

Prognostic value of the neutrophil-to-lymphocyte ratio in critically ill patients with severe pneumonia

Valeur pronostique du rapport neutrophiles/lymphocytes chez les patients gravement malades atteints de pneumonie sévère

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ABSTRACT

Introduction : Community-acquired pneumonia (CAP) is one of the main reasons for admission to intensive care. Several studies have suggested the potential role of the neutrophil-to-lymphocyte ratio (NLR) in risk stratification and prognosis prediction in septic patients. Our objective was to evaluate the prognostic value of NLR on admission to intensive care in patients hospitalized for CAP.

Methods : We conducted a prospective, single-center, observational cohort study in the medical intensive care unit over a six-month period, from July 2024 to December 2024. We included patients over 18 years of age admitted to intensive care for CAP.

Results : We included 126 patients with a median age of 68 years and a gender ratio of 1.13. The main comorbidities were diabetes (48.8%), hypertension (47.6%), and dyslipidemia (41.2%). The APACHE II and SAPS II scores were 7.7 ± 4.4 and 24 ± 7.4 points, respectively. Invasive mechanical ventilation was indicated in 30 patients (23.8%). Thirty-one patients (24.6%) were in shock and 31 patients (24.6%) had ARDS. The mortality rate was 46% with a median length of stay of 5 days. The median NLR was 8.85. An NLR > 9 was associated with mortality ($p < 10^{-3}$) with an AUC = 0.69, sensitivity = 62%, and specificity = 64%. It was associated with an increased risk of shock ($p=0.03$), acute respiratory distress syndrome ($p=0.01$) and acute renal failure ($p=0.04$).

Conclusion : NLR is a relevant biomarker that can determine the short-term prognosis in patients hospitalized for CAP.

Key words : Neutrophil, Lymphocyte, Ratio, ICU, Prognostic, Pneumonia.

RÉSUMÉ

Introduction : La pneumonie communautaire (PC) est l'une des principales causes d'admission en soins intensifs. Plusieurs études ont suggéré le rôle potentiel du rapport neutrophiles/lymphocytes (RNL) dans la stratification du risque et le pronostic chez les patients septiques. Notre objectif était d'évaluer la valeur pronostique du RNL à l'admission en soins intensifs chez les patients hospitalisés pour PC.

Méthodes : Nous avons mené une étude de cohorte observationnelle prospective monocentrique dans l'unité de soins intensifs médicaux sur une période de six mois, de juillet 2024 à décembre 2024. Nous avons inclus les patients de plus de 18 ans admis en soins intensifs pour une pneumonie communautaire.

Résultats : Cent vingt-six patients ont été inclus, d'âge médian de 68 ans et présentant un sex-ratio de 1,13. Les principales comorbidités étaient le diabète (48,8 %), l'hypertension (47,6 %) et la dyslipidémie (41,2 %). Les scores APACHE II et SAPS II étaient respectivement de $7,7 \pm 4,4$ et $24 \pm 7,4$. Une ventilation mécanique invasive a été indiquée chez 30 patients (23,8 %). Trente et un patients (24,6 %) étaient en état de choc et 31 patients (24,6 %) présentaient un SDRA. Le taux de mortalité était de 46 %, avec une durée médiane d'hospitalisation de 5 jours. Le rapport neutrophiles/lymphocytes (NLR) médian était de 8,85. Un NLR > 9 était associé à la mortalité ($p < 10^{-3}$), avec une aire sous la courbe (AUC) de 0,69, une sensibilité de 62 % et une spécificité de 64 %. Il était associé à un risque accru de syndrome de détresse respiratoire aiguë ($p=0,01$) et d'insuffisance rénale aiguë ($p=0,04$).

Conclusion : Le NLR est un biomarqueur pertinent qui peut déterminer le pronostic à court terme chez les patients hospitalisés pour une pneumonie communautaire.

Mots clés : Rapport, Neutrophile, Lymphocyte, Pneumonie, Unité de soins intensifs, Pronostic

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INTRODUCTION

Community-acquired pneumonia (CAP) remains one of the most frequent and severe infectious diseases worldwide, which represents a leading cause of hospitalization and mortality among adults. In the United States, CAP accounted for more than 800,000 hospitalizations and over 400,000 emergency department visits in 2014, with approximately 102,000 deaths annually. Reported mortality rates reach 13% at 1 month, 23% at 6 months, and more than 30% at 12 months after hospitalization (1-5).

Early identification of high-risk patients is crucial to guide timely management and improve outcomes. Traditional prognostic tools such as the Pneumonia Severity Index (PSI) and CURB-65 score are widely used for initial risk stratification (6,7). The CURB-65 is one of the most frequently used and consists of 5 factors: confusion, urea >7 mmol/L, respiratory rate >30 breaths/minute, systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg and age > 65 years (7). However, these scoring systems, though widely used, have notable limitations: relative complexity, limited accuracy in reflecting treatment response and reduced predictive value in critically ill patients (8).

To overcome these limitations, several biomarkers of systemic inflammation have been investigated, including white blood cell (WBC) count, C-reactive protein (CRP), procalcitonin (PCT), and various cytokines (9,10). Nevertheless, their predictive accuracy remains debated, and their cost or limited availability often restricts their use in daily practice. Hence, there is a growing interest in simple, inexpensive, and readily available markers for CAP prognosis.

The neutrophil-to-lymphocyte ratio (NLR), calculated as the absolute neutrophil count divided by the absolute lymphocyte count, is an easily obtainable parameter from routine blood tests. Initially described by Zahorec in 2001 as an indicator of systemic inflammation and stress in critically ill patients, the NLR has since been explored in a wide range of conditions (11-13). In CAP, several studies have reported that elevated NLR values are associated with increased disease severity and worse outcomes (14-16). However, evidence specifically addressing severe CAP in intensive care settings remains limited. The present study aimed to assess the prognostic value of the NLR at ICU admission in patients with severe CAP, with a particular focus on its association with intrahospital mortality.

METHODS

Study design and setting

We conducted a prospective, monocentric, observational cohort study in the medical intensive care unit (ICU) over a six-month period, from July 2024 to December 2024. The study protocol was reviewed and approved by the institutional ethics committee of the Hospital, and the requirement for informed consent was waived due to the

observational design.

Study population

Inclusion criteria were:

- Consecutive adult patients (≥18 years) admitted to the ICU with a diagnosis of severe CAP were included.
- CAP was defined according to the Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) criteria, requiring the presence of a new pulmonary infiltrate on chest radiography plus at least one compatible clinical symptom (cough, sputum production, dyspnea, fever, pleuritic chest pain, or hemoptysis) without recent hospitalization.

Exclusion criteria were:

- An alternative diagnosis established after discharge (e.g., pulmonary edema, pulmonary embolism, tuberculosis, or lung cancer),
- antibiotic therapy initiated >24 hours prior to enrollment,
- absence of differential WBC counts,
- hematological disorders, current or recent corticosteroid therapy (within the past 3 months), chemotherapy or radiotherapy within 4 weeks before admission.

Data collection

At admission, demographic characteristics, comorbidities, clinical findings, and severity scores (PSI, SOFA) were recorded. Laboratory tests included complete blood count with differential, CRP, and PCT when available. The NLR was calculated as the ratio of absolute neutrophil count to absolute lymphocyte count. Outcomes were recorded during hospitalization.

Outcomes

- The primary outcome was intrahospital mortality.
- Secondary outcomes included ICU length of stay, need for intubation and the use of vasopressors.

Sample size calculation

The sample size was calculated a priori using G*Power software (version 3.1) to ensure adequate power for detecting a significant association between admission neutrophil-to-lymphocyte ratio (NLR) and in-hospital mortality in patients with severe community-acquired pneumonia. Assuming a two-sided α level of 0.05, a statistical power of 80% ($1-\beta = 0.80$), and a moderate effect size (odds ratio ≈ 2.5) based on previous studies evaluating the prognostic performance of NLR in CAP, the minimum required sample size was estimated at 110 patients. To compensate for possible missing data or incomplete records, the target sample size was increased by approximately 10%, resulting in a planned enrollment of at least 120 patients.

Definitions

Acute Respiratory Distress Syndrome (ARDS)

The Global Definition of ARDS (2023), proposed by an international expert consensus, refines and expands the previous Berlin Definition (2012). Key updates include (17):

- Timing remains within 1 week of a known clinical insult or new/worsening respiratory symptoms.
- Imaging: expands criteria to include not only bilateral radiographic opacities, but also ultrasound findings (e.g., B-lines or consolidation), useful especially in resource-limited settings.
- Oxygenation metrics:
 - o Supports use of $\text{SpO}_2/\text{FiO}_2$ ratio (if $\text{SpO}_2 \leq 97\%$) as an alternative to $\text{PaO}_2/\text{FiO}_2$.
 - o Introduces a non-intubated ARDS category for patients on HFNO (≥ 30 L/min), non invasive ventilation or CPAP.

Resource-limited adaptation: allows ARDS diagnosis even without reliance on $\text{PaO}_2/\text{FiO}_2$, PEEP, or HFNO, enhancing applicability in diverse healthcare context

Acute kidney failure (AKF)

It is a decrease in rapid-onset glomerular filtration rate resulting in uremia and life-threatening short-term water-electrolyte disorders (18).

Healthcare-associated infections

Healthcare-associated infections acquired during the process of receiving health care that was not present during the time of admission. They may occur in different areas of healthcare delivery, such as in hospitals, long-term care facilities, and ambulatory settings, and may also appear after discharge (19).

Hemodynamically unstable

It is an acute circulatory failure, due to an imbalance between oxygen intake and needs (O_2), not spontaneously reversible, resulting in tissue hypoxia by (20):

- either a tissue perfusion defect causing a lack of O_2 intake (cellular hypoxia)
- and/or a defect in adenosine triphosphate production (energy deficiency)

Community-acquired pneumonia (CAP):

Defined as an acute pulmonary infection acquired outside the hospital or within 48 hours of admission, characterized by respiratory symptoms (e.g., cough, dyspnea, fever) and a new infiltrate on chest imaging, in the absence of recent hospitalization or healthcare-associated risk factors (21).

Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range) according to distribution and compared using the student's t-test or Mann-Whitney U test. Categorical variables were expressed as counts (percentages) and compared using the χ^2 test or Fisher's exact test. Multivariable logistic

regression was performed to identify independent predictors of mortality. Statistical significance was defined as a p-value <0.05 . Analyses were performed using JAMOVI 2.6.19.

Ethics approval : This study was approved by the Ethics Committee of Habib Thameur Hospital. Written informed consent was obtained from all participants or their legal representatives before inclusion.

RESULTS

Flow chart (Figure 1)

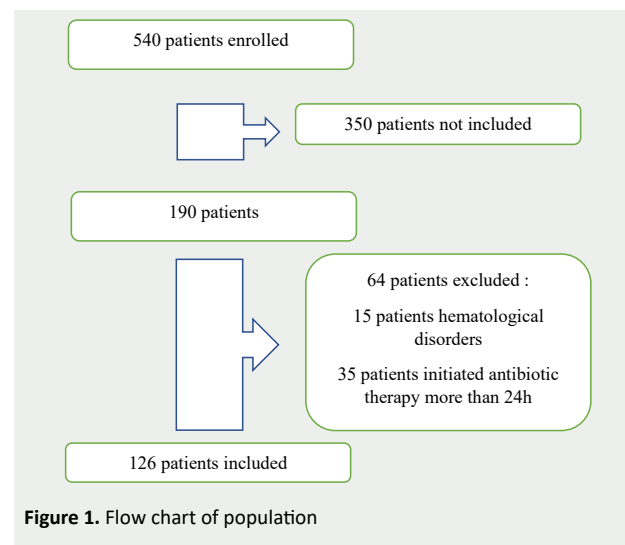


Figure 1. Flow chart of population

Demographic characteristics

The median age of our population was 68 years with sex ratio 1.13. Comorbidities are summarized in table 1. The mean Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAPS) II severity scores were 7.7 ± 4.4 and 24 ± 7.4 , respectively. The mean SOFA score was 4 ± 3 points. The mean Fine score was 6 ± 3 . Mainly symptoms presented at the ICU admission are summarized in Table 1. During ICU stay, all patients received antibiotics, for a median time of 8 days (interquartile range, 6–10 days). In 38 patients (30%), the corticosteroid prescribed was hemisuccinate hydrocortisone (300–400 mg/day). Moreover, 120 patients (95.2) received heparins, all patients received gastric prevention. For the ventilatory management ; 90 patients (71.4%) received conventional oxygen with non-invasive ventilation.

Outcomes

In our study, The clinical course is summarized in table 2. Mechanical ventilation maintained for a median of 4 days (interquartile range, 2–7 days). The mortality rate was 46%. The median of length of ICU stays was 5 days (interquartile range, 2–9 days).

Table 1. The mean characteristics of our population on hospital admission

Variable	Population (n=126)	Survived (n=68)	Died (n=58)	p-value
Age (yr)	66 ±15	66±16	65±14	0.66
Sex ratio (M/F)	1.13	1	1.32	0.47
BMI (kg/m ²)	29 (21–58)	28	30	0.2
Presence of comorbidities	110 (87.3)	56 (44.4)	54 (42.8)	0.8
Arterial hypertension (n,(%))	60 (47.6)	31 (24.6)	29 (23)	0.37
Diabetes (n,(%))	61 (48.8)	31 (24.6)	30 (23.8)	0.27
Cardiac Comorbidities (n,(%))	45 (35.7)	19 (15)	26 (20.6)	0.05
Dyslipidemia (n,(%))	52 (41.2)	40 (31.7)	12 (9.5)	0.02
Cancer (n,(%))	4 (3.1)	1 (0.7)	3 (2.4)	0.25
Asthma (n,(%))	3 (2.4)	3 (2.4)	0	0.74
COPD (n,(%))	16 (12.7)	8 (6.3)	8 (6.3)	0.95
CKD (n,(%))	14 (11.1)	6 (4.7)	8 (6.3)	0.28
Autoimmune disease (n,(%))	6 (4.8)	6 (4.8)	0	0.02
Temperature (°C) (moy±ET)	36.7±2.5	36.8±2.7	36.5±0.2	0.67
RR (cycles/min)	29.7±6.1	30±5.5	29±1.6	0.73
PaO ₂ /FIO ₂ ratio	132±2	141±1	128±2	0.07
CR (bpm)	88±17	92±17	88±9	0.23
Glasgow scale score (moy±ET)	14±1	14±1	14±1	0.67
Dyspnea (n,(%))	98 (77.7)	58 (46)	40 (31.7)	0.02
Fever (n,(%))	45 (35.7)	19 (15)	26 (20.6)	0.05
Cough (n,(%))	45 (35.7)	28 (22.2)	17 (13.4)	0.12
Confusion (n,(%))	24 (19)	10 (7.9)	14 (11.1)	0.11
Leucocytes (u/μl)	11950±5125	11196±4189	12836±6011	0.08
Neutrophiles (u/μl)	9751±4979	8751±3947	10984±5784	0.01
Lymphocytes (u/μl)	1194±700	1346±682	1017±685	0.008
CRP (mg/L)	168±118.2	149±117	191±115	0.04
Procalcitonin (mg/L)	6.8±18	3.41±12	10.7±23.8	0.01
Creatinine (mmol/dl)	172±160	160±171	186±146	0.36
Natremia (mEq/L)	133±13	132±17	134±7	0.67
Kaliemia (mEq/L)	4.2±0.7	4.2±0.77	4.3±0.73	0.92
Hemoglobin (mg/dl)	12.2±10.2	11.5±2.1	12.9±1.5	0.46
Platelets (u/μl)	264158 ± 153870	253161 ± 95831	277051 ± 202023	0.41
pH	7.38±0.11	7.38±0.11	7.37±0.12	0.74
PaO ₂ /FIO ₂ (mm Hg)	175±25	195±30	115±21	10 ⁻³
Neutrophil lymphocyte ratio	11.6±13	7.75±4.5	16.24±17.7	10 ⁻³

Values are presented as median (interquartile range) or number (%).Yr: years; M/F: male/female; BMI: body mass index;COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease, RR: respiratory rate; CR: cardiac rate

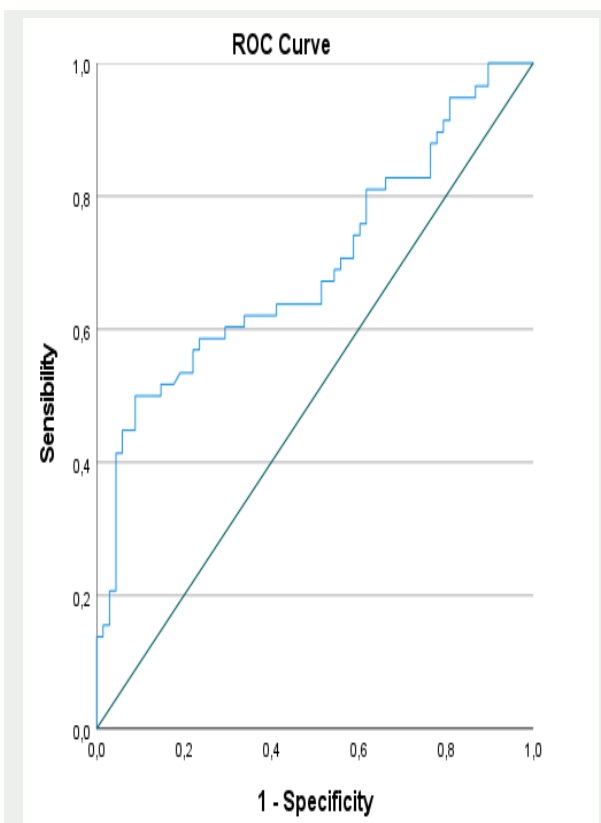
Table 2. The evolutive findings of the study

Parameter	Population (n=126)	Survived (n=68)	Died (n=58)	p-value
Need for IMV (%)	30 (23.8)	7 (5.5)	23 (18.2)	10 ⁻³
Shock	31 (24.6)	4 (3.1)	27 (21.4)	10 ⁻³
Nosocomial infection (%)	42 (33.3)	12 (9.5)	30 (23.8)	10 ⁻³
VAP (%)	40 (31.7)	10 (7.9)	30 (23.8)	0.002
ARDS (%)	31 (24.6)	3 (2.3)	28 (22.2)	10 ⁻³
AKF (%)	25 (19.8)	5 (3.9)	20 (15.8)	10 ⁻³

Values are presented as mean±standard deviation or numbers or percents; IMV: invasive mechanical ventilation; VAP: ventilator associated pneumonia; ARDS: acute respiratory distress syndrome, AKF: acute kidney failure.

Neutrophil Lymphocyte Ratio (NLR)

The median of NLR was 8.85 (interquartile range, 5.4 – 12.9) with a minimum 0.2 and maximum 90. The analysis showed a correlate between NLR and mortality ($p < 10^{-3}$). ROC curve analysis showed that the parameter exhibited a moderate discriminative ability, with an AUC of 0.696 ($p = 0.001$). The optimal threshold was 9, providing a sensitivity of 62% and a specificity of 64% for predicting the outcome. The analysis of curve ROC showed in figure 2.

**Figure 2.** The curve ROC analysis between NLR and mortality

The analysis demonstrated also that a NLR value superior of 9 was associated with increased risk of mortality, shock, ARDS and acute kidney failure (table 3).

Table 3. The analysis a NLR value

Parameter	NLR <9	NLR >9	p-value	OR	IC 95%
IVM (n, (%))	19 (15)	11 (8,7)	0.43	1,44	[0,37-5,5]
Shock (n, (%))	18 (14,2)	13 (10,3)	0.03	4,8	[1,15-20,3]
Sofa score	3	5	0.04	3,2	[1,4-11,2]
Fine score	4	7	0.01	5,2	[2,1-9,7]
AKF (n, (%))	11 (8,7)	14 (11,1)	0.03	3,9	[1,1-13,89]
ARDS (n, (%))	13 (10,3)	18 (14,2)	0.01	14,8	[3,8-57,7]
Mortality (n, (%))	24 (19)	31 (24,6)	10 ⁻³	1,8	[1,03-4,9]

IMV: invasive mechanical ventilation; AKF: acute kidney failure; ARDS: acute respiratory distress syndrome.

DISCUSSION

Our prospective cohort study of 126 patients admitted to the ICU with CAP demonstrated that the neutrophil-to-lymphocyte ratio (NLR) measured at admission was significantly associated with intra-hospital mortality. Patients with a NLR value greater than 9 at ICU admission were associated with a high risk to develop a AKF, shock and ARDS compared with patients with a low value. These findings reinforce the clinical utility of NLR as an easily accessible biomarker for risk stratification in critically ill patients with pneumonia.

Our results are consistent with a growing number of publications that support the role of NLR as a prognostic indicator in CAP. NLR reflects the balance between innate inflammation and adaptive immune suppression and has reproducible associations with severity, ICU admission, and short-term mortality in CAP; serial measurements and integration with clinical scores improve prognostic performance, but thresholds vary across settings.

NLR captures two complementary signals of the host response to pneumonia: neutrophil predominance as a marker of acute innate inflammation and relative lymphopenia as an indicator of stress-mediated or infection-associated adaptive immune suppression and physiological exhaustion, which together reflect disease severity and dysregulated host response. The combination of both mechanisms, resulting in a high NLR, has been interpreted as a surrogate of dysregulated host response to infection. This pathophysiological rationale supports the use of NLR as a biomarker of severity in infectious diseases, including pneumonia, sepsis, and COVID-19. This conceptual basis underpins observational studies that link higher NLR with worse clinical outcomes in CAP patients and with markers of severity in severe disease cohorts (22,23). The advantages and pathophysiological rationale of NLR have significant clinical implications:

1. The simple composite signal: Neutrophilia and lymphopenia are common and rapidly available from routine CBCs, so their ratio integrates systemic inflammatory activation with lymphocyte depletion without additional assays (22).
2. Reflects immune dysregulation: Rising NLR in severe CAP parallels other markers of host injury and has been associated with worse 30day prognosis, consistent with a pathophysiological model of hyperinflammation

plus impaired adaptive immunity (23).

3. Temporal dynamics matter: Changes in NLR over the first days after admission appear to track early treatment response and progression, suggesting that single static values incompletely represent evolving pathobiology.

The available literature consistently supports the prognostic value of the neutrophil-to-lymphocyte ratio (NLR) in patients with community-acquired pneumonia (CAP), although the strength of this association and the optimal cut-off values vary according to the study population, timing of assessment, and clinical outcome. Several studies have demonstrated that elevated admission NLR is associated with increased mortality and disease severity. Lee et al. reported that both admission NLR (cut-off ≈ 6.5) and day-4 NLR (cut-off ≈ 12) predicted 30-day mortality, with serial measurements providing greater prognostic accuracy than baseline values alone (24). Similarly, Tekin et al. found that an NLR >12 was significantly associated with ICU admission and mortality in a large cohort of hospitalized CAP patients (25). Zhang et al. showed that an NLR >11.2 predicted 30-day mortality (AUC = 0.79) and improved the predictive performance of the Pneumonia Severity Index when used in combination (26). More recently, Sharma et al. confirmed that an admission NLR of approximately 11.9 was an independent predictor of adverse outcomes, supporting the reproducibility of these findings across different populations (27).

Evidence specifically addressing critically ill patients with severe CAP remains limited. However, recent ICU-based studies consistently reported admission NLR cut-offs ranging from approximately 10 to 12, with acceptable predictive performance for mortality (22,25,28-30). Although these thresholds vary according to study design, patient characteristics, timing of assessment, and outcome definitions, they collectively support the prognostic value of NLR in severe CAP.

In our cohort, the optimal admission NLR cut-off identified by ROC analysis was 9, slightly lower than the thresholds reported in previous studies (25–27). This discrepancy may reflect the exclusive inclusion of ICU patients with severe CAP, in whom a lower NLR may already indicate profound systemic inflammation and immune dysregulation. Differences in blood sampling time, population characteristics, microbiological epidemiology, and methodological approaches may also account for the observed variability. These findings suggest that NLR cut-offs should be interpreted according to the clinical setting rather than as universal thresholds.

From a clinical perspective, NLR represents an attractive prognostic biomarker because it is inexpensive, readily available from routine complete blood counts, and easily applicable in daily practice, particularly in resource-limited settings. It may complement established severity scores, such as PSI, CURB-65, and SOFA, to improve early risk stratification of patients with severe CAP. Furthermore, previous studies demonstrated that serial NLR measurements provide additional prognostic information, with persistently elevated or increasing values being associated with poor outcomes, whereas

declining values reflect treatment response (22,24). This supports the potential role of dynamic NLR monitoring during ICU stay.

Overall, our findings reinforce the growing evidence that admission NLR is a simple and reliable predictor of in-hospital mortality in severe CAP. In our population, an NLR threshold of 9 showed clinically relevant prognostic performance and may help identify high-risk patients requiring closer monitoring and timely therapeutic interventions.

Several limitations should be acknowledged. First, this was a single-center study conducted in a tertiary ICU with a relatively small sample size, which may limit the generalizability of our findings. Second, variability in comorbidities, causative pathogens, and treatment strategies may have influenced patient outcomes. Third, we did not compare NLR with other inflammatory biomarkers, such as CRP or procalcitonin, nor evaluate their combined prognostic value. Finally, the optimal NLR threshold remains population-dependent, and long-term outcomes after hospital discharge were not assessed.

Future multicenter studies including larger and more diverse ICU populations are warranted to validate the optimal NLR threshold and determine whether integrating NLR into prognostic algorithms or clinical decision-making strategies can improve outcomes in patients with severe CAP.

CONCLUSION

In conclusion, admission NLR was independently associated with in-hospital mortality in critically ill patients with severe community-acquired pneumonia. Our findings suggest that NLR may represent a useful biomarker for early risk stratification in this population. Larger multicenter studies are warranted to validate the optimal prognostic threshold and confirm its clinical utility.

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