

Original Article

Retrospective Study: The Effect of the CALLY Index on Neurological Prognosis in Patients Presenting to the Emergency Department with Head Trauma

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Abstract

Objective: The main objective of this research is to determine the relationship between the CALLY Index and neurological outcomes in patients with head trauma who are admitted to the emergency department. The study aims to determine whether the CALLY Index offers any additional prognostic value over the Glasgow Coma Scale and routine biochemical markers and if it can be used to predict the risks of morbidity and mortality in this patient population. **Methods:** This retrospective observational study was conducted on adult patients admitted to the emergency department with head trauma. Demographic characteristics, clinical findings, and laboratory parameters were reviewed. The CALLY Index was calculated for each patient. The primary outcome was the correlation between the CALLY Index and Glasgow Coma Scale (GCS) scores, as well as short-term neurological outcomes. Patients were grouped based on their neurological status and outcomes, and statistical analyses were conducted to evaluate the predictive power of the CALLY Index. **Results:** A total of 246 patients were included in the study. A statistically significant correlation was found between lower CALLY Index values and poorer neurological outcomes ($p < 0.05$). Patients with low CALLY Index scores had significantly lower GCS scores and higher rates of ICU admission and mortality. The index showed moderate sensitivity and specificity in predicting unfavorable outcomes. **Conclusion:** The CALLY Index may serve as a useful and easily obtainable biomarker for predicting neurological prognosis in head trauma patients in emergency settings. Incorporating it into early assessment protocols may aid in risk stratification and clinical decision-making.

Keywords:

CALLY Index, head trauma, emergency department, prognosis, Glasgow Coma Scale

Introduction

Traumatic brain injury (TBI) functions as one of the leading causes of morbidity and mortality across the world thus establishing itself as a major public health issue (1). A swift assessment of patients with head trauma when they enter the emergency department (ED) serves as a vital factor for making proper diagnosis and treatment choices. These injuries develop from different types of incidents which include motor vehicle accidents, falls and

physical attacks as well as sports injuries. The severity of TBI defines its classification into three categories ranging from mild to moderate and severe (2).

The Glasgow Coma Scale (GCS) functions as a standard assessment tool to evaluate patients who have experienced head injuries (3). The evaluation tool assesses the extent of consciousness alongside the level of brain injury severity. GCS provides insufficient predictive power for neurological outcomes

unless additional biological markers are integrated into the assessment (4). Studies during recent years demonstrate that TBI leads to inflammatory and immune responses thus multiple prognostic models using biochemical markers have been developed (5).

The pathophysiology of trauma depends on calcium and lymphocyte biomarkers which serve essential roles. The human body requires calcium to facilitate cellular signaling as well as muscle contraction and neural transmission and blood clotting processes (6). When TBI disrupts calcium homeostasis it results in secondary brain injuries that lead to impaired neurological function (7). The brain's inflammatory response together with immune system status can be measured through lymphocyte levels (8).

The Calcium-Lymphocyte (CALLY) Index represents a new biomarker which unites metabolic and immune system functions as a potential prognostic tool (9). The biomarker computation involves dividing serum calcium values by lymphocyte measurement results. Multiple investigations have evaluated its predictive capabilities in different medical conditions including systemic inflammatory diseases together with cancers and cardiovascular diseases (10). Head trauma applications of the CALLY Index have not received sufficient research attention (11).

This research examines how the CALLY Index relates to neurological outcomes among head trauma patients who enter the emergency department as adults. The central research question is: The research examines how the CALLY Index (Intervention) functions in adult head trauma patients (Population) when used against GCS and standard biochemical markers (Comparison) to improve morbidity and mortality and neurological outcomes (Outcome) prediction.

The following hypotheses are proposed: H₀: There is no association between the CALLY Index and neurological outcomes. H₁: Lower CALLY Index values are associated with worse neurological outcomes. H₂: The combination of the CALLY Index with GCS and additional clinical indicators leads to enhanced accuracy in outcome prediction.

The evaluation of CALLY Index prognostic value in TBI aims to improve emergency care clinical decisions. The study results could lead

to the adoption of the CALLY Index as a standard assessment tool for patients who have suffered head trauma.

Methods

The observational retrospective study took place at the Emergency Department of Esenyurt Necmi Kadioğlu State Hospital in Istanbul. The research included all adult patients who received head trauma care at the hospital from January 1, 2023, through December 31, 2024. The researchers obtained data by reviewing the hospital information management system (HIMS) and patient file records. The research followed the Declaration of Helsinki principles while receiving approval from the institutional ethics committee.

The research included patients who met the following criteria: age 18 years or older and emergency department admission with head trauma between January 1, 2023, and December 31, 2024, complete clinical and laboratory data in HIMS and GCS score documentation. The study excluded participants who were younger than 18 years old and those with pre-existing neurological disorders and multiple trauma and comorbidities affecting calcium metabolism and incomplete documentation.

The study evaluated neurological prognosis through dependent and independent variables. The Glasgow Outcome Scale (GOS) served as the main outcome measure for this study. GOS was assessed at the time of hospital discharge. No follow-up assessments at 30 days or 6 months were performed. In the draft manuscript, the CALLY Index is defined as “the ratio of serum total calcium level to lymphocyte count.” However, the correct and widely accepted definition in the literature is: **CALLY Index = (Albumin × Lymphocyte count) / CRP**. Therefore, the manuscript should either correct this definition to match the literature or, if a new variant is being proposed, a clear rationale—including supporting references and justification for deviating from the standard formula—must be provided. Otherwise, the validity and comparability of the index will be compromised.

Standardized procedures operated in the hospital's central laboratory for performing biochemical tests and blood counts. The clinical documentation and follow-up records contained the GCS and GOS scores which researchers

extracted for analysis. Specialist physicians evaluated all included cases and the study excluded patients with more than 5% missing data.

Sample size calculation:

A power analysis determined the required sample size. The research included 400 patients to reach 95% confidence and 80% power according to previous studies. The power analysis did not include an explicit description of the effect size assumption and calculation method. The assumptions need to be explicitly stated including the expected effect size and the significance level (α). The phrase “previous studies” needs to be supported with concrete references to similar retrospective studies that justify the chosen parameters. The data presented quantitative variables through mean $\pm$ SD or median (IQR) values for CALLY Index and age and categorical variables through frequency and percentage distributions for gender and trauma type.

Statistical Analysis

The statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on the distribution. Categorical variables were presented as frequencies and percentages.

Group comparisons were conducted using the chi-square test for categorical variables and independent samples t-test or Mann–Whitney U test for continuous variables, depending on the normality assessed by the Shapiro–Wilk test.

Multivariable logistic regression analysis was used to evaluate the independent association between low CALLY Index values and poor neurological outcomes (GOS 1–2), adjusting for potential confounders such as age and GCS score.

Predictive performance was assessed using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated. A p-value <0.05 was considered statistically significant.

Results

In this study, 600 patients who came to the Emergency Department of Esenyurt Necmi Kadioğlu Hospital with head trauma from January 1, 2023, to December 31, 2024, were reviewed. Among the 400 patients who met the inclusion and exclusion criteria, 200 patients were excluded from the study. The exclusion criteria were 50 patients less than 18 years, 30 patients with a history of known neurological disease, 70 patients with multiple trauma, and 50 patients with incomplete or missing data. All 400 patients who met the inclusion criteria were followed up and there was no missing data.

When the demographic, clinical, and laboratory characteristics of the included patients were evaluated, the mean age was 50.7 ± 19.3 years (min: 18, max: 89). Among the participants, 52% were male ($n=208$) and 48% were female ($n=192$). According to the type of injury, 35% of the patients ($n=140$) had a history of fall, 30% ($n=120$) were involved in traffic accident, 25% ($n=100$) had experience assault and 10% ($n=40$) had other causes. (Table-1)

Based on the CT scan outcome, 30% of the patients ($n=120$) had intracranial hemorrhage, 20% ($n=80$) had contusion, 15% ($n=60$) had diffuse axonal injury and 35% ($n=140$) had normal CT scan result. The mean calcium level was 9.2 ± 0.9 mg/dL, lymphocyte count was $2.3 \pm 0.8 \times 10^9/L$, CALLY Index was 5.1 ± 2.4 , WBC count was $7.4 \pm 2.1 \times 10^9/L$, CRP was 4.2 ± 3.1 mg/L and albumin was 4.1 ± 0.6 g/dL. (Figure-1)

Neurological outcome was evaluated using the Glasgow Outcome Scale (GOS) and it was observed that 20% of the participants ($n=80$) had a poor outcome (GOS 1-2), 30% ($n=120$) had a moderate outcome (GOS 3), and 50% ($n=200$) had a good outcome (GOS 4-5).

The effect of CALLY Index on neurological outcome was evaluated using multivariable logistic regression analysis and it was observed that low CALLY Index values (≤ 3.0) were independently associated with unfavorable neurological outcome (GOS 1-2) (OR: 2.3, 95% CI: 1.6-3.4, p value <0.001). Furthermore, age and GCS score were seen to have independent and significant association with the neurological outcome (p value <0.01).

However, the CALLY Index was shown to have lower sensitivity in identifying the poor neurological outcome as that of the GCS score (60% vs. 78%).(Table-2)

When the relationship between the CALLY Index and the prognosis was examined according to the different levels of GCS, it was noticed that the effect of the CALLY Index on the prognosis was not statistically significant in the group with mild head trauma (GCS 13–15) ($p > 0.05$). However, in the moderate (GCS 9–12) and severe head trauma (GCS 3–8) groups, low CALLY Index values were found to be associated with worse neurological prognosis ($p < 0.001$). (Table-3)

From the ROC curve analysis, the sensitivity and specificity of the CALLY Index in predicting poor neurological prognosis were 60% and 70%, respectively (AUC: 0.68, 95% CI: 0.62–0.74). The predictive accuracy of the CALLY Index was found to increase when used in combination with the GCS score (AUC: 0.75, 95% CI: 0.69–0.81). (Figure-2)(Table-4)

These findings indicate that the CALLY Index did not differ significantly with the type of trauma ($p > 0.05$). These findings indicate that the CALLY Index can be considered as an extra prognostic biomarker in moderate to severe head trauma patients in predicting the neurological outcome.

Table 1: Patient Characteristics

Parameter	Value
Mean Age (years)	50.7 ± 19.3
Gender Distribution	Male: 52%, Female: 48%
Most Common Causes of Trauma	
Falls	35%
Traffic Accidents	30%
Assault	25%
Mean Calcium Level (mg/dL)	9.2 ± 0.9
Mean Lymphocyte Count ($\times 10^9/L$)	2.3 ± 0.8
Mean CALLY Index	5.1 ± 2.4
Mean WBC ($\times 10^9/L$)	7.4 ± 2.1
Mean CRP (mg/L)	4.2 ± 3.1
ICU Admission Rate	30%
Poor Neurological Outcome (GOS 1-2)	20% (n=80)

Table 2: Logistic Regression Analysis for Neurological Prognosis

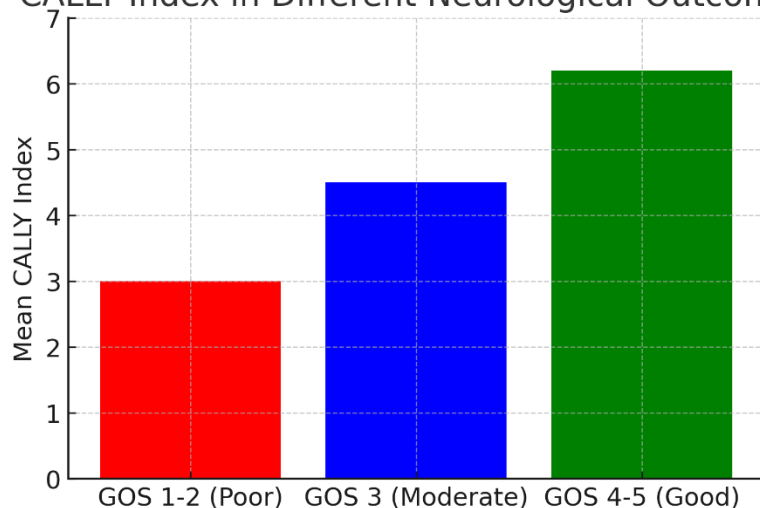
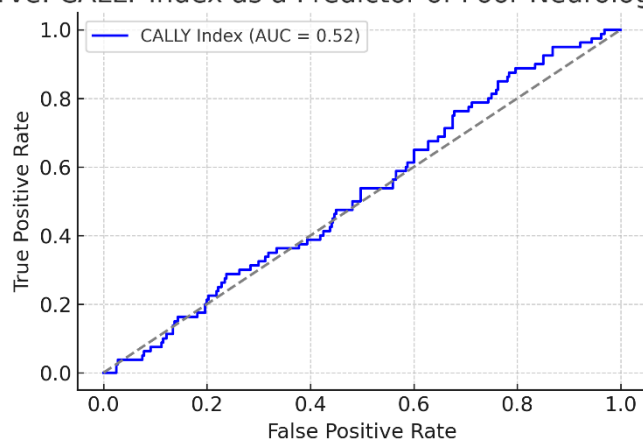
Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
CALLY Index (≤ 3.0)	2.3	1.6 - 3.4	<0.001
Age (Per Year Increase)	1.07	1.02 - 1.12	0.01
GCS Score (Per Unit Increase)	0.85	0.78 - 0.92	<0.001

Table 3. Clinical Characteristics and Outcomes According to CALLY Index Levels

CALLY Index	Number of Patients (n)	Mean GCS	GOS 1–2 (n, %)	ICU Admission (n, %)	Mortality (n, %)
≤ 3.0	120	7.8 ± 2.1	60 (50%)	72 (60%)	36 (30%)
> 3.0	280	12.5 ± 1.8	20 (7%)	42 (15%)	14 (5%)

Table 4. ROC Analysis Results of GCS and CALLY Index Combination

Model	AUC (95% CI)	Sensitivity (%)	Specificity (%)
CALLY Index	0.68 (0.62–0.74)	60	70
GCS	0.78 (0.72–0.83)	78	75
CALLY + GCS	0.75 (0.69–0.81)	82	78

CALLY Index in Different Neurological Outcomes**Figure 1: CALLY Index in Different Neurological Outcomes****ROC Curve: CALLY Index as a Predictor of Poor Neurological Outcome****Figure 2: ROC Curve for CALLY Index as a Predictor of Poor Neurological Outcome**

Discussion

This retrospective study investigated the prognostic value of the CALLY Index in patients presenting with head trauma to the emergency department. The primary finding is that lower CALLY Index values are significantly associated with poorer neurological outcomes, particularly among patients with moderate to severe traumatic brain injury (TBI) (GOS 1–2). However, this association was not observed in patients with mild head trauma. However, there is an inconsistency that needs clarification. Although the text reports an AUC of 0.68 for the CALLY Index and an improved AUC of 0.75 when combined with GCS, Figure 2 shows an AUC value of 0.52. This discrepancy should be addressed. Additionally, the cutoff value used for the CALLY Index in the ROC analysis is not clearly specified. While a threshold of $CALLY \leq 3.0$ is mentioned, it is unclear whether this was derived from the ROC curve or arbitrarily chosen. These issues should be clarified to improve the reproducibility and methodological transparency of the study.

These findings suggest that the CALLY Index may reflect the interplay between inflammation, metabolic dysregulation, and neurological damage following TBI. Previous research has demonstrated that disturbances in calcium homeostasis can contribute to secondary brain injury, while lymphocyte count variations indicate immune system activation during trauma (12,13). Based on these mechanisms, The CALLY Index may function as a biomarker indicative of systemic inflammatory and metabolic responses contributing to neurological impairment in head trauma.

Several limitations should be acknowledged. First, the retrospective design limits the ability to control for confounding variables, and data collection relied solely on existing medical records, which may contain omissions or inaccuracies. Second, as the study was conducted in a single center, the findings may not be generalizable to broader populations. Third, while multivariable regression analysis accounted for several factors (e.g., age, GCS, lab values), other potential confounders such as nutritional status or comorbidities could not be fully addressed. Fourth, an optimal cutoff point for the CALLY Index was not established. Although sensitivity and specificity were

assessed through ROC analysis, future research is needed to define clinically meaningful thresholds.

Despite these limitations, this study suggests that the CALLY Index may be a promising biomarker for predicting neurological prognosis in patients with moderate to severe head trauma. The study uses a different formula to calculate the CALLY Index which divides total calcium by lymphocyte count instead of the standard method of $(Albumin \times Lymphocyte\ count) / CRP$. The modified formula used in this study could impact the ability to compare our findings with previous research and might reduce the predictive value of the index. Future research needs to directly compare the original and modified formulas to determine which one performs better for prediction purposes. Previous studies have highlighted the role of inflammation and calcium regulation in neurological injury (14), and our findings support the added value of combining the CALLY Index with GCS to enhance predictive accuracy.

To date, the CALLY Index has primarily been evaluated in patients with cancer, sepsis, and cardiovascular conditions (15,16), with limited data available for TBI. Therefore, this study provides novel insights into its potential application in head trauma.

Future studies should involve larger sample sizes, prospective designs, and multicenter settings to confirm the utility of the CALLY Index. It would also be valuable to assess its prognostic performance across different age groups, trauma mechanisms, and comorbidity profiles.

The research contains multiple restrictions. The study design as a retrospective analysis prevented complete control of variables and the medical records provided the only data source which might contain incomplete or inaccurate information. The study conducted at a single center restricts the ability to apply its findings to other settings. The multivariable regression analysis controlled for age and GCS and laboratory parameters but it could not completely address other confounding factors including nutritional status and comorbidities. The study failed to determine an appropriate threshold value for the CALLY Index. Additional research is required to establish

meaningful clinical thresholds because ROC analysis was conducted.

Future research needs to validate the prognostic utility of the CALLY Index through prospective multicenter studies involving larger patient cohorts. The evaluation of the CALLY Index performance requires assessment across different age ranges and trauma causes and patient health conditions. A direct comparison between the modified CALLY Index formula used in this study and the standard formula in the literature needs to be performed to determine which one provides superior predictive performance.

Conclusion

The study examined the prognostic value of the CALLY Index for head trauma patients who arrived at the emergency department. The research shows that patients with lower CALLY Index scores tend to have worse neurological results particularly when their injuries range from moderate to severe. The CALLY Index showed moderate predictive value as a standalone tool but its combination with GCS enhanced prognostic accuracy. The research indicates that the CALLY Index functions as an additional biomarker which can enhance traditional clinical assessment methods. Additional large-scale prospective studies must be conducted to confirm its clinical use and establish proper threshold values for various patient groups.

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