ORIGINAL ARTICLE

# 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

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## 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 altered sensorium 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.[3] The components of this new score are enlisted in Table 1 below. Apart from addressing the shortcomings discussed 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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**Table 1:** Components of the GCS and FOUR score[3]

| *GCS score* | | *FOUR score* | |
|---|---|---|---|
| **Eye opening** | | **Eye response** | |
| 4 | Spontaneous | 4 | Eyelids open, tracking, or blinking to command |
| 3 | To speech | 3 | Eyelids open but not tracking |
| 2 | To pain | 2 | Eyelids closed, but open to loud voice |
| 1 | None | 1 | Eyelids closed, but open to pain |
| | | 0 | Eyelids remain closed with pain |
| **Best motor response** | | **Motor response** | |
| 6 | Obeying commands | 4 | Thumbs-up, fist, or peace sign |
| 5 | Localizing to pain | 3 | Localizing to pain |
| 4 | Withdrawal from pain | 2 | Flexion response to pain |
| 3 | Abnormal flexion response to pain | 1 | Extension response to pain |
| 2 | Extension response to pain | 0 | No response to pain or generalized myoclonus status |
| 1 | None | **Brainstem reflexes** | |
| | | 4 | Pupil and corneal reflexes present |
| **Verbal response** | | 3 | One pupil wide and fixed |
| 5 | Orientated | 2 | Pupil or corneal reflexes absent |
| 4 | Confused | 1 | Pupil and corneal reflexes absent |
| 3 | Inappropriate words | 0 | Absent pupil, corneal, and cough reflex |
| 2 | Incomprehensible sounds | **Respiration** | |
| 1 | None | 4 | Not intubated, regular breathing pattern |
| | | 3 | Not intubated, Cheyne–Stokes breathing pattern |
| | | 2 | Not intubated, irregular breathing |
| | | 1 | Breathes above ventilator rate |
| | | 0 | Breathes at ventilator rate or apnea |

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—"thumps 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.[2,9,10] 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.[11]) for the FOUR score and GCS score, respectively, with a correlation of .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

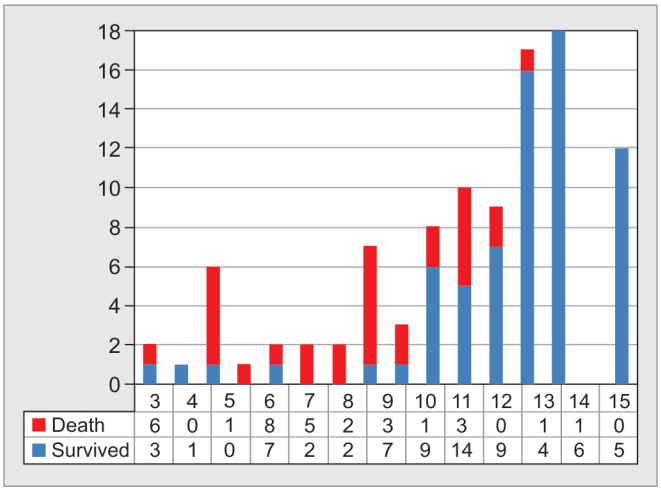


**Fig. 2:** FOUR score and outcomes

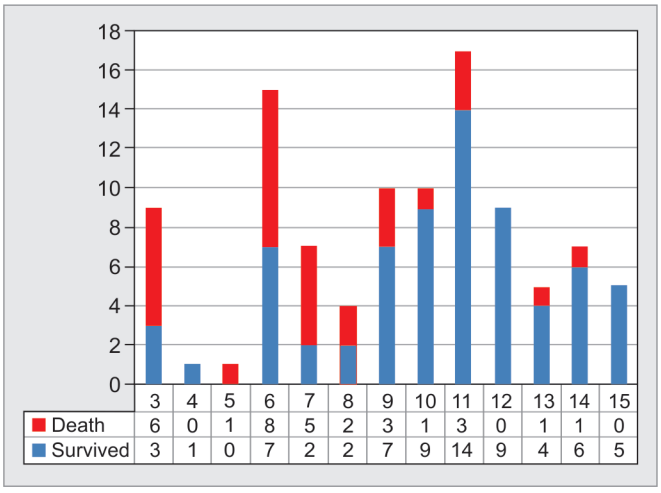


**Fig. 1:** GCS score and outcomes

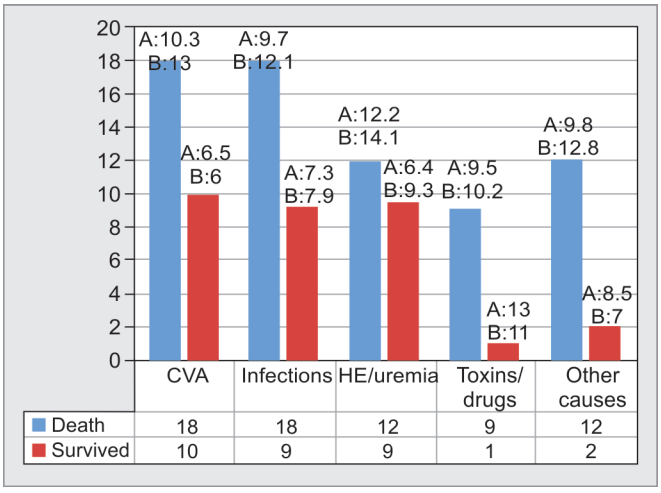


**Fig. 3:** Etiology-wise outcomes with mean GCS and FOUR scores

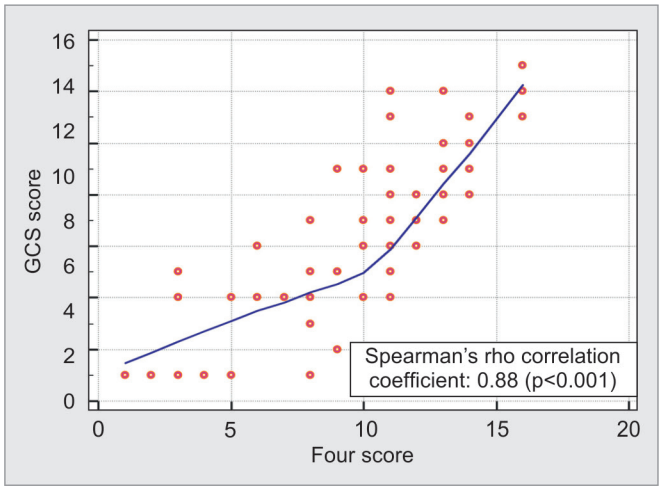


**Fig. 4:** Scatter diagram of Spearman's rho rank correlation between GCS score and FOUR score

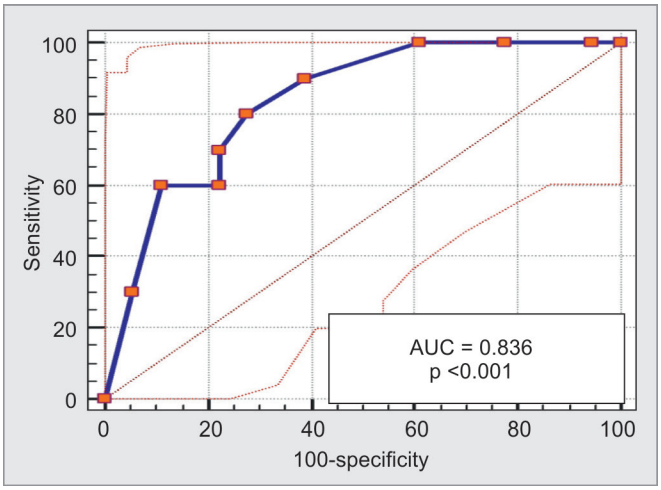


**Fig. 7:** AUC for GCS score in stroke cases ($n = 28$)

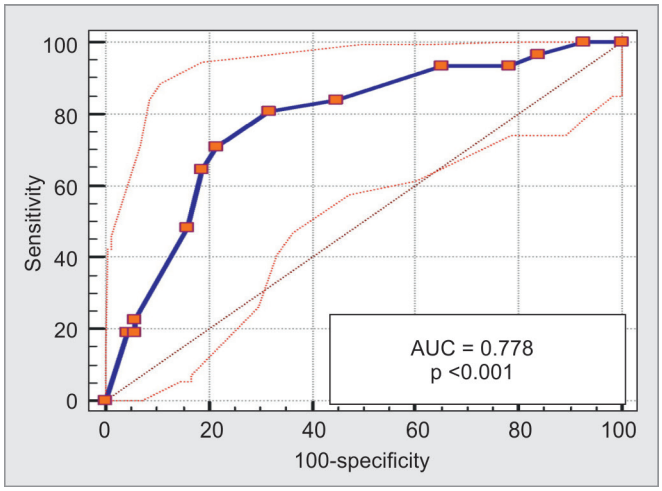


**Fig. 5:** AUC for GCS score in overall cases ($n = 100$)

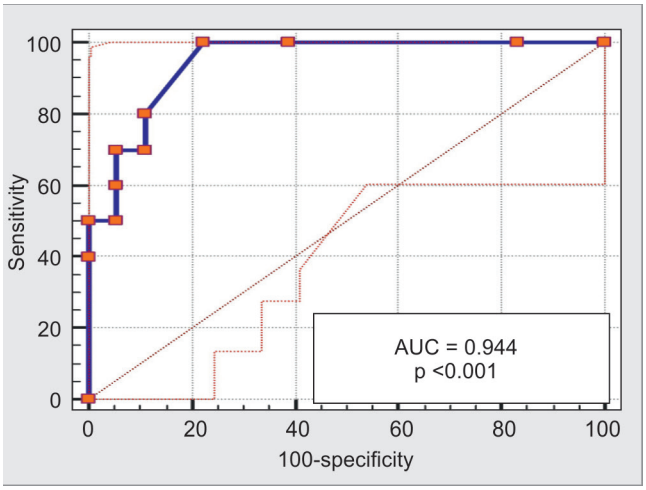


**Fig. 8:** AUC for FOUR score in stroke cases ($n = 28$)

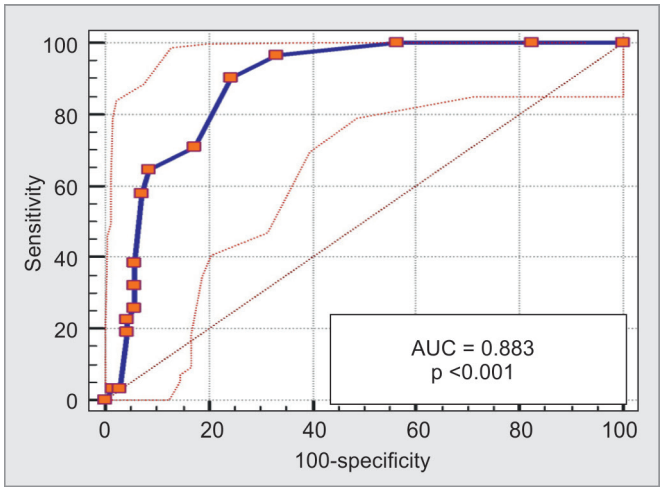


**Fig. 6:** AUC for FOUR score in overall cases ($n = 100$)

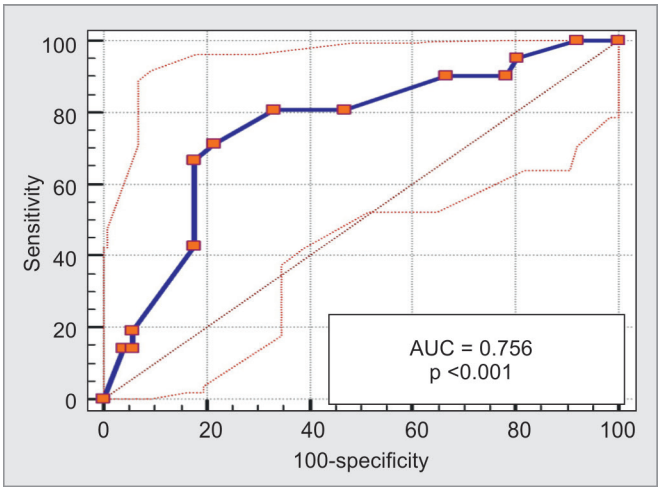


**Fig. 9:** AUC for FOUR score in overall cases ($n = 72$)

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 of 1-month mortality for every one-point rise in GCS score decreased by 33% (OR, 0.669; CI, 0.49–0.914), and for FOUR score model, it decreased 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.

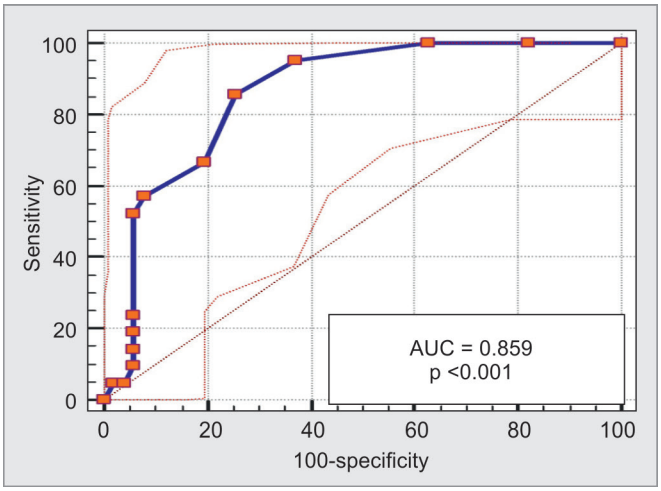


**Fig. 10:** AUC for FOUR score:nonstroke cases ($n$ = 72)

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, 0.604–0.89) 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.[8] reporting the coefficient as 0.91 and Iyer et al.[6] reporting it as 0.98 by first rater and 0.92 by the second rater.

**Table 2:** Comparison of statistical results for GCS and FOUR scores in the overall study, and stroke and nonstroke cases

| | *GCS score* | | | *FOUR score* | | |
|---|---|---|---|---|---|---|
| | All cases | Stroke | Nonstroke | All cases | Stroke | Nonstroke |
| AUROC curve | 0.778 | 0.836 | 0.756 | 0.883 | 0.944 | 0.859 |
| Standard error | 0.05 | 0.076 | 0.064 | 0.033 | 0.04 | 0.0438 |
| 95% Confidence interval | 0.684–0.855 | 0.687–0.985 | 0.631–0.881 | 0.804–0.939 | 0.87–1.00 | 0.757–0.93 |
| z statistic | 5.545 | 4.441 | 3.978 | 11.574 | 11.572 | 8.198 |
| Significance level $p$ (area = 0.5) | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Youden's index J | 0.4923 | 0.5222 | 0.4986 | 0.6568 | 0.7778 | 0.6022 |
| Associated criterion | ≤8 | ≤9 | ≤8 | ≤11 | ≤11 | ≤11 |
| Sensitivity | 70.97 | 80 | 71.43 | 90.32 | 100 | 85.71 |
| Specificity | 78.26 | 72.22 | 78.43 | 75.36 | 77.78 | 74.51 |
| | | | **Binary logistic regression test** | | | |
| GCS/FOUR-score-only model—OR | 0.717 | 0.669 | 0.738 | 0.672 | 0.583 | 0.714 |
| 95% Confidence interval | (0.611–0.841) | (0.49–0.914) | (0.612–0.889) | (0.569–0.794) | (0.408–0.834) | (0.589–0.865) |
| Significance | <0.001 | 0.012 | 0.001 | <0.001 | 0.003 | 0.001 |
| Homer and Lemeshow significance | 0.669 | 0.555 | 0.38 | 0.005 | 0.56 | 0.049 |
| Full model with covariates—OR | 0.712 | 0.642 | 0.733 | 0.657 | 0.43 | 0.681 |
| 95% Confidence interval | (0.604–0.839) | (0.452–0.911) | (0.604–0.89) | (0.552–0.782) | (0.191–0.967) | (0.55–0.842) |
| Significance | <0.001 | 0.013 | 0.002 | <0.001 | 0.041 | <0.001 |
| Homer and Lemeshow significance | 0.622 | 0.187 | 0.707 | 0.211 | 0.672 | 0.754 |
| Covariates: OR (significance) | | | | | | |
| Age | 0.993 (0.60) | 0.962 (0.33) | 0.998 (0.89) | 0.98 (0.21) | 0.93 (0.34) | 0.982 (0.29) |
| Sex | 0.942 (0.90) | 1.589 (0.64) | 0.856 (0.79) | 0.805 (0.69) | 18.01 (0.23) | 0.592 (0.42) |
| Diagnosis: stroke/nonstroke | 1.373 (0.57) | – | – | 1.185 (0.32) | – | – |

To test the discrimination of the two scoring systems, most studies used AUC value. In the meta-analysis by Foo et al.,[11] 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.[7] 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.[11] Thus, for every one-point increase in FOUR score, odds of in-hospital mortality decrease by 7 to 41%. Kishor et al.[8] 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.

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