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The Lactate-to-Albumin Ratio Predicts Short and Long-Term Mortality in Patients with Traumatic Brain Injury: A Retrospective Cohort Study from the MIMIC-IV Database

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Article

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Abstract

Background

Traumatic brain injury (TBI) exhibits significant prognostic heterogeneity, necessitating reliable early prognostic markers. The lactate-to-albumin ratio (LAR), a composite marker of tissue hypoxia and systemic inflammation, still needs to be validated as a prognostic indicator for TBI in a large-scale cohort.

Methods

This study utilized the MIMIC-IV database (V3.1) to enroll adult patients with traumatic brain injury (TBI) who were admitted to the ICU for the first time. The primary exposure variable was LAR within 24 hours of admission. The primary outcomes included all-cause mortality at 28 days, 90 days, and 365 days, as well as mortality during the ICU stay. Kaplan— Meier survival analysis compared survival differences across LAR quartiles. Univariate and multivariate Cox proportional hazards regression models assessed the association between LAR and mortality risk, yielding hazard ratios (HR) and 95% confidence intervals (CI). Restricted cubic spline (RCS) analysis evaluated the dose-response relationship between LAR and mortality. Subgroup analyses by age, sex, surgery, sepsis, hypertension, and diabetes further examined this association.

Results

In the multivariable-adjusted model (Model 5), patients in the Q4 group exhibited significantly elevated mortality risks compared to the Q1 group: ICU mortality (HR = 2.20, 95% CI: 1.09–4.42, P = 0.027), 28-day mortality (HR = 1.83, 95% CI: 1.16–2.89, P = 0.009), 90-day mortality (HR = 1.71, 95% CI: 1.15–2.54, P = 0.008), and 365-day mortality (HR = 1.77, 95% CI: 1.24–2.53, P = 0.002). Restricted cubic spline analysis demonstrated a linear positive correlation between LAR and mortality risk (P for nonlinearity > 0.05). Subgroup analysis revealed effect modification of the association between LAR and prognosis in patients with sepsis (P for interaction < 0.001).

Conclusion

LAR is an independent predictor of both short-term and long-term mortality in TBI patients. This readily obtainable metric facilitates early risk stratification.

1. Introduction

Traumatic brain injury (TBI) constitutes a major global public health challenge, ranking as one of the leading causes of death and long-term disability in young and middle-aged adults, while also imposing

significant socioeconomic burdens[1]. Despite substantial advances in neurocritical care over the past few years, outcomes for TBI patients remain highly variable. Accurate prediction of individual patient outcomes is critical for guiding clinical decision-making, optimizing resource allocation, and communicating with families[1]. The pathophysiological process of TBI involves both primary injury and complex secondary injury. Secondary injury encompasses multiple pathways, including cerebral hypoperfusion, inflammatory storm, oxidative stress, and apoptosis, which critically influence neurological recovery. Biomarkers play a vital role in assessing injury severity and predicting prognosis during this process. The Glasgow Coma Scale (GCS) remains the most widely used clinical assessment tool, though factors like sedation or alcohol may compromise its accuracy. Consequently, identifying objective, readily accessible laboratory biomarkers as complementary measures remains a research priority. Despite existing serum biomarker studies, their clinical application remains limited[2, 3] Lactate is the end product of anaerobic metabolism, and hyperlactatemia serves as a critical indicator of tissue hypoxia and shock. In TBI patients, elevated blood lactate levels not only reflect systemic hypoperfusion but may also be closely associated with cerebral ischemia caused by increased intracranial pressure and insufficient cerebral perfusion pressure. Conversely, serum albumin, synthesized by the liver, is a negative acute-phase reactant. Hypoalbuminemia reflects the body's inflammatory state, poor nutritional status, and impaired synthetic function, and has been proven to be an independent predictor of increased mortality in various critically ill patients[4]In recent years, composite indicators integrating multiple pathophysiological pathways have demonstrated superior predictive performance. The lactate-to-albumin ratio (LAR) simultaneously captures two core pathological states: "tissue hypoxia" and "inflammation." Studies indicate that LAR holds prognostic predictive value for patients with sepsis, heart failure, aneurysmal subarachnoid hemorrhage, and moderate-to-severe TBI[5–7]. The systematic evaluation of the relationship between LAR and mortality at different time points (including 28 days, 90 days, 365 days, and during the ICU stay) in TBI patients using large public databases remains unexplored. Therefore, this study aims to use the MIMIC-IV large-scale ICU database and employ a rigorous retrospective cohort study design to test the following hypothesis: LAR is an independent predictor of both short- and long-term mortality in individuals with traumatic brain injury (TBI).

2. Methods

2.1 Study Design and Data Sources

We conducted a retrospective cohort study utilizing the MIMIC-IV (3.1) database, a large, open, and publicly accessible resource. The latest version, MIMIC-IV v3.1, includes detailed data on approximately 546,028 patients, encompassing 94,458 ICU admissions from hospitalizations between 2008 and 2019. This extensive database provides a solid foundation for clinical research, offering valuable insights into patient outcomes and treatment patterns[8]. The database was approved by MIT and Beth Israel Deaconess Medical Center, and consent was obtained to collect raw data. It includes demographic information, vital signs, laboratory tests, disease diagnosis codes (ICD-9 and ICD-10), and survival

outcomes. Furthermore, the MIMIC-IV database anonymizes patient information, thus eliminating the need for informed consent.

2.2 Study Population

Our team initially screened 3,975 patients with brain injury admitted to the ICU for the first time from the MIMIC-IV database. Exclusion criteria: 1. ICU admission duration < 24 hours; 2. Age < 18 years; 3. Absence of lactate or albumin measurements during the initial ICU admission. We excluded 2,145 patients with missing lactate data and 762 patients with missing albumin data. Ultimately, 1,020 eligible TBI patients were included for further analysis (Fig. 1).

2.3 Data Extraction and Variable Definition

Relevant data were extracted from MIMIC-IV using PostgreSQL language tools. Extracted variables included demographics, vital signs, laboratory tests, and scores. Demographic and vital sign variables comprised age, sex, body mass index, heart rate, systolic blood pressure, diastolic blood pressure, Laboratory tests included lactate, albumin, lymphocyte count, neutrophil count, platelet count, white blood cell count, red blood cell count, hemoglobin, blood urea nitrogen, creatinine, blood glucose, anion gap, bicarbonate, calcium, chloride, potassium, sodium, prothrombin time, international normalized ratio, and creatine kinase. Comorbidities and medical history include hypertension, myocardial infarction, congestive heart failure, diabetes, kidney disease, liver disease, sepsis, malignancy, chronic lung disease, and neurosurgical procedures. Disease severity scores include the GCS, SAPS II, and SOFA scores. Mortality and survival outcomes: Survival days, in-ICU mortality, 28-day mortality, 90-day mortality, 365-day mortality.

LAR Definition: In this study, the lactate-to-albumin ratio (LAR) was chosen as the primary variable of interest. LAR was calculated based on the lactate and albumin levels measured within 24 hours of ICU admission. If multiple measurements were available within this period, the earliest recorded value was selected. The primary endpoints of this study were mortality during the ICU stay, as well as at 28 days, 90 days, and 365 days following ICU admission in patients with traumatic brain injury.

2.4 Statistical Analysis

Continuous variables underwent Shapiro-Wilk normality testing. Normally distributed variables were expressed as mean ± standard deviation (Mean ± SD) and compared between groups using analysis of variance (ANOVA). Non-normally distributed variables were expressed as median (interquartile range) [M (IQR)] and compared between groups using the Kruskal-Wallis H test. Categorical variables are presented as counts (percentages) [n (%)], with intergroup comparisons conducted using chi-square tests or Fisher’s exact tests as appropriate. Patients were stratified into four quartiles based on LAR: Q1 (lowest), Q2, Q3, and Q4 (highest). Baseline characteristics were compared across these quartiles. Survival curves were generated using the Kaplan-Meier method, and differences in survival rates between LAR quartiles were assessed with log-rank tests. Univariate and multivariate Cox proportional hazards regression models were employed to explore the association between LAR and mortality risk at

various time points. Results were reported as hazard ratios (HR) with 95% confidence intervals (CI). Five stepwise-adjusted covariate models were developed as follows: Model 1: Unadjusted (crude model)Model 2: Adjusted for age and sex, Model 3: Adjusted for age, sex, body mass index, systolic blood pressure, diastolic blood pressure, and heart rate, Model 4: Adjusted for laboratory parameters, Model 5: Fully adjusted for comorbidities (hypertension, diabetes, congestive heart failure, chronic lung disease, chronic kidney disease, sepsis, and malignant neoplasms). This model represents the final fully adjusted model. Additionally, Restricted Cubic Splines (RCS) were used in Cox regression models with LAR as a continuous variable to flexibly assess the relationship between LAR and mortality risk, while also testing for potential nonlinearity. Subgroup analyses were performed by age, hypertension, diabetes, sepsis, chronic kidney disease, and neurosurgical procedures to account for confounding factors within each group. All data analyses were performed using the Storm Statistics platform (Zstats software, v1.0, www.zstats.net) and the R language (version 4.5.1). A p-value of < 0.05 was considered statistically significant.

3. Results

3.1 Patient Baseline Characteristics

A total of 1,020 eligible TBI patients were ultimately enrolled. After stratification into four groups based on LAR quartiles, baseline characteristics for each group are presented in Table 1. Among the 1020 enrolled subjects, 254 (24.9%) were assigned to Group 1, 254 (24.9%) to Group 2, 256 (25.1%) to Group 3, and 256 (25.1%) to Group 4. Significant intergroup differences were observed across multiple baseline and clinical outcome measures. Age at admission differed significantly between groups (median 63.0 years [IQR 43.8–76.0]; $p < 0.001$), with Group 4 participants being the youngest (53.5 years [33.8–70.0]). Significant differences in hemodynamic parameters were noted: Group 4 had higher heart rates (94.5 beats/min [81.0–111.0], total group 88.0 beats/min [74.0–102.0]; $p < 0.001$), and Group 1 had higher systolic blood pressure (136.0 mmHg [121.0–152.0], total group 129.0 mmHg [114.0–146.0]; $p < 0.001$). Laboratory parameters revealed significant intergroup differences: inflammatory markers (lymphocytes $p = 0.018$, neutrophils $p = 0.003$, platelet count $p < 0.001$, WBC count $p < 0.001$), metabolic indicators (glucose $p < 0.001$, anion gap $p < 0.001$, bicarbonate $p < 0.001$), coagulation parameters (PT $p < 0.001$, INR $p < 0.001$), and organ function markers (creatinine $p < 0.001$, BUN $p = 0.008$, CK $p = 0.015$). Significant differences in disease severity scores were observed across groups, including GCS ($p = 0.002$), SAPS II ($p = 0.004$), and SOFA scores ($p < 0.001$). Clinical outcomes revealed significant differences in survival time (21.0 days [7.0–124.0]; $p < 0.001$) and ICU length of stay (4.5 days [2.0–10.4]; $p = 0.030$). Analysis of comorbidities revealed statistically significant differences in the prevalence of hypertension (39.3%; $p = 0.001$), liver disease (10.0%; $p < 0.001$), sepsis (65.7%; $p = 0.002$), and chronic lung disease (12.9%; $p = 0.008$). Mortality rates at all time points showed significant differences: ICU mortality (10.7%; $p < 0.001$), 28-day mortality (22.6%; $p < 0.001$), 30-day mortality (22.7%; $p < 0.001$), 90-day mortality (28.2%; $p = 0.006$), and 365-day mortality (34.3%; $p = 0.018$) all showed significant differences. No statistically significant differences were found in BMI, diastolic blood pressure, red blood cell count, serum

potassium levels, length of hospitalization, or comorbidities such as diabetes, malignancy, or need for renal replacement therapy.

3.2 Survival Analysis

Kaplan-Meier survival curves clearly demonstrated that across different time intervals (ICU admission, 0–28 days, 0–90 days, 0–365 days), patients in the LAR Q4 group consistently exhibited the lowest cumulative survival rates. In contrast, those in the Q1 group showed the highest survival rates (Log-rank $P < 0.001$). The survival curves diverged markedly, particularly in the early period (0–28 days), indicating that LAR effectively distinguishes mortality risk in patients during the initial phase of hospitalization.

Figure 2. Kaplan-Meier curves depicting survival rates during ICU admission at 28, 90, and 365 days for TBI patients, stratified by LAR quartiles.

3.3 Multivariate Cox Regression Analysis of LAR and Mortality Risk

Univariate Cox regression showed a significant association between higher LAR and mortality at all time points, which remained after multivariate adjustment.. In the final fully adjusted model (Model 5), with Q1 as the reference group, the independent associations of Q4 with mortality risk were as follows: ICU mortality (HR = 2.20, 95% CI: 1.09–4.42, P = 0.027), 28-day mortality (HR = 1.83, 95% CI: 1.16–2.89, P = 0.009), 90-day mortality (HR = 1.71, 95% CI: 1.15–2.54, P = 0.008), and 365-day mortality (HR = 1.77, 95% CI: 1.24–2.53, P = 0.002).

Table 2. Multivariate Cox regression analysis of the mortality association between LAR and TBI

Table 2
Multivariable Associations between the Highest Lactate-to-Albumin Ratio (LAR) Quartile (Q4) and Mortality Using Sequentially Adjusted Cox Proportional Hazards Models

Mortality Endpoint	Model 1: HR (95% CI) P	Model 2: HR (95% CI) P	Model 3: HR (95% CI) P	Model 4: HR (95% CI) P	Model 5: HR (95% CI) P
ICU mortality	4.18 (2.31–7.56) < .001	3.07 (1.66–5.66) < .001	3.11 (1.67–5.80) < .001	2.23 (1.13–4.40) 0.021	2.20 (1.09–4.42) 0.027
28-day mortality	2.65 (1.82–3.88) < .001	2.38 (1.62–3.51) < .001	2.30 (1.55–3.42) < .001	1.82 (1.17–2.83) 0.008	1.83 (1.16–2.89) 0.009
90-day mortality	2.23 (1.60–3.10) < .001	2.07 (1.48–2.89) < .001	2.00 (1.43–2.82) < .001	1.71 (1.17–2.52) 0.006	1.71 (1.15–2.54) 0.008
365-day mortality	2.09 (1.56–2.80) < .001	1.98 (1.47–2.66) < .001	1.91 (1.41–2.58) < .001	1.79 (1.27–2.53) < .001	1.77 (1.24–2.53) 0.002
Note: The reference value is Q1, and the table only lists Q4 results. For details, see the supplementary materials.					
HR: Hazard Ratio, CI: Confidence Interval					
Model1: Crude					
Model2: Adjust: gender, age					
Model3: Adjust: gender, age, BMI, heart_rate, sbp, dbp					
Model4:Adjust: gender, age, BMI, heart_rate, sbp, dbp, lymphocytes, neutrophils, platelet, wbc,rbc, hemoglobin, bun, creatinine, glucose, anion_gap, bicarbonate, calcium, chloride, potassium, sodium, pt, inr, ck					
Model5: Adjust: gender, hypertension, myocardial_infarct, congestive_heart_failure, diabetes, renal_disease, liver_disease, sepsis, malignant_cancer, chronic_pulmonary_disease, surgery, age, BMI, heart_rate, sbp, dbp, lymphocytes, neutrophils, platelet, wbc, rbc, hemoglobin, bun, creatinine, glucose, aniongap, bicarbonate, calcium, chloride, potassium, sodium, pt, inr, ck, GCS					

3.4 Dose-Response Relationship

As shown in Fig. 3, we analyzed the association between LAR and clinical outcomes at different time points using a restricted cubic spline model. Across all four time dimensions (28-day, 90-day, 365-day mortality, and ICU length of stay), the trend lines for odds ratios (ORs) showed a consistent pattern: ORs increased monotonically with rising LAR, indicating a sustained association between higher LAR and increased risk of adverse patient outcomes. The “P for nonlinear” values in all graphs were substantially greater than 0.05 (28 days: 0.823; 90 days: 0.642; 365 days: 0.355; ICU days: 0.851). This indicates that the association pattern between LAR and outcome risk lacks statistically significant nonlinear components, further supporting a linear association model.

Figure 3. Restricted cubic spline plots of LAR association with 28-day, 90-day, and 365-day ICU length of stay and mortality in TBI patients.

3.5 Forest Plot of Subgroup Analyses:

Subgroup analyses revealed that the significant association between LAR and 365-day mortality persisted across age groups, genders, and hypertension status (all interaction P > 0.05). No significant difference in overall mortality risk was observed during ICU stay (HR = 0.95, P = 0.550). However, diabetes (HR = 4.69, P < 0.001), renal disease (HR = 6.00, P < 0.001), and sepsis (HR = 1.40, P < 0.001) were influential risk factors for mortality. For the 28-day prognosis, the overall risk remained non-significant (HR = 1.10, P = 0.248). Diabetes (HR = 2.28, P = 0.007), kidney disease (HR = 2.24, P = 0.037), and sepsis (HR = 2.92, P < 0.001) remained significantly influential, though their effects were attenuated compared to the ICU period. At 90 days, the overall risk showed no difference (HR = 1.11, P = 0.175). Sepsis remained a significantly strong risk factor (HR = 3.36, P < 0.001), while the hazard ratios for other factors became non-significant. After 365 days, sepsis continued to have an adverse impact (P < 0.001). Interaction analysis revealed that the effect of sepsis on prognosis varied across patient subgroups (all interaction P values < 0.05).

Figure 4. Forest plot of subgroup analysis results.

4. Discussions

1. Traumatic brain injury (TBI) is caused by head impacts, shocks, or vibrations, or penetrating head injuries that disrupt the brain's normal function. [9]Although traumatic brain injury (TBI) is typically caused by sudden head trauma, its effects on patients can be lifelong and progressively evolving[10]. Traumatic brain injury (TBI) affects around 70 million people globally each year, making it a significant public health issue and the leading cause of death and disability from traumatic injuries[11, 12]. This study systematically examined the relationship between the lactate-to-albumin ratio (LAR) at different time points (during ICU admission, 28 days, 90 days, and 365 days) and mortality in TBI patients admitted to the ICU, using the large public ICU database MIMIC-IV version 3.1. Our main finding is that high admission LAR independently predicts both short-term and long-term all-cause mortality in TBI patients. Compared with the lowest LAR quartile (Q1), patients in the highest quartile (Q4) were older, had significantly lower GCS scores at admission, faster heart rates, and lower systolic blood pressure. Laboratory findings in Q4 patients revealed more severe metabolic and inflammatory states, characterized by extremely high lactate levels, extremely low albumin levels, and elevated glucose, serum creatinine, and inflammatory markers. Additionally, Q4 patients had higher rates of comorbidities such as sepsis and chronic kidney disease (all intergroup comparisons P < 0.05) (Table 1). These findings indicate that high LAR correlates with poorer physiological status and greater disease severity. After comprehensive adjustment in the multivariable Cox regression model, patients in the highest LAR quartile (Q4) had a significantly higher mortality risk than those in the lowest quartile (Q1) (Table 2). Furthermore, Restricted Cubic Spline (RCS) analysis revealed a continuous, near-linear dose-response relationship between LAR and mortality risk (Fig. 3). These findings show that LAR, as a comprehensive biomarker, is valuable for risk stratification and prognosis prediction in TBI patients. Subgroup analyses suggest that risk factors exert a distinct, temporally dependent, and hierarchical influence on outcomes. This study demonstrates that risk factors impact prognosis with clear temporal dependence and

hierarchy. During the initial hospitalization phase (ICU stay), pre-existing conditions (particularly diabetes and kidney disease) represent the primary risk factors for mortality, underscoring the critical importance of rigorous management of underlying conditions during the critical phase. Sepsis remained the most potent risk factor throughout, underscoring infection control as a critical priority in ICU management. Over time, the impact of underlying conditions like diabetes and kidney disease gradually diminished after 28 days. This suggests that if patients successfully navigate the most critical acute phase, these factors become less decisive for mid-term outcomes. However, sepsis' influence remained robust at 90 days, indicating persistent damage. One year post-injury, the overall mortality risk significantly increases, strongly suggesting the presence of late complications or sequelae affecting long-term survival. The persistent significant impact of sepsis indicates that severe infection during the acute phase may inflict profound, irreversible damage to the patient's body, severely compromising long-term survival rates. Research indicates that LAR possesses moderate predictive power for mortality in patients with sepsis or septic shock and aids in identifying high-risk individuals[13]. Future research is needed to clarify the pathophysiological role of LAR in non-septic TBI patients and to assess its viability as a potential therapeutic target.

2. Comparison with Previous Research and New Insights from This Study

Our findings align closely with recent trends in LAR research within critical care settings. Lee et al.'s pioneering study specifically targeting TBI patients demonstrated significant associations between admission LAR and 24-hour mortality (AUC 0.805) and massive transfusion requirements (AUC 0.735). Our research not only validates LAR's predictive value for early adverse events but, crucially, extends the predictive time window to 365 days, confirming LAR's utility in forecasting long-term outcomes. This indicates that physiological stress and inflammatory states at admission profoundly influence the recovery trajectory of TBI patients. In addition, the study by Xu Jianguo et al. indicated that LAR serves as an independent prognostic factor for mortality in patients with moderate to severe TBI, with predictive efficacy (AUC = 0.78) that even surpasses that of individual GCS, lactate, or albumin levels. Our study further validates this conclusion using a larger sample (from the MIMIC-IV database). It enhances the reliability of the findings through more rigorous statistical adjustments (multivariate Cox regression and RCS analysis). Notably, the prognostic value of LAR is not specific to TBI. Studies indicate that LAR serves as an effective prognostic indicator across diverse conditions, including acute pancreatitis, sepsis, cirrhosis with sepsis, myocardial infarction, and cardiac arrest[7, 14–19]. This cross-disease consistency suggests that the "hypoxia-inflammation" imbalance represented by LAR may constitute a standard, core pathophysiological pathway in critically ill patients, thereby conferring broad applicability.

3 The increasing prevalence of traumatic brain injury (TBI) remains a major public health concern. Therefore, early prediction of patient prognosis and development of appropriate treatment strategies are crucial for improving outcomes in TBI patients. On one hand, serum albumin is a negative acute-phase reactant. Under severe stress and inflammatory conditions, impaired hepatic albumin synthesis

combined with increased vascular permeability leading to albumin extravasation collectively cause hypoalbuminemia. Low albumin levels indicate impaired inflammatory control and nutritional status, which adversely affect tissue repair and immune defense. This increases the risk of complications such as infection, ultimately leading to poor outcomes. The causes of hypoalbuminemia following traumatic brain injury are multifactorial, including initial injury-related blood loss, consumption due to secondary oxidative stress damage, and physiological hypoalbuminemia resulting from massive crystalloid fluid infusion. Previous research has established a link between lower serum albumin levels following TBI and increased mortality[20]. Hypoalbuminemia in TBI patients is linked to poor outcomes, likely due to cerebral edema and increased intracranial pressure from inadequate intravascular osmotic pressure. Additionally, lower albumin levels may indicate a stronger systemic inflammatory response, which is associated with worse outcomes in TBI patients[21]. Conversely, serum lactate is a well-established marker of tissue hypoperfusion. It is associated with organ failure and mortality across a variety of clinical contexts, such as sepsis, trauma, and critical illness in children[6, 17, 22–26]. Furthermore, multiple studies have investigated the predictive value of serum lactate levels for outcomes in TBI patients[21, 27, 28]Most of these studies indicate that elevated serum lactate levels are associated with a poorer prognosis in TBI patients. Lactate is the end product of anaerobic glycolysis. Elevated levels directly reflect systemic or localized cerebral tissue hypoperfusion and hypoxia, though multiple factors, including liver and kidney function, influence them. Following TBI, increased intracranial pressure or systemic hypotension can reduce cerebral blood flow, leading to lactate accumulation. Several studies examining the relationship between lactate and TBI patient prognosis have yielded inconsistent conclusions[28]. One study indicated that TBI patients with serum lactate levels below 5 mmol/L might have higher survival rates than those with higher lactate levels [29]. To improve the predictive value of serum lactate, researchers introduced the lactate-to-albumin ratio (LAR), combining the clinical relevance of lactate and albumin. Its utility was validated across various patient cohorts[5–7]. These findings indicate that LAR may be more effective than lactate alone in predicting mortality in critically ill patients. Additionally, recent studies have shown that LAR provides better prognostic value than lactate alone in predicting survival after cardiac arrest at hospital discharge[15]. A 2022 study also suggested that the lactate-albumin ratio is a useful prognostic indicator for patients with moderate to severe traumatic brain injury (TBI)[30]. However, this study enrolled only 273 patients, focused on moderate-to-severe cases, and did not evaluate long-term outcomes. The advantage of LAR lies in its simultaneous capture of two key pathophysiological processes: tissue hypoxia and inflammatory states. In the context of TBI, mechanisms of secondary brain injury include tissue hypoxia due to cerebral hypoperfusion and the subsequent intense inflammatory response. Our study found that patients in the high LAR group exhibited elevated lactate levels and reduced albumin levels, accompanied by lower GCS scores and higher systemic inflammatory markers—findings consistent with these pathophysiological processes. Therefore, LAR may provide a more comprehensive evaluation of physiological disturbances in TBI patients than any single marker.

4 Clinical Significance and Potential Applications

The most prominent clinical advantage of LAR lies in its simplicity and cost-effectiveness. Lactic acid and albumin are routine tests for ICU admissions, requiring no additional costs or procedures for calculation. This makes LAR highly suitable as a rapid risk stratification tool, particularly in settings with relatively limited medical resources. Clinicians can rapidly identify TBI patients at extremely high risk of mortality by calculating LAR early in the admission phase. For high-risk patients, this prompts closer monitoring and more aggressive intervention strategies—such as more frequent neurological assessments, earlier imaging reviews, proactive hemodynamic management, and enhanced nutritional support—to improve outcomes.

Additionally, our dose-response analysis showed a continuous, linear increase in mortality risk with higher LAR, without any evident plateau or saturation point. This indicates that mortality risk increases progressively with higher LAR values, providing a theoretical basis for dynamically monitoring LAR changes to assess treatment response. Future studies may explore the feasibility of using dynamic LAR changes as a therapeutic target.

5. Study Strengths and Limitations

Strengths of this study include: Extensive follow-up duration covering multiple critical time points from short-term to long-term outcomes; Advanced and rigorous statistical methods, including multi-model adjustment and RCS analysis, effectively controlling for confounding biases. However, this study has several limitations. First, as a retrospective observational analysis, even after adjusting for multiple known confounders, the influence of residual or unmeasured confounding cannot be completely ruled out. Second, all data were derived from a single center. Although the MIMIC-IV database is considered high-quality, the external validity of our results still needs confirmation in other populations and in multicenter prospective studies. Third, LAR was calculated from a single lactate and albumin measurement within the first 24 hours after admission, so we were unable to determine whether temporal changes in LAR might have superior prognostic value. Monitoring LAR trends over time may represent a valuable future research direction.

5. Conclusion

This study confirms that the lactate-albumin ratio (LAR) independently predicts all-cause mortality during ICU stay, as well as at 28 days, 90 days, and 365 days in traumatic brain injury patients. Elevated LAR values are associated with a higher mortality risk. This easily calculable, low-cost ratio comprehensively reflects tissue perfusion and inflammatory status, offering potential as a practical tool for clinicians to perform early risk stratification, identify high-risk groups, and optimize clinical decision-making for TBI patients.

Declarations

Ethical Approval and Consent to Participate

Research encompassing human subjects was evaluated and authorized by ethics boards at the Massachusetts Institute of Technology (MIT) and Beth Israel Deaconess Medical Center (BIDMC). Per federal regulations and organizational protocols, written informed consent was waived for this investigation.

Publication Consent

All authors have read and approved the final version of this manuscript and authorize its publication .

Availability of Data and Materials

The data analyzed in this study were derived from the Intensive Care Medical Informatics Market IV (MIMIC-IV) clinical database and were used subject to the following permissions and restrictions: only eligible users were allowed access to the data, they had to complete specified training (including CITI data training or sample-only studies), and they had to sign a data use agreement. To access these datasets, submit a request directly to PhysioNet at https://physionet.org/; https://doi.org/10.13026/s6n6-xd98.

Competing Interests

The authors declare no competing interests.

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Author Contributions

Xiang Gao was responsible for study design and data analysis; Peng Yan contributed to experimental design and data collection; Xin Li contributed to writing and revising the manuscript.

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Tables

Table 1 is available in the Supplementary Files section.

Figures

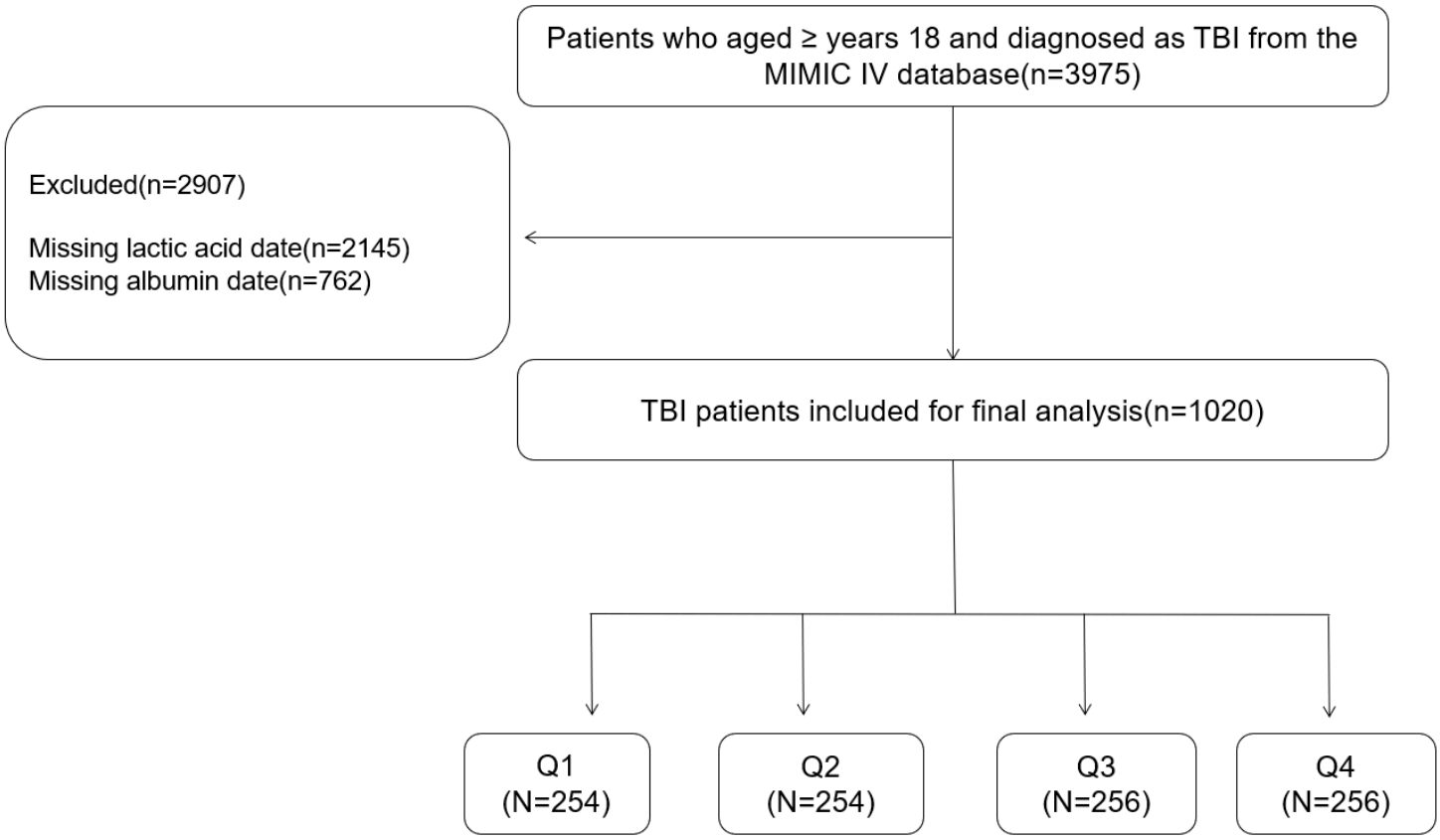


Figure 1

A flowchart of the population screening.

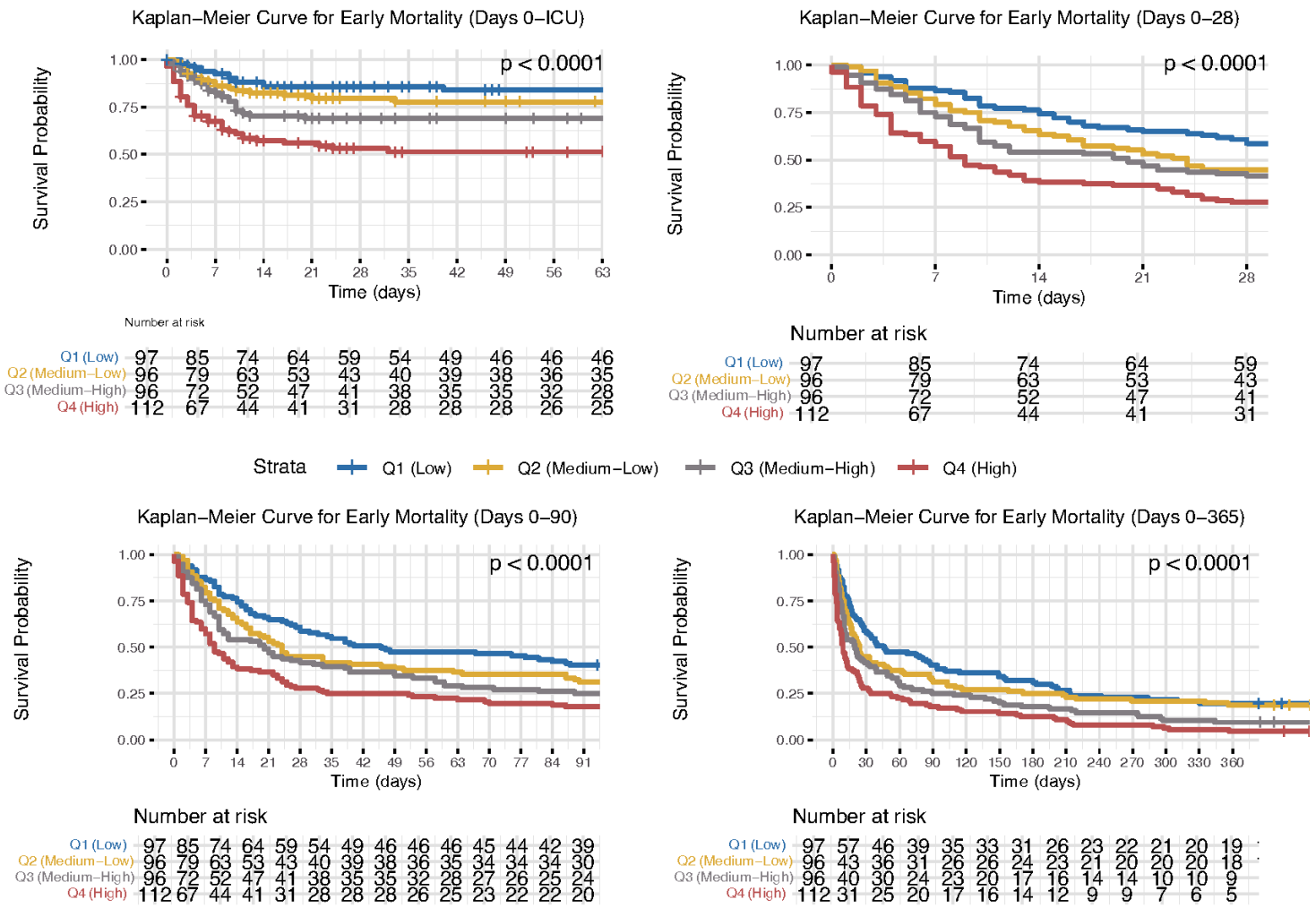


Figure 2

Kaplan-Meier curves depicting survival rates during ICU admission at 28, 90, and 365 days for TBI patients, stratified by LAR quartiles.

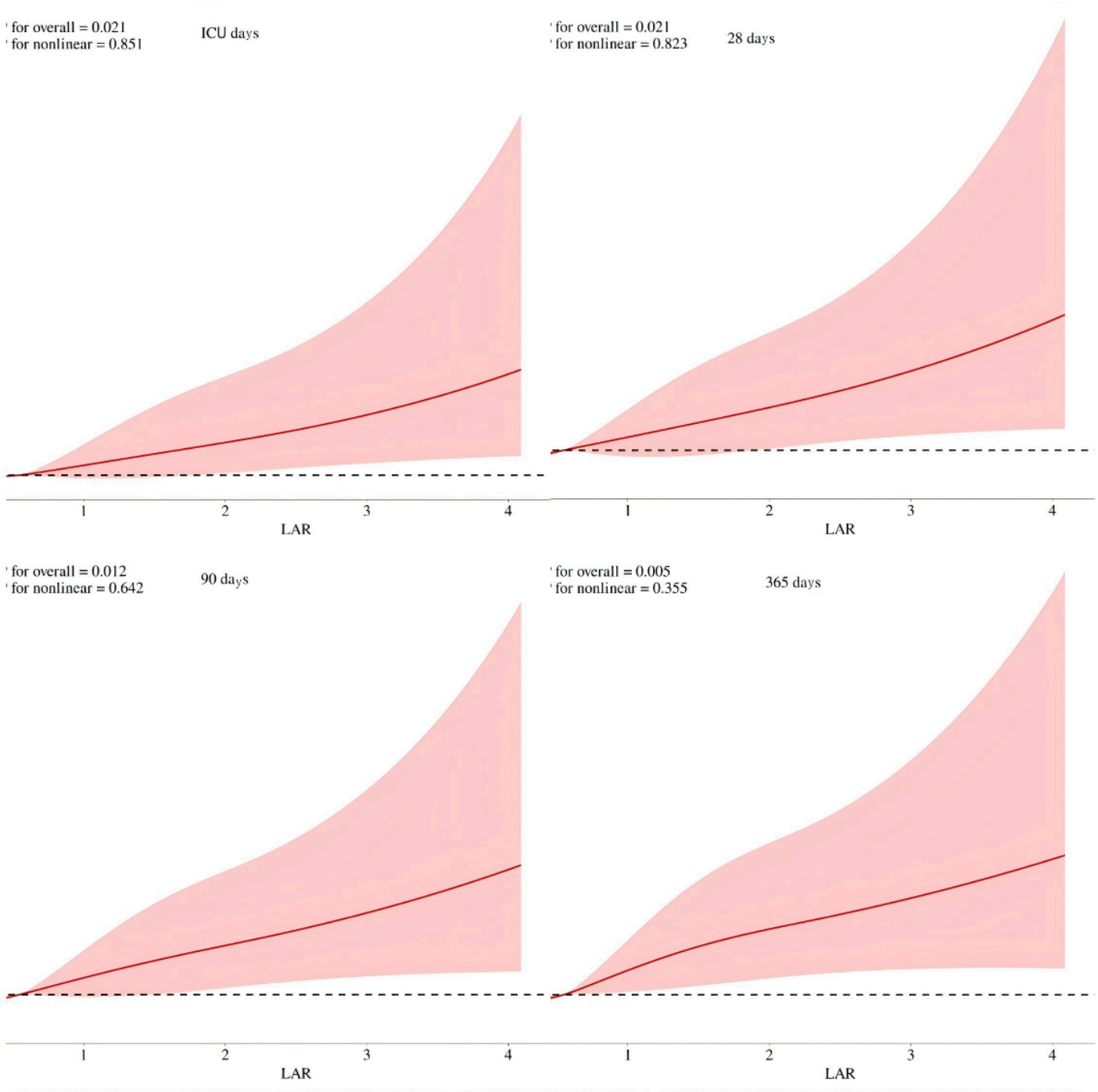


Figure 3

Restricted cubic spline plots of LAR association with 28-day, 90-day, and 365-day ICU length of stay and mortality in TBI patients.

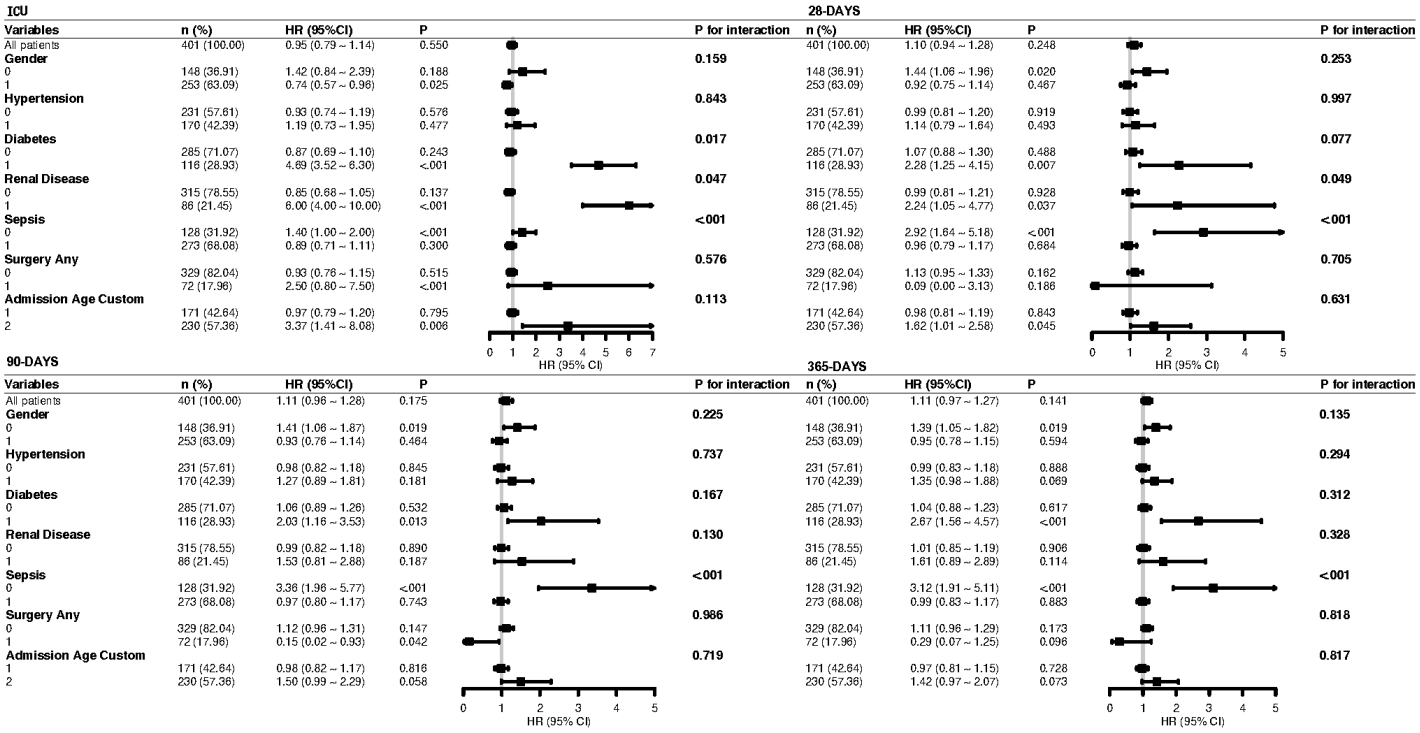


Figure 4

Forest plot of subgroup analysis results.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TABLE1BaselinecharacteristicsaccordingtoLARindexquartiles..docx