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ORIGINAL ARTICLES

Comparison Between the GCS And the 'Full Outline of UnResponsiveness' Score in Predicting 30-Day Mortality in Patients with Impaired Consciousness Due to Stroke

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Abstract

Background: *The Full Outline of UnResponsiveness (FOUR) score was introduced to overcome the limitations of the widely used Glasgow Coma Scale (GCS).* ***Objective:*** *The aim of the study was to evaluate the predictive ability of the GCS versus the FOUR score on 30-day mortality in patients with impaired consciousness due to stroke.* ***Materials and methods:*** *This prospective observational study was carried out among stroke patients with impaired consciousness admitted to the Department of Neurology of Chattogram Medical College & Hospital. A total of one hundred and thirty-two patients with evidence of stroke on computed tomography of the head were included. GCS and FOUR scores were assessed after enrollment in the study. The primary outcome measure was 30-day mortality after onset of stroke. A total of 128 patients were finally analyzed.* ***Results:*** *Mean (±SD) age was 62.6 (±11.5) years, and 54.7% were male. The types of stroke constituted ischemic, hemorrhagic, and subarachnoid hemorrhage in a proportion of 48.4%, 45.3%, and 6.3%, respectively. The mean (range) GCS score was 6.78 (3.0-10.0) and FOUR score was 9.72 (2-13). The 30-day mortality rate was 54.7%. In terms of predictive power for 30-day mortality, the area under the receiver operating characteristic curve (AUROC) (95% CI) for the GCS was 0.756 (0.673-0.838), and for the FOUR score was 0.909 (0.858-0.961). The difference in the AUROC values between the two coma scale scores (0.153) was statistically significant (p= 0.002, by Z test). With a cutoff score of 10.5, the FOUR score predicted 30-day mortality with a sensitivity and specificity of 93.1% and 81.4% respectively. For GCS, a cutoff score 6.5 had a sensitivity of 91.4% and* 52.9% specificity. Subjects with the FOUR score of 2-11 had an 8.02-fold higher hazard of 30-day mortality (HR 8.02, 95% CI *3.21-20.04) compared to those with the score of 12 and above. Those with a GCS score of 3-7 had a 4.88-fold higher hazard of 30-day mortality (HR 4.88, 95% CI 2.97-8.03) compared to those with a score of 8 and above.* ***Conclusion:*** *Our study revealed FOUR score was significantly better than GCS in predicting 30-day mortality in patients with impaired consciousness due to stroke.*

Keywords: *Stroke; Consciousness; FOUR score; Full Outline of UnResponsiveness; Outcome.*

Background

Predicting the prognosis in patients with stroke at the earlier stages can help physicians make proper decisions and accomplish appropriate management.[1,2] Various factors play a role in determining the outcome in stroke patients and as such, scales efficient in monitoring clinical trends and having the ability to anticipate outcomes with

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acceptable accuracy in stroke patients have been aspired for a long time. Several studies have been performed to evaluate the outcomes in stroke patients and, various scales have been used for this purpose.[3]

Stroke can cause a wide variety of symptoms one of which is impairment of consciousness. Various tools have been used to assess and measure disorders of consciousness.[4] Clinical scoring systems using physical examination variables help clinicians assess the level of consciousness (LOC), gauge clinical improvement or deterioration, and predict outcomes in patients with stroke in the acute stage. Frequent brain imaging, either by Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) is not feasible in most places, and clinical scoring methods are used to detect patients who may benefit from frequent monitoring, appropriate therapeutic support, referral to the intensive care units (ICU) or high dependency units at an earlier stage.[5]

The GCS was devised in 1974 keeping focus on patients with traumatic brain injury. This scale comprises three components that assess eye opening, verbal response, and motor response. It is the most widely used neurological scoring system in the world.[6,7] This scale consistently predicts mortality across a wide group of patients in Bangladesh.[8,9] Despite its widespread use, some shortcomings of GCS have been described. The verbal component of the GCS cannot be tested in patients having aphasia or endotracheal intubation. It does not possess some important clinical parameters, namely brainstem reflexes and breathing patterns, and thus, it may not be able to identify different stages of brain herniation as well as conditions like vegetative state, minimally conscious state, locked-in syndrome or brain death.[10]

Considering the limitations of GCS and overcoming those, the 'Full Outline of UnResponsiveness' (FOUR) score was constructed to assess the level of consciousness.[10] They validated this score first in patients admitted to a neuro-intensive care unit.10 The score includes four components of neurologic assessment—eye response, motor response, brainstem reflexes, and respiration—each with a score of 0 to 4. The sum score ranges from 0 to 16, with 16 indicating the highest possible score.10 Additionally, the eyes must be able to track or blink to command for scoring a maximum of 4 in the eye response component. The absence of voluntary tracking may guide the recognition of patients with possible vegetative states while documentation of two blinks on command would help find a locked-in syndrome.10 In some of the validation studiescarried out in various subsets of patients with impaired consciousness, the FOUR scores performed comparably to the GCS in predicting outcomes.[11-13]

The performance of the FOUR score has probably not yet been validated in Bangladesh. A well-structured coma scale like the FOUR score, capable of assessing important areas of brain function, might be useful for clinicians in resource-limited settings to evaluate patients with altered consciousness more elaborately and possibly improve the appropriateness of their subsequent triage. Henceforth, we felt the need to validate the scale in our setting. The current study was therefore aimed to compare the GCS with the FOUR score in predicting 30-day mortality outcomes in patients with impaired consciousness due to stroke admitted to a tertiary care teaching hospital in Bangladesh. We hypothesized that the FOUR score is superior to the GCS in terms of predicting 30-day mortality in patients with impaired consciousness due to stroke.

Materials and methods

This prospective observational study was conducted in the Department of Neurology, Neurosurgery and Intensive Care Unit (ICU) of Chattogram Medical College & Hospital, Bangladesh, from March 2019 to February 2021. Informed consent was obtained from patients' caregivers. The study protocol was approved by the Ethical Review Committee of Chittagong Medical College (Memo number: CMC/PG/2021/680 on January 19, 2021).

Adult patients (age more than 18 years) with impairment of consciousness due to stroke confirmed by brain imaging with duration of stroke

from onset not more than seven days were included in this study. Patients with clinical and imaging evidence suggestive of brain tumors or demyelination, subdural or epidural hematoma, traumatic brain injury; those who received sedatives, neuromuscular blocking agents, or anesthesia within the past 24 hours of entry to the study; those with clinical and radiological evidence of pneumonia or pulmonary edema; patients with stroke and impaired consciousness but having hypoglycemia, hyponatremia, urinary tract infection, pneumonia, hepatic or renal impairment, history of poisoning or drug intoxication were excluded. Patients whose symptoms resolved before 24 hours from onset were also excluded.

All relevant data were noted in a structured case record form. All patients with a clinical diagnosis of stroke and impaired consciousness were subjected to undergo an urgent non-contrast CT scan of the head as soon as possible. Soon after that, those who were diagnosed with stroke were enrolled and physically examined.

GCS and FOUR scores were assessed just after the patients had been enrolled, and this was used to predict the outcome mea- sures. The interval between the onset of stroke and assessment of GCS and FOUR scores was approximately three days on average in the current study. Thirty-day mortality from stroke onset was the outcome measure which was obtained either by direct patient evaluation in the outpatient department or by a telephonic interview with the patient's caregiver/ family member.

Data were analyzed using Statistical Package for Social Science (SPSS) for Windows version 23.0 software. The discriminato- ry values of GCS and FOUR scores for predicting 30-day mortality were studied using ROC curve analyses with the calculation of AUC. The difference between two AUCs was tested by Z test. The Youden index was used to determine optimal cutoffs for categorical transformations of the GCS and FOUR scores in the data set to predict 30-day mortality. Cox proportional hazard regression was used to calculate hazard ratios to determine the association between the scores and 30-day mortality. Values of $p < 0.05$ were established as indicating a significance threshold.

Results

A total of 132 subjects were enrolled out of 148 subjects screened for eligibility. Sixteen patients were excluded for not meeting the inclusion criteria. Four patients were lost to follow-up at the end. Out of 128 patients, 62 (48.4%) patients were diagnosed to have ischemic stroke, 58 (45.3%) had hemorrhagic stroke, and the rest of the 8 (6.3%) patients had subarachnoid hemor- rhage. The thirty-day mortality rate was 54.7% (70/128). Gender, FOUR score, and GCS were significantly different between the survivors and those who died; the latter group showed significantly lower scores than those who survived ($P < 0.001$) [Table I].

The AUROC in predicting 30-day mortality for GCS was 0.756 (95% CI: 0.673-0.838) and for FOUR scores was 0.909 (95% CI: 0.858-0.961) for FOUR score (Figure 1 and Table 2). The difference in the AUROC values between two score (0.153) was statistically significant ($p= 0.002$, by Z test).

Table-I

Characteristics of the study sample

Characteristics	Total (n=128)	Survivors (n=58)	Deceased (n=70)	P value
Age, years	62.6±11.5	63.1±11.4	62.2±11.7	0.650*
Sex				
Male	70 (54.7)	26 (44.8)	44 (62.9)	0.041†
Female	58 (45.3)	32 (55.2)	26 (37.1)	
FOUR score	9.7 ± 2.6	11.5±0.7	8.2±2.7	<0.001*
GCS score	6.8 ± 1.8	7.7±0.9	6.0±1.9	<0.001*

Data were expresses as mean ±SD or frequency (%)., FOUR: Full outline of unresponsiveness, GCS: Glasgow Coma Scale, *Independent sample t test, †Chi-square test.

With a cutoff score of 10.5, the FOUR score predicted 30-day mortality with a sensitivity of 93.1% and specificity of 81.4%. For GCS, a cutoff score of 6.5 showed a sensitivity of 91.4% and specificity of 52.9% (Table II).

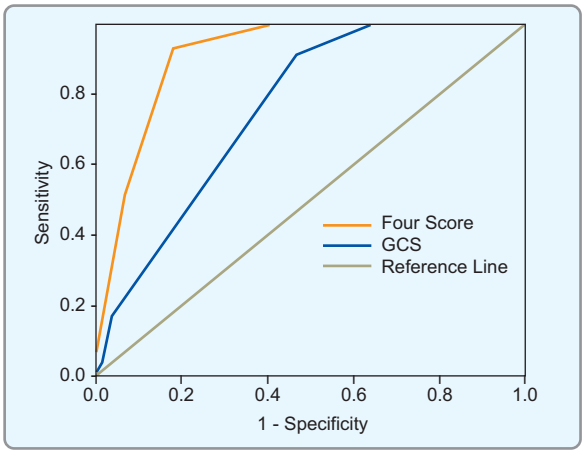

Figure 1: *Receiver operating characteristic curves comparing GCS and FOUR score in predicting 30-day mortality.*

Using the Youden index, the optimal point of maximizing sensitivity and specificity for 30-day mortality prediction was 11 for the FOUR score and 7 for the GCS score. Following univariate and multivariate Cox regression analysis, both scores were predictive of mortality. Compared to patients with the FOUR score of 12 and above, those with the score of 2–11 had significantly higher unadjusted hazards of 30-day death, HR (95% CI) of 8.028 (3.222-20.006). In the adjusted analysis, the mortality hazard was 8.022-fold (95% CI 3.211-20.039, p <0.001) higher in those with the FOUR score of 2–11 compared to those with the FOUR score of 12-16. For the GCS score, those with the score of 3–7 had higher unadjusted hazards of 30-day case fatality HR (95% CI) of 4.640 (2.847-7.562). In the adjusted analysis, the mortality hazard was 4.883-fold higher (95% CI

2.969-8.033, p <0.001) in those with the GCS score of 3–7 compared to those with the GCS score of 8 and above (Table III).

Table-II

Performance of GCS and FOUR score for predicting 30-day mortality

Variables	Cut-off score	Youden index	Sensitivity (%)	Specificity (%)	AUROC (95% CI)	P value
GCS	6.5	44.3	91.4	52.9	0.756 (0.673-0.838)	<0.001
FOUR score	10.5	74.5	93.1	81.4	0.909 (0.858-0.961)	<0.001

CI: Confidence interval, GCS: Glasgow Coma Scale, FOUR: Full Outline of UnResponsiveness, AUROC: Area Under the Receiver Operating Characteristic curve

Table-III

Unadjusted and adjusted hazard ratios from proportional hazards regression using the FOUR and GCS scores to predict 30-day mortality

Variable	Unadjusted HR (95% CI)	Adjusted HR* (95% CI)	p value
FOUR score			
12-16	Reference	Reference	<0.001
2-11	8.03 (3.22-20.01)	8.02 (3.21-20.04)	
GCS			
8-15	Reference	Reference	<0.001
3-7	4.64 (2.85-7.56)	4.88 (2.97-8.03)	

*Adjusted for age and sex. HR: Hazard Ratio; GCS: Glasgow Coma Scale; FOUR: Full Outline of UnResponsiveness

Discussion:

Present study findings support the hypothesis that the FOUR score could be regarded as superior to the GCS in assessing 30-day mortality in patients with impairment of consciousness due to stroke. In the current study, the 30-day mortality rate was 54.7%. Another study conducted in Iran among stroke patients found mortality that was nearer to but slightly lesser than our one.[14] The outcome of stroke patients with impaired consciousness depends on stroke etiology, the extent and duration of altered consciousness, the development of systemic illness, and the quality of post-stroke care and rehabilitation. While the survival rate of ischemic stroke patients with no impairment in consciousness can be more than 90%, it goes below 30% in patients who become comatose.[15] Patients with hemorrhagic stroke and subarachnoid hemorrhage (45.3% and 6.3%, respectively) constituted more than half of the population in the present study altogether.

In the present study, the AUROC showed FOUR score and GCS to be good at discriminating cumulative survivors and the deceased up to 30 days from the onset of stroke.

The discrimination power of the FOUR score was better than the GCS. These interesting findings of the current study indicate that the FOUR score can be used parallel to GCS or even replace the GCS provided the FOUR score undergoes further validation among larger populations and bigger setups in our country. Similarly, another study reported a higher AUROC value of the FOUR scores than the GCS in predicting survival in 300 patients admitted to an ICU.[17] However, the difference was not statistically significant in their study.[17] Abdallah et al. compared the performances of FOUR and GCS scores in terms of 30-day mortality prediction in patients from the emergency room with varying etiology; the AUROC (95% CI) for mortality prediction for the FOUR score and the GCS score also lacked statistical significance.[5]

The present study demonstrated comparatively good sensitivity and specificity of the FOUR score cutoff value to predict 30-day mortality. For GCS, a cutoff score of 6.5 showed a sensitivity of 91.4% and a specificity of 52.9%, with the Youden index of 44.3%. With a cutoff score 10.5, the FOUR score predicted 30-day mortality with a sensitivity of 93.1% and specificity of 81.4% with the Youden index of 74.5%. The study of Ramazani and his colleague also reported a lower Youden index for GCS compared to a higher value for the FOUR score for discriminating survivors from the deceased in a cohort of MICU patients.[17]

Moreover, the adjusted HR for the FOUR score to predict 30-day mortality was higher than the HR for GCS (8.028 versus 4.883). These findings are consistent with two other studies which found that both the GCS and FOUR scores were equally able to predict survival and overall functional status even after adjusting for age, sex, and alertness group.[5,12]

Though the majority of the patients in the current study were included from the general ward setting, there were two patients with stroke from the ICU. These patients' GCS and FOUR scores were 3 and 2, respectively. For intubated patients in the ICU, the FOUR score is more suitable since it does not have a verbal component in its assessment as opposed to the GCS. Furthermore, those with the lowest GCS score of 3 can be further categorized using the FOUR score based on the assessment of brainstem reflexes and breathing patterns.10,16 These data suggest that the FOUR score might hold greater value when evaluating patients in deeper stages of coma. In the present study, there was no patient with the lowest FOUR score of '0' due to the scarcity of intensive care facilities in our setting and we got only two patients from the ICU. As a consequence, the study has been unable to make any conclusion regarding the predictive properties of both scores at the lowest values.

The strength of our study includes the prospective nature of data collection. However, a few limitations should be considered when considering the study findings. All the samples were from a single tertiary care hospital in a resource-limited setup that hindered the escalation of necessary care when required. Mixing of cases from different settings could have led to bias. Inter-observer reliability of the two scores was not assessed in this study. Finally, in the analysis, it was not possible to control

for all factors determining mortality and functional outcome in such a group of stroke patients with varying etiology.

Conclusion

This prospective observational study showed that the GCS and the FOUR scores are good scales for predicting 30-day mortality; however, the FOUR scores showed significantly better discrimination than the GCS in predicting mortality.

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Conflict of interest:

The authors declare no conflict of interest in this study.

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