Usefulness of full outline of unresponsiveness score to predict extubation failure in intubated critically-ill patients: A pilot study

Tarek Said, Anis Chaari, Karim Abdel Hakim, Dalia Hamama, William Francis Casey

ABSTRACT

Objective: To assess the usefulness of the full outline of unresponsiveness (FOUR) score in predicting extubation failure in critically ill intubated patients admitted with disturbed level of conscious in comparison with the Glasgow coma scale (GCS).

Patients and Methods: All intubated critically ill patients with a disturbed level of consciousness were assessed using both the FOUR score and the GCS. The FOUR score and the GCS were compared regarding their predictive value for successful extubation at 14 days after intubation as a primary outcome measure. The 28-day mortality and the neurological outcome at 3 months were used as secondary outcome measures.

Results: Eighty-six patients were included in the study. Median age was 63 (50–77) years. Sex-ratio (M/F) was 1.46. On admission, median GCS was 7 (3–10) while median FOUR score was 8.5 (2.3–11). A GCS ≤ 7 predicted the extubation failure at 14 days after intubation with a sensitivity of 88.5% and specificity of 68.3%, whereas a FOUR score <10 predicted the same outcome with a sensitivity of 80.8% and a specificity of 81.7%. The areas under the curves was significantly higher with the FOUR score than with GCS (respectively 0.867 confidence interval [CI]: 95% [0.790–0.944] and 0.832 CI: 95% [0.741–0.923]; P = 0.014). When calculated before extubation, FOUR score <12 predicted extubation failure with a sensitivity of 92.3% and a specificity of 85%, whereas a GCS <12 predicted the same outcome with a sensitivity of 73% and a specificity of 61.7%. Both scores had similar accuracy for predicting 28-day mortality and neurological outcome at 3 months.

Conclusion: The FOUR score is superior to the GCS for the prediction of successful extubation of intubated critically ill patients.

Key Words: Extubation, full outline of unresponsiveness score, glasgow coma scale

INTRODUCTION

Daily assessment of comatose critically ill patients is an integral part of working in intensive care units. The Glasgow coma scale (GCS), originally designed to assess head trauma patients, has become the most widely used assessment tool worldwide for critically ill patients with an altered sensorium.[1] However, the GCS has its inherent shortcomings which include inconsistent interobserver reliability, concerns over its ability to predict the extent of the brain damage, the impracticality of verbal response assessment in intubated patients or in patients with dysphasia, the exclusion of brain stem functions from the GCS, and

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the inability to detect subtle changes in neurological status.[2,3]

The full outline of unresponsiveness (FOUR) score was proposed by investigators from the Mayo Clinic in 2005.[4] Unlike the GCS, it does not depend on a verbal response, which makes it an attractive tool in intubated patients.[3] Since its introduction in the Mayo Clinic, the FOUR score has been validated through observational studies within different types of patient population.[6‑11] In the majority of these studies, FOUR score was found to be equivalent to the GCS regarding the inter-rater reliability and correlation with outcome. However, to the best of our knowledge, there were no studies to evaluate the predictive value of the FOUR score regarding short-term extubation failure in critically ill intubated patients with an altered sensorium. In fact, several studies suggest that in neurocritical patients, neurologic disabilities can be responsible for delayed extubation and/or increased risk for extubation failure.[12‑14]

In this prospective observational study, we compared the predictive value of the FOUR score against the GCS in terms of short-term extubation failure in intubated critically ill patients.

PATIENTS AND METHODS

This observational prospective study was conducted in a 12-bedded Intensive Care Unit (ICU) over a period of 6 months (between December 1, 2014 and May 31, 2015). The study was approved by our hospital Ethics Committee.

All intubated adult patients admitted with a disturbed level of consciousness (GCS ≤8) and requiring intubation, and mechanical ventilation was included in the study. Patients admitted with a tracheostomy and those needing continuous heavy sedation or infusion of muscle relaxants for more than 24 h were excluded from the study.

In our intensive care unit, all the patients are sedated with remifentanil alone or combined to propofol. The dose of the sedative drugs was adjusted aiming to achieve a Richmond Agitation Sedation Scale of −3.[15] The assessment of the conscious level was carried out by one of the ICU physicians, within the first 24 h following intubation, using both the FOUR score and the GCS. If a sedative agent was being administered, the assessment was commenced after 3-4 h of sedation vacation. Both scores were calculated before extubation, once the weaning process was considered as successful. The record of each assessment also included the mark given to each component of each score (motor, verbal and eye for the GCS and motor, verbal, respiration, and brainstem for the FOUR score). The following data were also recorded on admission for all the included patients:

- Age, sex, comorbidities (diabetes, hypertension, stroke, chronic obstructive pulmonary disease, and chronic kidney disease) and the cause of admission to the ICU.
- The FOUR score and the GCS were compared regarding their predictive value for successful extubation at 14 days after intubation as a primary outcome measure. A patient was considered successfully extubated if he was maintained off mechanical ventilation, breathing spontaneously, and without definitive airway management for at least 48 h. The 28-day mortality and the neurological outcome at 3 months were used as the secondary outcome measures. The neurological outcome at 3 months after ICU admission was assessed by the estimation of the modified Rankin score.[16] Hence, the patient with a modified Rankin score ranging from 3 to 6 was considered as having poor neurological outcome.

Included patients were divided into two groups: Those with extubation failure (extubation failure (+) group) and those with successful extubation (extubation failure (−) group) at 14 days of intubation. Qualitative variables were expressed as percentages, whereas quantitative variables were expressed as means ± standard deviation or median (quartiles). The normal distribution of the quantitative variables was checked by the Kolmogorov–Smirnov test and Shapiro–Wilk test. Univariate analysis was performed to compare the two groups according to their baseline characteristics. Qualitative variables were compared by the Chi-square test or by the Fischer’s exact test, whereas quantitative variables were compared by the t-test or the Mann–Whitney test as appropriate. Sensitivity and specificity of each score in predicting extubation failure at 14 days of intubation were obtained from the receiver operating characteristics (ROC) curves. The Youden index with a 95% confidence interval (CI) was calculated for each score. The areas under the curves (AUC) were compared using DeLong test.

The two scores were also compared according to the secondary outcomes (day-28 mortality and neurological outcome at 3 months after admission to the ICU) with the same statistical modalities. All the tests were two-sided. P < 0.05 was considered statistically significant. All the statistics were performed using the R package (version 3.1.3).

RESULTS

Baseline characteristics

During the study period, 101 intubated patients were admitted to our intensive care unit. Eighty-six patients met the inclusion criteria. Median age was 63 (50–77) years. Sex-ratio (M/F) was 1.46. Leading causes for ICU admission were septic shock (43%), cardiac arrest (19.8%), and acute ischemic or hemorrhagic stroke (15.1%). Only
18 patients (21%) had no previous medical history. The main comorbidities were diabetes mellitus (62.8%), arterial hypertension (67.4%), ischemic heart disease (23.3%), ischemic stroke (17.4%), and chronic obstructive pulmonary disease (5.8%). Vasopressor support was required in 58 patients (67.4%). Median GCS was 7 (3–10). The median values for the different components of the GCS were 4 (1–5) for the motor response and 3 (1–4) for the eye movements. The verbal response was rated 1 for all the patients. Median FOUR score was 8.5 (2.3–11). The median value of its components were 2 (0–3) for the motor response as well as the eye response and 4 (1–4) for the brainstem. The median value of the respiratory response was 1 (1–1) (as all patients were intubated, the respiratory score range was 0–1). The univariate analysis showed that the two studied groups had similar baseline characteristics except for the age which was significantly higher for extubation failure (+) group [Table 1].

Primary outcome

Sixty patients (69.8%) failed the extubation trial by day 14. The incidence of swallowing or cough impairment as main cause leading to reintubation was significantly higher in the extubation failure (+) group (respectively 40% and 7.7%; P = 0.002). Both the GCS and the FOUR score were significantly lower in the extubation failure (+) group than the extubation failure (−) group [Table 2]. A GCS ≤7 predicted the extubation failure at 14 days after intubation with a sensitivity of 88.5% and specificity of 68.3% (Youden index = 0.57 CI: 95% [0.35–0.7]), whereas a FOUR score ≤9 predicted the same outcome with a sensitivity of 80.8% and a specificity of 81.7% (Youden index = 0.62 CI: 95% [0.44–0.77]). The FOUR score was more accurate in predicting extubation failure at 14 days of intubation. In fact, the AUC was significantly higher with the FOUR score than with GCS (respectively 0.867 CI: 95% [0.790–0.944] and 0.832 CI: 95% [0.741–0.923]; P = 0.014) [Figure 1]. Moreover, the FOUR score and the GCS calculated before extubation were significantly lower in the extubation failure (+) group [Table 2]. The FOUR score calculated before extubation was the most accurate to predict extubation failure by day 14, whereas the GCS calculated concomitantly had the worst sensitivity and specificity to predict the outcome [Table 3].

Secondary outcomes

The analysis of the ROC curves showed that a GCS ≤8 predicted 28-day mortality with a sensitivity of 84.4% and a specificity of 77.8% (Youden index = 0.62 CI: 95% [0.43–0.75]). On the other hand, a FOUR score ≤9 predicted the same outcome with a sensitivity of 84.4% and a specificity of 79.6% (Youden index = 0.64 CI: 95% [0.45–0.78]). There was no significant difference between the AUCs of the two studied scores regarding day 28 mortality [Figure 2].

Similarly, the GCS and the FOUR score had comparable predictive values for the poor neurological outcome at 3 months after admission. In fact, a GCS ≤ 8 predicted poor neurological outcome with a sensitivity of 100% and a specificity of 71% (Youden index = 0.71 CI: 95% [0.59–0.81]) whereas a FOUR score ≤9 predicted the same outcome with a sensitivity of 100% and

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**Table 1:** Comparison of extubation failure (+) and extubation failure (−) groups according to demographic characteristics

| Characteristic                          | Extubation failure (+), n = 60 | Extubation failure (−), n = 26 | P      |
|----------------------------------------|---------------------------------|---------------------------------|--------|
| Age (years), median (quartiles)        | 68.5 (54.3–78.8)                | 52 (41–70)                      | 0.004  |
| Gender (male/female)                   | 39/21                           | 12/14                           | 0.102  |
| Cause of admission, n (%)              |                                 |                                 |        |
| Cardiac arrest                         | 13 (21.7)                       | 4 (15.4)                        | 0.964  |
| ACS                                    | 3 (5)                           | 3 (11.5)                        | 0.381  |
| Septic shock                           | 28 (46.7)                       | 9 (34.6)                        | 0.300  |
| ARF                                    | 2 (3.3)                         | 3 (11.5)                        | 0.160  |
| Acute stroke                           | 11 (18.3)                       | 2 (7.7)                         | 0.327  |
| Others                                 | 3 (5.1)                         | 5 (2.4)                         | 0.053  |
| Comorbidities, n (%)                   |                                 |                                 |        |
| Hypertension                           | 42 (70)                         | 16 (61.5)                       | 0.442  |
| Diabetes                               | 41 (68.3)                       | 13 (50)                         | 0.106  |
| COPD                                   | 2 (3.3)                         | 3 (11.5)                        | 0.160  |
| Cardiac disease                        | 16 (26.7)                       | 4 (15.4)                        | 0.255  |
| CKD                                    | 17 (28.3)                       | 5 (19.2)                        | 0.374  |
| CVA                                    | 11 (18.3)                       | 4 (15.4)                        | 0.990  |
| GCS before extubation                  | 10 (7–12)                       | 12 (11–13)                      | <0.001 |
| FOUR score before extubation           | 10 (8–12)                       | 12 (11–13)                      | <0.001 |

**Table 2:** Comparison of extubation failure (+) and extubation failure (−) groups according to Glasgow coma scale and full outline of unresponsiveness score parameters

| Score                          | Extubation failure (+), n = 60 | Extubation failure (−), n = 26 | P       |
|-------------------------------|---------------------------------|---------------------------------|---------|
| GCS score, median (quartiles) |                                 |                                 |         |
| Motor                         | 2 (1–4)                         | 5 (5.5–3)                       | <0.001  |
| Eyes                          | 1.5 (1–4)                       | 4 (3.8–4)                       | <0.001  |
| Verbal                        | 1 (1–1)                         | 1 (1–1)                         | 0.99    |
| Total                         | 5.5 (3–9)                       | 10 (9.9–3)                      | <0.001  |
| FOUR score, median (quartiles)|                                 |                                 |         |
| Eye                            | 0.5 (0–3)                       | 3 (3–4)                         | <0.001  |
| Motor                          | 0.5 (0–2)                       | 3 (3.3–2.5)                     | <0.001  |
| Brainstem                      | 2 (1–4)                         | 4 (4–4)                         | <0.001  |
| Reaction                       | 1 (1–1)                         | 1 (1–1)                         | 0.028   |
| Total                          | 4.5 (2–10)                      | 11 (11–12)                      | <0.001  |

**Table 3:** Sensitivity and specificity of the full outline of unresponsiveness score and the Glasgow coma scale to predict day 14-extubation failure

| Score on admission | Threshold | Sensitivity (%) | Specificity (%) | AUC (CI 95%)     |
|--------------------|-----------|-----------------|-----------------|-----------------|
| FOUR score on admission | 10        | 80.8            | 81.7            | 0.87 (0.79–0.94)|
| GCS on admission | 7         | 88.5            | 68.3            | 0.83 (0.74–0.92)|
| FOUR score day 14 | 12        | 92.3            | 85              | 0.95 (0.90–0.99)|
| GCS day 14        | 12        | 73              | 61.7            | 0.71 (0.60–0.82)|

FOUR: Full outline of unresponsiveness, GCS: Glasgow coma scale.
Said, et al.: FOUR score to predict extubation failure

There was no significant difference between the AUCs of the two studied scores regarding the prediction of poor neurological outcome at 3 months after admission [Figure 3].

**DISCUSSION**

Our results show that the FOUR score calculated either on admission or before extubation is more accurate than the GCS in predicting the extubation failure at 14 days post intubation. On the other hand, when we compared the FOUR score and the GCS regarding prediction of mortality at 28 days and poor neurological outcome at 3 months after admission, we found that the predictive value of the FOUR score is not superior to that of the GCS.

Since its introduction in 2005, the FOUR score has been investigated against the GCS and it was found to have a similar if not higher prediction of mortality and poor neurological outcome in general ICU population, traumatic brain injury patients, stroke patients, and patient admitted after cardiac arrest. Concerns have been reported regarding the accuracy of using the GCS, especially in intubated ICU patients due to the impracticality of assessing the verbal response. Usually, assessors omit this component resulting in an incomplete assessment. A verbal score of one in an intubated patient does not tell much about the actual ability to communicate and articulate. It was observed that some physicians and nurses might opt to estimate a verbal score despite the limitations imposed by intubation. On the other hand, the FOUR score carries potential advantages that merit its use in intubated critically ill patients. It adds eye-tracking to the eye opening of the GCS, thus incorporating the assessment of midbrain and pontine function. It replaced the verbal response by hand gestures, allowing for testing the afferent language processing in intubated patients. No motor response and myoclonic status epilepticus are equally scored as 0, which correctly reflects their poor neurological outcome in anoxic brain injury.

In our study, we have evaluated the predictive value of the FOUR score against the GCS on admission regarding extubation failure as a primary outcome variable. Neurological impairment reflected in a low GCS was found to be an independent risk factor for extubation failure. In a systematic review including 9 studies, Wang et al. reported that poor gag reflex, low GCS (7–9 T), and the inability to follow command were significantly associated with extubation failure. Our study corroborates these findings as the incidence of gag and swallowing impairment was significantly higher in the group of patients who failed the extubation trial. In fact, an intact cough reflex provides reasonable assurance of ability to clear bronchial secretions after extubation.
and it was shown to be associated with successful extubation.\[32\] Having incorporated all these detailed neurological examinations and deferring the use of a verbal response, we have found the FOUR score to have a better and more accurate correlation with extubation outcome compared to the GCS in intubated patients. Interestingly, we found that the FOUR score was able to predict extubation failure even when it was calculated on admission. This finding may be related to the assessment of the brainstem reflexes and the respiratory function which deeply interfere with the weaning process. The higher accuracy of the FOUR score calculated before extubation highlight the usefulness of this score as a follow-up tool as it reflects the improvement of few patients since their admission which made their weaning and extubation feasible.

Regarding prediction of 28-day mortality and poor neurological outcome 3 months after admission, we could not find a statistically significant difference between the FOUR score and the GCS. This finding is in accordance with the results of a recent study that examined the FOUR score against the GCS regarding prediction of early and late mortality.\[5\] In fact, Gorji et al. found that the FOUR score is more accurate than the GCS in predicting early mortality in 80 intubated patients with traumatic brain injury, whereas there was no statistically significant difference in predicting late mortality.\[5\]

The first limitation to our study may be the small sample size. A larger sample may bolster the results. Second, the use of sedative agents may be considered a limitation. However, in our ICU we largely depend on short-acting agents such as remifentanil and propofol for routine sedation of intubated patients.

**CONCLUSION**

Our study showed that the FOUR score is superior to the GCS in the prediction of successful extubation of intubated critically ill patients in the general ICU population. Larger cohort studies are needed to evaluate both scores regarding the prediction of 28-day mortality and poor neurological outcome 3 months after admission.

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Conflicts of interest
There are no conflicts of interest.

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