**Title page**


**The Scandinavian Stroke Scale is equally as good as the National Institutes of Health Stroke Scale in identifying 3-month outcome**

Torunn Askim PhD[1,2], Julie Bernhardt PhD[3,4], Leonid Churilov PhD[3,5], Bent Indredavik MD PhD[1,6]


[1]Department of Neuroscience, Faculty of Medicine, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

[2]Department of Physiotherapy, Faculty of Health and Social Science, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

[3]Stroke Division, Florey Institutes of Neuroscience and Mental Health, Melbourne, Australia

[4]Faculty of Health Sciences, La Trobe University, Melbourne, Australia

[5]School of Mathematical and Geospatial Sciences, RMIT University, Melbourne, Australia

[6]Stroke Unit, Department of Medicine, St. Olavs Hospital, Trondheim, Norway


Corresponding author: Torunn Askim, Department of Neuroscience, NTNU, Faculty of Medicine, Postbox 8905, 7491 Trondheim, Norway. Email: torunn.askim@ntnu.no, Telephone: +4799589235

Short title: Measurement properties of NIHSS and SSS


Key words: Acute stroke, prediction, outcome assessment, ROC curve, Neurologic examination

Abstract

Background: National Institutes of Health Stroke Scale (NIHSS) is the first choice among stroke scales while the Scandinavian Stroke Scale (SSS) is an alternative scale easy to apply in the clinic.

Aim: The present study aimed to compare the ability of SSS against NIHSS to identify patients being dead or dependent at 3-month follow-up.

Methods: This was a prospective study including patients with acute stroke. NIHSS and SSS were obtained during index hospital stay. Receiver Operating Characteristics (ROC) curve was used to determine the optimal dichotomization of NIHSS and SSS by using modified Rankin Scale (mRS)>2 at 3-month follow-up as the criterion standard. Positive and negative predictive values (PPV and NPV) were calculated.

Results: A total of 104 patients (mean age 79 years, 57.7% male) were included. Median (IQR) NIHSS and SSS score were 6.0 (2.0-11.8) and 43.5 (30.0-51.0) respectively. The AUCs were 0.769 and 0.796 for NIHSS and SSS, respectively, chi2 p=0.303. The best cut point for NIHSS was 6/7 points (PPV=76.2%, NPV=69.0%) while for SSS it was 42/43 points (PPV=71.4%, NPV=73.2%).

Conclusions: SSS was equally as good as NIHSS in identifying patients who died or were dependent at 3-month follow-up and its measurement properties should be further investigated.

Introduction

National Institutes of Stroke Scale (NIHSS) is a well-established and extensively used measure in acute stroke treatment and also recommended for use in clinical trials after stroke (1). The reliability of the scale is clear but some items have consistently shown moderate to low inter-rater reliability (Kappa score less than 0.75). These items are level of consciousness, gaze, facial palsy, ataxia and dysarthria (2;3). The ability of NIHSS to identify 3 months outcome has shown to be superior to other stroke scales like the Canadian Neurological Scale and the Middle Cerebral Artery Neurological Score (1). Furthermore, a baseline NIHSS score $\leq 6$ is associated with high probability of good recovery, and the ability to predict 6 months outcome is shown to be equally good at 2 days versus 5 days or 9 days post stroke (4;5).

The Scandinavian Stroke Scale (SSS) is an alternative stroke scale, frequently used in Scandinavian countries and recently also validated in the Portuguese language (6). Inter-rater reliability of the items varies from excellent for conscious level, orientation and gait, (kappa 0.84, 0.86 and 1.0 respectively) to moderate for facial palsy (kappa 0.59) (6). In a multivariate logistic regression model, neurological recovery as measured by the SSS change score during the first week after onset of stroke was shown to be an independent predictor of good functional outcome (7;8).

The advantage of SSS is its simplicity which makes it easy to perform repeated measures in the very acute phase after stroke (9). However, the ability of SSS to identify outcome at 3 months after onset of stroke has not been validated. As NIHSS is regarded as the gold standard measure, the purpose of the present study was to compare the SSS against the NIHSS to identify patients dead or dependent at 3-month follow-up. A secondary aim was to

compare their ability to identify outcome in patients from different age groups and with different severity levels.

Methods

This was a prospective cohort study with an initial assessment within 14 days after onset of stroke and a follow-up assessment conducted in the patient's home three months later.

All patients admitted to the Stroke Unit at Trondheim University Hospital, Norway, with the diagnosis of stroke were eligible for inclusion, except for those with a devastating stroke receiving end-of-life palliative care. Eligible patients were included if they were able and willing to sign informed consent. Patients who were not able to give informed consent were also included if their next of kin gave oral consent to participation. The study was approved by the Regional Committee of Medical and Health Research Ethics and Norwegian Social Science Data Services.

Age, gender, time since stroke, stroke type, Oxfordshire Classification of Stroke, NIHSS, total score ranges from 0 (no symptoms) to 42 and Scandinavian Stroke Scale, total score ranges from 0 to 58 (no symptoms) were assessed at baseline. At three months follow-up a home visit was conducted for all patients still alive. Death or dependency 3 months after stroke was determined by modified Rankin Scale (mRS) (11). Two well trained assessors did the baseline assessments. The same assessor obtained the NIHSS and the SSS score. A third assessor who was blinded to the initial assessment did the follow-up assessments.

Statistical Analysis

Descriptive statistics were used for the baseline characteristics. Primary outcome was comparison of the area under the Receiver Operating Characteristics (ROC) curve (AUC) for both NIHSS and SSS. The Chi-square test was used to compare the AUCs for NIHSS and SSS. ROC curve analysis was used to determine the optimal dichotomization of NIHSS and SSS respectively, using Youden's criteria (12). The criterion standard was mRS>2. Since SSS ranges from 0 to 58 with 0 as the worst score and NIHSS ranges from 0 to 42 with 42 as the worst score, the SSS sum score was transformed to an SSS inverse score according to the following equation; SSS inverse = Maximum SSS score minus original SSS score. The SSS inverse score was used in the ROC analysis to make it possible to compare the two scales. In all other analysis, the original score of SSS has been reported. Sensitivity and specificity were reported for the optimal dichotomization, while positive and negative predictive values were standardized to a 50% pre-test chance of responding. For the sub-group analysis, patients were divided into subgroups according to age (dichotomized at 80 versus 81 years) and according to stroke severity (NHISS < 8, NIHSS 8-16, NIHSS >16). The statistical analysis were conducted using IBM SPSS Statistics version 19 and Stata v13.

Results

Over 18 months, 124 patients were included, which makes up 23% of all patients admitted to the stroke unit during this period. Two patients were excluded because inclusion exceeded 14 days post stroke, one patient was found not to have stroke and six patients were excluded because of incomplete data at baseline. Eleven patients were lost to follow-up leaving a total of 104 patients included in the analysis.

At baseline, the median age was 81 years and 57.7 % were male. Median (IQR) NIHSS and SSS score were 6.0 (2.0-11.75) and 43.5 (30.0-51.0) respectively (Table 1).

At 3-month follow-up, a total of 59 patients were classified as dependent (mRS>2) and 45 as independent. Nine patients (15.3%) died in the 3-month follow-up interval. The ROC curve (Figure 1) revealed an AUC of 0.769 and 0.796 for NIHSS and SSS respectively, p=0.303. The optimal dichotomization was between 6 and 7 points for NIHSS (64.4% sensitivity and 80.0% specificity) while for SSS it was between 42 and 43 points (69.5% sensitivity and 82.2% specificity).

Ninety-three patients (89.4%) were equally classified as dependent or independent with SSS and NIHSS while 11 (10.6%) patients were incongruent in classification.

Table 2 displays the predictive values standardized to a 50% pre-test chance of being dependent. The PPVs showed a 76% chance of being dependent at 3-months post stroke if the NIHSS score was 7 points or more and a 71% chance of being dependent if the SSS score was 42 points or less. The NPVs were 69% and 73% for NHISS and SSS respectively.

The results from subgroup analysis are displayed in Table 3, showing no significant differences between the two scales for any of the subgroups. However, both scales showed better measurements properties for patients of older age (≤80 years) and those with moderate strokes (NIHSS 8-16).

Discussion

This study showed that SSS was equally good as NIHSS in identifying patients dead or dependent 3 months after stroke. The subgroup analysis showed that the measurement properties for both scales were better for patients with moderate strokes and for those of older age.

Modified Rankin Scale>2 is the most widely used definition of death and dependency after stroke (13). Using this definition as the criterion standard for the ROC analysis revealed an AUC of 0.769 for NIHSS and 0.796 for SSS which should be regarded as adequate (14). Even though the AUC for SSS was slightly larger compared to NIHSS, there were no statistically significant differences between the two scales.

From a clinical perspective the PPV and NPV are of even greater interest. However, these two values are known to be prevalence dependent. To make comparison between scales more feasible the predictive values should be standardized to a 50% pre-test chance of responding. A NPV of 73% for SSS and 69% for NIHSS means that patients have a 73% chance of truly being independent if the initial SSS score is 43 points or more or a 69% chance if the NIHSS score is 6 points or less, indicating that SSS is superior to NIHSS in ruling out the problem. However, the PPV was 71% for SSS versus 76% for NIHSS indicating that NIHSS might be better than SSS in predicting the chance of being dependent at 3 months. Whether one should use the PPV or the NPV is a matter of discussion. From the patients' perspective it might be of greater value to know the chance of being independent while for the health care system it might be of greater value to know the chance of being in need for future health care services.

Even though the measurement properties of NIHSS and SSS are equally good in their ability to identify outcome, the superiority of SSS lies with its simplicity and ease to perform in the

clinic. An example is the difference in measuring motor function between the two scales. While in the NIHSS patients are asked to keep their limb against gravity for 10 seconds, which means that you need a watch, in the SSS patients must keep their limb against manual resistance to get a full score. This advantage of SSS is of particular importance when repeated measures of selected items are used to detect early neurological deterioration (9).

In the NIHSS muscle power is measured in both the affected and the unaffected limb, while SSS only measures the affected limb. This might indicate that the two scales act differently in patients with first ever and recurrent stroke. Future studies should therefore assess measurement properties in these subgroups of patients.

The present study included a rather unselected stroke sample, however, the prevalence of death (15.5 % at 3 months) and dependency seems to be a bit lower comparable to the general stroke population (15). Hence, the next step should be to validate the predictive capacity of SSS and NIHSS in a new patient sample.

In conclusion, SSS showed equally good measurement properties as NIHSS. The SSS is a simple tool, easy to apply in the acute clinical setting and its measurement properties should be further investigated.

Disclosures: None

Reference List

1. Muir KW, Weir CJ, Murray GD, Povey C, Lees KR. Comparison of neurological scales and scoring systems for acute stroke prognosis. Stroke 1996; 27: 1817-1820.

2. Meyer BC, Lyden PD. The modified National Institutes of Health Stroke Scale: its time has come. Int J Stroke 2009; 4: 267-273.

3. Dewey HM, Donnan GA, Freeman EJ, Sharples CM, Macdonell RA, McNeil JJ, et al. Interrater reliability of the National Institutes of Health Stroke Scale: rating by neurologists and nurses in a community-based stroke incidence study. Cerebrovasc Dis 1999; 9: 323-327.

4. Adams HP, Jr., Davis PH, Leira EC, Chang KC, Bendixen BH, Clarke WR, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology 1999; 53: 126-131.

5. Kwakkel G, Veerbeek JM, van Wegen EE, Nijland R, Harmeling-Van der Wel BC, Dippel DW. Predictive value of the NIHSS for ADL outcome after ischemic hemispheric stroke: does timing of early assessment matter? J Neurol Sci 2010; 294: 57-61.

6. Luvizutto GJ, Monteiro TA, Braga G, Pontes-Neto OM, de Lima Resende LA, Bazan R. Validation of the scandinavian stroke scale in a multicultural population in Brazil. Cerebrovasc Dis Extra 2012; 2: 121-126.

7. Jorgensen HS, Reith J, Nakayama H, Kammersgaard LP, Raaschou HO, Olsen TS. What determines good recovery in patients with the most severe strokes? The Copenhagen Stroke Study. Stroke 1999; 30: 2008-2012.

8. Christensen H, Boysen G, Truelsen T. The Scandinavian stroke scale predicts outcome in patients with mild ischemic stroke. Cerebrovasc Dis; 20: 46-48.

9. Birschel P, Ellul J, Barer D. Progressing stroke: towards an internationally agreed definition. Cerebrovasc Dis 2004; 17: 242-252.

10. Gray LJ, Ali M, Lyden PD, Bath PM. Interconversion of the National Institutes of Health Stroke Scale and Scandinavian Stroke Scale in acute stroke. J Stroke Cerebrovasc Dis 2009; 18: 466-468.

11. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. Stroke 2007; 38: 1091-1096.

12. Youden WJ. Index for rating diagnostic tests. Cancer 1950; 3: 32-35.

13. Stroke Unit Trialists Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane database of systematic reviews (online) 2013; 9: CD000197

14. StrokeEngine. Statistical evaluation criteria for outcome measures. 2015 [accessed 2016 July]. Available from: http://www.strokengine.ca/statistics/

15. Appelros P, Jonsson F, Asberg S, Asplund K, Glader EL, Asberg KH, et al. Trends in stroke treatment and outcome between 1995 and 2010: observations from Riks-Stroke, the Swedish stroke register. Cerebrovasc Dis 2014; 37: 22-29.

Table 1. Baseline characteristics

|  | N=104 |
|---|---|
| Male, n (%) | 60 (57.7) |
| First ever stroke, n (%) | 76 (73.1) |
| Age | |
| Mean (SD) | 79.1 (9.0) |
| Days since stroke | |
| Median (IQR) | 6.0 (4.0-9.0) |
| SSS score | |
| Median (IQR) | 43.5 (30.0-51.0) |
| NIHSS score | |
| Median (IQR) | 6.0 (2.0-11.75) |
| Severity groups, n (%) | |
| Mild stroke (NIHSS < 8) | 63 (60.6) |
| Moderate stroke (NIHSS 8-16) | 27 (26.0) |
| Severe stroke (NIHSS > 16) | 14 (13.5) |
| Stroke Classification, n (%) | |
| Infarction | 81 (77.9) |
| Haemorrhage | 21 (20.2) |
| Unknown | 2 (1.9) |

SD, standard deviation; IQR, Inter quartile range; SSS, Scandinavian Stroke Scale; NIHSS,

National Institutes of Health Stroke Scale

Table 2. Predicitive values for National Institutes of Health Stroke Scale (NIHSS) and Scandinavian Stroke Scale (SSS) with mRS>2 as the criterion standard.

| | True positive | False positive | True negative | False negative | Sensitivity | Specificity | PPV* | NPV* |
|---|---|---|---|---|---|---|---|---|
| SSS (42/43) | 41 | 8 | 37 | 18 | 69.5% | 82.2% | 71.4% | 73.2% |
| NIHSS (6/7) | 38 | 9 | 36 | 21 | 64.4% | 80.0% | 76.2% | 69.0% |

PPV: positive predictive value; NPV: Negative predictive value; mRS: modified Rankin Scale *predictive values were standardized to a 50% pre-test chance of responding

Table 3. Subgroup analysis

| All patients | NIHSS | SSS | p-value* |
|---|---|---|---|
| AUC | 0.769 | 0.796 | 0.303 |
| Sensitivity | 64.4 | 69.5 | |
| Specificity | 80.0 | 80.2 | |
| Optimal cutoff | 6/7 | 42/43 | |

Age > 80 years (n=54)

| | NIHSS | SSS | p-value |
|---|---|---|---|
| AUC | 0.806 | 0.827 | 0.592 |
| Sensitivity | 68.4 | 76.3 | |
| Specificity | 87.5 | 81.2 | |
| Optimal cutoff | 6/7 | 45/46 | |

Age ≤ 80 years (n=50)

| | NIHSS | SSS | p-value |
|---|---|---|---|
| AUC | 0.755 | 0.778 | 0.613 |
| Sensitivity | 66.7 | 76.2 | |
| Specificity | 62.1 | 75.9 | |
| Optimal cutoff | 5/6 | 42/43 | |

NIHSS < 8 (n=63)

| | NIHSS | SSS | p-value |
|---|---|---|---|
| AUC | 0.608 | 0.632 | 0.709 |
| Sensitivity | 65.4 | 61.5 | |
| Specificity | 54.1 | 64.9 | |
| Optimal cutoff | 2/3 | 48/49 | |

NIHSS 8-16 (n=27)

| | | | |
|---|---|---|---|
| AUC | 0.809 | 0.901 | 0.246 |
| Sensitivity | 78.9 | 84.2 | |
| Specificity | 75.0 | 87.5 | |
| Optimal cutoff | 10/11 | 33/34 | |

NIHSS > 16**(n=14)

NIHSS; National Institutes of Health Stroke Scale, SSS; Scandinavian Stroke Scale, AUC;

Area Under the Curve

*Chi-square test for differences in AUC

** The Receiver Operating Characteristics (ROC) curves could not be drawn because no

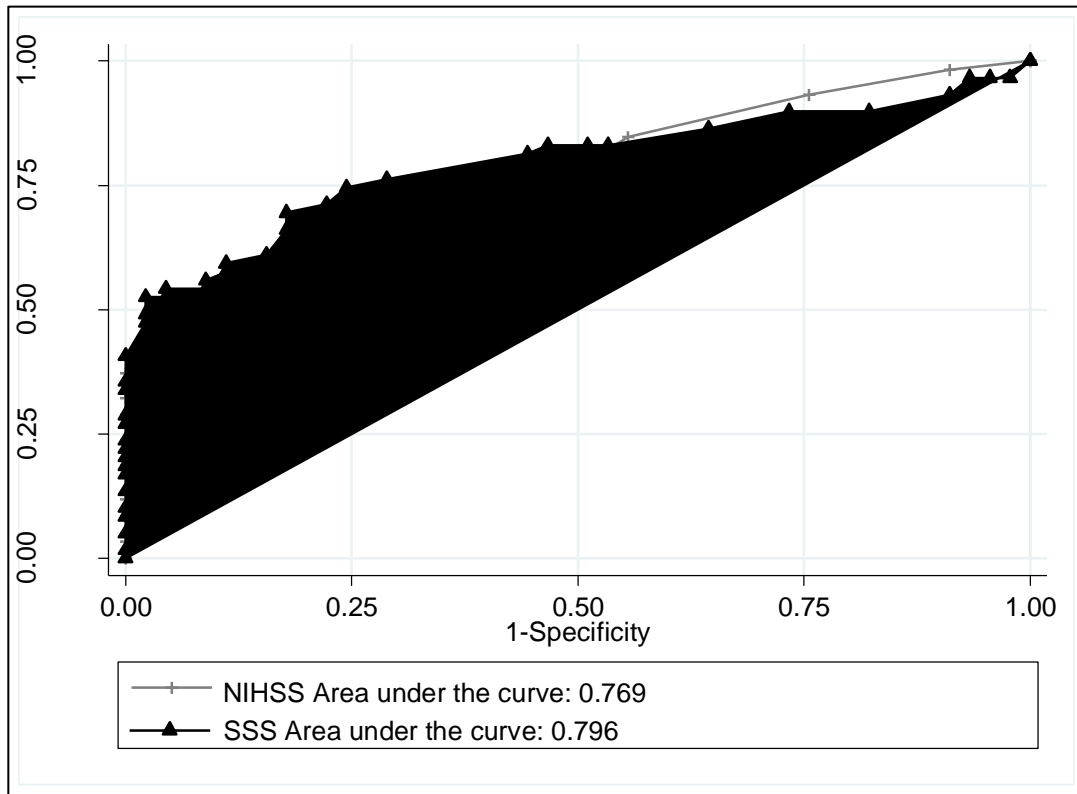patients were classified as independent at 3-month follow-up

Figure 1.

Legend

Figure 1. Receiver Operating Characteristics (ROC) curves for National Institutes of Stroke

Scale (NIHSS) and Scandinavian Stroke Scale (SSS) with mRS>2 as criterion standard