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ORIGINAL RESEARCH

Limited Utility of the CALLY Index in Enhancing Mortality Prediction for Trauma Patients in Intensive Care Units: A Retrospective Analysis

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Background: Accurate prognostication for trauma patients in intensive care units (ICUs) remains challenging. This study investigated whether incorporating the C-reactive protein-albumin-lymphocyte (CALLY) index into traditional ICU scoring systems could enhance mortality prediction for trauma patients.

Methods: A retrospective cohort study was performed on 1242 trauma patients hospitalized to a Level I trauma center ICU from January 1, 2016, to December 31, 2023. The CALLY index was computed using the formula = [albumin (g/dL) × lymphocyte count (10^9/L)]/CRP (mg/L) and was incorporated with APACHE II, MPM II, MPM24 II, MPM48 II, and TRISS for predicting mortality outcomes. The predictive performance was assessed utilizing the area under the receiver operating characteristic curve (AUC).

Results: Integration of the CALLY index with APACHE II resulted in a minimal AUC increase from 0.811 to 0.812. It did not alter the AUC for MPM II, MPM24 II, or MPM48 II models (0.826, 0.845, and 0.832, respectively). For TRISS, adding the CALLY index slightly decreased the AUC from 0.731 to 0.725. The calibration curves suggest that adding the CALLY index did not markedly improve agreement between predicted and actual mortality.

Discussion: Unlike its proven efficacy in chronic conditions, the CALLY index did not significantly enhance mortality prediction in trauma patients when combined with traditional scoring systems. The reason that CALLY index did not enhance predictive power may be attributed to the acute, dynamic nature of trauma physiology, which differs from the steady-state conditions observed in chronic diseases. Further research is required to develop or refine prognostic tools specifically tailored to the unique physiological responses of trauma patients in ICU settings.

Conclusion: For ICU clinicians, these results imply that the CALLY index provides minimal improvement in mortality risk assessment for trauma patients.

Keywords: the C-reactive protein-albumin-lymphocyte index, CALLY index, trauma, intensive care unit, ICU, prognostic scoring systems, mortality

Introduction

The management of trauma patients in the intensive care unit (ICU) can be problematic due to the complicated interplay of injuries, nutritional condition, and systemic immunoinflammatory reactions, making a clear prognosis to guide therapy and resource allocation challenging. Conventional trauma outcome assessments, such as the Trauma Score and Injury Severity Score (TRISS),[1–3] and ICU scoring systems, such as the Acute Physiology and Chronic Health Evaluation (APACHE)[4,5] and Mortality Probability Models (MPM),[4,6,7] are widely used to predict the outcomes of trauma critical ill patients in ICU. APACHE II is a general critical illness severity score based on acute physiology and comorbidities. It correlates with mortality risk in trauma ICU patients and offers robust prognostic accuracy.[8] However, APACHE II is not trauma-specific and relies on extensive laboratory data, limiting its immediate utility during initial trauma resuscitation.[8] MPM II is another ICU mortality model calculated at admission (with updates at 24–72 hours) that emphasizes simplicity

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and uses fewer variables.[8] In a Level I trauma center study, the 24-hour MPM II had the highest discrimination (AUC 0.92) for ICU trauma mortality, outperforming APACHE II and TRISS.[4] Still, like APACHE, MPM II was developed on general ICU populations and may overlook trauma-specific factors.[4] TRISS is a trauma-focused score combining anatomic injury severity (ISS), physiologic response (RTS), age, and injury mechanism to estimate survival. TRISS is a longstanding benchmark in trauma outcome prediction, but it relies on limited variables and coefficients derived from older datasets.[9] Its accuracy diminishes in patients with extreme injury severity (especially severe neurotrauma), leading to misprediction of mortality in high-risk groups.[9] These challenges underscore that trauma prognostication remains difficult – heterogeneous injury patterns and evolving clinical care can reduce the accuracy of APACHE II, MPM II, and TRISS in a modern trauma ICU setting.[9] So far, these models may not effectively comprehend a patient's nutritional status and immunoinflammatory response, therefore incorporating such biomarkers (eg with additional clinical and laboratory variables) into the prediction method may be advantageous.

The C-reactive protein-albumin-lymphocyte (CALLY) index has garnered significant attention as an innovative biomarker by incorporating three crucial parameters: serum albumin, lymphocyte count, and C-reactive protein (CRP), thus offering a thorough evaluation of a patient's nutritional and immunoinflammatory condition.[10–16] The standard range for the C-reactive protein-albumin-lymphocyte (CALLY) index is generally delineated by certain cutoff values that signify various prognostic implications. A CALLY index below 0.65 correlates with adverse outcomes, including reduced overall and disease-free survival in individuals with specific malignancies, such as oral cavity squamous cell carcinoma and hepatocellular carcinoma.[17] The CALLY index has been demonstrated to be a significant predictive marker in patients receiving surgery for cholangiocarcinoma,[16] colorectal cancer,[18] epithelial ovarian cancer,[19] as well as gastric cancer[12,20] and serves as a cost-effective and therapeutically pertinent instrument.[10–16]

Unlike chronic disease processes, trauma triggers a unique acute pathophysiological response. Severe injury causes an abrupt release of damage-associated molecular patterns and a systemic inflammatory response syndrome (SIRS), followed closely by a compensatory anti-inflammatory response (CARS).[21,22] This acute, biphasic immune cascade is a hallmark of trauma and contrasts with the sustained, low-grade inflammation seen in chronic conditions.[23,24] Patients with chronic illnesses (eg advanced malignancy or organ failure) experience persistent immune activation and gradual nutritional decline over time, which drive prognostic markers like C-reactive protein and lymphocyte count.[23,24] By contrast, trauma's pathophysiology is dominated by sudden inflammatory and stress responses, and these trauma patients may undergo hypermetabolism and catabolism, which intensifies nutritional deficiencies and hinders immunological function, hence complicating recovery.[22,25,26] Furthermore, the consequences of traumatic injury may result in problems such as sepsis, systemic inflammatory response syndrome, and multiple organ dysfunction syndrome.[27–29] It remains uncertain whether prognostic indices derived from chronic disease cohorts have similar utility in the trauma setting.[23,24] Therefore, the potential significance of the CALLY index in enhancing the information that is provided by conventional ICU scoring methods is noteworthy. The study sought to determine whether the integration of the CALLY index into current scoring systems like as APACHE II, MPM II, and TRISS could enhance the predictive accuracy for in-hospital mortality among trauma patients in the ICU. The research will involve a retrospective analysis of recorded trauma data spanning eight years at a Level I trauma center.

Methods

Enrollment of Patients and Data Collection

This retrospective study examined medical records from the Trauma Registry System for the period of January 1, 2016, to December 31, 2023, and it was carried out at a Level I trauma facility in southern Taiwan. The study was approved by the Institutional Review Board with the number 202401468B0 before to starting. The data of each trauma patient was prospectively input into the systems by two well-trained accredited nurses following the examination of the responsible trauma surgeon. The study included all trauma patients who were hospitalized in the ICU. Those patients without CRP or albumin data were removed from the study cohort. Exclusion criteria include persons without CALLY data, those with hanging injuries, and individuals with incomplete demographic information. The research methodology involved systematically recording patients' gender, age, comorbidities, Glasgow Coma Scale (GCS) scores, Injury Severity Scores (ISS), and in-hospital mortality. The CALLY index was determined by multiplying the albumin level by the lymphocyte count, then dividing the result by the CRP level as follows: CALLY index = [albumin (g/dL) × lymphocyte count (10^9/L)]/CRP (mg/L).[30] To evaluate the CALLY index's predictive power, the study utilized existing mortality prediction models from the trauma registry database, including APACHE II,[5] MPM II (at ICU admission),[4,6,7] MPM24 II (24 hours post-admission), MPM48 II (48 hours post-admission), and TRISS,[1–3] providing a comprehensive comparative analysis of prognostic tools in trauma care.

Statistical Analysis

Statistical analyses were conducted using a combination of R version 4.1.3 and SPSS for Windows version 23.0 (IBM Inc., Chicago, IL, USA). For non-parametric data, the Mann–Whitney *U*-test was applied, while associations between categorical variables were assessed using the Chi-square test. Continuous variables were expressed as median with interquartile range (IQR) to account for potential skewness in the data distribution. The predictive performance of the models was quantified using the area under the receiver operating characteristic curve (AUC-ROC), calculated with the pROC package in R. Model calibration was assessed through calibration curves, calibration intercept, and calibration slope with all parameters computed using the rms package in R. This method allows for a comprehensive evaluation of each model's predictive performance and discriminative ability across various threshold settings. To ensure robust statistical inference, a significance level of α = 0.05 was adopted for all analyses, with two-tailed p-values below this threshold considered statistically significant.

Results

Study Patient Cohort

Figure 1 illustrates that 3540 trauma patients in the ICU from 2016 to 2023 were selected from the Trauma Registry System. A total of 1242 trauma patients admitted to the ICU were designated as the study cohort after excluding 7 patients with hanging injuries, 24 patients with incomplete demographic data, and 2267 patients with absent CALLY data. Out of them, 1090 patients survived, whilst 152 people did not.

Patients and Injury Demographics

There was no difference regarding the sex predominance in the deceased or survival patients (Table 1). Non-survivors were older (median age 67.50 vs 57.00 years, p<0.001) and had higher severity scores, including APACHE II (median 32.23 vs

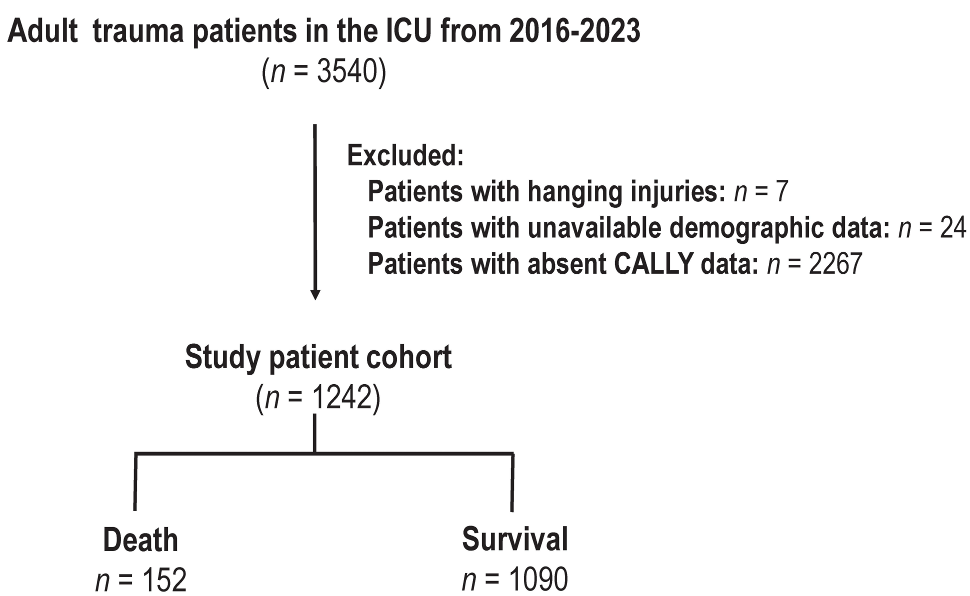

Figure 1 Algorithm in the selection of study patient cohort.
Abbreviations: CALLY, the C-reactive protein-albumin-lymphocyte index; ICU, Intensive Care Unit.

Table 1 Patients and Injury Demographic in the Deceased and Survival Patients

Variables	Death n = 152	Survival n = 1090	P
Sex			0.715
Male, n (%)	106 (69.7)	740 (67.9)	
Female, n (%)	46 (30.3)	350 (32.1)	
Age, years	67.50 [49.50, 79.25]	57.00 [40.00, 70.00]	<0.001
APACHE II	32.23 [23.49, 49.68]	14.62 [7.62, 23.49]	<0.001
TRISS	0.80 [0.40, 0.91]	0.94 [0.82, 0.97]	<0.001
MPM II	33.40 [17.20, 57.02]	11.10 [6.53, 18.78]	<0.001
MPM II 24	24.36 [14.76, 47.88]	7.64 [4.26, 12.97]	<0.001
MPM II 48	26.70 [16.57, 49.99]	9.89 [5.42, 16.45]	<0.001
CALLY	1.74 [0.39, 7.15]	1.67 [0.56, 6.94]	0.380
Albumin, g/dL	3.10 [2.60, 3.60]	3.50 [3.10, 3.90]	<0.001
Lymphocyte count, 10^9/L	1.23 [0.73, 2.45]	1.20 [0.70, 2.18]	0.639
CRP, mg/L	3.82 [0.87, 10.29]	3.90 [0.92, 9.07]	0.893
Comorbidities			
CVA, n (%)	8 (5.3)	51 (4.7)	0.909
HTN, n (%)	69 (45.4)	349 (32.0)	0.001
CAD, n (%)	20 (13.2)	91 (8.3)	0.073
CHF, n (%)	3 (2.0)	7 (0.6)	0.216
DM, n (%)	41 (27.0)	239 (21.9)	0.197
ESRD, n (%)	14 (9.2)	31 (2.8)	<0.001
GCS	7.00 [4.00, 11.00]	11.00 [9.00, 15.00]	<0.001
ISS	25.00 [17.75, 34.00]	20.00 [16.00, 25.00]	<0.001
ICU stay, days	9.00 [4.00, 18.00]	6.00 [4.00, 13.00]	0.003

Note: The continuous data is presented as median [IQR].
Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; CAD, coronary artery disease; CALLY, the C-reactive protein-albumin-lymphocyte index; CHF, congestive heart failure; CI, confidence interval; CVA, cerebral vascular accident; CLR, C-Reactive Protein to Lymphocyte Ratio; DM, diabetes mellitus; ESRD, end-stage renal disease; GCS, Glasgow Coma Scale; HTN, hypertension; IQR, interquartile range; ICU, Intensive Care Unit; ISS, injury severity score; MPM, Mortality Probability Mo TRISS, Trauma Score and Injury Severity Score.

14.62, p<0.001), lower TRISS (median 0.80 vs 0.94, p<0.001), and higher MPM II scores (all p<0.001). Non-survivors also exhibited lower albumin levels (median 3.10 vs 3.50 g/dL, p<0.001), lower GCS scores (median 7.00 vs 11.00, p<0.001), and higher ISS (median 25.00 vs 20.00, p<0.001). Comorbidities such as hypertension (45.4% vs 32.0%, p = 0.001) and end-stage renal disease (9.2% vs 2.8%, p<0.001) were more prevalent in non-survivors than those survivors. Notably, we observed no significant differences in lymphocyte count, C-reactive protein levels, or CALLY scores between the deceased and survival patients. Non-survivors had longer ICU stays (median 9.00 vs 6.00 days, p = 0.003).

Evaluation of Adding CALLY Index to Improve Mortality Prediction Models

As demonstrated in Figure 2, adding the CALLY index to the APACHE II model resulted in a very marginal increase, with the AUC increasing slightly from 0.811 to 0.812 but not significantly. Furthermore, when assessing the MPM II, MPM24 II, and MPM48 II models, the CALLY index integration had no effect on the AUC values, which remained at 0.826, 0.845, and 0.832, respectively. Notably, the TRISS model, which had an initial AUC of 0.731, saw a modest fall to 0.725 after adding the CALLY index. Statistically, these AUC differences (ranging from +0.001 to –0.006) are negligible and did not reach significance. This suggests that incorporating CALLY failed to enhance the prognostic models' ability to distinguish survivors from non-survivors in this trauma ICU cohort. In conclusion, the CALLY index does not considerably improve the predicted performance of the APACHE II and MPM models, and it may even slightly reduce the performance of the TRISS model. These results indicate that the CALLY index may not be a universally advantageous addition to all mortality prediction models in trauma care.

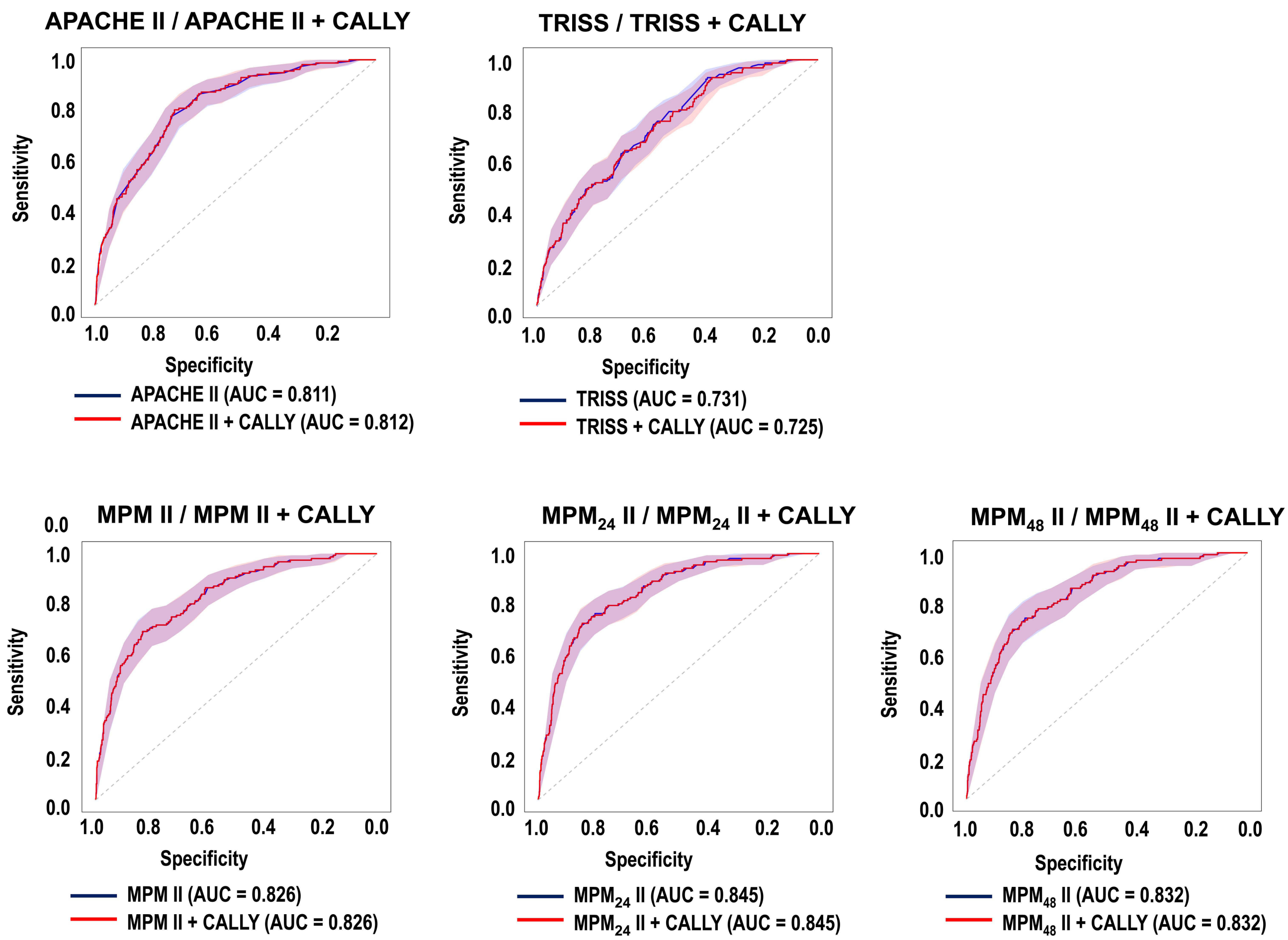

Figure 2 Evaluation of prediction performance by AUC with 95% confidence interval with the addition of the C-reactive protein-albumin-lymphocyte (CALLY) index in the mortality prediction models.

Calibration Curve of Adding CALLY Index in the Mortality Prediction Models

Figure 3 illustrates calibration curves for five mortality prediction models incorporating the CALLY index. Calibration reflects how well a model's predicted mortality probabilities align with actual observed mortality rates. In an ideally calibrated model, predictions match outcomes across all risk levels (points falling on the 45° line of identity). In these plots, however, the observed-vs-predicted trends deviate from the ideal line, indicating areas of miscalibration. In these plots, however, the observed-vs-predicted trends deviate from the ideal line, indicating areas of miscalibration. Notably, the TRISS + CALLY model appears to under-predict mortality for high-risk trauma patients (its curve falls below ideal at the high end), while still slightly over-predicting in low-risk groups – a pattern consistent with an overall calibration slope >1 (indicating underestimation at high risk and overestimation at low risk). The APACHE II and MPM-based models with CALLY show relatively closer alignment but still exhibit mild miscalibration in extreme risk strata, suggesting that adding the CALLY index did not markedly improve agreement between predicted and actual mortality.

Discussion

Although the CALLY index has shown significant prognostic value across various cancers[13,16,18,31] and in infectious diseases.[32] Our study reveals a significant divergence from previous findings, showing that incorporating the CALLY index into traditional ICU scoring systems (APACHE II, MPM II, MPM24 II, MPM48 II, and TRISS) did not significantly enhance predictive performance for mortality outcome in trauma patients in the ICU. This contrasts with its effectiveness in chronic conditions like cancer and COVID-19, likely due to key differences between acute trauma and chronic diseases. While chronic diseases progress over weeks to months, allowing CALLY components to reach a steady

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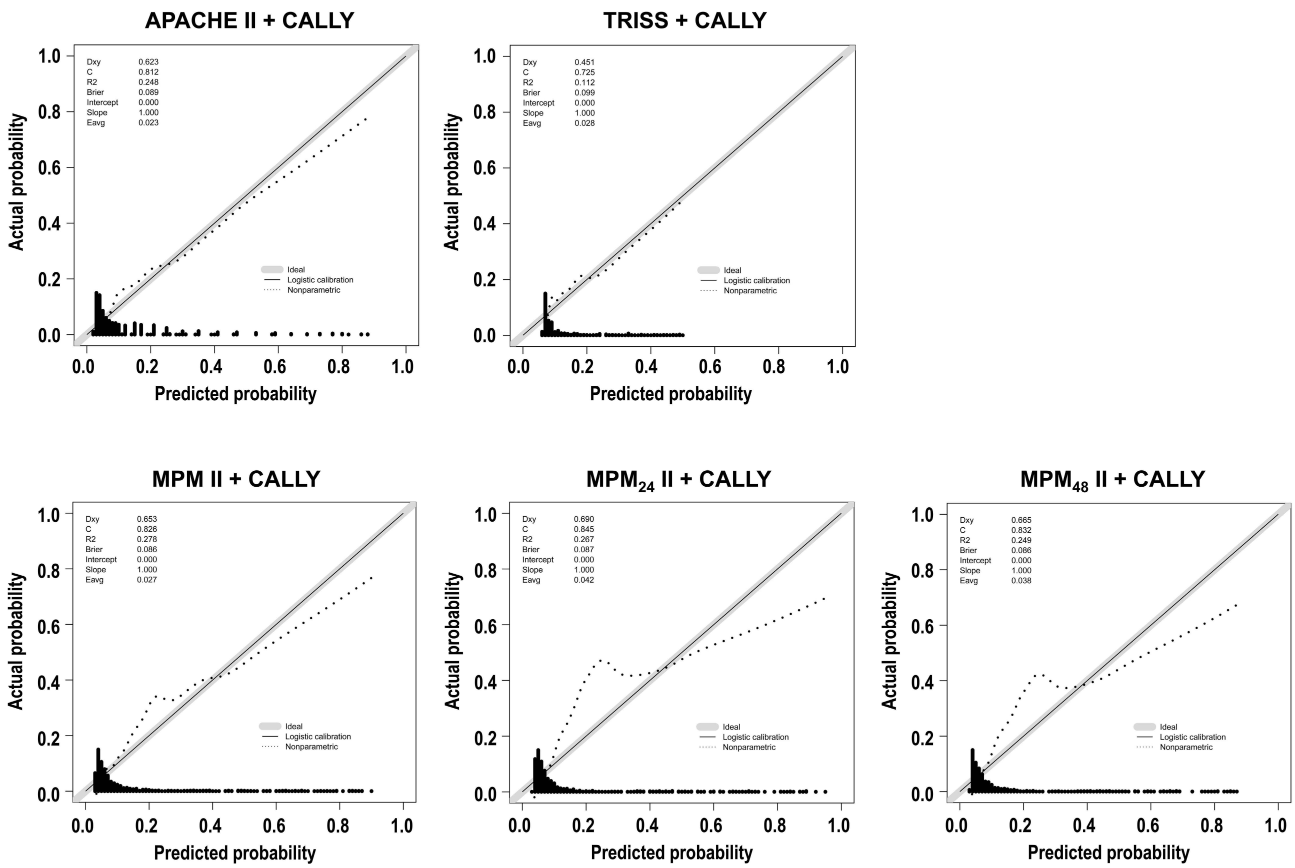

Figure 3 The calibration curves for five mortality prediction models incorporating the CALLY index.
Abbreviations: C, Concordance index; Dxy, Somers' Dxy rank correlation; R^2, Nagelkerke's R-squared; Brier, Brier score; APACHE, Acute Physiology and Chronic Health Evaluation; CALLY, the C-reactive protein-albumin-lymphocyte index; MPM, Mortality Probability Mo TRISS, Trauma Score and Injury Severity Score.

state,[33,34] trauma patients experience rapid fluctuations due to immediate interventions.[35] The inflammatory response in trauma is highly variable, depending on injury type and severity,[36] and patients have diverse baseline health statuses suddenly altered by injury. These factors may limit the CALLY index's ability to capture the complex, dynamic physiological changes in trauma patients, reducing its effectiveness in this context compared to chronic conditions.

The CALLY index's prognostic power diverges between chronic illnesses and acute trauma may be attributed by fundamental differences in pathophysiology. In chronic conditions such as advanced cancers, long-standing infections, or end-stage organ failure, patients endure persistent systemic inflammation and immune dysregulation over weeks to months, coupled with gradual nutritional decline.[37–39] This results in chronically elevated CRP, hypoalbuminemia, and lymphopenia, which reach a steady state and reflect disease severity. Therefore, a low CALLY index (high CRP, low albumin/lymphocyte) strongly predicts worse outcomes in cancers and other chronic diseases, where it signifies ongoing metabolic-inflammation and immunosuppression. By contrast, severe trauma elicits a swift, biphasic immune response: an immediate surge of inflammatory mediators followed by a compensatory anti-inflammatory response.[40–42] This acute immune whirlwind causes volatile CRP and lymphocyte levels rather than stable changes. Trauma also triggers hypermetabolism and catabolism, acutely lowering albumin independent of prior nutrition.[43,44] Additionally, life-saving interventions in trauma such as fluid resuscitation, surgeries, or transfusions may rapidly alter inflammatory and nutritional parameters. These dynamic immunometabolic shifts prevent the CALLY components from equilibrating, diminishing its prognostic utility in trauma patients.

Several limitations must be acknowledged when interpreting the findings of this study. The retrospective form of our study constrains our capacity to control all possible confounding variables and may result in selection bias. Moreover, as a single-center study, the applicability of our findings to other contexts or populations may be constrained. The exclusion of patients without CALLY data, who constituted a significant fraction of the patient group, may introduce selection bias and undermine the representativeness of our sample. Furthermore, owing to data constraints, CALLY was assessed solely at admission rather than through time-dependent analysis, precluding examination of dynamic trajectories or temporal variations (eg, early versus late-phase patterns). Serial assessments of the CALLY index may yield valuable prognostic insights regarding its evolving predictive utility throughout ICU stay, though such approaches require further validation. Based on these findings, subsequent research might focus on monitoring variations in the CALLY index during the ICU admission to enhance comprehension of its predictive significance. Investigating its efficacy within particular trauma subgroups may uncover domains where it provides substantial benefit. Further investigation and studies of certain subgroups (such as severe trauma, infection, and comorbidities) may also be beneficial in order to comprehend the function of the CALLY index in these individuals with severe trauma. Future studies should focus on time-dependent inflammatory biomarkers and machine-learning–based models with a prospective multicenter validation to enhance mortality prediction accuracy in trauma ICU populations.

Conclusion

This study demonstrates that the CALLY index, despite its prognostic value in chronic conditions, does not significantly improve mortality prediction when integrated with traditional ICU scoring systems for trauma patients. The acute and dynamic nature of trauma physiology may limit the CALLY index's effectiveness in this context. These findings underscore the need for continued research to develop or refine prognostic tools specifically tailored to trauma patients' unique physiological responses in ICU settings, potentially exploring other biomarkers or combinations of existing tools.

Data Sharing Statement

De-identified data could be supplied only upon request for academic research projects via the corresponding author.

Ethic Statement

The Institutional Review Board (IRB) at Chang Gung Memorial Hospital approved the investigation, with approval number 202400927B0. The IRB waived the necessity for a informed consent owing to the retrospective examination of registration data within the study design. All patient data were de-identified prior to analysis, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki and approved by the institutional review board.

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Disclosure

The authors declare no conflicts of interest in this work.

References

1. Indurkar SK, Ghormade PS, Akhade S, Sarma B. Use of the Trauma and Injury Severity Score (TRISS) as a predictor of patient outcome in cases of trauma presenting in the trauma and emergency department of a tertiary care institute. *Cureus*. 2023;15:e40410. doi:10.7759/cureus.40410
2. Schluter PJ. The Trauma and Injury Severity Score (TRISS) revised. *Injury*. 2011;42:90–96. doi:10.1016/j.injury.2010.08.040
3. Champion HR, Sacco WJ, Carnazzo AJ, Copes W, Fouty WJ. Trauma score. *Crit Care Med*. 1981;9:672–676. doi:10.1097/00003246-198109000-00015
4. Wu SC, Chou SE, Liu HT, et al. Performance of prognostic scoring systems in trauma patients in the intensive care unit of a trauma center. *Int J Environ Res Public Health*. 2020;17:7226. doi:10.3390/ijerph17197226

5. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13:818–829.
6. Lemeshow S, Teres D, Klar J, Avrunin JS, Gehlbach SH, Rapoport J. Mortality Probability Models (MPM II) based on an international cohort of intensive care unit patients. *JAMA*. 1993;270:2478–2486.
7. Lemeshow S, Klar J, Teres D, et al. Mortality probability models for patients in the intensive care unit for 48 or 72 hours: a prospective, multicenter study. *Crit Care Med*. 1994;22:1351–1358. doi:10.1097/00003246-199409000-00003
8. Kaya M, Yildirim H, Toprak M, Ulu M. Comparison of trauma scoring systems for predicting mortality in emergency department patients with traffic-related multiple trauma. *Diagnostics*. 2025;15:1563.
9. Ha M, Yu S, Kim BC, Choi HJ. Nationwide evaluation of the validity of the trauma and injury severity score method in Korean regional trauma centers using multi-institutional large-scale data. *J Korean Med Sci*. 2024;39:e288. doi:10.3346/jkms.2024.39.e288
10. Fukushima N, Masuda T, Tsuboi K, et al. Prognostic significance of the preoperative C-reactive protein-albumin-lymphocyte (CALLY) index on outcomes after gastrectomy for gastric cancer. *Surg Today*. 2024;54:943–952. doi:10.1007/s00595-024-02813-1
11. Furukawa K, Tsunematsu M, Tanji Y, et al. Impact of C-reactive protein-albumin-lymphocyte (CALLY) index on prognosis after hepatectomy for colorectal liver metastasis. *Surg Oncol*. 2023;47:101911. doi:10.1016/j.suronc.2023.101911
12. Hashimoto I, Tanabe M, Onuma S, et al. Clinical impact of the C-reactive protein-albumin-lymphocyte index in post-gastrectomy patients with gastric cancer. *In Vivo*. 2024;38:911–916. doi:10.21873/invivo.13518
13. Li J, Zhang S, Hu X, Huang T, Chen M. Correlation between the C-reactive protein (CRP)-albumin-lymphocyte (CALLY) index and the prognosis of gastric cancer patients after gastrectomy: a systematic review and meta-analysis. *Surg Today*. 2024. doi:10.1007/s00595-024-02921-y
14. Özdemir S, Özkan A. The importance of the CALLY index as a non-invasive prognostic biomarker in SARS-CoV-2 infected patients: an analytical study: CALLY index in SARS-CoV-2 infection. *Med Sci Discov*. 2023;10:6. doi:10.36472/msd.v10i7.967
15. Takeda Y, Sugano H, Okamoto A, et al. Prognostic usefulness of the C-reactive protein-albumin-lymphocyte (CALLY) index as a novel biomarker in patients undergoing colorectal cancer surgery. *Asian J Surg*. 2024;47:3492–3498. doi:10.1016/j.asjsur.2024.03.054
16. Tsunematsu M, Haruki K, Taniai T, et al. The impact of C-reactive protein-albumin-lymphocyte (CALLY) index on the prognosis of patients with distal cholangiocarcinoma following pancreaticoduodenectomy. *Ann Gastroenterol Surg*. 2023;7:503–511. doi:10.1002/ags3.12637
17. Tsai YT, Ko CA, Chen HC, et al. Prognostic value of CRP-Albumin-Lymphocyte (CALLY) index in patients undergoing surgery for oral cavity cancer. *J Cancer*. 2022;13:3000–3012. doi:10.7150/jca.74930
18. Yang M, Lin SQ, Liu XY, et al. Association between C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with colorectal cancer: from the investigation on nutrition status and clinical outcome of common cancers study. *Front Immunol*. 2023;14:1131496. doi:10.3389/fimmu.2023.1131496
19. Wang W, Gu J, Liu Y, et al. Pre-treatment CRP-Albumin-Lymphocyte Index (CALLY Index) as a prognostic biomarker of survival in patients with epithelial ovarian cancer. *Cancer Manag Res*. 2022;14:2803–2812. doi:10.2147/cmar.S359968
20. Nakashima K, Haruki K, Kamada T, et al. Usefulness of the C-Reactive Protein (CRP)-Albumin-Lymphocyte (CALLY) index as a prognostic indicator for patients with gastric cancer. *Am Surg*. 2024;90:2703–2709. doi:10.1177/00031348241248693
21. Yang YW, Wu CH, Tsai HT, et al. Dynamics of immune responses are inconsistent when trauma patients are grouped by injury severity score and clinical outcomes. *Sci Rep*. 2023;13:1391. doi:10.1038/s41598-023-27969-7
22. Dobson GP, Morris JL, Letson HL. Immune dysfunction following severe trauma: a systems failure from the central nervous system to mitochondria. *Front Med*. 2022;9:968453. doi:10.3389/fmed.2022.968453
23. van de Vyver M. Immunology of chronic low-grade inflammation: relationship with metabolic function. *J Endocrinol*. 2023;257:e220271. doi:10.1530/joe-22-0271
24. Zotova N, Zhuravleva Y, Chereshnev V, Gusev E. Acute and chronic systemic inflammation: features and differences in the pathogenesis, and integral criteria for verification and differentiation. *Int J Mol Sci*. 2023;24:1144. doi:10.3390/ijms24021144
25. Poblete RA, Pena J, Kuo G, et al. Immunonutrition with Omega-3 fatty acid supplementation in severe TBI: retrospective analysis of patient characteristics and outcomes. *Neurotrauma Rep*. 2024;5:574–583. doi:10.1089/neur.2024.0005
26. Jandari S, Rezvani R, Yousefian S, et al. The effect of low dietary inflammatory index score formula on inflammatory, metabolic, and clinical outcomes in critically ill traumatic brain injury patients: a single-blind randomized controlled pilot study. *Food Sci Nutr*. 2023;11:3365–3375. doi:10.1002/fsn3.3326
27. Ye J, Hu X, Wang Z, et al. The role of mtDAMPs in the trauma-induced systemic inflammatory response syndrome. *Front Immunol*. 2023;14:1164187. doi:10.3389/fimmu.2023.1164187
28. Mileković M. Trauma-induced systemic inflammatory response: a comprehensive review. *J Surg Res Prac*. 2023.
29. Janicova A, Relja B. Neutrophil phenotypes and functions in trauma and trauma-related sepsis. *Shock*. 2021;56:16–29. doi:10.1097/shk.0000000000001695
30. Feng J, Wang L, Yang X, Chen Q. Clinical significance of preoperative CALLY index for prognostication in patients with esophageal squamous cell carcinoma undergoing surgery. *Sci Rep*. 2024;14:713. doi:10.1038/s41598-023-51109-w
31. Zhuang J, Wang S, Wang Y, Wu Y, Hu R. Prognostic value of CRP-Albumin-Lymphocyte (CALLY) index in patients undergoing surgery for breast cancer. *Int J Gen Med*. 2024;17:997–1005. doi:10.2147/ijgm.S447201
32. Zhang J, Zhao Q, Liu S, Yuan N, Hu Z. Clinical predictive value of the CRP-albumin-lymphocyte index for prognosis of critically ill patients with sepsis in intensive care unit: a retrospective single-center observational study. *Front Public Health*. 2024;12:1395134. doi:10.3389/fpubh.2024.1395134
33. Frey A, Martin D, D'Cruz L, Fokas E, Rödel C, Fleischmann M. C-reactive protein to albumin ratio as prognostic marker in locally advanced non-small cell lung cancer treated with chemoradiotherapy. *Biomedicines*. 2022;10:598. doi:10.3390/biomedicines10030598
34. Dou L, Shi M, Song J, et al. The prognostic significance of C-reactive protein to albumin ratio in newly diagnosed acute myeloid leukaemia patients. *Cancer Manag Res*. 2022;14:303–316. doi:10.2147/cmar.S343580
35. Gong Y, Tang Y, Xue Y, Chen L. Impact of intraoperative allogenic and autologous transfusion on immune function and prognosis in patients with hepatocellular carcinoma. *Medicine*. 2020;99:e22568. doi:10.1097/md.0000000000022568
36. Vijapur SM, Vaughan LE, Awan N, DiSanto D, McKernan GP, Wagner AK. Treelet transform analysis to identify clusters of systemic inflammatory variance in a population with moderate-to-severe traumatic brain injury. *Brain Behav Immun*. 2021;95:45–60. doi:10.1016/j.bbi.2021.01.026
37. Zhang L, Bonomi PD. Immune system disorder and cancer-associated cachexia. *Cancers*. 2024;16:1709. doi:10.3390/cancers16091709

38. Efron PA, Brakenridge SC, Mohr AM, et al. The persistent inflammation, immunosuppression, and catabolism syndrome 10 years later. *J Trauma Acute Care Surg*. 2023;95:790–799. doi:10.1097/ta.0000000000004087
39. Thakir TM, Wang AR, Decker-Farrell AR, et al. Cancer therapy and cachexia. *J Clin Invest*. 2025;135. doi:10.1172/jci191934
40. Meza Monge K, Ardon-Lopez A, Pratap A, Idrovo JP. Targeting inflammation after hemorrhagic shock as a molecular and experimental journey to improve outcomes: a review. *Cureus*. 2025;17:e77776. doi:10.7759/cureus.77776
41. Meza Monge K, Rosa C, Sublette C, Pratap A, Kovacs EJ, Idrovo JP. Navigating hemorrhagic shock: biomarkers, therapies, and challenges in clinical care. *Biomedicines*. 2024;12:2864. doi:10.3390/biomedicines12122864
42. Huang C-Y, Wu S-C, Liao K-H, Lin P-C, Chien P-C, Hsieh C-H. Integration of stress and immunoinflammatory indices into Intensive Care Unit scoring systems for mortality prediction in trauma patients: a retrospective cohort study. *Formosan J Surg*. 2025;58:161–167. doi:10.1097/fs9.0000000000000215
43. Stepanovic L, Govindarajulu U, Agriantonis G, et al. Albuminemia as a potential predictor of clinical outcomes in patients with severe Traumatic Brain Injury (TBI). *J Clin Med*. 2025;14:7499. doi:10.3390/jcm14217499
44. Nicholson T, Belli A, Lord JM, Hazeldine J. The impact of trauma relevant concentrations of prostaglandin E(2) on the anti-microbial activity of the innate immune system. *Front Immunol*. 2024;15:1401185. doi:10.3389/fimmu.2024.1401185