Original Article

Cukurova Anestezi ve Cerrahi Bilimler Dergisi

Glasgow Coma Scale–Pupil Score and C-Reactive Protein-to-Albumin Ratio as Predictors of In-Hospital Mortality in Moderate-to-Severe Traumatic Brain Injury

Kadir Arslan[1], *Deniz Yasemin Keleş Duran*[1], *Ayca Sultan Sahin*[1]

[1] Department of Anesthesiology and Reanimation, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Türkiye

***Correspondence:** Kadir Arslan, MD; kadir.arslan@sbu.edu.tr

Abstract

Aim: Traumatic brain injury (TBI) is a serious clinical condition associated with high mortality and neurological sequelae. This study aims to evaluate the prognostic role of the Glasgow Coma Scale–Pupils score (GCS-P) and the C-reactive protein-to-albumin ratio (CAR) on mortality in patients with moderate and severe TBI. **Methods:** In this retrospective observational study, patients with moderate-to-severe TBI admitted to and treated in the ICU between January 2021 and June 2023 were included. Patients were classified into survivors and non-survivors. Demographic and clinical characteristics, GCS, GCS-P, and CAR were recorded. CAR was calculated by dividing the CRP level by the albumin level obtained from routine blood tests at admission. **Results:** The study cohort comprised 177 patients, with an in-hospital mortality rate of 22%. In non-survivors, GCS and GCS-P scores were significantly lower and CAR was significantly higher (all $p < 0.001$). In multivariable analysis, GCS-P (OR = 0.425, $p = 0.028$) and CAR (OR = 1.275, $p = 0.022$) were independent predictors of mortality. The cut-off for GCS-P was ≤4.5 (AUC = 0.863) and for CAR ≥0.07 (AUC = 0.721). **Conclusion:** In patients with moderate-to-severe TBI admitted to the ICU, GCS-P score and CAR are independent predictors of in-hospital mortality. The combined use of GCS-P, reflecting neurological status, and CAR, reflecting systemic inflammation and nutritional status, may provide additional prognostic value.

Keywords: Traumatic brain injury; Glasgow Coma Scale–pupils score; GCS; C-reactive protein-to-albumin ratio; Mortality

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1. Introduction

Traumatic brain injury (TBI) refers to structural brain damage or physiological disruption of brain function caused by an external mechanical force. Although its worldwide incidence has been increasing, approximately 70 million individuals are affected annually[1]. TBI is one of the leading causes of long-term neurological disability and mortality worldwide, with reported mortality rates as high as 30–40% among critically ill patients with severe TBI[2,3]. Therefore, timely recognition of ICU-admitted TBI patients likely to have unfavorable outcomes is pivotal for directing intensive therapeutic approaches and ultimately reducing the risk of death.

The GCS score has long been used as the primary clinical tool for assessing TBI severity. However, especially in moderate and severe TBI, the prognostic accuracy of GCS alone may be limited. Consequently, the GCS-P, which assesses the pupillary light reflex, has been developed as a more comprehensive indicator of neurological injury. Recent studies have demonstrated that GCS-P may be a stronger predictor of mortality and poor neurological outcomes than the conventional GCS[5,6].

TBI is not merely a localized brain injury but also a multidimensional disease process characterized by a pronounced systemic inflammatory response[7,8]. The C-reactive protein-to-albumin ratio (CAR) has emerged as a simple parameter integrating acute inflammation and physiological reserve into a single measure. In recent years, CAR has been reported to be associated with mortality and adverse clinical outcomes in sepsis, trauma, and critical illness[9,10]. However, data regarding the combined evaluation of CAR with neurological scores in patients with moderate and severe TBI remain limited.

In this retrospective observational study, the prognostic roles of GCS-P and CAR were investigated in critically ill patients with moderate-to-severe TBI managed in the ICU.

2. Materials and Methods

2.1. Study Design and Population

Following approval from the Institutional Review Board (date: 13.08.2025, KAEK/2025.08.191), this retrospective study was initiated. The study was conducted in accordance with the principles of the Declaration of Helsinki. Patients with TBI admitted to and managed in the ICU at the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, between January 2021 and June 2023 were included. Inclusion criteria: age ≥18 years, isolated head trauma, ICU admission within 24 hours of injury, moderate-to-severe TBI (GCS < 13). Exclusion criteria: requirement for cardiopulmonary resuscitation within the first 24 hours post-trauma, ICU length of stay <24 hours or death within initial 24 hours, absence of cranial CT imaging, active viral or bacterial infection including COVID-19, and missing data.

2.2. Data Collection

Patients' demographic characteristics, primary diagnoses, trauma type and etiology, comorbidities, neurosurgical intervention status, pupillary reactivity, GCS, GCS-P, and APACHE-II scores at ICU admission were recorded. Laboratory parameters collected from routine admission tests included hemoglobin, platelet count, CRP, albumin, neutrophil count, lymphocyte count, and lactate. CAR was calculated as CRP (mg/L) / albumin (g/dL). The study cohort was stratified into survivors and non-survivors based on in-hospital mortality[4].

2.3. Glasgow Coma Scale, GCS-Pupils Score, and APACHE-II Score

GCS is a clinical scoring system for assessing neurological status in trauma patients, ranging from 3 to 15. TBI severity was classified as mild (13–15), moderate (9–12), and severe (≤8)[11,12,13]. GCS-P integrates the total GCS score with the pupillary light reflex. Pupillary reactivity was coded as the pupil reactivity score (PRS): 0 if both pupils reactive, 1 if one non-reactive, 2 if both non-reactive. As only moderate-to-severe TBI patients were included (GCS < 13), GCS-P values ranged from 1 to 12. APACHE-II incorporates age, previous health status, and 12 physiological variables to predict disease severity and mortality risk in ICU patients[14].

2.4. C-Reactive Protein-to-Albumin Ratio

CAR was calculated to assess the combined prognostic impact of systemic inflammation and nutritional status. By reflecting both the inflammatory response and the decrease

in albumin, a negative acute-phase reactant related to nutritional status, CAR is considered a more comprehensive prognostic biomarker than CRP or albumin alone. Recent studies have reported that CAR demonstrates high prognostic performance, particularly for early in-hospital mortality and adverse clinical outcomes[15].

2.5. Statistical Analysis

SPSS version 26.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. Normality was assessed by the Shapiro–Wilk test. Data are presented as n (%), median (Q1–Q3), or mean ± SD. Comparisons of normally distributed variables used the independent-samples t-test; non-normally distributed variables used the Mann–Whitney U test; categorical variables used the Chi-square or Fisher's exact test. Multivariable logistic regression identified independent predictors of mortality. ROC analysis evaluated prognostic performance; optimal cut-offs were determined using the Youden index. $P < 0.05$ was statistically significant. Sample size was estimated using G*Power 3.1 (minimum 140 patients required; effect size 0.5, α 0.05, power 80%).

3. Results

Among 189 initially eligible patients, 12 were excluded. Ultimately, 177 patients were enrolled, including 39 non-survivors. The median age was 41 years (IQR: 27–62), and 81.4% were male. The in-hospital mortality rate was 22% (39/177). Non-survivors were significantly older (median age 53 vs. 39 years, $p = 0.049$). Blunt trauma was predominant (96.6%). The proportion of severe TBI was significantly higher in non-survivors (94% vs. 48%, $p < 0.001$). Overall, 51.4% of patients underwent neurosurgical intervention, with no significant difference between groups ($p = 0.152$). Non-survivors had significantly lower GCS (3 vs. 10) and GCS-P scores (2 vs. 10) and higher APACHE-II scores (27.6 vs. 15.4, all $p < 0.001$). Hemoglobin (11.9 vs. 13.1 g/dL) and albumin were lower, while CRP (9.3 vs. 3.5 mg/L), CAR (0.3 vs. 0.1), and lactate (3.6 vs. 2.5 mmol/L) were higher in non-survivors (Table 1).

Table 1. Clinical characteristics of the study population

Variable	All (n=177)	Survivors (n=138)	Non-survivors (n=39)	p
Age (years) Median (Q1–Q3)	41 (27–62)	39 (27–57)	53 (28–79)	0.049
Female n (%)	33 (18.6)	25 (18.1)	8 (20.5)	0.734
Male n (%)	144 (81.4)	113 (81.9)	31 (79.5)	
Blunt trauma n (%)	171 (96.6)	135 (97.8)	36 (92.3)	0.122
Neurosurgery n (%)	91 (51.4)	67 (48.6)	24 (61.5)	0.152
Comorbidity n (%)	54 (30.5)	38 (27.5)	16 (41.0)	0.106
ICU stay (days)	7 (4–14)	6 (3–12)	15 (7–22)	<0.001
GCS-P score	8 (3–12)	10 (6–12)	2 (2–4)	<0.001
Both pupils reacting n (%)	113 (63.8)	107 (77.5)	6 (15.4)	<0.001
One pupil reacting n (%)	41 (23.2)	20 (14.5)	21 (53.8)	
No pupil reacting n (%)	23 (13.0)	11 (8.0)	12 (30.8)	
GCS score	8 (4–12)	10 (6–12)	3 (3–5)	<0.001
APACHE-II score Mean±SD	18.9±10.2	15.4±7.3	27.6±8.4	<0.001
Hemoglobin (g/dL) Mean±SD	12.9±2.1	13.1±1.9	11.9±2.4	0.046
Platelets (10^9/L)	263±75	268±73	245±82	0.161
CRP (mg/L)	5.2 (1.7–22.6)	3.5 (1.4–18.7)	9.3 (4.6–45.3)	<0.001
Albumin (g/L)	38.6 (33.9–43.5)	40.5 (35.9–44.2)	32.9 (27.0–37.2)	<0.001
CAR	0.1 (0.04–0.6)	0.1 (0.03–0.4)	0.3 (0.1–1.5)	<0.001
Neutrophil (10^9/L)	9.0 (7.9–12.1)	8.9 (7.7–11.7)	9.8 (8.9–15.2)	0.099
Lymphocyte (10^9/L)	1.2 (1.0–1.8)	1.2 (1.0–1.7)	1.4 (0.9–1.9)	0.724
Lactate (mmol/L)	2.6 (1.8–3.6)	2.5 (1.8–3.5)	3.6 (1.9–3.7)	0.030

ICU: Intensive care unit; GCS: Glasgow Coma Scale; GCS-P: Glasgow Coma Scale–pupils score; APACHE-II: Acute Physiology and Chronic Health Assessment-II; CRP: C-reactive protein; CAR: C-reactive protein-to-albumin ratio. Data are presented as median (Q1–Q3), mean ± SD, or n (%).

Falls (42.4%), traffic accidents (41.2%), and assault (9.6%) were the leading causes of TBI (Table 2).

Regarding primary radiological diagnoses, acute subdural hematoma was most frequent (29.4%), followed by subarachnoid hemorrhage (26.0%) and epidural hematoma (19.2%) (Table 3).

Table 2. Trauma etiologies

Etiology	All n (%)	Survivors n (%)	Non-survivors n (%)
Falls	75 (42.4)	49 (35.5)	26 (66.7)
Traffic accidents	73 (41.2)	64 (46.4)	9 (23.1)
Assault	17 (9.6)	16 (11.6)	1 (2.6)
Work accidents/crush	7 (4.0)	7 (5.1)	0
Gunshot wounds/explosions	5 (2.8)	2 (1.4)	3 (7.7)

Table 3. Primary radiological diagnoses

Primary Diagnosis	All n (%)	Survivors n (%)	Non-survivors n (%)	p
Acute subdural hematoma	52 (29.4)	37 (26.8)	15 (38.5)	0.185
Subarachnoid hemorrhage	46 (26.0)	33 (23.9)	13 (33.3)	
Epidural hematoma	34 (19.2)	29 (21.0)	5 (12.8)	
Intracerebral hematoma	22 (12.4)	18 (13.0)	4 (10.3)	
Cerebral contusion	16 (9.0)	15 (10.9)	1 (2.6)	
Brain edema	7 (4.0)	6 (4.3)	1 (2.6)	

In multivariable regression, GCS was not an independent predictor of mortality ($p = 0.229$). In contrast, GCS-P ($p = 0.028$), CAR ($p = 0.022$), and APACHE-II ($p < 0.001$) independently predicted mortality (Table 4).

ROC analysis demonstrated AUC values of 0.852 for GCS, 0.863 for GCS-P, 0.721 for CAR, and 0.872 for APACHE-II (Table 5).

Table 4. Multivariable logistic regression analysis of mortality prediction

Variable	Odds Ratio	95% CI	p-value
GCS score	1.716	0.711–4.140	0.229
GCS-P score	0.425	0.198–0.913	0.028
CAR	1.275	1.036–1.570	0.022
APACHE-II score	1.165	1.080–1.257	<0.001

GCS: Glasgow Coma Scale; GCS-P: GCS–pupils score; CAR: C-reactive protein-to-albumin ratio; APACHE-II: Acute Physiology and Chronic Health Assessment-II.

Table 5. Mortality prediction performance of GCS, GCS-P, CAR, and APACHE-II scores

Variable	Cut-off	Sensitivity	Specificity	AUC (95% CI)
GCS	≤6.5	0.846	0.746	0.852 (0.792–0.912)
GCS-P	≤4.5	0.795	0.862	0.863 (0.807–0.920)
CAR	≥0.07	0.949	0.442	0.721 (0.640–0.801)
APACHE-II	≥19.5	0.846	0.717	0.872 (0.817–0.926)

GCS: Glasgow Coma Scale; GCS-P: GCS–pupils score; CAR: C-reactive protein-to-albumin ratio; APACHE-II: Acute Physiology and Chronic Health Assessment-II; AUC: area under the curve.

4. Discussion

In this study involving patients with moderate-to-severe TBI managed in the ICU, GCS-P score and CAR emerged as independent predictors of in-hospital mortality, while

the standard GCS was not an independent predictor in multivariable analysis. Epidemiological studies have reported that falls and traffic accidents are the most common causes of TBI, while subarachnoid hemorrhage and acute subdural hematoma are the most frequently observed primary radiological pathologies[16]. Friedrich et al. reported an in-hospital mortality rate of 27.5% in patients with isolated TBI and identified advanced age, elevated lactate, and higher CAR as independent predictors of mortality[17]. Our observed mortality rate was consistent with the literature.

Although GCS has long been the basis for clinical classification in TBI, factors such as sedation, endotracheal intubation, and the inability to reliably assess motor responses may limit its sensitivity. The GCS-P score was developed to address this limitation by incorporating the pupillary light reflex. Large-scale studies including CENTER-TBI and TRACK-TBI have shown that GCS-P outperforms GCS in predicting mortality[18,19]. Another study of over 1,000 patients with severe TBI found that GCS-P was strongly associated with in-hospital mortality, with lower scores more clearly distinguishing poor outcomes[6]. In our study, the AUC for GCS-P (0.863) was slightly higher than for GCS (0.852), and while GCS did not remain significant in multivariable analysis, GCS-P did, highlighting the role of brainstem function in early prognosis.

TBI is accompanied by a pronounced systemic inflammatory response closely associated with clinical prognosis. Albumin, a negative acute-phase reactant, decreases early after trauma due to capillary leakage, increased protein catabolism, and impaired hepatic synthesis, and has been identified as an independent predictor of mortality in TBI[23,24,25]. CAR integrates two opposing acute-phase reactants into a single parameter, providing a more comprehensive representation of the balance between the inflammatory response and metabolic reserve. Wang et al. demonstrated that CAR values were significantly higher in non-survivors with moderate-to-severe TBI[9], and Friedrich et al. confirmed that elevated CAR was independently associated with in-hospital mortality in isolated TBI[17]. Consistent with the literature, our study also showed significantly elevated CAR in the mortality group, and CAR remained an independent predictor in multivariable analysis.

The prognostic performance analysis revealed AUC values of 0.863 for GCS-P, 0.872 for APACHE-II, and 0.721 for CAR. Although APACHE-II is not a trauma-specific scoring system, its strong independent association with mortality supports the critical role of systemic organ dysfunction in determining outcomes in TBI[4]. The identification of all three parameters as independent predictors of in-hospital mortality indicates that TBI prognosis is determined not only by the severity of neurological injury but also by the accompanying systemic physiological derangement and inflammatory response.

Study Limitations

This study has certain limitations. First, the retrospective design precludes complete control over unmeasured confounding variables. Second, only admission CRP and albumin levels were evaluated; temporal changes in CAR were not analyzed. Third, the effects of prehospital interventions, sedative medication use, and delayed neurological deterioration on GCS and pupillary assessments could not be entirely excluded. Fourth, the absence of long-term functional outcome measures (such as the Glasgow Outcome Scale) limited comparison with established prognostic models.

5. Conclusion

The GCS-P score and CAR were identified as independent predictors of in-hospital mortality in patients with moderate-to-severe TBI. Although the conventional GCS was not identified as an independent predictor in multivariable analysis, GCS-P, which incorporates pupillary reactivity, demonstrated superior discriminative performance (AUC = 0.863). The CAR, as a practical biomarker reflecting systemic inflammation and

impaired nutritional reserve, was independently associated with mortality (AUC = 0.721). The combined use of these two parameters may enhance early risk stratification in moderate-to-severe TBI and contribute to clinical decision-making. Future prospective multicenter studies with larger cohorts are warranted to validate these findings.

Author Contributions: All authors contributed to the study conception and design. Data collection and analysis were performed by K.A. and D.Y.K.D. The first draft was written by K.A. and all authors commented on previous versions. K.A., D.Y.K.D., and A.S.S. supervised the whole process and critically reviewed the manuscript. All authors read and approved the final manuscript.

Ethical Approval: This study was approved by the Institutional Review Board at University of Health Sciences, Istanbul Kanuni Sultan Süleyman Training and Research Hospital (approval number: KAEK/2025.08.191, date: 13.08.2025). The study was conducted in accordance with the Declaration of Helsinki. Informed consent was waived due to the retrospective design.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Generative AI: No artificial intelligence-based tools or generative AI technologies were used in this study.

Data Availability: Due to institutional privacy policies, the datasets are not publicly available but are available from the corresponding author upon reasonable request.

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