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ORIGINAL ARTICLE

National Institutes of Health Stroke Scale in patients with primary intracerebral hemorrhage

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Abstract

Background The National Institutes of Health Stroke Scale (NIHSS) is able to predict mortality and functional outcome in patients with ischemic stroke. Its role in primary intracerebral hemorrhage (ICH) is not clear. The objective of our study was to investigate whether NIHSS is a reliable instrument of clinical monitoring and correlates with mortality and functional outcome in ICH.

Methods One hundred fifty-six consecutive subjects with primary ICH were included. We evaluated NIHSS at admission. The functional state after a 30-day and a 3-month-long follow-up was assessed by the modified Rankin Scale (mRS). Spearman's rank correlation coefficient analysis was used for statistics. Sensitivity, specificity, positive predictive value, negative predictive value, global accuracy, and ROC curve were computed using the median score 7 as NIHSS cutoff and the score 4 as mRS cutoff.

Results Median NIHSS score at admission was 7 (16–4); the mean (± SD) was 10.82 (± 8.27). Thirty-two patients (20.5%) died within 30 days and other 22 (14.1%) within 3 months. The median mRS score at 3 months was 4 (6–1); the mean (± SD) was 3.38 (± 2.42). We found a statistically significant correlation between initial NIHSS score and mRS score after 30 days (0.74) and 3 months (0.66, $p < 0.01$). Sensitivity was 93.5 and 92.2%, specificity 82.3 and 69.6%, and GA 87.8 and 80.8%, respectively, at 1 and 3 months. The 1- and 3-month ROC curves comparing initial NIHSS and mRS showed a fitted area as 0.914 and 0.833, respectively.

Conclusions NIHSS is a reliable tool of clinical monitoring and correlates with 30-day and 3-month mortality and functional outcome in subjects with ICH.

Keywords Intracerebral hemorrhage · Prognosis · NIHSS

Introduction

Primary intracerebral hemorrhage (ICH) is a major cause of death and disability. It contributes to about 10 to 15% of all strokes in western countries [1] and to about 30% of all strokes among Asians [2]. The 1-month fatality rate is about 42% in unselected cohorts [3]. The incidence of ICH is 24.6 per 100,000 person-years (95% confidence interval 19.7–30.7), ranging from 1.8 to 129.6 per 100,000 person-years in different studies [4]. The relatively low incidence (compared with ischemic stroke) and the high early case fatality means that relatively few patients are available for long-term follow-up, and therefore the available data on prognosis are imprecise.

ICH has a worse prognosis than ischemic stroke and no specific therapy has been proven to reduce mortality in randomized controlled trials. However, a careful management in a neurological intensive care unit as well as in a stroke unit does appear to improve outcomes [5, 6]. A systematic strategy is important for correct management, based on clinical stabilization and intensive control of elevated blood pressure, avoiding secondary insults.

There is growing evidence that ICH is a dynamic phenomenon and hematoma expansion can be observed within the first 24 h after symptom onset, predominantly in the early hours [7, 8]. In clinical practice, it is crucial to have practical and reliable instruments of accurate clinical monitoring and prediction of prognosis. Therefore, a simple, validated scale that predicts, with sufficient accuracy, mortality within 30 days

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and good long-term functional outcomes could facilitate interviews with patients and their relatives in terms of decisions for invasive and/or supportive care.

The National Institutes of Health Stroke Scale (NIHSS) is commonly used in patients presenting with acute ischemic stroke. It consists of 15 items with a total maximum score of 42 points. A score of zero indicates no clinically relevant neurological abnormality. If the patient score is more than 20, it usually indicates a dense paralysis with impaired consciousness. It is well known that NIHSS correlates with mortality and functional outcome in patients with ischemic stroke. Even if NIHSS is commonly used in primary ICH too, its role in this clinical setting is not clear. Thereafter, it is not known if NIHSS has a prognostic value in these subjects.

In a retrospective study, Cheung et al. [9] found that NIHSS, performed on admission in Asian patients with intracerebral hemorrhage, can be used to predict mortality at 30 days and at 5 years, as well as good functional outcome at 5 years, with an acceptable sensitivity and specificity. No prospective studies are present in literature on this topic, nor in Caucasian people. The objective of our study was to investigate prospectively whether NIHSS is a reliable instrument of clinical monitoring and correlates with mortality and functional outcome in patients presenting with spontaneous ICH.

Subjects and methods

We prospectively included in the study all consecutive patients observed in the acute phase of ICH, confirmed by cerebral CT scan, at our stroke unit since 1 August 2011 to 31 March 2016. A neurologist certified in the use of NIHSS (CF) evaluated the scores in all subjects at the admission to our stroke unit (in all cases within 24 h from the stroke clinical onset). We systematically followed all patients after discharge and a neurologist certified in the use of the modified Rankin Scale (mRS) (CF) evaluated the functional status after 30 days (± 3 days), as well as after a 3-month-long follow-up, by direct clinical observation. No patient was lost at the follow-up. Spearman's rank correlation coefficient analysis was used for statistics. Sensitivity, specificity, global accuracy, and receiver operating characteristic (ROC) curves were computed, using the median score 7 as NIHSS cutoff and the score 4 as mRS cutoff, by ROC analysis web-based calculator (www.jrocfit.org—John Eng).

Results

We included in the study 156 consecutive subjects observed because of primary ICH. Baseline patients' features and NIHSS distribution are shown in Table 1.

NIHSS was calculated at admission in stroke unit (6.1 + 4.9 h since symptom onset). The mean NIHSS score (± SD) at admission was 10.82 (± 8.27) with a median score (interquartile range) of 7 (16–4). Thirty-two patients (20.5%) died within 30 days and other 22 more (14.1%) died within 3 months. The 3-month global fatality rate was 54/156 (34.6%). The mean mRS score (± SD) (score 6 for patients who died) at 3 months was 3.38 (± 2.42) with a median score (interquartile range) of 4 (6–1). In patients whose admission NIHSS fell within the first quartile (0–4), unfavorable outcome occurred in 7 out of 48 cases (14%; odds ratio vs. the rest of the sample 0.33, CI 0.13–0.80, $p = 0.01$). In patients whose admission NIHSS fell within the second quartile but was higher than that of the first (5–7), unfavorable outcome occurred in 10 out of 31 cases (32%; odds ratio vs. the rest of the sample 0.40, CI 0.17–0.92, $p = 0.03$). In patients whose admission NIHSS fell within the third quartile but was higher than that of the second (8–16), unfavorable outcome occurred in 26 out of 39 cases (67%; odds ratio vs. the rest of the sample 0.63, CI 0.34–1.13, ns). In patients whose admission NIHSS fell within the fourth

Table 1 NIHSS score distribution by age, death, and clinical features

Characteristic	Whole cohort ($N = 156$)	Patients who died within 30 days ($N = 32$)	Patients who died within 3 months ($N = 54$)	NIHSS < = 7 at admission ($N = 79$)	NIHSS > 7 at admission ($N = 77$)	Patients with deep hypertensive primary ICH ($N = 94$)	Patients with lobar primary ICH ($N = 45$)
Mean age (± SD) (years)	75.95 (± 13.1)	83.83 (± 8.64)	83.66 (± 8.80)	74.27 (± 12.76)	77.69 (± 13.32)	74.95 (± 13.50)	78.78 (± 9.87)
Male/female	88/68	16/16	27/27	49/30	39/38	52/42	30/15
Mean initial NIHSS score (± SD)	10.82 (± 8.27)	20.22 (± 7.78)	16.72 (± 8.68)	3.91 (± 1.92)	17.91 (± 5.93)	11.76 (± 7.58)	11.42 (± 9.12)
Median initial NIHSS score (interquartile range)	7 (16–4)	23 (26–15.5)	19 (21–5)	4 (6–2)	16 (18–14)	9 (12–4)	8 (19–3)

NIHSS National Institutes of Health Stroke Scale, *SD* standard deviation, *ICH* intracranial cerebral hemorrhage

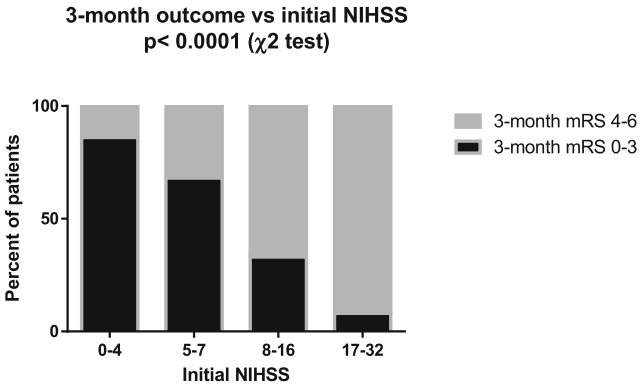

Fig. 1 Patients with unfavorable 3-month outcome increase with increasing baseline NIHSS score. See text for further details and explanations. NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale

quartile but was higher than that of the third (17–32), unfavorable outcome occurred in 35 out of 38 cases (92%; odds ratio vs. the rest of the sample 20.35, CI 5.90–70.13, $p < 0.0001$). Figure 1 summarizes these data.

We found a highly statistically significant correlation between initial NIHSS and mRS after 30 days (rank correlation coefficient, 0.74 $p < 0.01$) and after 3 months (rank correlation coefficient, 0.66, $p < 0.01$). Sensitivity was 93.5 and 92.2%, specificity was 82.3 and 69.6%, global accuracy was 87.8 and 80.8%, positive predictive value was 81.8 and 77.9%, and negative predictive value was 89.9 and 81.1%, respectively, at 30-day and 3-month follow-up. We carried out a ROC analysis using NIHSS = 7 and mRS = 4 as cutoff values. We chose those values because they represented the median values of either variable at admission (NIHSS), and respectively, at 1-month and at 3-month follow-up (mRS). The ROC curves at 1-month and at 3-month follow-up showed fitted areas as 0.914 and 0.833, respectively (Fig. 2). We analyzed separately also the accuracy in predicting dependency (dead patients excluded) as well as mortality alone. The findings are shown in Table 2.

Discussion

In our hospital-based study, we prospectively studied the application of the NIHSS and evaluated its prognostic value on mortality and disability in a consecutive group of patients with spontaneous ICH. Patients with very minor deficits (not hospitalized whatever the reason), those who refused admission, and those who died before admission were not included in our cohort. Patients with subarachnoid hemorrhage, usually admitted to neurosurgery, were also excluded. Although NIHSS is commonly used in patients with acute ischemic stroke, to our knowledge, this is the first prospective study in subjects with ICH. When the NIHSS was used to predict mortality and functional outcome at 1 and 3 months, it showed very good sensitivity (93.5 and 92.2% respectively) and good specificity (82.3 and 69.6% respectively), using the median score 7 as NIHSS cutoff and the score 4 as mRS cutoff. The predictive value on mortality was better for early (30 days) than that for late (3 months) mortality. We believed that the mRS cutoffs we adopted (0–3 vs 4–6) may be more useful in patients suffering from ICH characterized by a more severe prognosis in terms of mortality and disability in comparison to ischemic stroke.

NIHSS is a purely clinical scale, is easily administrable, and does not require the use of any additional diagnostic procedure. The application of a simple validated clinical scale, able to monitor clinical status, is useful for many reasons. ICH is a dynamic phenomenon and neurologic deterioration can be observed within the first 24–48 h due to edema, perilesional blood flow reduction, and hematoma expansion [8, 10]. Seventy-three percent of patients express some degree of hematoma growth; 30–40% of hematoma expand more than 30% from the baseline volume. The expansion is often associated with neurological deterioration and poor clinical outcome [11]. The NIHSS is a clinical measure of the severity of cerebral infarction; it is simple, valid, reliable, and routinely applied by neurologists all over the world. It emphasizes clinical changes and the immediate effect of therapies. Even if it has been introduced for

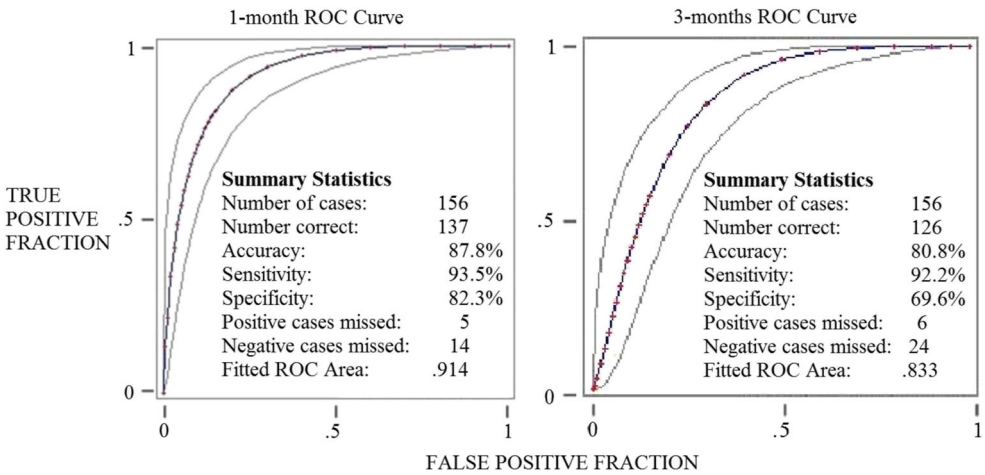

Fig. 2 ROC curves (cutoffs, NIHSS median score 7 and mRS median score 4) at 1- and 3-month follow-up (gray lines, 95% CI). ROC curves, receiver operator characteristic curves; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; CI, confidence interval

Table 2 Initial NIHSS score (cutoff > 7) accuracy in predicting dependency (mRS cutoff > 3, dead patients excluded) and mortality alone (mRS cutoff > 5) at 1- and 3-month follow-up (95% CI)

Dependency at 1 month ($N = 124$)	Dependency at 3 months ($N = 102$)	Death at 1 month ($N = 32$)	Death at 3 months ($N = 54$)
Sensitivity = 70.9 (59.6 to 80.6)	Sensitivity = 69.0 (56.9 to 79.5)	Sensitivity = 59.7 (50.5 to 68.4)	Sensitivity = 63.7 (53.6 to 73.0)
Specificity = 85.7 (71.5 to 94.6)	Specificity = 93.6 (78.6 to 99.2)	Specificity = 87.5 (71.0 to 96.5)	Specificity = 75.9 (62.4 to 86.5)
GA = 76.6 (68.2 to 83.7)	GA = 69.6 (59.7 to 78.3)	GA = 65.4 (57.4 to 72.8)	GA = 67.9 (60.0 to 75.2)
PPV = 90.3 (81.5 to 95.2)	PPV = 96.1 (86.4 to 98.9)	PPV = 94.9 (88.0 to 97.9)	PPV = 83.3 (75.3 to 89.1)
NPV = 61.0 (52.1 to 69.3)	NPV = 56.9 (47.9 to 65.4)	NPV = 35.9 (30.4 to 42.9)	NPV = 52.6 (45.1 to 60.0)

NIHSS National Institutes of Health Stroke Scale, *mRS* modified Rankin Scale, *CI* confidence interval, *GA* global accuracy, *PPV* positive predictive value, *NPV* negative predictive value

ischemic stroke, it has been frequently used in ICH as a monitoring tool [12–14]. In the PREDICT/Sunnybrook ICH CTA study [11], early neurological worsening was defined as worsening of ≥ 4 points in the NIHSS score at 24 h compared with baseline, just like in the therapeutic trials of acute ischemic stroke. Similarly, two other studies [13, 14] used the NIHSS to demonstrate early improvement after stereotactic aspiration of deep ICH. This approach is obvious and easily understandable, but so far it has never been validated.

About the prediction of ICH outcome, several prediction models have been developed using different factors known to influence prognosis like age, ICH location, baseline hematoma volume, anticoagulation use, and the presence and severity of intraventricular hemorrhage (IVH). ICH score [15] and FUNC score [16] are the most used. The ICH score takes in account age, Glasgow Coma Scale (GCS) score, infratentorial location, IVH presence, and ICH volume. The FUNC score uses age, premedical history of cognitive impairment, GCS score, ICH location, and ICH volume. The ICH score is an accurate predictor of outcome assessed as 30-day mortality and is useful as risk stratification; however, its prognostic value on disability was not assessed. The FUNC score was able to predict functional outcome, but the predictive accuracy was not calculated. Neither is based exclusively on clinical variables. In comparison to these two predictive scores, NIHSS is of course less accurate but is easier, is less time-consuming, and is purely clinical. Moreover, it does not require additional learning or training, being already used for ischemic stroke. A formal comparison between the predictive value of these two scales and the NIHSS would go beyond the scope of our present article, and will be investigated in our future research.

Our study has several limitations; we did not evaluate the correlation between NIHSS and hematoma volume and location, which heavily influence prognosis. This may be a future evolution of the study. However, our principal intent was to evaluate the impact on clinical management of a purely clinical scale. Therefore, the little number of infratentorial hemorrhages included did not allow a separate evaluation in this subgroup. We cannot exclude that the clinical value of NIHSS in monitoring patients with infratentorial hemorrhages might be lower. This, however, is a limitation of NIHSS in ischemic stroke, too.

Conclusions

In conclusion, NIHSS assessment, performed at admission by a certified neurologist is a reliable tool of clinical monitoring and correlates with the 30-day and 3-month mortality and functional outcome among survivors. While additional information such as age, precise location and size of the hemorrhage, its possible intraventricular and subarachnoid extension, body temperature, and blood pressure may improve prognostic precision, the clinician may find the NIHSS sufficient for most clinical management decisions and counseling.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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