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ORIGINAL ARTICLE

Association between advanced lung cancer inflammation index and in-hospital mortality in ICU patients with community-acquired pneumonia: A retrospective analysis of the MIMIC-IV database

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Abstract

Objective: The objective of the present study was to explore the correlation between the advanced lung cancer inflammation index (ALI) and in-hospital mortality among patients diagnosed with community-acquired pneumonia (CAP).

Methods: Data from the Medical Information Mart for Intensive Care-IV database were adopted to analyze the in-hospital mortality of ICU patients with CAP. Upon admission to the ICU, fundamental data including vital signs, critical illness scores, comorbidities, and laboratory results, were collected. The in-hospital mortality of all CAP patients was documented. Multivariate logistic regression (MLR) models and restricted cubic spline (RCS) analysis together with subgroup analyses were conducted.

Results: This study includes 311 CAP individuals, involving 218 survivors as well as 93 nonsurvivors. The participants had an average age of 63.57 years, and the females accounted for approximately 45.33%. The in-hospital mortality was documented to be 29.90%. MLR analysis found that ALI was identified as an independent predictor for in-hospital mortality among patients with CAP solely in the Q1 group with ALI ≤ 39.38 (HR: 2.227, 95% CI: 1.026–4.831, $P=0.043$). RCS analysis showed a nonlinear relationship between the ALI and in-hospital mortality, with a turning point at 81, and on the left side of the inflection point, a negative correlation was observed between ALI and in-hospital mortality (HR: 0.984, 95% CI: 0.975–0.994, $P=0.002$). The subgroup with high blood pressure showed significant interaction with the ALI.

Conclusion: The present study demonstrated a nonlinear correlation of the ALI with in-hospital mortality among individuals with CAP. Additional confirmation of these findings requires conducting larger prospective investigations.

KEYWORDS

advanced lung cancer inflammation index, community-acquired pneumonia, in-hospital mortality, MIMIC-IV database, nonlinear relationship

1 | INTRODUCTION

Community-acquired pneumonia (CAP) is not only a major cause of infectious fatalities worldwide but also a common reason for admissions to intensive care units (ICUs).[1,2] The global annual mortality rate for CAP ranges from 50,000 to 100,000 cases,[3] with a hospitalization fatality rate from 20% to 50%.[4] Although ICU mortality rates have remained constant over the past 10 years, CAP still has a significant impact on the global healthcare system. It is crucial to promptly identify high-risk CAP patients to improve their prognosis.

Various factors, such as age, overall health, and body mass index (BMI), can influence the prognosis of pneumonia. BMI can variably affect the progression and recovery of pneumonia. A meta-analysis highlights the obesity paradox, demonstrating that while obesity increases the risk of pneumonia, it also has a complex relationship with mortality rates.[5] A low BMI could suggest malnutrition or underlying health issues, potentially compromising the body's immune system and impeding recovery from pneumonia. Recent studies have emphasized the use of several blood biomarkers, including CAP,[6,7] in the early identification and prediction of pneumonia. Studies have indicated a correlation between serum albumin (ALB) levels and in-hospital mortality in patients with CAP.[8] Additionally, the neutrophil-to-lymphocyte (NLR) ratio may have predictive value in detecting adverse outcomes in individuals with CAP.[9]

In 2013, the advanced lung cancer inflammation index (ALI) was proposed by Jafri with his colleagues.[10] To calculate this indicator, multiply the BMI by ALB and then divide by the NLR. The calculation method for BMI is weight (kilograms) divided by the square of height (meters). NLR is a marker of inflammation, while BMI and ALB are markers of general nutritional status. A reduced ALI is considered an independent predictive factor for survival in gastric, lung, as well as colorectal malignancies in the field of oncology.[11–13]

There has been limited research on the relationship of ALI with the clinical outcomes of CAP patients. We aimed to explore the correlation of ALI with in-hospital mortality in CAP patients in ICUs to provide significant insights for the clinical care of CAP patients.

2 | METHODS

This retrospective cohort analysis utilized de-identified data of patients admitted between 2008 and 2019 from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, involving health information from patients at Beth Israel Deaconess Medical Center in Boston, Massachusetts. The study covered admissions. The MIMIC-IV (v2.0) dataset was available at https//physionet.org/. Feng Yang, the original author of this study, accessed this database upon completing the Collaborative Institutional Training Initiative (CITI) course and passing exams on "Conflicts of Interest" and "Data or Specimens Only Research" (ID 57620670). We obtained the necessary credentials to access and retrieve data from the database. This study was exempted from approval by the Institutional Review Board of China Rehabilitation Research Center.

Patients diagnosed with CAP were included. The CAP diagnosis was established according to the recommendations set forth by the American Thoracic Society and the Infectious Diseases Society of America (ATS/IDSA). Diagnostic information on admission was collected using the International Classification of Diseases (ICD)-9 as well as ICD-10 codes. Exclusion criteria were as follows: (1) patients with multiple admissions for CAP, with only data from the first admission being considered; (2) patients who were not admitted to the ICU; (3) patients lacking serum ALB data within 24 h of ICU admission; (4) patients without 24-h records of weight and height following ICU admission; and (5) patients without 24-h records of neutrophil and lymphocyte following ICU admission (Figure 1).

NLR was a ratio of neutrophil count to lymphocyte count in the bloodstream. The ALI, a measure of inflammation in advanced lung cancer cases, was determined by dividing the product of BMI and serum ALB by the NLR. ALI was selected as the primary variable for this study. Initial measurements of BMI, serum ALB, and NLR were taken upon admission to the ICU. This study considered a wide range of variables as potential confounders, including age, gender, vital signs (heart rate, systolic blood pressure [SBP], diastolic blood pressure [DBP], mean blood pressure [MBP], respiratory rate), comorbidities (myocardial infarction, congestive heart failure [HF], cerebrovascular disease, chronic pulmonary disease [CPD], mild liver disease, renal disease, malignant cancer, severe liver disease, metastatic solid tumor, sepsis, high blood pressure [HBP], diabetes), treatment (mechanical ventilation [MV]), and laboratory indicators (white blood cells [WBC], platelets, hemoglobin, ALB, serum creatinine, blood urea nitrogen, serum sodium, serum potassium, serum chloride), as well as the sequential organ failure assessment (SOFA). PostgreSQL software (v15) together with Navicat Premium software (v15) were used to extract data.

The primary outcome was the overall fatality rate observed during hospitalization.

The distribution of continuous data was examined by Kolmogorov–Smirnov test. Continuous data with normal distribution were reported as mean ± standard deviation (SD) and those with skewed distribution were presented as median and interquartile range (IQR). Categorical variables were presented numerically along with their corresponding percentages. Baseline characteristics were compared using T-tests, one-way analysis of variance (ANOVA), or Kruskal–Wallis tests for continuous data, as well as chi-square testing for categorical data. Multivariate logistic regression (MLR) analysis was carried out to determine the independent risk factors for in-hospital mortality. Multicollinearity among covariates in the fully adjusted models was assessed using the variance inflation factor (VIF), with a threshold of VIF less than 10 for all covariates. Model I does not account for any variables. Model II includes age and sex as adjusted variables. The fully adjusted model (Model III) additionally includes adjustments for sepsis, HBP, severe liver disease, creatinine, platelets, and SOFA. The predictive capability for in-hospital survival was evaluated using a receiver operating characteristic (ROC) analysis and the area under the curve (AUC) was calculated. Restricted cubic spline (RCS) and linear spline regression

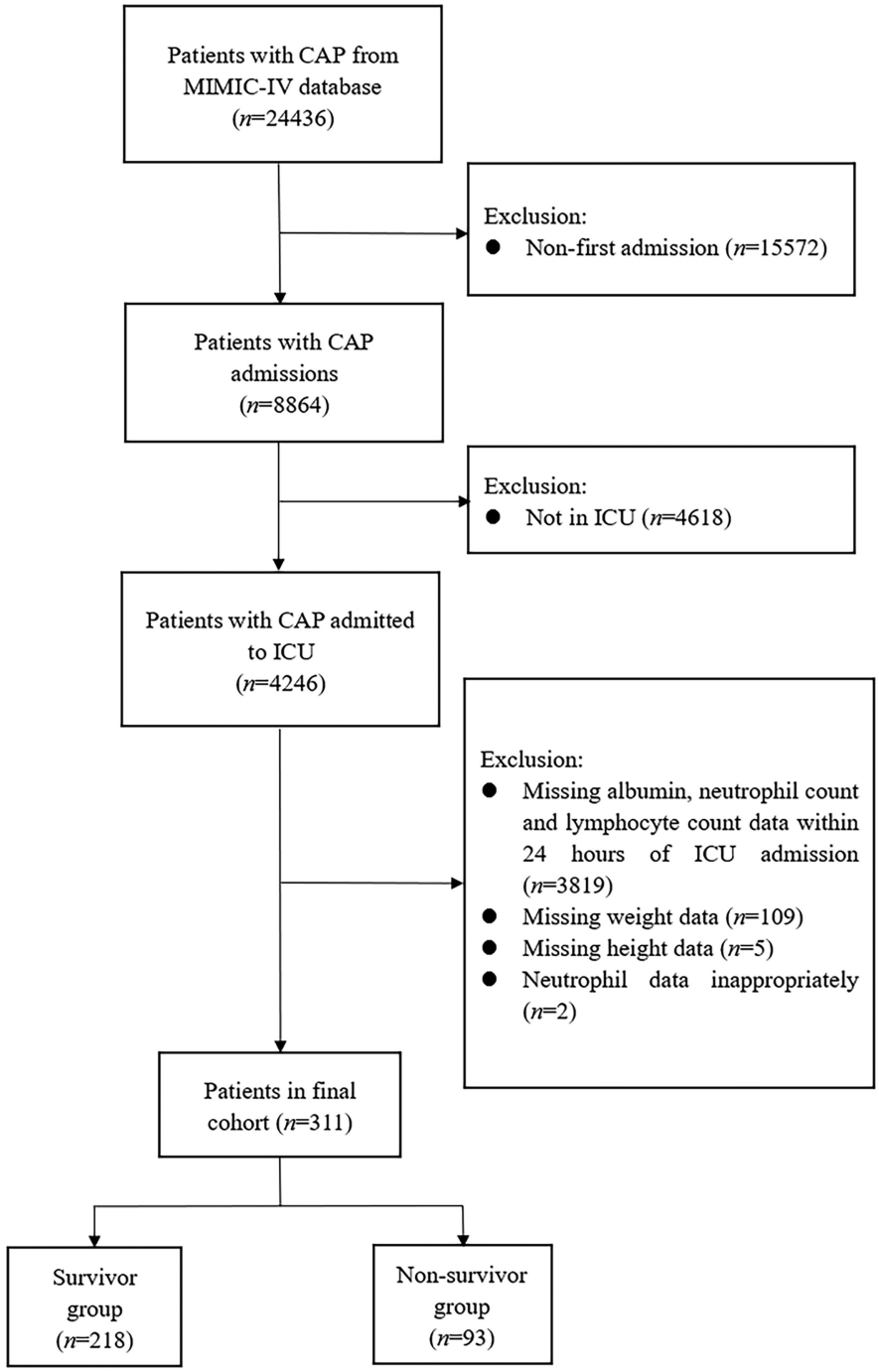

FIGURE 1 Flowchart of participants in the study. CAP, community-acquired pneumonia; ICU, intensive care unit; MIMIC-IV, medical information mart for intensive care.

analysis were adopted to demonstrate the nonlinear relationship of ALI with in-hospital mortality in CAP patients. Subgroup analyses were further conducted to examine the impact of ALI. The analyses were performed using SPSS 24.0 and R 4.1.3. Significance was assessed based on a two-tailed $P < 0.050$.

3 | RESULTS

Table 1 presents the baseline characteristics of patients who survived and those who did not. A total of 311 patients were included, among which 141 (45.33%) were female and 170 (54.66%) were male. The median age was 63.57 years (range: 53.00–73.91). The in-hospital mortality rate was 29.90%. Analysis revealed that deceased patients with CAP were characterized by advanced age, elevated heart rates, higher levels of blood urea nitrogen, higher levels of creatinine, and higher SOFA ratings compared to the survivors. Additionally, 41.93% of nonsurviving patients had concurrent HF, while 19.35% of this group experienced severe liver disease complications. Upon admission, laboratory tests showed significantly lower lymphocyte levels in the nonsurvivors compared to the survivors [0.71 (0.40, 1.21) vs. 1.07 (0.70, 1.63), $P < 0.001$]. The nonsurvivors also exhibited lower levels of platelet count, hemoglobin, serum sodium, serum chloride, and ALI compared to the survivors ($P < 0.050$).

TABLE 1 Comparison of baseline characteristics between survivors and nonsurvivors[a].

Variables	Total ($n=311$)	Survivors ($n=218$)	Nonsurvivors ($n=93$)	*P*
Age, years	63.57 (53.00, 73.91)	62.03 (52.15, 73.01)	67.28 (57.16, 76.21)	0.009*
Gender, *n* (%)				0.772
Female	141 (45.33)	100 (45.87)	41 (44.08)	
Male	170 (54.66)	118 (54.12)	52 (55.91)	
BMI (kg/m^2)	29.25 (24.34, 35.01)	28.72 (24.19, 33.56)	30.61 (25.39, 37.06)	0.071
SOFA score	7.64 ± 4.06	6.82 ± 3.69	9.58 ± 4.24	<0.001*
Comorbidities				
Sepsis, *n* (%)	275 (88.42)	187 (85.77)	88 (94.62)	0.026*
Myocardial infarction, *n* (%)	29 (9.32)	18 (8.25)	11 (11.82)	0.321
HBP, *n* (%)	102 (32.79)	79 (36.23)	23 (24.73)	0.048*
Congestive heart failure, *n* (%)	116 (37.29)	77 (35.32)	39 (41.93)	0.269
Cerebrovascular disease, *n* (%)	40 (12.86)	29 (13.30)	11 (11.82)	0.722
Chronic pulmonary disease, *n* (%)	101 (32.47)	68 (31.19)	33 (35.48)	0.459
Mild liver disease, *n* (%)	55 (17.68)	33 (15.13)	22 (23.65)	0.071
Diabetes without cc, *n* (%)	57 (18.32)	42 (19.26)	15 (16.12)	0.513
Diabetes with cc, *n* (%)	43 (13.82)	30 (13.76)	13 (13.97)	0.960
Renal disease, *n* (%)	67 (21.54)	41 (18.80)	26 (27.95)	0.072
Malignant cancer, *n* (%)	38 (12.21)	22 (10.09)	16 (17.20)	0.080
Severe liver disease, *n* (%)	38 (12.21)	20 (9.17)	18 (19.35)	0.012*
Metastatic solid tumor, *n* (%)	22 (7.07)	9 (4.12)	13 (13.97)	0.002*
Treatment				
MV	178 (57.23)	121 (55.50)	57 (61.29)	0.345
Vital signs				
Heart rate (beats/min)	109 (93, 124)	105 (90, 120)	116 (102, 132)	<0.001*
SBP (mmHg)	143 (129, 159)	143.50 (130, 159)	139 (126, 159)	0.294
DBP (mmHg)	87 (76, 102)	88 (77, 104)	86 (76, 97)	0.276
MBP (mmHg)	102 (91, 117)	104 (92, 118)	100 (90, 112)	0.235
Resp rate (beats/min)	30 (26, 34)	29 (26, 34)	31 (26, 34)	0.238
Laboratory tests				
WBC (K/uL)	13 (9.50, 18)	12.70 (9.30, 18.10)	13.50 (9.60, 17.70)	0.578
Neutrophil (K/uL)	10.90 (7.27, 15.51)	10.60 (7.07, 15.50)	11.54 (7.81, 15.66)	0.392
Lymphocytes (K/uL)	0.99 (0.55, 1.56)	1.07 (0.70, 1.63)	0.71 (0.40, 1.21)	<0.001*
Hemoglobin (g/dL)	10.60 (8.50, 12.40)	10.90 (8.70, 12.70)	10 (8.40, 11.40)	0.042*
Platelets (K/μL)	184 (116, 242)	192 (126, 252)	156 (84, 220)	0.015*
Albumin (g/L)	29.62 ± 6.26	30.05 ± 5.98	28.61 ± 6.80	0.063
BUN (mg/dL)	24 (16, 43)	22 (14, 36)	33 (19, 55)	<0.001*
Creatinine (mg/dL)	1.20 (0.80, 2)	1 (0.70, 1.70)	1.50 (1, 2.40)	<0.001*
Sodium (mEq/L)	138 (134, 142)	138 (135, 142)	136 (132, 142)	0.031*
Potassium (mEq/L)	4.20 (3.70, 4.70)	4.10 (3.70, 4.70)	4.40 (3.80, 4.80)	0.209
Cl (mEq/L)	102 (97, 106)	103 (99, 106)	100 (94, 105)	0.003*
ALI	83.21 (39.38, 154.48)	95.70 (45.97, 165.43)	53.42 (30.78, 121.49)	0.005*

Abbreviations: ALI, advanced lung cancer inflammation index; BMI, body mass index; BUN, blood urea nitrogen; Cl, chloride; DBP, diastolic blood pressure; HBP, high blood pressure; diabetes without cc, diabetes without chronic complications; diabetes with cc, diabetes with chronic complications; MBP, mean blood pressure; MV, mechanical ventilation; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; WBC, white blood cell.

[a]Values expressed as *n* (%), mean ± SD, or median [IQR].

*$P<0.050$.

TABLE 2 Baseline characteristics of participants categorized by ALI[a].

Variables	ALI quartiles				P
	Q1 (*n* = 78)	Q2 (*n* = 77)	Q3 (*n* = 78)	Q4 (*n* = 78)	
Age, years	63.42 (54.70, 74.71)	66.62 (52.73, 74.83)	63.30 (53.48, 73.46)	61.86 (52.81, 72.07)	0.721
Male, *n* (%)	46 (58.97)	44 (57.69)	45 (57.14)	35 (44.87)	0.253
BMI (kg/m^2)	25.84 (21.74, 31.76)	28.99 (23.35, 34.19)	30.21 (25.78, 36.14)	31.91 (28.16, 38.06)	<0.001*
SOFA score	8.84 ± 3.69	7.11 ± 4.06	7.06 ± 4.32	7.55 ± 3.95	0.020*
In-hospital mortality	33 (42.30)	25 (32.46)	16 (20.51)	19 (24.35)	0.016*
Comorbidities					
Sepsis, *n* (%)	72 (92.30)	70 (91.02)	66 (84.41)	67 (85.89)	0.361
Myocardial infarction, *n* (%)	3 (3.84)	7 (9.09)	10 (12.82)	9 (11.53)	0.226
HBP, *n* (%)	26 (33.33)	22 (28.20)	31 (39.74)	23 (29.48)	0.435
Congestive heart failure, *n* (%)	27 (34.61)	28 (37.17)	36 (45.45)	25 (32.05)	0.284
Cerebrovascular disease, *n* (%)	10 (12.82)	10 (12.82)	9 (11.68)	11 (14.10)	0.973
Chronic pulmonary disease, *n* (%)	33 (42.30)	23 (29.48)	24 (31.16)	21 (26.92)	0.181
Mild liver disease, *n* (%)	17 (21.79)	19 (24.35)	7 (9.09)	12 (15.38)	0.049*
Diabetes without cc, *n* (%)	10 (12.82)	9 (11.53)	25 (32.46)	13 (16.66)	0.003*
Diabetes with cc, *n* (%)	11 (14.10)	8 (11.53)	13 (15.58)	11 (14.10)	0.729
Renal disease, *n* (%)	21 (26.92)	17 (23.07)	14 (16.88)	15 (19.23)	0.534
Malignant cancer, *n* (%)	10 (12.82)	8 (10.25)	8 (10.39)	12 (15.38)	0.735
Severe liver disease, *n* (%)	12 (15.38)	12 (15.38)	3 (3.89)	11 (14.10)	0.075
Metastatic solid tumor, *n* (%)	9 (11.53)	5 (6.41)	4 (5.19)	4 (5.12)	0.347
Treatment					
MV	44 (56.41)	40 (51.94)	48 (61.53)	46 (58.97)	0.665
Vital signs					
Heart rate (beats/min)	112.50 (98, 123)	109 (94, 122)	108 (92, 125)	106.50 (90, 125)	0.773
SBP (mmHg)	137.50 (126, 153)	140 (126, 158)	148 (132, 167)	145.50 (133, 161)	0.016*
DBP (mmHg)	84 (75, 97)	85 (74, 99)	92.50 (79, 105)	90 (79, 106)	0.023*
MBP (mmHg)	99 (89, 110)	101 (88.50, 112)	106.50 (96, 122)	104 (92, 118)	0.008*
Resp rate (beats/min)	32 (27, 36.50)	30 (26, 34)	29.50 (25, 34)	28 (24, 32)	0.009*
Laboratory tests					
WBC (K/μL)	17 (11.90, 23)	13.50 (10.50, 17.50)	12.70 (10.10, 17.90)	9.85 (6.50, 13)	<0.001*
Neutrophil (K/μL)	15.70 (11.76, 21.66)	11.76 (9.19, 15)	10.39 (7.78, 13.88)	6.47 (4.10, 9.18)	<0.001*
Lymphocytes (K/μL)	0.50 (0.33, 0.74)	0.79 (0.58, 1.09)	1.24 (1.03, 1.78)	1.59 (0.97, 2.23)	<0.001*
Hemoglobin (g/dL)	10.10 (8.30, 11.90)	10.50 (8.80, 12.70)	11.05 (9, 13.20)	10.85 (8.70, 12.30)	0.201
Platelets (K/μL)	163 (110, 264)	189 (121, 226)	200 (137, 260)	155.50 (78, 226)	0.066
Albumin (g/L)	27.39 ± 6.60	29.01 ± 6.35	30.32 ± 5.60	31.76 ± 5.71	<0.001*
BUN (mg/dL)	39 (17, 55)	23.50 (15, 40)	22 (17, 34)	21.50 (12, 33)	0.001*
Creatinine (mg/dL)	1.35 (0.80, 2.70)	1.10 (0.70, 1.70)	1.20 (0.80, 1.70)	1.10 (0.70, 1.60)	0.080
Sodium (mEq/L)	137.50 (133, 143)	138 (134, 142)	137 (135, 140)	139 (135, 142)	0.700
Potassium (mEq/L)	4.40 (3.70, 4.90)	4.30 (3.80, 4.70)	4.35 (3.90, 5.10)	4.05 (3.60, 4.50)	0.036*
Cl (mEq/L)	101 (97, 106)	101 (97, 106)	102 (98, 105)	103 (99, 106)	0.704

Abbreviations: ALI, advanced lung cancer inflammation index; BMI, body mass index; BUN, blood urea nitrogen; Cl, chloride; DBP, diastolic blood pressure; diabetes without cc, Diabetes without chronic complications; diabetes with cc, diabetes with chronic complications; HBP, high blood pressure; MBP, mean blood pressure; MV, mechanical ventilation; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; WBC; white blood cell.

[a]Values expressed as *n* (%), mean ± SD, or median [IQR].

*$P < 0.050$.

TABLE 3 Univariate logistic regression analysis of risk factors for in-hospital mortality.

Variables	HR	95% CI	*P*
Age	1.021	1.004–1.037	0.011*
Male	1.074	0.659–1.751	0.772
BMI	1.029	1.003–1.056	0.028*
SOFA score	1.197	1.119–1.281	<0.001*
Sepsis	2.917	1.097–7.758	0.032*
Myocardial infarction	1.490	0.674–3.293	0.324
HBP	0.578	0.334–0.998	0.049*
Congestive heart failure	1.322	0.804–2.173	0.270
Cerebrovascular disease	0.874	0.416–1.833	0.722
Chronic pulmonary disease	1.213	0.726–2.025	0.460
Mild liver disease	1.737	0.948–3.180	0.074
Diabetes without cc	0.805	0.421–1.539	0.513
Diabetes with cc	1.018	0.504–2.053	0.960
Renal disease	1.675	0.951–2.950	0.074
Malignant cancer	1.851	0.923–3.712	0.083
Severe liver disease	2.376	1.191–4.737	0.014*
Metastatic solid tumor	3.773	1.552–9.171	0.003*
MV	1.269	0.773–2.083	0.346
Heart rate	1.024	1.013–1.036	<0.001*
SBP	0.997	0.986–1.008	0.617
DBP	0.992	0.979–1.005	0.249
MBP	0.995	0.985–1.005	0.331
Resp rate	1.024	0.989–1.060	0.170
WBC	1.010	0.979–1.042	0.515
Neutrophil	1.010	0.979–1.041	0.520
Lymphocytes	0.565	0.387–0.825	0.003*
Hemoglobin	0.908	0.822–1.002	0.055
Platelets	0.996	0.993–0.999	0.009*
Albumin	0.689	0.465–1.021	0.064
BUN	1.018	1.007–1.029	0.001*
Creatinine	1.231	1.049–1.443	0.010*
Sodium	0.974	0.940–1.009	0.147
Potassium	1.155	0.884–1.509	0.288
Cl	0.956	0.926–0.986	0.005*
ALI			
Q1 group	2.277	1.148–4.516	0.019*
Q2 group	1.492	0.738–3.016	0.264
Q3 group	0.801	0.376–1.704	0.565
Q4 group	REF		

Abbreviations: ALI, advanced lung cancer inflammation index; BMI, body mass index; BUN, blood urea nitrogen; CI, confidence interval; Cl, chloride; diabetes without cc, diabetes without chronic complications; diabetes with cc, diabetes with chronic complications; DBP, diastolic blood pressure; HR, hazard ratio; HBP, high blood pressure; MBP, mean blood pressure; MV, mechanical ventilation; REF, reference; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; WBC, white blood cell.

*$P < 0.050$.

The study participants were divided into quartiles based on their ALI levels: Quartile 1 (Q1, ≤39.38), Quartile 2 (Q2, 39.38–83.21), Quartile 3 (Q3, 83.21–154.48), and Quartile 4 (Q4, ≥154.48). As presented in Table 2, significant variations were found in BMI, SOFA score, in-hospital mortality, mild liver disease, diabetes without chronic complications, SBP, DBP, MBP, respiratory rate, WBC count, neutrophil count, lymphocyte count, serum ALB levels, blood urea nitrogen levels, and serum potassium levels across the different ALI groups. The remaining demographic variables, comorbidities, vital signs, results of laboratory tests, and MV use were all similar across these four groups ($P > 0.050$, Table 2).

Univariate analysis revealed a correlation between an increased risk of in-hospital mortality and factors such as age, BMI, SOFA scores, severe liver disease, metastatic solid tumors, sepsis, heart rate, creatinine, blood urea nitrogen, and ALI in the Q1 group. Conversely, HBP, lymphocyte count, platelet count, and serum chloride were linked to a reduced risk of in-hospital mortality. According

TABLE 4 Multivariable logistic regression models evaluating the association between ALI and in-hospital mortality.

	Model I			Model II			Model III		
ALI quartiles	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Q1 group	2.277	1.148–4.516	0.019*	2.220	1.107–4.452	0.025*	2.227	1.026–4.831	0.043*
Q2 group	1.492	0.738–3.016	0.264	1.441	0.706–2.942	0.315	1.718	0.784–3.762	0.176
Q3 group	0.801	0.376–1.704	0.565	0.780	0.363–1.675	0.525	1.006	0.432–2.343	0.989
Q4 group	REF			REF			REF		
P for trend			0.005*			0.007*			0.016*

Abbreviations: ALI, advanced lung cancer inflammation index; CI, confidence interval; HBP, severe liver disease, creatinine, platelets; HR, hazard ratio; Model I: unadjusted; Model II: Model I + age, gender; Model III: Model II + sepsis; REF, reference; SOFA score.
*$P < 0.050$.

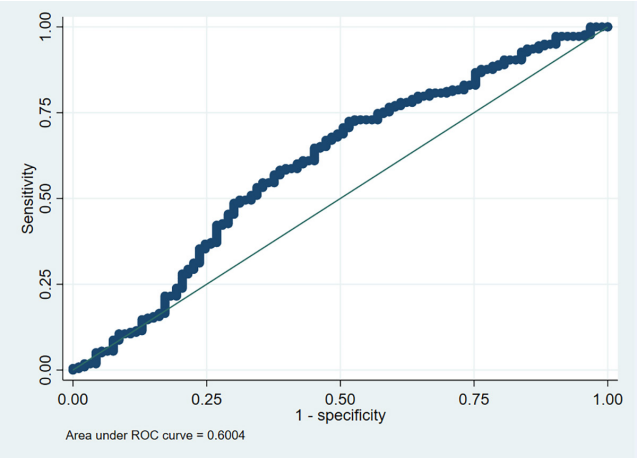

FIGURE 2 ROCs curve for in-hospital survival.

to Table 3, there was no statistically significant association between in-hospital mortality and various clinical factors, including gender, myocardial infarction, congestive HF, cerebrovascular disease, CPD, mild liver disease, diabetes, renal disease, malignant cancer, MV, SBP, DBP, MBP, respiratory rate, WBC count, neutrophil count, hemoglobin level, ALB level, sodium level, potassium level, and ALI in the Q2 and Q3 groups.

MLR analysis was carried out to determine if different levels of ALI were in relation to in-hospital mortality from CAP. The results from the models are presented in Table 4. After adjusting for age and gender, the model showed a significant association between ALI and in-hospital mortality from CAP solely in the Q1 group [hazard ratio (HR): 2.220, 95% confidence interval (CI): 1.107–4.452, $P = 0.025$]. Even after considering additional factors, the relationship between ALI and in-hospital mortality from CAP in the Q1 group remained significant (HR: 2.227, 95% CI: 1.026–4.831, $P = 0.043$) (Table 4). The analysis indicated that ALI in the Q1 group was a significant predictor for in-hospital mortality among patients with CAP. Figure 2 illustrates the predictive capability of ALI for in-hospital survival using ROC curves, with an AUC of 0.600.

RCS analysis revealed a nonlinear relationship between ALI and in-hospital all-cause mortality, as shown in Figure 3 ($P = 0.004$ for nonlinearity). As shown in Table 5, the inflection point was determined to be 81. On the left side of the inflection point, a negative correlation was observed between ALI and in-hospital mortality (HR: 0.984, 95% CI: 0.975–0.994, $P = 0.002$). However, the association between ALI and in-hospital mortality on the right side of the inflection point was similar, without any statistical significance (HR = 0.999, 95% CI: 0.999–1.000, $P = 0.720$).

As shown in Table 6, stratified analysis was performed based on age, gender, HBP, congestive HF, CPD, and MV use. The findings indicated no significant interaction of ALI with each category ($P > 0.050$), except for the subgroup of HBP ($P = 0.029$).

4 | DISCUSSION

We investigated the association of ALI with in-hospital mortality among ICU patients. A cohort of 311 individuals diagnosed with CAP from the MIMIC-IV dataset was analyzed. After adjusting for other variables, a statistically significant connection was observed between the Q1 group of ALI and in-hospital mortality due to CAP. Using the RCS approach, this study explored the relationship between ALI and in-hospital mortality, revealing a nonlinear link between the two. The results demonstrated an inverse relationship between ALI levels below 81 and in-hospital mortality, while ALI levels beyond 81 did not exhibit a meaningful association with in-hospital mortality. Subgroup analysis showed that, except for the HBP group, there was no significant interaction between ALI and the other subgroups.

ALI was assessed through components such as BMI, serum ALB levels, and the NLR, providing a thorough evaluation of an individual's inflammatory status and nutritional condition. This dual approach is crucial in the context of lung cancer, as inflammation and malnutrition can significantly impact patient prognoses.[14] Studies by Shibutani et al.[15] and Liu et al.[11] have demonstrated the prognostic significance of ALI in various cancers, such as unresectable metastatic colorectal cancer and gastrointestinal cancer,

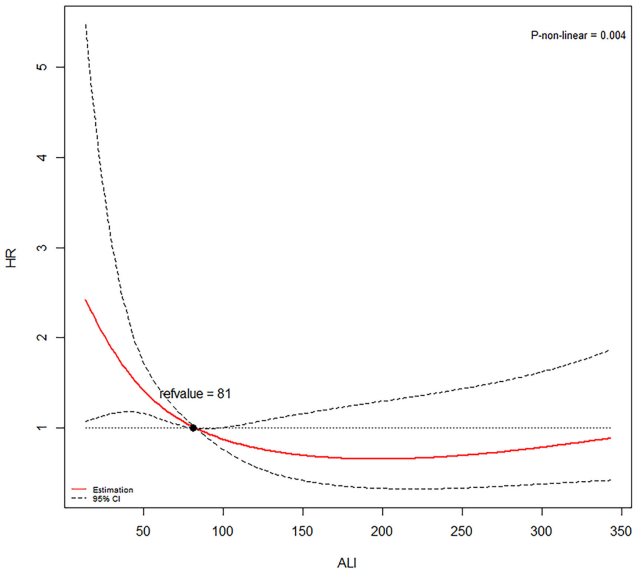

FIGURE 3 The relationship of ALI with in-hospital mortality.

TABLE 5 Analysis of nonlinear relationship between ALI and in-hospital mortality.

	HR	95% CI	*P*
ALI <81	0.984	0.975–0.994	0.002*
ALI >81	0.999	0.999–1.000	0.720
Likelihood ratio test			0.005*

Abbreviations: ALI, advanced lung cancer inflammation index; HR, hazard ratio; CI, confidence interval.

*$P < 0.050$.

indicating its potential as a novel prognostic marker beyond its conventional association with lung cancer. Recently, scholars have identified ALI < 334.96 to be an independent prognosis risk factor for acute coronary syndrome patients who underwent percutaneous coronary intervention.[16] This study suggested that ALI could serve as a novel biomarker in therapeutic settings. Despite the recognized importance of inflammation and nutrition in the context of CAP, research regarding the predictive value of ALI in CAP patients is lacking. The relationship between CAP and BMI is complex, with studies showing varying associations between high BMI and severe outcomes in different age groups. Bramley et al.[17] demonstrated an association between higher BMI and ICU admission in pediatric patients, but no such relationship was observed in adults with severe CAP. In another study, individuals classified as obese (BMI > 30 kg/m^2) exhibited lower rates of all-cause mortality during a 6-year period compared to those with a normal weight, confirming the established phenomenon of the "obesity paradox."[18] Conversely, another study found a connection between severe thinness (BMI < 16 kg/m^2) and increased 30-day mortality in CAP patients.[19] Studies have also shown that low blood ALB levels upon admission independently predict mortality in CAP patients.[20] Ma et al.[21] conducted a study and discovered a link between lower ALB levels at admission and higher short-term mortality rates in CAP patients. The NLR is a valuable laboratory tool for assessing infectious diseases.[22] Studies have demonstrated that a single NLR measurement is useful for evaluating disease severity and predicting prognosis in individuals with CAP.[23–25] Our study highlighted the significant impact of systemic inflammation and nutritional status on the prognosis of CAP and proposed a new measure that could improve outcome prediction. This finding suggests the need for a more comprehensive approach in both research and clinical practice for CAP, recommending the inclusion of ALI in standard prognostic assessments to enhance treatment options and patient outcomes.

This study demonstrated several strengths. The initial study aimed to investigate the correlation between ALI and in-hospital mortality in patients with CAP. RCS curves were used to analyze the nonlinear correlation between ALI and in-hospital mortality in diagnosed CAP patients. A subgroup analysis was conducted to validate the accuracy of the results.

There were multiple limitations associated with this research. The study was conducted at a single location, which may introduce selection bias and therefore needs confirmation in various international settings. Additionally, the data obtained from public databases contained numerous missing values, which prevented their use in the research. In the future, it is necessary to use datasets from multiple institutions in different countries and ethnic groups to further verify the reliability of research results. The research sample was limited to CAP patients admitted to the ICU, highlighting the need to confirm the findings with CAP patients treated in standard hospital wards. The study only focused on the initial values of ALI upon admission to the ICU and did not investigate its dynamic evolution values, thus overlooking the potential impact of ALI's dynamic changes. In future studies, attention should be paid to the values of ALI during the treatment process and at discharge, and further analysis of the prognostic value of dynamic changes in ALI for CAP should be conducted. In this study, only two demographic variables, age and gender, were included to analyze the impact on the relationship between ALI and mortality. In future studies, more demographic variables, such as age, gender, race, marriage, and income, need to be included to further analyze the impact of demographic variables on the relationship between ALI and mortality.

5 | CONCLUSION

The study identified a nonlinear correlation between ALI and in-hospital mortality among individuals with CAP. ALI showed an inverse relationship with in-hospital mortality up to a certain threshold, beyond which there was no significant association between ALI and in-hospital mortality. To further validate these findings, larger prospective studies need to be conducted.

AUTHOR CONTRIBUTIONS

Feng Yang conceptualized and designed the project, and was responsible for data collection. Wei Gao contributed to the project's

TABLE 6 Subgroup analyses of the association between ALI and in-hospital mortality.

	ALI quartiles					
	Q1 group	Q2 group	Q3 group	Q4 group		
Subgroup	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	*P* for trend	P for interaction
Age						0.343
<65 years	1.530 (0.544–4.301)	1.148 (0.376–3.501)	0.673 (0.201–2.248)	1 (REF)	0.288	
≥65 years	3.624 (1.093–12.016)	2.302 (0.728–7.279)	1.584 (0.460–5.458)	1 (REF)	0.025*	
Gender						0.051
Female	1.305 (0.386–4.408)	1.508 (0.468–4.856)	0.762 (0.191–3.034)	1 (REF)	0.467	
Male	4.987 (1.525–16.305)	2.853 (0.854–9.526)	1.879 (0.542–6.514)	1 (REF)	0.004*	
HBP						0.029*
No	3.623 (1.398–9.384)	1.594 (0.632–4.021)	0.959 (0.340–2.700)	1 (REF)	0.004*	
Yes	0.745 (0.162–3.412)	1.518 (0.312–7.393)	0.795 (0.170–3.702)	1 (REF)	0.898	
Congestive heart failure						0.729
No	2.537 (0.928–6.931)	2.199 (0.772–6.261)	1.234 (0.377–4.037)	1 (REF)	0.042*	
Yes	1.494 (0.382–5.840)	1.151 (0.291–4.552)	0.779 (0.206–2.936)	1 (REF)	0.395	
Chronic pulmonary disease						0.454
No	1.858 (0.700–4.928)	1.283 (0.507–3.243)	1.032 (0.380–2.802)	1 (REF)	0.195	
Yes	7.464 (1.214–45.857)	8.335 (1.166–59.566)	2.843 (0.391–20.669)	1 (REF)	0.022*	
MV use						0.177
No	2.450 (0.676–8.877)	1.539 (0.437–5.423)	0.561 (0.111–2.836)	1 (REF)	0.084	
Yes	2.198 (0.775–6.236)	1.858 (0.628–5.493)	1.429 (0.490–4.167)	1 (REF)	0.119	

Abbreviations: ALI, advanced lung cancer inflammation index; HR, hazard ratio; CI, confidence interval; HBP, high blood pressure; MV, mechanical ventilation; REF, reference.

*$P < 0.050$.

conceptualization and design, and oversaw administration and supervision. Feng Yang, Lianjun Gao, Cuiping Xu, and Qimin Wang conducted data analysis. All authors collaborated on drafting, reviewing, and editing the manuscript. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

None declared.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Institutional Review Boards (IRB) of Institutional Review Boards of Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

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REFERENCES

1. Aliberti S, Reyes LF, Faverio P, et al. Global initiative for meticillin-resistant Staphylococcus aureus pneumonia (GLIMP): an international, observational cohort study. *Lancet Infect Dis*. 2016;16(12):1364-1376. doi:10.1016/s1473-3099(16)30267-5
2. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA*. 2009;302(21):2323-2329. doi:10.1001/jama.2009.1754
3. Jain S, Self WH, Wunderink RG, et al. Community-acquired pneumonia requiring hospitalization among U.S. Adults. *New Engl J Med*. 2015;373(5):415-427. doi:10.1056/NEJMoa1500245
4. Khawaja A, Zubairi AB, Durrani FK, Zafar A. Etiology and outcome of severe community acquired pneumonia in immunocompetent adults. *BMC Infect Dis*. 2013;13:94. doi:10.1186/1471-2334-13-94
5. Nie W, Zhang Y, Jee SH, Jung KJ, Li B, Xiu Q. Obesity survival paradox in pneumonia: a meta-analysis. *BMC Med*. 2014;12(1):61. doi:10.1186/1741-7015-12-61

6. Menéndez R, Méndez R, Aldás I, et al. Community-acquired pneumonia patients at risk for early and long-term cardiovascular events are identified by cardiac biomarkers. *Chest*. 2019;156(6):1080-1091. doi:10.1016/j.chest.2019.06.040
7. Jeong JH, Heo M, Lee SJ, Jeong YY, Lee JD, Yoo JW. Clinical usefulness of red cell distribution width/albumin ratio to discriminate 28-day mortality in critically ill patients with pneumonia receiving invasive mechanical ventilation, compared with Lacate/albumin ratio: a retrospective cohort study. *Diagnostics (Basel, Switzerland)*. 2021;11(12). doi:10.3390/diagnostics11122344
8. Zhao L, Bao J, Shang Y, et al. The prognostic value of serum albumin levels and respiratory rate for community-acquired pneumonia: a prospective, multi-center study. *PLoS One*. 2021;16(3):e0248002. doi:10.1371/journal.pone.0248002
9. Lv C, Chen Y, Shi W, Pan T, Deng J, Xu J. Comparison of different scoring Systems for Prediction of mortality and ICU admission in elderly CAP population. *Clin Interv Aging*. 2021;16:1917-1929. doi:10.2147/cia.S335315
10. Jafri SH, Shi R, Mills G. Advance lung cancer inflammation index (ALI) at diagnosis is a prognostic marker in patients with metastatic non-small cell lung cancer (NSCLC): a retrospective review. *BMC Cancer*. 2013;13:158. doi:10.1186/1471-2407-13-158
11. Liu X-R, Wang L-L, Zhang B, et al. The advanced lung cancer inflammation index is a prognostic factor for gastrointestinal cancer patients undergoing surgery: a systematic review and meta-analysis. *World J Surg Oncol*. 2023;21:81. doi:10.1186/s12957-023-02972-4
12. Zhang Y, Chen B. Prognostic value of the advanced lung cancer inflammation index in patients with lung cancer: a meta-analysis. *Dis Markers*. 2019;2019:2513026. doi:10.1155/2019/2513026
13. Xie H, Huang S, Yuan G, et al. The advanced lung cancer inflammation index predicts short and long-term outcomes in patients with colorectal cancer following surgical resection: a retrospective study. *PeerJ*. 2020;8:e10100. doi:10.7717/peerj.10100
14. Song M, Zhang Q, Song C, et al. The advanced lung cancer inflammation index is the optimal inflammatory biomarker of overall survival in patients with lung cancer. *J Cachexia Sarcopenia Muscle*. 2022;13(5):2504-2514. doi:10.1002/jcsm.13032
15. Shibutani M, Maeda K, Nagahara H, et al. The prognostic significance of the advanced lung cancer inflammation index in patients with unresectable metastatic colorectal cancer: a retrospective study. *BMC Cancer*. 2019;19:241. doi:10.1186/s12885-019-5468-9
16. Wang X, Wei C, Fan W, et al. Advanced lung cancer inflammation index for predicting prognostic risk for patients with acute coronary syndrome undergoing percutaneous coronary intervention. *J Inflamm Res*. 2023;16:3631-3641. doi:10.2147/jir.S421021
17. Bramley AM, Reed C, Finelli L, et al. Relationship between body mass index and outcomes among hospitalized patients with community-acquired pneumonia. *J Infect Dis*. 2017;215(12):1873-1882. doi:10.1093/infdis/jix241
18. Braun N, Hoess C, Kutz A, et al. Obesity paradox in patients with community-acquired pneumonia: is inflammation the missing link? *Nutrition*. 2017;33:304-310. doi:10.1016/j.nut.2016.07.016
19. Lee J, Kim K, Jo YH, et al. Severe thinness is associated with mortality in patients with community-acquired pneumonia: a prospective observational study. *Am J Emerg Med*. 2015;33(2):209-213. doi:10.1016/j.ajem.2014.11.019
20. Matsuo A, Takamori A, Kawaura F, et al. Risk for prolonged hospitalization and mortality in aged community acquired pneumonia patients: a retrospective study in Japan. *J Clin Biochem Nutr*. 2020;67(3):302-306. doi:10.3164/jcbn.20-85
21. Ma CM, Wang N, Su QW, et al. Age, pulse, urea, and albumin score: a tool for predicting the short-term and long-term outcomes of community-acquired pneumonia patients with diabetes. *Front Endocrinol*. 2022;13:882977. doi:10.3389/fendo.2022.882977
22. Yoon NB, Son C, Um SJ. Role of the neutrophil-lymphocyte count ratio in the differential diagnosis between pulmonary tuberculosis and bacterial community-acquired pneumonia. *Ann Lab Med*. 2013;33(2):105-110. doi:10.3343/alm.2013.33.2.105
23. Zhang HF, Ge YL, Wang HY, et al. Neutrophil-to-lymphocyte ratio improves the accuracy and sensitivity of pneumonia severity index in predicting 30-day mortality of CAP patients. *Clin Lab*. 2019;65(10):1867-1873. doi:10.7754/Clin.Lab.2019.190226
24. Ge YL, Zhang HF, Zhang Q, et al. Neutrophil-to-lymphocyte ratio in adult community-acquired pneumonia patients correlates with unfavorable clinical outcomes. *Clin Lab*. 2019;65(5):839-844. doi:10.7754/Clin.Lab.2018.181042
25. Cataudella E, Giraffa CM, Di Marca S, et al. Neutrophil-to-lymphocyte ratio: an emerging marker predicting prognosis in elderly adults with community-acquired pneumonia. *J Am Geriatr Soc*. 2017;65(8):1796-1801. doi:10.1111/jgs.14894

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