A Comparison of Full Outline of UnResponsiveness Score with Glasgow Coma Scale Score in predicting Outcomes among Patients with Altered Mental Status admitted to the Critical Care Unit

Praveen K Javvaji1, Padmaja Nagatham2, Ramachandra RI Venkata3, Harivarsha Puttam4, Sanjo K John5, Hemapiya Karavalla6, Tulasiram Pulivarthi7

ABSTRACT

Aim: Comparison of the Full Outline of UnResponsiveness (FOUR) score with the Glasgow Coma Scale (GCS) score to find the better scoring system for predicting outcomes among patients in the critical care unit.

Materials and methods: This is a prospective observational study. It included 100 patients of altered sensorium, whose GCS and FOUR scores were calculated at admission and followed up till death or discharge to note the outcome. Individual demographics and diagnosis were recorded, and the results were analyzed statistically.

Results: The correlation between the two scores was excellent, with the Spearman's correlation coefficient of 0.88. Discrimination ability of the two scoring systems, as assessed by the area under the receiver operating characteristic curve, was 0.778 for GCS score and 0.883 for FOUR score (p < 0.001). When area under the curve (AUC) was calculated exclusively in stroke cases, it was 0.836 for GCS score and 0.944 for FOUR score. Among nonstroke cases, the AUC was 0.756 and 0.859, respectively. However, the 95% confidence limits were overlapping among the corresponding scores.

Conclusion: The above study concludes that there is a good correlation between GCS and FOUR scores in predicting outcomes. Superiority of FOUR score could not be established statistically in view of overlapping confidence limits. However, it performed at par with GCS in prognosticating mortality among patients with altered sensorium.

Clinical significance: In critically ill patients with altered sensorium, explaining the prognosis to the attendants is a challenge for the physician. The commonly used GCS score has several shortcomings, especially in intubated patients. Use of the FOUR score can overcome these shortcomings and help in prognostication of these patients. In view of its good correlation with GCS score and equal efficacy in predicting outcomes in varied etiologies, it can be used as a good alternative to the GCS score.

Keywords: Altered sensorium, Full Outline of UnResponsiveness score, Glasgow Coma Scale score.

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INTRODUCTION

Glasgow Coma Scale (GCS) is a widely used method to assess the brain function and to estimate outcomes in patients with altered mental status. It was introduced by Teasdale and Jennett in 1974 to bring uniformity in the clinical assessment of consciousness.1,2 Although the test was devised to be used in patients with brain injury, it is used extensively in other etiologies like stroke, drowning, infections, cardiac arrest, and metabolic causes leading to altered sensorium.3,4 The score has an excellent correlation to the outcome and good interobserver reliability.1 However, GCS has several drawbacks. Firstly, there is no provision to grade verbal component of GCS in intubated patients. Several patients in altered sensorium will require assisted ventilation. Inability to access such condition can undermine the effectiveness of the scoring system.4,6 Secondly, in the motor component of GCS, the withdrawal response may be mistaken as a flexor response causing an error in scoring.4 Thirdly, brainstem reflexes are not used in the GCS, which is found to be closely related to mortality in several studies.6,7

Given these shortcomings, Wijdicks et al. introduced the FOUR score in 2005.5 The components of this new score are enlisted in Table 1 below. Apart from addressing the shortcoming above, the new score also includes the assessment of the breathing pattern. The need for assisted ventilation correlates with the severity of the disease and hence with the outcome.8 Also, the FOUR score can identify the locked-in state (pseudo-coma) and persistent vegetative state where the patient’s eyes are open, but the tracking of the examiner’s finger cannot be performed. There

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A comparison of the FOUR and GCS score

Table 1: Components of the GCS and FOUR Score

<table>
<thead>
<tr>
<th>Eye opening</th>
<th>GCS score</th>
<th>FOUR score</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Spontaneous</td>
<td>Eyelids open, tracking, or blinking to command</td>
</tr>
<tr>
<td>3</td>
<td>To speech</td>
<td>Eyelids open but not tracking</td>
</tr>
<tr>
<td>2</td>
<td>To pain</td>
<td>Eyelids closed, but open to loud voice</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td>Eyelids closed, but open to pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Eyelids remain closed with pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best motor response</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Obeying commands</td>
</tr>
<tr>
<td>5 Localizing to pain</td>
</tr>
<tr>
<td>4 Withdrawal from pain</td>
</tr>
<tr>
<td>3 Abnormal flexion response to pain</td>
</tr>
<tr>
<td>2 Extension response to pain</td>
</tr>
<tr>
<td>1 None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Motor response</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Thumbs-up, fist, or peace sign</td>
</tr>
<tr>
<td>3 Localizing to pain</td>
</tr>
<tr>
<td>2 Flexion response to pain</td>
</tr>
<tr>
<td>1 Extension response to pain</td>
</tr>
<tr>
<td>0 No response to pain or generalized myoclonus status</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brainstem reflexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Pupil and corneal reflexes present</td>
</tr>
<tr>
<td>3 One pupil wide and fixed</td>
</tr>
<tr>
<td>2 Pupil or corneal reflexes absent</td>
</tr>
<tr>
<td>1 Pupil and corneal reflexes absent</td>
</tr>
<tr>
<td>0 Absent pupil, corneal, and cough reflex</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Not intubated, regular breathing pattern</td>
</tr>
<tr>
<td>3 Not intubated, Cheyne–Stokes breathing pattern</td>
</tr>
<tr>
<td>2 Not intubated, irregular breathing</td>
</tr>
<tr>
<td>1 Breaths above ventilator rate</td>
</tr>
<tr>
<td>0 Breaths at ventilator rate or apnea</td>
</tr>
</tbody>
</table>

There are several modifications in the motor response components in the FOUR score. Generalized myoclonus status is included and given a score of “zero.” Withdrawal from pain is clubbed into decorticate response (flexion response) as it is often difficult to differentiate the two. The component “obeying commands” is replaced by a more specific response—"thumbs up, fist or peace sign." This has the added advantage of testing the patient’s alertness. These modifications are thought to increase the effectiveness of the new score in predicting outcomes reliably.

Since the introduction of the FOUR score, there have been several studies comparing it with the GCS. Most of them concluded that the FOUR score is better than the GCS score in predicting mortality and morbidity. However, the majority of these have been among patients of traumatic brain injury. In the present study, the comparison is made between the two scores in patients of altered sensorium from nontraumatic causes admitted to a critical care unit (CCU).

Materials and Methods

Study Design and Setting
This was a prospective observational study, at a tertiary care teaching hospital, in the CCU of the Department of General Medicine, Sri Venkateswara Medical College, Tirupati, from November 2018 to October 2019.

Sample Size Calculation
The sample size was estimated by the comparison of the receiver operating characteristic (ROC) curve method using Medcalc software. We selected type 1 error as 0.05 and type 2 as 0.20 (power of 80%). Values of 0.8 and 0.64 were used for the area under the curve (AUC) values 1 and 2 (as observed in the meta-analysis study by Foo et al.). For the FOUR score and GCS score, respectively, with a correlation of 0.6 in positive and negative groups. The ratio of sample size was selected as 2. We obtained a sample size of 93. We planned to include 100 patients.

Inclusion Criteria
Patients with a GCS score less than 15, or those in confusion or with a diminished or absent response to verbal or physical stimuli, were included in the study.

Exclusion Criteria
Patients aged younger than 12 years and chronic cases like Alzheimer’s, schizophrenia, and those with an altered mental status of more than a week were excluded. A patient who develops cardiac arrest during emergency treatment was excluded. Patients with known psychiatric illness were excluded from the study.

Methodology
The study population was drawn from consecutive patients who were admitted to the CCU with altered mental status, who met the inclusion and exclusion criteria. After obtaining informed consent from attendants, data were collected related to the patient’s demographic characteristics, chief complaints, and duration of illness. All patients underwent full medical and neurologic clinical evaluation at the time of admission. The neurologic condition was
judged by evaluating the GCS and FOUR scores, and patients were
followed until death or discharge. The final diagnosis and outcome
were noted in each case. Patients discharged before 1 month were
contacted at the end of 1 month to note the outcome in terms of
death or survival.

Statistical Analysis
Data were analyzed using Medcalc software version 19.1.3 (for
Windows 10). Spearman’s rho coefficient was used to test the
correlation between GCS and FOUR scores. The ROC curve was
used to test the discriminating ability of the two scoring systems
in predicting outcomes. The odds ratio (OR) by binary logistic
regression was used to test their predictive power. The predictive
scores were entered as ordinals, and OR adjusted for age, sex,
and diagnosis was calculated. Internal validation was done using
bootstrap technique with 1,000 replications. The goodness of fit for
the logistical regression model was tested by Hosmer–Lemeshow
test. Microsoft Office 2019 was used for graphical representation
of data.

Results
Among 100 patients studied, 59 were males and 41 were females.
The median GCS score was 10, and the median FOUR score was
12. Patient’s ages ranged between 12 and 86 years, with a median
age of 55 years. Figures 1 and 2 show frequencies of outcomes for
a total score of GCS and FOUR, respectively. Overall, the mortality
increased with an increase in the total score as assessed by both
GCS and FOUR scores.

In Figure 3, the data on etiology-wise survivors and nonsurvivors are illustrated. The major contributors to etiology,
were cerebrovascular accidents (28%) and infective causes
(27%). Hepatic encephalopathy (14%) and uremia (7%) together
constituted 21% of cases, whereas drugs and toxins accounted for
10% of cases. Other causes, which included metabolic or reversible
causes like seizures (4%), hypercapnia (3%), dyselectrolytemia (3%),
somatoform disorder (2%), hypoglycemia (1%), and hypoxia (1%),
accounted for 10% of cases. Median GCS score and FOUR score are
also represented in each group in the chart. Overall, there were 31
deaths and 69 survivors. Among the patients who died, the median
GCS score was 7, and among survivors, it was 11. The median FOUR
score among these groups was 8 and 13, respectively.

In all the etiologies, except in toxins and drug group, the mean
score by both the scoring systems was higher among survivors and
lower among nonsurvivors. Interestingly, in other causes (which
include mostly reversible etiologies), the difference in median GCS
score between survivors and nonsurvivors was only 1, while the
difference in FOUR score was 5.5. However, on statistical analysis,
this observation was found insignificant (AUC 0.60, with a p value
of 0.794 for GCS score and AUC 0.71, with a p value of 0.487 for
FOUR score).

The correlation between GCS and FOUR scores in predicting
mortality was calculated by using Spearman’s rho rank correlation.
It showed an excellent correlation with the coefficient of 0.88
(p < 0.001), as illustrated by the scatter diagram (Fig. 4). The
discrimination ability of the two scoring systems was assessed by
the AUROC curve. In Figures 5 to 10, the ROC curve for GCS and
FOUR scores is shown for various subgroups. The AUC for all cases
of altered sensorium was 0.778 for GCS score (Fig. 2) and 0.883 for
FOUR score (Fig. 3) with p < 0.001 for both the scores. By the binary
logistic regression model with GCS score, the OR was 0.717 (95% CI,
0.611–0.841), whereas for the model with FOUR score, the OR was
0.672 (95% CI, 0.569–0.794). Hence for every unit increase in GCS
score at admission, the chances of mortality at the end of 1 month
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A comparison of the FOUR and GCS score

Fig. 4: Scatter diagram of Spearman's rho rank correlation between GCS score and FOUR score

Fig. 5: AUC for GCS score in overall cases (n = 100)

Fig. 6: AUC for FOUR score in overall cases (n = 100)

Fig. 7: AUC for GCS score in stroke cases (n = 28)

Fig. 8: AUC for FOUR score in stroke cases (n = 28)

Fig. 9: AUC for FOUR score in overall cases (n = 72)
A comparison of the FOUR and GCS score
decrease by about 28%, whereas in the FOUR score, it decreases by 33%. With the full model using patients’ age, sex, and diagnosis (stroke and nonstroke cases) as covariates, the OR was 0.712 (95% CI, 0.604–0.839) for GCS score and 0.657 (95% CI, 0.552–0.782) for FOUR score.

In Figures 7 to 10, AUC was calculated for stroke and nonstroke cases separately. In the stroke cases, AUC for GCS score was 0.836 (p < 0.001), and for the FOUR score, it was 0.944 (p < 0.001). By logistic model with GCS score, the odds decreased by about 28%, whereas in the FOUR score, it decreases by 42% (OR, 0.583; CI, 0.408–0.834). By full model with covariates, OR was 0.642 (CI, 0.452–0.911) and 0.43 (0.191–0.967), respectively.

Among nonstroke cases, the AUC for GCS score was 0.756 (p < 0.001), and for FOUR score, AUC was 0.859 (p < 0.001). The OR was 0.738 (CI, 0.612–0.889) and 0.714 (CI, 0.589–0.865), respectively, by logistic model with GCS and FOUR scores. With covariates of age and sex, the OR was 0.733 (CI, 0.604–0.849) and 0.681 (CI, 0.55–0.842), respectively. Table 2 compares the results of all the statistical analyses of the study. From the table, it can be noted that the significance of Hosmer–Lemeshow test for FOUR-score-only model was low. However, by Omnibus test of model coefficient, the model had a significance of <0.001, suggesting a good fitness of the model. Also, the results of the OR were not found to be significant in subgroups of stroke cases, for both the models of GCS score and the full model of FOUR score.

**Discussion**
The FOUR score was developed to aid in predicting outcomes among intubated patients in whom the verbal component could not be assessed. Since its introduction, several studies were done, comparing it with the GCS score, testing the correlation between the two, and their discriminative ability in predicting outcomes. In this study, the correlation between the two scores was found excellent, with the Spearman correlation coefficient of 0.88. This was comparable to previous studies, with Kishor et al. reporting it as 0.91 and Iyer et al. reporting it as 0.98 by first rater and 0.92 by the second rater.
To test the discrimination of the two scoring systems, most studies used AUC value. In the meta-analysis by Foo et al., it is observed that the AUC for FOUR score and GCS score for predicting 1-month mortality ranges from 0.62 to 0.99 in different studies, with overlapping confidence limits in corresponding studies. In Kishor et al. study, AUC for FOUR score is 0.82 (CI, 0.73–0.91), whereas in the Ghelichkhani et al. study, it is 0.99 (CI, 0.97–1.0). The same for GCS score is 0.79 (CI, 0.74–0.91) and 0.97 (CI, 0.95–1.0), respectively. In the present study, the AUC was 0.778 (95% CI, 0.68–0.85) and 0.883 (95% CI, 0.804–0.939), respectively, for all cases combined. For stroke cases, the AUC was 0.836 (95% CI, 0.69–0.98) and 0.944 (95% CI, 0.87–1.00), respectively, for GCS and FOUR scores. For cases other than stroke, it was 0.756 (95% CI, 0.63–0.88) and 0.859 (95% CI, 0.76–0.93), respectively.

Foo et al. in their meta-analysis note that 17 studies assessed FOUR score by logistic regression for in-hospital mortality. The OR score among these studies ranges from 0.93 to 0.59 by the unadjusted model. Thus, for every one-point increase in FOUR score, odds of in-hospital mortality decrease by 7 to 41%. Kishor et al. note OR of 0.70 (95% CI, 0.6–0.82) for FOUR score, whereas Iyer et al. report an OR of 0.84 (CI, 0.72–0.88). In the present study, the OR was 0.672 (95% CI, 0.569–0.794) for FOUR score among all cases, suggesting a 33% decrease in mortality for a unit increase in FOUR score. For the GCS, Kishor et al. report OR of 0.66 (CI, 0.55–0.79), and Vivek et al. note it as 0.75 (95% CI, 0.68–0.84). In our study, this was found to be 0.717 (CI, 0.611–0.841).

Thus, like all the previous studies, the present study suggests that the FOUR score is comparable to the GCS score in predicting mortality. This was true in both stroke and nonstroke cases. However, owing to overlapping CIs between the corresponding GCS and FOUR scores, the superiority of the FOUR score could not be established with complete confidence.

**Conclusion**

The above study proves that there is a good correlation between GCS and FOUR scores in predicting outcomes, even in nontraumatic cases. Both the scoring systems have good discrimination ability in predicting mortality in both stroke and nonstroke cases. The superiority of FOUR score over the GCS score, in prognosticating mortality, could not be established adequately in the present study. However, it was not found to be inferior either. Given the higher number of patients requiring endotracheal intubation in CCUs and difficulties in evaluating GCS score among them, the FOUR score can serve as a good alternative. The sample size was the major limitation of the study, owing to which no robust conclusions could be made, especially among etiological subgroups. Further studies will be required to compare the effectiveness of FOUR score with that of GCS in individual etiologies using a more extensive study group, especially among nontraumatic and nonstroke causes, where studies are lacking.

**References**