Systemic inflammatory markers as a supplement to nutrition risk screening of ICU patients

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ABSTRACT

Background and Objectives: Critical illness often leads to life-threatening organ dysfunction, requiring intensive care. This catabolic condition significantly affects nutrition, causing muscle loss, weakness, and an increased risk of malnutrition, which complicates recovery. Traditional nutritional assessment tools often face limitations in critically ill patients. Systemic inflammation may improve the accuracy of nutritional risk screening. **Methods and Study Design:** Data from the MIMIC-IV database were analyzed. The study aimed to assess the prognostic value of inflammatory markers combined with the mNUTRIC score. Survival analyses were conducted using Kaplan-Meier curves and Cox regression models to evaluate the association between these markers and patient mortality at 30-day, 60-day, and 90-day intervals. **Results:** A total of 2,628 ICU patients were included. High C-reactive protein (CRP; cut-off value 75.2 mg/L) had a hazard ratio (HR) of 1.345 (Log-rank $p = 0.004$), high neutrophil-to-lymphocyte ratio (NLR; cut-off value 8.16) had an HR of 1.266 (Log-rank $p = 0.021$), and albumin (cut-off value 35 g/L) was associated with an HR of 0.576 (Log-rank $p < 0.001$). For 60-day and 90-day mortality, similar trends were observed, with significant p-values. **Conclusions:** Combining inflammatory markers such as CRP, NLR, and albumin with the mNUTRIC score enhances mortality prediction in critically ill patients, improving clinical decision-making. Further research with larger, multicenter cohorts is needed.

Key Words: critical illness, malnutrition, nutritional risk screening, systemic inflammation, inflammatory markers

INTRODUCTION

Critical illness is characterized by life-threatening dysfunction of vital organs, often requiring intensive care unit (ICU) admission for life-sustaining treatments, such as mechanical ventilation.[1,2] In addition to the illness itself, sedation is used to induce unconsciousness and prolonged immobilization, along with hypermetabolic and hypercatabolic state of critical illness, which reduces utilization of nutrients, food intake, rapid loss of fat and body mass, inflammation, anorexia, gastrointestinal disorders and metabolic disorders, leading to protein breakdown, muscle loss, and weakness.[3–5] This catabolic state significantly hampers physical function and increases the likelihood of compromised nutritional status in critical patients.[6] Patients with pre-existing chronic diseases, malnutrition, or reduced food intake prior to ICU admission are more likely to experience severe nutritional deficits and associated

complications during their critical illness.[7–10] These effects can persist for years, further deteriorating their overall condition.[11–15]

Clinical nutrition societies evaluate nutritional risk of patients in ICUs. The European Society for Clinical Nutrition (ESPEN) defines patients who stay longer than 48 hours in the ICU as risky for malnutrition.[16,17] Conversely, the American Society for Parenteral and Enteral Nutrition (ASPEN) suggests using the Nutritional Risk Screening (NRS2002) or the Nutrition Risk in Critically Ill (NUTRIC) score.[18,19] NRS2002 classifies patients with 3 or higher as risky for malnutrition. Individuals with 6 or higher on the original NUTRIC score (mNUTRIC score) or 5 or more on the modified NUTRIC score (excluding interleukin-6) score have high nutritional risk.[20]

The Global Leadership Initiative on Malnutrition (GLIM), established in 2019, aims to standardize the diagnosis of malnutrition through consensus report.[21] The standardization process involves two main steps: risk screening and diagnostic assessment. Initially, the patient's nutritional status is confirmed, and the risk of malnutrition is evaluated. Following this, patients are assessed based on two etiological and three phenotypic criteria. A malnutrition diagnosis is made if the patient meets at least one etiological and one phenotypic criterion.[22] Nutrition assessments in the ICU can be challenging for bedridden and sedated patients who may not be able to provide accurate diet and weight histories. Critically ill patients often have significant fluid shifts, complicating attempts to obtain a dry weight and muscularity at the bedside.[9]

Systemic inflammation is a known contributor to malnutrition. It causes decreased food intake, altered metabolism, high energy expenditure, muscle catabolism, and muscle wasting.[23] According to GLIM, it is an important indicator for malnutrition. In clinical settings, inflammation can be assessed by laboratory indicators; systemic inflammation can often be measured by variations in peripheral blood components and biomarkers such as neutrophils, lymphocytes, and C-reactive protein (CRP).[24]

This study investigated whether inflammatory markers alone, used after an initial positive nutrition risk screening, could serve as an alternative method for assessing nutritional status in critically ill patients. Inflammatory status was assessed using a set of commonly available laboratory biomarkers such as IBI, CRP, neutrophil-to-lymphocyte ratio (NLR) and serum albumin.[25–27] Specific cutoff values for these markers were obtained based on their association with survival to identify patients as malnourished or non-malnourished. Diagnostic accuracy of the method based on inflammatory markers was evaluated to provide evidence-based recommendations on improving practicality of GLIM criteria in critically ill

cohorts and selecting appropriate laboratory markers for inflammatory status in nutritional evaluation.

MATERIALS AND METHODS

Population

All patient data used in this study came from Medical Information Mart for Intensive Care database (MIMIC-IV, version 3.1) a large, de-identified database database of patients admitted to the emergency department or Intensive Care Unit at Beth Israel Deaconess Medical Center in Boston, Massachusetts. Data were collected from the database,[28,29] which is available at: https://mimic.mit.edu/. Due to the extensive volume of ICU-specific data, the MIMIC-IV database has become a highly sought-after resource for clinical decision support, predictive modeling, critical care outcomes research, and other areas. The database includes data from 2008 to 2022, such as laboratory results, treatment information, vital signs, length of stay, and other patient-specific details. To protect patient privacy, all personal data were de-identified, and patient IDs were replaced with random identifiers. As the data were anonymous, ethical approval and informed consent were waived. The collection and creation of the research resource were reviewed and approved by the Beth Israel Deaconess Medical Center Institutional Review Board, which also waived the need for informed consent and approved the project involving data sharing.

Supplementary Figure 1 presents the process of selecting the study sample from the MIMIC-IV database (version 3.1), which initially contained 546,028 admissions, 364,627 patients, and 94,458 ICU stays. The study focused on ICU patients with available data on CRP, NLR, albumin, and IBI, resulting in a cohort of 4,204 patients. Exclusion criteria were applied: patients under 18 years of age (n=0), ICU stays shorter than 48 hours (n=1,073), and those with missing data that prevented nutritional risk screening (n=503). This resulted in a final cohort of 2,628 patients for analysis.

Ethical review

The human participant studies were approved by the Institutional Review Boards of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. Written informed consent was not required in accordance with national regulations and institutional policies.

Data collection and outcome

We extracted data from the MIMIC-IV database to calculate the NRS2002 and mNUTRIC scores, along with data on various inflammatory markers, all measured within the first 24 hours of ICU admission. To efficiently extract and manage the data, we used Structured Query Language (SQL), ensuring the accuracy of data collection by retrieving relevant clinical measurements from each patient's first 24 hours in the ICU. The outcome we selected were 30-day all-cause mortality, 60-day all-cause mortality and 90-day all-cause mortality.

Nutritional risk screening and inflammatory marker utilization

This study primarily employed the NRS2002 and mNUTRIC for initial nutritional screening. Based on their efficacy in distinguishing critically ill patients, the superior method was selected for integration with inflammatory markers in subsequent research. Serum inflammatory markers previously reported were utilized to assess inflammatory burden, including the IBI, CRP, NLR, and albumin. The IBI was calculated as CRP (mg/dL) multiplied by NLR. Optimal cut-off values for these markers were determined using the standardized log-rank statistic via the R.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as counts and percentages (%). Group differences in continuous variables were assessed using the Student's t-test, with non-parametric Kruskal-Wallis tests employed for non-normally distributed variables. Categorical variables were compared using the chi-square test, with Fisher's correction applied as needed. Survival rates and curves were estimated for each group using the Kaplan-Meier method, with group comparisons conducted using the log-rank test. Univariate and multivariate Cox regression analyses were utilized to assess the relationship between various combinations of nutritional risk screening and inflammatory biomarkers with all-cause mortality, employing different adjusted models. Subgroup analysis was conducted to explore interactions between exposure factors and outcomes. Harrell’s concordance index (C-index) was employed to compare the discriminative performance of the original screening method with the nutritional risk screening based on IBI, CRP, NLR, and ALB for predicting all-cause mortality.

RESULTS

Baseline characteristics

A total of 2,628 patients were included in this study, with baseline clinical characteristics presented in Table 1. Among the patients, 56.00% (1,472 patients) were male, with a median age of 65 years (IQR: 52.00–75.00). The median body mass index (BMI) was 27.86 (IQR: 24.16–33.06). Regarding racial distribution, 57.20% (1,504 patients) of the patients were white, 11.80% (310 patients) were black, and 27.72% were from other racial groups, including Asian, Hispanic, or Latino, and those with an unknown race. The majority of patients were admitted to the Medical Intensive Care Unit (MICU), accounting for 23.60% (620 patients), followed by the Neurological ICU (NCU) with 22.60% (594 patients), Surgical ICU (SICU) with 19.30% (506 patients), and Coronary Care Unit (CCU) with 18.90% (496 patients). In terms of comorbidities, 28.80% (757) had type 2 diabetes mellitus, 34.40% (905) had pneumonia, and 8.79% (231) had chronic obstructive pulmonary disease (COPD). A majority of patients (83.60%, 2,197) received mechanical ventilation, with a median ventilation time of 75.92 hours (IQR: 35.68–173.97 hours). Additionally, the median NRS2002 score was 4.00 (IQR: 3.00–6.00), and the median mNUTRIC score was 4.00 (IQR: 4.00–5.00), indicating a high nutritional risk in most patients. Laboratory data showed a median CRP level of 73.75 mg/L (IQR: 19.70–147.73) and a median white blood cell count of 11.10 × 10^9/L (IQR: 8.00–15.70), suggesting systemic inflammation. The mortality rates within 30 days, 60 days, and 90 days were 14.54% (382 patients), 19.44% (511 patients), and 22.41% (589 patients), respectively, indicating a high risk of mortality.

Comparison of different nutrition risk screening tool

We compared the discriminative ability of NRS2002 and mNUTRIC scores in predicting mortality. As shown in Figure 1, both scores significantly differentiated survival probabilities between groups. The NRS2002 score significantly affected survival at 30 days (HR = 2.26), 60 days (HR = 2.12), and 90 days (HR = 2.30) ($p < 0.001$). The mNUTRIC score also showed significant survival differences at 30 days (HR = 3.87), 60 days (HR = 3.62), and 90 days (HR = 3.24) ($p < 0.001$). Considering that the mNUTRIC score demonstrated more prominent discriminative ability, we primarily chose the mNUTRIC score combined with various inflammatory markers for further research.

Comparison of various inflammatory markers

Based on the optimal cut-off values of various inflammatory markers, patients were categorized into high-risk and low-risk groups, and the corresponding Kaplan-Meier (KM) survival curves were generated (Supplementary Figure 2). For CRP (A), the optimal cut-off value was 75.2; for NLR (B), the optimal cut-off value was 8.16; For Albumin (C), although the statistically derived optimal cut-off value was 23 g/L, clinical practice generally defines hypoalbuminemia in critically ill patients as serum albumin levels below 30–35 g/L. Therefore, we adopted 35 g/L as the cut-off value in subsequent analyses 30; for IBI (D), the optimal cut-off value was 68.8. At these cut-off points, significant changes in the rank statistics occurred, effectively stratifying the patient population into high-risk and low-risk groups. The results (Figure 2) showed that patients with higher CRP (cut-off value of 75.2) had significantly lower survival rates compared to those with lower CRP (Log-rank $p = 0.004$, HR = 1.345 [1.098–1.646]). Patients with higher NLR (cut-off value of 8.16) also had lower survival rates (Log-rank $p = 0.021$, HR = 1.266 [1.036–1.547]). Patients with lower albumin (cut-off value of 35) had a lower survival rate (Log-rank $p < 0.001$, HR = 0.576 [0.437–0.759]). However, the difference in survival between patients with higher or lower IBI (cut-off value of 68.8) was not significant (Log-rank $p = 0.204$, HR = 0.869 [0.699–1.08]). These results indicate that CRP, NLR, and albumin have significant prognostic value in predicting survival, while IBI has a weaker predictive effect (Supplementary Figure 3). Therefore, we chose to use mNUTRIC combined with CRP, NLR, and albumin for evaluation.

Comparison of different combinations of the mNUTRIC score and inflammatory markers

Based on different combinations of inflammatory markers and the mNUTRIC score, we plotted Kaplan-Meier (KM) survival curves for 30 days, 60 days, and 90 days (Figure 3 and Supplementary Figure 4). The results showed significant differences in survival rates between high-risk and low-risk groups at different time points (30 days, 60 days, and 90 days). Specifically, in the mNUTRIC and CRP combination, patients with higher CRP had lower survival rates than those with lower CRP (Log-rank $p < 0.001$, HR = 0.716 [0.564–0.881]); in the mNUTRIC and NLR combination, patients with higher NLR had significantly lower survival rates than those with lower NLR (Log-rank $p < 0.001$, HR = 0.847 [0.669–0.998]); and in the mNUTRIC and Albumin combination, patients with lower albumin levels had lower survival rates at all time points (Log-rank $p < 0.001$, HR = 0.793 [0.571–0.925]). These results suggest that combining the mNUTRIC score with inflammatory markers (such as CRP, NLR, and Albumin) can more effectively differentiate patients' survival prognosis, particularly in survival analyses at 30, 60, and 90 days.

Subsequently, we computed C-statistics for various combinations (Table 2). The results revealed that integrating the mNUTRIC score with different inflammatory markers enhanced the predictive accuracy for mortality. The C-statistic for the mNUTRIC score is 0.706. When combined with CRP, NLR and Albumin, the C-statistics improve to 0.714, 0.708 and 0.715, respectively, with improvement of 0.08, 0.02 and 0.09 with *p*-values below 0.001.This suggests that adding inflammatory markers to the mNUTRIC score improves the prediction accuracy for mortality.

Prognostic performance of different combinations of the mNUTRIC score and inflammatory markers

Cox regression analysis was used to compare the prognostic performance of different combinations of mNUTRIC score and inflammatory markers for 30-day, 60-day and 90-day mortality prediction (Table 3, Supplementary Table 1 and 2). All combinations of mNUTRIC score and CRP, NLR and albumin improved mortality prediction at each time point. The HRs for the high-risk group defined by mNUTRIC, compared with the low-risk group, were 1.721, 1.680, and 1.620 at 30, 60, and 90 days, respectively (all $p<0.001$). The HRs of mNUTRIC and CRP were 2.889, 2.619 and 2.375 at the same time points (all $p<0.001$) and the HRs of mNUTRIC and NLR were 2.538, 2.349 and 2.275 (all $p<0.001$) and the HRs of mNUTRIC and albumin were 3.252, 3.170 and 2.866 (all $p<0.001$). The results suggest that the combination of mNUTRIC and inflammatory markers, including albumin, significantly improves the ability to predict mortality even after adjustment for age, sex, BMI, ICU admission mode, ventilation status and comorbidities.

In our subgroup analysis, we assessed the prognosis efficiency of mNUTRIC and inflammatory markers such as albumin, CRP, and NLR(Supplementary Figure 5-7). Combined with albumin significantly improved prognosis accuracy in subgroups. Combining mNUTRIC with CRP significantly improved mortality prediction accuracy (HR) in high risk groups. Combining mNUTRIC and NLR showed strong predictive power (HR) in high risk patients. Forest plots show the reliability and efficiency of combinations across different patients and show that pairing mNUTRIC with specific inflammatory markers improves mortality prediction accuracy.

DISCUSSION

Our results show that combining inflammatory markers with the mNUTRIC score greatly improves mortality risk prediction in critically ill patients. The mNUTRIC score has superior

discriminant power for 30-day, 60-day and 90-day mortality than NRS2002 score. Inflammatory markers such as CRP, NLR and albumin play a key role in mortality prediction: higher CRP and NLR levels or lower albumin levels contribute to significantly lower survival rates. Furthermore, the combination of the mNUTRIC score with these inflammatory markers more effectively differentiated survival probabilities, with the combination of mNUTRIC and albumin showing the best prognostic performance. C-statistics analysis also demonstrated that adding inflammatory markers significantly improved the discrimination ability of the mortality prediction model. Therefore, the study suggests that incorporating inflammatory markers with existing nutritional risk screening tools can more accurately predict mortality risk in critically ill patients and provide more precise management strategies for clinicians.

Currently, research on the application of GLIM in the ICU is still limited. A meta-analysis included five studies, which showed that 15% to 68% of patients were diagnosed with malnutrition using the GLIM criteria,[31] while 48% to 75% of malnourished patients were identified using the Subjective Global Assessment (SGA). The overall sensitivity of the meta-analysis was 65.3% (95% CI: 34.9%-86.9%), and the overall specificity was 88.8% (95% CI: 58.1%-97.8%). Despite its application value in ICU patients, the effectiveness of the GLIM criteria remains limited.The GLIM guidelines for critically ill patients recommend that malnutrition be assessed within 48 hours of ICU admission using phenotypic criteria (such as weight loss, low BMI, and low muscle mass) and etiological criteria (including inflammation and inadequate food intake/assimilation), particularly for overweight and obese patients, when feasible.[32,33] Other malnutrition diagnosis methods using similar criteria may also be applied or integrated with the GLIM criteria.[22] Our study provides evidence-based support for the application of the GLIM criteria in the ICU, particularly enhancing and refining the inflammatory component of the etiological criteria.

Moreover, the study introduces a new perspective: in clinical practice within the ICU, assessing nutritional status after screening for nutrition risk presents certain challenges, especially for bedridden and sedated patients, who may be unable to provide accurate dietary and weight histories. Additionally, critically ill patients often experience significant fluid shifts, complicating the accurate determination of dry weight and muscle mass assessment.[6–9,12] As pointed out in the study by Milanez et al., the application of the GLIM criteria in critically ill patients also faces difficulties.[34] In their study, the GLIM criteria could be applied to 377 out of 450 patients (83.7%). However, among the 73 patients who could not be diagnosed with malnutrition, 42.5% failed to meet the phenotypic criteria, mainly due to a lack of muscle mass data when using normal BMI and unintentional weight loss standards.

Similarly, 68.5% of patients could not meet the etiological criteria, as, despite confirming normal energy intake, they lacked inflammation data. Given these factors, a key question arises: can nutritional status be assessed solely through the inflammatory component of the etiological criteria following nutrition risk screening, and can this be used for GLIM diagnosis in ICU patients? Our preliminary results suggest that this approach can effectively differentiate survival outcomes in critically ill patients, but further prospective studies are needed to validate its feasibility.

Brown et al. conducted a meta-analysis that revealed significant variability in the prognostic predictive ability of the GLIM criteria across different inflammation and intake reduction measures.[35] The authors suggested that differences in the etiological assessment criteria contribute to the varying prognostic capabilities of GLIM in predicting the survival of cancer patients. Systemic inflammation is a key pathological criterion for diagnosing malnutrition based on the GLIM criteria. It is widely believed that many diseases or conditions are caused by or lead to inflammation. Malnutrition may be caused by inflammation-induced muscle catabolic loss, anorexia, metabolic changes, and associated micronutrient deficiencies, which are particularly evident in critically ill patients. Our study also contributes to the expansion of the inflammatory criterion in the GLIM standards.[36–38] A study by Xie et al. on cancer patients further corroborated that the GLIM criteria based on IBI/CRP/NLR/ALB performs better than the original GLIM standards in predicting long-term prognosis in cancer patients (Chi-square values: 1.316 vs. 78.321 vs. 74.740 vs. 88.719 vs. 100.921).[25] The ALB-based GLIM standard showed the best prognostic accuracy. The GLIM standard based on inflammatory markers is an independent predictor of long-term prognosis in cancer, with malnourished patients having a 45% higher risk of poor long-term outcomes compared to those without malnutrition. This study provides valuable insights into the integration of inflammatory markers with the mNUTRIC score for enhancing the prediction of mortality risk in critically ill patients. The results show that inflammatory markers such as CRP, NLR, and albumin can be used to predict mortality outcomes more accurately when combined with mNUTRIC score. This combination enables clinicians to better understand nutritional and inflammation status of critically ill patients and provides better prognosis in the ICU.

This study provides important insights into the role of inflammatory markers in the prediction of mortality for critically ill patients, but several limitations must be acknowledged. The data were obtained from only one database (MIMIC-IV) with mostly patients from Beth Israel Deaconess Medical Center (Boston, MA), and thus the results may not be generalized

to other populations, or different healthcare settings (for example, different geographical regions or types of hospitals (rural versus urban). Future work might address this limitation by replicating the results in multiple centers and regions to improve external validity and to investigate how mNUTRIC and inflammatory markers perform in different healthcare settings.. Second, since this study is retrospective, it is unable to establish causal relationships. Prospective cohort studies would help confirm these findings and validate the use of mNUTRIC combined with inflammatory markers as part of a nutritional assessment framework. Lastly, while this study demonstrated the potential of inflammatory markers in predicting mortality, it did not explore the impact of nutritional interventions on patient outcomes. Future research should investigate how early identification of nutritional risk through inflammatory biomarkers affects clinical decisions, such as whether to initiate enteral or parenteral nutrition, and whether these interventions improve patient outcomes.

Future research can further refine and validate the role of inflammatory markers in ICU nutrition assessments in several ways. Longitudinal studies with extended follow-up periods would help determine whether early nutritional risk identification impacts long-term survival, functional recovery, and quality of life. Interventional studies could evaluate the effectiveness of using inflammatory markers in clinical decision-making by administering targeted nutritional interventions to patients at high nutritional risk. Research into broader inflammatory marker panels or more advanced inflammatory profiles (such as cytokines or genetic markers) could provide a more comprehensive understanding of the inflammatory state in critically ill patients. Additionally, multi-center and international studies would help confirm the applicability of the findings across diverse patient populations and healthcare settings. Finally, applying machine learning techniques to develop predictive models combining inflammatory markers, mNUTRIC scores, and other clinical variables would assist clinicians in real-time risk stratification, improving decision-making and management for ICU patients. Addressing these research gaps will optimize nutritional management and improve outcomes for critically ill patients through early and accurate risk identification.

Conclusions

This study shows that inflammatory markers and the mNUTRIC score improve mortality risk prediction in critically ill patients. Markers such as CRP, NLR, and albumin improve mortality risk prediction when combined with the mNUTRIC score, providing more reliable information on ICU patients' nutritional and inflammation status than traditional tools such as NRS2002 and the original mNUTRIC.. Despite promising results, retrospective design and

single data set reliance are limitations of the study. Future work should validate results with multi-center prospective studies and consider larger inflammatory marker panels. Using advanced machine learning technologies could further refine predictive models and help clinicians in real-time risk stratification. This paper advocates for inclusion of inflammatory markersinflammatory markers in nutrition assessment of critically ill patients, thus improving mortality risk prediction and patient management in ICU. Further work should be done to confirm results and optimize nutritional care for this vulnerable population.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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REFERENCES

1. 1. Kayambankadzanja RK, Schell CO, Gerdin Wärnberg M, Tamras T, Mollazadegan H, Holmberg M, et al. Towards definitions of critical illness and critical care using concept analysis. BMJ Open. 2022;12:e060972. https://doi.org/10.1136/bmjopen-2022-060972.
2. Odutola PO, Olarewaju A, Shah P. Effectiveness of atrial natriuretic peptide in the treatment of critically ill patients: a systematic review and meta-analysis. J Clin Med. 2025;14:3267. https://doi.org/10.3390/jcm14103267.
3. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute skeletal muscle wasting in critical illness. JAMA. 2013;310:1591–1600. https://doi.org/10.1001/jama.2013.278481.
4. Herridge MS, Azoulay É. Outcomes after critical illness. N Engl J Med. 2023;388:913–924. https://doi.org/10.1056/NEJMra2104669.
5. Mayer KP, Thompson Bastin ML, Montgomery-Yates AA, Pastva AM, Dupont-Versteegden EE, Parry SM, et al. Acute skeletal muscle wasting and dysfunction predict physical disability at hospital discharge in patients with critical illness. Crit Care Lond Engl. 2020;24:637. https://doi.org/10.1186/s13054-020-03355-x.
6. Reignier J, Rice TW, Arabi YM, Casaer M. Nutritional Support in the ICU. BMJ. 2025;388:e077979. https://doi.org/10.1136/bmj-2023-077979.
7. de Man AME, Gunst J, Reintam Blaser A. Nutrition in the intensive care unit: From the acute phase to beyond. Intensive Care Med. 2024;50:1035–1048. https://doi.org/10.1007/s00134-024-07458-9.
8. Heyland DK, Ortiz A, Stoppe C, Patel JJ, Yeh DD, Dukes G, et al. Incidence, risk factors, and clinical consequence of enteral feeding intolerance in the mechanically ventilated critically ill: an analysis of a

multicenter, multiyear database. Crit Care Med. 2021;49:49–59. https://doi.org/10.1097/CCM.0000000000004712.

9. Ridley EJ, Lambell K. Nutrition before, during and after critical illness. Curr Opin Crit Care. 2022;28:395–400. https://doi.org/10.1097/MCC.0000000000000961.
10. De Waele E, Rosseel Z, Pen JJ. Post-ICU nutrition: the neglected side of metabolic support. Curr Opin Crit Care. 2023;29:360–362. https://doi.org/10.1097/MCC.0000000000001057.
11. Rousseau A-F, Prescott HC, Brett SJ, Weiss B, Azoulay E, Creteur J, et al. Long-term outcomes after critical illness: recent insights. Crit Care Lond Engl. 2021;25:108. https://doi.org/10.1186/s13054-021-03535-3.
12. Viner Smith E, Lambell K, Tatucu-Babet OA, Ridley E, Chapple L-A. Nutrition considerations for patients with persistent critical illness: A narrative review. JPEN J Parenter Enteral Nutr. 2024;48:658–666. https://doi.org/10.1002/jpen.2623.
13. Pardo E, Lescot T, Preiser J-C, Massanet P, Pons A, Jaber S, et al. Association between early nutrition support and 28-day mortality in critically ill patients: the FRANS prospective nutrition cohort study. Crit Care Lond Engl. 2023;27:7. https://doi.org/10.1186/s13054-022-04298-1.
14. Moisey LL, Merriweather JL, Drover JW. The role of nutrition rehabilitation in the recovery of survivors of critical illness: underrecognized and underappreciated. Crit Care Lond Engl. 2022;26:270. https://doi.org/10.1186/s13054-022-04143-5
15. Jubina LE, Locke A, Fedder KR, Slone SA, Soper MK, Kalema AG, et al. Nutrition in the intensive care unit and early recovery influence functional outcomes for survivors of critical illness: A prospective cohort study. JPEN J Parenter Enteral Nutr. 2023;47:888–895. https://doi.org/10.1002/jpen.2538.
16. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr Edinb Scotl. 2019;38:48–79. https://doi.org/10.1016/j.clnu.2018.08.037.
17. Singer P, Blaser AR, Berger MM, Calder PC, Casaer M, Hiesmayr M, et al. ESPEN practical and partially revised guideline: clinical nutrition in the intensive care unit. Clin Nutr Edinb Scotl. 2023;42:1671–1689. https://doi.org/10.1016/j.clnu.2023.07.011.
18. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (SCCM) and american society for parenteral and enteral nutrition (a.S.P.E.N.). J Parenter Enter Nutr. 2016;40:159–211. https://doi.org/10.1177/0148607115621863.
19. Cogle SV, Hallum M, Mulherin DW. Applying the 2022 ASPEN adult nutrition support guidelines in a 2024 ICU. Nutr Clin Pract. 2024;39:1055–1068. https://doi.org/10.1002/ncp.11188.
20. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Crit Care Lond Engl. 2011;15:R268. https://doi.org/10.1186/cc10546.

21. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition – a consensus report from the global clinical nutrition community. Clin Nutr. 2019;38:1–9. https://doi.org/10.1016/j.clnu.2018.08.002.
22. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Pisprasert V, et al. The GLIM consensus approach to diagnosis of malnutrition: a 5-year update. Clin Nutr Edinb Scotl. 2025;49:11–20. https://doi.org/10.1016/j.clnu.2025.03.018.
23. White JV, Guenter P, Jensen G, Malone A, Schofield M, Academy Malnutrition Work Group, et al. Consensus statement: academy of nutrition and dietetics and american society for parenteral and enteral nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). JPEN J Parenter Enteral Nutr. 2012;36:275–283. https://doi.org/10.1177/0148607112440285.
24. Xie H, Yuan K, Ruan G, Wei L, Zhang H, Ge Y, et al. Improving the assessment of malnutrition in cancer: using systemic inflammatory markers as a supplement to the inflammation items of the GLIM criteria. Clin Nutr Edinb Scotl. 2023;42:2036–2044. https://doi.org/10.1016/j.clnu.2023.08.020.
25. Xie H, Ruan G, Ge Y, Zhang Q, Zhang H, Lin S, et al. Inflammatory burden as a prognostic biomarker for cancer. Clin Nutr Edinb Scotl. 2022;41:1236–1243. https://doi.org/10.1016/j.clnu.2022.04.019.
26. Huang Z, Fu Z, Huang W, Huang K. Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: a meta-analysis. Am J Emerg Med. 2020;38:641–647. https://doi.org/10.1016/j.ajem.2019.10.023.
27. Islam MM, Satici MO, Eroglu SE. Unraveling the clinical significance and prognostic value of the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index, and delta neutrophil index: an extensive literature review. Turk J Emerg Med. 2024;24:8–19. https://doi.org/10.4103/tjem.tjem_198_23.
28. Goldberger AL, Amaral LA, Glass L, Hausdorff JM, Ivanov PC, Mark RG, et al. PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. Circulation. 2000;101:E215–E220. https://doi.org/10.1161/01.cir.101.23.e215.
29. Johnson AEW, Bulgarelli L, Shen L, Gayles A, Shammout A, Horng S, et al. MIMIC-IV, a freely accessible electronic health record dataset. Sci Data. 2023;10:1. https://doi.org/10.1038/s41597-022-01899-x.
30. Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. JPEN J Parenter Enteral Nutr. 2019 Feb;43(2):181-193. doi: 10.1002/jpen.1451.
31. Díaz G, Correia MITD, Gonzalez MC, Reyes M. The global leadership initiative on malnutrition criteria for the diagnosis of malnutrition in patients admitted to the intensive care unit: a systematic review and meta-analysis. Clin Nutr Edinb Scotl. 2023;42:182–189. https://doi.org/10.1016/j.clnu.2022.12.007.
32. Wischmeyer PE, Bear DE, Berger MM, De Waele E, Gunst J, McClave SA, et al. Personalized nutrition therapy in critical care: 10 expert recommendations. Crit Care Lond Engl. 2023;27:261. https://doi.org/10.1186/s13054-023-04539-x.

33. Thibault R, Bear DE, Fischer A, Montejo-González JC, Hiesmayr M, Tamási P, et al. Implementation of the ESPEN guideline on clinical nutrition in the intensive care unit (ICU): It is time to move forward!: A position paper from the “nutrition in the ICU” ESPEN special interest group. Clin Nutr ESPEN. 2023;57:318–330. https://doi.org/10.1016/j.clnesp.2023.06.033.
34. Milanez DSJ, Razzera EL, Lima J, Silva FM. Feasibility and criterion validity of the GLIM criteria in the critically ill: A prospective cohort study. J Parenter Enter Nutr. 2023;47:754–765. https://doi.org/10.1002/jpen.2536.
35. Brown D, Loeliger J, Stewart J, Graham KL, Goradia S, Gerges C, et al. Relationship between global leadership initiative on malnutrition (GLIM) defined malnutrition and survival, length of stay and post-operative complications in people with cancer: a systematic review. Clin Nutr. 2023;42:255–268. https://doi.org/10.1016/j.clnu.2023.01.012.
36. Stumpf F, Keller B, Gressies C, Schuetz P. Inflammation and nutrition: friend or foe? Nutrients. 2023;15:1159. https://doi.org/10.3390/nu15051159.
37. Massironi S, Viganò C, Palermo A, Pirola L, Mulinacci G, Allocca M, et al. Inflammation and malnutrition in inflammatory bowel disease. Lancet Gastroenterol Hepatol. 2023;8:579–590. https://doi.org/10.1016/S2468-1253(23)00011-0.
38. Fatyga P, Pac A, Fedyk-Łukasik M, Grodzicki T, Skalska A. The relationship between malnutrition risk and inflammatory biomarkers in outpatient geriatric population. Eur Geriatr Med. 2020;11:383–391. https://doi.org/10.1007/s41999-020-00303-4.

Table 1. Clinical characteristics

Characteristic	Overall n=2628
Gender, male, n (%)	1,472 (56.00)
Age, years, median (IQR)	65.00(52.00, 75.00)
BMI, median (IQR)	27.86(24.16, 33.06)
Race	
Asian	90 (3.42)
Black	310 (11.80)
Hispanic or Latino	96 (3.65)
White	1,504 (57.20)
Other	138 (5.25)
Unknown	490 (18.60)
ICU mode	
CCU	496 (18.90)
MICU	620 (23.60)
ICU	412 (15.70)
NCU	594 (22.60)
SICU	506 (19.30)
Malignant tumor, yes, n (%)	242 (9.21)
Type 2 Diabetes Mellitus, yes, n (%)	757 (28.80)
Pneumonia, yes, n (%)	905 (34.40)
COPD, yes, n (%)	231 (8.79)
Ventilation, yes, n (%)	2,197 (83.60)
Ventilation Time,hours,median (IQR)	75.92 (35.68, 173.97)
Apache, median (IQR)	8.00 (7.00,10.00)
Sofa, median (IQR)	4.00 (2.00,7.00)
Charlson, median (IQR)	5.00 (3.00,7.00)
Oasis, median (IQR)	33.00 (27.00,39.00)
NRS2002, median (IQR)	4.00 (3.00, 6.00)
mNUTRIC, median (IQR)	4.00 (4.00, 5.00)
White Blood Cell Count, $\times 10^9$/L, median (IQR)	11.10 (8.00, 15.70)
Red Blood Cell Count, $\times 10^9$/L, median (IQR)	3.69 (3.09, 4.25)
Platelet Count, $\times 10^9$/L, median (IQR)	210.00 (147.00, 286.00)
Hemoglobin, g/dL, median (IQR)	109.00(91.00, 126.00)
Neutrophil Count, $\times 10^9$/L, median (IQR)	9.09 (6.34, 12.43)
Lymphocyte Count, $\times 10^9$/L, median (IQR)	1.22 (0.82, 1.57)
C-Reactive Protein, mg/L, median (IQR) =	73.75 (19.70, 147.73)
Albumin, g/L, median (IQR)	30.00 (26.00, 34.00)
Neutrophil-to-Lymphocyte Ratio, median (IQR)	7.62 (4.70, 12.76)
Inflammatory Burden Index, median (IQR)	51.08 (14.52, 120.41)
Number of Diagnoses, count, median (IQR)	24.00 (17.00, 32.00)
ICU Stay Duration, days, median (IQR)	5.30 (3.14, 10.61)
Hospital Stay Duration, days, median (IQR)	16.10 (9.16, 28.69)
Death within 30 days, yes, n (%)	382 (14.54)
Death within 60 days, yes, n (%)	511 (19.44)
Death within 90 days, yes, n (%)	589 (22.41)

BMI, body mass index; CCU, coronary care unit; MICU, medical intensive care unit; ICU, intensive care unit; NCU, neurological care unit; SICU, surgical intensive care unit; COPD, chronic obstructive pulmonary disease; NRS2002, nutritional risk screening 2002; mNUTRIC, modified nutritional risk in critically ill.

Table 2. Comparative analysis of the discrimination of the mNUTRIC Combined with inflammation marker and the original mNUTRIC for overall survival

Discrimination Ability	C-statistic	Difference	p value
mNUTRIC	0.706	Ref	
mNUTRIC+CRP	0.714	0.08	<0.001
mNUTRIC+NLR	0.708	0.02	<0.001
mNUTRIC+Albumin	0.715	0.09	<0.001

mNUTRIC, Modified Nutritional Risk in Critically Ill; CRP, C-reactive Protein; NLR, Neutrophil-to-Lymphocyte Ratio

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Table 3. Cox regression analysis comparing high- vs. low-risk groups defined by the mNUTRIC and mNUTRIC combined with inflammatory markers for 30-day survival

Categories	Model a	p value	Model b	p value	Model c
mNUTRIC	1.721 (1.586,1.868)	<0.001	1.655 (1.499,1.826)	<0.001	1.614 (0.827,1.306)
mNUTRIC+CRP	2.889 (2.356,3.543)	<0.001	2.166 (1.735,2.705)	<0.001	2.078 (1.663,2.595)
mNUTRIC+NLR	2.538 (2.062,3.122)	<0.001	1.895 (1.519,2.364)	<0.001	1.835 (1.470,2.290)
mNUTRIC+ Albumin	3.252 (2.647,3.994)	<0.001	2.520 (1.997,3.180)	<0.001	2.383 (1.885,3.012)

mNUTRIC, Modified Nutritional Risk in Critically Ill; CRP, C-reactive Protein; NLR, Neutrophil-to-Lymphocyte Ratio; BMI, body mass index; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease
Model a: Not adjusted.
Model b: Adjusted for age, sex, BMI, ICU mode.
Model c: Adjusted for age, sex, BMI, ICU mode, ventilation, diabetes mellitus, malignant tumor, pneumonia, COPD.

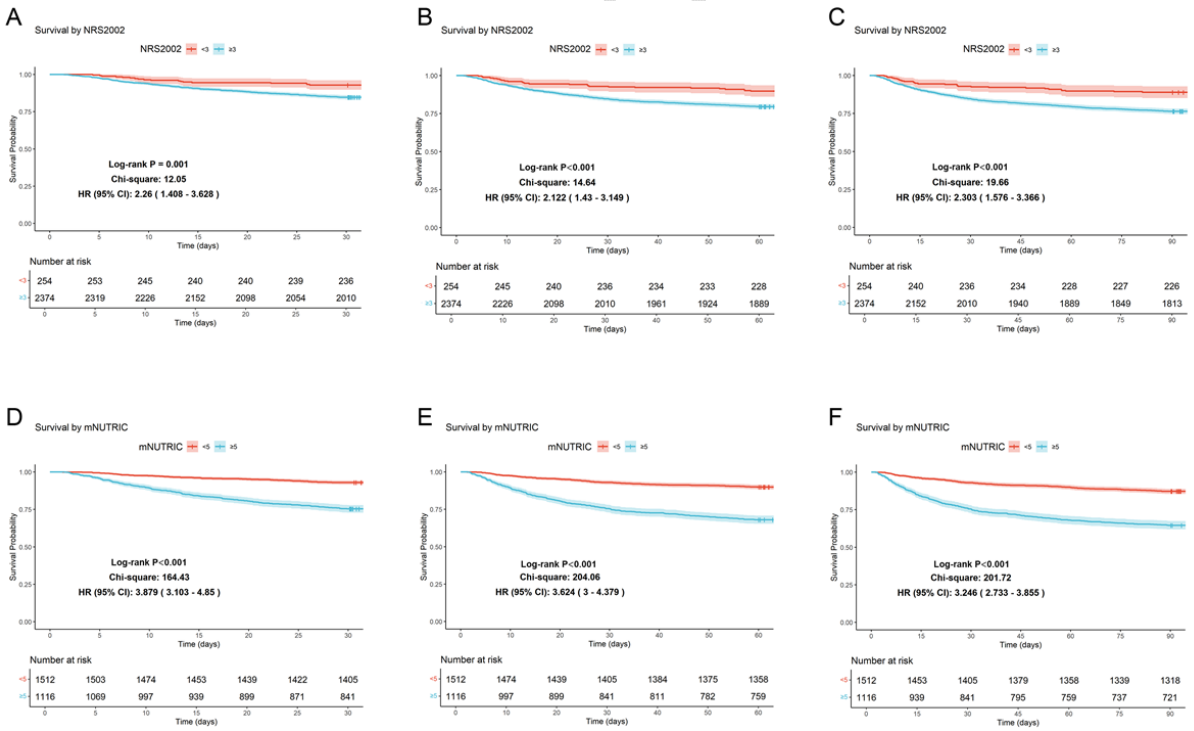

Figure 1. Kaplan-Meier survival curves for overall survival stratified by NRS2002 and mNUTRIC scores.(A-C) Survival curves stratified by NRS2002 for ICU patients at different time points: 30 days (A), 60 days (B), and 90 days (C).(D-F) Survival curves stratified by mNUTRIC scores for ICU patients at 30 days (D), 60 days (E), and 90 days (F)

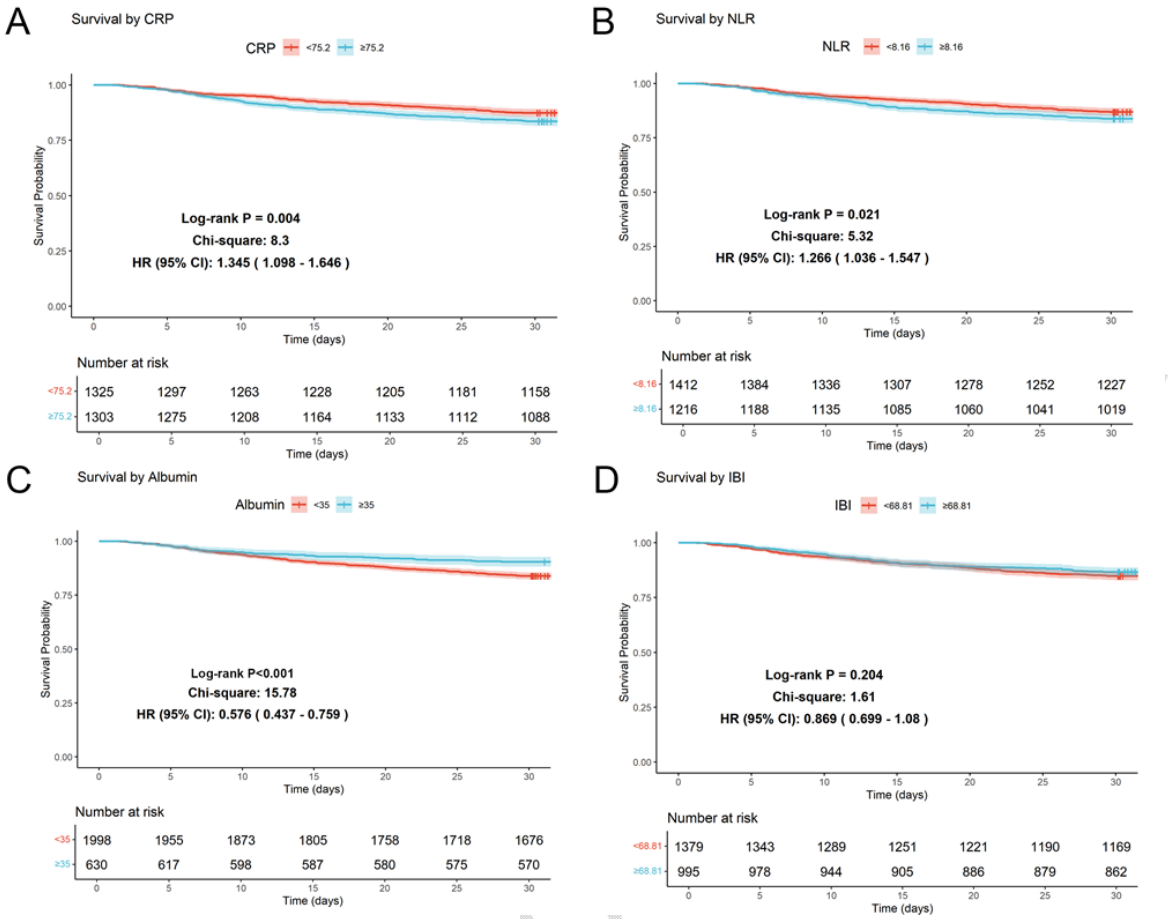

Figure 2. Kaplan-Meier survival curves for 30-day survival stratified by inflammatory markers (CRP, Albumin, NLR, and IBI). A, C-reaction protein; B, Neutrophil to lymphocyte ratio; C, Albumin; D, inflammatory burden index

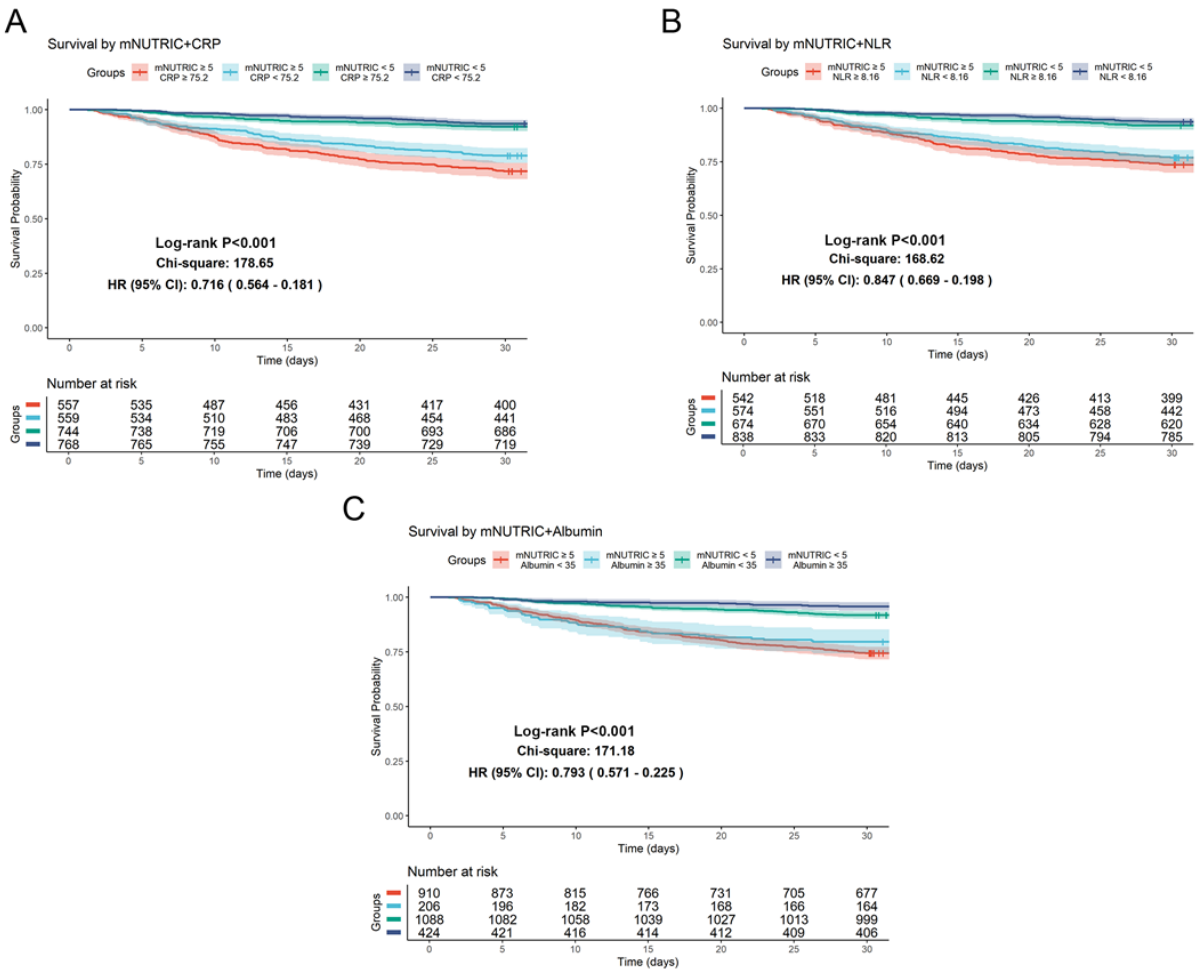

Figure 3. Kaplan-Meier survival curves for 30-day survival stratified by the combined mNUTRIC scores and inflammatory markers (CRP, NLR, and albumin). A, mNUTRIC and C-reaction protein; B, mNUTRIC and neutrophil to lymphocyte ratio; C, mNUTRIC and albumin