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Original Article

EVALUATION OF CONSCIOUSNESS STATUS USING THE GCS AND FOUR SCORE IN ICU PATIENTS PROGRESSING TO BRAIN DEATH

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ABSTRACT

Introduction: Brain death (BD) represents the irreversible loss of all brain functions. Early diagnosis plays a critical role in the organ donation process. This study aimed to compare the intervals between the day the Glasgow Coma Scale (GCS) first reached 3 or the Full Outline of UnResponsiveness (FOUR) score first reached 0, and the day of BD confirmation.

Methods: In this retrospective, single-center study, adult ICU patients with confirmed BD between 2018 and 2024 were included. Patients were assessed daily using the GCS and FOUR score. Imminent brain death (IBD) was defined as the day on which the GCS first reached 3 (IBD-GCS) and the day on which the FOUR score first reached 0 (IBD-FOUR). The intervals between these days and the day of formal BD confirmation were calculated and compared.

Results: A total of 62 patients were included. The time from ICU admission to BD confirmation was 5 (3–7) days. IBD-GCS preceded BD confirmation by 3 (2–5) days, while IBD-FOUR preceded it by only 1 (1–2) day. This difference was statistically significant ($p<0.001$).

Conclusion: Both scales are useful in the evaluation of patients with BD; however, a FOUR score of 0 occurs much closer in time to formal BD confirmation than a GCS of 3. Because the FOUR score also incorporates brainstem reflexes and respiratory drive, it may be a more informative tool for monitoring progression toward BD in the ICU.

Keywords: Brain Death, Imminent Brain Death, FOUR Score, Glasgow Coma Scale, Brainstem Reflexes

INTRODUCTION

Brain death (BD) is clinically defined as the irreversible and complete loss of all brain functions. This diagnosis holds critical importance for the termination of life support treatments and the initiation of organ donation processes (1). The ongoing global shortage of organ donors has made the timely and accurate diagnosis of BD both an ethical and clinical necessity. Delays in BD diagnosis may negatively impact not only potential organ donors but also the survival prospects of patients awaiting transplantation.

According to national regulations, the primary criteria for BD diagnosis include the presence of a clinical condition explaining deep coma, the absence of brainstem reflexes (light reflexes, oculocephalic and vestibulo-ocular reflexes, corneal, pharyngeal, and tracheal reflexes), the absence of spontaneous respiratory effort, and a positive apnea test. Standardized tools such as the Glasgow Coma Scale (GCS) and the Full Outline of UnResponsiveness (FOUR) score are commonly used to assess the level of consciousness (2,3). In cases of diagnostic uncertainty, ancillary tests such as electroencephalography, evoked potentials, and cerebral blood flow studies may be employed (2). Nevertheless, despite the availability of these diagnostic modalities, ambiguities and delays in BD confirmation remain common and continue to negatively impact organ donation rates (4).

Organ transplantation relies on both cadaveric and living donors, with cadaveric donation forming the foundation of most national transplant programs. The efficiency of this process depends largely on the early identification of potential donors. In this context, the concept of imminent brain death (IBD) has been proposed as a strategy to facilitate timely donor recognition. Similarly, the Organ Procurement and Transplantation Network define *imminent neurological death* as a condition in ventilated patients with severe neurological injury who demonstrate the loss of at least three brainstem reflexes, underscoring the importance of early identification of patients at high risk of progression to BD (5). A related but distinct definition was proposed by de Groot et al., who defined IBD as a GCS of 3 with the loss of at least three of six brainstem reflexes, or a FOUR score of 0 (6).

Previous studies have compared coma assessment scales across various neurological conditions. Although the GCS remains the most widely used tool in clinical practice, it has notable limitations in differentiating advanced disorders of consciousness (7,8). In contrast, the FOUR score, which incorporates

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assessments of brainstem reflexes and respiratory drive, provides a more comprehensive evaluation and may offer advantages in detecting the level of consciousness (3).

This study aimed to compare the timing of a GCS of 3 and a FOUR score of 0 relative to the formal confirmation of BD in intensive care unit (ICU) patients. We further examined the ability of each scale to identify patients at high risk of progression to BD and to determine which scale occurs closer in time to confirmed BD. Ultimately, we aimed to evaluate whether a more comprehensive assessment of consciousness could enable earlier recognition of BD and support more timely and effective decision-making in organ donation.

METHODS

This retrospective, single-center study was conducted in the ICU of a hospital between February 2018 and December 2024. The study was approved by the institutional ethics committee (13.12.2023/264; revision date: 09.02.2026) and conducted in accordance with the Declaration of Helsinki.

Adult patients (≥18 years) with irreversible severe brain injury who were mechanically ventilated were screened for eligibility. Only patients with confirmed brain death (BD) were included in the final analysis; patients who died of cardiac arrest before BD could be confirmed were excluded. Eligibility criteria required a core body temperature of ≥36°C, absence of hypotensive shock, and no metabolic, electrolyte, or acid–base disturbances. Potential confounding factors such as drug effects or intoxication were excluded. Neurological assessments were performed only after ensuring the absence of residual sedative effects, defined as a period equivalent to at least five elimination half-lives or subtherapeutic serum drug levels.

All eligible patients were evaluated daily by using the GCS and the FOUR score. These prospectively documented scores were retrieved retrospectively from the patient charts. The diagnosis of IBD was determined using two distinct criteria:

1. IBD-GCS: Patients with irreversible severe brain injury, deep coma under mechanical ventilation, and a GCS score of 3.
2. IBD-FOUR: Patients with irreversible severe brain injury, deep coma under mechanical ventilation, and a FOUR score of 0, defined as E0 (no eye opening to pain), M0 (no motor response or generalized myoclonus), B0 (absence of pupillary, corneal, and cough reflexes), and R0 (absence of spontaneous breathing or presence of apnea).

All time intervals were calculated from the day of ICU admission (day 0). IBD-GCS and IBD-FOUR days were defined as the first day on which a GCS of 3 or a FOUR score of 0, respectively, was recorded under the eligibility conditions described above. These operational thresholds, adopted from previously published IBD frameworks (5,6,9), were not intended to represent validated diagnostic criteria for BD itself, but rather reproducible reference points for measuring temporal proximity to formal BD confirmation. The BD day was defined as the day on which BD was formally confirmed according to national regulations.

Recorded parameters included age, sex, diagnosis, ancillary tests performed for BD confirmation, donor status, time from admission to death, and the timing of IBD-GCS and IBD-FOUR relative to confirmed BD.

Statistical analysis: All statistical analyses were performed using IBM SPSS for Windows version 29.0 (IBM Corp., Armonk, NY, USA). Kolmogorov-Smirnov's test was used to assess the normality assumption. Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile range (IQR), as appropriate. Categorical variables were summarized as

Table 1. Demographic and clinical characteristics of patients diagnosed with BD

Variables	Overall cohort (n=62)
Age, mean ± SD	45.4 ± 17.8
Sex, n (%)	
Male	44 (71)
Female	18 (29)
Admission Diagnosis, n (%)	
HIE	17 (27.4)
ICH	15 (24.2)
SAH	13 (21.0)
TBI	13 (21.0)
Others*	4 (6.4)
Ancillary tests, n (%)	
EEG	42 (67.7)
CT Angiography	57 (91.9)
Donor Status, n (%)	
Yes	9 (14.5)
No	53 (85.5)
Time from admission to death days, median (IQR)	8 (5-10)

Abb. SD: Standard deviation, IQR: Interquartile range, HIE: Hypoxic ischemic encephalopathy, ICH: Intracranial hemorrhage, SAH: Subarachnoid hemorrhage, TBI: Traumatic brain injury, EEG: Electroencephalography, CT angiography: Computed tomography angiography. *Others: 1 meningoencephalitis, 2 hemorrhagic transformation of ischemic stroke, 1 malignant brain neoplasm.

counts and percentages. Comparisons of dependent groups were conducted using the Wilcoxon signed-rank test and Friedman's two-way ANOVA. Dunn's test was applied for post-hoc multiple comparisons. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 62 patients (44 males, 18 females) with confirmed BD were included in the analysis and the mean age was 45.4 ± 17.8 years. Regarding ICU admission diagnoses, the most common etiology was hypoxic ischemic encephalopathy (HIE) (27.4%), followed by intracranial hemorrhage (ICH) (24.2%), subarachnoid hemorrhage (SAH) (21.0%) and traumatic brain injury (TBI) (21.0%). Among the 10 patients who underwent decompressive surgery, 4 had SAH, 4 had ICH, 1 had meningoencephalitis, and 1 had hemorrhagic transformation of ischemic stroke. Additionally, one patient with a malignant brain neoplasm underwent external ventricular drainage placement. Among ancillary tests, EEG was performed in 42 patients (67.7%), while CT angiography was obtained in 57 patients (91.9%). Only 9 patients' (14.5%) families gave consent to organ donation. After BD confirmation, all non-donor patients subsequently developed cardiac arrest under continued support. The median time from ICU admission to death was 8 (5–10) days in the overall study population (Table 1).

Table 2. Comparison of the time to GCS=3, FOUR=0, and BD confirmation (days from ICU admission)

Variables	Median (IQR), days
IBD-FOUR	3 (2-5)
IBD-GCS	1 (1-1)
BD	5 (3-7)
p[a]	**<0.001**
Post-Hoc Tests	**p[b]**
IBD FOUR vs BD	**<0.001**
IBD GCS vs BD	**<0.001**
IBD FOUR vs IBD GCS	**<0.001**

Abb. IBD: Imminent Brain Death, FOUR: Full Outline of UnResponsiveness, GCS: Glasgow Coma Scale, BD: Brain Death, IQR: Interquartile range, [a]Friedman's two-way ANOVA [b]Dunn's test

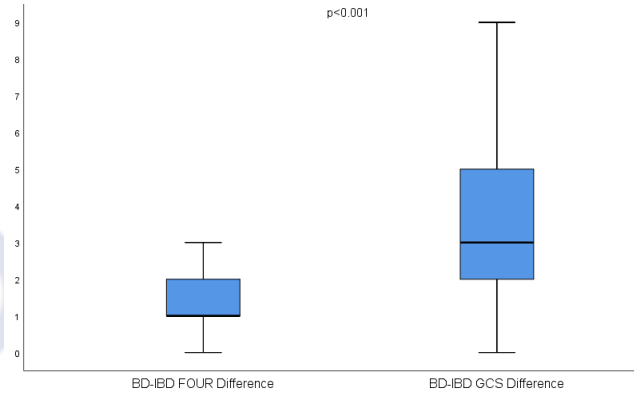
The progression toward BD during ICU follow-up was evaluated using the GCS and FOUR score. The median time from ICU admission to BD confirmation was 5 (3–7) days. A GCS of 3 was reached at a median of 1 (1–1) day, and a FOUR score of 0 was reached at a median of 3 (2–5) days after admission (p<0.001).

Table 3. Comparison of the time to GCS=3, FOUR=0, and BD confirmation between donor and non-donor patients

Variables	Donor (n=9)	Non-Donor (n=53)	p[a]
IBD GCS, median (IQR)	1 (1-1)	1 (1-1)	0.452
IBD FOUR, median (IQR)	3 (1–5)	3 (2–5)	0.322
BD, median (IQR)	5 (4–8)	5 (3–7)	0.864

Abb. IBD: Imminent Brain Death, FOUR: Full Outline of UnResponsiveness, GCS: Glasgow Coma Scale, BD: Brain Death, IQR: Interquartile range [a]Mann–Whitney U test.

Figure 1. Box plots show the interval between reaching a GCS of 3 or a FOUR score of 0 and the day of BD confirmation.



Consequently, the interval between reaching the respective score and BD confirmation was 3 (2–5) days for the GCS and 1 (1–2) day for the FOUR score (Table 2). Although both intervals were significantly shorter than the actual time to BD confirmation, the interval for the FOUR score was significantly shorter than that for the GCS (1 vs. 3 days, p<0.001) (Table 2, Figure 1).

No significant differences were observed between donor and non-donor patients regarding the time to GCS=3, FOUR=0, or BD confirmation (Table 3).

DISCUSSION

In this study, we found that a FOUR score of 0 occurred substantially closer in time to formal BD confirmation than a GCS of 3. Both scales reached their respective threshold values in all patients; however, a GCS of 3 was recorded a median of 3 days before confirmation, whereas a FOUR score of 0 was recorded a median of 1 day before confirmation.

Although the GCS remains the most widely used coma assessment tool in clinical practice, its ability to evaluate advanced stages of neurological deterioration is limited by its exclusive focus on cortical responses. In contrast, the FOUR score incorporates key physiological components, including brainstem reflexes and respiratory drive, which are central to the pathophysiology of BD. This broader neurological framework likely explains why a FOUR score of 0 occurred closer in time to BD confirmation than a GCS of 3 in our cohort. Accordingly, GCS-based assessments may overestimate early neurological failure by reflecting cortical unresponsiveness rather than complete loss of brain function.

An important consideration is that a FOUR score of 0 requires the absence of pupillary, corneal, and cough reflexes and of respiratory drive, and therefore overlaps substantially with the clinical criteria for BD. The closer proximity of the FOUR score to BD confirmation is thus partly expected. Nevertheless, a median interval of 1 day remained between the first FOUR score of 0 and formal confirmation. This residual interval most likely reflects the time required for repeated clinical examinations, apnea testing, ancillary tests, and documentation, rather than further neurological deterioration. From a practical standpoint, a FOUR score of 0 may serve as a trigger to initiate the formal BD evaluation and donor coordination process without delay.

Previous studies have examined the role of coma assessment scales in identifying patients who are approaching BD. Zappa et al. reported that both the FOUR score and GCS demonstrated high sensitivity but low specificity in detecting IBD, supporting their

utility in identifying high-risk patients (9). Unlike Zappa et al., whose cohort allowed calculation of sensitivity and specificity by including patients who did not progress to BD, the present study was restricted to patients with confirmed BD; consequently, our findings cannot address the diagnostic performance of either score and instead characterize the temporal relationship between each operational threshold and BD confirmation among patients who did progress to BD. Extending these findings, our study adds a temporal dimension by demonstrating that a FOUR score of 0 occurs closer in time to confirmed BD than a GCS of 3. This distinction is clinically relevant, as this temporal information may help guide the intensity of monitoring and decision-making in the ICU.

Comparative studies of the GCS and FOUR score have yielded inconsistent results across different neurological populations. Several investigations have reported the superiority of the FOUR score in predicting hospital length of stay and morbidity among patients with TBI (10,11). Similarly, serial FOUR score assessment has been shown to predict overall mortality in elderly medical ICU patients, supporting its broader prognostic utility beyond the specific context of BD (12). However, other studies have shown similar prognostic performance between the FOUR score and the GCS, indicating that their relative utility may vary according to clinical context (13,14). More recently, another study proposed combining the FOUR and GCS scores to create a composite tool for assessing the level of consciousness in patients with impaired neurological status (15). Together, these findings support the FOUR score as a reliable tool for identifying patients approaching BD.

The limitations of the GCS become particularly evident in advanced neurological deterioration. Because it does not assess brainstem reflexes or respiratory activity, the GCS may indicate a loss of neurological function earlier than is physiologically accurate. Supporting this view, several studies have suggested that the FOUR score may offer certain advantages over the GCS in assessing consciousness in mechanically ventilated patients (16-19). Consistent with these observations, in our study a GCS of 3 was reached substantially earlier than a FOUR score of 0 relative to BD confirmation, suggesting that GCS-based assessments may overrepresent early cortical unresponsiveness rather than complete brain failure. This underscores the value of more comprehensive assessment tools when evaluating the progression toward BD in the ICU.

Regarding organ donation, the donor conversion rate in our study was 14.5%, which is consistent with previously reported national data (20) but remains lower than the rates observed in many international series (21). Similar to previous studies, which found that clinical variables were not associated with donation outcomes (22, 23), we did not find a significant association between coma scores and donor status (Table 3). This finding suggests that factors beyond neurological scoring, such as cultural attitudes, family awareness, and institutional protocols, play a more decisive role in determining donation outcomes. Nevertheless, previous studies have emphasized that earlier confirmation of BD may facilitate organ donation (24, 25). In this respect, the closer temporal proximity of the FOUR score to BD confirmation may indirectly support the earlier identification of potential donors and contribute to a more organized and timely donation process, even if it does not directly influence donor conversion rates.

Study Limitations: This study has several limitations. Its retrospective design, single-center setting, and relatively small sample size may limit the generalizability of the findings. A key limitation of this study is the inclusion of only patients who progressed to confirmed BD, introducing a potential selection bias. This design limits the generalizability of the findings and precludes the evaluation of the predictive performance of the GCS and FOUR scores in patients who do not progress to BD. Therefore, future multicenter, prospective studies are warranted.

CONCLUSION

In this study, a FOUR score of 0 occurred substantially closer in time to formal BD confirmation than a GCS of 3, likely to reflect the more comprehensive assessment of brainstem function and respiratory drive provided by the FOUR score. While both scales remain valuable for identifying patients at risk, the FOUR score's comprehensive assessment of neurological function may offer advantages in monitoring patients approaching BD and supporting timely clinical decision-making in the ICU. Further prospective, multicenter studies are needed to validate these findings and to clarify their implications for clinical decision-making and organ donation practices.

Ethics Committee Approval: The study received approval from Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital ethical board (13.12.2023/264, revision date: 09.02.2026).

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