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REVIEW ARTICLE

The Full Outline of UnResponsiveness (FOUR) Score and Its Use in Outcome Prediction: A Scoping Systematic Review of the Adult Literature

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Abstract

Background: The Full Outline of UnResponsivness (FOUR) score is a neurological assessment score. Its theoretical benefit over preexisting scores is its evaluation of brainstem reflexes and respiratory pattern which may allow better assessment of patients with severe neurologic impairment.

Objective: Our goal was to perform a scoping systematic review on the available literature for FOUR score and outcome prediction in critically ill patients. The primary outcome of interest was patient global outcome, as assessed by any of: mortality, modified Rankin Score, Glasgow Outcome Score, or any other functional or neuropsychiatric outcome. Information on interobserver reliability was also extracted.

Methods: MEDLINE and five other databases were searched. Inclusion criteria were: humans, adults, and children; prospective randomized controlled trial; prospective cohort, cohort/control, case series, prospective, and retrospective studies. Two reviewers independently screened the results. Full texts for citations passing this initial screen were obtained. Inclusion and exclusion criteria were applied to each article to obtain final articles for review. Results on adult populations are presented here. Data are reported following the preferred reporting items for systematic reviews and meta-analyses guidelines.

Results: The initial search yielded 1709 citations. Of those used, 49 were based on adult and 6 on pediatric populations. All but 8 retrospective adult studies were performed prospectively. Patient categories included traumatic brain injury, intraventricular hemorrhage, intracerebral hemorrhage, subarachnoid hemorrhage, ischemic stroke, general/combined neurology and neurosurgery, post-cardiac arrest, medicine/general critical illness, and patients in the emergency department. A total of 9092 adult patients were studied. Fourteen studies demonstrated good interobserver reliability of the FOUR score. Nine studies demonstrated prognostic value of the FOUR score in predicting mortality and functional outcomes. Thirty-two studies demonstrated equivalency or superiority of the FOUR score compared to Glasgow Coma Score in prediction of mortality and functional outcomes.

Conclusions: The FOUR score has been shown to be a useful outcome predictor in many patients with depressed level of consciousness. It displays good inter-rater reliability among physicians and nurses.

Keywords: FOUR score, Prognosis, Clinical scoring, Critical illness, Neurological illness

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Table 1 Neurological grading scales

Full Outline of UnResponsiveness Score		Glasgow Coma Scale	
Eye response		Eye opening	
E4	Eyelids open or opened, tracking or blinking to command	E4	Spontaneous
E3	Eyelids open but not tracking	E3	To verbal command
E2	Eyelids closed but open to loud voice	E2	To pain
E1	Eyelids closed but open to pain	E1	None
E0	Eyelids remain closed with pain		
Motor response		Verbal response	
M4	Thumbs-up, fist or peace sign	V5	Oriented
M3	Localizing to pain	V4	Confused
M2	Flexion response to pain	V3	Inappropriate words
M1	Extension to pain	V2	Incomprehensible sounds
M0	No response to pain or generalized myoclonus status	V1	None
Brainstem reflexes		Motor response	
B4	Pupil and corneal reflexes present	M6	Follows commands
B3	One pupil wide and fixed	M5	Localizes pain
B2	Pupil or corneal reflexes absent	M4	Withdraws from pain
B1	Pupil and corneal reflexes absent	M3	Flexion to pain
B0	Absent pupil, corneal and cough reflex	M2	Extension to pain
		M1	None
Respiration			
R4	Not intubated, regular breathing pattern		
R3	Not intubated, Cheyne–Stokes breathing		
R2	Not intubated, irregular breathing		
R1	Breathes above ventilator rate		
R0	Breathes at ventilator rate or apnea		

ROC = 0.92, 95% CI 0.87–0.97). In medicine patients, Rohaut et al. [20] demonstrated the predictive value of the FOUR score in predicting 28-day mortality (*c*-index of 0.76, 95% CI 0.67–0.84). Other outcomes studied include admission to an intensive care unit [23], overt hepatic encephalopathy [18] and discharge to home or a rehabilitation facility [19]. "Appendix E" of the supplementary materials displays the tabulated results from these studies.

One study [26] examined the use of various weaning parameters (including the FOUR score) in predicting extubation failure in general neurology and neurosurgical patients. The authors found no significant difference in FOUR score between patients who failed extubation and those who were successfully extubated.

Prognostic Value When Compared to the GCS

Thirty-two studies [1, 6, 7, 9, 11, 12, 16, 25, 27–51] demonstrated equivalency or superiority of the FOUR score compared to GCS in the prediction of mortality and functional outcomes. Four of these studied patients in the emergency department [6, 7, 27, 30], 8 studied general medical and critical illness patients [9, 11, 12, 29, 31, 45, 48, 49], 11 studied traumatic brain injury patients [25, 34–36, 40–45, 47], and 10 studied other neurology/neurosurgery patients (6 studied general neurology and neurosurgical patients [16, 28, 33, 37, 49, 50], 2 studied ischemic stroke patients [38, 39], 1 studied intraventricular hemorrhage patients [32] and 1 studied aneurysmal subarachnoid patients [51]).

Table 2 displays the studies focusing on emergency department populations. Multiple authors demonstrated equal or superior prognostic value of the FOUR score in predicting mortality; for example, Eken et al. [30] showed AUC ROC = 0.788 for FOUR (95% CI 0.722–0.844) and AUC ROC = 0.735 for GCS (95% CI 0.655–0.797) in predicting in-hospital mortality ($p = 0.0001$). Similarly, Stead et al. [6] demonstrated OR = 0.67 for FOUR (95% CI 0.53–0.84) versus OR = 0.68 for GCS (95% CI 0.56–0.83) in predicting in-hospital mortality ($p < 0.001$).

Table 3 displays the studies on general medical/critically ill patients. Outcomes studied in this population include those in the intensive care unit (ICU) [49], in-hospital [6, 7, 27, 31] and 28-day mortality [45], successful extubation [45], the ability to become a potential organ donor [29], and other functional outcomes based on the GOS, modified Rankin Scale and Glasgow–Pittsburgh cerebral performance categories [9, 12, 45, 48]. All demonstrated equivalency or superiority of the FOUR score; for example, Wijdicks et al. [49] demonstrated AUC ROC = 0.742 (95% CI 0.694–0.790) for FOUR and AUC ROC = 0.715 for GCS (95% CI 0.663–0.768) in predicting in-ICU mortality ($p = 0.001$).

Table 4 outlines the studies on traumatic brain injury patients, while Table 5 highlights the other studies on neurology/neurosurgery patient populations. Values for AUC ROC were similar across studies in predicting in-hospital mortality; generally AUC ROC ≥ 0.80 [1, 34, 39, 40, 43, 44, 47]. Mortality was studied at various other time points [35, 46], along with functional outcome based on the GOS, the Karnofsy Performance Score, the Acute Physiology and Chronic Health Evaluation II score and the modified Rankin Scale [34, 36, 40, 41, 43, 44]. Again, all illustrate the equivalent or superior ability of the FOUR score to predict mortality and functional outcomes when compared to GCS.

One study [52] conducted in post-resuscitation encephalopathy patients studied the motor components of both the FOUR score and GCS to predict poor prognosis, and found a lower sensitivity of the FOUR score in outcome prediction (68.7% sensitivity for FOUR, 95% CI 41.4–88.9 vs. 87.5% sensitivity for GCS, 95% CI 61.6–92.6).

Quality of Evidence

Quality of evidence was assessed using the RTI Item Bank on Risk of Bias and Precision of Observational Studies [4]. Based on its itemized list of questions, there was an overall low risk of bias in the studies included in this review.

Discussion

We aimed to perform a scoping review of the FOUR score and its use in outcome prediction. The existing literature around the FOUR score generally demonstrates that it possesses prognostic value alone and in comparison with the GCS, as exemplified through 9 and 32 mainly prospective studies, respectively.

In predicting extubation failure, however, Ko et al. [26] failed to show predictive value for the FOUR score as well as all other weaning parameters they chose to study, including rapid shallow breathing index and spontaneous breathing trial. In neurology and neurosurgical patients, the ability to forcefully cough and actively clear secretions is of importance in successful extubation, and perhaps not specifically assessed by the FOUR score. However, the authors also had missing data regarding etiology of respiratory failure and inaccurate fluid balance, which may have contributed to their negative results. In contrast, Said et al. [45] published a pilot study among a general ICU population, and did show superiority of the FOUR score compared to GCS in predicting successful extubation at 14 days post-intubation.

In comatose patients post cardiopulmonary arrest, Topcuoglu et al. [52] examined the motor parts of the GCS and FOUR score in outcome prediction and showed