Lestvica NIHSS (National Institutes of Health Stroke Scale) in kratkoročna (30-dnevna) umrljivost bolnikov z ishemično možgansko kapjo

Predicting short-term (30-day) mortality in patients with ischemic stroke using the baseline score of the National Institutes of Health Stroke Scale

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Izvleček

Namen: *Lestvica NIHSS (National Institutes of Health Stroke Scale) je bila razvita predvsem za napoved izhoda po možganski kapi. Cilj naše raziskave je bil ugotoviti uporabnost te lestvice za napoved kratkoročne (30-dnevne) umrljivosti pri bolnikih z ishemično možgansko kapjo.*

Metode: *V raziskavo so bili vključeni vsi bolniki (n=402; 216 moških in 186 žensk), ki so bili v obdobju enega leta hospitalizirani zaradi akutne ishemične možganske kapi. Podatke o prisotnosti sladkorne bolezni in kajenju smo pridobili z vprašalnikom. Pri sprejemu so imeli vsi bolniki izmerjen sistolični in diastolični krvni tlak. Izračunali smo indeks telesne mase. Laboratorijske preiskave so bile opravljene v*

Abstract

Purpose: *The National Institutes of Health Stroke Scale (NIHSS) was developed to measure neurologic outcome and recovery in patients with stroke. The aim of our study was to establish the validity of the NIHSS on short-term (30-day) mortality in patients with ischemic stroke.*

Methods: *All 402 patients (216 males) with acute ischemic stroke hospitalized over 1 year were included in the study. Information on the presence of diabetes mellitus and smoking habits was obtained by a questionnaire. Systolic and diastolic blood pressure was measured upon hospital admission. The body mass index was calculated. Laboratory data were assessed in the first 24*

prvih 24. urah. Ocena nevrološkega stanja ob sprejemu je bila opravljena z lestvico NIHSS. Bolnike smo nato sledili 30 dni.

Rezultati: *Povprečna starost v raziskavo vključenih bolnikov je bila 70,89 let (od 36 do 96 let). Ženske so bile starejše od moških (P<0,0001). V 30-tih dnevih je umrlo 49 (12,2%) bolnikov. Bolniki, ki so umrli, so imeli ob sprejemu višjo oceno po lestvici NIHSS (P=0,0001), bili so starejši (P=0,013), imeli so višji hsCRP (P=0,0001) in nižje albumine (P=0,016). S pomočjo Cox multivariable regression analize so bili napovedniki 30 dnevne umrljivosti NIHSS (P=0,0001), celotni holesterol (P=0,004) in LDL holesterol (P=0,016). Ko smo dodali v analizo starost so NIHSS (P=0,0001), celotni holesterol (P=0,006) in LDL holesterol (P=0,025) ostali napovedniki umrljivosti.*

Zaključek: *Lestvica NIHSS je dober napovednik kratkoročnega (30-dnevnega) izhoda pri bolnikih z akutno ishemično možgansko kapjo.*

h after stroke onset. The National Institutes of Health Stroke Scale (NIHSS) was employed upon hospital admission. Patients were then followed up for 30 days.

Results: *The mean age of patients was 70.89 years (range, 36–96 years). Women were older than men (P<0.0001). There were 49 (12.2%) deaths in the first 30 days. Patients who died had a higher NIHSS score upon hospital admission (P=0.0001), were older (P=0.013), had higher high-sensitivity C-reactive protein (hsCRP) levels (P=0.0001) and lower albumin levels (P=0.016). With Cox multivariable regression analyses, NIHSS score (P=0.0001) as well as levels of total cholesterol (TC) (P=0.004) and low-density lipoprotein-cholesterol (LDL-C) (P=0.016) were predictors of 30-day mortality. After the addition of age as a variable, NIHSS score (P=0.0001) as well as levels of TC (P=0.006) and LDL-C (P=0.025) remained predictors of mortality.*

Conclusion: *The NIHSS is a good predictor of outcome in short-term (30-day) mortality in patients with ischemic stroke.*

INTRODUCTION

Application of the results from clinical trials focusing on stroke to clinical practice needs interpretation and integration of stroke–outcome measures. No single outcome measure can be used to describe or predict all dimensions of recovery and disability after acute stroke. Several tools can be used to measure stroke outcomes, but they are used inconsistently between trials and their relevance may not be clear to practicing physicians (1). Authorities favor functional outcome scales such as the modified Rankin Scale or Barthel Index (2). However, they are crude and potentially insensitive measures of outcome after stroke (3). Handicap scales and disability scales may reflect outcomes of greater relevance to patients. Neurologic scales may provide greater statistical power than disability scales and/or handicap scales. Consequently, there may be an increased chance of detecting the effect of a treatment using a neurologic scale (3). Scales that measure neurological deficits or specific body functions can be used for triage and to guide acute-treatment decisions.

The National Institutes of Health Stroke Scale (NIHSS) has been widely favored in clinical trials focusing on acute stroke. It was developed to measure neurologic outcome and recovery in patients with stroke. The NIHSS is a 15-item impairment scale that provides a quantitative measure of key components of a standard neurological examination (Table 1). The scale can be used to assess the level of consciousness, extraocular movements, visual fields, the function of facial muscle, strength of the extremities, sensory function, coordination (ataxia), language (aphasia), speech (dysarthria), and hemiinattention (neglect) (4, 5). The NIHSS can be used to measure the overall degree of neurologic impair-

Table 1: *National Institutes of Health Stroke Scale (NIHSS)*

1a Level of consciousness	0=Alert	1=Not alert, arousable	2=Not alert, obtunded	3=Unresponsive	
1b Questions	0=Answers both correctly	1=Answers one correctly	2=Answers neither correctly		
1c Commands	0=Performs both tasks correctly	1=Performs one task correctly	2=Performs neither task		
2 Gaze	0=Normal	1=Partial gaze palsy	2=Total gaze palsy		
3 Visual fields	0=No visual loss	1=Partial hemianopsia	2=Complete hemianopsia	3=Bilateral hemianopsia	
4 Facial palsy	0=Normal	1=Minor paralysis	2=Partial paralysis	3=Complete paralysis	
5a Left motor arm	0=No drift	1=Drift before 10 s	2=Falls before 10 s	3=No eff ort against gravity	4=No movement
5b Right motor arm	0=No drift	1=Drift before 10 s	2=Falls before 10 s	3=No eff ort against gravity	4=No movement
6a Left motor leg	0=No drift	1=Drift before 5 s	2=Falls before 5 s	3=No eff ort against gravity	4=No movement
6b Right motor leg	0=No drift	1=Drift before 5 s	2=Falls before 5 s	3=No effort against gravity	4=No movement
7 Ataxia	0=Absent	1=One limb	2=Two limbs		
8 Sensory	0=Normal	1=Mild loss	2=Severe loss		
9 Language	0=Normal	1=Mild aphasia	2=Severe aphasia	3=Mute or global aphasia	
10 Dysarthria	0=Normal	1=Mild	2=Severe		
11 Extinction/inattention	0=Normal	1=Mild	2=Severe		

ment (6). It is one of the most reliable and valid instruments of clinical measurement in stroke (7, 8) It was also shown to be highly correlated with the Barthel Index, modified Rankin Scale and Glasgow Outcome Score at 90 days (5). The NIHSS was designed to assess differences in interventions in patient care as an initial assessment tool and planning post-acute care (1, 9).

The NIHSS has established reliability and validity for use in prospective clinical research, and predictive validity for long-term stroke outcome (1). Less is known about the validity in short-term outcome. The aim of the present study was to establish the validity of the NIHSS on short-term (30-day) mortality in patients with ischemic stroke.

MATERIAL AND METHODS

The present study involved 402 patients with acute ischemic stroke hospitalized over 1 year. A very experienced neurologist reviewed all cases. Stroke was defined according to World Health Organization (WHO) criteria (10). Ischemic stroke was diagnosed if the patient had an appropriate clinical event and had a brain CT that showed a compatible low-density lesion or was normal. Events resolving completely in <24 h were diagnosed as transient ischemic attack (TIA) and such patients were excluded from the study. Patients were then followed up for 30 days.

Baseline data were collected for all patients (Table 2). Information on the presence of diabetes mellitus (DM) and smoking habits was obtained by a questionnaire.

Table 2: *Baseline data of patients with acute ischemic stroke (N=402)*

Age (mean ± SD; years)	70.89 ± 11.6
DM (presence; yes/no)	103/299
SBP (mmHg)	61/341
SBP (mean ± SD; mm Hg)	155.29 ± 25.36
DBP (mean ± SD; mm Hg)	89.89 ± 13.84
BMI (mean ± SD; kg/m^2)	27.32 ± 4.50
NIHSS (mean ± SD; score)	9.61 ± 5.38
TC (mean ± SD; mmol/l)	5.15 ± 1.29
HDL-C (mean ± SD; mmol/l)	1.23 ± 0.36
LDL-C(mean ± SD; mmol/l)	3.16 ± 1.08
TGs (mean ± SD; mmol/l)	1.92 ± 2.21
hsCRP (mean ± SD; mg/L)	17.74 ± 35.70
Albumin (mean ± SD; g/L)	40.11 ± 5.07

SBP = systolic blood pressure upon hospital admission; DBP = diastolic blood pressure upon hospital admission; BMI = body mass index; NIHSS = National Institutes of Health Stroke Scale upon hospital admission; hsCRP = high-sensitivity C-reactive protein; DM = diabetes mellitus; TGs = triglycerides; HDL-C = high-density lipoprotein-cholesterol; LDL-C = low-density lipoprotein-cholesterol; TC = total cholesterol.

Data were obtained from patients and/or their relatives. Patients were divided into two subgroups according to smoking habits: smokers (present or former) and non-smokers. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured upon hospital admission. The body mass index (BMI) was calculated. The NIHSS was also employed upon hospital admission (6). Laboratory data were assessed in the first 24 h after stroke onset. These included serum levels of cholesterol (total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C)), triglycerides (TGs), high-sensitivity C-reactive protein (hsCRP) and albumin. All were measured by routine laboratory methods.

STATISTICAL ANALYSES

Data were analyzed with SPSS ver12.0.1 (SPSS, Chicago, IL, USA) and MedCalc ver9.3.9.0 for Windows software. The Mann–Whitney test was used to compare the data of patients who survived or died. Univariate analyses for all variables were used to discover possible associations between 30-day mortality and conventional risk factors. Cox multivariable regression analyses were used to discover the predictors of 30-day mortality. In the first model of Cox multivariable regression analyses we included: sex; presence of DM and smoking; SBP and DBP upon hospital admission; the BMI; the NIHSS; lipid (TC, HDL-C, LDL-C, TGs) levels; hsCRP level; and albumin level. In the second model, previous variables were included and age added.

To obtain the baseline NIHSS score as the cutoff point for discriminating between patients who survived and those who died, receiver operating characteristic (ROC) curves were constructed and the area under the ROC curve (AUC) with 95% confidence intervals (CIs) calculated. P<0.005 was considered significant.

RESULTS

The study population comprised 402 subjects (216 males). The mean age of patients was 70.89 years (range, 36–96 years). Women were older than men (74.96 vs. 67.38 years, P<0.0001). There were 49 (12.2%) deaths in the first 30 days after the episode of ischemic stroke. No statistically significant differences in sex between patients who died or survived was found, but women who died were older than men (78.6 vs. 67.6 years), and this difference was significant (P=0.003).

When comparing patients who died or survived, we found that patients who died had a higher NIHSS score upon hospital admission (P=0.0001), were older (P=0.013), had a higher hsCRP level (P=0.0001) and lower albumin level (P=0.016) (Table 3). No differences in the presence of DM and smoking between patients who died or survived were found. There was also no difference in SBP or DBP upon hospital admission, lipid levels, and the BMI between patients who died or survived (Table 3).

With univariate analysis only the association between 30-day mortality after ischemic stroke and the NIHSS

Table 3: *Data of patients who survived or died*

	SURVIVED	DIED	P
Age/mean ± SD (years)	70.44 ± 11.32	74.08 ± 13.14	0.013
DM presence (yes/no)	91/262	12/37	NS*
Smoking presence (yes/no; %)	55/298; 15.6	6/43; 12.2	NS*
SBP (mmHg)	155.53 ± 25.05	153.57 ± 27.71	NS*
DBP (mmHg)	89.90 ± 13.66	89.80 ±15.21	NS*
BMI (kg/m^2)	27.35 ± 4.35	27.14 ± 5.47	NS*
NIHSS, mean ± SD (score)	9.03 ± 5.0	13.78 ± 6.15	0.0001
TC, mean ± SD (mmol/L)	5.22 ± 1.29	4.68 ± 1.19	0.01
HDL-C, mean ± SD (mmol/L)	1.23 ± 0.36	1.17 ± 0.40	NS*
LDL-C, mean ± SD (mmol/L)	3.19 ± 1.10	2.92 ± 0.96	NS*
TGs, mean ± SD (mmol/L)	1.95 ± 2.27	1.73 ± 1.62	NS*
hs CRP, mean ± SD (mg/L)	16.13 ± 35.47	29.32 ± 35.61	0.0001
Albumin, mean ± SD (g/L)	40.39 ± 4,86	38.10 ± 6.03	0.016

NS = not significant upon hospital admission*

SBP = systolic blood pressure upon hospital admission; DBP = diastolic blood pressure upon hospital admission; BMI = body mass index; NIHSS = National Institutes of Health Stroke Scale upon hospital admission; hsCRP = high-sensitivity C-reactive protein; DM = diabetes mellitus; TGs = triglycerides; HDL-C = high-density lipoprotein-cholesterol; LDL-C = low-density lipoprotein-cholesterol; TC = total cholesterol.

score (P=0.0001) and TC (P=0.024) was found. No association between mortality and age, presence of DM, smoking, SBP and DBP upon hospital admission, the BMI, as well as levels of LDL-C, HDL-C, TGs, hsCRP and albumin was found.

With Cox multivariable regression analyses in the first model, NIHSS score (P=0.0001), as well as levels of TC (P=0.004) and LDL-C (P=0.016) were predictors of 30-day mortality. In the second model, age (P=0.262) was not a predictor of 30-day mortality, but the NIHSS score (P=0.0001) as well as levels of TC (P=0.006) and LDL-C (P=0.025) remained predictors of mortality.

The AUC of the ROC curve for predicting mortality in the first 30 days was 0.747 (95% CI, 0.702–0.789) (Figure 1). For patients with ischemic stroke, the optimal cutoff score of the baseline NIHSS score to predict death in the first 30 days was NIHSS >9 with a sensitivity of 81.63% (95% CI, 68.0–91.2%) and specificity of 62.89% (57.6–67.9%).

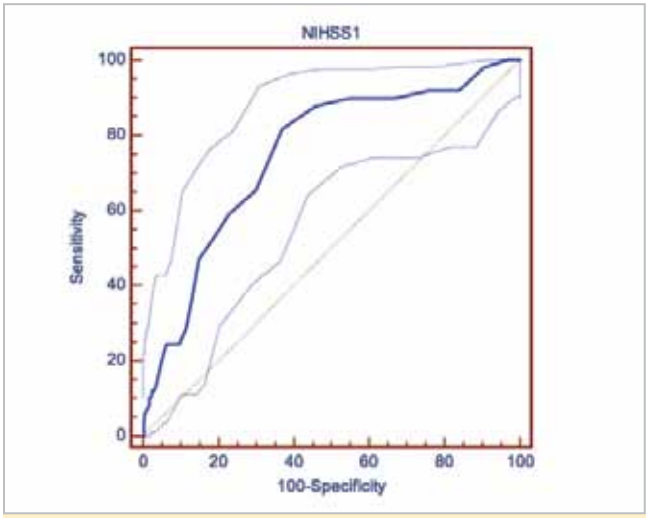

Figure 1. *Receiver operating characteristic (ROC) curve of the baseline NIHSS score for predicting death in the first 30 days.*
NIHSS1, National Institutes of Health Stroke Scale upon hospital admission.

DISCUSSION

The present study showed that the baseline NIHSS score is good predictor of short-term (30-day) mortality. Comparing patients who survived or died in the first 30 days from hospital admission we found that patients who died had a higher baseline NIHSS score. The association between 30-day mortality and NIHSS score was found with univariate analyses, and Cox multivariable regression analyses showed that NIHSS score was an independent predictor of 30-day mortality. It is well known that the NIHSS has

established reliability and validity for use in prospective clinical research, as well as predictive validity for long-term stroke outcome (1, 11, 12). Less is known about the validity of the NIHSS on short-term mortality. Muir et al. found that outcome at 3 months assessed by simple and clinically relevant criteria was best predicted by the baseline NIHSS score (6). The NIHSS was better at predicting outcome than the Canadian Neurological Scale (CNS) and Middle Cerebral Artery Neurological Sore (MCANS) in that study (6). Outcome was categorized as "alive at home", "alive in care" or "dead". Unlike the CNS, MCANS, Scandinavian Stroke Scale and European Stroke Scale, the NIHSS is not weighted in an arbitrary fashion towards the motor function of limbs, but instead reflects the overall degree of neurological deficit. In post-hoc analyses by stroke subtype enrolled in an acute stroke trial, baseline NIHSS scores were strongly predictive of outcome at 7 days and 3 months (13). Excellent outcome was achieved by almost two-thirds of patients with a score of ≤3 at day 7 and very few patients with baseline scores of >15 had excellent outcome after 3 months (13). Baird et al. in their study included 66 patients with ischemic stroke from Boston (MA, USA) and 63 patients with ischemic stroke from Melbourne (VIC, Australia) (14). In both groups, the NIHSS was a good predictor of stroke recovery at 3 months, particularly at high and low scores, but with less certainty in the middle range (14). Sato et al. included 310 patients with ischemic stroke and found that the baseline NIHSS score predicted outcome at 3 months in anterior- and posterior-circulation strokes (11). Because there are few validated models for the prediction of in-hospital mortality after ischemic stroke, Smith et al. used data from the Get With The Guidelines-Stroke Program to derive and validate prediction models for the risk of in-hospital mortality due to ischemic stroke (15). The NIHSS provided substantial incremental information on short-term mortality risk in that study, and was the strongest predictor of mortality (15).

It is also important that the intra-observer reliability of the NIHSS is high. Initial rating and re-rating 3 months later showed an interclass correlation coefficient (ICC) of 0.93 (16). An ICC of 1 suggests perfect reliability and an ICC of 0.8 is, in general, deemed to represent excellent reliability (17). Inter-observer reliability is also high, with an overall ICC of 0.95 (16).

In our study for patients with ischemic stroke, the optimal cutoff score of the baseline NIHSS to predict death in the first 30 days was NIHSS >9 with a sensitivity of 81.63% and specificity of 62.89%. Muir et al. chose a cutoff of 13 on the baseline NIHSS score and found that all patients above that score had poor outcome at 3 months (6). A NIHSS score ≥16 forecasted a high probability of death or severe disability, whereas a score of ≤6 forecast good recovery at 3 months in the Trial of Org 10172 in Acute Stroke Treatment (TOAST) trial (13). Schlegel et al. in a retrospective study confirmed the importance of the categorization of NIHSS (13). Patients with a NIHSS score ≤5 were most strongly associated with discharge home, those with a NIHSS score of 6–13 with rehabilitation, and those with a NIHSS score >13 with long-term nursing facility (12). Compared with patients with a NIHSS score ≤5, patients with a NIHSS score >13 were nearly tenfold more likely to require rehabilitation and more than 100-fold more likely to be placed in a nursing facility (12). Appeleros and Terent in a prospective study included all 377 patients within a municipality who had first-ever non-subarachnoidal stroke during 1 year (18). Of patients with a baseline NIHSS score <4, 75% were functionally independent after 1 year, 17% were functionally dependent, and 8% were dead (18).

In the present study, women who suffered a stroke were older than men. A similar finding was reported and this finding is widely accepted in the general population (19, 20). Patients in our study who died were older, and this finding is in accordance with those from other studies. In the study by MacWalter et al. (21), patients aged >85 years were more than eight-times more likely to die compared with patients aged <59 years. No difference in sex between patients who died was found in the present study, but women were older compared with men, which has been reported previously (22, 23). In the present study, hsCRP levels were higher in patients who died. High levels of

CRP in serum is related to the risk of cerebrovascular and cardiovascular events (24, 25). However, no large study has prospectively assessed the value of CRP levels for short-term and long-term stratification of patients with ischemic stroke for assessment of the prognosis. The patients in the present study who died had lower serum values of TC and albumin. Together with higher hsCRP values, a possible association between malnutrition, inflammation and atherosclerosis is suggested. No difference in the presence of known risk factors for ischemic stroke (hypertension, DM, smoking, SBP, DBP) was found in patients who survived or died in the present study.

Our study has potential limitation that patients who were treated at home were not included, but according to habits in our region it is very unlikely and rare that patients are home-treated.

In conclusion, the NIHSS is a good predictor of outcome in short-term (30-day) mortality in patients with ischemic stroke. Beside the NIHSS, levels of TC and LDL-C were predictors of 30-day mortality. The cut-off score of the baseline NIHSS for a bad outcome in the first 30 days was >9.

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