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Research Article

Comparison of the Full Outline of Unresponsiveness score with Glasgow coma scale in comatose patients: A diagnostic study

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Abstract:

Background: Coma is defined as a significant reduction in the level of consciousness, leading to a state of unarousable unresponsiveness.

Aim: This study aimed to compare the reliability and outcome predictive value of GCS and Full Outline of Unresponsiveness (FOUR) scores in comatose patients.

Methods: This prospective observational study was conducted on 128 comatose patients admitted in the intensive care units (ICUs) of Farshchian and Besat hospitals in Hamadan, Iran. Patients were hospitalized due to neurological disorders and traumatic brain injury. Pearson's correlation-coefficient was used to evaluate the correlations between FOUR and GCS scores, and Cohen's *kappa coefficient* was applied to assess the inter-rater agreement. Data analysis was performed in SPSS version 19 at the significance level of P<0.05.

Results: Interobserver agreement of the FOUR score was 0.761, 0.938, and 0.958 on days 1, 3, and 10, respectively. Correlation-coefficient of inter-rater agreement for FOUR score was higher compared to GCS, which was considered favorable for both scales. According to both observers, ROC curve showed a higher predictive value for the FOUR score compared to GCS, while the difference was not significant.

Implications for Practice: According to the results of this study, FOUR score has an excellent reliability in the assessment of consciousness level in comatose patients. Compared to GCS, FOUR has a higher predictive value to measure the level of consciousness in patients admitted in the ICU.

Keywords: FOUR score, Glasgow coma scale, Consciousness, Brain injuries

Introduction

Coma is defined as a significant reduction in the level of consciousness, leading to a state of unarousable unresponsiveness. In addition to losing their consciousness and awareness, comatose patients are not able to respond to environmental stimuli due to sensory deprivation (1).

As major neurological components, cerebral cortex and reticular activating system play a pivotal role in maintaining the consciousness; coma might occur following the injuries in either or both these compartments (1). Measurement of the level of consciousness in patients with severe brain trauma is a remarkable medical challenge.

Cerebrovascular diseases are responsible for the mortality of 7.8 million individuals across the world each year. Moreover, statistics suggest that these disorders account for 13% of all deaths in different populations. Strokes are the fourth main cause of mortality, following cardiac diseases, cancer, and chronic pulmonary disease. Severe vascular brain injury may lead to coma due to nonvascular (e.g., stroke and trauma) and vascular lesions, which induce coma through exogenous intoxication and metabolic dysfunction (2, 3). Since loss of consciousness might be an indication for brain injury, measurement of consciousness level is critical in patients who are in a coma for any reason (4).

Consciousness level in comatose patients is evaluated based on several tools with variable classified criteria, all of which are used to predict the prognosis of the patients with loss of consciousness admitted in intensive care units (ICUs) or emergency sections (4).

Recent studies have reported different predictive values for the measurement tools of consciousness level in comatose patients. Glasgow coma scale (GCS) is a valid, reliable instrument routinely used for assessing the level of consciousness (5), especially in patients with traumatic brain injury. However, GCS has several limitations (4); for instance, GCS could not accurately measure the level of consciousness in comatose patients with endotracheal intubation. Additionally, this scale cannot assess the respiratory status and brain reflexes of comatose patients (6).

With this background in mind, application of a reliable, valid measurement tool without the mentioned restrictions is critical for the evaluation of consciousness level in comatose patients. Full outline of unresponsiveness (FOUR) is a relatively new instrument used to measure the level of consciousness in comatose patients. This scale examines four main domains of neurological function, including eye response, motor response, brainstem reflexes, and respiratory pattern. Some of the advantages of the FOUR score are easy application and assessment of consciousness level in intubated patients. Furthermore, this scale could be used to evaluate the vegetative state of comatose patients (7).

Considering the strengths of FOUR score in the measurement of consciousness level, this study aimed to compare the reliability and outcome predictive values of FOUR score and GCS in comatose patients.

Materials and Methods

This prospective observational study was conducted on all the comatose patients admitted in the ICUs of Farshchian and Besat hospitals in Hamadan, Iran. Sample population consisted of all the comatose patients with neurological disorders and traumatic brain injury without conscious response to external stimuli. Sample size was calculated at 128 cases using consecutive sampling.

Before the study, required permit was obtained from the authorities of Hamadan University of Medical Sciences to implement research procedures. Consciousness level of the patients was assessed based on the FOUR score and GCS on the first, third, and 10th day of hospitalization. Measurement of consciousness level in each patient was performed twice (by a nurse and physician) within a short interval. Moreover, observers were trained before the study in order to become familiar with the evaluation and scoring system of the applied scales.

Primary information of the patients, including demographic characteristics and diagnosis, were collected from their medical records, and other data were recorded in self-made questionnaires by the observers.

Data analysis was performed in SPSS version 19 using descriptive statistics to describe qualitative and quantitative variables. In addition, t-test and χ^2 were applied to compare quantitative and qualitative variables, respectively. Correlations between the FOUR score and GCS were determined using Pearson's correlation-coefficient, and Cohen's *kappa coefficient* was applied to determine the inter-rater agreement. Moreover, receiver operating characteristic (ROC) curve was used to assess the outcome predictive power of FOUR and GCS. In this study, P value of less than 0.05 was considered statistically significant.

Results

Among the studied patients, 61.7% and 38.3% were male and female, respectively, and mean age of the subjects was 54.25±23.8 years. With respect to gender and age, mean age of female and male patients was 61.59±21.35 and 49.69±24.22 years, respectively. Comparison of the age of subjects based on gender was indicative of a significant difference between men and women (P=0.006).

In terms of the cause of coma, 67.2% of the patients were hospitalized due to head trauma, and 32.8% were admitted due to a cerebrovascular event (i.e., stroke). During ten days, 37.5% of the patients died, while 62.55% survived.

Mean age and gender of the patients based on the causes of unconsciousness and outcomes are presented in **Table 1**

Table 1. Mean age and gender of patients based on cause of coma and outcome

Variables		**Cause of coma**		**P-value**	**Outcome**		**P-value**
		Head trauma (%)	*CVA (%)		Survival (%)	Death (%)	
Gender	Female	23.9	44.8	0.165	41.2	33.3	0.372
	Male	67.1	55.2		58.8	66.7	
Age (year)		Mean±SD			Mean±SD		
		36.15±14.81	76.08±10.46	0.001	50.75±22.46	60.08±25.04	0.013

***CVA:** cerebrovascular accident*

According to the information in this table, mean age of the comatose patients with head trauma and stroke had no significant difference (P<0.001). On the other hand, mean age of the surviving patients was lower compared to those who died at the end of the study (P=0.013).

Comparison of mean level of consciousness by two observers is shown in **Table 2**

.**Table 2.** Mean consciousness level by two observers

Variables	Day of admission	Observers	Mean±SD	P-value
*FOUR score	1	Nurse	5.97±2.53	0.454
		Physician	5.74±2.46	
	3	Nurse	5.60±3.39	0.746
		Physician	5.47±3.27	
	10	Nurse	5.44±4.70	0.958
		Physician	5.41±4.80	
**GCS	1	Nurse	5.32±1.44	0.544
		Physician	5.21±1.50	
	3	Nurse	5.34±1.92	0.768
		Physician	5.27±1.88	
	10	Nurse	5.53±2.87	0.779
		Physician	5.63±2.93	

***FOUR:** Full outline of unresponsiveness; ****GCS:** Glasgow coma scale*

According to the information in this table, interobserver variation had no significant difference on days 1, 3, and 10 of hospitalization. Comparison of mean FOUR and GCS scores between observers based on the gender and age of patients is presented in tables 3, respectively

.**Table 3.** Mean FOUR score and GCS between observers based on gender and age

Variables	Day of admission	Observers	Gender Mean±SD		P-value	Age Mean±SD		**P-value**
FOUR score	1	Nurse	Female	6.22±2.38	0.322	Less than 50 years	5.36±2.32	0.701
			Male	5.82±2.63	0.829	More than 50 years	6.38±2.61	0.511
		Physician	Female	5.74±2.46	0.322	Less than 50 years	5.22±2.21	0.701
			Male	5.72±2.53	0.829	More than 50 years	6.10±2.58	0.511
	3	Nurse	Female	6.42±3.18	0.624	Less than 50 years	5.28±2.87	0.867
			Male	5.08±3.43	0.981	More than 50 years	6.12±2.97	0.804
		Physician	Female	6.12±2.97	0.624	Less than 50 years	5.76±3.69	0.867
			Male	5.07±3.40	0.981	More than 50 years	5.61±3.54	0.804
	10	Nurse	Female	6.10±4.48	0.703	Less than 50 years	6.11±4.67	0.683
			Male	5.03±4.82	0.833	More than 50 years	6.49±4.83	0.676
		Physician	Female	5.75±4.50	0.703	Less than 50 years	4.97±4.70	0.683
			Male	5.20±5	0.833	More than 50 years	4.65±4.67	0.676
GCS	1	Nurse	Female	5.36±1.48	0.585	Less than 50 years	4.92±1.2	0.816
			Male	5.29±1.43	0.748	More than 50 years	4.86±4.5	0.569
		Physician	Female	5.20±1.47	0.585	Less than 50 years	5.6±1.54	0.816

			Male	5.21±0.748	0.748	More than 50 years	5.45±1.60	0.569
	3	Nurse	Female	6±2.02	0.579	Less than 50 years	5.01±1.56	0.953
			Male	4.93±1.75	0.928	More than 50 years	5.03±1.73	0.692
		Physician	Female	5.77±1.97	0.579	Less than 50 years	5.57±2.12	0.953
			Male	4.96±1.77	0.928	More than 50 years	5.44±1.98	0.692
	10	Nurse	Female	5.91±2.43	0.625	Less than 50 years	6.05±3.11	0.717
			Male	5.29±3.10	0.527	More than 50 years	5.16±2.64	0.975
		Physician	Female	5.67±2.51	0.625	Less than 50 years	6.28±3.30	0.717
			Male	5.60±3.18	0.527	More than 50 years	5.17±2.56	0.975

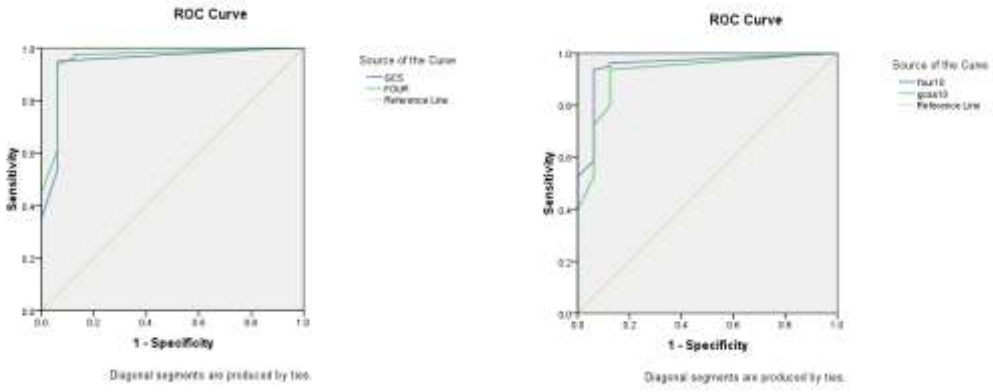
Interobserver agreement of the FOUR score was 0.761, 0.938, and 0.958 on the first, third and 10th day of admission, respectively, which was relatively high (P=0.001). As for GCS, this value was determined at 0.841, 0.939, and 0.914 on the first, third, and 10th day of hospitalization, respectively. This high level of interobserver agreement cannot be coincidental (P=0.001).

According to the results of this study, internal reliability of the FOUR score was 0.795, while it was 0.697 for GCS; this high level of agreement cannot be coincidental (P=0.001). In general, irrespective of the length of hospital stay (days), inter-rater reliability was estimated at 0.68.

Comparison of the FOUR score and GCS based on Spearman's correlation-coefficient between the observers on the first, third, and 10th day in terms of the gender and age of patients is shown in tables 4, respectively. On day 10 of hospitalization, ROC curve was used to compare the outcome predictive value of the FOUR score with GCS in patients with non-metabolic coma **(Figure 1)**.

Table 4. Comparison of correlation-coefficient and inter-rater agreement of FOUR score and GCS on different days of admission based on gender and age

Scale	Day of admission	Gender			Age (year)		
		Spearman's rho		P-value	Spearman's rho		P-value
		Female	Male		<50	>50	
FOUR score	1	0.721	0.939	0.001	0.886	0.841	0.001
	3	0.947	0.970		0.974	0.956	
	10	0.954	0.961		0.952	0.964	
GCS	1	0.719	0.916	0.001	0.875	0.816	0.001
	3	0.962	0.918		0.881	0.969	
	10	0.978	0.897		0.911	0.915	



(A) **(B)**

Figure 1. ROC curve for FOUR score and GCS

According to both observers in this study, ROC curve showed a higher predictive value for the FOUR score compared to GCS, while the difference was not considered significant.

Discussion

In the present study, we compared the interobserver reliability of the FOUR score and GCS, and the results were indicative of an excellent correlation between these scales. Moreover, interobserver agreement of these instruments was relatively high. In general, no significant difference was observed between the inter-rater agreement of the FOUR score and GCS on various days of admission in comatose patients.

While the inter-rater agreement of the FOUR score was higher compared to GCS, no significant difference was observed between these tools in this regard. Therefore, it could be concluded that the FOUR score is a reliable scale for the measurement of consciousness level in comatose patients.

According to the ROC curve, outcome predictive value of the FOUR score was higher compared to GCS. In other words, FOUR score is more reliable in the prediction of outcomes in comatose patients compared to GCS.

Previous studies have denoted excellent inter-rater agreement for the FOUR score and GCS (8, 9). Similar to the current research, in a study by Idrovo et al., a nurse and physician measured the consciousness level of patients with acute stroke. In the mentioned study, correlation-coefficient between the FOUR score and GCS was reported to be 0.78, while the inter-rater agreement was estimated at 0.8, which is slightly higher than the value obtained in our study (10).

Another study in this regard also confirmed the higher interobserver reliability of the FOUR score compared to GCS with no significant difference, which is consistent with the results of the current research (11).

Our findings are in line with the results obtained by Tadrisi et al., which suggested the excellent inter-rater reliability of the FOUR score. However, correlation-coefficient of the FOUR score and GCS was higher in the mentioned research compared to our study, which could be attributed to the differences of the evaluators. In the present study, inter-rater agreement was assessed by one nurse and one physician, while the observers in the study by Tadrisi et al. included the main researcher, four nurses, and an anesthesiology resident (total: six observers) (12).

In another study by Fischer et al., inter-rater agreement of GCS was reported to be higher among ICU staff, while the FOUR score had a higher inter-rater agreement among neurologists. However, the difference in this regard was not considered significant (13). Compared to the present study, inter-rater agreement of the FOUR score was higher (82%) in the mentioned research, which could be due to the conditions of the evaluators. In the study by Fischer et al., observers consisted of neurologists and ICU staff, while in our research, inter-rater agreement was compared between a nurse and physician as the observers. Furthermore, the study by Fischer et al. was conducted on a larger sample size (n=267) compared to our research.

Similar to the present study, inter-rater agreement of the FOUR score was reported to be excellent by Iyer et al. According to their findings, outcome predictive value of the FOUR score based on the ROC curve was 0.75, while it was 0.76 for GCS. This accentuates the high predictive power of the FOUR score and GCS for poor neurological outcomes. These values are lower compared to our findings, which could be due to the variable characteristics of the patients (e.g., age difference). Similar to the current study, findings of Iyer et al. were indicative of the favorable predictive value of the FOUR score in the prognosis of comatose patients, which further highlights the advantages of this scale over GCS (8).

Consistent with the aforementioned findings, inter-rater agreement was reported to be excellent for both the FOUR score (0.97) and GCS (0.95) in a study by Peng et al. Furthermore, outcome predictive value based on the ROC curve was determined at 0.83 and 0.815 for GCS and FOUR score, respectively (9). This is more similar to our findings compared to the results obtained by Iyer et al.

Findings of the current study are in congruence with the results obtained by Stead et al. In the mentioned research, the FOUR score was compared between three study groups, including physicians, residents and nurses. According to the findings, correlation-coefficient of the FOUR score and GCS was 0.88, and both scales were reported to have a high outcome predictive power (14).

In the present study, outcome predictive power of the FOUR score was observed to be higher compared to GCS according to the ROC curve, which is in line with the findings of Peng et al. (9) and Gorji et al. (15). In another study conducted by Eken et al., ROC curve showed the predictive value of the FOUR score and GCS to be 0.77 and 0.72, respectively in terms of patient mortality during three months. Moreover, predictive power for poor neurological outcomes was estimated at 0.75 and 72 for the FOUR score and GCS, respectively (16).

In comparison with GCS, the FOUR score has higher clarity and easier application in determining the consciousness level of comatose patients. Although the reliability of GCS is relatively high in assessing the level of consciousness, this scale could not be used effectively to measure the consciousness level of patients with intubation.

On the other hand, the FOUR score could be used to identify the locked-in syndrome, brain herniation signs, and brainstem abnormalities in patients with cerebrovascular event (10, 17). Considering the high reliability and outcome predictive power of the FOUR score, as well as its easy application compared to GCS, this scale could be a viable alternative to GCS to measure the level of consciousness in ICUs and critical care units.

Implications for Practice

Loss of consciousness is considered a significant indication of traumatic brain injury. Given the importance of timely diagnosis and treatment in patients with brain injury, use of a valid, reliable tool to measure the consciousness level of comatose patients should be prioritized. According to the results of this study, the FOUR score has an excellent

reliability in the assessment of the level of consciousness in comatose patients. Moreover, this scale has a higher predictive value compared to GCS in the evaluation of consciousness level in patients admitted in the ICU.

Limitations and recommendations

Due to limited financial resources, one of the drawbacks of the present study was the small number of observers to verify the validity and reliability of the FOUR score and GCS. Therefore, it is recommended that future studies in this regard assess the reliability and validity of these scales by a larger number of evaluators. In addition, further investigation in larger sample sizes with prolonged follow-ups might be required.

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