

ORIGINAL RESEARCH



Association of C-reactive protein-to-lymphocyte ratio and mortality outcome in patients with trauma admitted to an intensive care unit

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Abstract

Background: Inflammation and immune dysregulation shape outcomes after major trauma, yet practical biomarkers that add prognostic value in the intensive care unit (ICU) are limited. The C-reactive protein-to-lymphocyte ratio (CLR) integrates inflammatory burden and host immune status. This study aimed to evaluate the association between CLR at admission and in-hospital mortality among adult trauma patients admitted to the ICU, and to characterize the discriminate performance of CLR. **Methods:** This was a retrospective single-center cohort study at a level I trauma center in southern Taiwan, including consecutive adults (≥ 20 years) with traumatic injury admitted to the ICU from 2016–2022. Patients with burns, hanging, drowning, incomplete Injury Severity Score (ISS), or missing laboratory data were excluded. The final analytic cohort comprised 1985 patients (217 deaths, 1768 survivors). **Results:** Higher CLR was independently associated with mortality (multivariable odds ratio (OR), 1.03; 95% confidence interval (CI), 1.01–1.06; $p = 0.021$). Other independent predictors included older age, end-stage renal disease, lower Glasgow Coma Scale score, and higher ISS. Receiver operating characteristic (ROC) analysis identified a CLR cutoff of 93.6 with high specificity but low sensitivity (specificity, 0.874; sensitivity, 0.230; area under curve (AUC), 0.515). Compared with CLR < 93.6 , CLR ≥ 93.6 was associated with higher adjusted odds of death (adjusted OR, 1.71; 95% CI, 1.16–2.51; $p = 0.007$) and longer length of stay (mean 24.4 vs. 18.9 days; $p < 0.001$). Survival curves differed significantly between CLR groups (log-rank $p = 0.007$). **Conclusions:** Admission CLR correlates with mortality risk and prolonged hospitalization in ICU trauma patients, but its standalone discriminative performance is poor. CLR may help flag a high-risk subgroup given its specificity, yet it should be used only in conjunction with established clinical variables and injury-severity measures. Prospective, multicenter studies with serial CLR measurements and comparison to other inflammatory ratios are warranted.

Keywords

Trauma; Mortality; Prognosis; Intensive care unit; Injury severity score; C-reactive protein-to-lymphocyte ratio

1. Introduction

Managing critically ill patients with trauma in the intensive care unit (ICU) is difficult because of the complexity and severity of their injuries [1], and trauma-induced immunosuppression increases infections, complications, and mortality [2]. Physiologic severity scores, such as the Acute Physiology and Chronic Health Evaluation, Sequential Organ Failure Assessment, and Simplified Acute Physiology Score, predict outcomes and support risk stratification [3–5]. However, urgent settings may preclude timely collection of the comprehensive data they require, and the C-reactive protein-to-lymphocyte ratio (CLR) offers a practical alternative in such

circumstances. Across conditions, elevated CLR is associated with worse short-term outcomes in severe acute respiratory syndrome coronavirus 2 infection—including higher risks of critical illness, mortality, and severe presentation in the emergency department [6]—and has also been shown to predict survival in non-small cell lung cancer and adverse outcomes in colorectal liver metastases [7, 8]. CLR also tracks acute pancreatitis severity and outcomes in dilated cardiomyopathy [9, 10], differentiates perforated versus acute appendicitis [11], and identifies postoperative surgical site infection after lumbar procedures [12] and periprosthetic joint infection [13]. As a simple, rapidly obtainable composite reflecting infection burden and host immunity, CLR can facilitate the

early identification of high-risk patients and guide targeted therapy [10, 14]. In trauma, C-reactive protein (CRP) levels increase rapidly post-injury, reaching a peak approximately on day 3 and corresponding with the severity of trauma and tissue damage. Persistent elevation suggests complications such as infection [15]. Lymphocyte counts commonly fall in the acute phase, reflecting immune dysregulation. The trajectory of lymphocyte fluctuations within the first seven days is significant for predicting late prognosis in patients with severe trauma [16], and the shift in early lymphocyte count may be utilized to predict prognosis in patients with trauma [17]. By combining the inflammatory response indicated by CRP levels with immune status reflected by lymphocyte counts, the CLR may offer valuable prognostic information for patients with trauma.

Despite the extensive use of CLR as a prognostic marker in nontraumatic conditions, its role in trauma remains unexplored. In particular, there has been little investigation into the predictive significance of CLR in trauma patients with critical illness in the ICU. Only one study has identified CLR as a meaningful predictor of 30-day mortality in older individuals after hip fracture surgery [18]. This study confirmed CLR as a strong indicator of mortality, revealing that patients who succumbed within 30 days exhibited markedly elevated preoperative CLR compared with survivors [18]. In contrast, CLR showed limited discriminative power as a standalone predictor of mortality in individuals with traumatic brain injury, although a significant association with mortality was still observed [19]. This difference emphasizes the necessity for larger-scale research to determine the predictive value of CLR in ICU patients with general trauma. The purpose of this study was, therefore, to determine the predictive significance of CLR in critically ill trauma patients admitted to the ICU.

2. Materials and methods

2.1 Patient enrollment and study design

Medical documents that were registered between 01 January 2016, and 31 December 2022 were offered by the Trauma Registry System at a Level I trauma center in southern Taiwan. Data from the Trauma Registry System were entered by two qualified registry nurses and then curated and validated by a trauma surgeon before being entered in the database. All patients with trauma admitted to the ICU aged 20 years or older were included. Patients sustained injuries from all causes of trauma, including motorcycle accidents, vehicle accidents, striking at/against objects, penetration injuries, and falls. Patients with an incomplete Injury Severity Score (ISS), unavailable laboratory data, or particular trauma mechanisms, such as burns, hangings, and drowning, were excluded from the study. For this investigation, both patients' medical records and the institutional trauma registry were systematically reviewed. Key demographic and clinical variables, including sex, age, and preexisting comorbidities, were extracted. Trauma-specific data included the mechanism of trauma, CLR, Glasgow Coma Scale (GCS), Abbreviated Injury Scale (AIS), ISS, and Trauma and Injury Severity Scores (TRISS). Additionally, outcome measures, such

as in-hospital mortality and length of hospital stay, were meticulously documented. Laboratory data of the patients were derived from the initial analysis of blood samples collected upon admission to the emergency room. The CLR was calculated by dividing the patient's CRP level (mg/L) by the lymphocyte count ($10^9/L$). Comorbidities were recorded according to International Classification of Diseases, 10th revision (ICD-10) codes in the patients' medical records. Cerebrovascular accidents (CVAs) were identified using ICD-10 codes, I63.x for cerebral infarction and I64 for unspecified stroke. Hypertension (HTN) corresponded to I10, which denotes essential (primary) hypertension. Coronary Artery Disease (CAD) is classified as I25.x, which represents chronic ischemic heart disease. Congestive Heart Failure (CHF) is coded as I50.x, covering various types of heart failure. Diabetes mellitus (DM) falls under codes E08–E13, with E11 commonly used for type 2 diabetes. End-stage renal disease (ESRD) is specifically coded as N18.6.

2.2 Statistical analysis

Categorical variables were compared between deceased and surviving patients using the chi-square test. Odds ratios (OR) with 95% confidence intervals were derived to assess the strength and direction of associations. Levene's test was used to confirm the homogeneity of variances, followed by analysis of variance for comparing normally distributed continuous variables, which are reported as mean \pm standard deviation (SD). The Mann-Whitney U test was utilized for non-normally distributed continuous variables, presented as median and interquartile range (IQR). We performed univariable and multivariable analyses to ascertain independent risk factors for death. The area under the receiver operating characteristic curve (AUC) was employed to ascertain the appropriate CLR cutoff value for predicting death, utilizing the Youden index. Patients were subsequently classified into groups according to whether their CLR readings exceeded or fell below this threshold. Adjusted odds ratios (AORs) were calculated for key variables, such as age, ESRD, GCS score, and ISS. All statistical analyses were performed using IBM SPSS Statistics (Version 23, IBM, Armonk, NY, USA), with a significance level set at $p < 0.05$.

3. Results

3.1 Enrollment of the study patient cohort

The study cohort consisted of 26,605 trauma patients from the Trauma Registry System, spanning the years 2016 to 2022 (Fig. 1). Of these, 24,193 were adults aged 20 years or older. There were 3540 adult patients that were hospitalized to the ICU. After removing patients with burns ($n = 65$), hanging injuries ($n = 5$), drowning ($n = 1$), missing lab data ($n = 1480$), and inadequate ISS data ($n = 4$), the final study group consisted of 1985 patients. Within this cohort, 217 deaths occurred, and 1768 patients survived.

Trauma patients in the Trauma Registry System (2016–2022)

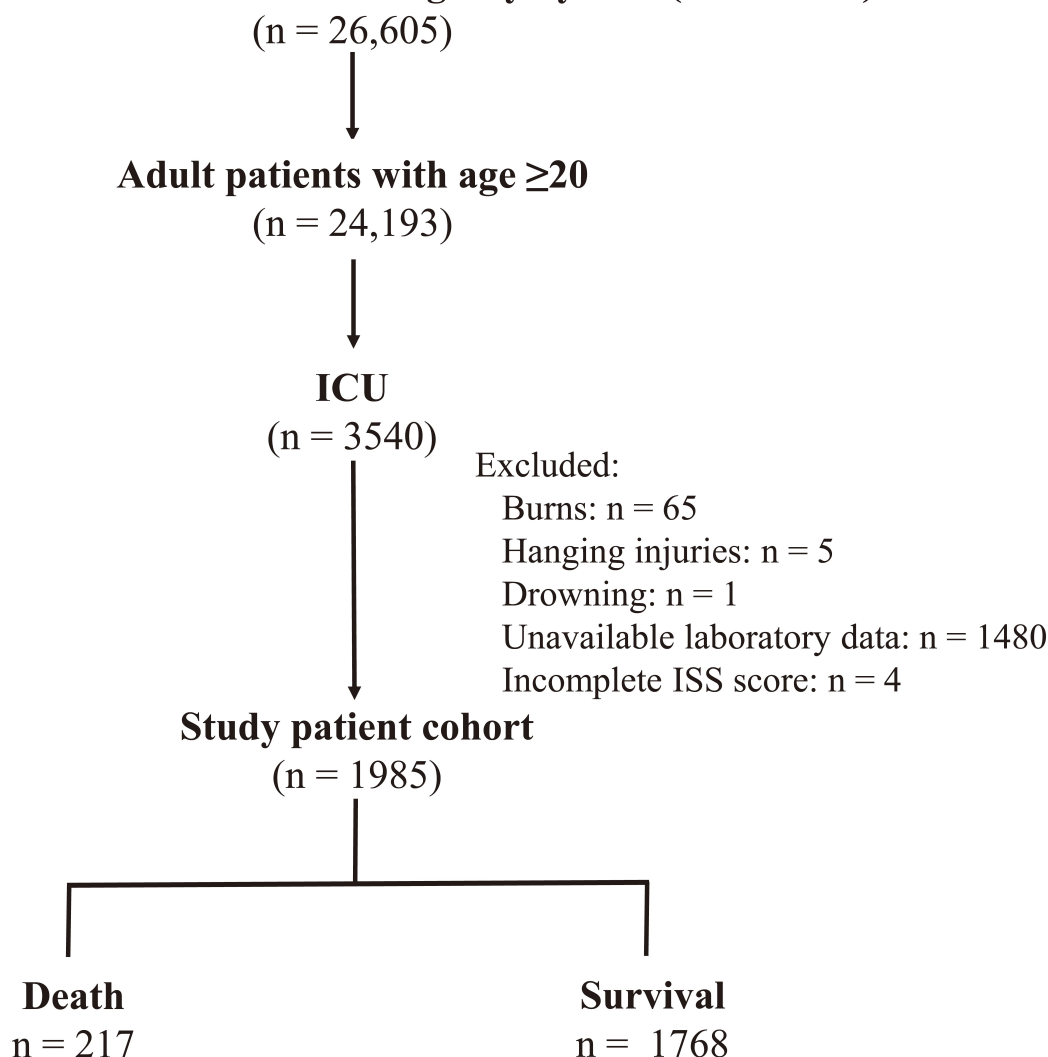


FIGURE 1. Enrollment process of adult trauma patients into the study cohort. ICU: intensive care unit; ISS: injury severity score.

3.2 Injury and clinical characteristics of deceased and surviving patients

The demographic and clinical characteristics of the deceased and surviving patients within the study cohort are presented in Table 1, which emphasizes the substantial disparities between the two groups. Survivors were considerably younger than deceased patients (mean age 56.2 years vs. 65.0 years, $p < 0.001$). They exhibited significantly elevated CRP levels (70.4 vs. 57.2 mg/L; $p = 0.006$) and higher CLR (62.1 vs. 43.8; $p = 0.001$). The prevalence of comorbidities, such as HTN (46.1% vs. 34.6%; $p = 0.001$), CAD (14.7% vs. 8.3%; $p = 0.002$), and ESRD (8.3% vs. 2.6%; $p < 0.001$), was significantly higher in the deceased than in surviving patients. The deceased patients had significantly lower GCS scores (median 7 vs. 15; $p < 0.001$) and more severe injuries, as reflected in higher AIS scores for the head/neck (86.2% vs. 74.2%; $p < 0.001$) and lower AIS score for abdomen (12.4% vs. 20.0%; $p = 0.007$), as well as higher ISS (median 25 vs. 18; $p < 0.001$) than the surviving patients. The TRISS of the deceased patients was significantly lower than that of the surviving patients ($0.62 \pm$

0.31 vs. 0.87 ± 0.19 ; $p < 0.001$). Patients who died had a shorter hospital stay than those who survived (mean 14.8 vs. 20.2 days; $p < 0.001$).

3.3 Univariable and multivariable analysis of factors associated with mortality

Table 2 shows that older age (OR, 1.03; $p < 0.001$), higher CLR (OR, 1.03; $p = 0.001$), higher CRP levels (OR 1.03, $p = 0.007$), and having comorbidities, like high blood pressure (OR, 1.62; $p = 0.001$), CAD (OR, 1.91; $p = 0.002$), or ESRD (OR, 3.39; $p < 0.001$), were all significantly linked to a higher risk of mortality in patients with trauma.

Lower GCS scores (OR, 0.83; $p < 0.001$) and higher ISS (OR, 1.07; $p < 0.001$) were also significantly associated with mortality. The multivariate analysis identified higher CLR (AOR, 1.03; 95% CI 1.01–1.06; $p = 0.021$) as an independent risk factor for mortality, but neither CRP level nor lymphocyte count alone were associated with the patient's mortality. In addition, older age (AOR, 1.03; $p < 0.001$) and the presence of ESRD (AOR, 3.37; $p < 0.001$) were significantly associated

TABLE 1. Patient and injury characteristics of the deceased and survived patients.

Variables	Death n = 217	Survival n = 1768	OR (95% CI)	p
Male, n (%)	153 (70.5)	1143 (64.6)	1.31 (0.96–1.78)	0.087
Age, yr (mean ± SD)	65.0 ± 18.2	56.2 ± 19.7	-	<0.001
CLR	62.1 ± 109.8	43.8 ± 67.4	-	0.001
CRP (mg/L)	70.4 ± 85.6	57.2 ± 65.1	-	0.006
Lymphocyte (10 ⁹ /L)	2.1 ± 1.6	1.9 ± 1.4	-	0.120
Comorbidities, n (%)				
CVA	12 (5.5)	85 (4.8)	1.16 (0.62–2.16)	0.641
HTN	100 (46.1)	611 (34.6)	1.62 (1.22–2.15)	0.001
CAD	32 (14.7)	147 (8.3)	1.91 (1.26–2.88)	0.002
CHF	3 (1.4)	11 (0.6)	2.24 (0.62–8.09)	0.207
DM	54 (24.9)	371 (21.0)	1.25 (0.90–1.73)	0.186
ESRD	18 (8.3)	46 (2.6)	3.39 (1.93–5.95)	<0.001
GCS, median (IQR)	7 (3–15)	15 (10–15)	-	<0.001
AIS ≥2, n (%)				
Head/neck	187 (86.2)	1312 (74.2)	2.17 (1.45–3.23)	<0.001
Face	37 (17.1)	304 (17.2)	0.99 (0.68–1.44)	0.958
Thorax	73 (33.6)	539 (30.5)	1.16 (0.86–1.56)	0.342
Abdomen	27 (12.4)	354 (20.0)	0.57 (0.37–0.86)	0.007
Extremity	78 (35.9)	674 (38.1)	0.91 (0.68–1.22)	0.533
ISS, median (IQR)	25 (16–29)	18 (16–25)	-	<0.001
TRISS	0.62 ± 0.31	0.87 ± 0.19	-	<0.001
Hospital stay (d)	14.8 ± 25.3	20.2 ± 16.4	-	<0.001

AIS: Abbreviated Injury Scale; CAD: coronary artery disease; CHF: congestive heart failure; CI: confidence interval; CVA: cerebral vascular accident; CRP: C-reactive protein; CLR: CRP (mg/L)/Lymphocyte (10⁹/L); DM: diabetes mellitus; ESRD: end-stage renal disease; GCS: Glasgow Coma Scale; HTN: hypertension; IQR: interquartile range; ISS: injury severity score; OR: odds ratio; SD: standard deviation; TRISS: The Trauma and Injury Severity Score.

TABLE 2. Univariable and multivariable analysis of factors associated with mortality in trauma patients admitted to intensive care unit.

Mortality	Univariable analysis			Multivariable analysis		
	OR	CI	p	AOR	CI	p
Age (yr)	1.03	(1.02–1.03)	<0.001	1.03	(1.02–1.04)	<0.001
CLR	1.03	(1.01–1.04)	0.001	1.03	(1.01–1.06)	0.021
CRP (mg/L)	1.03	(1.01–1.05)	0.007	0.99	(0.96–1.02)	0.347
Lymphocyte (10 ⁹ /L)	2.03	(0.83–4.99)	0.121	1.74	(0.55–5.43)	0.344
HTN	1.62	(1.22–2.15)	0.001	1.05	(0.75–1.49)	0.770
CAD	1.91	(1.26–2.88)	0.002	1.59	(0.99–2.55)	0.053
ESRD	3.39	(1.93–5.95)	<0.001	3.37	(1.76–6.45)	<0.001
GCS	0.83	(0.81–0.86)	<0.001	0.84	(0.82–0.87)	<0.001
ISS	1.07	(1.05–1.09)	<0.001	1.05	(1.04–1.07)	<0.001

CAD: coronary artery disease; CI: confidence interval; CRP: C-reactive protein; CLR: CRP (mg/L)/Lymphocyte (10⁹/L); ESRD: end-stage renal disease; GCS: Glasgow Coma Scale; HTN: hypertension; ISS: injury severity score; OR: odds ratio; AOR: adjusted odds ratio.

with increased mortality. Additionally, lower GCS scores (AOR, 0.84; $p < 0.001$) and higher ISS (AOR, 1.05; $p < 0.001$) were significant predictors of mortality.

3.4 Comparison of patients grouped by value of CLR

Fig. 2 shows the ROC curve analysis for CLR in predicting mortality. An optimal CLR cutoff value of 93.6 was determined. At this cutoff, the specificity was 0.874; however, the predictive performance of CLR was poor (AUC, 0.515; sensitivity, 0.230). As shown in Table 3, patients were stratified into high (≥ 93.6) and low (< 93.6) CLR groups to compare demographics and clinical outcomes.

Patients with high CLR scores were more likely to be male (75.0% vs. 63.7%; $p < 0.001$) and older (mean age 60.3 vs. 56.7 years; $p = 0.004$). They also had a higher prevalence of comorbidities, such as CVAs (7.4% vs. 4.5%; $p = 0.042$) and ESRD (6.2% vs. 2.7%; $p = 0.002$). The high CLR group showed a greater incidence of significant thoracic injuries (AIS ≥ 2) (37.9% vs. 29.7%; $p = 0.007$) and extremity injuries (47.8% vs. 36.3%; $p < 0.001$). The ISS was higher in the high CLR group (median 20 vs. 20, $p = 0.048$) than in the low CLR group. Mortality was significantly higher in patients with high CLR scores than in those with low CLR scores (18.4% vs. 9.78%; $p < 0.001$), with an AOR of 1.71 (95% CI 1.16–2.51; $p = 0.007$). The patients with high CLR scores also had longer hospital stays (mean 24.4 vs. 18.9 days; $p < 0.001$) than those with low CLR scores. The Kaplan-Meier survival curves demonstrated a significant difference between the high and low CLR groups, with a Log Rank test $p = 0.007$ (Fig. 3).

4. Discussion

This study demonstrated that the CLR is a significant independent risk factor for mortality among patients with trauma admitted to the ICU. In these patients, a high CLR level correlates with longer hospital stays and increased mortality. However, CLR alone has poor predictive ability for mortality outcomes, as shown by its limited accuracy (AUC, 0.515; sensitivity, 0.230). Some studies in various clinical settings [9, 10, 12] have reported a strong predictive value of CLR; however, this result contradicts their findings. Trauma involves diverse acute injury mechanisms that trigger distinct inflammatory responses, unlike chronic conditions characterized by prolonged inflammation. Furthermore, complex and heterogeneous nature of trauma, often affecting multiple organ systems, makes it challenging for a single biomarker, such as CLR, to accurately predict outcomes across diverse cases. Various diseases have proposed different CLR cutoff values for diagnostic purposes. Tondangu *et al.* [6] found that in patients with coronavirus disease 2019, CLR thresholds of 78.3 and 159.5 for predicting infection and mortality showed sensitivities of 79% and 48% and specificities of 47% and 70%, respectively. Unlike CLR cutoff values of 21.25, 30.835, and 0.45, which are respectively suggested for the Omicron BA.2.2 variant infection [20], acute pancreatitis [10], and acute appendicitis perforation [11], this study identified an optimal CLR cutoff of 93.6 for predicting mortality in ICU trauma patients. Considering that the predictive performance of CLR in patients with trauma in the ICU is poor (AUC, 0.515) and has low sensitivity (0.230) but high specificity (0.874), a high CLR may indicate specific inflammatory or infectious conditions and identify patients at high risk for mortality, while its utility as a standalone predictor of trauma mortality is limited. This study demonstrated that patients with high CLR require more

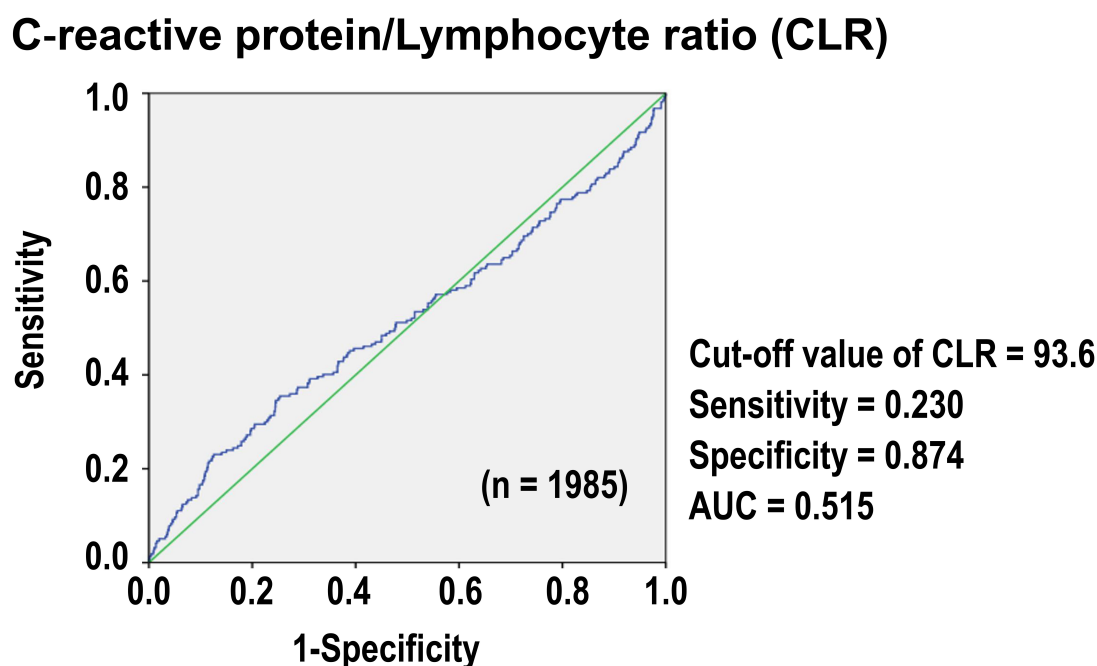


FIGURE 2. Performance characteristics of the C-reactive protein/Lymphocyte ratio (CLR) for predicting mortality. AUC: area under curve.

TABLE 3. Comparative analysis of patients with high and low C-reactive protein/Lymphocyte ratio (CLR) based on the optimal cut-off value of 93.6.

	CLR		OR (95% CI)	p
	≥93.6 n = 272	<93.6 n = 1713		
Male, n (%)	204 (75.0)	1092 (63.7)	1.71(1.28–2.28)	<0.001
Age, yr (mean ± SD)	60.3 ± 19.4	56.7 ± 19.7	-	0.004
Comorbidities, n (%)				
CVA	20 (7.4)	77 (4.5)	1.69 (1.01–2.81)	0.042
HTN	110 (40.4)	601 (35.1)	1.26 (0.97–1.63)	0.087
CAD	20 (7.4)	159 (9.3)	0.78 (0.48–1.26)	0.302
CHF	1 (0.4)	13 (0.8)	0.48 (0.06–3.70)	0.474
DM	68 (25.0)	357 (20.8)	1.27 (0.94–1.71)	0.120
ESRD	17 (6.2)	47 (2.7)	2.36 (1.34–4.18)	0.002
GCS, median (IQR)	15 (8–15)	15 (9–15)	-	0.106
AIS ≥2, n (%)				
Head/neck	194 (71.3)	1305 (76.2)	0.78 (0.59–1.03)	0.083
Face	38 (14.0)	303 (17.7)	0.76 (0.53–1.09)	0.131
Thorax	103 (37.9)	509 (29.7)	1.44 (1.11–1.88)	0.007
Abdomen	57 (21.0)	324 (18.9)	1.14 (0.83–1.56)	0.427
Extremity	130 (47.8)	622 (36.3)	1.61 (1.24–2.08)	<0.001
ISS, median (IQR)	20 (16–27)	20 (16–25)	-	0.048
Mortality, n (%)	50 (18.38)	167 (9.78)	2.09 (1.48–2.95)	<0.001
Mortality AOR*	-	-	1.71 (1.16–2.51)	0.007
Hospital stay (d)	24.4 ± 24.8	18.9 ± 16.1	-	<0.001

AIS: Abbreviated Injury Scale; AOR: adjusted odds ratio; CAD: coronary artery disease; CHF: congestive heart failure; CI: confidence interval; CRP: C-reactive protein; CLR: CRP (mg/L)/Lymphocyte ($10^9/L$); CVA: cerebral vascular accident; DM: diabetes mellitus; ESRD: end-stage renal disease; GCS: Glasgow Coma Scale; HTN: hypertension; IQR: interquartile range; ISS: injury severity score; OR: odds ratio; SD: standard deviation. *Mortality adjusted by age, ESRD, GCS, and ISS.

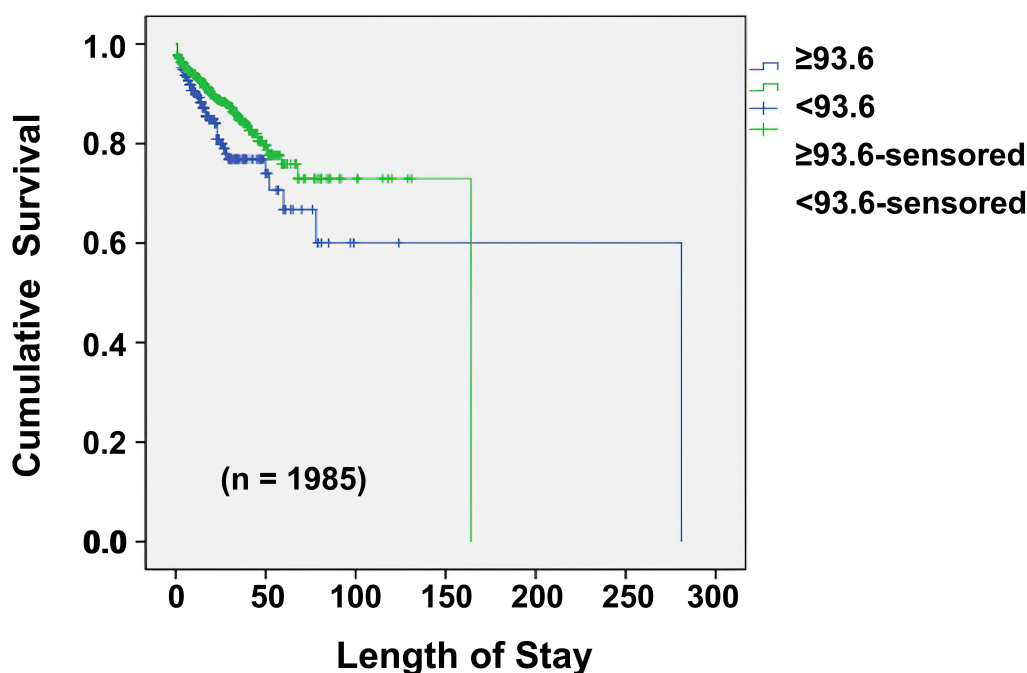


FIGURE 3. Kaplan-Meier survival curves of the high and low CLR groups.

focused care. By integrating CLR with other clinical variables, healthcare providers may be able to improve risk assessment and personalize interventions to improve patient outcomes.

Several factors may explain why CLR underperforms as a prognostic tool in trauma compared with its utility in other diseases. Trauma patients constitute a heterogeneous cohort exhibiting varied damage patterns and physiological responses, making a single inflammation-based index less universally predictive. After a major trauma, innate-like lymphocytes surge during the hyperacute response. Studies report increased natural killer (NK) and natural killer T (NKT) cells within hours, but the profound lymphopenia developing 4–12 h later and persisting beyond 48 h is linked to multiple organ dysfunction and mortality [19]. Those trauma patients with lymphocyte counts $\leq 0.5 \times 10^9/\text{L}$ at 48 h have an approximately 45% risk of mortality. In parallel, CRP, an Interleukin-6 (IL-6)-dependent acute-phase protein, rises rapidly after injury and peaks by day 3 [19]. This mirror image of CRP elevation and lymphocyte decline underlies the CRP-to-lymphocyte ratio, a composite biomarker reflecting inflammation and immune status. In addition, this study highlights the lack of significance of individual CRP and lymphocyte counts in the multivariable analysis. However, CLR combines these markers to capture the balance between systemic inflammation and immune competence. These data suggest that CLR may reflect the interplay of inflammatory burden and immune suppression better than either marker alone. Studies of specific diseases with more homogeneous patient groups have demonstrated that CLR is more effective compared with a diverse patient population [9, 10, 12]. This study discovered additional important characteristics linked to mortality, including age, GCS score, ISS, and preexisting illnesses, such as ESRD. These factors may have a more significant influence on patient outcomes than CLR alone [20]. Outcomes after trauma (especially severe injuries, such as traumatic brain injuries) depend heavily on injury severity and timely surgical or critical care interventions, which can overshadow systemic inflammatory markers [19]. In cases of isolated traumatic brain injuries, a high CLR correlated with mortality; however, its discriminative capacity was inadequate and became insignificant after correcting for injury severity [19]. This suggests that CLR in trauma largely reflects the underlying injury complexity rather than serving as an independent predictor. Furthermore, the acute immune responses to trauma are dynamic. Current evidence indicates that CLR in trauma primarily mirrors the severity of shock and tissue injury, rather than providing novel prognostic insights. In critically injured patients, a high CLR is often driven by an intense acute-phase reaction (marked by elevated CRP levels) coupled with stress-induced lymphocyte changes, which are hallmarks of severe hemorrhagic shock and trauma stress [21]. CRP levels rise within hours and peak around the third day post-injury [22], in proportion to tissue damage, whereas lymphocyte counts often decrease in the acute phase due to stress-induced immunosuppression. Such fluctuating kinetics imply that a single CLR measurement on admission may miss critical changes over time [19]. Indeed, persistent lymphopenia or secondary spikes in CRP levels can signal complications, such as organ failure or infection, later in the disease course [23, 24]. Reliance on the admission

CLR value without accounting for its evolution or the timing of interventions is a potential limitation. In summary, the complexity of trauma, with variable injury profiles and rapidly evolving inflammation, likely blunts the prognostic precision of CLR.

This study has some limitations. First, this retrospective, single-center study may not generalize to all trauma populations or healthcare environments, and the potential for selection bias remains a concern. Second, the imbalanced number of survivors and deaths may have affected the findings and overall perception of the prognostic value of CLR. Third, laboratory data were dynamic and may have fluctuated during admission. In this study, laboratory data were derived from the initial analysis of blood samples collected upon admission to the emergency room. However, the time lag between arrival in the emergency room and admission to the ICU may vary, leading to bias in data assessment. Moreover, omitting patients with incomplete data, especially those lacking laboratory results, may have heightened bias if these individuals routinely differed from the included cohort. Treatment interventions (*e.g.*, intubation or surgery) varied across patients with different injuries. In this study, we could infer that management differences did not significantly affect the outcomes. Finally, although the study concentrated on in-hospital mortality as the principal outcome, it neglected to investigate other significant clinical endpoints, like functional outcomes, quality of life, or long-term survival, which could offer a more comprehensive understanding of CLR levels in trauma patients. Addressing these limitations in future prospective multicenter research using consistent data collection techniques would assist in a deeper understanding of the CLR level and outcomes for trauma patients. Furthermore, the comparison of CLR with other ratios, such as neutrophil-to-lymphocyte ratio (NLR), PLR, and the CRP/albumin ratio, and the exploration of heterogeneity in subgroups (*e.g.*, traumatic brain injuries, elderly, or poly-trauma patients) may provide additional information regarding the role of CLR in the trauma patients with critical illness.

5. Conclusions

This study demonstrated that a high CLR correlates with a longer hospital stay and increased mortality. However, CLR alone possesses little predictive value and should not be utilized as a solitary clinical indicator for traumatic patients with critical illness. The heterogeneity of trauma and dynamic immune responses likely explain why CLR alone underperforms. Future prospective, multicenter studies should incorporate serial CLR measurements and compare it with other inflammatory ratios to improve risk stratification.

AVAILABILITY OF DATA AND MATERIALS

The raw data could be provided via corresponding author only for academic research.

AUTHOR CONTRIBUTIONS

PJK—writing. CYH—manuscript drafting. KHL—literature research. CHT—table creation. WTS—maintenance of the registered trauma database. SYH—statistical analysis. CHH—study design, proof-reading, and supervision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Institutional Review Board (IRB) of the Chang Gung Memorial Hospital with approval number 202400890B0. The requirement for informed consent was waived by IRB because it entailed a retrospective review of registered trauma data.

ACKNOWLEDGMENT

We thank the Biostatistics Center at Kaohsiung Chang Gung Memorial Hospital for assisting us with statistical analyses.

FUNDING

This study was supported by a grant from Chang Gung Memorial Hospital CDRPG8M0022.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

- [1] Rubano JA, Vosswinkel JA, McCormack JE, Huang EC, Shapiro MJ, Jawa RS. Unplanned intensive care unit admission following trauma. *Journal of Critical Care*. 2016; 33: 174–179.
- [2] Moore K. Infections in trauma patients: prevention begins in the emergency department. *Journal of Emergency Nursing*. 2015; 41: 170–171.
- [3] Tekin B, Kiliç J, Taşkın G, Solmaz İ, Tezel O, Başgöz BB. The comparison of scoring systems: SOFA, APACHE-II, LODS, MODS, and SAPS-II in critically ill elderly sepsis patients. *The Journal of Infection in Developing Countries*. 2024; 18: 122–130.
- [4] Chung J, Ahn J, Ryu JA. Beyond SOFA and APACHE II, novel risk stratification models using readily available biomarkers in critical care. *Diagnostics*. 2025; 15: 1122.
- [5] Kahraman F, Yılmaz AS, Ersoy İ, Demir M, Orhan H. Predictive outcomes of APACHE II and expanded SAPS II mortality scoring systems in coronary care unit. *International Journal of Cardiology*. 2023; 371: 427–431.
- [6] Tonduang N, Le Borgne P, Lefebvre F, Alame K, Bérard L, Gottwalles Y, *et al.*; Crems Network Clinical Research in Emergency Medicine and Sepsis Clr. Prognostic value of C-reactive protein to lymphocyte ratio (CLR) in emergency department patients with SARS-CoV-2 infection. *Journal of Personalized Medicine*. 2021; 11: 1274.
- [7] Hwang JJ, Hur JY, Eo W, An S, Kim DH, Lee S. Clinical significance of C-reactive protein to lymphocyte count ratio as a prognostic factor for survival in non-small cell lung cancer patients undergoing curative surgical resection. *Journal of Cancer*. 2021; 12: 4497–4504.
- [8] Taniai T, Haruki K, Hamura R, Fujiwara Y, Furukawa K, Gocho T, *et al.* The prognostic significance of C-reactive protein-to-lymphocyte ratio in colorectal liver metastases. *Journal of Surgical Research*. 2021; 258: 414–421.
- [9] Qi B, Yang ZJ, Huang N, Zheng WB, Gui C. Exploring the diagnostic and

prognostic value of the C-reactive protein/lymphocyte ratio for dilated cardiomyopathy based on a real-world study. *Scientific Reports*. 2023; 13: 18889.

- [10] Chen X, Lin Z, Chen Y, Lin C. C-reactive protein/lymphocyte ratio as a prognostic biomarker in acute pancreatitis: a cross-sectional study assessing disease severity. *International Journal of Surgery*. 2024; 110: 3223–3229.
- [11] Koyuncu S, Ismail O. The role of C-reactive protein to lymphocyte ratio in the differentiation of acute and perforated appendicitis. *Turkish Journal of Trauma and Emergency Surgery*. 2020; 26: 760–764.
- [12] Wu X, Ma X, Zhu J, Chen C. C-reactive protein to lymphocyte ratio as a new biomarker in predicting surgical site infection after posterior lumbar interbody fusion and instrumentation. *Frontiers in Surgery*. 2022; 9: 910222.
- [13] Shi W, Jiang Y, Tian H, Wang Y, Zhang Y, Yu T, *et al.* C-reactive protein-to-albumin ratio (CAR) and C-reactive protein-to-lymphocyte ratio (CLR) are valuable inflammatory biomarker combination for the accurate prediction of periprosthetic joint infection. *Infection and Drug Resistance*. 2023; 16: 477–486.
- [14] Ngiam JN, Liong TS, Chew NWS, Li TY, Chang ZY, Lim ZY, *et al.* Serum creatinine to absolute lymphocyte count ratio effectively risk stratifies patients who require intensive care in hospitalized patients with coronavirus disease 2019. *Medicine*. 2022; 101: e30755.
- [15] Mouliou DS. C-reactive protein: pathophysiology, diagnosis, false test results and a novel diagnostic algorithm for clinicians. *Diseases*. 2023; 11: 132.
- [16] Dong X, Wang C, Liu X, Bai X, Li Z. The trajectory of alterations in immune-cell counts in severe-trauma patients is related to the later occurrence of sepsis and mortality: retrospective study of 917 cases. *Frontiers in Immunology*. 2020; 11: 603353.
- [17] Lee DH, Lee BK, Lee SM, Cho YS, Yun SW. Association of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios with in-hospital mortality in the early phase of severe trauma. *Turkish Journal of Trauma and Emergency Surgery*. 2021; 27: 290–295.
- [18] Balta O, Altınayak H, Gürlü Balta M, Astan S, Uçar C, Kurnaz R, *et al.* Can C-reactive protein-based biomarkers be used as predictive of 30-day mortality in elderly hip fractures? A retrospective study. *Turkish Journal of Trauma and Emergency Surgery*. 2022; 28: 849–856.
- [19] Huang CY, Wu SC, Yen YH, Yang JC, Hsu SY, Hsieh CH. Assessing the predictive utility of the C-reactive protein-to-lymphocyte ratio for mortality in isolated traumatic brain injury: a single-center retrospective analysis. *Diagnostics*. 2024; 14: 2065.
- [20] Xiao B, Wu Y, Liang H, Xiao J, Han Y, Yang Z, *et al.* C-reactive protein to lymphocyte ratio is a significant predictive factor for poor short-term clinical outcomes of SARS-CoV-2 BA.2.2 patients. *Frontiers in Public Health*. 2023; 11: 1168375.
- [21] Lalwani S, Gera S, Sawhney C, Mathur P, Lalwani P, Misra MC. Mortality profile of geriatric trauma at a level 1 trauma center. *Journal of Emergencies, Trauma, and Shock*. 2020; 13: 269–273.
- [22] Fu G, Chen T, Wu J, Jiang T, Tang D, Bonaroti J, *et al.* Single-cell transcriptomics reveals compartment-specific differences in immune responses and contributions for complement factor 3 in hemorrhagic shock plus tissue trauma. *Shock*. 2021; 56: 994–1008.
- [23] Wang ZY, Du W, Liu XZ, Li Y, Liu J. Elevation of C-reactive protein and homocysteine levels as reliable biomarkers for assessing injury severity and prognosis in traumatic brain injury. *Scientific Reports*. 2025; 15: 18819.
- [24] Aldewereld Z, Connolly B, Banks RK, Reeder R, Holubkov R, Berg RA, *et al.* Risk factors for prolonged infection and secondary infection in pediatric severe sepsis. *Infection*. 2025; 53: 241–251.

How to cite this article: Pao-Jen Kuo, Ching-Ya Huang, Kuan-Hao Liao, Ching-Hua Tsai, Wei-Ti Su, Shiun-Yuan Hsu, Ching-Hua Hsieh. Association of C-reactive protein-to-lymphocyte ratio and mortality outcome in patients with trauma admitted to an intensive care unit. *Signa Vitae*. 2026; 22(2): 96-103. doi: 10.22514/sv.2025.183.