Original Article

Full Outline of Unresponsiveness score and the Glasgow Coma Scale in prediction of pediatric coma

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BACKGROUND: This study was done to compare the admission Full Outline of Unresponsiveness (FOUR) score and Glasgow Coma Scale (GCS) as predictors of outcome in children with impaired consciousness.

METHODS: In this observational study, children (5–12 years) with impaired consciousness of <7 days were included. Children with traumatic brain injury, on sedatives or neuromuscular blockade; with pre-existing cerebral palsy, mental retardation, degenerative brain disease, vision/hearing impairment; and seizure within last 1 hour were excluded. Primary outcomes: comparison of area under curve (AUC) of receiver operating characteristic (ROC) curve for in-hospital mortality. Secondary outcomes: comparison of AUC of ROC curve for mortality and poor outcome on Pediatric Overall Performance Category Scale at 3 months.

RESULTS: Of the 63 children, 20 died during hospital stay. AUC for in-hospital mortality for GCS was 0.83 (CI 0.7 to 0.9) and FOUR score was 0.8 (CI 0.7 to 0.9) [difference between areas -0.0250 (95% CI 0.0192 to 0.0692), Z statistic 1.109, $P=0.2674$]. AUC for mortality at 3 months for GCS was 0.78 (CI 0.67 to 0.90) and FOUR score was 0.74 (CI 0.62 to 0.87) ($P=0.1102$) and AUC for poor functional outcome for GCS was 0.82 (CI 0.72 to 0.93) and FOUR score was 0.79 (CI 0.68 to 0.9) ($P=0.2377$), which were also comparable. Inter-rater reliability for GCS was 0.96 and for FOUR score 0.98.

CONCLUSION: FOUR score was as good as GCS in prediction of in-hospital and 3-month mortality and functional outcome at 3 months. FOUR score had a good inter-rater reliability.

KEY WORDS: Altered sensorium; Neuro-intensive care; Neuro-monitoring; Neuroinfection; Tropical neurology

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INTRODUCTION

Evaluation of altered consciousness in children is a challenge and an important aspect of emergency care. There is no objective measure to communicate and document the severity of coma as distinct from vital signs. Clinicians frequently rely upon clinical scores or scales to record the level of consciousness. The Glasgow Coma Scale (GCS) is by far the most widely used and popular scoring system for this purpose. It was designed to assess individuals with head trauma, but it's increasingly being used in patients with non-traumatic

coma as well. Several limitations of the GCS have been encountered on its use. It has limitations in inter-observer agreement; it is hard to use in non-verbal or intubated patients; it lacks brainstem reflexes; the sub-scores are not equally represented in the total scores; and there are concerns regarding its predictive abilities. Newer scales have not been met with wide acceptance. However, a recently validated new coma scale the "Full Outline of Unresponsiveness (FOUR) score" has generated interest worldwide. The main highlights of this 16-point score are the exclusion of the verbal component of GCS,

and the inclusion of brainstem reflexes and respiratory pattern. The "FOUR score" was first validated in the neurological-neurosurgical ICU and showed favourable characteristics.^[1] Over the last ten years or so it has been demonstrated to be useful in adults with stroke,^[2] trauma^[3] and non-traumatic coma.^[1] It has been used by trainees, nurses, ICU staff and neurologists.^[1,4] It has been shown to have good inter-rater reliability and predictive ability comparable to GCS.^[4] In a pooled analysis of prospectively studied patients with traumatic and non-traumatic coma, the predictive ability of FOUR score was reported to be as good as that of GCS.^[5]

The FOUR score has been evaluated in children with altered consciousness in only a few studies.^[3,6-8] It still needs to generate more data on the use of FOUR score in children, especially those with non-traumatic coma. This study aimed to compare the predictive ability of FOUR score and Glasgow Coma Scale (GCS) in 5 to 12-year-old children admitted in the pediatric emergency with impaired consciousness.

METHODS

This prospective observational study was conducted over ten months (September 2013 to June 2014) in a tertiary care referral children hospital of Post-Graduate Institute of Medical Education and Research. The protocol was approved by the institutional ethics committee of the hospital. A written informed consent was obtained from the primary caregivers of the participating children.

Enrolment criteria

Children presenting to the pediatric emergency with altered level of consciousness were screened for eligibility. The inclusion criteria were children aged 5–12 years, with impaired consciousness of less than 7 days duration. The exclusion criteria were head trauma; any episode of seizure in the preceding one hour; administration of sedatives, or neuromuscular relaxants; and intellectual, motor, visual, or hearing impairment.

FOUR score

Wijdicks and colleagues in 2005 proposed a new coma scale named the FOUR score.^[1] The FOUR score has four testable components (E, eye responses; M, motor responses; B, brainstem reflexes; and R, respiration). All components have five subscores from zero to four. The eye response (E) is graded as: eyelids remain closed with

pain (0), eyelids closed but opens to pain (1), eyelids closed but opens to loud voice (2), eyelids open but not tracking (3), and eyelids open or opened, tracking or blinking to command (4). The motor responses (M) are graded as: no response to pain or generalized myoclonus status epilepticus (0), extensor posturing (1), flexion response to pain (2), localizing to pain (3), and thumbs up, fist, or peace sign to command (4). The brain stem reflexes (B) are graded as: absent pupil, corneal, and cough reflex (0), pupil and corneal reflexes absent (1), pupil or corneal reflexes absent (2), one pupil wide and fixed (3), and pupil and corneal reflexes present (4). The respiration (R) is graded as: breathes at ventilator rate or apnea (0), breathes above ventilator rate (1), not intubated and irregular breathing pattern (2), not intubated and Cheyne-Stokes breathing pattern (3), and not intubated and regular breathing pattern (4).

Training and administration of the scores

All raters were trainee resident doctors in pediatrics. They were provided with a background of the score and shown the 30 minutes with the standardized video examples included in a DVD prepared by the developers of the FOUR score.^[9] GCS is the routine scale administered to all children admitted in the pediatric emergency as a part of initial TRIAGE at our center. All eligible children additionally underwent a scoring based on FOUR score. All raters were given a one-page hand-out with written instructions describing both FOUR score and GCS. The GCS and FOUR scores were applied by each rater within one hour of admission. For the purpose of the study, the verbal GCS score of intubated patient was taken as one. The further care of the child was left to the treating team and a note of all events till discharge was made. The functional outcome of the survivors was assessed by the Pediatric Overall Performance Category (POPC) at three months following discharge. Values of POPC between 1 and 3 were taken as good outcome, whereas values of 4 or 5 and death were taken as poor outcome.

Outcome measures

The primary outcome was the comparison of area under the curve (AUC) of receiver operating characteristic (ROC) curve for in-hospital mortality. The secondary outcomes were the comparison of AUC of ROC curve for 3-month mortality and a poor outcome on Pediatric Overall Performance Category Scale (POPC) at 3 months.

Statistical analysis

Continuous variables were expressed by mean $\pm$ standard deviation, ordinal variables as median and range. The predictive value of GCS and FOUR score in predicting the outcome (mortality, 3 months mortality, poor functional outcome on POPC at 3 months) was established by receiver operator curve (ROC) by calculating area under the curve (AUC) values and 95% confidence intervals (CIs). For the purpose of sample size calculation, an AUC value for ROC of GCS in children for prediction of in-hospital mortality was assumed as 0.7 and the expected clinically relevant area under the curve for FOUR score was anticipated at 0.8.^[10] The rank correlation between both the scores and outcome was taken as 0.7. When α -level was kept as 0.05 and β -level as 0.20, the estimated sample size was 70. Inter-rater reliability was assessed using the interclass coefficient in a subgroup of children evaluated by two raters.

RESULTS

During the study period, 157 children with altered sensorium were assessed for eligibility. Of these, 63 children (33 boys, mean age 7.4 $\pm$ 2.1 years) meeting study criteria were enrolled (Figure 1). All children were assessed and rated by Rater-1 (AJ). Twenty-seven children were assessed by two independent observers (Rater 1 and Rater 2). The second raters were

Figure 1. Flow of the screened and enrolled children in the study.

different trainee resident doctors in pediatrics posted in the emergency room. The mean duration of impaired consciousness in the study group was 2.1 $\pm$ 1.8 days. The median value of GCS in the whole study group was 8 (IQR 6 to 11) and that of FOUR score was 11 (IQR 9 to 13). The suspected cause for impaired consciousness was neuroinfection in 34 children, an non-infection in 29 children. Among infectious causes, the most common cause of impaired consciousness was acute viral meningoencephalitis ($n=16$), followed by tuberculous meningitis ($n=5$) and bacterial meningitis ($n=5$). Among non-infectious causes, epilepsy with seizure recurrence ($n=7$), hepatic encephalopathy ($n=5$) and intoxication/envenomation ($n=4$) were the three leading causes.

Comparison of GCS and FOUR score in predicting mortality

Of the 63 enrolled children, 20 died during the hospital stay. The median GCS at admission in those dying in the hospital was 6 (IQR 4.25 to 7) as compared with survivors whose admission median GCS was 10 (IQR 7 to 11). The median FOUR score at admission in those dying in hospital was 9.5 (IQR 7.25 to 11) as compared with survivors whose score was 12 (IQR 11 to 14). On the ROC curve analysis, area under curve (AUC) for in-hospital mortality for GCS was 0.83 (CI 0.7 to 0.9) and FOUR score was 0.8 (CI 0.7 to 0.9), which were comparable [difference between areas 0.0250 (95%CI 0.0192 to 0.0692), Z statistic 1.109, $P=0.2674$]. Furthermore, on univariate analysis those who survived were significantly less likely to have shock and poorly reactive pupils at admission (Table 1), and higher mean scores and subscores on the two coma

Table 1. Demographic and clinical characteristics of the study population stratified by the primary outcome (in-hospital mortality)

Variables	Survived ($n=43$)	Died in hospital ($n=20$)	<i>P</i> value
Age (years)	7.4 $\pm$ 2.1	7.4 $\pm$ 2	0.9
Male sex, n (%)	23 (53.4)	10 (50)	1
Fever, n (%)	25 (58.1)	17 (85)	0.046
Vomiting, n (%)	23 (53.5)	15 (75)	0.16
Seizure, n (%)	25 (58.1)	9 (45)	0.41
Headache, n (%)	8 (18.6)	2 (10)	0.48
Cough, n (%)	5 (11.6)	5 (25)	0.26
Shock, n (%)	3 (7)	8 (40)	0.003
Meningeal signs, n (%)	5 (11.6)	3 (15)	0.07
Non-reactive or sluggish pupils, n (%)	0	7 (35)	<0.001
Hepatomegaly, n (%)	8 (18.6)	8 (40)	0.18
Intubated, n (%)	37 (86)	16 (80)	0.7
Duration of ventilation (days)	3.8 $\pm$ 4.7	3.5 $\pm$ 4.5	0.8

Values in parenthesis indicate percentage within the group.

scales (Table 2).

Of the 63 enrolled children, two more children died during 3 months follow-up. So the total deaths by 3 months were 22. AUC for mortality at 3 months for GCS was 0.78 (CI 0.67 to 0.90) and FOUR score was 0.74 (CI 0.62 to 0.87) [difference between areas 0.0399 (95%CI 0.00907 to 0.0889)].

Functional outcome of survivors was assessed using Pediatric Overall Performance Category Scale (POPC) score at 3 months. Children with POPC score of 1–3 were assigned as a good outcome and children with score of 4, 5 or death were assigned as a poor outcome. Twenty-nine (including 22 who died) children had a poor outcome and thirty-four children had a good outcome. AUC for poor functional outcome for GCS and FOUR score were comparable (Table 3).

Table 2. The admission coma scores of the study population stratified by the primary outcome (In -hospital mortality)

Coma score/Subscore	Survived (n=43)	Died in hospital (n=20)	P value
GCS			
Subscore eye response	2.4±0.9	1.3±0.6	<0.001*
Subscore verbal response	2.4±1.3	1.2±0.4	0.002
Subscore motor response	4.2±1.0	3.2±1.3	<0.001*
Total	9.1±2.5	5.8±1.9	<0.001
FOUR score			
Subscore eye response	1.7±1.3	0.6±1.1	0.001
Subscore motor response	2.4±0.8	1.7±0.9	0.007
Subscore brainstem reflexes	3.9±0.15	3.4±1.1	0.054*
Subscore respiration	3.7±0.7	3.0±1.1	0.017*
Total score	11.8±2.2	8.8±3.0	<0.001

*: variable was non-parametrically distributed; P value derived from "t test" adjusted for unequal variances; equality of variances was compared using Levene's test for equality of variances.

To assess the inter-rater reliability, 27 children were rated by two raters on the GCS and FOUR scores. For GCS the interclass correlation co-efficient was 0.93 (95%CI 0.867 to 0.970) for single measures and 0.96 (95%CI 0.970 to 0.985) for average measures. For FOUR score the interclass correlation co-efficient was 0.97 (95%CI 0.930 to 0.985) for single measures and 0.98 (95%CI 0.964 to 0.992) for average measures. Both GCS and FOUR score had a good inter-rater reliability as evidenced by a high interclass coefficient.

DISCUSSION

In this study, the new coma scale "FOUR score" was assessed in the emergency room (ER) by trainee residents as raters. The raters with a short training were able to use this scale and use it in the emergency rooms. We confirmed that the FOUR score is a good predictor of in-hospital mortality, and 3-month outcome in children with coma. Our study adds to the little but accumulating data on use of this scale in children with impaired consciousness (Table 4). The strength of our study is that we used mortality as primary outcome measure, thus avoiding any subjectivity in outcome assessment. Additionally, we used the functional outcome measure (Pediatric Overall Performance Category) to assess long-term outcome. This study had a prospective design and well defined inclusion and exclusion criteria.

Both GCS and FOUR score had excellent agreement between observers. GCS is a part of TRIAGE at our center and is done in all children admitted to the emergency ward and a good agreement among observers

Table 3. Comparison of GCS and FOUR score based on area under curve of ROC curve

Variable compared	GCS (95%CI)	FOUR score (95%CI)	Differences in AUC (95%CI)	Z statistic	Significance level
In-hospital mortality	0.83 (0.73 to 0.92)	0.80 (0.69 to 0.91)	0.0250 (0.0192 to 0.0692)	1.109	P=0.2674
Three-month mortality	0.78 (0.67 to 0.90)	0.74 (0.62 to 0.87)	0.0399 (0.00907 to 0.0889)	1.597	P=0.1102
Poor outcome at 3 months outcome on POPC scale	0.82 (0.72 to 0.93)	0.79 (0.68 to 0.90)	0.0294 (0.0194 to 0.0782)	1.181	P=0.2377

Table 4. Comparison of studies on FOUR score in children with coma

Author; Year of publication	Number	Population studied	Raters and setting	Prediction of death by GCS	Prediction of death by FOUR score
Kochar et al; 2014 ^[8]	70	5–18 years, non traumatic coma	Pediatric neurology, fellow, ward and ICU	0.916	0.940
Büyükcem et al; 2012 ^[3]	100	2–17 year, traumatic coma	Physicians and residents, emergency	0.965	0.975
Khajehet et al; 2014 ^[7]	200	Mean age 4.4 years, children, non trauma PICU	ICU	–	–
Cohen et al; 2009 ^[12]	–	–	Critical care nurse, ICU	0.77	0.81
Current study	63	5–12 years	Pediatric resident trainee, emergency room	0.83	0.80

GCS: Glasgow coma scale; FOUR: full outline of unconsciousness score; ICU: intensive care unit.

was thus not surprising. However, the equally good agreement among observers while using the FOUR score was remarkable, indicating that the performance and interpretation of components of FOUR score were not difficult for a pediatric resident working in the ER.

FOUR score was proposed by Wijdicks and colleagues in 2005 to address the deficiencies of the popular GCS.^[1] Initially, this scale was validated in adults and followed by recent reports in children (Table 2). The score has been used to determine outcomes in patients with traumatic coma and non-traumatic coma. Secondly, it has been used by doctors, nurses and specialists in different settings and found to be useful.^[1,5,6,8,11,12] GCS was initially tested in individuals with traumatic coma whereas the FOUR score was initially tested in neurointensive care settings and included patients with surgical and medical conditions.^[1] In the present study, most of the children with impaired consciousness had febrile encephalopathy secondary to tropical neuro-infections. The scores performed well in this setting of tropical neuro-infections. We, however, did not assess how the FOUR score assessment altered management of individual patients. Another stated advantage of FOUR score over GCS is that it can be applied in the intubated patients without substitute scores and thus may be suitable for patients in the ICU. In fact, in a recent study of 1 645 critically ill patients, Wijdicks and colleagues^[13] reported FOUR score to be better than GCS in predicting ICU mortality. Similar studies in children, though desired, are lacking. It has also been reported that FOUR score is better than GCS in predicting outcome in some situations like hypoxic ischemic encephalopathy after cardiac arrest.^[11] We could not compare the two scores for individual conditions due to a small sample.

Any scale that has to be widely used has to be simple, reliable and help in prediction and clinical decision making. In this regard, GCS score is more familiar to physicians and healthcare workers and easier than FOUR score. FOUR score has more items, requires more time, and possibly harder to remember.^[4] However, FOUR score provides more neurologic details than GCS, so it cannot replace a detailed neurological examination. Nevertheless, in the emergency settings, the standardized assessment of respiration, brain stem reflexes and pupillary reactions using FOUR score may help in recognition of possible brain death, herniation syndromes and prompt urgent medical and surgical intervention. Because of the different advantages and disadvantages of the two coma scales, it is worthwhile to evaluate the two

scales further. The possible areas of exploration could be an assessment of each scale in different settings (ER and ICU, intubated versus non-intubated), in various etiologies, and severities of coma (e.g., for GCS <5). Another important aspect that needs careful comparison is how absolute scores and serial changes in scores impact management at bedside. The FOUR score has to show unequivocal advantage over GCS in more than one aspect to become the new gold standard coma scale.

Our study had several limitations. The study was under-powered to detect any differences in AUC of less than 0.1 between GCS and FOUR score. So the question of superiority of one score over the other remains unsettled after this study. We did not explore the role of this score to detect and communicate serial changes in children with coma. Since this study only reflected admission ratings and outcome, it may not truly reflect the predictive ability of the scores. Researchers have shown that changes in scores have a predictive value in comatose individuals,^[11] and comparing serial changes in the two scores may have provided a better understanding of the predictive ability of the scores.

CONCLUSION

The new coma scale "FOUR score" is reliably used in the emergency room setting by pediatrics trainee residents. We found the FOUR score could be used as good as GCS in predicting in-hospital mortality and three-month outcome in children with non-traumatic coma.

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Contributors: Jamal A proposed the study and wrote the first draft. All authors read and approved the final version of the paper.

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