nutrición clínica y Dietética Hospitalaria

Artículo Original

Nutr Clín Diet Hosp. 2024; 44(3):253-260
DOI: 10.12873/443wullur

Neutrophil-Lymphocyte Ratio, prognostic nutritional index and CRP - Albumin Ratio significantly predict mortality in ICU patients with low nutrition risk

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Recibido: 10/mayo/2024. Aceptado: 12/julio/2024.

ABSTRACT

Introduction: The dynamic ICU environment requires the use of accurate prognostic indicators to assess patient outcomes and guide clinical interventions. Nutritional status and inflammation are important factors influencing patient outcomes in the ICU. Several prognostic indicators have been proposed to evaluate the prognostic value of NLR, PNI, and CRP to Albumin Ratio in predicting mortality in ICU patients with different levels of nutritional risk.

Methods: This observational retrospective cohort study was conducted in the ICU of Wahidin Sudirohusodo Hospital, Indonesia, from April 2022 to March 2023. All patients admitted to the ICU during the study period were considered. Data collected from medical records included patient demographics, clinical characteristics, prognostic indicators, and outcomes. Bivariate and multivariate regression analysis was used to evaluate the associations between prognostic indicators and mortality both in low-risk and high-risk subgroup. The results were presented as hazard ratios (HRs) with 95% confidence intervals (CIs). To predict accuracy of prognostic biomarker, Receiver Operating Characteristic (ROC) curve analysis was conducted. The area under the ROC curve (AUC) was calculated to evaluate the discriminative ability of each biomarker

Result: In a study of 1,106 ICU patients. The length of stay in the ICU and hospital for survivors is shorter than for non-survivors. Hazard ratio analysis showed that higher PNI significantly reduced the risk of death (unadjusted HR 0.914, adjusted HR 0.910), whereas higher CAR and NLR were associated with increased risk of death (CAR unadjusted HR 1.020, adjusted HR 1.017; unadjusted NLR HR 1.018, adjusted HR 1.014). This effect was less pronounced in patients at high nutritional risk, with nonsignificant HR values. ROC curve analysis showed that CRP/Albumin (AUC: 0.696), NLR (AUC: 0.575), and PNI (AUC: 0.325).

Conclusion: NLR, PNI, and CAR are valuable prognostic indicators in ICU settings, providing crucial information on mortality risk especially in patients with low nutritional risk. The data supports their use in clinical assessments to tailor interventions that address inflammation and nutritional deficits.

KEYWORDS

Intensive Care, mortality, Inflammation, biomarker panel.

INTRODUCTION

Intensive Care Unit (ICU) patients often experience severe physiological stress due to underlying conditions, surgery, or trauma, which can affect immune responses and nutritional status. The dynamic environment of the ICU necessitates the use of accurate prognostic indicators to assess patient outcomes and guide clinical interventions. Nutritional status and inflammation are critical factors influencing patient outcomes in the ICU. Malnutrition is prevalent among critically ill patients and is associated with increased morbidity and mortality[1,2]. Simultaneously, inflammatory responses reflect the body's reaction to infection, trauma, or surgery. The interplay between nutrition and inflammation in critically ill patients underscores the importance of understanding how these factors impact patient outcomes[3,4].

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Several prognostic indicators have been proposed to evaluate the outcomes of critically ill patients, including the Neutrophil-to-Lymphocyte Ratio (NLR), Prognostic Nutritional Index (PNI), and CRP-to-Albumin Ratio (CAR). NLR is a simple marker that represents the ratio of neutrophils to lymphocytes. Elevated NLR has been associated with poor outcomes in various clinical settings, including sepsis, cardiovascular diseases, and cancer[3,5,6]. In ICU patients, NLR serves as a marker of systemic inflammation, with higher values indicating a heightened inflammatory response and worse prognosis[7,8]. The PNI is calculated based on serum albumin levels and lymphocyte count. It serves as an indicator of nutritional and immune status. Lower PNI values are associated with malnutrition and poorer outcomes in surgical and critically ill patients[1,9,10]. The PNI reflects both the patient's nutritional reserves and immune function. The CAR combines CRP, an acute-phase reactant, and albumin, a marker of nutritional status. The ratio provides insight into the balance between inflammation and nutrition. Elevated CAR has been linked to increased mortality in ICU patients, as well as in patients with sepsis, cancer, and cardiovascular diseases[11,12]. The CAR is particularly useful because it accounts for both inflammatory and nutritional aspects of patient health[13,14].

While previous research has established the prognostic value of NLR, PNI, and CAR in various clinical settings, there is limited information on their predictive capabilities in ICU patients with different levels of nutritional risk. The objective of this study is to evaluate the prognostic value of the Neutrophil-to-Lymphocyte Ratio, Prognostic Nutritional Index, and CRP-to-Albumin Ratio in predicting mortality in ICU patients with different levels of nutritional risk.

METHODS

Study Design

An observational retrospective cohort study conducted in the Intensive Care Unit (ICU) of Wahidin Sudirohusodo from April 2022 to March 2023. Participants was all the patient admitted to the ICU during the study period. Patients were excluded if they were younger than 18 years of age or lacking necessary data for the analysis. The study was approved by the ethics committee of the university and hospital which ensure the confidentiality of all the patient's data throughout the research process. The ethic protocol member No: 969/UN4.6.4.5.31/ PP36/ 2023.

Data Collection

Data for the study were collected from medical records, which provided detailed information on patient demographics, clinical characteristics, prognostic indicators and clinical outcomes. Demographic data included age, sex, height, weight, and body mass index (BMI). The clinical characteristics collected included the admission category and nutritional risk. The nutritional risk was assessed using the mNutric score. Prognostic indicator data included NLR, PNI, and CAR. The clinical outcomes assessed included ICU and hospital length of stay (LOS), duration of mechanical ventilation, and ICU mortality.

Statistical Analysis

The normality of continuous data was assessed using the Shapiro-Wilk test to evaluates normal distribution of dataset. Depending on the distribution, continuous variables were expressed as either mean ± standard deviation (SD) or median and interquartile range (IQR). Categorical variables were presented as numbers and percentages. For continuous variables, the Student's t-test or Mann-Whitney U test was used for two-group comparisons, while one-way ANOVA or Kruskal-Wallis test was used for more than two groups. For categorical variables, the chi-square test was used, depending on the sample size and distribution of the categories. Bivariate and multivariate regression analysis was used to evaluate the associations between prognostic indicators and mortality both in low-risk and high-risk subgroup. The results were presented as hazard ratios (HRs) with 95% confidence intervals (CIs). Both unadjusted and adjusted models were used, with adjustments made for potential confounders, including age, sex, BMI, and admission type. To assess the predictive accuracy of the Neutrophil-to-Lymphocyte Ratio (NLR), Prognostic Nutritional Index (PNI), and C-reactive Protein to Albumin Ratio (CAR) in forecasting ICU mortality, Receiver Operating Characteristic (ROC) curve analysis was conducted. The area under the ROC curve (AUC) was calculated to evaluate the discriminative ability of each biomarker. AUC values closer to 1 indicate excellent predictive accuracy, whereas values near 0.5 suggest no predictive benefit over random chance. This analysis helps to elucidate which biomarkers can effectively distinguish between patient outcomes, particularly in terms of mortality risk. Statistical analysis for the study was performed using SPSS 25.0 (IBM Corp., Armonk, NY). A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 1,189 patients were admitted to the ICU from April 2022 to March 2023. Among these, 83 patients were excluded from the study due to being under 18 years of age, leaving a final sample size of 1,106 patients for analysis. The demographic and clinical characteristics of the study population are summarized in Table 1.

The patients' median age was 50 years (IQR: 37–60) for survivors and 55.5 years (IQR: 41–67) for non-survivors, with a significant difference ($p < 0.001$). Regarding sex, 54.4% of the survivors were women, whereas the majority of non-survivors (58%) were men, highlighting a statistically significant difference ($p < 0.001$). The survivors and non-survivors had similar heights, with median heights of 160 cm (IQR: 155–165) in both groups, showing no significant dif-

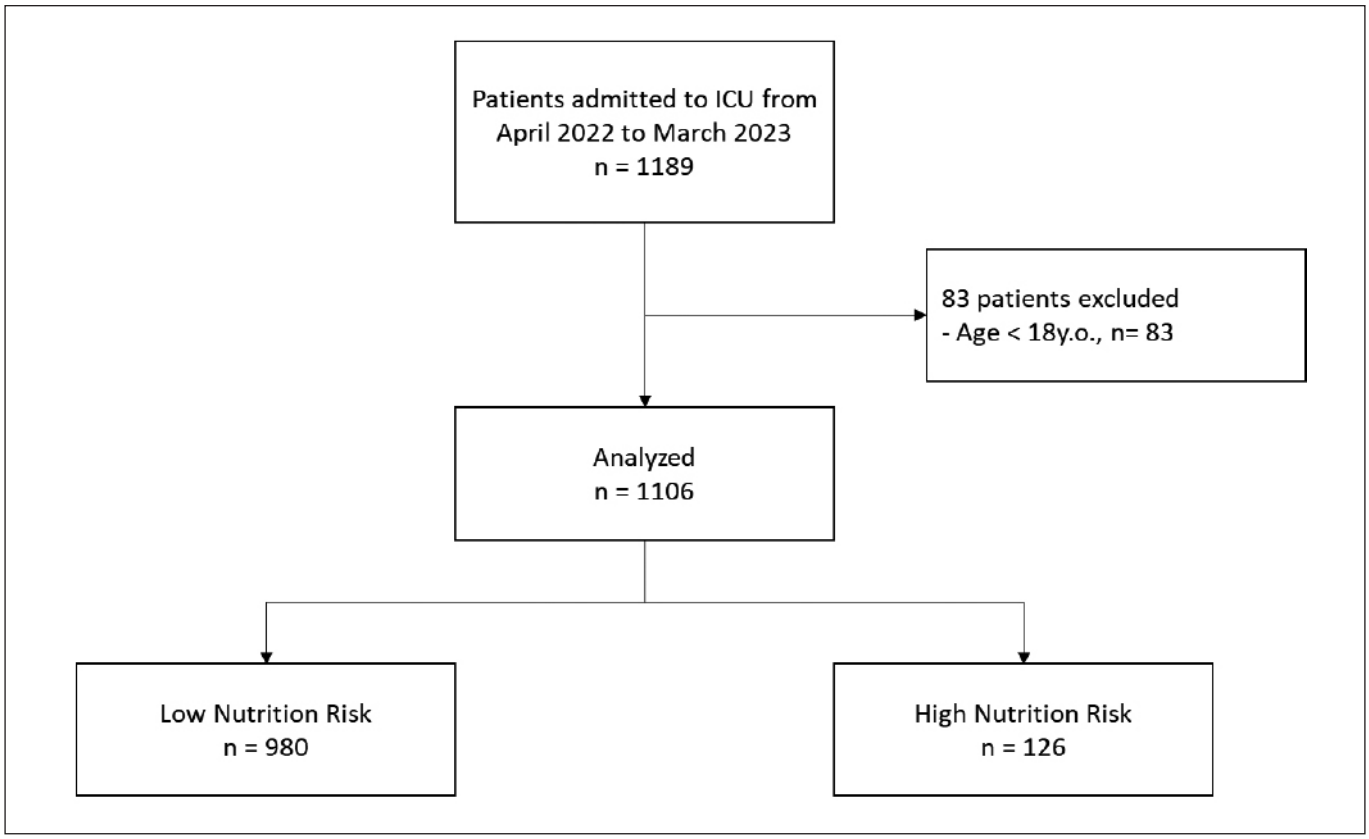


Figure 1. Flowchart of the study patients

Table 1. Baseline characteristics of the study patients

	Survivors	Non Survivors	p Value
Age, year	50 [37, 60]	55.5 [41, 67]	<0.001
Sex			<0.001
Men	401 (45.6)	131 (58)	
Woman	479 (54.4)	95 (42)	
Height, cm	160 [155, 165]	160 [155, 165]	0.105
Weight, kg	60 [50, 63]	60 [50, 64]	0.235
BMI, kg/m2	22.22 [20.56, 24.61]	22.22 [20.81, 23.92]	0.690
BMI Category			0.921
<18.5	94 (10.7)	21 (9.3)	
18.5 - 22.9	412 (46.8)	102 (45.1)	
23 - 24.9	192 (21.8)	53 (23.5)	
25 - 29.9	165(18.8)	46 (20.4)	
>30	17 (1.9)	4 (1.8)	

Data are presented as n (%) or median (interquartile range).
BMI, Body Mass Index.

Table 1 continuation. Baseline characteristics of the study patients

	Survivors	Non Survivors	p Value
Admission Type			<0.001
Medical	84 (37.2)	123 (14)	
Surgical	142 (62.8)	757 (86)	
mNutric Score			<0.001
Low Risk	830 (94.3)	150 (66.4)	
High Risk	50 (5.7)	76 (33.6)	
Total Lymphocyte Count	939 [663, 1340]	792 [485, 1185]	0.001
Neutrophil to Lymphocyte Ratio	12.73 [8.38, 20.1]	16.58 [9.42, 25.51]	0.034
Prognostic Nutritional Index	34.2 (6.8)	29.7 (6.8)	<0.001
CRP to Albumin Ratio	5.36 [4.33, 37.41]	9.39 [19.23, 64.11]	<0.001
ICU LOS, days	1 [1, 5]	6 [2, 11]	<0.001
Hospital LOS, days	8 [6, 20]	16 [9, 28]	<0.001
Mechanical Ventilation, days	0 [0, 2]	4 [1, 10]	<0.001

Data are presented as n (%) or median (interquartile range).
ICU, Intensive Care Unit; LOS, Length of Stay; CRP, C-Reactive Protein; mNutric Score, modified Nutrition risk in critically lll.

Table 2. Relationship between Prognostic Indicator and Mortality

	Unadjusted			Adjusted*		
	Hazard ratio	95% CI	p Value	Hazard ratio	95% CI	p Value
Total Study Population						
PNI	0.914	0.892 - 0.937	<0.001	0.910	0.887 - 0.934	<0.001
CAR	1.020	1.013 - 1.026	<0.001	1.017	1.011 - 1.024	<0.001
NLR	1.018	1.008 - 1.027	<0.001	1.014	1.005 - 1.023	0.002
Subgroup Analysis						
Low Nutrition Risk						
PNI	0.917	0.892 - 0.944	<0.001	0.909	0.882 - 0.937	<0.001
CAR	1.021	1.013 - 1.028	<0.001	1.019	1.011 - 1.027	<0.001
NLR	1,015	1.003 - 1.026	<0.001	1.015	1.003 - 1.027	0.011
High Nutrition Risk						
PNI	0.961	0.907 - 1.019	0.188	0.978	0.948 - 1.008	0.148
CAR	0.999	0.984 - 1.014	0.880	0.997	0.981 - 1.014	0.751
NLR	1.004	0.992 - 1.017	0.507	1.005	0.990 - 1.020	0.541

* Adjusted for age, sex, BMI, Admission Type.
PNI, Prognostic Nutritional Index; CAR, CRP to Albumin Ratio; Neutrophil to Lymphocyte Ratio.

ference (p = 0.105). The survivors and non-survivors had similar median weights of 60 kg, although the distribution was slightly different, and this was not statistically significant (p = 0.235). The BMI of both groups was also similar, with a median of 22.22 kg/m², and no significant difference (p = 0.690). The admission type differed significantly between survivors and non-survivors (p < 0.001). Among survivors, 37.2% were medical admissions, while 62.8% were surgical. In contrast, among non-survivors, 14% were medical, and 86% were surgical. Nutrition risk, assessed using the mNUTRIC score, was significantly different between the groups (p < 0.001). The majority of survivors (94.3%) had low nutrition risk, while most non-survivors (86%) had high nutrition risk. The median total lymphocyte count was significantly higher in survivors (939, IQR: 663–1340) compared to non-survivors (792, IQR: 485–1185), with a significant difference (p < 0.001). The median Neutrophil-to-Lymphocyte Ratio (NLR) was lower in survivors (12.73, IQR: 8.38–21.00) than in non-survivors (16.58, IQR: 9.42–25.71), also significantly different (p = 0.003). The Prognostic Nutritional Index (PNI) was higher in survivors (34.2, IQR: 6.8) compared to non-survivors (29.7, IQR: 6.8), with a significant difference (p < 0.001). The CRP-to-Albumin Ratio (CAR) was lower in survivors (5.36, IQR: 3.43–7.41) compared to non-survivors (9.39, IQR: 3.71–19.23), also significantly different (p < 0.001). The median length of stay in the ICU was shorter for survivors (1 day, IQR: 1–5) compared to non-survivors (6 days, IQR: 2–11), with a significant difference (p < 0.001). The median hospital length of stay was shorter for survivors (8 days, IQR: 2–20) compared to non-survivors (16 days, IQR: 8–28), also significantly different (p < 0.001). The median duration of mechanical ventilation was shorter for survivors (0 days, IQR: 0–1) compared to non-survivors (4 days, IQR: 1–10), with a significant difference (p < 0.001).

For the total study population, the unadjusted HR for Prognostic Nutritional Index (PNI) was 0.914 (95% CI: 0.892–0.937; p < 0.001). This indicates that higher PNI is associated with lower mortality. The adjusted HR for PNI, which accounts for potential confounding factors such as age, sex, BMI, and admission type, remained significant at 0.910 (95% CI: 0.887–0.934; p < 0.001). The unadjusted and adjusted HRs for CRP-to-Albumin Ratio (CAR) were 1.020 (95% CI: 1.013–1.026; p < 0.001) and 1.017 (95% CI: 1.011–1.024; p < 0.001), respectively, suggesting that higher CAR is associated with increased mortality. Similarly, the Neutrophil-to-Lymphocyte Ratio (NLR) showed significant associations with mortality, with unadjusted and adjusted HRs of 1.018 (95% CI: 1.008–1.027; p < 0.001) and 1.014 (95% CI: 1.005–1.023; p = 0.002), respectively. In the low nutrition risk group, all three indicators (PNI, CAR, and NLR) were significantly associated with mortality both in the unadjusted and adjusted models. For example, the unadjusted HR for PNI was 0.917 (95% CI: 0.892–0.944; p < 0.001) and the adjusted HR was 0.909 (95% CI: 0.882–0.937; p < 0.001). However, in the high nutrition risk group, the associations were less pronounced. The unadjusted and adjusted HRs for PNI were not significant, with values of 0.961 (95% CI: 0.907–1.019; p = 0.188) and 0.978 (95% CI: 0.948–1.008; p = 0.148), respectively. The unadjusted and adjusted HRs for CAR were also non-significant, with values of 0.999 (95% CI: 0.984–1.014; p = 0.880) and 0.997 (95% CI: 0.981–1.014; p = 0.751), respectively. The unadjusted and adjusted HRs for NLR were similarly non-significant, with values of 1.004 (95% CI: 0.992–1.017; p = 0.507) and 1.005 (95% CI: 0.990–1.020; p = 0.541), respectively.

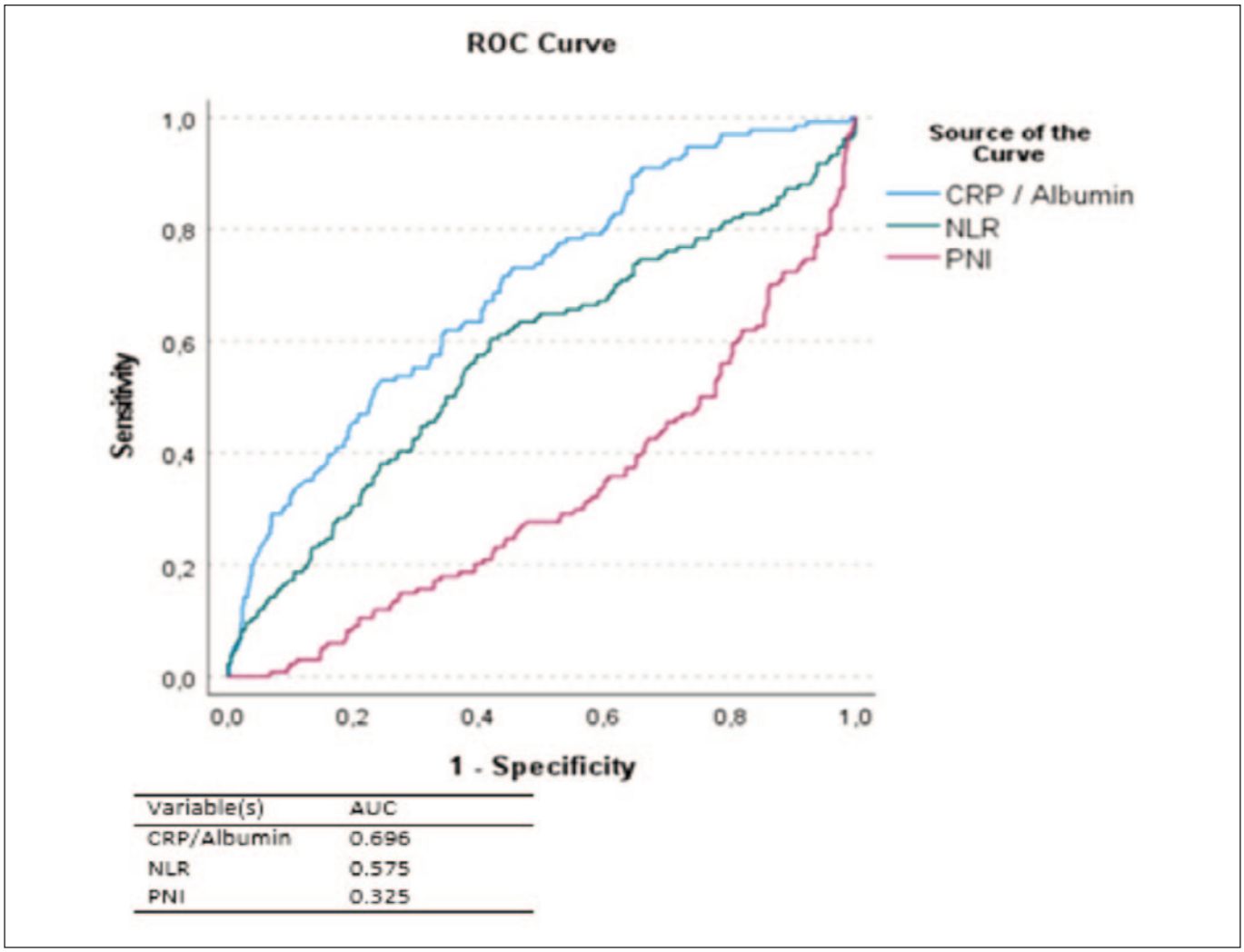
The predictive factor accuracy of C-reactive protein to albumin ratio (CRP/Albumin), neutrophil to lymphocyte ratio (NLR), and Prognostic Nutritional Index (PNI) was assessed using Receiver Operating Characteristic (ROC) curve analysis. Figure 2 depicts the ROC curves for each test variable to predict mortality. The area under the ROC curve (AUC) for CRP/Albumin was 0.696, indicating a good diagnostic ability to differentiate between patient groups. NLR demonstrated a fair diagnostic performance with an AUC of 0.575. The PNI showed a poor discriminative ability with an AUC of only 0.325

DISCUSSION

In this observational cohort study, we evaluated the prognostic value of the Neutrophil-to-Lymphocyte Ratio (NLR), Prognostic Nutritional Index (PNI), and CRP-to-Albumin Ratio (CAR) in predicting mortality among ICU patients. Our findings indicate that all three indicators significantly predict mortality in this population, particularly among those with low nutrition risk. The unadjusted and adjusted hazard ratios for NLR, PNI, and CAR were all significant in the total population and among patients with low nutrition risk. However, among patients with high nutrition risk, the prognostic significance of these indicators was less pronounced[15-17].

In critically ill patients, the intricate interplay between inflammation, immune function, and nutritional status plays a pivotal role in determining clinical outcomes. Elevated NLR may signify an exaggerated inflammatory response in patients with low nutrition risk, characterized by an imbalance between pro-inflammatory neutrophils and anti-inflammatory lymphocytes, contributing to tissue damage, organ dysfunction, and increased mortality risk[18-21]. Similarly, the CRP-albumin ratio reflects the balance between inflammatory markers and nutritional status. Elevated levels of CRP, indicative of systemic inflammation, coupled with decreased levels of albumin, suggestive of malnutrition, underscore the multifaceted nature of critical illness in these patients[22,23]. These biomarkers not only reflect the severity of the inflammatory response but also provide insights into the nutritional adequacy and immune competence of the individual, crucial determinants of clinical outcomes.

The differences in prognostic predictability between patients with low and high nutrition risk may stem from the un-



Variable(s)	AUC
CRP/Albumin	0.696
NLR	0.575
PNI	0.325

Figure 2. ROC Curve Analysis of CRP/Albumin, NLR, and PNI to Predict Mortality

derlying pathophysiology of critical illness and the dynamic interplay between inflammation, immune function, and nutritional status. Patients with high nutrition risk may exhibit more profound and persistent inflammation, reflecting a dysregulated immune response and systemic inflammatory cascade, potentially overshadowing the effectiveness of traditional prognostic markers such as NLR, PNI, and CRP-albumin ratio in predicting mortality risk[24-27]. Moreover, the impact of nutritional status on immune function may be more pronounced in patients with high nutrition risk, further complicating the prognostic assessment. Malnutrition-induced immune dysfunction can exacerbate the inflammatory response and predispose patients to adverse outcomes, making it challenging to discern the independent prognostic significance of individual biomarkers[28,29].

The demonstrated predictability of NLR, PNI, and CAR as mortality indicators in ICU patients with low nutritional risk suggests significant clinical implications for monitoring and intervention. The utility of these markers can be extended to devise personalized treatment strategies, where the inflammation and nutritional status of each patient are regularly assessed and addressed. For instance, elevated NLR and CAR values might prompt immediate anti-inflammatory interventions, while low PNI could necessitate nutritional support measures. Integrating these indicators into routine clinical practice could potentially accelerate decision-making processes, enhance patient monitoring, and improve outcomes by enabling more tailored and timely interventions. Future studies could explore the integration of these markers into clinical protocols and examine their impact on the management strategies and recovery rates of ICU patients[30-33].

Our study has several limitations. First, this was an observational cohort study, which limits our ability to establish causality between the prognostic indicators and mortality. Future randomized controlled trials are needed to further investigate these relationships. Second, our study was con-

ducted in a single centre hospital, which may limit the generalizability of our findings to other settings. However, the large sample size and diverse patient population enhance the external validity of our results. Third, we used retrospective data from medical records, which may be subject to data quality issues. However, the use of standardized clinical measurements and robust statistical analyses mitigates this limitation. Finally, while we adjusted for several potential confounders, residual confounding cannot be ruled out. Future studies should consider additional confounding factors, such as comorbidities and treatment interventions, to further elucidate the relationships between these prognostic indicators and mortality.

CONCLUSION

Study demonstrates that the Neutrophil-to-Lymphocyte Ratio, Prognostic Nutritional Index, and CRP-to-Albumin Ratio are significant predictors of mortality in ICU patients with low nutrition risk. These indicators provide valuable prognostic information and underscore the importance of addressing both inflammation and nutritional status in critically ill patients.

ACKNOWLEDGEMENTS

The author would like to express gratitude to all teachers at the Nutrition Department, Faculty of Medicine, Hasanuddin University

REFERENCES

1. Huang Y, Zhang Q, Li P, Chen M, Wang R, Hu J, et al. The prognostic nutritional index predicts all-cause mortality in critically ill patients with acute myocardial infarction. BMC Cardiovasc Disord. 2023 Jul 4;23(1):339.
2. Xu T, Zhang SM, Wu HM, Wen XM, Qiu DQ, Yang YY, et al. Prognostic significance of prognostic nutritional index and systemic immune-inflammation index in patients after curative breast cancer resection: a retrospective cohort study. BMC Cancer. 2022 Nov 3;22(1):1128.
3. Regolo M, Vaccaro M, Sorce A, Stancanelli B, Colaci M, Natoli G, et al. Neutrophil-to-Lymphocyte Ratio (NLR) Is a Promising Predictor of Mortality and Admission to Intensive Care Unit of COVID-19 Patients. J Clin Med. 2022 Apr 16;11(8):2235.
4. Chen L, Bai P, Kong X, Huang S, Wang Z, Wang X, et al. Prognostic Nutritional Index (PNI) in Patients With Breast Cancer Treated With Neoadjuvant Chemotherapy as a Useful Prognostic Indicator. Front Cell Dev Biol. 2021 Mar 30;9.
5. Zinellu A, Zinellu E, Mangoni AA, Pau MC, Carru C, Pirina P, et al. Clinical significance of the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in acute exacerbations of COPD: present and future. European Respiratory Review. 2022 Dec 31;31(166):220095.
6. Zhang X, Wei R, Wang X, Zhang W, Li M, Ni T, et al. The neutrophil-to-lymphocyte ratio is associated with all-cause and cardiovascular mortality among individuals with hypertension. Cardiovasc Diabetol. 2024 Apr 2;23(1):117.
7. Asghar MS, Akram M, Yasmin F, Najeeb H, Naeem U, Gaddam M, et al. Comparative analysis of neutrophil to lymphocyte ratio and derived neutrophil to lymphocyte ratio with respect to outcomes of in-hospital coronavirus disease 2019 patients: A retrospective study. Front Med (Lausanne). 2022 Jul 22;9.
8. Man MA, Rajnoveanu RM, Motoc NS, Bondor CI, Chis AF, Lesan A, et al. Neutrophil-to-lymphocyte ratio, platelets-to-lymphocyte ratio, and eosinophils correlation with high-resolution computer tomography severity score in COVID-19 patients. PLoS One. 2021 Jun 28;16(6):e0252599.
9. Liu M, Sun M, Zhang T, Li P, Liu J, Liu Y, et al. Prognostic Nutritional Index (PNI) as a potential predictor and intervention target for perioperative ischemic stroke: a retrospective cohort study. BMC Anesthesiol. 2023 Aug 10;23(1):268.
10. Wang HB, Xu XT, Tian MX, Ding CC, Tang J, Qian Y, et al. Prognostic values of the prognostic nutritional index, geriatric nutritional risk index, and systemic inflammatory indexes in patients with stage IIB–III cervical cancer receiving radiotherapy. Front Nutr. 2023 Mar 2;10.
11. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci. 2022 Mar 26;23(7):3636.
12. Shi Y, Zhang Y, Niu Y, Chen Y, Kou C. Prognostic role of the prognostic nutritional index (PNI) in patients with head and neck neoplasms undergoing radiotherapy: A meta-analysis. PLoS One. 2021 Sep 14;16(9):e0257425.
13. Liu B, Lv D. Prognostic value of C-reactive protein to albumin ratio for mortality in acute kidney injury. BMC Nephrol. 2023 Feb 25;24(1):44.
14. Jang JH, Hong S, Ryu JA. Prognostic Value of C-Reactive Protein and Albumin in Neurocritically Ill Patients with Acute Stroke. J Clin Med. 2022 Aug 29;11(17):5067.
15. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci. 2022 Mar 26;23(7):3636.
16. Regolo M, Vaccaro M, Sorce A, Stancanelli B, Colaci M, Natoli G, et al. Neutrophil-to-Lymphocyte Ratio (NLR) Is a Promising Predictor of Mortality and Admission to Intensive Care Unit of COVID-19 Patients. J Clin Med. 2022 Apr 16;11(8):2235.
17. Huang Y, Zhang Q, Li P, Chen M, Wang R, Hu J, et al. The prognostic nutritional index predicts all-cause mortality in critically ill patients with acute myocardial infarction. BMC Cardiovasc Disord. 2023 Jul 4;23(1):339.
18. Wu X, Luo Q, Su Z, Li Y, Wang H, Liu Q, et al. Neutrophil-to-lymphocyte ratio as a predictor of mortality in intensive care unit patients: a retrospective analysis of the Medical Information Mart for Intensive Care III Database. BMJ Open. 2021 Nov 11;11(11):e053548.

19. Liu J, Liu Y, Xiang P, Pu L, Xiong H, Li C, et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. J Transl Med. 2020 Dec 20;18(1):206.

20. Tanık VO, Akdeniz E, Çınar T, Şimşek B, İnan D, Kıvrak A, et al. Higher C-Reactive Protein to Albumin Ratio Portends Long-Term Mortality in Patients with Chronic Heart Failure and Reduced Ejection Fraction. Medicina (B Aires). 2024 Mar 7;60(3):441.

21. Jang JH, Hong S, Ryu JA. Prognostic Value of C-Reactive Protein and Albumin in Neurocritically Ill Patients with Acute Stroke. J Clin Med. 2022 Aug 29;11(17):5067.

22. Liu B, Lv D. Prognostic value of C-reactive protein to albumin ratio for mortality in acute kidney injury. BMC Nephrol. 2023 Feb 25;24(1):44.

23. Uzum Y, Turkkan E. Predictivity of CRP, Albumin, and CRP to Albumin Ratio on the Development of Intensive Care Requirement, Mortality, and Disease Severity in COVID-19. Cureus. 2023 Jan 10;

24. Sarejloo S, Shojaei N, Lucke-Wold B, Zelmanovich R, Khanzadeh S. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as prognostic predictors for delirium in critically ill patients: a systematic review and meta-analysis. BMC Anesthesiol. 2023 Feb 21;23(1):58.

25. Di Rosa M, Sabbatinelli J, Soraci L, Corsonello A, Bonfigli AR, Cherubini A, et al. Neutrophil-to-lymphocyte ratio (NLR) predicts mortality in hospitalized geriatric patients independent of the admission diagnosis: a multicenter prospective cohort study. J Transl Med. 2023 Nov 21;21(1):835.

26. Akkaya S, Cakmak U. Association between C-Reactive Protein to Albumin Ratio and Multi-Vessel Coronary Artery Disease in Patients with Stable Coronary Artery Disease. J Pers Med. 2024 Mar 31;14(4):378.

27. Li J, Zhu P, Li Y, Yan K, Tang X, Xu J, et al. A novel inflammatory biomarker, high-sensitivity C-reactive protein-to-albumin ratio, is associated with 5-year outcomes in patients with type 2 diabetes who undergo percutaneous coronary intervention. Diabetol Metab Syndr. 2023 Feb 6;15(1):14.

28. Drăgoescu AN, Pădureanu V, Stănculescu AD, Chiuțu LC, Tomescu P, Georgmăneanu C, et al. Neutrophil to Lymphocyte Ratio (NLR)—A Useful Tool for the Prognosis of Sepsis in the ICU. Biomedicines. 2021 Dec 30;10(1):75.

29. Dolapoglu A, Avci E, Kiris T. The predictive value of C-reactive protein to albümin ratio for ascending aort progression in patients with ascending aortic diameter of 40–50 mm. J Cardiothorac Surg. 2022 Oct 4;17(1):254.

30. Toyokawa T, Muguruma K, Yoshii M, Tamura T, Sakurai K, Kubo N, et al. Clinical significance of prognostic inflammation-based and/or nutritional markers in patients with stage III gastric cancer. BMC Cancer. 2020 Dec 3;20(1):517.

31. Shao Y, Lai Q cheng, Duan Q, Ge P, Ye L. Nutritional indices at admission are associated with mortality rates of patients in the intensive care unit. Eur J Clin Nutr. 2022 Apr 17;76(4):557–63.

32. Wu X, Luo Q, Su Z, Li Y, Wang H, Liu Q, et al. Neutrophil-to-lymphocyte ratio as a predictor of mortality in intensive care unit patients: a retrospective analysis of the Medical Information Mart for Intensive Care III Database. BMJ Open. 2021 Nov 11;11(11):e053548.

33. Regolo M, Vaccaro M, Sorce A, Stancanelli B, Colaci M, Natoli G, et al. Neutrophil-to-Lymphocyte Ratio (NLR) Is a Promising Predictor of Mortality and Admission to Intensive Care Unit of COVID-19 Patients. J Clin Med. 2022 Apr 16;11(8):2235.