. NIHSS-8 scores were calculated from the admission NIHSS score. To assess inter-rater reliability, the NIHSS-8 score was prospectively scored in a subgroup of 64 patients suspected with acute ischemic stroke. In that patient subgroup, EMS performed NIHSS-8 scoring upon patient arrival in the emergency department triage unit. A blinded stroke team member then scored the full 15-item NIHSS within 5 minutes of EMS evaluation.

All suspected stroke patients evaluated by the stroke team underwent noncontrast CT and CT angiography (CTA) as part of the standard acute stroke assessment. CTA was performed using a 40-mL bolus of intravenous contrast (Ultravist 370, Bayer HealthCare, Whippany, NJ, USA). Images were acquired from the aortic arch to the top of the lateral ventricles. The presence or absence of LVO was assessed on admission CTA and defined as a target occlusion for EVT in the anterior circulation: either an occlusion of the M1 segment of the medial cerebral artery) or an internal carotid artery–M1 tandem occlusion. Other LVO (isolated common or internal carotid artery, more distal medial cerebral artery occlusions, anterior cerebral artery occlusions, and posterior territory LVO) were regarded as non-LVO patients as these are not routinely treated with EVT and evidence for EVT treatment in these subgroups is currently lacking. The presence or absence of a causal LVO in the cohort was reviewed by 2 experienced vascular neurologists and correlated with clinical data. Disagreement was resolved by consensus. Patients with incidental findings of cerebral artery occlusions deemed as noncausal for the current stroke were regarded as

NIHSS-8 Item	Scoring Definition	Score
1. LOC	0-alert (A) 1-rousable to minor stimulation (V) 2-rousable only to painful stimulation (P) 3-reflex response or un-rousable (U)	
2. LOC Questions – Ask patient's age and current month (Must be exact)	0-Both correct 1-one correct or dysarthria, foreign language 2-Neither correct	
3. Commands – opens/close eyes, grip and release non paretic hand Other 1 step commands or mimic ok)	0-Both correct (Ok if impaired by weakness) 1-One correct 2-Neither correct	
4. Best Gaze – Test horizontal eye movements tracking object/face	0-Normal 1-partial gaze, abnormal gaze in 1 or both eyes 2- Forced eye deviation or total paresis which cannot be overcome	
5. Facial Palsy – Show teeth, close eyes tight, raise eyebrows. If stuporous, check symmetry of grimace to pain	0-Normal 1-Minor paralysis, flat NLF, asymmetrical smile 2-Partial paralysis (lower face) 3-Complete paralysis (upper & lower face)	
6. Motor Arm - arms outstretched 90deg (sitting or 45 deg (supine) for 10secs. Encourage best effort. Score for Left and then Right arm.	0-No drift for 10 secs 1-drift but does not hit bed 2-Some antigravity effort but can't sustain 3-Unable to overcome gravity, minimal proximal movement present 4-No movement at all X-Unable to assess due to amputation, fusion,fx etc	Left: Right:
7. Dysarthria – read or repeat list of words (see reverse of page)	0-Normal 1-mild-mod slurred speech but intelligible 2-Unintelligible or mute X-intubation or mechanical barrier	
8. Extinction / Neglect – simultaneously touch patient on both hands or legs with their eyes closed, show fingers in both visual fields.	0-Normal none detected 1-neglect or extinction to double simultaneous stimulation in any modality (sensory, visual) OR visual/sensory loss on one side 2-profound neglect in both visual and sensory modalities	
Total Score		

Figure 1. *Eight-item NIHSS-8. Abbreviations: LOC, level of consciousness; NIHSS-8, National Institutes of Health Stroke Scale-8; NLF, nasolabial fold.*

non-LVO patients. Patients without admission CTA were excluded from further evaluation.

Patients were grouped into 3 categories based on acute noncontrast CT and 24-hour follow-up magnetic resonance imaging (MRI) results: confirmed ischemic stroke, confirmed intracranial hemorrhage (ICH), or stroke mimic/transient ischemic attack (TIA). Confirmed ischemic stroke was defined as any patient referred to the stroke team with acute symptoms suggestive of stroke and a diffusion-restrictive lesion on MRI performed 24 hours after admission. ICH was defined as any patient with acute stroke symptoms and acute hemorrhage visible on admission noncontrast CT brain. Patients without a 24-hour MRI diffusion lesion or acute hemorrhage were diagnosed as stroke mimics or TIA.

Statistical Analysis

SPSS version 20 (IBM Corp., Released 2011, IBM SPSS Statistics for Windows, Armonk, NY) and STATA version 14.1 (StataCorp LP 2015, College Station, TX) software were used to perform the statistical analysis. Simple descriptive statistics were used to document patient characteristics. We used a Mann–Whitney *U* test to compare NIHSS and NIHSS-8 scores between patient subgroups. We used area under the receiver operating characteristic curve (AUC) to assess the accuracy of the NIHSS-8 and different NIHSS-8 cutoff scores to identify the presence of an LVO. We calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detection of target LVO for each individual NIHSS-8 cutoff score using standard 2×2 contingency table methodology. The Youden index was used to determine the optimum cutoff score for detection of target LVO. Inter-rater agreement on the subgroup of patients simultaneously scored was assessed using linear-weighted kappa statistics for ordinal data.[12] Kappa values of .41-.60, .61-.80, .81-.99 indicate *moderate, substantial*, and *near perfect* agreement, respectively.[13,14]

Results

Patient Characteristics

The final validation dataset included 551 consecutive patients with suspected ischemic stroke for whom the

Table 1. *Patient characteristics*

	N = 551
Age (median, IQR)	73 (IQR 62-81)
Gender (male, %)	287 (52%)
Subclassification (n, %)	551
Confirmed ischemic stroke	381 (69%)
ICH	55 (10%)
Other	115 (21%)
NIHSS score (median, IQR)	
General population	9 (IQR 4-17)
Confirmed ischemic stroke	11 (IQR 5-19)
Ischemic stroke with LVO	18 (IQR 14-22)
Ischemic stroke without LVO	6 (IQR 4-11)
NIHSS-8 score (median, IQR)	
General population	5 (IQR 2-10)
Ischemic stroke with LVO	11 (IQR 8-14)
Population without LVO	4 (IQR 2-7)

Abbreviations: ICH, intracranial hemorrhage; IQR, interquartile range; LVO, large vessel occlusion; n, number of patients; NIHSS-8, National Institutes of Health Stroke Scale-8.

Table 2. *Distribution of large vessel occlusion sites*

Site of LVO	n
M1	102
ICA-M1 tandem	34
	n = 136
"Nontarget" occlusion	
CCA-ICA	27
ICA-M2 tandem	2
M2	23
A1	0
Vertebrobasilar	9
P1	2
	n = 63
Total	199

Abbreviations: CCA-ICA, common carotid artery or internal carotid artery; ICA-M1 tandem, internal carotid artery and M1 segment of medial cerebral artery tandem; ICA-M2 tandem, internal carotid artery and M2 segment of medial cerebral artery tandem; LVO, large vessel occlusion; M1, M1 segment of medial cerebral artery; M2, M2 segment of medial cerebral artery; n, number of patients; P1, P1 segment of posterior cerebral artery.

hospital stroke team was activated by EMS. All patients received noncontrast CT brain and CTA within 1 hour from clinical assessment. Thirty-four patients were excluded prior to analysis due to lack of admission CTA. No patients were excluded because of incomplete NIHSS. In that same time period, a total of 1866 (acute and nonacute) stroke patients were admitted to the hospital.

Male patients comprised 52% of the cohort (n = 287). Median age at time of evaluation was 73 (interquartile range [IQR] 62-81) (Table 1). Three hundred eighty-one (381) patients had a confirmed ischemic stroke, 55 patients had an ICH, and 115 patients were diagnosed with a TIA or stroke mimic (Table 1). The median NIHSS in the general population of patients suspected with acute stroke (N = 551) was 9 (IQR 4-17). The median NIHSS in the population of patients confirmed with acute ischemic stroke (n = 381) was 11 (IQR 5-19).

A causal LVO eligible for EVT was present in 136 patients (42% of patients confirmed with ischemic stroke): 102 patients had an isolated M1 occlusion and 34 patients had an internal carotid artery–M1 tandem lesion. Another 63 patients had an intracranial occlusion that was not considered a target for EVT, of whom 11 patients had a posterior circulation occlusion. Distribution of LVO occlusion sites is illustrated in Table 2. Zero patients labeled stroke mimic or TIA had an LVO. In the confirmed ischemic stroke population with LVO (n = 136), the median NIHSS was 18 (IQR 14-22) (Table 1). NIHSS scores in patients with ischemic stroke with LVO were significantly higher than in patients confirmed with stroke without LVO (median NIHSS of 6; IQR 4-11; $P < .0001$), but not in patients with a nontarget LVO (median NIHSS of 17, IQR 11-21; $P = .18$) (Table 1).

Validation of the NIHSS-8

The median NIHSS-8 in the cohort of patients suspected with acute ischemic stroke (N = 551) was 5 (IQR 2-10) (Table 1). LVO patients (n = 136) had a median NIHSS-8 score of 11 (IQR 8-14) (Table 1). There was a significant difference between the median NIHSS-8 score of patients with an LVO (n = 136) and patients without an LVO (n = 415), who had a median NIHSS-8 of 4 (IQR 2-7; P value for difference < .0001) (Table 1). The median NIHSS-8 score in patients with a non-target LVO (n = 63) was 9 (IQR 5-13), which was significantly lower than in patients with an LVO eligible for EVT (P value for difference = .026). Distribution of NIHSS-8 scores for patients with an LVO or nontarget LVO and patients without LVO is depicted in Figure 2.

The NIHSS-8 score showed a good accuracy at identifying patients with an LVO eligible for EVT (AUC of .82; 95% confidence interval [CI] .78-.86) in a population of patients with suspected ischemic stroke (N = 551) (Fig 3). In patients with a confirmed ischemic stroke (n = 381), the NIHSS-8 score also had a good accuracy for detection of an LVO (AUC of .77; 95% CI .73-.81). In comparison, the full NIHSS in the population of patients suspected with ischemic stroke (N = 551) had an AUC of .81 (95% CI .77-.85) for detection of an LVO (Fig 3). The accuracy of individual NIHSS items to predict LVO in patients presumed with acute ischemic stroke can be found in the supplementary data (Table S1, Figure S1).

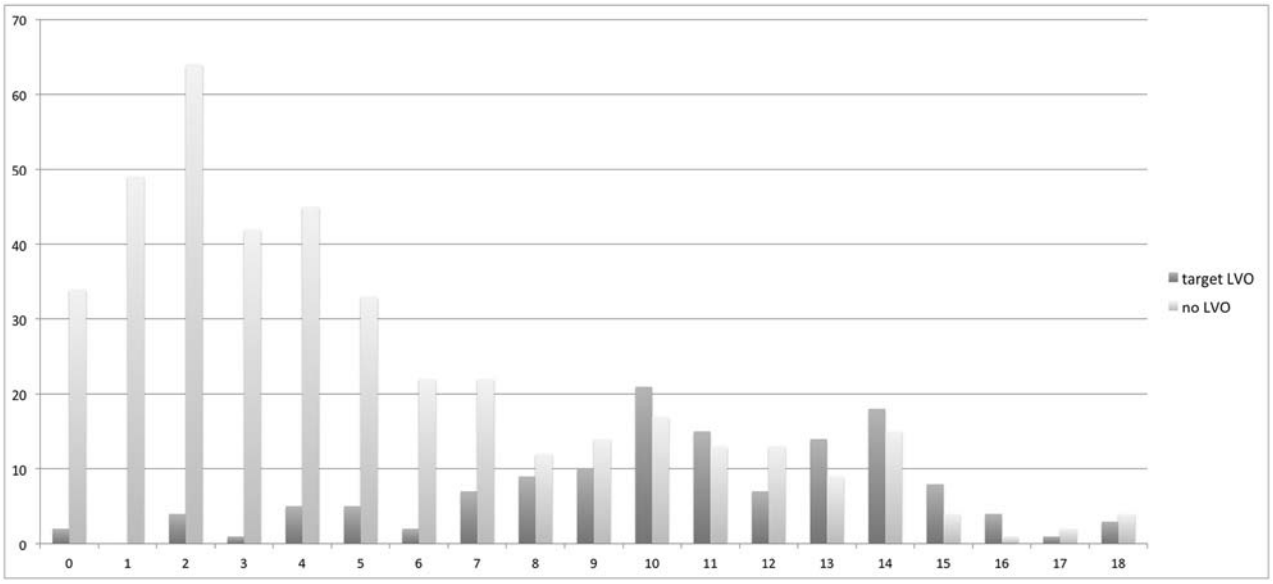

Figure 2. *Distribution of patients with a large vessel occlusion and without large vessel occlusion (y-axis) per NIHSS-8 score (x-axis). Abbreviation: NIHSS-8, National Institutes of Health Stroke Scale-8.*

An NIHSS-8 score of 8 or more most accurately discriminated between patients with and without LVO eligible for EVT. An NIHSS-8 cutoff value of 8 or more had a sensitivity of .81, specificity of .75, PPV of .52, NPV of .92, accuracy of .77, and Youden index of .56 (Fig 4). For detailed sensitivity, specificity, PPV, NPV, accuracy, and Youden index for different NIHSS-8 cutoff values, see supplementary data (Table S2).

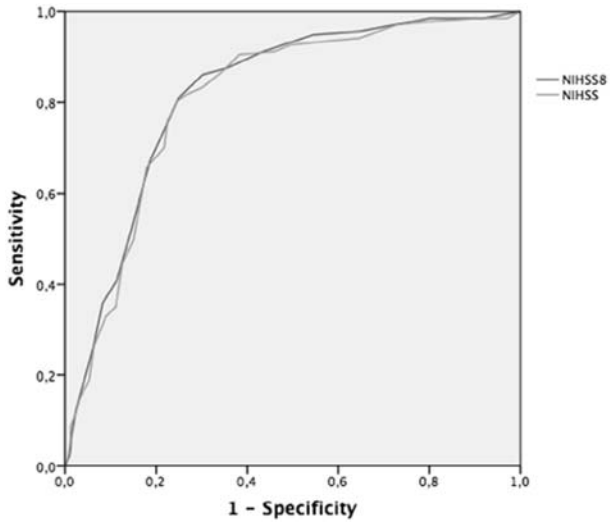

Figure 3. *ROC of the accuracy of the NIHSS-8 score and NIHSS score to identify patients with a large vessel occlusion in a population of patients suspected with ischemic stroke. AUC NIHSS-8 score = .82. AUC NIHSS score = .81. Abbreviations: AUC, area under the ROC curve; NIHSS-8, National Institutes of Health Stroke Scale-8; ROC, receiver operating curve.*

Reliability of the NIHSS-8

EMS and the hospital stroke team reached substantial agreement on NIHSS-8 rating, with an overall linear-weighted Cohen's kappa of .69. This agreement was preserved when a cutoff value of 8 or more was used (linear-weighted kappa = .67). Inter-rater agreement was substantial for all NIHSS-8 items, except for level of consciousness assessment (linear-weighted kappa .54; moderate agreement), facial weakness (linear-weighted kappa .54; moderate agreement), dysarthria (linear-weighted kappa .53; moderate agreement), gaze (linear-weighted kappa .43; moderate agreement), commands (linear-weighted kappa .34; fair agreement) and neglect (linear-weighted kappa .26; fair agreement). Additional information on the inter-rater reliability for each NIHSS-8 cutoff value can be found in the supplementary data (Tables S3 and S4).

Discussion

We have demonstrated that the NIHSS-8 can accurately detect patients with acute ischemic stroke with an LVO eligible for EVT. We assessed the accuracy of this 8-item version of the NIHSS in 551 consecutive patients suspected with acute ischemic stroke (i.e., an aggregate population of acute ischemic stroke, acute hemorrhagic stroke, TIA, and stroke mimics) for whom the hospital acute stroke team was activated within 4.5 hours from stroke symptom onset after assessment by EMS. Although all intracranial and extracranial LVO were captured, only proximal occlusions of the anterior circulation were regarded as target occlusions for EVT. As opposed to the NIHSS, the NIHSS-8 significantly differed between

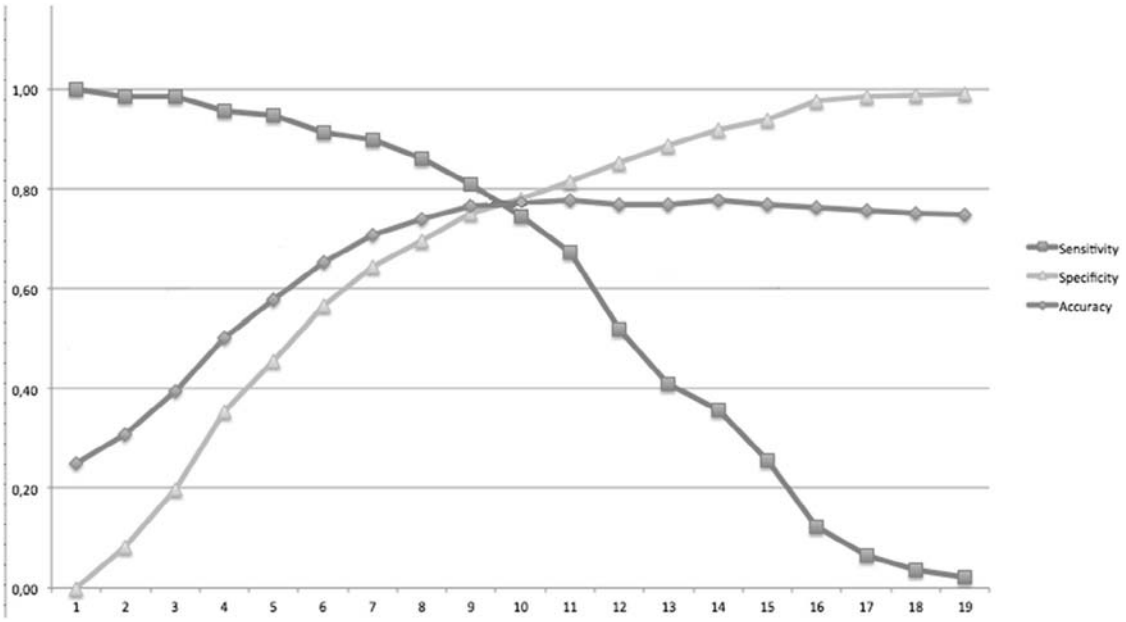

Figure 4. *Sensitivity, specificity, and accuracy for NIHSS-8 cutoff values. Abbreviation: NIHSS-8, National Institutes of Health Stroke Scale-8.*

patients with an LVO eligible for EVT and patients with an intracranial occlusion that was not a target for EVT. A cutoff score of 8 or more had a high sensitivity, specificity, and accuracy for detection of a target LVO, which was comparable to other prehospital stroke scales (Table 3).[15-22] There was substantial agreement between stroke specialists and EMS for use of the overall NIHSS-8, which was preserved when the scale wass used as a cutoff tool.

In the past, different stroke scales have been applied in an effort to identify patients with LVO with variable success rates.[15-22] However, only 3 other prehospital stroke scales were validated on a general cohort of patients suspected with acute ischemic stroke.[15,18,21] Other scales used a cohort of patients confirmed with ischemic stroke, which differs from the population assessed by EMS. Furthermore, except for the Rapid Arterial oCclusion Evaluation scale, existing prehospital stroke scales validated for detection of LVO were used by stroke specialists instead of EMS.[15-17,19-22] Therefore, for most prehospital scales, usefulness of these scales *in the field* remains to be determined. To our knowledge this is the only prehospital stroke scale for detection of LVO validated by stroke specialists for which inter-rater reliability with EMS was assessed.

Our study has several limitations and caveats. First of all, although the sensitivity and specificity of the NIHSS-8

Table 3. *Comparison of prehospital stroke scales for detection of large vessel occlusion*

Prehospital stroke scale	Patient population	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV
3ISS[15]	Presumed ischemic stroke	.86*	≥4	.67	.92	.74	.89
LAMS[16]	Confirmed ischemic stroke	.86	≥4	.81	.89	7.36†	.21†
NIHSS for LVO[17]	Confirmed ischemic stroke/TIA	/	≥9	/	/	.86	/
RACE[18]	Presumed ischemic stroke	.82	≥5	.85	.68	.42	.94
CPSSS[19]	Confirmed ischemic stroke	.67	≥2	.83	.40	1.4†	.4†
CPSSS[20]	Confirmed ischemic stroke	.85	≥2	.70	.87	5.3†	.3†
FAST-ED[21]	Presumed stroke	.81	≥4	.60	.89	.72	.82
PASS[22]	IV rt-PA-treated presumed ischemic stroke	.75	≥2	.64	.83	.67	.81
NIHSS-8	Presumed stroke	.82	≥8	.81	.75	.52	.92

Abbreviations: AUC, area under the receiver operating characteristic curve of the overall scale; CPSSS, Cincinnati Prehospital Stroke Severity Scale; FAST-ED: Field Assessment Stroke Triage for Emergency Destination; 3ISS, 3-Item Stroke Scale; IV, intravenous; LAMS, Los Angeles Motor Scale; LVO, large vessel occlusion; NIHSS-8, National Institutes of Health Stroke Scale-8; NPV, negative predictive value; PASS, Prehospital Acute Stroke Severity scale; PPV, positive predictive value; RACE, Rapid Arterial Occlusion Evaluation scale; rt-PA, recombinant tissue plasminogen activator; TIA, transient ischemic attack.

*Overall accuracy, not AUC.

†Positive and negative likelihood ratio.

is comparable to existing prehospital stroke scales for detection of LVO (which range from .60-.85 to .40-.92, respectively; Table 3), a substantial proportion of stroke patients with a target LVO would remain undetected (15%-20%) or may be misdirected. This significantly limits the usefulness of any existing prehospital stroke scale for detection of LVO. Second, although this study tried to evaluate the usefulness of the NIHSS-8 in a more general population of patients suspected with ischemic stroke evaluated by EMS, this retrospective analysis could not correct for existing EMS screening tools and stroke team activation paradigms, which may have selected a higher number of actual patients with ischemic stroke and a higher number of patients with a target LVO. Also, because of local stroke care organization, this scale was validated on a patient cohort with stroke symptom onset within a 4.5-hour window from assessment. Although unlikely to significantly impact these results, the accuracy of this scale in patients with symptoms beyond the 4.5-hour window is uncertain. Moreover, as for most other prehospital stroke scales, prospective validation in a prehospital setting for this scale remains to be carried out. Third, whereas inter-rater reliability is substantial, agreement on several individual items was fair to moderate, which may reflect the need for more intensive continuous training, and assessment of inter-rater reliability was performed on a small subpopulation. Further validation on a larger population is therefore needed. Also, some individual NIHSS items included in our scale did not have the highest accuracy for LVO identification. As we assessed the accuracy of this existing scale, we could not correct for the possible inferiority of this scale when compared with the 8 most accurate NIHSS items. Fourth, although we included scientifically proven EVT target occlusions, in the future, evidence may be obtained for the benefit of EVT of more distal medial cerebral artery occlusions and posterior circulation occlusions. Inclusion of these vessel occlusions in the LVO target group did not significantly change the accuracy of this scale (AUC .83) (supplementary data Fig S2, A,B). And finally, the NIHSS-8 was derived from the hospital admission NIHSS as opposed to a prehospital evaluation. A prospective validation is therefore needed to confirm the accuracy of the scale and possible impact of this score on EVT rates and patient outcomes.

Summary

In summary, we show that an existing. short 8-item version of the NIHSS-8 accurately identifies the presence of an LVO eligible for EVT in patients with acute ischemic stroke. The score can be used by EMS in a general population of patients presumed with acute ischemic stroke with reasonable reliability.

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Appendix: Supplementary Material

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2017.03.020.

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