

Beyond the GCS: an integrative review of new tools for neurological assessment in the intensive care unit for adult patients

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Abstract

The Glasgow Coma Scale (GCS) is a widely used clinical tool for assessing impaired consciousness, but concerns arise when applied to intubated patients or those receiving analgesics, sedatives, and paralytics because verbal scores are not evaluable. Furthermore, the GCS does not differentiate the neurological status of the patient once intubated, resulting in poor reliability in neurological assessment, and clinical indicators that may reflect the severity of the coma are not included in the GCS. This study explores alternative tools for neurological assessment in Intensive Care

Units (ICUs) when GCS is impractical. Conducting an integrative review of studies from 2018 to 2022, we identified seven relevant papers. Results indicate the FOUR score as a promising GCS alternative, particularly in cases where the GCS is unavailable. Automated pupillometry also demonstrated the potential for monitoring neurologically impaired ICU patients. These tools, independent of verbal responses and applicable to sedated patients, offer improved accuracy in assessing consciousness. The study emphasizes the importance of adopting such alternatives, and addressing GCS limitations, and highlights the need for further research and implementation to enhance patient care in ICU settings.

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Introduction

The alteration of the state of consciousness represents a very frequent neurological emergency in some contexts, including the intensive care unit but there is still no evidence that defines a uniform way of evaluating this condition. Numerous behavioral scales have been validated and developed, both for rehabilitation and intensive settings, which allow to determine the level of consciousness and allow an accurate diagnosis of the type of alteration.¹ The universal clinical scale used to evaluate altered consciousness is the Glasgow Coma Scale (GCS). It was created for the evaluation of patients with head trauma and then became the most widely used scale for the assessment of the state of consciousness of acute patients with both medical and traumatic pathologies.² Despite widespread use, numerous concerns have been expressed about the accuracy of the GCS score in intubated patients and those receiving analgesics, sedatives, and paralytics - as verbal scores cannot be evaluated. Furthermore, GCS does not differentiate the neurological condition of the patient once intubated and is unreliable in neurological assessment.³ Therefore, it becomes necessary to find alternative tools, that can be used in Intensive Care Units, in case of the absence of the GCS score capable of evaluating and combining the motor and ocular components and that do not depend on the verbal response. One of the alternative tools available for a correct and effective neurological and consciousness assessment, where the GCS score is poorly reliable or cannot be applied, is the Full Outline of UnResponsiveness score (FOUR)⁴ and the automated pupillometry.⁵

Assessment tools

The pupillary reflex is one of the most used prognostic factors in the assessment of the severity of a head injury. The scores evaluating the level of consciousness and the functions of the brain stem were used to create an extended index of clinical severity starting from the Glasgow Coma Scale Pupils Score (GCS-P) analysis. It aims to improve the accuracy of prognostic evaluation in traumatized patients by including the photomotor reflex among the parameters of GCS evaluation.^{6,7} Pupillary reflex was quanti-

fied to achieve the new assessment scale, introducing the concept of Pupil Reactivity Score (PRS). PSR can range from 0 to 2, the PRS is obtained by subtracting it from the GCS (range 3-15) to obtain the GCS-P (range 1-15) (Table 1). A new scale for state of consciousness assessment, the Full Outline of UnResponsiveness (FOUR), has recently been proposed.⁸ This scale introduces elements that allow a more accurate neurological evaluation referring to four components: eye-opening, motor response, brain stem reflexes, and respiratory pattern.⁹ Each component is a 5-point scale, ranging from 0 to 4, with a combined FOUR score ranging from 0 to 16, where 16 indicates the highest level of consciousness, while the lowest score is zero, indicating brain death¹ (Figure 1, Table 2). The FOUR score can be used in multiple intensive settings, it is easy to teach, learn, and administer, and it also provides essential information for accurate assessment of patients with impaired state of consciousness.⁴ In contrast to GCS, where abnormal reflexes of the brain stem are not included among the clinical indicators evaluated, in FOUR the reflexes of the brain stem examined are: pupillary and corneal reflex.¹⁰

Aim of this review

Specifically, this review aimed to answer the following question: is it possible to identify the limitations of the Glasgow Coma Scale and to find alternative assessment tools capable of assessing the consciousness of patients admitted to the Intensive Care Unit?

Materials and Methods

We chose to conduct an integrative review, based on Dhollande *et al.*¹¹ Integrative reviews assimilate research data from various research designs to reach conclusions that are comprehensive and reliable.¹²

The search for bibliographical sources was conducted between March and October 2022, through PubMed, SCOPUS, Web Of Science, CINAHL, and Cochrane Library.

The research strategy used is based on the P&PICO methodology (Table 3).

Picos model

(P) Population- subject of the question: adult male and female patients admitted to an intensive care unit with brain damage, who are in a coma or intubated.

(I) Intervention - object of investigation: assessment of the state of consciousness through the use and comparison of GCS,

Table 1. Pupil Reactivity Score (PRS).

2	No pupil shows the photomotor reflection
1	Only one pupil shows the photomotor reflex
0	Both pupils show the photomotor reflex

Table 2. Full Outline of UnResponsiveness Score (FOUR Score).

Ocular response	
Action	Score
Open or open, tracer or flashing eyelids	4
Open but not tracer eyelids	3
Closed eyelids but open to verbal recall	2
Closed eyelids but open to painful stimulus	1
Eyelids remain closed even after painful stimulation	0
Motor response	
Action	Score
Thumb up, fist up or peace signal	4
Localization to pain	3
Flexion response to pain	2
Response in extension to pain	1
No pain response or generalized myoclonus state	0
Reflexes of the brain stem	
Action	Score
Presence of pupils and corneal reflexes	4
A wide and fixed pupil	3
No pupillary or corneal reflexes	2
No pupillary and corneal reflexes	1
Absence of pupillary, corneal and coughing reflex	0
Breathing	
Action	Score
Not intubated, regular breathing	4
Not intubated, Cheyne-Stokes breath	3
Not intubated, irregular breathing	2
Breathe over the ventilator frequency	1
Breathe at respiratory rate or apnea	0

Table 3. Question according to P&PICO methodology.

Question according to the P&PICO methodology				
Population	Problem	Intervention	Comparison	Outcome
Assisted adults hospitalized at ICU neurological, in a comatose state and/or intubated	Poor reliability of GCS score in cases selected	Assessment of the state of consciousness by FOUR and pupillometer	The use of GCS for the neurological assessment	Highlight the GCS limits and suggest alternative tools of assessment
Search terms				
ICU Intensive care unit Adult	Neurologic Examination	Pupillometry FOUR Full Outline of Unresponsiveness score	Glasgow Coma Scale GCS score	Neuro benefit

FOUR score, and automated pupillometer.

(C) Comparison - applicable alternative intervention: the alternative intervention to GCS for the assessment of the state of consciousness is represented using FOUR scales and an automated pupillometer.

(O) Outcome - result: highlight the limits of GCS in the assessment of the state of consciousness and propose alternative tools that combine the ocular and motor components.

(S) Study design: includes simultaneous assessment of consciousness by two scales: the FOUR and GCS scales and neurological assessment with automated pupillometer, based on strict criteria of inclusion and exclusion.

The query strings used in the databases were constructed using the keywords with the appropriate boolean operators. For this review, we chose to focus our search on 2018-2022. These dates were selected to capture the most up-to-date trends in this context as it is broadly accepted that research currency spans 3-5 years. Only publications in English with abstract and full-text availability have been examined, the selection criteria used for the studies are described in Table 4.

Results and Discussion

From the first research, 139 citations were identified. After reading the title and abstracts, 32 publications were relevant to the topic. After the retrieval of the full texts and the full reading of the articles, 7 articles met the criteria of inclusion and exclusion of the revision (Figure 2).

These studies included a more complete neurological assessment in the assisted with traumatic brain injury (TBI), a synopsis of the selected studies is shown in Table 5.

The results of the research showed that to date, several studies have been conducted for the evaluation of the usefulness and reliability of the FOUR score compared to GCS, with the aim of including the FOUR score among the clinical evaluation tools, especially in the absence of the GCS score. Over the years many limitations have emerged regarding the use of the Glasgow Coma Scale: inconsistent inter-observer reliability, the impossibility of testing the verbal component in intubated patients, in those receiving paralytic, analgesic, and sedative, absence of evaluation of brain stem reflexes and poor correlation between outcome and low GCS index.³ Moreover, the withdrawal response in the motor component of GCS can be mistaken for a flexor response, leading to a score error. The study conducted by Brennann and colleagues⁷ ana-

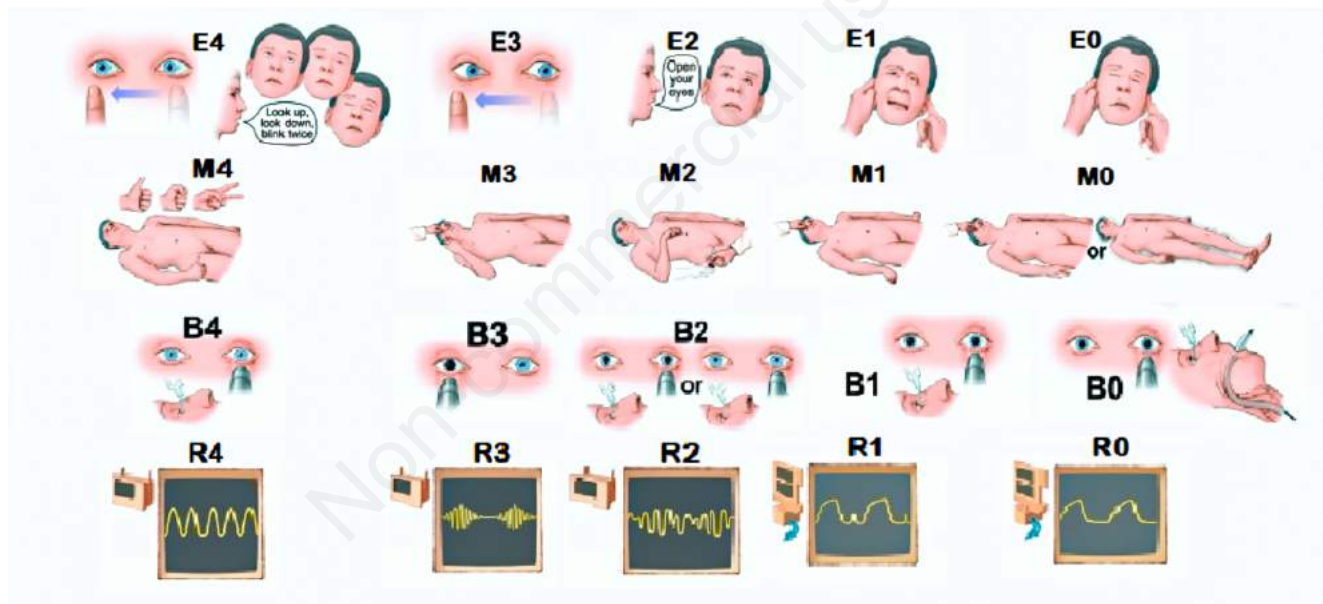


Figure 1. Description of Full Outline of UnResponsiveness (FOUR) score (adapted from Iyer et al. 2009;4 reproduction permission has been requested and granted by the author).

Table 4. Inclusion and exclusion criteria for studies

Inclusion criteria	Exclusion criteria
Adult population	Paediatric population
Patients admitted to general ICU or neurological ICU	Patients admitted in non-intensive settings
Peer-reviewed scientific papers	Discussions papers, editorial and opinions, dissertations thesis
Years from 2018 to 2022	Articles published prior to 2018 and after 2022
English language	
Articles with full text and abstract available	

lyzed data from 15,900 patients from the CRASH and IMPACT studies, the two largest studies in patients with TBI, to evaluate whether the combination of GCS and photomore reflex could provide more accurate information on the outcome of patients compared to the two factors taken individually. From the study emerges that the simple addition of the photomore reflex to the GCS allows obtaining a score that combines the easy applicability necessary in the traumatological field to the greater prognostic precision useful in the correct management of the patient, with results similar to those obtained with more complex assessment scales.

The FOUR score has several advantages: it is not complex to use, it distinguishes various states of unconsciousness between them, provides important details on brain stem reflexes, and requires minimal need for neurological testing in states of impaired consciousness.^{12,13} The assessment of the state of consciousness, using FOUR, can be carried out in all patients, including patients with tracheostomy. Through the application of the FOUR scale, it is possible to detect the presence of an uncal hernia, locked-in syn-

drome, and the beginning of a vegetative state - all conditions in which the GCS score does not provide much information.¹⁴

The FOUR score adds additional information to the GCS eye-opening, including eye tracking, so that mesencephalic and pontine functions are included in the assessment of the state of consciousness. The final category of the FOUR score refers to the different respiratory models. Respiration is evaluated as spontaneous regular or irregular, Cheyne-Stokes breath, intubated but independent of ventilation, dependent ventilation, or absent breath. The assessment of the state of consciousness, with the use of FOUR, can be performed in all patients, including those with an endotracheal tube and it is a good predictor in the prognosis of critically ill clients.⁴ Whereas eye and motor components of the GCS represent the global impact of the neurotrauma on the brain, the brainstem and respiratory pattern components of the FOUR score are perhaps assessing more specific brainstem injury, hence the variation seen between patients with different severities of TBI.¹⁵

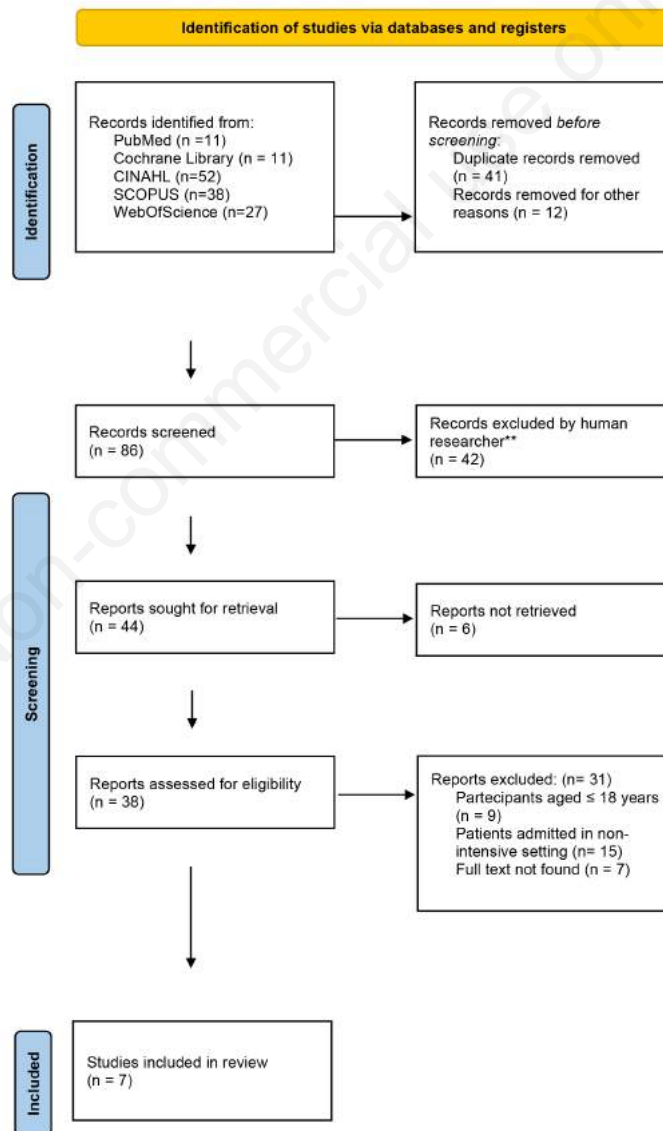


Figure 2. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.

Table 5. Studies analyzed in the review.

Author/Year	Aims	Type of study	Subjects included	Conclusions
Bremner <i>et al.</i> , ⁷ 2018	Assess if the combination of GCS and photomotor reflexion can provide more accurate information on the outcome of patients compared to the two factors taken individually	Prospective study	Data analysis of 15,900 individuals from CRASH and IMPACT, the two largest TBI studies	The addition of the photomotor reflex to the GCS allows to obtain a score that combines the easy applicability necessary in the traumatological field to the greater prognostic precision useful in the correct management of the patient, with results similar to those obtained with more complex assessment scales
Bayraktar <i>et al.</i> , ¹⁹ 2019	Study aim to assessing the reliability of FOUR and GCS scores by comparing the values assigned by specialists to assisted persons in anaesthesia and reanimation and neurosurgical ICU	Prospective study	Were recruited 79 persons between the ages of 18 and 65 who were treated for at least 24 hours in ICU and who did not receive sedation	The consistency demonstrated by the scores attributed by two different professionals for the same patient demonstrates the ease of application of GCS and FOUR. However, due to the additional parameters of FOUR, the latter is more effective in evaluating the subject who is unconscious or dependent on mechanical ventilation
Olsen <i>et al.</i> , ²⁰ 2020	Evaluate how FOUR score and automated pupillometry add meaning and clinical information in an intensive care context, comparing it with GCS score and manual pupil assessment	Prospective observational study	Patients admitted to a Neurointensive Unit	The training of nursing staff in the use of FOUR score and automated pupillometer is a good strategy to implement frequent monitoring in neurointensive units. Both assessment tools provide more clinical information than GCS and the study demonstrates how FOUR score is a better predictor of outcomes, prognosis and mortality than GCS
Ramazani <i>et al.</i> , ²³ 2019	Evaluate FOUR score and GCS ability in predicting the outcomes (Survivors, nonsurvivors) in Medical Intensive Care Unit (MICU)	Observational and prospective study	300 patients admitted to medical ICU. Excluded from the study population were patients with a length of ICU stay <24 h and brain death at the time of admission	Both FOUR score and GCS are valuable scales for predicting outcomes in patients admitted to the MICU; however, the FOUR score showed better discrimination and calibration than GCS, so it is superior to GCS in predicting outcomes in this patients population
Temiz <i>et al.</i> , ²² (2018)	To evaluate the effectiveness and the use of Glasgow Coma Score (GCS) and Full Outline of Unresponsiveness (FOUR) score by nurses in the follow-up and evaluation of patients admitted to the neurosurgical intensive care unit for cranial surgery or head trauma	Cross-sectional study	47 patients calculated who were admitted to the intensive care unit for cranial surgery or head trauma	Concordance between nurses was found high both for GCS and FOUR. The FOUR score is as effective as GCS on the follow-up of patients who are managed in the neurosurgical intensive care units.
Foo <i>et al.</i> , ¹⁵ 2019		Systematic review	Patients admitted to dedicated neuroscience centers	FOUR score overall has a close relationship to in-hospital mortality and poor functional outcome in patients with impaired consciousness. Further comparison of FOUR score and GCS, and with GCS-P, may, in subgroups of patients, identify relative merits of FOUR score
Almojuela <i>et al.</i> , ²¹ 2019	To perform a scoping systematic review on the available literature for FOUR score and outcome prediction in critically ill patients	Systematic review		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

The literature shows the ease of application of GCS and FOUR, however, due to the additional parameters of FOUR, the second one is more effective in evaluating the unconscious subject or dependent on mechanical ventilation¹⁶⁻¹⁸ since it has a better correlation and a higher predictive value with the need for ventilation, the stay in ICU and the GOS score compared to GCS, in patients with traumatic brain injury.¹⁹ The reliability of the FOUR score is excellent and the agreement between the evaluators is similar to GCS. The probability of intrahospital death is higher for the lower FOUR's total score. The FOUR score provides more details related to neurological status than GCS^{8,10} and can be used as an alternative to the GCS scale as there is no significant difference in evaluators, it has a satisfactory prognostic value, good specificity, and sensitivity.¹⁸ It also emerged that the new FOUR score is an insightful clinical tool in detecting subtle changes in neurological status as well as GCS, the prognosis of mortality for patients with altered sensory was similar to GCS¹⁹ but the evaluation of cortical function and brain stem gave additional value to FOUR, this score provides more neurological information compared to GCS and can be used by any intensive care nurse, even by those who have less experience.²⁰ It has been studied in a wide variety of critically ill patients, both with and without neurologic pathology in predicting mortality and functional outcomes. It displays good inter-rater reliability among physicians and nurses.²¹

Also, GCS and FOUR scores were compared in patients with brain tumors or TBI at the intensive care unit and the FOUR score was found to be just as effective and reliable as GCS. FOUR and GCS scores have been found to have a high interclass correlation coefficient between practitioners. The correlation for both scales is quite strong. This conclusion is thought to help decrease mistakes when evaluating intensive care unit patients and a more accurate evaluation can be made.²² In a study recently conducted to evaluate the FOUR score and the ability of GCS to predict the outcomes (survivors, non-survivors) in a medical intensive care unit (MICU), both scores were found to be reliable Scales and showed acceptable discrimination power but the FOUR score showed better discrimination and calibration than GCS for predicting outcomes in hospitalized MICU patients. The higher accuracy of the FOUR score compared to the GCS makes it an advisable predictive model for patients who are admitted to the medical ICU²³ (Table 6). New technologies were also adopted to support the medical staff in assessing neurological status. The pupillometer is an automated portable device, easy to use and economical, and has the advantage of making accurate and reproducible quantitative measurements and evaluations.⁶ Automated pupillometry evaluates the pupillary reflex in light, or photomotor reflex, the diameter, the shape of the pupil, the latency time, the rate of constriction and dilation, and the percentage of amplitude reduction.²⁴ The values calculated by the pupillometer are displayed on the screen showing

an algorithm that takes into account all these variables as input to obtain a composite score that defines the pupillary response index (Neurological Pupil Index)²⁵ (Figure 3 and 4).



Figure 3. NPi-300 Automated Pupillometry® (From: NeurOptics' NPi-300 Automated Pupillometer, US (reproduction permission has been requested and granted by the author).



Figure 4. NPi-300 Automated Pupillometry® (From: NeurOptics' NPi-300 Automated Pupillometer, US (reproduction permission has been requested and granted by the author).

Table 6. Comparison between Glasgow Coma Scale (GCS) and Full Outline of UnResponsiveness Score (FOUR score).

GCS	FOUR score
Three major components:	Four components (E ₄ , M ₄ , B ₄ , R ₄) with maximum score of 4 points each:
<ul style="list-style-type: none"> • Eye 4 points • Motor 6 points • Verbal 5 points 	<ul style="list-style-type: none"> • Eye response • Motor response • Brainstem reflexes • Respiratory pattern
Limited utility in intubated patients and children with limited language development	Includes testing for intubated patients and brainstem reflexes
Key component of other ICU severity of illness scales	Useful in detecting patients with locked-in-syndrome and VSs
Widely used and validated for more than 30 years	Multicenter trials and validation are pending

A study has recently been conducted to study the relationship between GCS and dilation rate (DV) through 42,229 observations in patients with brain damage and an average age of 58.9 years, of which 49.11% are female. The study showed that higher GCS is associated with faster DV, and that automated pupillometry can be a biomarker of injury where neurological examination is limited.²⁶

In 2019 a systematic review was published to evaluate the specific results associated with the use of the automated pupillometer in the monitoring of critical patients with neurological impairment receiving assistance in an intensive care environment.²⁷ The study also aims to examine whether the use of the pupillometer in this population has any effect on outcomes and to assess potential limitations to a wider adoption of automated pupillometry. It has emerged as a crucial tool in neurocritical care, allowing the detection of elevated intracranial pressure and imminent neurological deterioration at an early stage.²⁸⁻³⁰

At the moment there are no guidelines approving the routine use of automated pupillometry in an intensive care environment despite has received more attention in recent years as a predictive tool for delirium in ICU through evaluation of the pupillary reflex of both eyes immediately after hospitalization through the use of a portable infrared pupillometer³¹ being an effective triage tool in brain trauma patients.³² However, the increase in research and studies supports the usefulness of automated pupillometry because of the greater accuracy and reliability compared to manual pupillary examination, in detecting pupillary changes indicating an increase in intracranial pressure and detecting the level of sedation and analgesia, it also offers a more accurate and objective assessment, with only one-third of non-reactive pupils^{28,33-36} and half of anisocoria cases detected.³⁷

Limitations

The integrative review consists of different empirical sources and, therefore, no particular criterion for assessing the quality of the studies exists,³⁸ but the strict inclusion criteria in the review can be evaluated not only as a strength but also as a limitation that might have resulted in relevant studies being excluded. Therefore, the study might have reporting bias, since, for example, only English-language studies with at least an abstract available were included.

Conclusions

The purpose of this integrative review is to describe tools capable of making complete assessments of the neurological status of patients admitted to intensive care units and that are better predictors of mortality and morbidity in head injury. Two primary evaluation tools are proposed and analyzed: FOUR score and automated pupillometry, capable of exceeding the limits of GCS for a more calibrated and complete assessment of the neurological state and consciousness of the patient in the ICU. The FOUR score is not higher than GCS but the combination of visual and motor components is essential for an even more complete neurological assessment. The FOUR score can be used in multiple intensive settings, is easy to teach, learn, and administer, and also provides essential information for accurate assessment of patients with impaired states of consciousness. In contrast to GCS, where abnormal reflexes of the brain stem are not included among the clinical indicators evaluated, FOUR also includes pupillary and corneal reflex evaluation. The score showed a prognostic value comparable to that provided by GCS but offers indisputable advantages: it can be

used in intubated patients, can distinguish vegetative states from minimally responsive states, and detect the “locked-in syndrome”.

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