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Article

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Posted Date: November 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11338485/v1

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Additional Declarations: No competing interests reported.

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Funding

This study was supported by the Talent Fund of Guizhou Provincial People's Hospital (Grant No. [2023] 31).

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Abstract

Background

The association between early albumin-corrected neutrophil-to-lymphocyte ratio (ACNLR) and in-hospital mortality in critically ill patients with pneumonia remains unclear. This study aimed to clarify this relationship using two large critical care databases.

Methods

Patients with pneumonia were retrospectively identified from the Medical Information Mart for Intensive Care IV (MIMIC-IV) and the eICU Collaborative Research Database (eICU-CRD). ACNLR was calculated as the neutrophil-to-lymphocyte ratio divided by serum albumin concentration using laboratory measurements obtained within the first 24 hours after intensive care unit admission. Multivariable logistic regression and restricted cubic spline analyses were used to investigate the association between ACNLR and in-hospital mortality. Subgroup analyses and propensity score-based sensitivity analyses were also performed.

Results

A total of 1,378 patients from MIMIC-IV and 3,426 patients from eICU-CRD were included. In-hospital mortality was 27.4% and 16.8%, respectively. Higher ACNLR was independently associated with increased in-hospital mortality after multivariable adjusting. In the fully adjusted model, each 1-standard deviation increase in ACNLR was associated with higher mortality in both MIMIC-IV (OR = 1.19, 95% CI: 1.06–1.33, $P = 0.003$) and eICU-CRD (OR = 1.28, 95% CI: 1.16–1.41, $P < 0.001$). Patients in the highest ACNLR quartile also had significantly higher mortality than those in the lowest quartile in both cohorts. Restricted cubic spline analyses showed a nonlinear positive association between ACNLR and in-hospital mortality, with consistent findings across sensitivity analyses.

Conclusions

Higher early ACNLR was independently associated with increased in-hospital mortality in critically ill patients with pneumonia. ACNLR may serve as a simple and readily biomarker for early mortality risk stratification in pneumonia-related critical illness.

Keywords: albumin-corrected neutrophil-to-lymphocyte ratio; pneumonia; intensive care unit; in-hospital mortality; MIMIC-IV; eICU-CRD; inflammation; albumin;

Introduction

Pneumonia, as a major clinical manifestation of lower respiratory infection, remains a substantial cause of morbidity and mortality worldwide and imposes a considerable burden on healthcare systems, particularly among critically ill patients[1]. According to the Global Burden of Disease analysis, lower respiratory infections were responsible for approximately 2.50 million deaths and 98.7 million disability-adjusted life-years worldwide in 2023, with older adults and vulnerable populations carrying a particularly high burden[2]. In critically ill patients, pneumonia may progress rapidly and is frequently accompanied by extrapulmonary complications, including acute respiratory distress syndrome, septic shock, acute kidney injury, and multiple organ dysfunction, which further increase the need for organ support and prolong ICU care[3]. These complications not only increase healthcare costs and ICU resource utilization, but may also impose substantial social and family burdens through prolonged hospitalization, functional decline, and loss of productivity[4, 5]. Although advances in antimicrobial therapy, respiratory support, and organ-protective strategies have improved the management of pneumonia, mortality among patients requiring intensive care remains considerable. Identification of biomarkers for early mortality risk stratification is therefore essential in the management of patients with pneumonia, particularly those admitted to the intensive care unit (ICU). Early risk stratification may help clinicians identify patients who require closer monitoring, timely escalation of respiratory or hemodynamic support, and more individualized therapeutic strategies, while also supporting triage decisions and rational allocation of ICU resources[6, 7].

The systemic inflammatory response plays a central role in the progression and prognosis of pneumonia. The neutrophil-to-lymphocyte ratio (NLR), derived from routine peripheral blood counts, reflects the balance between neutrophil-mediated innate inflammatory activation and lymphocyte-mediated adaptive immune regulation. Previous systematic reviews and meta-analyses based mainly on hospitalized patients with community-acquired pneumonia have suggested that elevated NLR is associated with increased mortality and adverse clinical outcomes, indicating its potential value as a simple and readily available inflammatory biomarker for pneumonia prognosis[8, 9]. However, NLR alone cannot fully reflect the nutritional reserve and systemic inflammatory burden of critically ill patients. Serum albumin is not only a marker of nutritional status but also a negative acute-phase protein that decreases during systemic inflammation, capillary leakage, hepatic dysfunction, and catabolic stress[10]. Hypoalbuminemia has been consistently associated with disease severity and increased mortality in acutely ill and critically ill patients[11]. Because inflammation and hypoalbuminemia frequently coexist in severe infection and critical illness, composite indices integrating inflammatory and nutritional information may provide more

comprehensive prognostic value than either biomarker alone. The albumin-corrected neutrophil-to-lymphocyte ratio (ACNLR), which combines NLR and serum albumin, is an inexpensive and easily obtainable biomarker based on routine laboratory tests. Previous studies have suggested that ACNLR and related NLR–albumin composite indices are associated with mortality in sepsis, severe sepsis or septic shock, and other critically ill populations[12–14]. Nevertheless, evidence regarding the early prognostic value of ACNLR in ICU patients with pneumonia remains limited. Therefore, this study focused on exploring the association between early ACNLR and in-hospital mortality in ICU patients with pneumonia using the MIMIC-IV and eICU-CRD databases, with the aim of providing additional evidence for early risk stratification and clinical management of critically ill patients with pneumonia.

Methods

Study design and data source

This retrospective cohort study was conducted using two publicly available critical care databases. The Medical Information Mart for Intensive Care IV version 3.1 (MIMIC-IV v3.1) database was used as the primary cohort. MIMIC-IV contains deidentified electronic health records of patients admitted to the emergency department or intensive care units at Beth Israel Deaconess Medical Center between 2008 and 2022. The eICU Collaborative Research Database version 2.0 (eICU-CRD v2.0) was used as the external cohort. eICU-CRD is a multicenter critical care database containing deidentified data from more than 200,000 ICU admissions across 335 ICUs in 208 hospitals in the United States between 2014 and 2015. Access to both databases was granted after completion of the required data-use training and certification by one author (Yunpeng Luo; certification number: 71292458). Because this study used publicly available, de-identified data and did not involve identifiable personal information, the requirement for informed consent was waived.

Study population

Adult patients aged 18 years or older with a diagnosis of pneumonia were eligible for inclusion. Pneumonia was identified using diagnostic records and ICD codes in each database. For patients with multiple ICU admissions, only the first ICU stay was retained. Patients were excluded if they had an ICU length of stay less than 24 hours, ventilator-associated pneumonia, aspiration pneumonia, missing laboratory measurements required to calculate ACNLR within the first 24 hours after ICU admission, or missing primary outcome information. The same eligibility criteria were applied to both the MIMIC-IV and eICU-CRD cohorts whenever possible, and the detailed patient selection process is shown in Figure 1.

Data extraction and variable definitions

Structured Query Language (SQL) was used in Navicat Premium software (version 16) to extract data from eligible patients with pneumonia in the MIMIC-IV and eICU-CRD databases according to predefined variable definitions and time windows. For each eligible ICU stay, demographic characteristics, vital signs, laboratory parameters, treatment-related variables, comorbidities, disease severity scores, and outcome information were extracted. Laboratory variables required to calculate ACNLR, including absolute neutrophil count, absolute lymphocyte count, and serum albumin, were obtained within the first 24 hours after ICU admission. Treatment-related variables, including mechanical ventilation, vasoactive drug use, and renal replacement therapy, were identified during the early ICU period according to treatment records.

The neutrophil-to-lymphocyte ratio (NLR) was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. Albumin-corrected neutrophil-to-lymphocyte ratio (ACNLR) was defined as NLR divided by serum albumin concentration. In the primary analysis, ACNLR was analyzed both as a standardized continuous variable and as a categorical variable. ACNLR quartile cutoffs were derived from its distribution in the MIMIC-IV cohort. To ensure consistency between the primary and external cohorts, the same MIMIC-IV-derived quartile boundaries were subsequently applied to categorize patients in the eICU-CRD cohort.

Outcomes

The primary outcome was in-hospital mortality, defined as death occurring before hospital discharge. In-hospital mortality was identified using death records and hospital discharge status in the MIMIC-IV and eICU-CRD databases. For the main regression analyses, in-hospital mortality was treated as a binary outcome. For the cumulative incidence analysis, follow-up time was calculated from ICU admission to in-hospital death, discharge alive, or 28 days after ICU admission, whichever occurred first. Discharge alive before in-hospital death was treated as a competing event.

Statistical analysis

All analyses were performed using R software (version 4.6.0; R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as medians with interquartile ranges and compared using the Kruskal – Wallis test. Categorical variables were summarized as frequencies with percentages and compared using the chi-square test or Fisher's exact test, as appropriate. Missing covariate data

were handled using multiple imputation by chained equations; variables required to calculate ACNLR and the primary outcome were not imputed. Twenty imputed datasets were generated, and estimates from the main regression analyses were pooled using Rubin's rules. Multivariable logistic regression was used to evaluate the association between ACNLR and in-hospital mortality in the MIMIC-IV and eICU-CRD cohorts separately. ACNLR was analyzed both as a standardized continuous variable and as MIMIC-IV-derived quartile categories. Three models were constructed, including an unadjusted model, a demographic-adjusted model, and a fully adjusted model. Restricted cubic spline analysis was performed to assess potential nonlinearity. Cumulative incidence curves were generated for 28-day in-hospital death after ICU admission, with discharge alive treated as a competing event, and compared using Gray's test. Subgroup analyses were performed across predefined clinical strata, with interaction terms added to the fully adjusted models.

Sensitivity analyses were conducted in the pooled MIMIC-IV and eICU-CRD cohort using propensity score matching and inverse probability of treatment weighting. High ACNLR was defined as ACNLR >7.13. Propensity scores were estimated using clinically relevant baseline covariates and database source. Covariate balance was assessed using standardized mean differences, with values <0.1 considered acceptable. Logistic regression was fitted in the original pooled cohort, the matched cohort, and the weighted cohort. Propensity score-based sensitivity analyses were performed within each imputed dataset, and estimates were pooled using Rubin's rules. Results were reported as odds ratios with 95% confidence intervals, and a two-sided P value <0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 1,378 ICU patients with pneumonia were included in the MIMIC-IV cohort. Baseline characteristics stratified by MIMIC-IV-derived ACNLR quartile categories are presented in Table 1. Patients with higher ACNLR levels tended to have lower serum albumin levels, higher NLR and white blood cell counts, greater disease severity, and more pronounced physiological or laboratory abnormalities. Vasopressor use and antibiotic exposure also differed across ACNLR quartiles.

The eICU-CRD cohort included 3,426 ICU patients with pneumonia, and baseline characteristics according to the same MIMIC-IV-derived ACNLR quartile cutoffs are summarized in Supplementary Table 1. In this cohort, higher ACNLR levels were similarly associated with older age, lower albumin levels, higher NLR and white blood cell counts, higher APACHE scores, and greater vasopressor use, whereas mechanical ventilation showed only a modest and statistically non-significant increase across ACNLR categories. Baseline characteristics according to in-hospital mortality status are shown in Supplementary Table 2. In both cohorts, non-survivors generally had higher inflammatory burden, lower albumin levels, more severe physiological and laboratory abnormalities, and more frequent use of mechanical ventilation and vasopressors than survivors.

Association between ACNLR and in-hospital mortality

In both cohorts, higher ACNLR was significantly associated with increased in-hospital mortality. In the MIMIC-IV cohort, each 1-SD increase in ACNLR was associated with higher mortality risk in Model 1, Model 2, and Model 3. After full adjustment, the association remained significant (OR 1.19, 95% CI 1.06–1.33; P = 0.003). When ACNLR was analyzed as a categorical variable, patients with ACNLR >7.13 had a significantly higher risk of in-hospital mortality compared with those with ACNLR ≤2.05 in the fully adjusted model (OR 1.572, 95% CI 1.088–2.272; P = 0.016), with a significant trend across increasing ACNLR categories (P for trend = 0.003).

Consistent results were observed in the eICU-CRD external cohort. Each 1-SD increase in ACNLR was independently associated with higher in-hospital mortality in the fully adjusted model (OR 1.277, 95% CI 1.158–1.408; P < 0.001). Patients with ACNLR >7.13 also had a significantly increased mortality risk compared with the reference group (OR 1.863, 95% CI 1.389–2.498; P < 0.001), and the trend across ACNLR categories remained significant (P for trend <0.001).

Nonlinear association between ACNLR and in-hospital mortality

Restricted cubic spline analyses were performed to further evaluate the dose–response relationship between ACNLR and in-hospital mortality. In the MIMIC-IV cohort, ACNLR was significantly associated with in-hospital mortality after multivariable adjustment (P for overall <0.001), and the association showed evidence of nonlinearity (P for nonlinear = 0.014). The adjusted mortality risk remained relatively stable at lower ACNLR levels and increased progressively at higher ACNLR levels.

A similar pattern was observed in the eICU-CRD external cohort. The overall association between ACNLR and in-hospital mortality was significant (P for overall <0.001), with a significant nonlinear relationship (P for nonlinear <0.001). The adjusted risk increased more prominently in the higher range of ACNLR values, supporting the consistency of the nonlinear association across the two cohorts.

Cumulative incidence of in-hospital mortality

The cumulative incidence curves of in-hospital mortality according to ACNLR categories are shown in Figure 3. In both the MIMIC-IV and eICU-CRD cohorts, patients in the highest ACNLR category consistently showed the greatest cumulative incidence of in-hospital mortality during the 28-day follow-up period, and the differences among ACNLR categories were statistically significant in both cohorts (Gray's test, $P < 0.001$).

In the MIMIC-IV cohort, the lowest cumulative incidence was observed in Q2, whereas the curves for Q1 and Q3 were relatively similar. In contrast, Q4 showed a clearly higher cumulative incidence throughout follow-up. In the eICU-CRD cohort, Q1 and Q2 showed comparable cumulative incidence curves, while Q3 demonstrated an intermediate increase in mortality risk and Q4 remained the group with the highest cumulative incidence. Overall, these findings suggest that although the detailed risk pattern differed slightly between cohorts, elevated ACNLR was consistently associated with a higher cumulative burden of in-hospital mortality, particularly among patients in the highest ACNLR category.

Subgroup analyses

Subgroup analyses were performed to evaluate whether the association between ACNLR and in-hospital mortality differed across clinically relevant strata (Figure 4). In the MIMIC-IV cohort, the association between higher ACNLR and in-hospital mortality was generally consistent across subgroups defined by age, sex, mechanical ventilation, vasoactive drug use, chronic pulmonary disease, congestive heart failure, and renal disease. No significant interactions were observed across the predefined subgroups. Similar findings were observed in the eICU-CRD external cohort. The direction of association between ACNLR and in-hospital mortality was broadly consistent across the examined subgroups, and no significant interactions were observed for age, sex, mechanical ventilation, vasoactive drug use, chronic pulmonary disease, congestive heart failure, or renal disease. Overall, these findings suggest that the association between elevated ACNLR and in-hospital mortality was not substantially modified by the evaluated clinical characteristics.

Propensity score-based sensitivity analyses in the pooled cohort

In the pooled MIMIC-IV and eICU-CRD cohort, high ACNLR was consistently associated with increased in-hospital mortality in both the original and propensity score-adjusted analyses. In the original pooled cohort, high ACNLR was associated with higher in-hospital mortality in the unadjusted model (OR 1.739, 95% CI 1.500–2.016; P < 0.001), and this association remained significant after full adjustment (OR 1.471, 95% CI 1.245–1.738; P < 0.001). After propensity score matching, high ACNLR remained significantly associated with increased mortality in both the unadjusted model (OR 1.385, 95% CI 1.163–1.649; P < 0.001) and the fully adjusted model (OR 1.450, 95% CI 1.194–1.761; P < 0.001). Similar results were observed in the IPTW-weighted cohort, with high ACNLR associated with increased in-hospital mortality in the unadjusted model (OR 1.396, 95% CI 1.195–1.631; P < 0.001) and the fully adjusted model (OR 1.457, 95% CI 1.229–1.727; P < 0.001). In addition, no significant interaction was observed between high ACNLR and database source (OR 1.148, 95% CI 0.811–1.623; P for interaction = 0.436), suggesting that the association was consistent between the MIMIC-IV and eICU-CRD cohorts.

Discussion

The present dual-database retrospective cohort study provides evidence that early albumin-corrected neutrophil-to-lymphocyte ratio (ACNLR) is independently associated with in-hospital mortality among ICU patients with pneumonia. Higher early ACNLR was associated with increased mortality risk in the MIMIC-IV cohort, and this association was replicated in the eICU-CRD cohort. The excess mortality risk was mainly concentrated among patients with markedly elevated ACNLR values, whereas lower or intermediate ACNLR levels were not consistently associated with increased risk. Restricted cubic spline analysis further demonstrated a nonlinear association between ACNLR and mortality, with risk increasing predominantly at higher ACNLR values. Subgroup analyses showed no significant effect modification across clinically relevant strata. In the pooled cohort, the association between high ACNLR and in-hospital mortality also remained consistent after propensity score matching and inverse probability of treatment weighting. Taken together, these findings suggest that early ACNLR may serve as a simple and clinically accessible inflammation–nutrition biomarker for mortality risk stratification in ICU patients with pneumonia.

Our findings are consistent with previous studies showing that inflammatory and nutritional biomarkers are closely related to adverse outcomes in pneumonia and critical illness. Pneumonia is a heterogeneous infectious syndrome with substantial variation in host inflammatory response, immune status, nutritional reserve, and organ dysfunction, all of which may influence clinical outcomes[15, 16]. NLR has been widely evaluated

as a readily available marker of systemic inflammation and immune dysregulation. In a multicenter cohort of hospitalized patients with community-acquired pneumonia, elevated NLR was independently associated with adverse outcomes, including ICU admission, prolonged hospitalization, and in-hospital mortality[17]. NLR has also been reported to predict mortality in general ICU populations, suggesting that neutrophil–lymphocyte imbalance may reflect a broader inflammatory and immune disturbance in critical illness[18]. These findings support the clinical relevance of NLR as an accessible inflammatory marker in both pneumonia and critical care settings.

Serum albumin is another clinically important prognostic biomarker. Previous studies in patients hospitalized with community-acquired pneumonia have shown that lower albumin levels are associated with increased mortality and poorer clinical outcomes[19, 20]. Similarly, hypoalbuminemia has been associated with increased mortality in critically ill patients, reflecting not only poor nutritional reserve but also systemic inflammation, increased vascular permeability, hepatic dysfunction, and disease severity[21, 22]. Therefore, albumin may provide prognostic information that is not fully captured by leukocyte-derived inflammatory indices alone. The prognostic value of albumin-based composite biomarkers has also been increasingly reported in critically ill populations. Previous studies have shown that the C-reactive protein-to-albumin ratio is associated with mortality in ICU patients[23, 24]. In addition, the lactate-to-albumin ratio has been reported to predict ICU admission and mortality in hospitalized patients with community-acquired pneumonia[25]. In elderly ICU patients with pneumonia, neutrophil percentage-to-albumin ratio has further shown prognostic value[26]. This body of evidence supports the concept that inflammation–nutrition composite indices may capture complementary information on systemic inflammation, immune-inflammatory status, nutritional reserve, and illness severity. Our findings extend this evidence to critically ill patients with pneumonia and support the potential role of ACNLR in early risk stratification.

The biological plausibility of ACNLR may be explained by the combined effects of neutrophil-dominant inflammation, lymphocyte depletion, and hypoalbuminemia-related physiological vulnerability. In severe infection, excessive neutrophil activation may amplify cytokine release, oxidative stress, endothelial injury, microvascular dysfunction, and tissue damage, thereby contributing to organ dysfunction and adverse outcomes[27–29]. At the same time, lymphopenia may reflect impaired adaptive immunity and immune exhaustion; previous studies have shown that lymphopenia in pneumonia and sepsis is associated with dysregulated immune responses, greater disease severity, and increased mortality[30–32]. Serum albumin further complements this immune-inflammatory signal, as hypoalbuminemia in critical illness reflects not

only nutritional depletion but also systemic inflammation, increased capillary permeability, impaired hepatic synthesis, and accelerated catabolism[10, 22]. Consistent with this concept, NLR–albumin and neutrophil–albumin composite indices, including the neutrophil-to-lymphocyte-to-albumin ratio and neutrophil percentage-to-albumin ratio, have shown prognostic value in critically ill patients with sepsis, septic shock, or pneumonia[12, 14, 26, 33]. Therefore, elevated ACNLR may represent the coexistence of heightened inflammatory burden, impaired immune reserve, and reduced nutritional–physiological reserve, which may partly explain its association with in-hospital mortality in critically ill patients.

The nonlinear association observed in the restricted cubic spline analysis provides further insight into the prognostic pattern of ACNLR. Rather than increasing uniformly across the entire range of values, mortality risk appeared to remain relatively stable at lower ACNLR levels and increased more prominently among patients with markedly elevated ACNLR. Consistent with the spline findings, categorical analyses also showed that the excess mortality risk was mainly concentrated among patients in the highest ACNLR category. This pattern suggests that the prognostic significance of ACNLR may be driven primarily by patients with substantial inflammatory activation and impaired nutritional–physiological reserve, rather than by a simple linear increase across the full spectrum of values. From a clinical perspective, markedly elevated ACNLR may identify a subgroup of ICU patients with pneumonia who have concurrent inflammation, immune dysregulation, and reduced physiological reserve. These patients may be more vulnerable to organ dysfunction and adverse outcomes and may therefore benefit from closer monitoring, early reassessment, and risk-directed management.

Several limitations of this study should be acknowledged. First, this was a retrospective observational study, and therefore causality between ACNLR and in-hospital mortality cannot be established. Second, although multivariable adjustment, subgroup analyses, and propensity score-based sensitivity analyses were performed, residual confounding from unmeasured factors, such as microbiological characteristics, appropriateness of antimicrobial therapy, radiographic severity, inflammatory cytokine profiles, fluid balance, and specific nutritional interventions, cannot be completely excluded. Third, ACNLR was calculated using laboratory data obtained during the early phase of ICU admission, and dynamic changes in ACNLR over time were not evaluated. Serial measurements may provide additional prognostic information and warrant further investigation. Fourth, pneumonia was identified using database-derived diagnostic records, and misclassification may have occurred despite efforts to exclude ventilator-associated pneumonia and aspiration pneumonia. Fifth, although our findings

were externally replicated in the eICU-CRD cohort, both databases were derived from the United States, which may limit the generalizability of the results to other healthcare systems and populations. Finally, while ACNLR was independently associated with mortality, whether incorporating ACNLR into existing clinical risk prediction models can improve discrimination, calibration, and clinical utility remains to be determined.

Conclusions

In conclusion, elevated early albumin-corrected neutrophil-to-lymphocyte ratio was independently associated with increased in-hospital mortality among ICU patients with pneumonia. This association was observed in both the MIMIC-IV and eICU-CRD cohorts and remained consistent across subgroup and propensity score-based sensitivity analyses. As a simple and readily available inflammation–nutrition composite biomarker derived from routine laboratory tests, ACNLR may provide useful prognostic information for early risk stratification in critically ill patients with pneumonia. Further prospective multicenter studies are warranted to validate these findings and to determine whether incorporating ACNLR into existing clinical risk assessment strategies can improve prognostic assessment and patient management.

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Declarations

Ethics approval and consent to participate

This study used publicly available, de-identified data from the MIMIC-IV and eICU-CRD databases. Access to both databases was granted after completion of the required training and approval of the data use agreement. Because the data were de-identified and no identifiable personal information was involved, additional institutional ethics approval and informed consent were not required for this secondary analysis.

Consent for publication

Not applicable.

Availability of data and materials

The data used in this study were obtained from two publicly accessible critical care databases hosted on PhysioNet: the Medical Information Mart for Intensive Care IV version 3.1 (MIMIC-IV v3.1; https://physionet.org/content/mimiciv/3.1/) and the eICU Collaborative Research Database version 2.0 (eICU-CRD v2.0; https://physionet.org/content/eicu-crd/2.0/). Access to both databases requires completion of the required training and approval of the data use agreement. The data were used in accordance with the respective data use agreements. No new primary data were generated in this study. The analytic datasets can be reproduced from the original databases using the eligibility criteria, variable definitions, and time windows described in the Methods section. Additional details regarding data extraction and analysis are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by the Talent Fund of Guizhou Provincial People's Hospital (Grant No. [2023] 31). The funder had no role in the study design, data extraction, statistical analysis, interpretation of results, manuscript preparation, or decision to submit the manuscript for publication.

Authors' contributions

LH and YW contributed equally to this work and share first authorship. LH was responsible for data extraction, formal analysis, visualization, and drafting of the original manuscript. YW contributed to methodology, data curation, formal analysis, and drafting of the original manuscript. QZ contributed to data curation, literature review, and manuscript revision. JY contributed to methodology, result interpretation, and critical revision of the manuscript. BW and YL contributed equally to this work and share corresponding authorship. BW and YL conceived and supervised the study, interpreted the results, and critically revised the manuscript. YL also contributed to methodology and statistical analysis. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

574 **Table 1**. Baseline characteristics and in-hospital mortality of patients stratified by MIMIC-IV-derived ACNLR quartile categories in the MIMIC-
575 IV cohort.

Variables	Overall (n= 1378)	Q1 (≤2.05) (n=345)	Q2 (2.06–3.53) (n= 344)	Q3 (3.54–7.13) (n= 344)	Q4 (>7.13) (n= 345)	*P*
Population characteristics, median [IQR]						
Age (years)	65.00 [54.00, 75.75]	63.00 [50.00, 74.00]	66.00 [55.00, 75.00]	66.00 [55.00, 77.00]	67.00 [56.00, 76.00]	0.008
Male, n (%)	736 (53.4)	176 (51.0)	179 (52.0)	196 (57.0)	185 (53.6)	0.42
Race						0.084
White, n (%)	810 (58.8)	190 (55.1)	190 (55.2)	215 (62.5)	215 (62.3)	
Black, n (%)	107 (7.8)	33 (9.6)	31 (9.0)	24 (7.0)	19 (5.5)	
Asian, n (%)	38 (2.8)	15 (4.3)	9 (2.6)	4 (1.2)	10 (2.9)	
Other, n (%)	423 (30.7)	107 (31.0)	114 (33.1)	101 (29.4)	101 (29.3)	
BMI	28.23 [23.88, 33.38]	28.44 [24.30, 33.29]	28.52 [24.38, 34.46]	28.69 [23.47, 33.85]	27.34 [23.46, 32.41]	0.066
Vital signs, median [IQR]						
Heart rate (beats/min)	89.76 [77.84, 101.99]	88.65 [76.36, 102.00]	88.58 [78.66, 100.66]	90.26 [76.65, 102.08]	91.50 [79.23, 103.73]	0.134
Respiratory rate (breaths/min)	21.33 [18.45, 24.71]	21.28 [18.08, 24.55]	20.61 [18.24, 24.33]	21.37 [18.37, 24.78]	21.92 [19.17, 25.21]	0.052
Mean blood pressure (mmHg)	75.69 [70.41, 82.88]	76.50 [70.25, 83.74]	76.34 [70.68, 83.96]	74.67 [70.81, 81.22]	74.42 [69.09, 82.04]	0.054
SpO_2 (%)	96.12 [94.52, 97.76]	96.51 [94.65, 97.85]	96.06 [94.64, 97.78]	96.17 [94.63, 97.85]	95.69 [94.04, 97.46]	0.011
Temperature (°C)	36.90 [36.62, 37.31]	37.01 [36.71, 37.40]	36.91 [36.64, 37.32]	36.92 [36.65, 37.28]	36.80 [36.53, 37.17]	<0.001
Laboratory tests onset, median [IQR]						
Albumin (g/dL)	3.00 [2.52, 3.30]	3.10 [2.80, 3.50]	3.10 [2.70, 3.42]	2.90 [2.50, 3.30]	2.70 [2.30, 3.10]	<0.001
NLR	10.62 [6.02, 19.43]	3.67 [2.31, 5.00]	8.34 [7.08, 10.00]	14.60 [11.42, 17.20]	31.34 [24.03, 46.21]	<0.001

ACNLR	3.53 [2.05, 7.13]	1.21 [0.73, 1.63]	2.80 [2.45, 3.18]	5.00 [4.24, 5.94]	11.85 [8.93, 16.80]	<0.001
Hemoglobin (g/dL)	9.70 [8.20, 11.40]	9.60 [7.80, 11.30]	10.00 [8.47, 11.60]	9.60 [8.20, 11.30]	9.60 [8.20, 11.20]	0.052
Platelet(×10^9/L)	170.00 [107.00, 250.75]	147.00 [70.00, 222.00]	182.00 [120.00, 257.00]	173.50 [123.75, 257.00]	183.00 [111.00, 276.00]	<0.001
RDW (%)	15.30 [14.00, 17.30]	15.30 [13.90, 17.80]	15.30 [13.70, 17.02]	15.20 [14.20, 17.02]	15.50 [14.10, 17.50]	0.148
WBC (×10^9/L)	13.35 [9.03, 19.30]	9.60 [5.50, 14.10]	12.35 [8.70, 16.70]	14.85 [10.40, 20.62]	17.70 [12.80, 24.40]	<0.001
Anion gap	16.00 [13.00, 19.00]	15.00 [13.00, 18.00]	15.00 [13.00, 18.00]	16.00 [13.00, 19.00]	16.00 [14.00, 20.00]	0.001
Bicarbonate (mmol/L)	21.00 [18.00, 24.00]	22.00 [19.00, 24.00]	22.00 [18.00, 25.00]	21.00 [17.00, 24.00]	20.00 [17.00, 24.00]	0.013
BUN (mg/dL)	28.00 [17.00, 48.00]	22.00 [13.00, 35.00]	28.00 [18.75, 44.00]	29.00 [19.00, 48.00]	37.00 [19.00, 58.00]	<0.001
Calcium (mg/dL)	7.90 [7.30, 8.50]	8.00 [7.40, 8.60]	8.00 [7.50, 8.60]	7.90 [7.30, 8.43]	7.80 [7.20, 8.30]	<0.001
Chloride (mmol/L)	102.00 [98.00, 109.00]	103.00 [99.00, 109.00]	102.00 [98.00, 109.00]	102.00 [97.00, 110.00]	102.00 [96.00, 109.00]	0.125
Creatinine (mg/dL)	1.20 [0.80, 2.10]	1.10 [0.80, 1.70]	1.25 [0.88, 2.00]	1.20 [0.80, 2.20]	1.50 [0.90, 2.50]	<0.001
Sodium (mmol/L)	137.00 [133.00, 142.00]	138.00 [134.00, 142.00]	137.00 [134.00, 143.00]	137.00 [133.00, 143.00]	137.00 [133.00, 143.00]	0.325
Potassium (mmol/L)	4.30 [3.50, 4.90]	4.10 [3.50, 4.70]	4.30 [3.50, 4.82]	4.40 [3.60, 4.90]	4.50 [3.60, 5.00]	0.001
Glucose (mg/dL)	147.00 [118.25, 203.75]	136.00 [110.00, 172.00]	150.50 [120.00, 209.00]	154.00 [121.75, 203.25]	155.00 [122.00, 214.00]	<0.001
Treatment, n (%)						
Mechanical ventilation	733 (53.2)	163 (47.2)	188 (54.7)	196 (57.0)	186 (53.9)	0.065
Vasopressor use	534 (38.8)	129 (37.4)	114 (33.1)	137 (39.8)	154 (44.6)	0.018
RRT	76 (5.5)	12 (3.5)	22 (6.4)	18 (5.2)	24 (7.0)	0.196
Antibiotic type						0.001
0	168 (12.2)	54 (15.7)	52 (15.1)	39 (11.3)	23 (6.7)	
1	169 (12.3)	41 (11.9)	54 (15.7)	43 (12.5)	31 (9.0)	
2	402 (29.2)	84 (24.3)	100 (29.1)	112 (32.6)	106 (30.7)	
3	399 (29.0)	105 (30.4)	83 (24.1)	99 (28.8)	112 (32.5)	
>3	240 (17.4)	61 (17.7)	55 (16.0)	51 (14.8)	73 (21.2)	

Disease Severity Score, median [IQR]						
SOFA score	6.00 [4.00, 9.00]	6.00 [4.00, 10.00]	6.00 [4.00, 9.00]	6.50 [4.00, 9.00]	7.00 [4.00, 10.00]	0.047
APS III	53.00 [39.00, 70.00]	49.00 [34.00, 65.00]	49.50 [37.75, 65.00]	55.00 [40.75, 70.00]	59.00 [45.00, 79.00]	<0.001
Charlson comorbidity index	5.00 [3.00, 8.00]	5.00 [3.00, 7.00]	5.00 [3.00, 8.00]	5.00 [3.00, 8.00]	6.00 [4.00, 8.00]	<0.001
Comorbidities, n (%)						
Myocardial infarct	237 (17.2)	43 (12.5)	63 (18.3)	65 (18.9)	66 (19.1)	0.062
Congestive heart failure	467 (33.9)	92 (26.7)	135 (39.2)	120 (34.9)	120 (34.8)	0.002
Dementia	59 (4.3)	17 (4.9)	13 (3.8)	17 (4.9)	12 (3.5)	0.689
Chronic pulmonary disease	465 (33.7)	87 (25.2)	127 (36.9)	123 (35.8)	128 (37.1)	0.002
Diabetes	397 (28.8)	91 (26.4)	107 (31.1)	104 (30.2)	95 (27.5)	0.477
Renal disease	307 (22.3)	55 (15.9)	87 (25.3)	86 (25.0)	79 (22.9)	0.01
Liver disease	306 (22.2)	69 (20.0)	78 (22.7)	73 (21.2)	86 (24.9)	0.442
Cancer	316 (22.9)	103 (29.9)	57 (16.6)	65 (18.9)	91 (26.4)	<0.001
Cerebrovascular disease	149 (10.8)	40 (11.6)	35 (10.2)	39 (11.3)	35 (10.1)	0.891
Outcomes, n (%)						
Hospital death	377 (27.4)	88 (25.5)	70 (20.3)	94 (27.3)	125 (36.2)	<0.001

Note: Values are presented as median [interquartile range] for continuous variables and n (%) for categorical variables. Patients were stratified according to MIMIC-IV-derived ACNLR quartile cutoffs: Q1 ≤2.05, Q2 2.06–3.53, Q3 3.54–7.13, and Q4 >7.13. Between-group comparisons were performed using the Kruskal–Wallis test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Albumin and hemoglobin are expressed in g/dL. ACNLR was calculated as NLR divided by serum albumin concentration. ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; BMI, body mass index; SpO_2, peripheral oxygen saturation; RDW, red cell distribution width; WBC, white blood cell count; BUN, blood urea nitrogen; APS III, Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; CCI, Charlson comorbidity index; RRT, renal replacement therapy

Table 2. Association between ACNLR and in-hospital mortality in the MIMIC-IV and eICU-CRD cohorts.

		Model 1 OR (95% CI)	*P*	Model 2 OR (95% CI)	*P*	Model 3 OR (95% CI)	*P*
MIMIC-IV cohort	Per 1-SD increase	1.13 (1.01-1.26)	0.029	1.12 (1.00-1.24)	0.045	1.19 (1.06-1.33)	0.003
	Q1 (≤2.05)	Reference		Reference		Reference	
	Q2 (2.06–3.53)	0.746 (0.52-1.07)	0.108	0.696 (0.48-1.00)	0.050	0.834 (0.56-1.24)	0.370
	Q3 (3.54–7.13)	1.098 (0.782-1.541)	0.588	1.030 (0.729-1.454)	0.869	1.203 (0.825-1.755)	0.336
	Q4 (>7.13)	1.659 (1.196-2.301)	0.002	1.578 (1.131-2.203)	0.007	1.572 (1.088-2.272)	0.016
	P for trend		<0.001		<0.001		0.003
eICU-CRD cohort	Per 1-SD increase	1.346 (1.225-1.479)	<0.001	1.272 (1.156-1.400)	<0.001	1.277 (1.158-1.408)	<0.001
	Q1 (≤2.05)	Reference		Reference		Reference	
	Q2 (2.06–3.53)	0.995 (0.720-1.375)	0.976	0.928 (0.669-1.287)	0.655	0.995 (0.709-1.398)	0.978
	Q3 (3.54–7.13)	1.307 (0.981-1.743)	0.067	1.147 (0.856-1.537)	0.357	1.219 (0.897-1.656)	0.206
	Q4 (>7.13)	2.120 (1.616-2.780)	<0.001	1.802 (1.366-2.377)	<0.001	1.863 (1.389-2.498)	<0.001
	P for trend		<0.001		<0.001		<0.001

Note: Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression models. ACNLR was analyzed as a cohort-specific standardized continuous variable and as MIMIC-IV-derived quartile categories. Q1 (ACNLR ≤2.05) was used as the reference group. Model 1 was unadjusted. Model 2 was adjusted for age, sex, race, and body mass index. Model 3 was adjusted for age, sex, race, body mass index, mean blood pressure, peripheral oxygen saturation, glucose, sodium, hemoglobin, bicarbonate, platelet count, vasoactive drug use, renal replacement therapy, cancer, congestive heart failure, cerebrovascular disease, renal disease, and chronic pulmonary disease. ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; OR, odds ratio; CI, confidence interval.

Table 3. Propensity score-based sensitivity analyses of high ACNLR and in-hospital mortality in the pooled MIMIC-IV and eICU-CRD cohort.

Model	Original cohort OR (95% CI)	*P* value	PSM-matched cohort OR (95% CI)	*P* value	IPTW-weighted cohort OR (95% CI)	*P* value
Unadjusted	1.739 (1.500-2.016)	<0.001	1.385 (1.163-1.649)	<0.001	1.396 (1.195-1.631)	<0.001
Fully adjusted	1.471 (1.245-1.738)	<0.001	1.450 (1.194-1.761)	<0.001	1.457 (1.229-1.727)	<0.001
Interaction analysis			**OR (95% CI)**		**P for interaction**	
High ACNLR × eICU-CRD			1.148 (0.811–1.623)		0.436	

Note: High ACNLR was defined as ACNLR >7.13, corresponding to the MIMIC-IV-derived 75th percentile cutoff and the lower boundary of the highest ACNLR quartile. The reference group comprised patients with ACNLR ≤7.13. The fully adjusted model included prespecified demographic characteristics, vital signs, laboratory parameters, treatment-related variables, comorbidities, and database source. Propensity score matching was performed using 1:1 nearest-neighbor matching with exact matching on database source. PSM, propensity score matching; IPTW, inverse probability of treatment weighting; OR, odds ratio; CI, confidence interval.

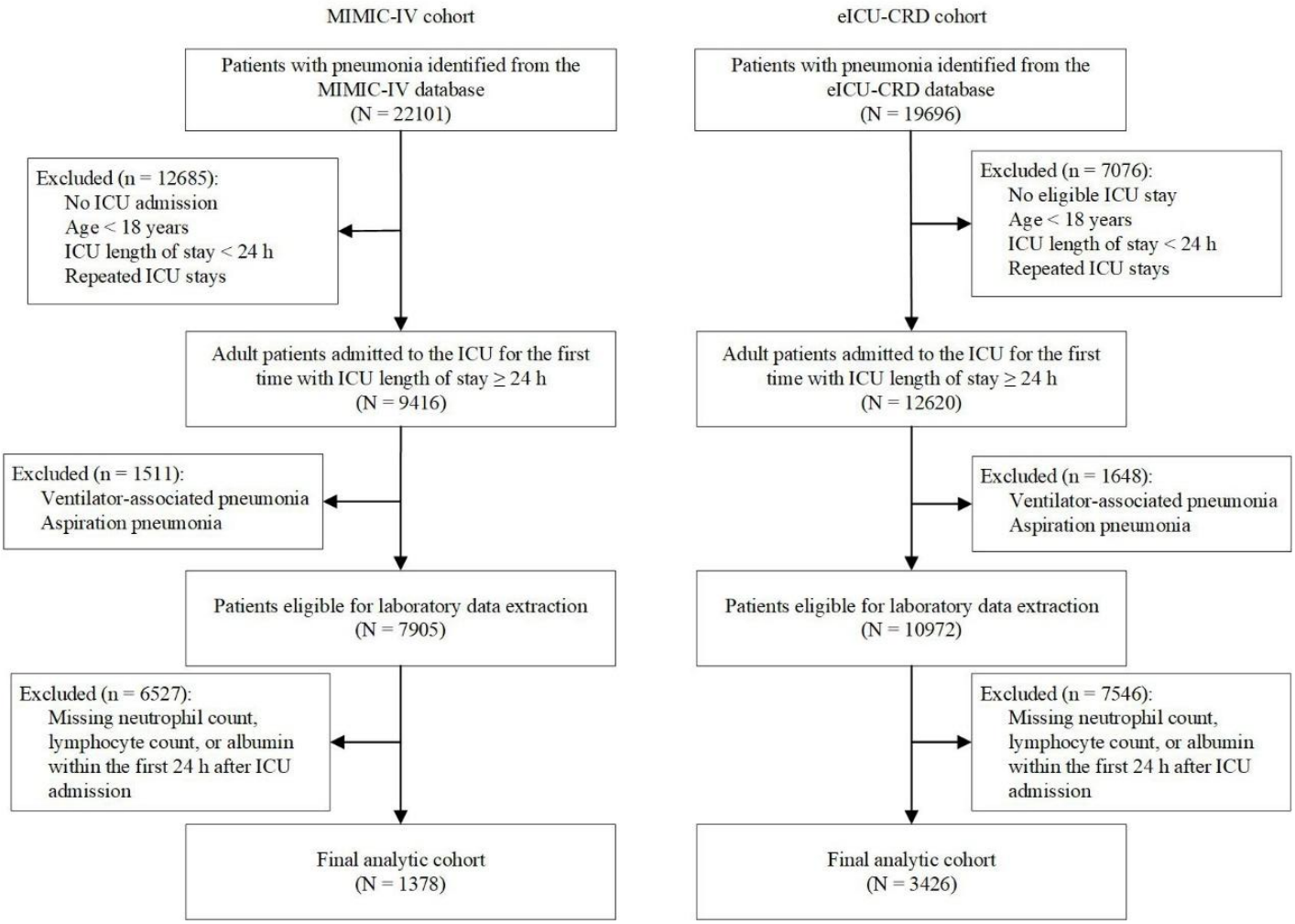


Figure 1: Flow chart of patient selection.

Note: Patient selection processes are shown separately for the MIMIC-IV and eICU-CRD cohorts. Adult patients with pneumonia were included, and only the first ICU stay was retained for patients with multiple ICU admissions. Patients were excluded if they had an ICU length of stay less than 24 hours, ventilator-associated pneumonia, aspiration pneumonia, missing laboratory measurements required to calculate ACNLR within the first 24 hours after ICU admission, or missing primary outcome information. ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; ICU, intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care IV; eICU-CRD, eICU Collaborative Research Database.

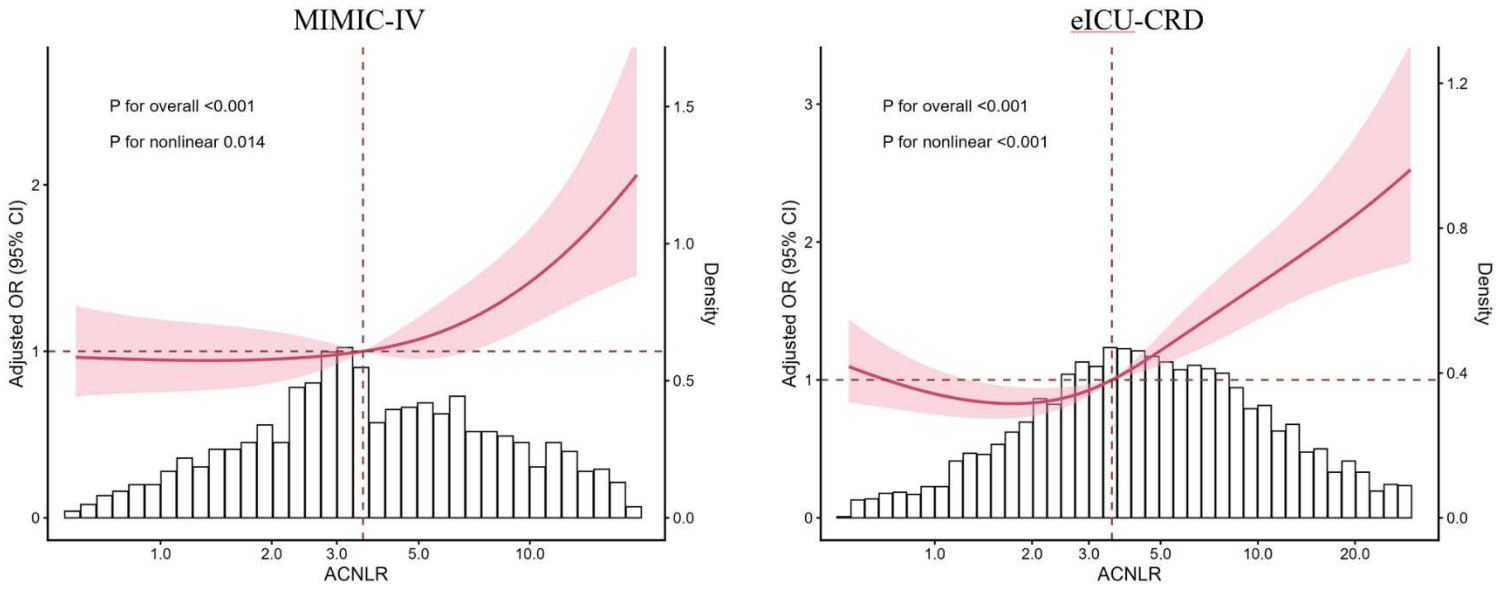


Figure 2. Restricted cubic spline curves for the association between ACNLR and in-hospital mortality in the MIMIC-IV and eICU-CRD cohorts.

Note: Restricted cubic spline curves show adjusted odds ratios for in-hospital mortality according to ACNLR levels. Solid lines represent adjusted odds ratios, shaded areas represent 95% confidence intervals, and histograms show the distribution of ACNLR. The horizontal dashed line indicates an odds ratio of 1.0, and the vertical dashed line indicates the reference value. Models were adjusted for the covariates included in the fully adjusted model. ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; OR, odds ratio; CI, confidence interval.

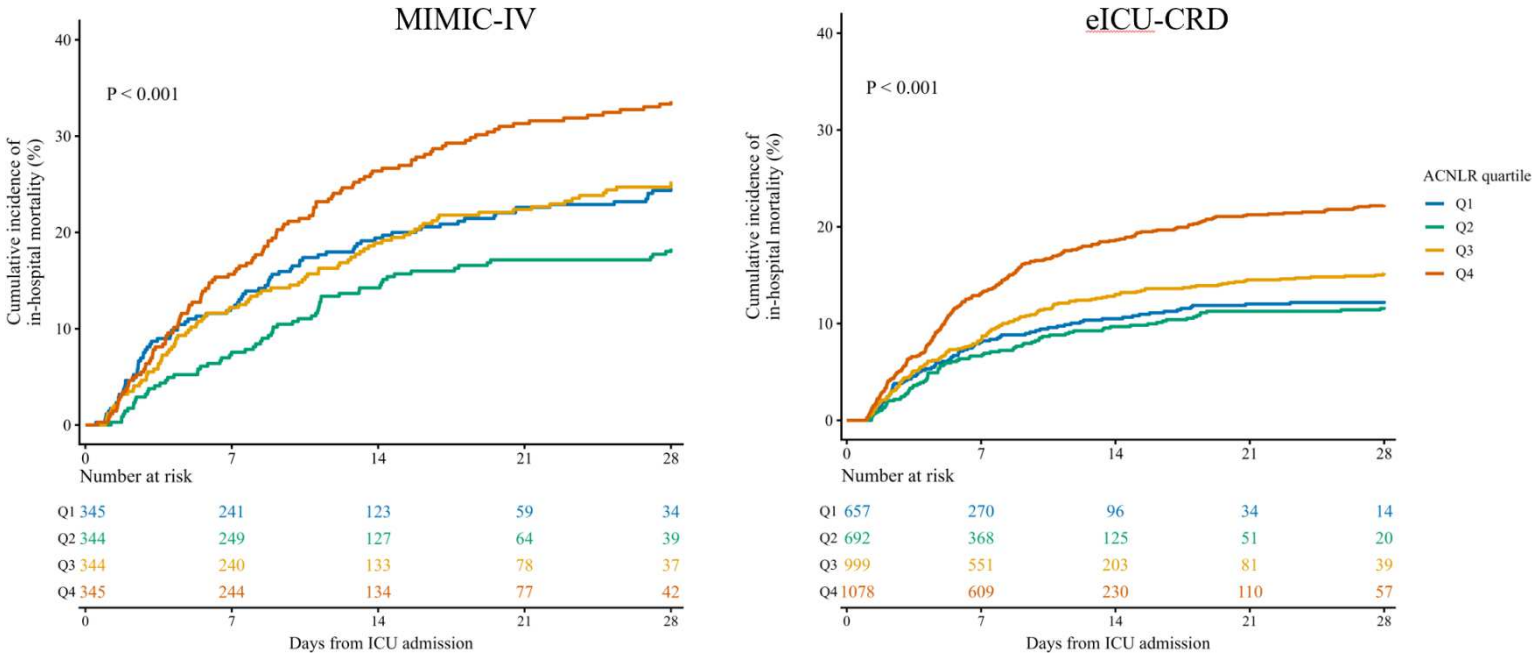


Figure 3. Cumulative incidence of in-hospital mortality according to ACNLR quartile categories in the MIMIC-IV and eICU-CRD cohorts.

Note: Cumulative incidence curves show the 28-day cumulative incidence of in-hospital death after ICU admission, with discharge alive treated as a competing event. Patients were stratified using MIMIC-IV-derived ACNLR quartile cutoffs. P values were calculated using Gray's test. ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; ICU, intensive care unit.

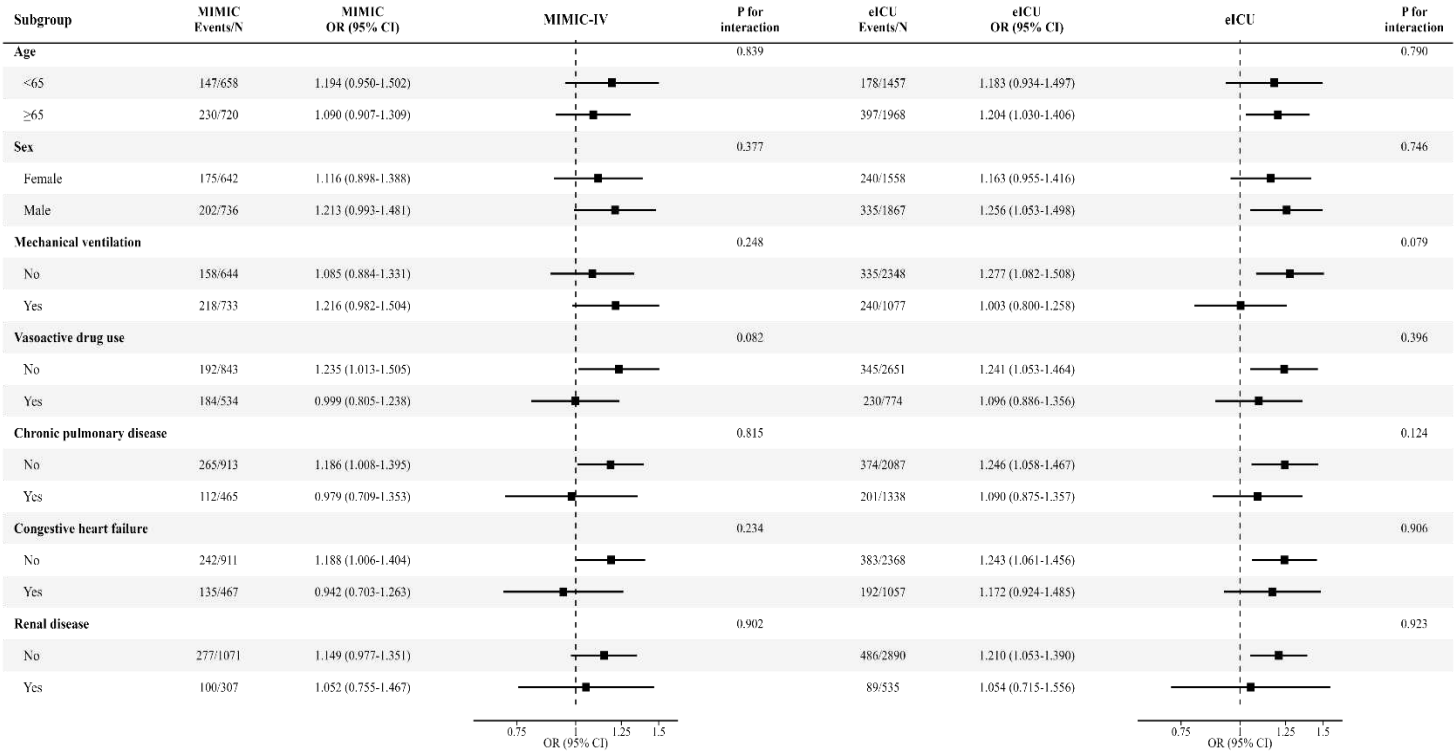


Figure 4. Subgroup analyses of the association between ACNLR and in-hospital mortality in the MIMIC-IV and eICU-CRD cohorts.

Note: Subgroup analyses were performed according to age, sex, mechanical ventilation, vasoactive drug use, chronic pulmonary disease, congestive heart failure, and renal disease. Odds ratios were estimated for each 1-SD increase in ACNLR within each subgroup. P values for interaction were calculated by adding interaction terms to the fully adjusted logistic regression models. ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; OR, odds ratio; CI, confidence interval.

Supplementary Table 1. Baseline characteristics and in-hospital mortality of patients stratified by MIMIC-IV-derived ACNLR quartile categories in the eICU-CRD cohort.

Variables	Overall (n= 3426)	Q1 (≤2.05) (n=657)	Q2 (2.06–3.53) (n= 692)	Q3 (3.54–7.13) (n= 999)	Q4 (>7.13) (n= 1078)	*P*
Population characteristics, median [IQR]						
Age (years)	68.00 [56.00, 79.00]	64.00 [51.00, 76.00]	67.00 [55.00, 78.00]	69.00 [57.00, 88.00]	70.00 [59.00, 80.00]	<0.001
Male, n (%)	1867 (54.5)	349 (53.1)	368 (53.2)	562 (56.3)	588 (54.5)	0.525
Race						<0.001
White, n (%)	2739 (79.9)	484 (73.7)	536(77.5)	825 (82.6)	894 (82.9)	
Black, n (%)	286 (8.3)	92 (14.0)	62 (9.0)	69 (6.9)	63 (5.8)	
Asian, n (%)	53 (1.5)	8 (1.2)	10 (1.4)	20 (2.0)	15 (1.4)	
Other, n (%)	348 (10.2)	73 (11.1)	84 (12.1)	85 (8.5)	106 (9.8)	
BMI	27.05 [22.83, 32.60]	27.70 [23.63, 33.68]	27.64 [23.74, 34.23]	27.26 [23.03, 32.74]	25.87 [21.92, 30.87]	<0.001
Vital signs, median [IQR]						
Heart rate (beats/min)	89.44 [78.94, 101.28]	88.76 [77.94, 100.99]	89.18 [79.38, 101.22]	88.86 [77.88, 100.72]	90.74 [80.24, 102.14]	0.112
Respiratory rate (breaths/min)	21.58 [18.16, 25.38]	21.32 [17.85, 25.60]	21.28 [17.96, 25.32]	21.54 [18.22, 25.17]	21.88 [18.37, 25.38]	0.276
Mean blood pressure (mmHg)	76.20 [69.60, 85.59]	78.10 [70.06, 88.22]	77.17 [70.72, 87.28]	76.18 [69.58, 85.17]	75.11 [69.00, 82.94]	<0.001
SpO_2 (%)	96.37 [94.84, 98.01]	96.49 [94.76, 98.00]	96.38 [94.70, 97.96]	96.37 [94.88, 98.02]	96.30 [94.89, 98.04]	0.874
Temperature (°C)	36.50[36.20, 36.83]	36.60 [36.20, 36.90]	36.60 [36.20, 36.90]	36.50 [36.20, 36.90]	36.40 [36.10, 36.80]	0.001
Laboratory tests onset, median [IQR]						
Albumin (g/dL)	2.70 [2.30, 3.10]	2.90 [2.50, 3.30]	2.80 [2.40, 3.20]	2.70 [2.30, 3.00]	2.40 [2.00, 2.90]	<0.001
NLR	11.89 [6.58, 21.85]	3.67 [2.44, 4.81]	7.72 [6.37, 9.10]	12.80 [10.73, 15.70]	29.69 [22.02, 45.00]	<0.001
ACNLR	4.52 [2.50, 8.45]	1.31 [0.82, 1.70]	2.78 [2.42, 3.18]	4.94 [4.15, 5.94]	11.66 [8.89, 17.63]	<0.001
Hemoglobin (g/dL)	10.60 [9.20, 12.10]	10.70 [9.20, 12.20]	10.90 [9.30, 12.33]	10.60 [9.20, 12.10]	10.50 [9.20, 11.90]	0.004
Platelet ($\times 10^9$/L)	193.00 [141.00, 263.00]	180.50 [130.75, 245.00]	193.00 [141.00, 253.00]	193.00 [146.00, 266.00]	202.00 [143.75, 276.25]	<0.001
RDW (%)	15.20 [14.00, 16.80]	15.10 [14.00, 16.60]	15.10 [13.90, 16.70]	15.00 [14.10, 16.80]	15.40 [14.20, 17.20]	0.004
WBC ($\times 10^9$/L)	11.91 [8.20, 17.10]	8.40 [5.84, 12.17]	10.50 [7.27, 14.25]	12.20 [8.70, 16.70]	15.80 [11.00, 21.83]	<0.001
Anion gap	11.00 [8.00, 14.00]	11.00 [8.00, 15.00]	11.00 [8.00, 14.00]	11.00 [8.00, 14.00]	11.00 [8.00, 14.00]	0.277
Bicarbonate (mmol/L)	24.00 [21.00, 28.00]	24.00 [21.00, 27.00]	24.00 [21.00, 28.00]	24.00 [21.00, 28.00]	24.00 [20.00, 27.70]	0.007
BUN (mg/dL)	25.00 [16.00, 41.00]	22.00 [14.00, 38.00]	22.00 [15.00, 36.75]	25.00 [17.00, 41.00]	27.00 [17.00, 45.00]	<0.001

Calcium (mg/dL)	8.20 [7.60, 8.70]	8.30 [7.70, 8.80]	8.20 [7.70, 8.80]	8.20 [7.60, 8.70]	8.10 [7.50, 8.60]	<0.001
Chloride (mmol/L)	103.00 [99.00, 108.00]	103.00 [99.00, 108.00]	103.00 [99.00, 107.00]	103.00 [99.00, 108.00]	103.00 [99.00, 108.00]	0.833
Creatinine (mg/dL)	1.15 [0.78, 1.90]	1.20 [0.78, 2.02]	1.11 [0.75, 1.93]	1.15 [0.80, 1.90]	1.14 [0.78, 1.88]	0.69
Sodium (mmol/L)	138.00 [135.00, 141.00]	138.00 [135.00, 141.00]	138.00 [135.00, 141.00]	138.00 [135.00, 141.00]	138.00 [135.00, 141.00]	0.016
Potassium (mmol/L)	4.10 [3.60, 4.50]	4.00 [3.60, 4.50]	4.00 [3.60, 4.50]	4.10 [3.70, 4.60]	4.00 [3.60, 4.60]	0.237
Glucose (mg/dL)	133.00[105.00,176.00]	121.00[96.00,162.75]	125.00[102.00,163.00]	137.00[110.00,175.00]	145.00[115.00,188.00]	<0.001
Treatment, n (%)						
Mechanical ventilation	1077(31.4)	182 (27.7)	219 (31.6)	320 (32.0)	356 (33.0)	0.128
Vasopressor use	774 (22.6)	117 (17.8)	143 (20.7)	236 (23.6)	278 (25.8)	0.001
RRT	140 (4.1)	39(5.9)	29 (4.2)	37 (3.7)	35 (3.2)	0.045
Antibiotic type						0.144
0	1818 (53.1)	349 (53.1)	353 (51.0)	544 (54.5)	572 (53.1)	
1	703 (20.5)	160 (24.4)	147 (21.2)	181 (18.1)	215 (19.9)	
2	617 (18.0)	102 (15.5)	134 (19.4)	184 (18.4)	197 (18.3)	
3	250 (7.3)	39 (5.9)	54 (7.8)	75 (7.5)	82 (7.6)	
>3	38 (1.1)	7 (1.1)	4 (0.6)	15 (1.5)	12 (1.1)	
Disease Severity Score, median [IQR]						
SOFA score	/	/	/	/	/	
APS III	/	/	/	/	/	
Charlson comorbidity index	/	/	/	/	/	
APACHE score	66.00[51.00,85.00]	60.00[47.00,78.00]	63.00[48.00,80.00]	67.00[52.50,85.00]	72.00[56.00,91.00]	<0.001
Comorbidities, n (%)						
Myocardial infarct	447 (13.0)	83 (12.6)	90 (13.0)	137 (13.7)	137 (12.7)	0.896
Congestive heart failure	1058 (30.9)	210 (32.0)	226 (32.7)	306 (30.6)	316 (29.3)	0.448
Dementia	234 (6.8)	34 (5.2)	50 (7.2)	81 (8.1)	69 (6.4)	0.118
Chronic pulmonary disease	1338 (39.1)	206 (31.4)	247 (35.7)	424 (42.4)	461 (42.8)	<0.001
Diabetes	1097 (32.0)	247 (37.6)	215 (31.1)	327 (32.7)	308 (28.6)	0.001
Renal disease	535 (15.6)	116 (17.7)	105 (15.2)	158 (15.8)	156 (14.5)	0.35
Liver disease	259 (7.6)	47 (7.2)	57 (8.2)	71 (7.1)	84 (7.8)	0.805

Cancer	671 (19.6)	117 (17.8)	120 (17.3)	185 (18.5)	249 (23.1)	0.005
Cerebrovascular disease	449(13.1)	98 (14.9)	90 (13.0)	122 (12.2)	139 (12.9)	0.451
Outcomes, n (%)						
Hospital death	575(16.8)	82 (12.5)	86 (12.4)	157 (15.7)	250 (23.2)	<0.001

Note: Values are presented as median [interquartile range] for continuous variables and n (%) for categorical variables. Patients in the eICU-CRD cohort were categorized using the ACNLR quartile cutoffs derived from the MIMIC-IV cohort: Q1 ≤2.05, Q2 2.06–3.53, Q3 3.54–7.13, and Q4 >7.13. Between-group comparisons were performed using the Kruskal–Wallis test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Albumin and hemoglobin are expressed in g/dL. ACNLR was calculated as NLR divided by serum albumin concentration. Variables not available or not directly comparable in the eICU-CRD cohort are indicated by "/".

Supplementary Table 2. Baseline characteristics of survivors and non-survivors in the MIMIC-IV and eICU-CRD cohorts.

	Patients from MIMIC-IV (n= 1378)				Patients from eICU-CRD (n= 3426)			
	Total (n=1378)	**Survival (n=1001)**	**Death (n=377)**	***P***	**Total (n=3426)**	**Survival (n=2851)**	**Death (n=575)**	***P***
Population characteristics, median [IQR]								
Age (years)	65.00[54.00,75.75]	64.00[52.00,75.00]	68.00[57.00,78.00]	<0.001	68.00[56.00,79.00]	67.00[55.00,78.00]	72.00[62.00,82.00]	<0.001
Male, n (%)	736(53.4）	534(53.3)	202(53.6)	0.986	1867 (54.5)	1532 (53.7)	335 (58.3)	0.052
Race				0.035				0.077
White, n (%)	810(58.8)	596(59.5)	214(56.8)		2739(79.9)	2271(79.7)	468(81.4)	
Black, n (%)	107(7.8)	87(8.7)	20(5.3)		286(8.3)	249(8.7)	37(6.4)	
Asian, n (%)	38(2.8)	29(2.9)	9(2.4)		53(1.5)	39(1.4)	14(2.4)	
Other, n (%)	423(30.7)	289(28.9)	134(35.5)		348(10.2)	292(10.2)	56(9.7)	
BMI	28.23[23.88,33.38]	27.99[23.71,33.41]	28.55[24.81,33.36]	0.206	27.05[22.83,32.60]	27.30[23.09,33.18]	25.60[22.06,30.61]	<0.001
Vital signs, median [IQR]								
Heart rate (beats/min)	89.76 [77.84, 101.99]	88.42 [76.76, 100.04]	95.00 [81.25, 107.88]	<0.001	89.44 [78.94, 101.28]	88.72 [78.35, 100.41]	93.86[81.74,106.76]	<0.001
Respiratory rate (breaths/min)	21.33 [18.45, 24.71]	20.74 [18.21, 24.16]	22.56 [19.82, 26.08]	<0.001	21.58 [18.16, 25.38]	21.33 [18.00, 25.00]	22.85[19.39,26.85]	<0.001
Mean blood pressure (mmHg)	75.69 [70.41, 82.88]	76.28 [70.88, 83.87]	73.95 [68.46, 79.81]	<0.001	76.20 [69.60, 85.59]	76.99 [70.31, 86.53]	72.71[67.49,80.72]	<0.001
SpO2 (%)	96.12 [94.52, 97.76]	96.37 [94.62, 97.90]	95.56 [94.09, 97.13]	<0.001	96.37 [94.84, 98.01]	96.41 [94.91, 97.99]	96.09[94.44,98.13]	0.042
Temperature (°C)	36.90[36.62,37.31]	36.92[36.65,37.34]	36.85[36.53,37.21]	<0.001	36.50[36.20,36.83]	36.50[36.20,36.90]	36.40[35.90,36.80]	<0.001
Laboratory tests onset, median [IQR]								
Albumin (g/dL)	3.00[2.52,3.30]	3.00[2.60,3.40]	2.80[2.30,3.20]	<0.001	2.70[2.30,3.10]	2.70[2.30,3.10]	2.40[2.00,2.80]	<0.001
NLR	10.62[6.02,19.43]	10.31[5.95,18.20]	11.43[6.24,26.00]	0.009	11.89[6.58,21.85]	11.39[6.42,20.49]	14.67[8.05,25.87]	<0.001
ACNLR	3.53[2.05,7.13]	3.35[2.01,6.46]	4.29[2.24,10.17]	<0.001	4.52[2.50,8.45]	4.23[2.38,7.87]	6.15[3.11,11.50]	<0.001
Hemoglobin (g/dL)	9.70[8.20,11.40]	9.90[8.40,11.60]	9.10[7.80,10.80]	<0.001	10.60[9.20,12.10]	10.70[9.20,12.20]	10.20[9.00,11.75]	<0.001
Platelet ($\times 10^9$/L)	170.00 [107.00, 250.75]	182.00 [119.00, 253.00]	147.00 [68.00, 238.00]	<0.001	193.00 [141.00, 263.00]	196.00 [145.00, 265.00]	181.00[122.50,250.00]	<0.001
RDW (%)	15.30 [14.00, 17.30]	15.00 [13.80, 16.70]	16.20 [14.70, 18.60]	<0.001	15.20 [14.00, 16.80]	15.10 [14.00, 16.60]	16.00[14.50,18.00]	<0.001
WBC ($\times 10^9$/L)	13.35 [9.03, 19.30]	12.90 [8.90, 18.10]	15.70 [9.50, 22.50]	<0.001	11.91 [8.20, 17.10]	11.66 [8.10, 16.71]	13.35[9.03,19.23]	<0.001

Anion gap	16.00 [13.00, 19.00]	15.00 [13.00, 18.00]	17.00 [14.00, 21.00]	<0.001	11.00 [8.00, 14.00]	11.00 [8.00, 14.00]	12.00[9.00,15.00]	<0.001
Bicarbonate (mmol/L)	21.00 [18.00, 24.00]	22.00 [18.00, 24.00]	20.00 [16.00, 24.00]	<0.001	24.00 [21.00, 28.00]	24.00 [21.00, 28.00]	23.00[19.00,27.00]	<0.001
BUN (mg/dL)	28.00 [17.00, 48.00]	25.00 [16.00, 41.00]	38.00 [23.00, 59.00]	<0.001	25.00 [16.00, 41.00]	24.00 [15.00, 39.00]	30.00[21.00,47.00]	<0.001
Calcium (mg/dL)	7.90 [7.30, 8.50]	7.90 [7.30, 8.50]	7.80 [7.20, 8.50]	0.215	8.20 [7.60, 8.70]	8.20 [7.70, 8.70]	8.00[7.40,8.50]	<0.001
Chloride (mmol/L)	102.00[98.00,109.00]	103.00[98.00,109.00]	101.00[96.00,108.00]	<0.001	103.00[99.00,108.00]	103.00[99.00,107.00]	104.00[99.00,109.00]	0.042
Creatinine (mg/dL)	1.20 [0.80, 2.10]	1.10 [0.80, 1.80]	1.60 [1.10, 2.80]	<0.001	1.15 [0.78, 1.90]	1.11 [0.77, 1.87]	1.31[0.85,2.13]	<0.001
Sodium (mmol/L)	137.00 [133.00, 142.00]	137.00 [134.00, 142.00]	136.00 [132.00, 143.00]	0.042	138.00 [135.00, 141.00]	138.00 [135.00, 141.00]	138.00[135.00,142.00]	0.045
Potassium (mmol/L)	4.30 [3.50, 4.90]	4.20 [3.50, 4.80]	4.50 [3.60, 5.10]	<0.001	4.10 [3.60, 4.50]	4.00 [3.60, 4.50]	4.10[3.60,4.70]	0.099
Glucose (mg/dL)	147.00[118.25,203.75]	144.00[118.00,195.00]	158.00[121.00,217.00]	0.004	133.00 [105.00,176.00]	133.00[105.00,176.00]	137.00[106.00,179.50]	0.215
Treatment, n (%)								
Mechanical ventilation	733(53.2)	515(51.4)	218(57.8)	0.04	1077 (31.4)	837 (29.4)	240(41.7)	<0.001
Vasopressor use	534(38.8)	350(35.0)	184(48.8)	<0.001	774 (22.6)	544 (19.1)	230(40.0)	<0.001
RRT	76(5.5)	40(4.0)	36(9.5)	<0.001	140 (4.1)	120 (4.2)	20(3.5)	0.489
Antibiotic type				0.029				0.693
0	168(12.2)	124(12.4)	44(11.7)		1818(53.1)	1509(52.9)	309(53.7)	
1	169 (12.3)	126 (12.6)	43 (11.4)		703 (20.5)	593 (20.8)	110（19.1）	
2	402 (29.2)	285 (28.5)	117 (31.0)		617 (18.0)	516 (18.1)	101（17.6）	
3	399 (29.0)	308 (30.8)	91 (24.1)		250 (7.3)	201 (7.1)	49（8.5）	
>3	240 (17.4)	158 (15.8)	82(21.8)		38(1.1)	32 (1.1)	6 (1.0)	
Disease Severity Score, median [IQR]								
SOFA score	6.00 [4.00, 9.00]	6.00 [3.00, 9.00]	9.00 [5.00, 12.00]	<0.001	/	/	/	/
APS III	53.00 [39.00, 70.00]	48.00 [36.00, 63.00]	68.00 [53.00, 87.00]	<0.001	/	/	/	/
Charlson comorbidity index	5.00 [3.00, 8.00]	5.00 [3.00, 7.00]	6.00 [4.00, 8.00]	<0.001	/	/	/	/
APACHE score	/	/	/		66.00[51.00,85.00]	63.00[50.00,80.00]	82.00[67.00,105.00]	<0.001
Comorbidities, n (%)								
Myocardial infarct	237(17.2)	165 (16.5)	72 (19.1)	0.286	447 (13.0)	357 (12.5)	90(15.7)	0.049
Congestive heart failure	467(33.9)	332(33.2)	135(35.8)	0.39	1058(30.9)	866(30.4)	192(33.4)	0.168
Dementia	59 (4.3)	43 (4.3)	16 (4.2)	1	234 (6.8)	192 (6.7)	42(7.3)	0.687

Chronic pulmonary disease	465 (33.7)	353 (35.3)	112 (29.7)	0.06	1338 (39.1)	1137 (39.9)	201(35.0)	0.031
Diabetes	397 (28.8)	301 (30.1)	96 (25.5)	0.106	1097(32.0)	930 (32.6)	167(29.0)	0.104
Renal disease	307 (22.3)	207 (20.7)	100 (26.5)	0.024	535 (15.6)	446 (15.6)	89(15.5)	0.971
Liver disease	306(22.2)	192(19.2)	114 (30.2)	<0.001	259 (7.6)	178 (6.2)	81(14.1)	<0.001
Cancer	316(22.9)	190(19.0)	126 (33.4)	<0.001	671(19.6)	512(18.0)	159 (27.7)	<0.001
Cerebrovascular disease	149(10.8)	104(10.4)	45(11.9)	0.467	449(13.1)	361(12.7)	88(15.3)	0.100

Note: Values are presented as median [interquartile range] for continuous variables and n (%) for categorical variables. Patients in the eICU-CRD cohort were categorized using the ACNLR quartile cutoffs derived from the MIMIC-IV cohort: Q1 ≤2.05, Q2 2.06–3.53, Q3 3.54–7.13, and Q4 >7.13. Between-group comparisons were performed using the Kruskal–Wallis test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Albumin and hemoglobin are expressed in g/dL. ACNLR was calculated as NLR divided by serum albumin concentration. Variables not available or not directly comparable in the eICU-CRD cohort are indicated by "/". ACNLR, albumin-corrected neutrophil-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; BMI, body mass index; SpO_2, peripheral oxygen saturation; RDW, red cell distribution width; WBC, white blood cell count; BUN, blood urea nitrogen; APACHE, Acute Physiology and Chronic Health Evaluation; RRT, renal replacement therapy.