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CLINICAL ARTICLE - BRAIN INJURY

Validation of a new neurological score (FOUR Score) in the assessment of neurosurgical patients with severely impaired consciousness

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Abstract
Background The Glasgow coma scale (GCS) was introduced as a scoring system for patients with impaired consciousness after traumatic brain injury (TBI). Since, it has become the worldwide standard in TBI assessment. The GCS has repeatedly been criticized for its several failures to reflect verbal reaction in intubated patients, and to test brain stem reflexes. Recently, the full outline of unresponsiveness (FOUR) score was introduced, which is composed of four clinically distinct categories of evaluation: eye reaction, motor function, brainstem reflexes and respiratory pattern. This study aims to validate the FOUR score in neurosurgical patients.
Methods FOUR score and GCS were assessed in a consecutive series of neurosurgical patients with severely impaired consciousness (GCS<9). Their correlation with the 30-day Glasgow outcome score (GOS) was compared. Patients admitted for TBI, spontaneous intracranial hemorrhage (intracerebral hemorrhage, aneurysmal subarachnoid hemorrhage, cerebellar hemorrhage), or malignant middle cerebral artery infarction were included.
Results We assessed a total of 101 patients (mean age=64y, SD=36.1y). The area under the curve (AUC) for mortality was 0.768 (P=0.0001) for the FOUR Score, and 0.699 (P= 0.001) for the GCS. For poor outcome (GOS=2-3) the FOUR score AUC was 0.683 (P=0.018), the GCS AUC was 0.682 (P=0.019). The FOUR score value for favorable outcome (GOS=4-5) was 0.748 (P=0.001), the corresponding GCS value was 0.704 (P=0.002).
Conclusions The FOUR score was more robust than the GCS in predicting mortality after 30 days in neurosurgical patients with severely impaired consciousness. There was no relevant difference in predicting poor and good outcome.

Keywords Assessment · Coma · Consciousness · FOUR score · Glasgow coma scale · Outcome

Portions of this study were presented at the 58th Annual Meeting of the German Society of Neurosurgery, Leipzig, Germany, April 27, 2007.

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Introduction

Structured assessment of coma and impaired consciousness is essential in monitoring critically ill neurosurgical patients. For this purpose the Glasgow coma scale (GCS) is the most commonly used grading scheme [25]. The GCS was original developed for patients with TBI, but has been validated for outcome prediction in several other causes of coma [3, 8, 13, 18, 21], and evolved into a general tool for assessment of unconsciousness. There are, however, difficulties regarding its qualified application, especially in deeply unconscious patients, and with implementation by inexperienced users [20], e.g., a noticeable number of such patients are intubated or suffer from additional facial trauma. In these cases the verbal score can only be guessed [17], thus rendering a reliable evaluation impossible [10].

In addition, although the relevance of brainstem functions for the clinical prognosis is high, it is not taken into account by the GCS [6, 11, 26]. Furthermore, breathing patterns, which are also not part of the GCS, may be related to the depth of coma [19]. Thus, subtle neurological changes may be overlooked by the GCS in its current form.

Altogether, the shortcomings of the Glasgow coma scale have led to repeated suggestions and conceptions of modifications [5], and of alternative coma scores. Because of lack of reliability or complicated handling, these scores were not widely accepted (e.g. Edinburgh-2 coma sScale [24], reaction level scale [23], comprehensive level of consciousness scale [22], Innsbruck coma scale [4])

The ease of use of the GCS may also have prevented other, possibly more detailed scales from introduction into daily routine.

Recently, the full outline of unresponsiveness (FOUR) score [28] was introduced by Wijdicks and colleagues in neurological patients with traumatic and nontraumatic disorders of the central nervous system and miscellaneous acute neurological conditions. This scale is supposed to take into account various levels of brain stem damage, and should thus allow for more precise clinical prognosis concerning patient outcome.

In the present study, we aimed at a validation of this new score in the assessment of newly admitted adult neurosurgical ICU-patients with severely impaired consciousness due to TBI, to spontaneous intracranial hemorrhage, or to malignant middle cerebral artery infarction.

Materials and methods

This consecutive prospective study involves 101 of initially 110 assessed patients from May 2006 until July 2007 who were all admitted to the neurological intensive care unit (ICU) of the University Medical Center department of neurosurgery, Bonn, Germany. This study follows the declaration of Helsinki as revised in Edinburgh in October 2000.

Newly admitted neurosurgical ICU patients older than 17 years with severely impaired consciousness defined by a GCS score under 9 were included. Nine patients in which the GOS after 30 days could not be determined by direct examination or telephone interview were subsequently excluded from the study.

Clinical assessment

In all patients the Glasgow coma scale score and the full outline of unresponsiveness (FOUR) score (Table 1) were assessed on the day of admission by a board certified neurologist (C. G.). The outcome was determined using the Glasgow outcome score (GOS)[14] at 30 days as part of the regular clinical outcome assessment.

The full outline of unresponsiveness (FOUR) score

The full outline of unresponsiveness score consists of four components: motor response, eye response, brain stem reflexes, and respiration. In every item the minimal score is zero, while the maximal score to reach is four. Thus, the total score ranges

Table 1 Comparison of the full outline of unresponsiveness score [28] [a] and the Glasgow coma scale [25]

Parameter	Score
Full outline of unresponsiveness score	
Eye response (E)	
Eyelids open or opened, tracking or blinking to command	E4
Eyelids open but not tracking	E3
Eyelids closed but open to loud voice	E2
Eyelids closed but open to pain	E1
Eyelids remain closed with pain	E0
Motor response (M)	
Thumbs-up, fist or peace sign	M4
Localizing to pain	M3
Flexion response to pain	M2
Extension response to pain	M1
No response to pain or generalized myoclonus status	M0
Brainstem reflexes (B)	
pupil and corneal reflexes present	B4
one pupil wide and fixed	B3
pupil or corneal reflexes absent	B2
pupil and corneal reflexes absent	B1
Absent pupil, corneal, and cough reflex	B0
Respiration (R)	
Not intubated, regular breathing patterns	R4
Not intubated, Cheyne–Stokes breathing pattern	R3
Not intubated, irregular breathing	R2
Breathes above ventilator rate	R1
Breathes at ventilator rate or apnea	R0
Glasgow coma scale	
Eye opening	
Spontaneous eye opening	4
Eye opening response to speech	3
Eye opening response to pain	2
No eye opening	1
Motor response	
Obeying commands	6
Localizing response to pain	5
Withdrawal from pain	4
Flexor response to pain	3
Extensor posturing to pain	2
No motor response to pain	1
Verbal response	
Orientation	5

Table 1 (continued)

Parameter	Score
Confused conversation	4
Inappropriate speech	3
Incomprehensible speech	2
No verbal response	1

[a] For the assessment of the eye reaction (E) make three attempts to figure out the best reaction. A score of E4 accords to at least three tracking reactions with open or opened eyes (in patients who are not able to open their eyes independently e.g. because of facial oedema or trauma) or alternatively to two blinking reactions on command. E3 typifies open eyes without tracking. Eye opening to voice is rated with E2, to a pain stimulus with E1. E0 is assessed if the patient shows no eye opening upon a pain stimulus

The motor response (M) score is taken from the best reaction of the upper limbs. M4 requires the performance of at least one of the three hand positions from the hand position test [29] - thumbs up, fist and the victory sign. Whether the patient is not able to act on an instruction, the reaction to pain should be examined by setting a stimulus on the temporomandibular or supraorbital nerve. A localizing reaction M3 is rated if the patient touches the examiner's hand whilst the stimulation. Flexion comes up to M2, an extension response to M1, no response to pain accords to M0

Within the category brain stem functions (B), the pupil and the corneal reflexes are tested; the best response is valued. The cough reflex is only examined in the case that both are absent. When pupil and corneal reflexes can be triggered on both sides, the reaction is rated with B4. Patients with one wide and fixed pupil receive B3 points. It is distinguished between absent pupil or corneal reflexes (B2) and the absence of both (B1). If in addition the cough reflex is missing, B0 is given

For respiration (R), the patient's breathing pattern is observed. Breathing self-dependently in a normal pattern corresponds with R4. Cheyne–Stokes (R3) and other irregular breathing patterns (R2) are differentiated. Intubated patients are assessed with R1 for breathing over ventilator rate or R0 for breathing on ventilator rate or apnea

from 0 as the worst to 16 as the best reaction. By suggestive naming the authors of the paper on the FOUR score aimed for the memorability of the new score. The FOUR score includes a motor and an eye movement category resembling the GCS sections. It does not contain the verbal reaction. Additionally, brainstem reflexes and breathing patterns are tested. The goal in this change was to withdraw information that does not increase the correlation with outcome and adding information which does. Altogether, adding selected information can lead to a better performance as well as leaving out selected information.

The assessment of the motor and the eye responses is similar to the Glasgow coma scale, though with some exceptions. The motor response category additionally contains the hand position test to detect subtle changes in alertness [29]. It also includes myoclonus, which is known to be associated with poor outcome [30]. Withdrawal and flexion response to pain are combined, as they may be mistaken or confused by inexperienced users.

Moreover, a locked-in syndrome can be detected, when a patient with opened eyes is not able to track the examiner's finger [15].

Brain stem functions, such as the pupillary light reflex, the corneal reflex, and the cough reflex are tested, which refer to the function of mesencephalon, pons, medulla oblongata, and the oculomotor nerve, respectively.

The respiratory observations include Cheyne–Stokes respiration, which is found to be in correlation to an intermediate prognosis, while other irregular breathing patterns and spontaneous hyperventilation are associated with a poor prognosis [2, 19]. Another potential advantage is that alteration of breathing patterns can show indication for mechanical ventilation [16]. In intubated patients, breathing over and breathing on ventilator rate or apnea are distinguished.

Statistical analysis

For every possible cut-off point, sensitivity and 1-specificity (false positive rate) were calculated. Out of these data sets, the coordinates of receiver operating characteristic curves (ROC) were generated. Accuracy of the scales was quantified by the area under the ROC curve (AUC). An AUC of 1.0 refers to a perfect test, while a perfectly inaccurate test has an AUC of 0.0. An area of 0.5 represents the chance diagonal, consequently a worthless test.

The relation of the FOUR score and the GCS score to mortality (GOS 1), poor outcome (GOS 2–3), and favorable outcome (GOS 4–5) at 30 days was estimated. We performed all data analysis with PASW Statistics, Version 18.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

Results

Patient characteristics

The 101 included patients suffered from traumatic brain injury (TBI) ($n=31$) and from non-traumatic brain damage (hypertensive intracerebral hemorrhage (ICH) ($n=30$), aneurysmal subarachnoid hemorrhage (SAH) ($n=33$), spontaneous cerebellar hemorrhage ($n=5$), and malignant middle cerebral artery infarction ($n=2$)). Assessed FOUR scores ranged from 0 to 13, GCS scores had a range from 3 to 8 (Table 2); 91 % ($n=91$) of the patients were intubated and sedated.

Scores and outcome

At 30 days, 32 (31.7 %) patients were deceased (GOS 1), 49 (48.5 %) had a poor outcome (GOS 2–3), and 19 patients (18.8 %) had a favorable outcome (GOS 4–5). Figure 1 shows the frequencies of the assessed total scores and subunit scores.

The correlation between FOUR score, GCS score and the patient outcome at 30 days is displayed in Table 3. The FOUR score had a slightly higher area under the curve (AUC) in predicting mortality with 0.768 ($p<0.001$; 95 % CI: 0.664–

Table 2 Characteristics of 101 patients with severely impaired consciousness

Age (years)	
Mean (range)	64 (18–91)
Sex (n)	
Male	52
Female	49
Diagnosis (n)	
Traumatic brain injury	31
Non-traumatic causes	
Aneurysmal subarachnoid hemorrhage	33
Nontraumatic intracerebral hemorrhage	30
Spontaneous cerebellar hemorrhage	5
Malignant media infarction	2
FOUR Score	
Mean (range)	5,6 (0–13)
GCS	
Mean (range)	4,7 (3–8)
GOS	
Mean (range)	2,5 (1–5)

0.872) compared to GCS AUC of 0.699 (p=0.001; 95 % CI: 0.595–0.802). AUC for poor outcome (GOS 2–3) was lower and equal for both scales, 0.682 (p=0.019; 95 % CI: 0.531–0.832) for FOUR score, and 0.683 (p=0.018; 95 % CI: 0.533–0.832) for GCS. Both scales also had comparable results in predicting favorable outcome (GOS 4–5). AUC was 0.748 (p=0.001: 95 % CI: 0.624–0.871) for FOUR Score and 0.727 (p=0.002; 95 % CI: 0.588–0.865) for GCS (Fig. 2).

In the subunits, the verbal response of the GCS showed the lowest correlation to outcome in this group of mostly intubated patients. The AUC for respiration patterns of the FOUR score was lower than the AUC of the total GCS and the AUC of the total FOUR score. The AUC for FOUR score brain stem reflexes exceeded the total GCS in predicting mortality, but not in predicting poor outcome and favorable outcome.

The maximum sum of sensitivity and specificity for mortality was at a total FOUR score of 4 (sensitivity=0.500; specificity=0.957) and a total GCS score of 5 (sensitivity=0.750; specificity=0.609). In this collective of patients, no mortality at 30 days was observed at FOUR Scores>9 and GCS scores>7.

Although, the differences in AUC values did not reach statistical significance, it should be noted that the difference

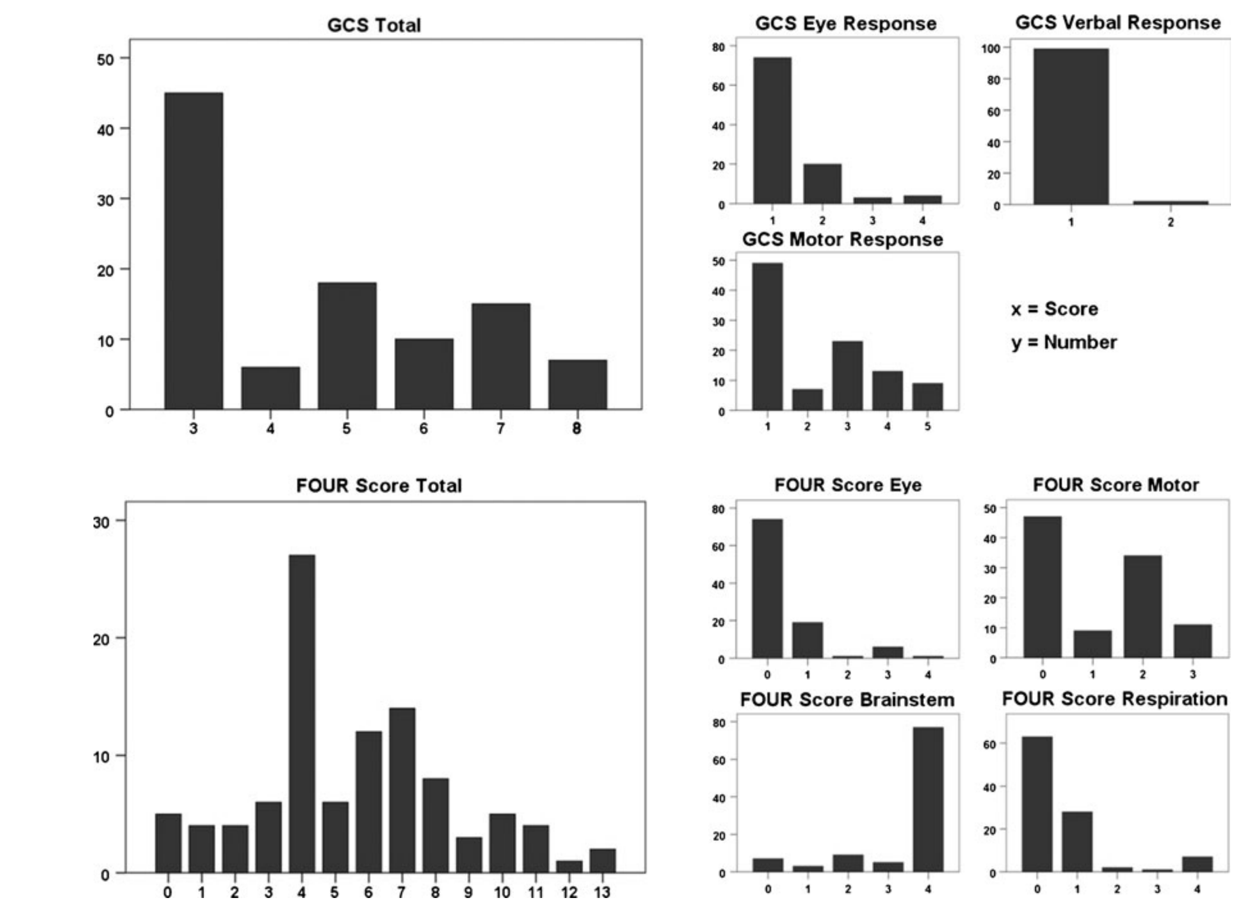

Fig. 1 Frequencies of assessed GCS and FOUR scores

Table 3 Correlation between initial score and outcome: area under the receiver operating characteristic curve

	Mortality GOS 1 (95 % CI)	Poor outcome GOS 2–3 (95 % CI)	Favorable outcome GOS 4–5 (95 % CI)
FOUR score total	0.768 (0.664–0.872)	0.682 (0.531–0.832)	0.748 (0.624–0.871)
FOUR Eye	0.590 (0.477–0.704)	0.558 (0.405–0.711)	0.588 (0.441–0.735)
FOUR Motor	0.661 (0.552–0.770)	0.689 (0.542–0.837)	0.722 (0.585–0.860)
FOUR Brainstem	0.743 (0.628–0.858)	0.526 (0.378–0.674)	0.619 (0.496–0.741)
FOUR Respiration	0.576 (0.460–0.693)	0.634 (0.487–0.790)	0.648 (0.498–0.797)
GCS total	0.699 (0.595–0.802)	0.683 (0.533–0.832)	0.727 (0.588–0.865)
GCS Eye	0.611 (0.499–0.722)	0.547 (0.395–0.700)	0.587 (0.441–0.733)
GCS Verbal	0.492 (0.369–0.614)	0.525 (0.371–0.679)	0.519 (0.374–0.664)
GCS Motor	0.677 (0.571–0.782)	0.709 (0.563–0.855)	0.744 (0.608–0.881)

in predictive power between GCS and FOUR score is particularly larger in patients with very low scores. The rate of mortality in patients with the lowest FOUR score was higher than in patients with the lowest GCS score. There was a range of FOUR scores from 0 to 6 for patients with GCS scores of 3, thus indicating higher capacity for differentiation in investigation of this subgroup.

Discussion

The FOUR score proved to be a fast and reliable method for the examination of our cohort of patients suffering from severely impaired consciousness, regardless the origin of their stupor, or coma, respectively. Its capacity for the prediction of mortality it was superior to the GCS. Although the Glasgow coma scale is used worldwide for standardized evaluation of unconsciousness, major deficiencies remain. A number of attempts have been made to improve the predictive power regarding the outcome. Many of the developed scoring systems were more complicated, and could not be established in clinical routine. Nevertheless, the “gold standard” role of the GCS remains disputable.

The authors of the FOUR score have developed a new scale to overcome the shortcomings of the Glasgow coma scale. At the same time, it encompasses the minimal requirements for neurological testing in cases of impaired consciousness [28]. The FOUR Score does not contain a verbal score but provides testing of brain stem reflexes and assessment of respiratory patterns. The difference entails testability in intubated patients in contrast to the GCS, which is especially advantageous for the intensive care unit.

We have found that the FOUR Score is easily implementable in a neurosurgical setting. The assessment can be undertaken within few minutes and is practicable in daily routine.

Prediction of outcome

Total scores of FOUR score and GCS showed similar correlations in predicting poor outcome and favorable outcome. In prognosticating mortality, the FOUR Score exceeded the predictive power of the GCS.

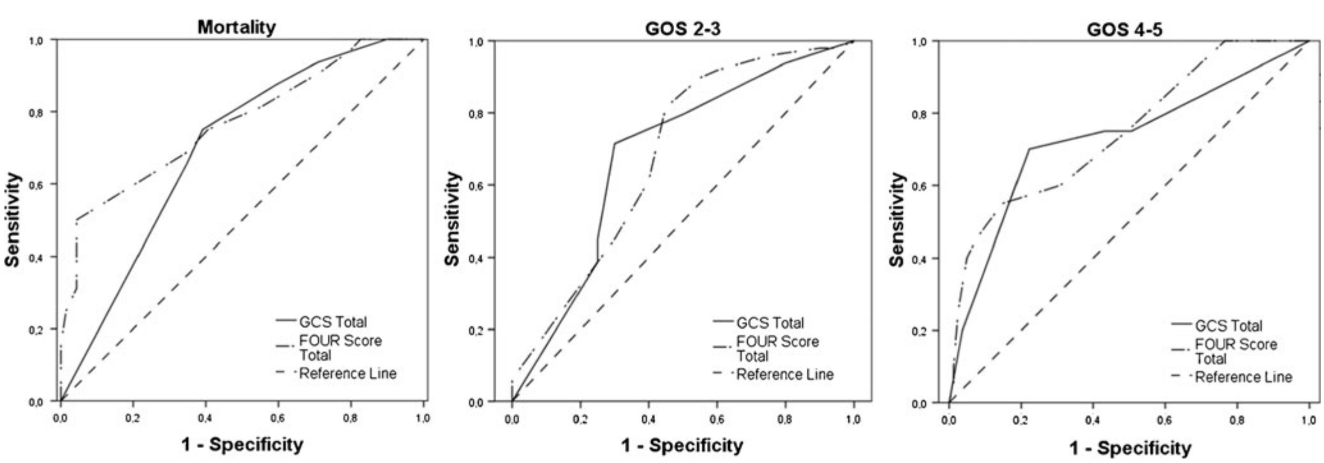

Fig. 2 Correlation between initial scores and outcome: Receiver operating characteristic curves

The verbal subscore of the GCS correlated least with good outcome, poor outcome as well as mortality, consistent with a rate of 90 % intubated patients and with the fact that verbal reaction cannot be evaluated in such a group of patients.

Appraisal of brain stem reflexes leads to more detailed information and is part of standardized evaluation of the neurological state in patients with impaired consciousness. In our collective, it allowed especially for further discrimination of the relatively large patient group with GCS 3, who had FOUR Scores from 0 to 6, facilitating analysis of the time course of clinical evolution. Accordingly, the brain stem reflexes subscore had the biggest AUC in predicting mortality.

Because most of our patients (90 %) were intubated at the time of assessment, the correlation of respiration patterns and outcome was narrowed. Capturing changes of respiratory patterns is not only an expedient way of predicting outcome [2, 16], but it may also give evidence upon which therapeutic decisions may be based.

Clinical practice

We consider that the FOUR Score is a useful instrument for predicting outcome and for neurological screening in the neurosurgical ICU. The FOUR Score captures essential aspects of the neurological status. For making optimal decisions and predicting outcomes as precisely as possible, further techniques apart from pure clinical assessment should be included [27]. Studies on classification of TBI based on magnetic resonance imaging have shown significant correlation between the identified locations of lesions and outcome of patients [12]. Moreover, evoked potentials especially somatosensory evoked potentials correlate with neurological outcome: E.g. bilateral absent somatosensory potentials correlate strongly with mortality [9, 32], and can be an additional tool for evaluation of unresponsive patients. Notwithstanding, one of the main objectives remains to appraise outcome based on an initial score.

Limitations of the study

As we had only one rater, we did not analyze interobserver reliability in neurosurgical staff, which has been reported to be comparable with the Glasgow coma scale's [1, 7]. In inexperienced neurological users, an even better reliability was found [31].

The comprehensive relevance of evaluation of breathing parameters could not be satisfactorily tested in this study due to the fact that most patients were intubated at admission.

We focused on the initial hospital stay of our patient population and assessed outcome at 30 days. For further validation, studies on the long term outcome should follow. This is important insofar a high proportion of such patients may undergo rehabilitation and develop further secondary complications affecting long-term clinical outcome.

Outcome was assessed according to the GOS and not to a more detailed scale. However, the GOS is an established and well validated scoring system, which provides the possibility of standardized discrimination between good and poor outcome and mortality, which we found was detailed enough for validating a coma score in deeply unconscious patients without providing much unused information.

Conclusions

The FOUR score is straightforward to apply and, at the same time, more refined in assessment of patients with severely impaired consciousness. In this study, the predictive value of the FOUR score concerning 30-day mortality was slightly higher than that of the GCS. This needs to be corroborated, however, in larger studies on distinct pathologies requiring neurocritical care. It is more accurate for the evaluation of patients with very low GCS scores. The FOUR score also offers a wider range of scale points in patients of whom the verbal part of the GCS cannot be performed. This facilitates assessment of clinical evolution. In prediction of poor outcome and favorable outcome after 30 days, both scales showed similar performance.

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Conflicts of interest None.

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Comment

Chen and coworkers provide a prospective consecutive single center study comparing the FOUR (full outline of unresponsiveness) score with the GCS (Glasgow coma scale) score in 101 neurosurgical patients with severely impaired consciousness. They conclude that the FOUR score is more robust in predicting mortality after 30 days. No relevant difference was found in predicting poor and good outcome.

In my opinion, this is an interesting paper with relevant results. However, there are also some aspects of this paper which have especially to be considered:

The GSC was originally developed for patients with traumatic brain injury. Within the last years, however, also the outcome of other causes of coma has been assessed using the GSC—as the authors describe in this paper. This is important not only because of the different causes of coma included in the present paper, but also in daily practice of critical care.

Another aspect is that in the present paper outcome was assessed at 30 days. One has to keep in mind that—especially in traumatic brain injury patients—progresses sometimes will be seen only within 6 months.

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