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Acute ischemic stroke prognostication, comparison between Glasgow Coma Score, NIHS Scale and Full Outline of UnResponsiveness Score in intensive care unit

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KEYWORDS

Acute stroke;
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Abstract *Background:* Stroke is the second most common cause of death worldwide and a frequent cause of adult disability in developed countries. No single outcome measure can describe or predict all dimensions of recovery and disability after acute stroke. Several scales have proven reliability and validity in stroke trials.

Objectives: The aim of the work was to evaluate the FOUR score predictability for outcome of patients with acute ischemic stroke in comparison with the NIHSS and the GCS.

Methods: 127 adult patients with acute ischemic stroke were enrolled. NIHSS, GCS, and FOUR score were collected at 24 and 72 h. Patients were prospectively followed up for the following outcomes; In-hospital or 30 days mortality and Modified Rankin Scale (mRS) at 3 months. The areas under receiver operating characteristic curve (AUC) were compared between the three scores.

Results: Twenty-five (19.7%) patients died, and seventy-two (56.7%) had unfavourable outcome. The NIHSS, the GCS, and the FOUR score were not different in predicting in-hospital mortality (AUC: 0.783, 0.779, 0.796 at 24-h and 0.973, 0.975, 0.977 at 72-h). The NIHSS, the GCS, and the FOUR score done at 24-h were not different in predicting unfavourable outcome (AUC: 0.893, 0.868, and 0.865, respectively). However, the NIHSS done at 72-h showed significantly higher AUC than the GCS score (0.958 versus 0.931, $p = 0.041$), and higher than the Four score (0.958 versus 0.909, $p = 0.011$).

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Conclusions: The GCS and the FOUR score are accurate predictors of mortality after acute ischemic stroke, and are equal in prediction to the NIHSS. The NIHSS is more accurate than the GCS and the FOUR score in predicting poor neurologic outcome.

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1. Introduction

Stroke is the second most common cause of death worldwide and a frequent cause of adult disability in developed countries. According to World Health Organization (WHO) estimates, 15 million people each year suffer strokes.[1,2]

No single outcome measure can describe or predict all dimensions of recovery and disability after acute stroke, several scales have proven reliability and validity in stroke trials.[3] Although measures of clinical stroke severity are critical for optimal discrimination of mortality risk, yet the NIHSS score was recorded infrequently in clinical practice. The time needed to perform even a short standardized stroke severity assessment is probably a barrier to more widespread use. Thus, simpler measures of stroke severity are needed.[4]

The aim of the work was to investigate the performance of the FOUR score in predicting outcome of patients with acute ischemic stroke in comparison with the NIHSS and the GCS.

2. Patients and methods

The study was carried out on 127 adult patients with acute ischemic stroke admitted consequently to the units of Critical Care Medicine Department of Alexandria Main University Hospital and Mustafa Kamel Military Hospital from the first of March to the 30th of September 2013. All patients were managed according to the American Heart Association/American Stroke Association guidelines for the management of patients with acute ischemic stroke.[5] However, none of the patients received thrombolytic therapy.

Informed consent was taken from the next of kin of every patient included in the study. The study had been approved by the local ethics committee of the faculty of medicine.

2.1. Inclusion criteria

- Adult patients (Age $\geqslant$ 18 year).
- With Acute Ischemic Stroke defined as "An episode of neurological dysfunction caused by focal cerebral ischemic injury based on symptoms persisting $\geqslant$ 24 h".[5]

2.2. Exclusion criteria

- Patients who were heavily sedated or receiving neuromuscular blocking agents.

2.3. Data collected

For every eligible patient the following data had been collected:

- *Age and Sex*.
- *Pre-existing comorbid conditions* were assessed and summarized in the Charlson Comorbidity Index (CCI).[6] The CCI is an extensively validated index and includes 19 diseases, which are weighted according to their association with mortality. The CCI reflects the cumulative increased likelihood of 1-year mortality: the higher the score, the more severe the burden of comorbidity. The system was developed originally as a prognostic indicator for patients of a general medical service with a variety of conditions. Its validity for use in stroke outcome studies has been shown recently.[7]
- All patients received a *CT scan of the brain on admission*. Diagnostic procedures such as Doppler ultrasound of the carotid arteries, MRI, and echocardiography were ordered when needed.
- *Stroke subtype classification* utilizing both the Oxfordshire Community Stroke Project[8] and the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) method.[9]
- *The National Institutes of Health Stroke Scale (NIHSS) score*[10] on the first and third days of admission.
- *Glasgow Coma Scale (GCS)*[11] on the first and third days of admission.
- *Full Outline of UnResponsiveness (FOUR)* Score[12] on the first and third days of admission.

2.4. Outcome measures

Enrolled patients were prospectively followed up for the following Outcomes:

In-hospital or 30 days mortality.
Modified Rankin Scale (mRS) at 3 months.[13]

- The scale is defined categorically with seven different grades; 0 indicates no symptoms, 5 indicates severe disability, and 6 indicates death.
- For the final prediction model mRS was dichotomized as unfavorable (score 3–6) versus favorable (score 0–2).

2.5. Statistical analysis

- Data are presented as mean with standard deviation (SD) or median with interquartile range (IQR) for continuous variables and as frequencies and percentages for categorical variables.
- A binary logistic regression analysis was performed to reveal the odds ratios of NIHSS, GCS and FOUR Score in predicting outcome measures. Analyses for scales considered unadjusted models as well as models which adjusted for age, sex, Charlson Index and Oxfordshire

Topographic class. Discrimination of the logistic models was assessed by calculating the area under receiver operating characteristic (ROC) curve. The best cut-off point was chosen as that one which maximizes the Youden index (sensitivity + specificity − 1). Comparison of the areas under ROC curves (AUC) was performed using the nonparametric technique described by DeLong et al.[14]

- To define best cut-off points for neuroworsening, ROC curves were depicted for the difference between day 1 and day 3 for the three scores (NIHSS, GCS and FOUR Score). The best cut-off point was chosen as that one which maximizes Specificity and Positive likelihood ratio.
- Data were analyzed by SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and ROC curve analyses were performed by MedCalc Version 12.5.0.0 (Frank Schoonjans, Mariakerke, Belgium). All hypotheses were constructed two-tailed and $p \leqslant 0.05$ was considered significant.

3. Results

Mean age was 62.40 ± 1.11 years (range 25–95). Sixty-eight patients (53.5%) were females. The median Charlson Index was one (range 0–4). Twenty- five patients (19.7%) died, seventy-two (56.7%) had unfavorable outcome. Patient characteristics are summarized in Table 1.

Table 1 Patient characteristics.

Study variable	Median (interquartile range)/ frequency (%)
Age (years)	63 (54–70)
Male gender	59 (46.5)
Charlson Index	1 (1–2)
NIHSS at 24-h	22 (16–30)
NIHSS at 72-h	20 (11–30)
GCS score at 24-h	8 (7–11)
GCS score at 72-h	10 (8–13)
FOUR score at 24-h	11 (9–15)
FOUR score at 72-h	12 (8–16)
TOAST classification	
Large artery atherosclerosis	53 (41.7)
Cardioembolism	39 (30.7)
Small artery occlusion	24 (18.9)
Stroke of other determined cause	4 (3.1)
Stroke of undetermined cause	7 (5.5)
Oxford-shire topographic classification	
Total anterior circulation infarcts	29 (22.8)
Partial anterior circulation infarcts	23 (18.1)
Lacunar infarcts	28 (22)
Posterior circulation infracts	47 (37)
Outcomes	
In-hospital mortality	25 (19.7)
Unfavorable outcome (mRS 3–6)	72 (56.7)

IQR = Interquartile range, NIHSS = National Institute of Health Stroke Scale, GCS = Glasgow Coma Scale, FOUR = Full Outline of UnResponsiveness, TOAST = Trial of Org 10172 in Acute Stroke Treatment.

3.1. Prediction of in-hospital mortality

Regarding day one scores, for every one point increase in NIHSS score there was an estimated 15% increased odds of experiencing in-hospital mortality (OR = 1.15; 95% CI, 1.07–1.24; $p < 0.001$). For every one point increase in GCS total score, there was an estimated 39% reduced odds of experiencing in-hospital mortality (OR = 0.61; 95% CI, 0.48–0.77; $p < 0.001$). Considering the FOUR score, for every one point increase in total score, there was an estimated 36% reduction in the odds of in-hospital mortality (OR = 0.64; 95% CI, 0.52–0.79; $p < 0.001$). These associations remained after adjustment for age, sex, Charlson Index and Oxfordshire class (Table 2).

Receiver operating characteristic (ROC) curves were estimated to compare prediction of in-hospital mortality by the three scores collected on day one (Table 2, Fig. 1A). The NIHSS AUC was 0.783, the sum of sensitivity and specificity was maximized at a NIHSS score of 25 (sensitivity = 0.84; specificity = 0.69). The GCS AUC was 0.779, the sum of sensitivity and specificity was maximized at a GCS of 8 (sensitivity = 0.84; specificity = 0.57). The FOUR score AUC was 0.796, the sum of sensitivity and specificity was maximized at a FOUR score of 11 (sensitivity = 0.84; specificity = 0.57). This difference between the three scores AUCs was not statistically significant.

Regarding day three scores, for every one point increase in NIHSS score there was an estimated 73% increased odds of experiencing in-hospital mortality (OR = 1.73; 95% CI, 1.35–2.21; $p < 0.001$). For every one point increase in GCS total score on admission, there was an estimated 75% reduced odds of experiencing in-hospital mortality (OR = 0.25; 95% CI, 0.13–0.48; $p < 0.001$). For every one point increase in the FOUR score, there was an estimated 74% reduction in the odds of in-hospital mortality (OR = 0.26; 95% CI, 0.24–0.55; $p < 0.001$). These associations remained after adjustment for age, sex, Charlson Index and Oxfordshire class (Table 2).

The NIHSS AUC was 0.973, the sum of sensitivity and specificity was maximized at a NIHSS score of 29 (sensitivity = 1; specificity = 0.89). The GCS AUC was 0.975, the sum of sensitivity and specificity was maximized at a GCS of 7 (sensitivity = 0.96; specificity = 0.92). The FOUR score AUC was 0.977, the sum of sensitivity and specificity was maximized at a FOUR score of 8 (sensitivity = 1; specificity = 0.86). This difference between the three scores AUCs was not statistically significant (Table 2, Fig. 1B).

3.2. Prediction of unfavorable outcome (mRS 3–6)

Regarding day one scores, for every one point increase in NIHSS score there was an estimated 28% increased odds of experiencing unfavourable outcome (OR = 1.28; 95% CI, 1.18–1.39; $p < 0.001$). For every one point increase in GCS total score, there was an estimated 55% reduced odds of experiencing unfavourable outcome (OR = 0.45; 95% CI, 0.34–0.59; $p < 0.001$). Considering the FOUR score, for every one point increase in total score, there was an estimated 45%

Table 2 Logistic regression models with receiver operating characteristic (ROC) curve analysis in predicting in-hospital mortality.

	Unadjusted model		Adjusted model[¶]		ROC	
	OR (95% CI)	*p*	OR (95% CI)	*p*	AUC (95% CI)	*p*
At 24-h:						
NIHSS	1.15 (1.07–1.24)	<0.001*	1.14 (1.05–1.24)	0.001*	0.783 (0.701–0.851)	<0.001*
GCS score	0.61 (0.48–0.77)	<0.001*	0.60 (0.44–0.80)	0.001*	0.779 (0.697–0.848)	<0.001*
FOUR score	0.64 (0.52–0.79)	<0.001*	0.66 (0.52–0.84)	0.001*	0.796 (0.715–0.862)	<0.001*
At 72-h:						
NIHSS	1.73 (1.35–2.21)	<0.001*	2.81 (1.37–5.78)	0.005*	0.973 (0.927–0.993)	<0.001*
GCS score	0.25 (0.13–0.48)	<0.001*	0.16 (0.06–0.47)	0.001*	0.975 (0.930–0.994)	<0.001*
FOUR score	0.26 (0.12–0.54)	<0.001*	0.19 (0.06–0.58)	0.003*	0.977 (0.933–0.995)	<0.001*

OR = Odds Ratio, CI = Confidence Interval, AUC = Area Under ROC Curve, NIHSS = National Institute of Health Stroke Scale, FOUR = Full Outline of UnResponsiveness, GCS = Glasgow Coma Scale.

[¶] Adjusted for Age, Sex, Charlson Index, and Oxfordshire Class.

* *p* is significant ⩽ 0.05.

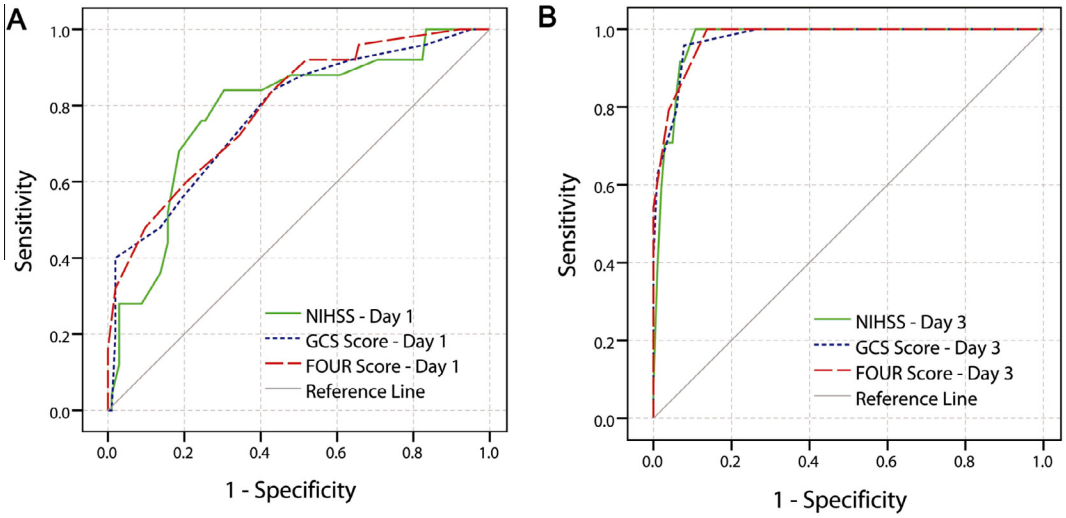

Figure 1 ROC curves comparing (A) 24-h & (B) 72-h NIHSS, GCS score and FOUR score in predicting In-hospital Mortality.

reduction in the odds of unfavourable outcome (OR = 0.55; 95% CI, 0.45–0.61; $p < 0.001$). These associations remained after adjustment for age, sex, Charlson Index and Oxfordshire class (Table 3).

The NIHSS AUC was 0.893, the sum of sensitivity and specificity was maximized at a NIHSS score of 22 (sensitivity = 0.76; specificity = 0.87). The GCS AUC was 0.868, the sum of sensitivity and specificity was maximized at a GCS of 8 (sensitivity = 0.81; specificity = 0.87). The FOUR score AUC was 0.865, the sum of sensitivity and specificity was maximized at a FOUR score of 11 (sensitivity = 0.79; specificity = 0.85). This difference between the three scores AUCs was not statistically significant (Table 3, Fig. 2A).

Regarding day three scores, for every one point increase in NIHSS score there was an estimated 36% increased odds of experiencing unfavourable outcome (OR = 1.36; 95% CI, 1.22–1.51; $p < 0.001$). For every one point increase in GCS total score on admission, there was an estimated 58% reduced odds of experiencing in-hospital mortality (OR = 0.42; 95% CI, 0.31–0.56; $p < 0.001$). For every one point increase in the FOUR score, there was an estimated 47% reduction in the odds of in-hospital mortality (OR = 0.53; 95% CI, 0.43–0.65; $p < 0.001$). These associations remained after adjustment for age, sex, Charlson Index and Oxfordshire class (Table 3).

The NIHSS AUC was 0.958, the sum of sensitivity and specificity was maximized at a NIHSS score of 19 (sensitivity = 0.86; specificity = 0.93). The GCS AUC was 0.931, the sum of sensitivity and specificity was maximized at a GCS of 10 (sensitivity = 0.84; specificity = 0.93). The FOUR score AUC was 0.909, the sum of sensitivity and specificity was maximized at a FOUR score of 11 (sensitivity = 0.84; specificity = 0.94). The NIHSS score showed significantly larger AUC than the GCS score and the FOUR score ($p = 0.041$ & 0.011, respectively), the difference between the GCS and FOUR score AUCs was not statistically significant (Table 3, Fig. 2B).

4. Discussion

The mean age of patients in the present study was 62.4 years; this is consistent with worldwide studies that quote mean ages between 31 and 88 years.[15–19] El Batch et al.[20] in an epidemiological study of 850 stroke patients admitted to Alexandria Main University Hospital reported a mean age of 67.2 years.

Table 3 Logistic regression models with receiver operating characteristic (ROC) curve analysis in predicting unfavorable outcome.

	Unadjusted model		Adjusted model[¶]		ROC	
	OR (95% CI)	*p*	OR (95% CI)	*p*	AUC (95% CI)	*p*
At 24-h:						
NIHSS	1.28 (1.18–1.39)	<0.001*	1.25 (1.14–1.36)	0.001*	0.893 (0.826–0.941)	<0.001*
GCS score	0.45 (0.34–0.59)	<0.001*	0.48 (0.35–0.65)	0.001*	0.868 (0.797–0.922)	<0.001*
FOUR score	0.55 (0.45–0.67)	<0.001*	0.56 (0.44–0.70)	0.001*	0.865 (0.794–0.920)	<0.001*
At 72-h:						
NIHSS	1.36 (1.22–1.51)	<0.001*	1.64 (1.31–2.06)	<0.001*	0.958 (0.906–0.986)	<0.001*
GCS score	0.42 (0.31–0.56)	<0.001*	0.29 (0.17–0.49)	<0.001*	0.931 (0.872–0.969)	<0.001*
FOUR score	0.53 (0.43–0.65)	<0.001*	0.41 (0.28–0.59)	<0.001*	0.909 (0.844–0.953)	<0.001*

OR = Odds Ratio, CI = Confidence Interval, AUC = Area Under ROC Curve, NIHSS = National Institute of Health Stroke Scale, FOUR = Full Outline of UnResponsiveness, GCS = Glasgow Coma Scale.
[¶] Adjusted for age, sex, Charlson Index, and Oxfordshire Class.
* *p* is significant ⩽ 0.05.

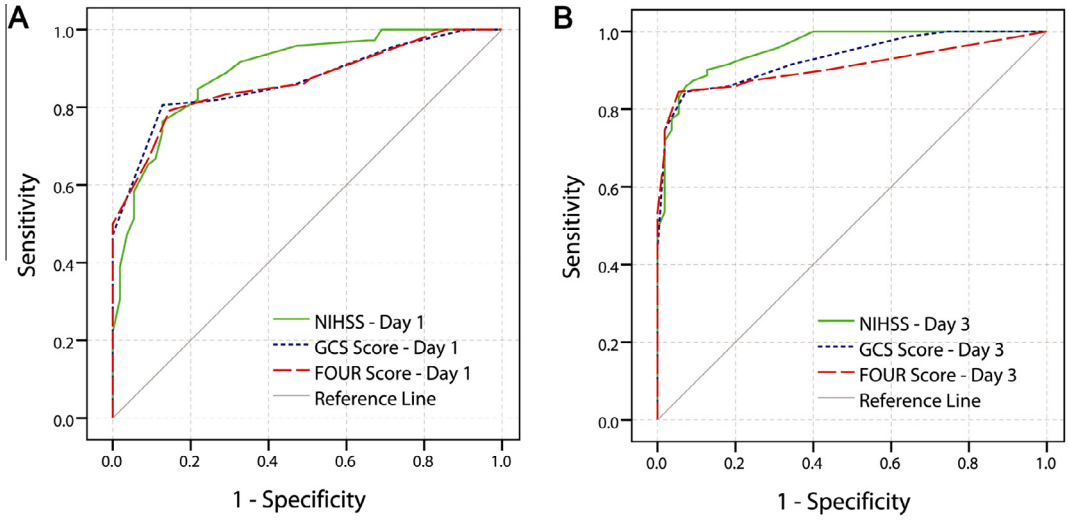

Figure 2 ROC curves comparing (A) 24-h & (B) 72-h NIHSS, GCS score and FOUR score in predicting Unfavorable Outcome.

Fifty-three percent of acute ischemic stroke admissions in this analysis were female. Different observations were reported in many studies[21–24] and the textbooks have often mentioned the incidence rates to be about 25–30% higher among men.[25] However, community-based studies from new parts of the world have been published, and these studies have changed the picture. In the study by Touze et al. from the United States, there were 14 149 male and 16 255 female strokes, which means that females outnumbered males by the factor 1.15. A recent systematic review found that women with stroke are more likely than men to have a parental history of stroke.[26]

The Charlson Index was scored on the basis of discharge *International Classification of Diseases, 9th Revision, Clinical Modification* coding. In the present study 21.3% had a Charlson Index of 0, 45.7% 1, 22% 2, 10.2% 3, and 0.8% 4, similar observation results were observed in a study of 960 enrolled ischemic stroke patients, 23% had a Charlson Index of 0, 34% 1, 22% 2, 12% 3, and 8% ⩾ 4.[7]

In the present study, twenty-five (19.7%) patients died during hospitalization and seventy-two (56.7%) had an unfavorable outcome at three months. Matching with that, El Batch et al.[20] reported a mortality rate of 25%.

When predicting in-hospital mortality; the NIHSS, the GCS score, the FOUR score, were independent predictors of mortality after controlling for common confounders on 24-h of admission as well as at 72 h via multiple logistic regression.

Stroke severity, assessed by NIHSS, is the single characteristic that was most strongly linked with mortality in the literature.[4,27-29] In the present study the NIHSS score showed a moderate accuracy in predicting in hospital mortality (AUC = 0.78). Different observations were reported by Jeng et al.[30] in an analysis of 1178 acute stroke patients admitted to stroke ICU reporting higher AUC for the NIHSS score in predicting in hospital mortality (AUC = 0.86). However, their study included 341 (40.2%) patients with hemorrhagic stroke and seventy (13.8%) patients with ischemic stroke receiving thrombolytic therapy. The present study included ischemic stroke patients only and none of them received thrombolytic therapy.

The GCS total score showed a moderate accuracy in predicting in-hospital mortality (AUC = 0.78). Similar observations were reported by Weir et al.[31] who in an analysis of 1517 acute stroke admissions to acute stroke unit found that GCS score had AUC of 0.79 in predicting in-hospital mortality. In contrast with that, Kocak et al. in a study of 100 acute stroke patients, reported AUC 0.62 for the GCS. However, their study addressed acute stroke including hemorrhagic stroke which had different mortality rates and patterns than ischemic stroke.[32]

In the present results, when comparing three scores in predicting in hospital mortality collected one day and the third day of admission there was no difference between the NIHSS score, the GCS scale and the FOUR score. This is consistent with previous studies that found no significant differences between the effectiveness of the FOUR score and the GCS scale but the FOUR score is more accurate than the GCS in assessment more neurological examination and the depth of coma, Sacco et al.[33] suggested that FOUR score is a reliable instrument to assess coma in stroke patients.

Kocak et al.[32] found that ROC curve analysis showed significant trending with both FOUR score and GCS for prognosis; the area under curve for the FOUR score ranged from 0.675 to 0.922 when measurements had been made on day 3 and the area under curve for the GCS scale ranged from 0.62 to 0.82 when measurements had been made on day 3 suggest that FOUR score is a useful scale for evaluation of acute stroke patients in the intensive care unit as a homogeneous group, with respect to the outcome estimation, which is similar to the present results that found all sub-scores of the FOUR and the GCS at third day had a good predictive value for mortality.

When it comes to prediction of an unfavorable outcome, the current study's results correspond to those reported by Idrovo et al.[15] the NIHSS score, the GCS, and the FOUR score predicted an unfavorable outcome. There were no significant differences for the predictive power of the two scoring methods. The NIHSS score had the highest AUC than the AUC of the GCS scale and the AUC of the FOUR score on the first day and the third day of admission in predicting unfavorable outcome.

The three scores showed more accurate prediction when done at 72 h than at 24 h. As time passes, the prognostic value of impairment severity becomes clearer. If deficits do not subside or improve after a few days, prognostication becomes more accurate. The NIHSS is robust between days 2 and 9 to predict outcome.[34,35]

5. Conclusions

The GCS and the FOUR score are accurate predictors of mortality after acute ischemic stroke, and are equal in prediction to the NIHSS.

The NIHSS is more accurate than the GCS and the FOUR score in predicting poor neurologic outcome.

Conflicts of interest

None declared.

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